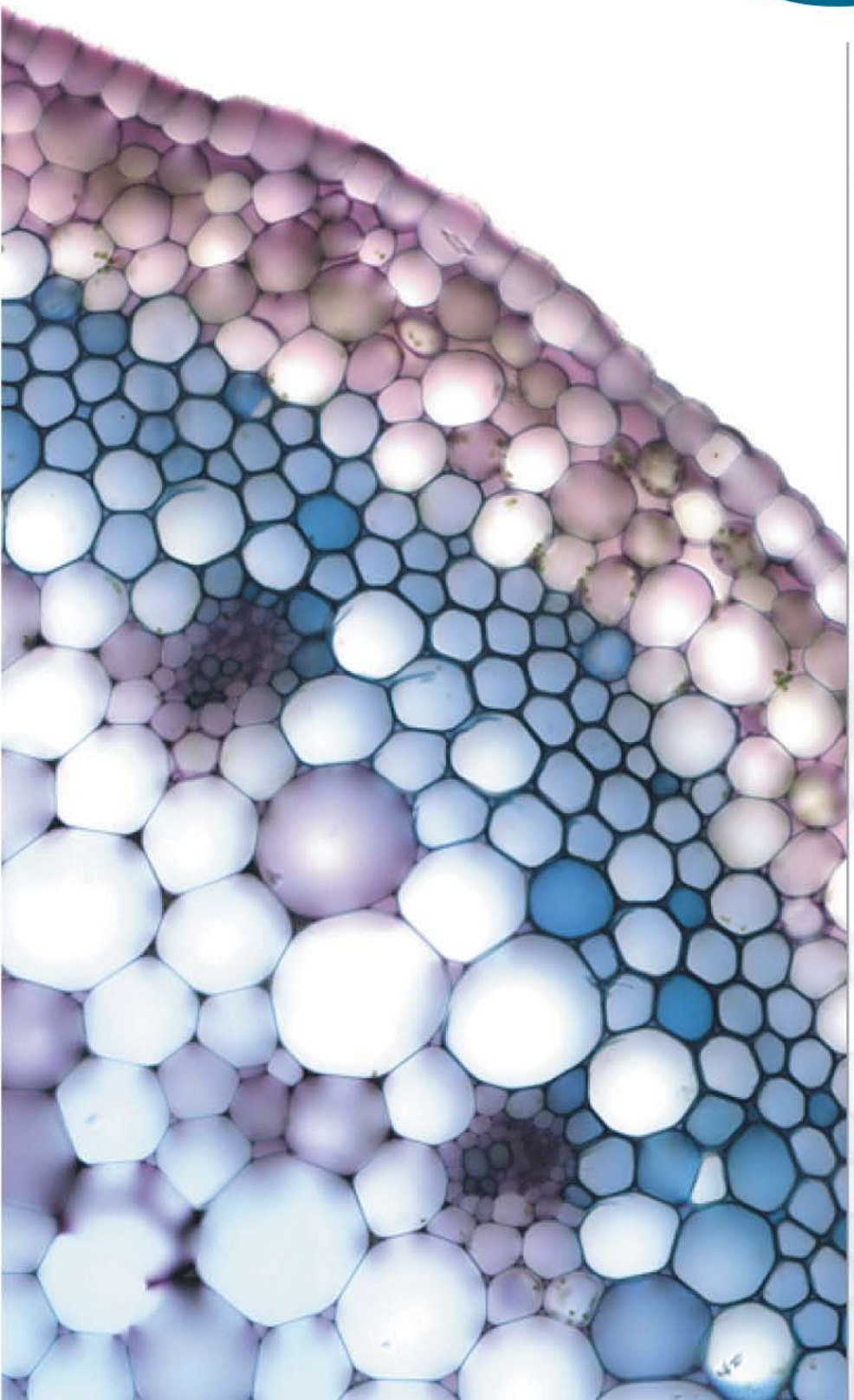
'09

ANNUAL REPORT

INSTITUTO GULBENKIAN DE CIÊNCIA | IGC



FUNDAÇÃO CALOUSTE GULBENKIAN

Instituto Gulbenkian de Ciência

'09

ANNUAL REPORT

INSTITUTO GULBENKIAN DE CIÊNCIA | IGC

The Instituto Gulbenkian de Ciência (IGC) is an international biomedical research and graduate training institute, founded and supported by the Calouste Gulbenkian Foundation, in Portugal. The IGC operates as a host institution, where research groups develop their research in complete financial and intellectual autonomy, underpinned by world-class services and facilities.

This Annual Report covers the Instituto Gulbenkian de Ciência's financial year, from 1st January to 31st December 2009.

COVER IMAGE
Gennaria diphylla, Gennaria.
Detail of stem section stained with TBO x40

ROB KESSELER
(Artist in residence at the IGC)

CONTENTS

06 ORGANISATION
08 FOREWORD BY THE DIRECTOR
15 THE IGC AT A GLANCE
18 RESEARCH GROUPS
- 20 Protein-Nucleic Acids Interactions – ALEKOS ATHANASIADIS
- 21 Plant Stress Signalling – ELENA BAENA GONZÁLEZ
- 22 Meiosis and Development – VITOR BARBOSA
- 23 Epigenetics and Soma – VASCO M. BARRETO
- 24 Variation: Development and Selection – PATRÍCIA BELDADE
- 25 Cell Cycle Regulation – MÓNICA BETTENCOURT DIAS
- 26 Quantitative Organism Biology – JORGE CARNEIRO
- 27 Population and Conservation Genetics – LOUNÈS CHIKHI
- 28 Neurobiology of Action – RUI COSTA
- 29 Lymphocyte Physiology – JOCELYNE DEMENGEOT
- 30 Plant Molecular Biology – PAULA DUQUE
- 31 Plant Development – JOSÉ FEIJÓ
- 32 Yeast Stress – LISETE FERNANDES
- 33 Telomeres and Genome Stability – MIGUEL GODINHO FERREIRA
- 34 Collective Dynamics – GABRIELA GOMES
- 35 Evolutionary Biology – ISABEL GORDO
- 36 Actin Dynamics – FLORENCE JANODY
- 37 Epigenetic Mechanisms – LARS JANSEN
- 38 Tissue Morphogenesis – MATHIAS KOEPPEN
- 39 Organogenesis – JOAQUIN RODRIGUEZ LÉON
- 40 Systems Neuroscience – ZACHARY MAINEN
- 41 Patterning and Morphogenesis – MOISES MALLO
- 42 Early Fly Development – RUI MARTINHO
- 43 Behavioural Neuroscience – MARTA MOITA
- 44 Animal Behaviour – RUI OLIVEIRA
- 45 Infection and Immunity – MICHAEL PARKHOUSE
- 46 Disease Genetics – CARLOS PENHA GONÇALVES
- 47 Computational Genomics – JOSÉ PEREIRA LEAL
- 48 Behaviour and Metabolism – CARLOS RIBEIRO
- 49 Membrane Traffic in Disease and Novel Therapies – MIGUEL SEABRA
- 50 Inflammation – MIGUEL SOARES
- 52 Stress and Cytoskeleton – HELENA SOARES
- 53 Evolution and Development – ÉLIO SUCENA
- 54 Mitosis – ÁLVARO TAVARES
- 55 Host-microorganism Interactions – LUÍS TEIXEIRA
- 56 Evolutionary Genetics – HENRIQUE TEOTÓNIO
- 57 Innate Behaviour – MARIA LUÍSA VASCONCELOS
- 58 Bacterial Signalling – KARINA XAVIER
- 59 Complex Adaptive Systems - LUÍS ROCHA

60 RESEARCH FELLOWS
- 62 Plant Genomics – JÖRG BECKER
- 63 Network Modelling – CLAUDINE CHAOUYIA
- 64 Lupus and Autoreactive Immune Repertoire – CONSTANTIN FESEL
- 65 Neuronal Structure and Function – INBAL ISRAELY
- 66 Neuroethology – SUSANA LIMA
- 67 Antigen presentation and T cell activation – ELISABETTA PADOVAN
- 68 Dopamine in Action Learning – JOSEPH PATON
- 69 Cardiac Regeneration – LUIS ROSÁRIO

70 EXTERNAL GROUPS
72 FACILITIES AND SERVICES
- 74 Animal Facilities
- 76 Transgenics Facility
- 77 Plant Facility
- 78 Cell Imaging Unit
- 80 Genomics Unit
- 82 Gene Expression Unit
- 83 Histology Unit
- 84 Bioinformatics and Computational Biology Unit
- 85 High Performance Computing Resource for Bioinformatics

86 RESEARCH STRUCTURES
92 PUBLICATIONS
105 AWARDS
108 RESEARCH FUNDING
111 GRADUATE TRAINING AND EDUCATION
- 112 PhD Programme in Integrative Biomedical Sciences
- 114 PhD Programme in Computational Biology (PDBC)
- 117 International Neuroscience Doctoral Programme (INDP)
- 120 Programme for Advanced Medical Research - Doctoral Programme for Physicians
- 122 GTPB – The Gulbenkian Training Programme in Bioinformatics

124 THESES
- 125 PhD Theses
- 125 MSc Theses
- 126 BSc Theses

127 SEMINARS, WORKSHOPS AND MEETINGS
- 128 Seminars at the IGC
- 140 Presentations by IGC researchers
- 156 Workshops, Courses and Meetings

159 PUBLIC ENGAGEMENT IN SCIENCE
- 160 Science Communication and Outreach
- 164 Fundraising

166 OTHER SERVICES
168 ACKNOWLEDGEMENTS

ORGANISATION

CALOUSTE GULBENKIAN FOUNDATION

The Calouste Gulbenkian Foundation is a Portuguese private institution of general public utility established by a clause in Calouste Sarkis Gulbenkian's will, in 1953. The purposes of the Foundation are charitable, artistic, educational and scientific.

BOARD OF TRUSTEES

EMÍLIO RUI VILAR
President
ISABEL MOTA
Trustee
DIOGO DE LUCENA
Trustee
EDUARDO MARÇAL GRILO
Trustee
ANDRÉ GONÇALVES PEREIRA
Non-executive Trustee
TERESA GOUVEIA
Trustee
MARTIN ESSAYAN
Trustee
EDUARDO LOURENÇO
Non-executive Trustee
ARTUR SANTOS SILVA
Non-executive Trustee

CALOUSTE GULBENKIAN FOUNDATION

SCIENTIFIC ADVISORY BOARD

The Scientific Advisory Board of the IGC oversees the scientific progress, graduate programmes, recruitment and overall performance of staff and research groups. The Scientific Advisory Board also advises the Board of the Calouste Gulbenkian Foundation on all matters of relevance to the mission of the Institute.

SYDNEY BRENNER (The Salk Institute, USA)
Chairman
JONATHAN HOWARD (University of Cologne, Germany)
MARTIN RAFF (University College London, UK)
GINÉS MORATA (Universidad Autónoma de Madrid, Spain)
NICOLE LE DOUARIN (Academie des Science, France)
DAVID SABATINI (New York University, USA)
KAI SIMONS (Max Planck Institute for Molecular Cell Biology and Genetics, Dresden, Germany)
SUSUMU TONEGAWA (Massachusetts Institute of Technology, USA)
RICHARD AXEL (Columbia University, USA)
JEAN-PIERRE CHANGEUX (Pasteur Institute, France)
TERRENCE SEJNOWSKY (The Salk Institute, USA)

IGC DIRECTOR
ANTÓNIO COUTINHO

IGC DEPUTY DIRECTOR
JOSÉ MÁRIO LEITE

DEPUTY TO THE DIRECTOR
JOCELYNE DEMENGEOT

FOREWORD BY THE DIRECTOR

With the end of the decade approaching, all sorts of listings on "the most important discoveries" started appearing, usually with 10 items each. It is tempting to do the same for the IGC, all the more so as the Institute did complete its first decade since the last reform, contrary to the century that has still to wait for another year. As in previous reports, I shall consider IGC's achievements as an institution, and will not single out particular scientific discoveries, for these represent the physiological behaviour of the institution itself, considered as an organism[1]. And I must start by something that we all knew, but has now received public confirmation: the IGC is a great place to work, one of the top 10 in the world outside the US, at least for "The Scientist", and at least for post-docs. Whatever objective value these surveys contain, they reflect the opinion of the users; as we host but a very small fraction of all those consulted, I take this ranking to mean that there are people around the world who hold the IGC's intellectual and human environment in high regard.

On previous occasions, I have expressed the view that the IGC is thought of and managed as if it were a living organism, and I shall insist here on that metaphor, hoping that the reader will readily translate the biology to the institutional level. If, as done recently, "organismality" is given a two-dimensional definition of high cooperation and low conflict (1), these 10 years have provided evidence, if necessary it was, for the "organismal" nature of the Institute. In turn, I am convinced that this was key to its fitness and adaptive performance. Today, the IGC is not a group of individuals that are indifferent to each other - with no conflict but no cooperation either; it is not a conventional society - characterised by levels of cooperation and conflict that are both high; and it is not a pack of competitors - full of conflicts and with no cooperation.

Organisms are born, develop and grow to maturity, turnover their components and regenerate at reproductive ages. They then age, decay and die. Higher organisms are composed of a variety of cell types, organs and systems, as if the "most interesting ways of living" were inexorably associated with increased intra-organismal complexity and diversification. Even the simplest forms of life, however, do require diversity of components, precisely to generate complementarities that allow for the necessary cooperation amongst them. Organisms grow to a given size that cannot be exceeded, a limitation that is imposed by various ratios of surface/volume, of weight/mass and others, which differ with the environments where evolution has shaped each type of organisms.

In the institutional metaphor as well, a large diversity of components and interactions are required to make up for an organism, which entertains its basic operation and produces "differentiated functions". At the IGC, these are clearly defined as biomedical research and education, but here again, diversity that ensures adaptive flexibility is key to the organisms' performance. The Institute is characterised by a wide diversity of components, first of all, as to the scientific interests of individual groups and the precise questions they address, the respective experimental systems, methodological approaches and techniques, even the relative importance given to either research or education. Components interact frequently, most often in preferred pathways, embodying a network from where the most critical "distributed" properties may emerge. Networks are characterised by their structure and their dynamics. Network connectivity (K/N values) should be high, for this ensures robustness in the operation, but not too high as to limit the range of dynamic behaviours. Each component may only enact a given number of productive interactions per unit of time: hence, the number of components in the network - the size of the institution, must be limited for optimal connectivity and emergent dynamics. Networks operate best when they are self-organised.

[1] If the relevance of discoveries were to be assessed by the respective number of citations, undoubtedly a poor way of doing it, the Web of Science gives the following list of the 10 most cited publications (discoveries) of the IGC since 1998 in this order: Regulatory T cells express receptors for bacterial products (TLRs); Carbon monoxide (CO) improves atherosclerotic lesions; CD4 T cell depletion in HIV patients correlates with immune activation, not with viral load; Notch signaling promotes human T cell differentiation from lymphoid precursors; Regulatory T cells suppress inflammation, but the elimination of microorganisms as well; Structural basis for the inhibition of BMP signaling by Noggin; CO protects endothelial cells from TNF-dependent apoptosis by activating NFkB; The transcriptome of Arabidopsis pollen differs from that of other organs in the plant; Adult IL-7-deprived mice maintain a long-lived compartment of B cells that are activated; Antigen-specificity of Regulatory T cells is required for disease suppression, but insufficient to ensure thymic selection.

Self-organisation, in turn, requires autonomy of components. It follows that institutional networks should not be hierarchical, and operate best if endowed with a horizontal structure. Ecological networks that are based on antagonistic interactions tend to fragment, while those made up of mutualistic interactions may "nest", in both cases leading to loss of an overall institutional structure and identity. Inside institutions, network fragmentation might thus occur by excess antagonism, but by inappropriate mutualism as well, and both must be fought with equal strength. In fact, excess mutualism actually represents antagonistic interactions between the subset of "outlier mutualists" against all the others, particularly if their interests are somewhat "differentiated". Dynamically, networks resist better both of those dangers if they contain appropriate numbers of "generalist", multi-connected components. Hence, it is critically relevant for the "organismality" of an institution to include individual scientists or groups who excel in a broad range of interests and research topics, even if they are (apparently) modestly productive in the conventional terms of papers, citations and money. Ideally, such generalists are prone to interact and enjoy intellectual exchange. They are also very useful in dealing with the frequent emergence of components that, by either their nature of for mere dynamic reasons, end up "isolated" from the productive network. In many cases, however, the very nature of such "disconnected" components provides for the most "unique" and exceptional performances, which, to be useful institutional contributions, must be "connected" by the generalists.

If anything, the IGC has grown somewhat larger than its ideal size, given its total scientific mass and specific weight, under current environmental conditions. Attention should be given, therefore, to possible risks of collapse, or fragmentation into disconnected subsets. Alternatively, there are not enough "generalists" at the IGC to ensure optimal dynamic behaviours of a unique network, to connect the "strange" outliers, to counteract the "nesting" of thematic programmes.

A research institution will have to adapt, with various degrees of success, to changing, often hostile environments, perhaps enduring various types of pathology, much as an organism does if it is not to perish. In this context, let us first agree on a critical point. To be an organism, all its components cooperate with each other to produce the physiological behaviours that ensure health, survival and reproduction. Self-organised cooperation, naturally emerging from the diversity of autonomous components is thus the model for a living institution. The cooperative nature of an organisms' architecture brings about a conclusion that is important for their understanding, but could well have been uttered by M. de La Palice: the better any of the components does, all others also gain; and vice versa: if any of the components fails, all others will suffer and eventually perish. I am certain that we all know this at the IGC.

Occasional conflicts among the organism's components result in pathology, which is also often due to mal-adaptation to the environment, starvation of essential nutrients, or infection by pathogens.

Metabolism is a relevant aspect of physiology, ensuring the energy for the basic operation, for differentiated functions, and for reproduction as well. Yet, whatever is necessary, the nutrients used in metabolism do not determine the nature of the organism. As Jerne used to say, (I do not know whether he borrowed it from someone else) "many things are necessary for the grass to grow, but they do not determine the kind of grass". Money alone will thus not produce an "organismal" research institution, even if it will allow for recruiting the most productive components. At best, money will suffice to establish a series of independent elements, often a pack of competitors, each of which would do as well being somewhere else, and providing nothing to the emergence of an institutional identity; that is, money alone will not create an institution with added value. The added value of a research institution is given by its collective knowledge, rationality and creativity, perhaps better, by its unique way of dealing with rationality and knowledge such that creativity is fostered. In turn, this is encoded in the institutional "germ-line", which imposes the value of individuals and of their freedom, and promotes their cooperation to form the organism "described" in the germ-line. Nevertheless, starvation of metabolic intake leads to all sorts of malfunctions that

might generate conflicts among the organisms' components. In the extreme, starvation may lead to death, usually in a protracted manner that calls for radical means to shorten the agony. On the other hand, organisms that are robustly well adapted to their environment feed on many different sources, such that they are not strictly dependent upon any of these. For an institution, the danger lies in a limited diversity of its sources of support: with high dependency on any one, the risk is that one particular source will determine, alone, the future evolution of the organism. In turn, the higher the intra-organismal diversity, the better the institutional possibilities to compete for resources in the environment.

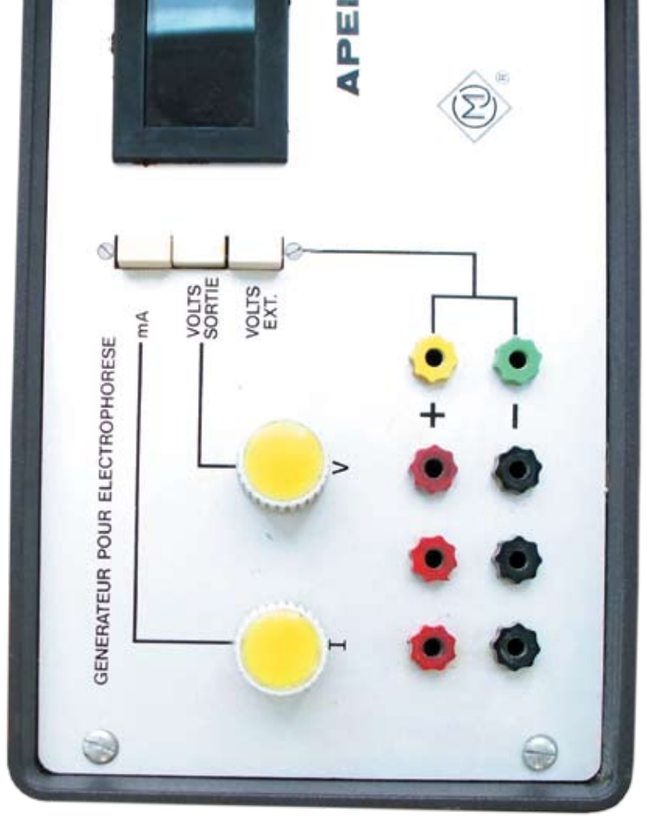
In the splendor and beauty of its diversity, life has evolved forms that differ dramatically in their potential for genetic variation, as the time required to duplicate their "germ-lines" may vary from some minutes to many years. Microbial infections of larger organisms may be taken to reflect the co-existence of such classes of life forms. For over a century, immunology has studied the mechanisms of animal resistance to infection, always with the central a priori that all evolution had done was to endow animals with "ridding" mechanisms against the microbes. Sadly, such mechanisms, while eliminating parasites, often also damage the host tissues, and disease is instead caused by the "ridding" response. This view of immune systems as biological warfare machines, however, has recently been, if not questioned, at least enriched by a novel, perhaps complementary, point of view. Survival and "fitness" have also been ensured, not by eliminating the infective microbes, but by evolving mechanisms that allow the organisms to "tolerate" the infection and thus adapt to it. Interestingly, at least some of these mechanisms involve extremely conserved, prototypic responses of cells and tissues to "stress", which "protect" host tissues from injury, be it directly caused by the infectious agent or by the response itself. It could be thought that infection, that is, invasion by other "germ-lines", carries a danger for an institution: the implantation of values (human, intellectual and scientific) that are foreign to its nature, may result in a chimera, in the best case, or in loss of the original "spirit" and "ethos". This is not necessarily the case, however, for many examples of symbiotic relationships exist in nature. Thus, eliminating infectious organisms may not always be the best strategy, because of the potential damage to institutional health. Rather, the most adaptive response may often be to "tolerate" the invader, actually using it for the host's benefit, by the gain in diversity and possibilities it represents, much like in a symbiotic interaction. These, by definition, are of mutual profit, in spite of whatever "germ-line" differences in values and goals. After all, mitochondria were once invasive bacteria. Interestingly as well, tolerance to "foreign" would best be achieved by re-enforcing the "stress resistance" of the institutional components, the whole process thus resulting in stimulation of the very values that characterise the original "germ-line".

For long-lived organisms, cancer - the selfish expansion of a component at the cost of all others and of the organism itself, represents a major threat. The tumour uses the host's resources for its own growth and advantage, until it eventually dies together with its host. Hence, the size of component groups in institutions must be regulated, either by letting expansionist forces from various groups equilibrate and neutralise each other, or by collective dependence in the physiological processes. The relationships between cancer and the host organism have received increased attention over the last few years, for they contribute to the initiation and expansion of the tumour (protected niches, for example), and may also determine various mechanisms of "resistance" or influence the outcome of therapies. Here again, the host's resistance seems to rely on re-calling physiological mechanisms that are at work in the organism before any cancer arises. It has long been known that cancer results from the accumulation of unique mutation events in single components, and it is thus a somatically acquired genetic disease. It is now clear, however, that the "germ-line" of the organism determines the risk of cancer development; so it is in our institutional metaphor. As with the fact that agents in the environment exist (physical, chemical or infectious) that markedly increase the rate at which mutations occur, reminding us of the cancer-preventive effects of "healthy life styles". Some such mutations occur in the fetus and are already present at birth; hence, prevention may be effective by carefully screening potentially "transformed" components, identifiable by self-centredness and conflict as they integrate the organism.

As mutations always occur at some frequency, whatever the "germ-line" or the "life style", cancer "check-ups" must be regular and tumour recession must be rapid, if the institution is to enjoy a healthy survival.

Successful organisms reproduce, the more the better, transmitting their "germ-line" to their progeny. Many genes make up for the "germ-line" of an organism, all are essential to encode each and everyone of its characters, the most "complex" of which require interactions amongst more than one, often many genes. Analyses of organisms discovered sub-unit processes, "modules", "pathways" and networks of interacting components, which ensure particular aspects of physiology of cells, organs and systems; many such sub-units are now well known, seemingly independent from each other. Upon appropriate analysis, however, it turns out that "germ-lines" (genomes) are ensembles that were shaped by evolution to function as units, the loss of any single component having consequences for the operation of the whole, of its fitness and its adaptive competence. Such is an organism. As any organism that reproduces is a point in the trajectory of life's evolution, so is an institution dedicated to research and education in the forward-going trajectory of science. Thus, already at birth, an institute must know what it wants to transmit to progenies, that is, it should have a "germ-line", composed of many genes that are as many principles. In the IGC's case, a lot of its germ-line owes to our creators and mentors, the values that inform the Calouste Gulbenkian Foundation, and those that the members of the Institute's Scientific Advisory Board personalise in the clearest manner. Some say that the Institute's germ-line, at least in what it contains of diversity, community and mutualism, of requirements for rigorous criticism and excellence, also originated from the "ethos" of the PhD programmes that had been established a few years ahead of the "new IGC".

Organisms reproduce in various ways: some by simply growing first, to then divide in two (never in three, for example) other organisms, of roughly the same size as the progenitor before it had grown; others have to go through a laborious process of producing a cell that is "germ-line only" (a gamete), only to conjugate it with another equivalent cell to produce an egg, which will then develop to a full organism. This process of "admixture" of genomes, while laborious, error-prone and energy-expensive, is so critical that even those organisms that reproduce by binary division have to use it from time to time. Similarly, species in which hermaphrodites exist regularly go back to crossing with different individuals, only to allow for wider admixtures of genes. This general rule seems to represent some sort of "horror clonicus", and aims at ensuring that diversity exists in the population of organisms. This, in turn, provides for the beauty of Biology: no two organisms are exactly the same, for even the mere duplication that precedes binary division is also error-prone, let alone the inexorable variability that is inherent to being alive, introduced by the randomness of environmental encounters and respective time sequences, which create individual histories. Some other "funny" species add to all this the amazing ability to reproduce through pieces of their (adult) bodies: if a planaria is cut in two (this time even in 3, or higher numbers), each piece will make up again for a whole organism; each time you stick a branch of some trees into fertile soil, this will result in a full tree of the same species. It is not a "new" tree, however, but the same tree "born again". For a science institution, reproduction is as essential, and in the IGC the mode has been both sexual and non-sexual. Thus, on the one hand, the Institute matures PhD students who carry some of the IGC's germ-line going to new environments, where they incorporate other "germ-lines", to then germinate and perhaps produce a new scientist. On the other hand, the Institute has also reproduced in the mode of planaria and plants, simply by shedding out groups that get established elsewhere, and grow to reach considerable sizes, sometimes by aggregating with others to form another complex organism, different from the IGC, but keeping at least some of the same "germ-line". It could be thought that the Institute has come of age to engage in yet another reproductive mode, this time in a fully sexual mode. This would require that the IGC's germ-line be admixed with another, hoping that the new hybrid organism will add to its expected "vigor" a higher level of diversity and differentiated functions. "Major transitions in evolution" have systematically been of a cooperative nature, leading to "more interesting", because more complex, forms of life, even when one of the cooperating components "disappears" in the process. What would our cells be, which



poor energy would they have available, if it were not for the mitochondria? What a beautiful, if adventurous and most generous, destiny for the original bacteria!

Already while growing, organisms "learn" new skills, a process that continues throughout life, often by trial and error, but the ability to learn requires a given "germ-line". Genomes do not determine what organisms learn, only the ability (or lack of it) to learn within a given domain of learnable things, and delimit this domain. In some cases, while nurturing the progeny, organisms also transmit acquired skills and knowledge about the environment, in a process that may be designated as "cultural inheritance". In addition to its own "germ-line", therefore, the IGC may also transmit, when reproducing, much of what it has learned over the years.

The year of 2009 celebrated "the survival of the fittest", and it may be appropriate for the IGC to celebrate its 10th anniversary, not because of being "the fittest", but because it did survive all hardships. The 1998 reform had left the IGC with only a few research groups, all labs essentially empty of heavy and light equipments, and in urgent need to undergo major reforms of buildings and infrastructure. The Foundation's investment had to be kept at the previous level, and there was no money for recruitment, for the whole budget had to be spent on creating attractive conditions to do science. With a reasonable working environment, and provided that a clear mission was announced, investigators would join. These "starting conditions" had an extraordinary advantage: those who would join would not come for the money, but to help with the mission and to carry on with the project. The plan was thus very simple: to invest in intellectual atmosphere and scientific excitement, in good services, equipment and working conditions, to keep the environment of a truly "open society", sharing strong principles while adopting very few rules, encourage risk, freedom, creativity and the uniqueness of individual contributions, and building it all on the solid basis of the basic values of science - rationality, doubt and critique, cooperation and optimism. In short, let us adopt the single, clear goal of doing good science and doing it the right way: progress will necessarily follow. Ten years later, it would seem that, thanks to the immense efforts of many "who joined", the plan seems to have worked, to some extent at least: the Foundation's investment has been kept essentially at the levels of 1997, but the total budget of the Institute is now roughly three times higher, thanks to increasing external funding secured by IGC scientists, through competitive national and international calls. Likewise, IGC scientific production (measured by papers, communications, academic theses, etc.) shows a steady rise since 1998; so too the impact of the research produced here is progressively rising: the number of citations of IGC's publications was nearly six times higher in 2009 than in 1998 (ISI Web of Science).

Science wishes to understand the world and ourselves through rational derivation of natural laws, and it expects that such knowledge will serve to solve problems, all sorts of problems of humankind. In Biology, one "applied" aim is to provide a science basis for medicine, thus improving the quality of health care. The last decades in Biology have brought about an astounding pace of progress, essentially derived from detailed component analyses. Yet, much has yet to be done in order to approach the properties of whole organisms, their organisation, operation and evolution, in ways that may be immediately useful for medicine. I had argued along these lines in the 1998 IGC report, and have later defended that medical education fosters predominant concerns and approaches to whole organisms, such that progress in Biology would seemly gain from more inputs from the medical side. One strategy would be to encourage MDs into basic research. This last year brought a new component to the IGC, which rapidly evolved to constitute a significant force in its operation: the students of the Advanced Medical Education Programme, MDs with several years of hospital training, who wish to get into science. Their arrival was looked at with some degree of suspicion by a few of the "basic" scientists, but very quickly their serious attitude, devotion, rigour and enthusiasm has convinced us all that they were making a considerable difference, not least by their maturity. The IGC was lucky enough to keep a few of these MDs in PhD thesis work, and we have continued to profit, along the year, from their medical education, interests and approach to questions. Looking at the commitment of this group of MDs and at their enthusiasm

with "real" science, seeing their rapid progress in critical understanding, and listening to their own views on how much they have changed in a few months only, it is clear that this Programme is a success. We all hope it will continue for many years to come. Another way to foster "organism-centered biology" would be to bring to the laboratories of basic research the questions that clinicians face in their wards. This amounts to inverting the established conviction that "translation" should proceed from "the bench to the bedside". Once again, Sydney Brenner has been a precursor, lecturing on the interest of doing research in humans, having MDs to produce most detailed and accurate "phenotypes", and scientists to unravel the molecular, cellular and systemic mechanisms representing the physio(patho)logical "mapping" of those phenotypes to "genotypes" that have become so much easier to determine these days. Today, there is reason to hope for a significant change in dominant views: a number of recent editorials have underlined the necessity of such approaches, and the NIH has opened a call specifically designed to do precisely that. There is, perhaps yet an alternative strategy to help bringing biomedical science to the organism level, which was rather evident at the IGC last year, at the "post-doc workshop" on Biophysics. This was, perhaps, one of the best workshops ever organised at the Institute. Component analysis in Biology has been deeply anchored into chemistry, and it has largely remained qualitative. The description of genomes and molecular components, of the metabolic, signaling and gene expression pathways of interacting molecules, has been prevalent; yet, very few approaches and experiments address quantitative aspects of the phenomenology, and it is rare that papers in molecular and cell biology speak of numbers of molecules, of reaction kinetics and rates, let alone concluding on a mathematical formula or a quantitative network model. At the risk of being unfair, it is a common notion that chemistry worries about detailed descriptions, while physics aims at general laws. Comforted by other indications that biophysics will take the front lines in the next decade(s), the hope is that the "physics spirit" and its usual concern with general laws and the derivation of quantitative descriptions will bring biology to the realm of organisms. It will not be too early.

The IGC was established by the Calouste Gulbenkian Foundation, and it has enjoyed the Foundation's support over the years. For the last three years, the Institute has gained a new and most active area of research on systems neuroscience, thanks to the vision of the Champalimaud Foundation to initiate here one of the Foundation's programmes. All of us at the IGC are deeply indebted to the Boards of Administration of both Foundations.

ANTÓNIO COUTINHO
Director

THE IGC AT A GLANCE

It is a sunny spring afternoon, and in the cobbled courtyard of the Instituto Gulbenkian de Ciência (IGC) tables are being set with white tablecloths, champagne bottles, and flutes. At around 5pm, people start to trickle out of the main building - students, post-docs, group leaders, staff - and gather round the tables, to celebrate the latest batch of research grants secured by IGC researchers. Or it could be the latest European Research Council grant everyone is celebrating. Indeed, such gatherings are common at the IGC. They underscore the dynamic, thriving nature of the institute, a consequence of the commitment, enthusiasm and drive of IGC researchers and staff, as the over 200 visitors to the IGC tell us.

In fulfilling its mission as a host institution and an 'entrance hall' into Portugal, the IGC identifies, educates, imports, incubates and exports new scientific leaderships, always with a view to setting up and developing research programmes of excellence and strengthening the country's scientific community. In 2009 seven new research groups joined the IGC - to carry out their research programmes in total intellectual and financial autonomy. Three groups left the institute for other research centres, two of which in Portugal. Thus, in all, 38 research groups and 8 small teams of Research Fellows made up the IGC in 2009.

Research at the IGC is organism centred, hypothesis driven, transverse and multidisciplinary in approach. The focus is on the genetic bases of development and evolution of complex systems, spanning evolutionary biology, genetics of complex diseases and of resistance to infections, cell biology, cell cycle and DNA repair, inflammation, immunity and auto-immune diseases, developmental biology in animals and plants, behavioural neurobiology, theoretical and computational biology.

The IGC research community is itself varied and multidisciplinary, combining biologists, biochemists, geneticists, physicists, mathematicians, clinicians, computer scientists. And not only are scientific backgrounds varied, but so are nationalities: the approximately 250 researchers - technicians, students, post-docs and group leaders - hail from 31 different countries, across five continents, making the IGC a truly international workplace.

Underpinning the large portfolio of research programmes, are state-of-the-art equipment, facilities and services, run by highly qualified and experienced support staff, many of which hold a PhD. From animal facilities to imaging and sequencing technology, all common equipment and services are freely accessible to all researchers, and are constantly being reviewed for updates and refurbishments. Research does not live from technology alone, so the IGC also provides support in other 'softer' aspects of research life: in grant application and project management for successful funding, in communicating IGC research and engaging the public in science, and the library provides up-to-date online subscriptions to over 16000 journals.

In 2009, just over 140 papers were published in international scientific journals, thus sustaining the trend for increasing publication and citation rates. IGC researchers presented over 300 talks at international meetings. Twelve PhD theses, nine Masters theses and one undergraduate thesis were prepared either partly or fully at the Institute. The year was particularly memorable in terms of scientific awards and funding obtained by IGC researchers. Besides the 45 projects approved for funding by the Fundação para a Ciência e a Tecnologia, 7 within the European Commission's 7th Framework Programme, three research groups were awarded research grants from the European Research Council (ERC), the most important funding organisation in Europe. The European Molecular Biology Organisation (EMBO) awarded two researchers with an installation grant and another with a Young Investigator Award. IGC scientists came away with many national awards, from cancer research to best practices in communicating with the public.

Graduate training has always been a strong commitment of the IGC, with four PhD programmes now being fully or partly hosted at the institute. When graduating, the students in these programmes, Portuguese and foreign, will join a noteworthy alumni network of 483, spread out across some of the world-leading research centres.

The PhD programmes ensure a steady flow of visiting scientists, thus contributing to what is an integral component of continuing graduate training: an international programme of invited seminars, regular meetings and workshops, being hosts to scientists on Sabbatical leave. Both these, and the more quirky TED talks organised by graduate students - on 'outer body' experience, tango or yoga - make for stimulating discussions and mentoring of the many young researchers at the Institute.

The IGC is in what has become known as the Oeiras Campus, home to several other basic and applied research centres in biology, biotechnology and chemistry, including the Oeiras Associated Laboratory, made up of the IGC, the Instituto de Tecnologia Química e Biológica (ITQB) and the Instituto de Biologia Experimental e Tecnológica (IBET). But collaborations extend beyond Oeiras and, indeed, beyond Portugal, to Europe, North and South America, through several networks and joint research programmes.

The town of Oeiras, where the IGC is located, is just 20km from Lisbon, on the coast. The IGC is at walking distance from the beach, and there is easy public transport access to Lisbon. The IGC's parent organisation, the Calouste Gulbenkian Foundation in Lisbon has both a fine arts and a contemporary art center, as well as a world class concert season, all of which IGC members have access to.

RESEARCH GROUPS

PROTEIN - NUCLEIC ACIDS INTERACTIONS

Alekos Athanasiadis

PhD in Structural Biology
University of Crete, Grece
E-mail: alekos@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/96

Sequence is not fate. Proteins demonstrate an impressive ability not only to recognise and bind to particular pieces of nucleic acids code but also to alter its information content by catalysing reactions that rearrange its sequence or specifically change one nucleotide for another.

Organisms have found in such mechanisms the means for creating sequence diversity, gloriously exemplified in the diversification of immunoglobulin genes. The recent realisation that multi-cellular organisms achieve phenotypic complexity without a parallel increase in number of genes has highlighted the importance of post-transcriptional RNA modifications in creating and fine-tuning a much larger repertoire of proteins originating from a small number of genes.

We are interested in the study of the molecular mechanisms involved in such diversification of RNA and DNA sequence as well as understanding the consequences of such processes for molecular evolution dynamics.

We are employing the tools of computational, molecular and structural biology in the study of the most widespread RNA editing process, mediated by Adenosine Deaminases Acting on RNA (ADARs). This editing process, which affects all animal species, is shown to create sequence variation for thousands of human pre-mRNAs (Athanasiadis et. al, 2004). When directed towards foreign nucleic acids, editing can also be a powerful tool for immunity towards pathogens. We are studying the role of ADAR1 in antiviral responses and how foreign nucleic acids are being distinguished from self.

RECOGNITION OF FOREIGN NUCLEIC ACIDS IN INNATE IMMUNITY

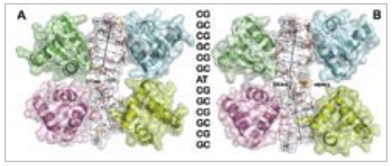
What are the molecular interactions that allow innate immunity to distinguish foreign from self nucleic acids? The Za domain family is found exclusively in proteins (ADAR1, DAI, E3L and PKZ) involved in the intracellular recognition of nucleic acids and the activation of interferon response. We are interested in characterising the interactions of the Za domains with DNA and RNA, understand how self and foreign nucleic acids are distinguished and how misrecognition can lead to autoimmune reactions.

We determined the crystal structure of the Zalpha domain of the RNA editing enzyme ADAR1 at 2.6 Å in complex with immunogenic CpG DNA sequences, adopting the left handed DNA conformation. The crystal structure reveals how Za can bind its cognate sequence in the left handed DNA conformation in the context of a natural DNA sequence. We have also managed to express and purify multi-domain regions of DAI, one of the cytoplasmic receptors for nucleic acids in vertebrates, and obtain (yet uncharacterised) crystals in the presence of activator DNA.

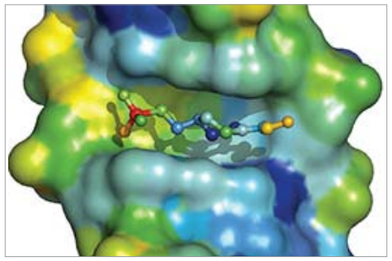
GROUP MEMBERS
Matteo De Rosa (Post-doc)
Delio Figueiredo (Trainee)

THIS GROUP COLLABORATES WITH:
Maas Stefan (Lehigh University, USA)
Alex Rich (Massachusetts Institute of Technology, USA)
Maria Armenia Carrondo (ITQB, Portugal)

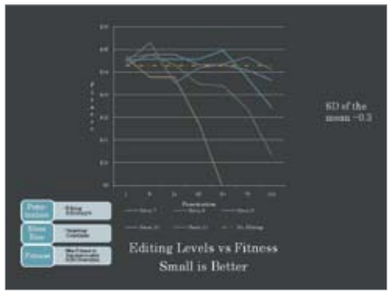
FUNDING
Marie Curie International Reintegration Grant, European Comission



Recognition of DNA CpG repeats by the Z-domain family, a DNA binding domain present in interferon response proteins involved in the recognition of foreign nucleic acids. The crystal structure in two different conditions with Tris (**A**) and HEPES (**B**) was determined in IGC at resolutions 2.8 and 2.6 Å, respectively.



A cavity formed at the junction between two CGCGCG segments can become site for intercalating agents. Here a HEPES molecule intercalates in the DNA helix.



Computational models of gene evolution in the presence or absence of RNA editing. Low levels of RNA editing are shown to accelerate evolution rates relative to the no editing controls (dashed yellow line). The plot shows the maximum fitness levels after 5000 generations of simulation under variable parameterization.

PLANT STRESS SIGNALING

Elena Baena González

PhD in Plant Physiology and Molecular Biology
University of Turku, Finland
E-mail: ebaena@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/94

In contrast to animals, plant growth and development are largely conditioned by environmental inputs. Stress can have a great impact on the decision to grow, to initiate organogenesis as well as on the characteristics of the newly formed organs. Often associated with stress is a reduction in photosynthesis and/or respiration, which in turn results in an energy deficit in the cell and a subsequent growth arrest. We use *Arabidopsis thaliana* as a model and a combination of cell-based assays, functional genomics, bioinformatics, mutant screens and genetics to understand how this stress-triggered energy deprivation is sensed, translated into an initial growth arrest and ultimately into plant adaptation, development and survival.

ENERGY SIGNALING IN THE STRESS RESPONSE

The aims for 2009 were to:

1. Establish the new laboratory;
2. Start gaining insight into the regulatory mechanisms that govern SnRK1 action and to further dissect this signaling pathway through the identification of novel components.

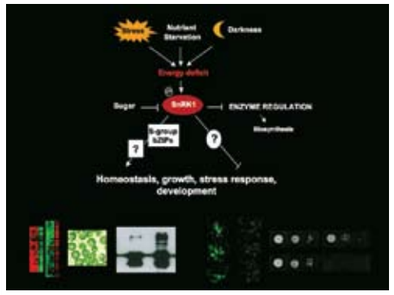
In 2009 we have:

1. Successfully set up the main techniques and facilities required for the work;
2. Recruited post-docs, a student and a technician;
3. Obtained preliminary results on new interacting partners for the SnRK1 kinase, on novel post-translational modifications and on the role of miRNAs downstream of SnRK1s.

GROUP MEMBERS
Américo Rodrigues (Visiting scientist/Post-doc)
Rafal Butowt (Post-doc)
Cláudia Martinho (PhD student)
Leonor Duarte (Technician/Trainee)

THIS GROUP COLLABORATES WITH:
Jen Sheen, Mark Borowsky, Brad Chapman
(Massachusetts General Hospital, USA)
Pedro L. Rodriguez Egea (Universidad Politécnica de Valencia, Spain)

FUNDING
Conselho de Reitores das Universidades Portuguesas (CRUP), Portugal
Marie Curie International Reintegration Grant, European Comission
European Molecular Biology Organization (EMBO)
Fundação para a Ciência e a Tecnologia (FCT), Portugal



Our main goal is to understand how the SnRK1 system integrates metabolic and environmental cues into growth and developmental patterns. To this end a deeper knowledge is required on how SnRK1s are regulated and therefore we are currently undertaking several complementary strategies to dissect and characterise in depth the SnRK1 signaling cascade.

MEIOSIS AND DEVELOPMENT

Vítor Barbosa

PhD in Genetics
University of Cambridge, UK
E-mail: vbarbosa@igc.gulenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/94

THIS GROUP WAS ESTABLISHED AT THE IGC IN MAY 2009

We use *Drosophila melanogaster* as a model to study the links between meiosis and oocyte polarity. In Drosophila females, the integrity of the meiotic chromatin is monitored by a checkpoint mechanism whose activation affects gamete viability. Persistent double strand breaks from meiotic recombination activate a conserved DNA damage response (DDR), which causes defects in the dorsal-ventral (DV) polarity of the eggshell. With a panel of germ line mutations we want to:

1. Characterise DDR pathways that monitor meiosis and understand how their activation affects oocyte polarity. We are also interested in finding new meiotic mechanisms under this surveillance.
2. Study the control of timing of DDR along oogenesis. Specifically, we want to know how DDR is activated by germ line-specific mobilisation of selfish elements at different points of oogenesis.
3. Understand the role of chromatid cohesion during meiosis. Cohesion is monitored by a meiotic DDR and affects transcription during meiosis. We want to understand how the transcriptional role of cohesion genes relates to DDR.

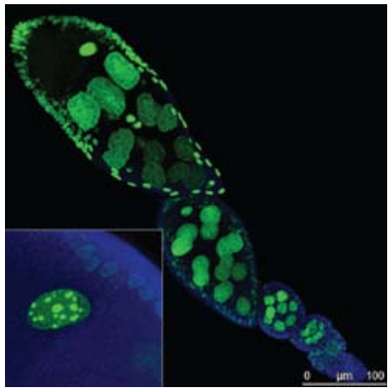
STUDIES OF CHROMATID COHESION DURING MEIOSIS IN *DROSOPHILA MELANOGASTER* REVEAL A NOVEL DNA DAMAGE CHECKPOINT PATHWAY ESSENTIAL FOR OOCYTE POLARITY

The aims of this project are to characterise the phenotype of dPds5 mutant germ cells in terms of their transcriptional activity using chromatin markers; to describe the localisation of functional tagged dPds5 transgenes in the oocyte with respect to other germ cells and soma; to test ed tags: GFP, Venus, Myc and FLAG.
Furthermore, we aim to identify earlier components of the checkpoint that monitor the meiotic function of dPds5, and define downstream effectors of the new DDR pathway identified through studies on dPds5 mutants.
We have achieved 40% partial characterisation of the dPds5 mutant germ cells by successfully staining two heterochromatic markers and two transcription markers.
Tagged proteins were localised to the oocyte in a different manner compared to all the other recognisable cell types in the ovary. Both results are consistent and point to a unique function in transcription by dPds5 in the oocyte.

GROUP MEMBERS
Sofia Leocádio (Technician, left October 2009)
Patrícia Silva (Technician)

THIS GROUP COLLABORATES WITH:
Caryn Navarro (Boston University School of Medicine, USA)

FUNDING
Marie Curie International Reintegration Grant
- Framework Programme 7, European Comission
Fundação para a Ciência e Tecnologia (FCT), Portugal



DROSOPHILA OVARIOLE SHOWING THE LOCALIZATION OF THE COHESION PROTEIN DPDS5 TAGGED WITH GFP UNDER THE CONTROL OF ACTIN PROMOTOR.
dPds5 co-localizes with DNA (blue) in all somatic nuclei and nurse cell (germ cell) nuclei where it presumably acts to establish and maintain chromatid cohesion. The localization of dPds5 in the oocyte is unique (inset) excluded from the meiotic chromatin and diffuse through the nucleoplasm accumulating in foci, which we hypothesise are transcriptional centers.

EPIGENETICS AND SOMA

Vasco Barreto

PhD in Immunology
Université Paris VI, France
E-mail: vbarreto@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/86

We are interested in expanding studies that have been classically associated with the antigen receptor (immunoglobulin) genes of B lymphocytes: random mono-allelic expression (RMAE) and DNA modification reactions, namely, somatic hypermutation (SHM) and class switch recombination (CSR).
RMAE is the most striking example of an epigenetic phenomenon, because at the level of each cell only one of two identical molecules (the alleles) is expressed. Understanding it implies: a) solving the lingering questions that still persist for the classical examples, such as the RMAE of the immunoglobulin genes; b) designing new model systems, in which the phenomenon can be studied at the level of the organism and fully captured in space and time; c) carrying out a phylogenetic evaluation of RMAE, which, with very few exceptions, is still lacking; d) performing new approaches on the global evaluation of how many and which genes are undergoing RMAE. We are currently studying the immunoglobulin genes as a model to dissect early epigenetic mechanisms that determine which allele is going to be expressed. We are also designing screens using model organisms and cell lines to identify additional regions in the genome undergoing random mono-allelic expression. SHM generates the required diversity to fuel the affinity maturation of antibodies. In contrast, CSR diversifies the effector functions of the antibodies. Activation-Induced Deaminase (AID) is essential for SHM and CSR, playing an important role in adaptive immunity. AID is intrinsically mutagenic and it has been implicated in B lymphomas and other neoplasias. First thought to be expressed only in activated B cells, AID was found to be expressed in the germline, which is counterintuitive. We are developing a directed evolution approach to isolate hypermutants of AID; we are also studying AID orthologues in a functional context; finally, we plan to develop murine models to study the impact of AID expression in cancer and in the germline.

STUDIES ON MONOALLELIC EXPRESSION

The aims of this study are:

1. Molecular analysis of sorted IgM and IgM b populations of individual B-cell clones.
2. Generation of transgenic zebrafish with artificial fluorescent allelic proteins.

We have shown that clones of IgM-expressing cells from different murine B cells progenitors grown *in vitro* are not committed to rearrange a given IgH allele before the other. We have made a suggestive observation that the same happens for the IgK locus.

STUDIES ON AID

This project has several aims, namely:

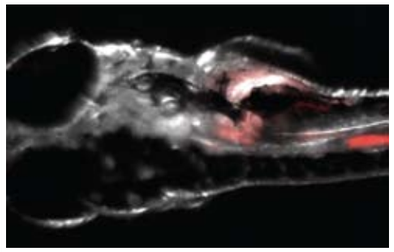
1. Testing the competence of AID from a shark species (which lacks CSR) to rescue CSR in murine AID deficient cells;
2. The optimisation of a directed evolution approach to isolate AID hypermutants;
3. Development of murine models to study the ectopic expression of AID in the tissues under chronic inflammation and in the germline.

We have shown that the AID from a shark can complement CSR in AID -/- murine cells. We have also characterised a new AID null mutant from patients with hyper-IgM syndrome.

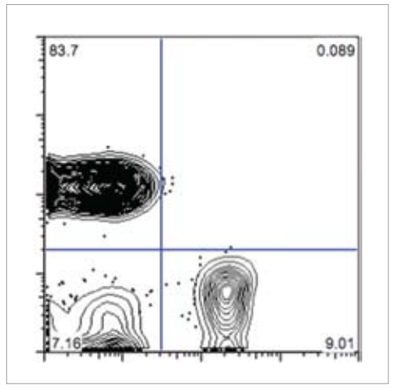
GROUP MEMBERS
Catarina Cortesão (Post-doc)
Clara Pereira (PhD student)
Thiago Guzzela (PhD Student)
Daniel Espadinha (MSc student)
Nadine Caratão (Lab technician)

THIS GROUP COLLABORATES WITH:
Paulo Vieira (Institut Pasteur, France)
Maria Vieria da Silva and Paula Gameiro
(Instituto Português de Oncologia, Portugal)

FUNDING
Associação Portuguesa Contra a Leucemia, Portugal
Núcleo Regional do Sul da Liga Portuguesa Contra o Cancro (LPCC)
– Bolsa Terry Fox, Portugal
Marie Curie Reintegration Grants, European Commission
Fundação para a Ciência e Tecnologia (FCT), Portugal



Transgenic zebra fish embryo with a heat shock-induced expression of a fluorescent protein. We are generating transgenic lines with artificial alleles, distinguishable by the expression of different fluorescent proteins.



Flow cytometry data of peripheral blood mononucleated cells from lethally irradiated mice. We are trying to reconstitute mice from single hematopoietic stem cells to evaluate stable epigenetic imprints.

VARIATION: DEVELOPMENT AND SELECTION

Patrícia Beldade

PhD in Evolution and Development
Leiden University, The Netherlands
E-mail: pbeldade@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/71
http://www.beldade.nl

My research in the area of evolutionary developmental biology is focused on trying to dissect the genetic and developmental basis of phenotypic variation and adaptation. Heritable phenotypic variation is the raw material of evolution by natural selection, and a universal property of biological systems - including traits of medical and economic importance. Understanding the mechanisms that generate phenotypic variation is, thus, a key challenge in contemporary biological research. What are the gene types (e.g. transcription factors versus enzymes), specific genes, and gene regions (e.g. regulatory versus coding sequence) that contribute to evolutionarily relevant variation? How do these genes lead to change in developmental programmes and translate into variant adult phenotypes and finally into phenotypic diversification? To address these and other questions my work has so far concentrated on a diverse and ecologically-relevant phenotype that represents a laboratory-tractable system for the dissection of variation in complex traits: color patterns on butterfly wings.

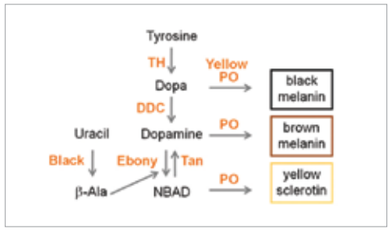
EVOLUTIONARY DIVERSIFICATION: GENETIC BASIS AND ADAPTIVE SIGNIFICANCE OF VARIATION IN BUTTERFLY WING PATTERNS

Study of the genetic basis of variation in eyespot size (an example of a complex morphological trait that is ecologically-relevant and extremely diversified) using gene mapping and expression-profiling approaches.
Building on markers (cf. Mol Ecol Res paper) and the linkage map (PLoS Genetics paper) published in 2009, we have continued to work on the genetic dissection of pigmentation variation. During 2009 we have focused on genes from the melanine synthesis pathway (affecting different phenotypes in insects -- see Sem Cell Dev Biol paper) and mapped a larval coloration mutation to the gene black, and on the Wingless-signaling pathway and cloned and developed markers for a number of candidate genes thought to play a role in the formation of and variation in adult wing patterns. A new post-doctoral researcher, Inês Conceição, was hired in the Summer of 2009 to continue to work on this project.

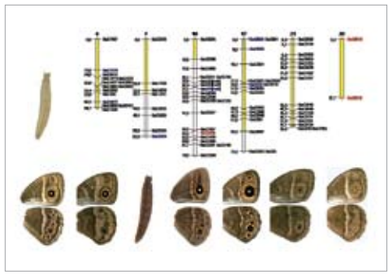
GROUP MEMBERS
Inês Conceição (Post-doc)
Ana Rita Mateus (PhD student)
Marisa Oliveira (MSc student, left September 2009)
Maria Adelina Jerónimo (Laboratory Technician/ Manager)

THIS GROUP COLLABORATES WITH:
Anthony Long (University of California, USA)
Bas Zwaan, Paul Brakefield (Leiden University, The Netherlands)
Filipa Abreu (IGC)

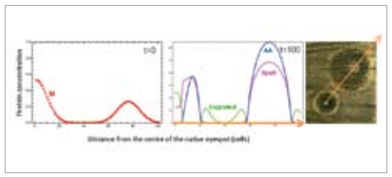
FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



Central components of the melanin synthesis pathway are shown, with enzymes in orange and pigments as well as pigment precursors in black. Different cells in the insect cuticle express different components of this pathway, and thus produce different colour pigments. (Adapted from Wittkopp and Beldade *Semin Cell Dev Biol* 2009).



Linkage map with visible markers (yellow shading corresponding to location of loci where spontaneous alleles produce the large phenotypic changes depicted on the bottom) and markers corresponding to genes expressed in developing wings during the stages of pattern formation. (Adapted from Beldade et al. *PLoS Genetics* 2009).



Modeling the genetic networks leading to the production of native and damage-induced pigmentation patterns. A gradient of a morphogen M (left panel) results in the expression of different transcription factors (middle panel) and the formation of concentric rings of different colours (right panel) around native sources of M (bottom) and sites of epidermal damage (top). (Adapted from M.Sc. thesis of student Marisa Oliveira (2009)).

CELL CYCLE REGULATION

Mónica Bettencourt Dias

PhD in Molecular Cell Biology
University College London, UK
E-mail: mdias@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/80
http://sites.igc.gulbenkian.pt/ccr/

In our laboratory, we study centriole and cilia biogenesis and function. In particular, we study the molecules and processes that regulate the architecture and number of those structures within a cell, in development and human disease. We contextualise our findings and take them further, as well as generating predictions, by studying the evolution of those structures.

REGULATION OF CENTRIOLE BIOGENESIS AND FUNCTION: AN INTEGRATIVE APPROACH

This project studies the evolution of centriole derived structures and their components.
Using computational and experimental studies, in collaboration with the Computational Genomics Laboratory at IGC, we proposed that a conserved group of proteins explains the conservation of centriole architecture, and that taxon and tissue-specific molecular innovations, gained through emergence, or duplication and divergence, play important roles in coordinating centriole biogenesis to different cellular contexts. This work, fully performed at the IGC and now in Press, contextualises the biogenesis and functions of the centriole structure, providing us with a conceptual, evolutionary framework, and suggesting strategies that we are now using to identify novel players in those processes. With the Computational Genomics laboratory, we are assembling a database using controlled vocabulary and linking protein repertoires with morphological diversity of centriole-related structures (www.centrioledb.org).

REGULATION OF THE TUMORIGENESIS-RELATED KINASE SAK/PLK4

The aim of this project is to study the regulation of the Kinase PLK4 and its role in centriole biogenesis
We showed that centrosome amplification is normally inhibited by degradation of PLK4, mediated by the SCF/Slimb (B-TRCP in Humans) ubiquitin ligase. This regulation is likely to be conserved. Because the SCF/B-TRCP complex plays an important role in cell-cycle progression, our results lead to new hypotheses on the control of centrosome number and how it may go awry in human disease, which we are now exploring.

REGULATION OF CENTRIOLE AND CILIA BIOGENESIS IN DEVELOPMENT AND HUMAN DISEASE

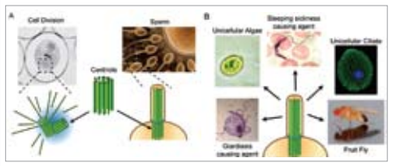
In this project we aim to study the regulation of centriole and cilia biogenesis in development and human disease.

Flagella formation: The first described intermediate in centriole assembly showing nine-fold symmetry is a structure called cartwheel. Bld10/CEP135 and SAS-6 are two components of the centriole proximal part, the cartwheel. We have recently found that Bld10 and SAS6 are likely to play a role in the formation of the tranzition zone. We hypothesise that similarly to the function of the cartwheel in procentriole assembly, the TZ may reinforce the nine-fold symmetry of the axoneme, and/or start the *de novo* formation of structures, such as the central pair of microtubules. We are exploring these parallels.
Centriole disappearance: The disappearance of centrioles during oogenesis might be central in avoiding partenogenesis. We are now describing the regulation of centrosome proteins in the female germline in order to get insights into the factors that regulate centriole disappearance.
In vitro centriole assembly: We have established an *in vitro* centriole assembly system using Xenopus extracts and shown that Xenopus PLK4 induces de novo centriole biogenesis. We are developing tools to follow centriole biogenesis both in fixed samples and in real time, by live imaging.

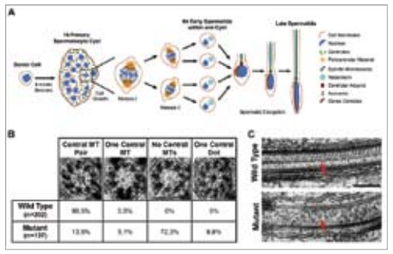
GROUP MEMBERS
Daniela Brito (Post-Doc)
Mariana Faria (Post-Doc)
Ana Rodrigues Martins (PhD student/ Post-Doc)
Zita Carvalho Santos (PhD student)
Filipe Leal (PhD student)
Inês Bento (PhD Student)
Inês Ferreira (PhD Student)
Francisco Freixo (MSc Student)
Pedro Machado (Technician)

THIS GROUP COLLABORATES WITH:
Eric Karsenti (EMBL,Germany)
David Glover (University of Cambridge. UK)
Michel Bornens (Institut Curie, France)
Keith Gull (University of Oxford, UK)
Juliette Azimzadeh (University of California, San Francisco, USA)
José Pereira-Leal, Miguel Godinho (IGC)

FUNDING
European Molecular Biology Organization (EMBO), Installation Grant
Fundação para a Ciência e Tecnologia (FCT), Portugal
Fundação para a Ciência e Tecnologia (FCT), Portugal and British Council



THE CENTRIOLE AND FLAGELLUM ARE CONSERVED STRUCTURES IN EUKARYOTES.
A - The centriole is crucial for cytoskeleton organisation and formation of cilia and flagella. **B** - The centriole is structurally and functionally conserved, from parasites (*Giardia lamblia* and *Trypanosoma cruzi*, causers of giardiasis and sleeping sickness), to small algae and ciliates (*Chlamydomonas reinhardtii* and *Tetrahymena thermophila*), to fruit flies and humans.



MALE FLIES MUTANT FOR A PROTEIN CONSERVED IN HUMANS ARE STERILE DUE TO DEFECTS IN FLAGELLA BIOGENESIS.
A - Spermatogenesis in *D.melanogaster*. A stem cell divides producing a gonial cell that undergoes four mitotic divisions producing a cyst of 16 primary spermatocytes. Each of these cells has four centrioles (shown in green) and undertakes a prolonged G2 before entering in meiosis I followed by meiosis II. These cells form a cyst of 64 spermatids, each with one centriole that templates the formation an axoneme, the structure that confers motility to the spermatids. **B** - Mutants that show defects in the biogenesis of the axoneme are sterile. In B. we represent and quantify the structural abnormalities observed in *DmBLD10* mutant sperm. The axonemes of these mutants show ninefold symmetry, but have defects in central microtubule pair formation. **C** - Longitudinal section showing lack of central pair in the mutant axoneme (arrows). Scale bar, 300 nm.

QUANTITATIVE ORGANISM BIOLOGY

Jorge Carneiro

PhD in Biomedicine
University of Porto, Portugal
E-mail: jcarneir@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/24
http://qobweb.igc.gulbenkian.pt/

Cells of multicellular organisms cooperate to ensure body development and maintenance. They do so in a collective distributed manner, without any master or plan. We investigate the multilevel mechanisms that give rise to whole organism properties, in search of general principles of organisation of natural systems and, eventually, the design of artificial systems.

QUANTITATIVE AND QUALITATIVE T CELL RECEPTOR REPERTOIRE REQUIREMENTS FOR IMMUNE TOLERANCE ESTABLISHMENT AND MAINTENANCE

We aim to clarify the mechanisms of selection of the repertoire of regulatory T cells in the thymus and the periphery. Our role is to develop the necessary modelling and statistical methods to quantify the properties of the repertoire of these cells. To date, all published studies on the repertoire of regulatory and conventional T cells are based on the enumeration of distinct TCR sequences present in the samples obtained from a two cell pool. We have introduced Poisson-abundance models that allow us to estimate the diversity and clonal size distribution of the original populations from which the samples were obtained, and to rigorously estimate the intersection between the repertoires of two populations. The statistical methods were compiled in a PAM package for the statistical software R, and is available from the group's website.

MORPHODYNAMIC MODELLING AND IMAGING OF SEA URCHIN SPERMATOZOA SWIMMING AND CHEMOTAXIS

The objective of this project is to gain insight into sea urchin spermatozoa flagellar morphodynamics, making use of state of the art imaging techniques and mathematical modelling. We want to understand how ligands from the egg or its surroundings regulate intracellular Ca^{2+} oscillations, and flagellar beating, to guide sperm towards the egg. We have developed the first spermatozoan model that integrates, in the same quantitative framework, the molecular signalling networks controlling intracellular Ca^{2+}, flagellum morphodynamics, and swimming behaviour, in the presence or absence of spatial environmental cues. This model has been validated using spermatozoa of *Lytechinus pictus* and *Strongylocentrotus purpuratus*: both respond to the egg chemoattractant Speract, but only the former display coherent chemotatic behaviour. The integrated model is able to qualitatively describe the trajectories of the spermatozoa of both species, pinpointing the quantitative differences in the sperm's sensorimotor system. We are now redeploying this model as an image analysis tool.

GENETIC AND BIOCHEMICAL CONTROL OF CERL2 ACTIVITY DURING EARLY DEVELOPMENT

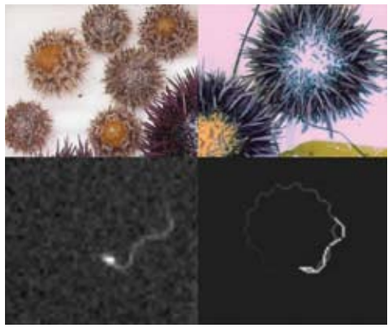
The general objective of this project is to study the regulation of Cerl2 gene expression, exploring several mutations. To gain quantitative insights into Cerl2 regulation of Nodal, our role is to develop mathematical models that take into account and try to reproduce the behaviour of the key players acting during the breaking of left/right symmetry in the node and its propagation to the lateral plate mesoderm, during early mouse embryogenesis.
We developed an integrated simulation framework that incorporates the basic knowledge on Nodal, Cerl2, and Lefty expression in the node and lateral plate mesoderm. This generic simulation explicitly describes:

1. Each epithelial cell;
2. The spatial arrangement and motion patterns of epithelia cells within the node and lateral plate mesoderm;
3. The paracrine activity of molecules in the medium bathing the cells;
4. The juxtacrine signals propagated by cell-to-cell contact;
5. The vesicle parcels and their transport in the node. Simulations of spatial patterning in the node and lateral plate mesoderm in wild type embryos and in mutants deficient in cerl2, lefty, and nodal flow, qualitatively reproduce the patterns of gene expression observed in wild type embryos, and, partially, the patterns observed in the mutants.

GROUP MEMBERS
Claudine Chaouiya (Visiting scientist)
Nuno Sepulveda (PhD student, left October 2009)
Tom Weber (PhD student)
Thiago Guzella (PhD student)

THIS GROUP COLLABORATES WITH:
Michal Or-guil (Institute for Theoretical Biology, Germany)
Alberto Darszon (Institute for Biotechnology, Mexico)
Jose Antonio Belo (University of Algarve, Portugal)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



Morphodynamic modelling and imaging of sea urchin spermatozoa swimming and chemotaxis, using imaging techniques and mathematical modeling.

POPULATION AND CONSERVATION GENETICS

Lounès Chikhi

PhD in Population Genetics
University Pierre et Marie Curie, France
E-mail: chikhi@igc.gulbenkian.pt and chikhi@cict.fr
url: http://www.igc.gulbenkian.pt/research/unit/88

The Population and Conservation Genetics Group (PCG) carries out research in the area of conservation and human population genetics. Genetic data can be used to reconstruct the recent demographic history of populations and species to identify key features of that history. For instance genetic data can be used to detect, quantify and date past population size changes such as collapses/bottlenecks and expansions. Admixture events whereby two or more populations "mix" to create new populations can also be analysed quantitatively. We are interested in understanding the statistical properties of genetic data in natural/wild or managed/domesticated populations (including breeds) to determine when and how genetic data can be used to make statements about the populations recent evolutionary history. Our work involves field and lab work together with data analysis, computer simulations, and the development of simulation tools.

DEMOGRAPHIC AND GENETIC RESPONSES TO HABITAT FRAGMENTATION AND HABITAT LOSS IN TWO LARGE FOREST MAMMALS

Within this project the aims are to sample and genotype populations of two endangered large mammals from Borneo (Pygmy elephant and orang-utan); to reconstruct the demographic history of these species and understand the effect of habitat fragmentation on their genetic diversity.
Very large number of elephant faecal samples were obtained by *B. Goossens* and *N. Othman* - 224 individuals were genotyped at 18 microsatellites - four papers published or accepted (two computer notes) - two free downloading software - but, large deficits in heterozygotes were observed in data - possibly due to the social structure or null alleles (technical issues). We encountered technical problems to validate genotypes at IGC (degraded DNA and samples).

LEMUR CONSERVATION, PHYLOGEOGRAPHY AND GENETICS IN FRAGMENTED HABITATS FROM MADAGASCAR AND THE COMOROS ARCHIPELAGO

The aims are to sample and genotype populations of endangered lemurs from the north and northwest of Madagascar, and estimate population sizes. Also, to reconstruct their demographic history and understand the effect of habitat fragmentation on their genetic diversity.
Non-invasive material has been collected and densities have been estimated for several Propithecus species. Papers have been published on both the genetic and density estimation work. Sampling of the Eulemur species has proven more difficult and sample sizes for wild animals are still limited.

GROUP MEMBERS
Reeta Shaarma (Post-doc)
Rita Rasteiro (PhD student)
Vitor Sousa (PhD student)
Erwan Quéméré (PhD student, left December 2009)
Bárbara Parreira (PhD student)
João Alves (Optimus Alive!Oeiras-IGC Fellow, left November 2009)
Jordi Salmona (Research Fellowship)
Tatiana Teixeira (Research Fellowship)

THIS GROUP COLLABORATES WITH:
Benot Goossens, Michael Bruford (Cardiff University, UK)
Benot Goossens (Danau Girang Field Center, Malaysia)
Nurzhafarina Othman (University Malaysia Sabah, Malaysia)
Marc Ancrenaz, Isabelle Lackman-Ancrenaz
(Kinabatangan Orang-utan Conservation Project, Malaysia)
Brigitte Cruouau-Roy (Université de Toulouse, France)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal
Fondation pour la Recherche sur la Biodiversité, France

GOLDEN CROWNED SIFAKA *(PROPITHECUS TATTERSALLI)*.
This is a species of lemur, living in the small Daraina region located in the very north of Madagascar. Our group has studied this species using genetic data extracted from fecal material collected in the field. We have also estimated the whole population size of this endangered species. (Copyright Erwan Quéméré)

ORANG-UTANS *(PONGO PYGMAEUS)*.
From the Sepilok Rehabilitation Center, Sabah, Malaysia, in the north of Borneo (Credit: Reeta Sharma).

BORNEAN ELEPHANTSW *(ELEPHAS MAXIMUS)*.
In the area around the Kinabatangan River, in Sabah, Malaysia. (Credit: Reeta Sharma)

NEUROBIOLOGY OF ACTION

Rui Costa

PhD in Biomedical Research
University of Porto, Portugal
E-mail: ruicosta@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/77

THIS GROUP WAS ESTABLISHED AT THE IGC IN APRIL 2009 AND IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

Animals have a distinctive ability to behave, i.e. to move and interact with their surroundings, which permits them to shift between environments and also to change their environment.

Did you ever stop to think why animals move? What type of nervous system organisation permits the generation of movement? How can actions be planned to achieve particular goals? To what extent they reflect the interaction with the environment or inherited programmes? Do similar movements always represent similar actions? How do sequences of actions emerge? And how do certain actions become compulsive?

The study of the neural mechanisms underlying our ability to act is a fascinating topic in neuroscience that has become truly multidisciplinary in recent years, integrating a considerable array of technologies and approaches. We use an integrative approach in mouse models to investigate the neurobiology of action in health and disease.

To study actions is to study the way we do things, which is different than studying how we remember stimuli, or facts and events. Some actions are innate or pre-wired (like swallowing, breathing, even grooming). Others are learned through trial and error throughout life. We currently focus on understanding the processes mediating the latter.

Our overall goal is to understand how changes in molecular networks in the brain modify neural circuits to produce experience-dependent changes in actions. In order to understand how actions are learned through trial and error, we subdivided our experiments into different components, or specific goals: how do we initiate and generate diverse actions? (trial); how do we form action sequences and improve the accuracy and speed of actions? (trial and error); and how do we learn that particular actions lead to particular outcomes? (goal of the action) and how do we form habits?

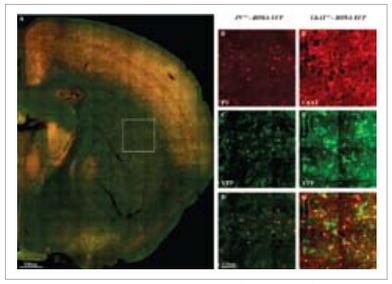
A growing body of evidence supports an important role of the basal ganglia in action initiation and selection, in learning sequences of actions and skills, and in learning goal-directed actions and habits. Therefore, we centered our efforts on investigating the cortico-basal ganglia mechanisms underlying these three processes using an across-level approach, from molecules to circuits.

We chose to implement this integrative approach in mice because they combine the power of genetics, a mammalian brain with canonical cortico-basal ganglia loops that can generate and propagate oscillatory activity, and the possibility of accurately quantifying simple behaviours like action initiation (with EMG recordings or using inertial sensors) and stereotypic skill learning, and more elaborate behaviours like goal-directed actions.

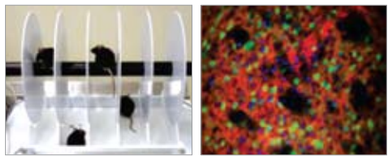
Our research programme will hopefully shed light on the mechanisms underlying the diversity of actions we perform, the automatisation of actions and the generalisation rules or ways to do it. Our research may also have important implications for understanding the relation between corticostriatal dysfunction and different neurodegenerative and psychiatric disorders.

GROUP MEMBERS
Rosalina Fonseca (Clinical Research Fellow)
Cristina Afonso (Post-doc)
Fatuel Aguilar (Post-doc)
Gabriela Martins (Pos-tdoc)
John Burkhardt (Post-doc)
Ana Mafalda Vicente (PhD Student)
Fernando Santos (PhD Student)
Pedro Ferreira (PhD Student)
Eduardo Ferreira (PhD Student)
Joana Almeida (Technician)
Sara Santos (Technician)
Vitor Paixão (Informatics Technician)

FUNDING
Marie Curie International Reintegration Grant, European Comission
ERC Starting Grant, European Research Council, Belgium



SPECIFICITY OF CRE EXPRESSION IN in *PV*^{Cre} AND *ChAT*^{Cre} MICE.
A - Montage of images from an adult brain section through the striatum demonstrating YFP colocalisation with PV in the *PV*^{Cre} mouse line crossed with a ROSA26-YFP reporter mouse. **B-G** - The inset in dorsolateral striatum depicts the location from where the smaller images were obtained. **B-D** - The first column demonstrates PV immuno-reactivity (in red; **B**), YFP expression (green; **C**), and colocalisation of both (yellow; **D**) in the *PV*^{Cre}*-ROSA-YFP* mouse striatum. **E-G** - The second panel shows ChAT immuno-reactivity (in red; **E**), YFP expression (green, **F**), and colocalisation of both (yellow; **G**) in a *ChAT*^{Cre}*-ROSA-YFP* mouse striatum. Scale bars = (A) 500µm; (D) 125µm for (B-G). (*by* Gabriela Martins)



THE ROLE OF DIFFERENT STRIATAL CIRCUITS IN ACTION LEARNING.
Left - Mice performing a behaviour task-walking on a rotating rod-which requires action learning that depends on striatal circuits in the brain. **Right** - Identification of striatal medium spiny neurons of the direct pathway expressing D1 dopamine receptor (in red) and striatal medium spiny neurons of the indirect pathway expressing D2 receptor (in green). Note the two populations do not overlap.

LYMPHOCYTE PHYSIOLOGY

Jocelyne Demengeot

PhD in Cellular and Molecular Biology
Université d'Aix-Marseille II, France
E-mail: jocelyne@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/37

The group is concerned with those properties of the immune system that guarantee tissue integrity as well as tolerance to commensals and food antigens, while maintaining the ability to mount efficient responses to infectious agents. We approach the cellular and molecular basis of immune regulation through the analysis of various mouse models of spontaneous or induced autoimmune and immuno-pathological inflammation. While most of our work has been concerned with understanding regulatory T cell origin, selection, maintenance and function, we have also investigated the regulation of B cell development and activation. Keeping in mind that the vertebrate immune system relies on the production of a very large diversity of antigen receptors through genomic rearrangement by the RAG recombinases, we also maintain a line of research assessing the consequences of deregulated RAG activity on genomic integrity and on lymphocyte homeostasis. Our group also has several collaborative interdisciplinary projects at the IGC. These include the analysis of human Systemic Lupus Erythematosus and the development of mathematical models of immune cell interactions. Further afield, we are involved in projects dealing with the evolutionary origin of immune regulation as well as the evolution and ecology of the commensal flora.

ORIGIN AND MAINTENANCE OF IMMUNE REGULATION

The aim of this project is to identify cell-cell interactions that are beneficial for Treg generation and maintenance.

While the essential role of thymic epithelial cells (TEC) in antigen specific Treg selection is no longer disputed, there is still doubt as to whether hematopoietic cells (HC) in the thymus would also shape the Treg repertoire, not only by negative selection but also by induction of Foxp3 expression. To tackle this issue we set up an experimental system where we could vary the nature of cells expressing and/or presenting the selecting antigen, through BM chimera and d10 embryonic thymus graft. We conclude that TEC are endowed with the specific ability to present and cross-present antigens to drive Treg differentiation (Manuscript in preparation).

We investigated the nature of the precursors that differentiate into Treg upon encounter of self and non-self antigen expressed in the periphery. We showed that peripherally administered antigens can gain access to the thymus and promote differentiation of thymocytes into Foxp3+ cells. Moreover we revealed that the maturation stage conditions the susceptibility of single positive Treg to differentiate into Treg, in the thymus and in the periphery (Manuscript submitted).

We are testing the effect of B cells on Treg, using both adoptive transfer experiments and mice deficient in various subsets of B cells. We have accumulated evidences to support the notion that B cells control the maintenance of Treg in the periphery, but not their production in the thymus. This work is in progress and will establish whether B cells affect Treg survival, expansion or peripheral induction due to their APC function, cytokine secretion or Ig secretion.

RAG1 AND RAG2 RECOMBINASES AND ABHERRENT GENOMIC ALTERATIONS

This project aims to experimentally evaluate the cost of deregulated and ectopic Rag expression.

We developed a novel assay, reporter of Rag mediated recombination. Cells transfected or infected with our novel reporter all fluoresce in Red, and, if they are recombined with a specific substrate, they would also fluoresce in Green. This assay was first used to test that embryonic fibroblasts from our recently established inducible Rag transgenic mice do rearrange if treated with the inducer. The assay was further explored to establish that it can be used to score specific RSS efficiency and also to screen tumors for those endowed with Rag activity (Manuscript in preparation).

GROUP MEMBERS
Marie-Louise Bergman (Post-Doc)
Andreia C. Lino (Post-Doc)
Leonor Sarmento (Post-Doc)
Joao H. Duarte (PhD student, left June 2009)
Maria Francisca Moraes-Fontes (PhD student, left May 2009)
Ricardo Paiva (PhD student)
Inês Trancoso (Msc student, left October 2009)

THIS GROUP COLLABORATES WITH:
Juan J Lafaille (Skirball Institute, NYU, USA)
Santiago Zelenay (Cancer Research, London, UK)
Luis Graca (Instituto de Medicina Molecular, Portugal)
Carlos Penha Gonçalves, Isabel Gordo, Karina Xavier (IGC)

FUNDING
Liga Portuguesa contra o Cancro/Foundation Terry Fox
Fundação para a Ciência e Tecnologia (FCT), Portugal

PLANT MOLECULAR BIOLOGY

Paula Duque

PhD in Biology
University of Lisbon, Portugal
E-mail: duquep@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/67

We use *Arabidopsis thaliana* as a model system to investigate how plants perceive and respond to environmental signals and endogenous developmental cues at the molecular level. In particular, we are focusing on the role of pre-mRNA splicing in the regulation of gene expression. The versatility of this mode of regulation suggests that it is likely to play an important contribution in ensuring the developmental plasticity and stress tolerance that are essential for plant survival. Another major ongoing project in the laboratory is examining the role of membrane transporters in plant resistance to herbicides and other chemical stresses.

SR PROTEINS AND THEIR FUNCTIONS IN PLANT STRESS RESPONSES

The general working hypothesis underlying this research project is that the functional complexity generated by alternative splicing is crucial in plant responses to environmental changes. Serine/arginine-rich (SR) proteins are essential splicing factors shown in animal systems to play a vital role in alternative splicing by affecting splice site selection in a concentration-dependent manner. This protein family remains poorly characterised in plants, which possess about twice as many SR proteins as animals owing to several duplication events. Our work has been addressing two key questions: i) whether plant SR proteins are involved in stress responses, and ii) whether duplicated plant SR genes are redundant or have evolved different functions.
We are employing reverse genetics to functionally analyse the 19-member Arabidopsis SR protein gene family, using a combination of knockout and RNAi techniques in association with overexpression studies. In support of our initial hypothesis, we have thus far shown that two plant-specific SR proteins play important roles in the response to environmental signals. The SR45 protein defines a negative regulator of sugar signaling during early seedling development, whose mode of action involves downregulation of the abscisic acid (ABA) pathway, via both reduction of the sensitivity to the phytohormone and a decrease in its glucose-induced endogenous accumulation. On the other hand, SCL30a controls drought and salt responses during seed germination by negatively regulating ABA signaling. Moreover, two SR paralogs, SCL33 and SCL30a, present different promoter activity patterns and knockout mutants for these genes display distinct phenotypes. We have thus shown that at least one duplicated gene pair in the Arabidopsis SR protein gene family is functionally non redundant, shedding light on a key open question in the field.

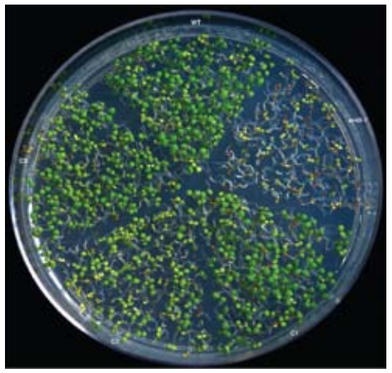
ROLE OF PLANT MDR TRANSPORTERS IN THE RESISTANCE TO HERBICIDES AND OTHER CHEMICAL STRESSES

The extensive use of herbicides to provide crop protection has led to the emergence of multiple resistant weeds, challenging agricultural practices. It is therefore crucial to understand the molecular basis of herbicide resistance and more globally of Multiple Drug Resistance (MDR), the simultaneous acquisition of resistance to a wide range of unrelated cytotoxic compounds. A living cell can achieve MDR by actively extruding toxic compounds via membrane pumps that catalyse the efflux of a broad range of chemically distinct substrates. A group at Instituto Superior Técnico (IST) has previously shown that two yeast MDR transporters, PDR5 and TPO1, determine the resistance to one of the most widely used herbicides worldwide, 2,4-D. Using a candidate gene strategy, we have selected Arabidopsis genes exhibiting homology to PDR5 and TPO1 and increased expression upon exposure to 2,4-D for heterologous expression in yeast and functional analysis in plants. In collaboration with the IST team, we have found that one of these genes, belonging to the Major Facilitator Superfamily (MFS), confers increased resistance to 2,4-D and other xenobiotic compounds - such as IAA (indole-3-acetic acid), Tl3+ and Al3+ - in yeast. Loss- and gain-of-function approaches in Arabidopsis are now showing that this MFS gene also confers resistance to 2,4-D and IAA in plants, confirming the effectiveness of the strategy employed and supporting our working hypothesis that plant MFS transporters play a role in 2,4-D resistance and MDR in general.

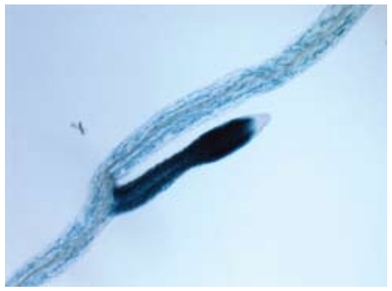
GROUP MEMBERS
Estelle Remy (Post-doc)
Sofia Carvalho (PhD Student)
Raquel Carvalho (PhD Student)
Inês Barbosa (Trainee)

THIS GROUP COLLABORATES WITH:
Isabel Sá-Correia (Instituto Superior Técnico, Portugal)
Elena Baena-González (IGC)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal

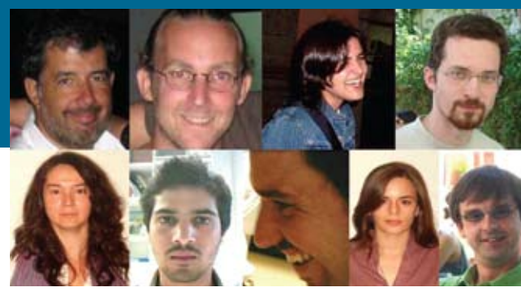


Glucose hypersensitivity is rescued in three independent complementation lines (C1, C2, and C3) expressing the *SR45* gene in the knockout (*sr45-1*) background.



GUS staining of transgenic plants shows that the *MFS5* promoter is highly active in lateral roots.

PLANT DEVELOPMENT



José A. Feijó

PhD in Cell Biology
University of Lisbon, Portugal
E-mail: jfeijo@fc.ul.pt
url: http://www.igc.gulbenkian.pt/research/unit/38

Research at the Plant Development group is concerned with developing integrated models of cellular growth and morphogenesis using the pollen tube as a biological model, ion dynamics as an experimental paradigm and theoretical modeling as an integrative tool.

ELECTROPHYSIOLOGICAL CHARACTERISATION OF MEMBRANE TRANSPORTERS FROM THE *ARABIDOPSIS THALIANA* POLLEN TUBE

This project aims at the systematic characterisation of ion transporters and channels of pollen protoplasts by patch-clamp and molecular genetics.
We have carried out patch-clamp characterisation of the first chloride-channels in pollen protoplasts and genetic characterisation and transport phenotype of three different classes of chlorides channels expressed in Arabidopsis pollen.

A SYSTEMS APPROACH TO APICAL CELL GROWTH

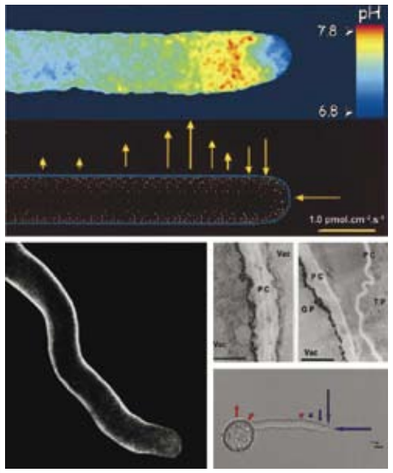
The aim is to develop integrative theoretical models that suficiently describe apical growth in terms of ion signaling and spatial synchronization.
The following results were achieved:

- definition of electrical equivalent models based on the individual fluxes described;
- Modelling of internal ion concentration based on membrane activity;
- Description of glutamate receptors as possible calcium channels in pollen.

GROUP MEMBERS
Erwan Michard (Post-doc)
Filipa Alves (Post-doc)
Kai Konrad (Post-doc)
Pedro Lima (PhD student)
Ana Barbara Santos (PhD Student)
Ana Catarina Silva (Technician, left December 2009)

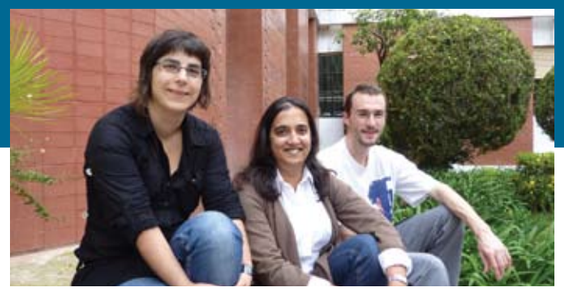
THIS GROUP COLLABORATES WITH:
Ana Bicho, Ana Lourenço (University of Lisbon - REQUIMTE, Portugal)
Alice Cheung (University of Massachusetts, USA)
Matthew Gilliham (University of Adelaide, Australia)
Christophe Maurel (INRA-Montpellier, France)
Rob Martienssen (Cold Spring Harbor Laboratory, USA)
Keith Slotkin (University of Ohio, USA)
Liam Dolan (Oxford University, UK)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



The pollen tube is a biological model to study cellular growth and morphogenesis combining the study of ion dynamics and mathematical modeling.

YEAST STRESS



Lisete Fernandes

PhD in Biochemistry
University of Lisbon, Portugal
E-mail: lisete@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/39

Adaptation and survival to intracellular and extracellular environmental challenges (stresses) are fundamental processes in all organisms. Pathogens and all micro-organisms in general are widely exposed to oxidative environments imposed by phagocytosis and chemical/physical stress agents, respectively. In fact, exposure to many fungicides and anti-cancer drugs generates oxidative stress; similarly, exposure to temperatures below the optimal value has effects on the intracellular oxidative environment. Primarily, adaptation/survival to environmental stresses depends on the accuracy and specificity of intracellular signal/stimuli propagation and efficient counter-acting/compensatory response(s). Despite the remodeling of gene expression at different steps, transcription by RNA polymerase II (pol II) is a crucial process under stress stimuli. In this respect, understanding how the 'oxidative stimuli' propagate in the cytoplasm to reach transcription factors and modulate nuclear events, is far from being a clear subject. In this context, in *Saccharomyces cerevisiae* we study: pol II machinery components as targets/signalling molecules of oxidative stimuli; cytoskeleton and related factors as vehicles for oxidative signaling. We are also interested in understanding adaptation from the population point of view.

MOLECULAR MECHANISMS BRIDGING PROTEIN FOLDING AND TRANSCRIPTION ACTIVATION

GimC, also designated prefoldin, is a cytoplasmatic complex composed of 6 distinct subunits (Gim1-Gim6 and Pfd1-Pfd6 in *Saccharomyces cerevisiae* and mammals, respectively) that promotes the formation of functional actin and tubulin, essential components of the cytoskeleton. GimC binds to nascent chains of these substrates, delivering them, after completion, to the chaperonine TRiC/CCT for efficient folding. However, the Gim proteins are not essential and data in the literature suggest alternative functions for several of the GimC subunits, e.g., archeabacteria contains a complex homologue of prefoldin and inherent substrates do not include actin/tubulin. Our results obtained with gim-mutants pinpoint different activities of each Gim subunit within the cell, in particular, under stresses. Because activation of transcription is the common regulated event in the cellular response(s) to the stress(es) that requires identified stress-gene(s), we want to assess the contribution of Gim(s) at different levels of transcription regulation.
We studied the effect of Gims on transcriptional activity of three selective DNA-binding signal regulators (responding to oxidative, osmotic and nutritional stimuli) and a general transcription factor. We found that Gim2 has a negative effect on the Yap1 inherent activation potential but a positive effect on Msn2. These findings were submitted for publication. Biological material, yeast strains and plasmids, were constructed to be used in two-hybrid screens in order to identify molecules that directly bridge Gim2 with transcriptional events.

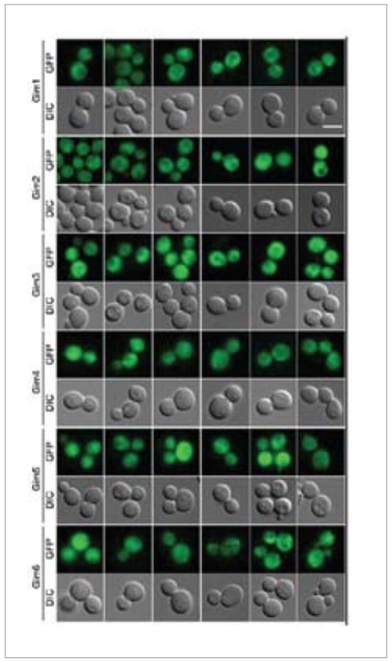
TRANSACTIVATOR YAP1 – CROSSROAD OF COLD AND OXIDATIVE STRESS SIGNALING PATHWAYS IN *SACCHAROMYCES CEREVISIAE*

The cytoskeleton network is a well-known target of oxidative stimuli, of cold as well as structurally essential for proper intracellular mobility of transcription factors such as the tumor suppressor gene p53 and Nrf2. The main activator of the yeast *Saccharomyces cerevisae* antioxidant response, Yap1, is also required for cold response and is regulated by cyto-nuclear translocation upon oxidative stimuli. So, by using yeast genetic systems, we aim to understand the importance of cytoskeleton for cold and oxidative stress towards nuclear events.
By analysing Yap1 and Msn2/4 activity under oxidative stress environments, our previous results uncoupled actin from microtubules contribution. The specificity of this data was acertained by the study of Msn2/4, a transactivator that also induced by osmotic stress.

GROUP MEMBERS
João Coelho (PhD student)
Ana Mafalda Cavaleiro (MSc student)
Dora Pinto (trainee)

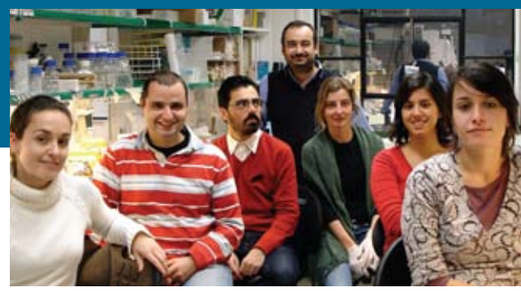
THIS GROUP COLLABORATES WITH:
Isabel Gordo (IGC)
Martine Collart (University of Geneve, Switzerland)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



Intracellular distribution of Gim-Gfp in the yeast *Saccharomnyces cerevisae*.

TELOMERE AND GENOME STABILITY



Miguel Godinho Ferreira

PhD in Cell Biology
University College London, UK
E-mail: mgferreira@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/69

Telomeres protect the ends of linear eukaryotic chromosomes from being recognised as deleterious DNA double strand breaks. Telomeres prohibit DNA repair, as it may lead to chromosome-end fusions - a source of genomic instability and a step in tumourigenesis. This fundamental function fades as telomeres get progressively shorter in cells of older people, thus limiting the capacity of tissue renewal and increasing the probability of cancer.
Our aim is to understand how telomeres block DNA damage responses and, when this function fails, how cells respond to unprotected chromosomes. Using fission yeast as a model system, we plan to identify key players and the mechanisms underlying these events.

UNCOVERING THE MECHANISMS PREVENTING CHECKPOINT DETECTION AT TELOMERES

Even though DNA repair and checkpoints are normally prevented at telomeres, upon replication fork passage, both ATM and ATR are activated without any interference in cell cycle progression. We discovered that this situation is mimicked throughout the cell cycle in cells devoid of Taz1, the dsDNA telomere binding protein in fission yeast. We showed that checkpoint activation at telomeres does not lead to cell cycle arrest, even though ATR and ATM are activated and DNA repair is ongoing. Dissecting the checkpoint signal transduction pathway, we showed that the chromatin binding protein Crb2/53BP1 is unable to be maintained at chromosome-ends, thus severing checkpoint signaling pathway. We further showed that this telomere function is under the control of the ssDNA telomere binding protein Pot1 and its partner Ccq1, a protein involved in chromatin remodeling. In absence of either Pot1 or Ccq1, checkpoints are promptly triggered at telomeres. We propose a model whereby telomeres normally initiate checkpoints every S phase, but signaling is interrupted due to local chromatin status.

IDENTIFICATION OF NOVEL COMPONENTS IN TELOMERE PROTECTION

For this purpose, we developed a novel direct assay for telomere protection in fission yeast using a linear plasmid. We validated this assay using known telomere protection mutants and used it to identify the mechanisms responsible for chromosome-end fusions. In parallel, we started screening the fission yeast whole genome deletion library looking for telomere protection factors on the available ca. 3,000 viable mutants. All telomere protection mutants described to date are non-essential, thus this strategy should produce several remaining players. Presently, we have screened half of the deletion library and plan to finish in spring 2010. To date, we have identified four new genes involved in telomere length regulation.

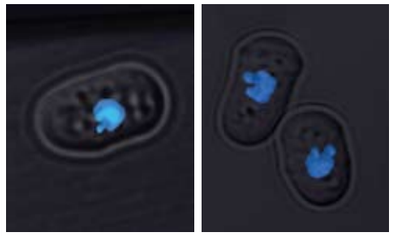
UNDERSTANDING THE EFFECTS OF CHROMOSOME REARRANGEMENTS

As consequence of telomere deprotection, chromosomes undergo breakage-fusion-bridge cycles resulting in gross chromosome rearrangements (GCRs). Even though most of these events are deleterious, several cells survive when telomere function is restored. We propose that GCRs, when not lethal, may be adaptative and potentially involved in speciation evolutionary processes. To test this, we generated ten GCR-containing fission yeast strains (2 inversions and 8 translocations) using a pre-established Cre-loxP system. These GCRs constitute the sole difference from the parental wt strain. We show that GCRs are neutral in normal growth conditions. As expected, we observed reduced viability of offspring in hybrid crosses that varied from 10-40%. In collaboration with Isabel Gordo (Evolutionary Biology Laboratory), we have devised ongoing experimental evolution experiments to test whether GCRs are capable of leading to further genetic isolation (and speciation) upon adaptation to non-optimal environments.

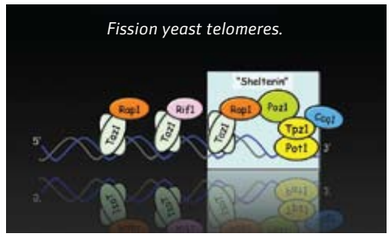
GROUP MEMBERS
Tiago Carneiro (Post-doc)
Clara Reis (Post-doc)
Ana Teresa Avelar (PhD Student)
Hugo Almeida (PhD Student)
Inês Tenente (MSc Student)
María Gallo (MSc Student)

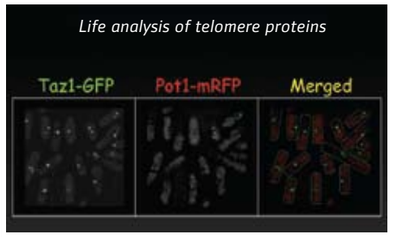
THIS GROUP COLLABORATES WITH:
Toru M. Nakamura (University of Illinois at Chicago, USA)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal
Toru M. Nakamura (University of Illinois at Chicago, USA)



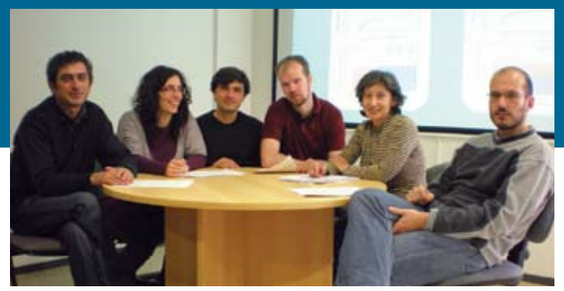
Left - Fission Yeast - *Schizosaccharomyces pombe*. **Right** - FISSION YEAST TELOMERES.





Life analysis of telomere proteins.

COLLECTIVE DYNAMICS



Gabriela Gomes

PhD in Mathematics
University of Warwick, UK
E-mail: ggomes@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/50

We study collective phenomena, such as self-organisation, criticality, and pattern formation, arising from spatial and temporal constraints in physical and biological systems, with a current focus on infectious disease ecology and evolution. The central theme of our research derives from a conceptual model of partial immunity whose collective outcome - the reinfection threshold - underlies a phenomenological transition in epidemic dynamics, with practical implications ranging from extreme geographical variability in the effect of vaccination programmes to destabilised transmission favouring polymorphism in antigenically diverse pathogens. We are interested in refining concepts and methodologies by performing specific experiments in the laboratory and in natural populations.

REINFECTION THRESHOLDS AND THE MANAGEMENT OF RECURRENT INFECTIONS

The aims of this project are:

1. To increase the accuracy and practical value of the reinfection threshold by focusing on specific infections;
2. To perform comparative studies across different infections, extract general trends, and standardise concepts for use in public health practice.

We have established a pivotal role for the reinfection threshold in a range of infectious diseases. In tuberculosis, communities that sustain transmission intensities above threshold are generally insensitive to vaccination. In pertussis, the recent ressurgence of the disease in developed countries is attributed to a decrease in transmission. In malaria, a threshold for elimination in regions of low to moderate transmission intensity has been identified. In diseases caused by antigenically diverse pathogens, such as influenza and dengue, a reinfection threshold has a destabilising effect that favours polymorphism.

MOLECULAR EPIDEMIOLOGY OF MYCOBACTERIUM TUBERCULOSIS IN PORTUGAL: IMPLEMENTING AND ANALYSING A DATABASE

Within this project we aim to:

1. To establish a system for genotyping Mycobacterium tuberculosis in Portugal;
2. To implement a database for tuberculosis that integrates clinical and molecular data;
3. Analyse the data.

The IGC Genomics Unit selected the SNPs and initiated the genotyping. The IGC Bioinformatics Unit initiated the database implementation.

EPIWORK - DEVELOPING THE FRAMEWORK FOR AN EPIDEMIC FORECAST INFRASTRUCTURE

This project aims to develop the framework for an epidemic forecast infrastructure. We have enhanced the Gripenet system to monitor the 2009 influenza pandemic in Portugal and Brazil. Mathematical models have been constructed for data interpretation.

COMPLEX SYSTEMS IN THE INFECTION DYNAMICS OF TUBERCULOSIS AND DENGUE

The aims of this project are:

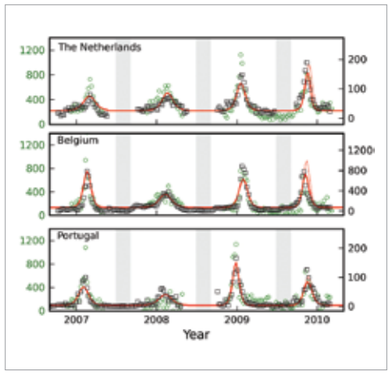
1. To develop mathematical models for the molecular epidemiology of tuberculosis in Portugal and Brazil;
2. To develop an internet-based system (inspired on Gripenet) to monitor dengue epidemics in Brazil (Denguenaweb).

We have initiated the development of mathematical models for the molecular epidemiology of tuberculosis. We have initiated the implementation of Denguenaweb.

GROUP MEMBERS
Flávio Coelho (Post-Doc)
Sander van Noort (PhD Student)
Ricardo Águas (PhD Student)
Paula Rodrigues (PhD Student, left October 2009)
Delphine Pessoa (MSc Student)
Vitor Faustino (Technician)

THIS GROUP COLLABORATES WITH:
José Pereira-Leal, Carlos Penha-Gonçalves, Ana Godinho (IGC)
Anabela Miranda, Cristina Furtado (Instituto Nacional de Saúde Dr Ricardo Jorge, Portugal)
Alessandro Vespignani (Institute for Scientific Interchange, Italy)
Lewi Stone (Tel Aviv University, Israel)
Dirk Brockmann (Max Planck Institute Gottingen, Germany)
Ronald Smallenburg (Grote Griepmeting.nl, The Netherlands)
John Edmunds (London School of Hygiene and Tropical Medicine, UK)
Olof Nyrén (Swedish Institute for Infectious Disease Control, Sweden)
Marc Van Ranst Rega (Institute for Medical Research, Belgium)
Shlomo Havlin (Bar Ilan University, Israel)
Stefano Merler (Fondazione Bruno Kessler, Italy)
Daniele Miorandi (Center for Research and Telecommunication Experimentation for NETworked communities, Italy)
Mário Silva (Faculdade de Ciências, University de Lisboa, Portugal)
Maurício Barreto (Instituto de Saúde Coletiva, Universidade Federal da Bahia, Brazil)

FUNDING
Epiwork, European Commission
Marie Curie Actions, European Commission
Fundação para a Ciência e a Tecnologia (FCT), Portugal
Convénio Fundação para a Ciência e a Tecnologia (FCT), Portugal, and Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)



Influenza epidemics in the Netherlands, Belgium and Portugal as monitored by Influenzanet (green circles), European Influenza Surveillance Network (black squares), and reconstructed by a mathematical model (red line). The area between dotted and full lines indicates the impact of the vaccination campaign against the influenza A (H1N1) 2009 pandemic virus.

EVOLUTIONARY BIOLOGY

Isabel Gordo

PhD in Biology
University of Edinburgh, UK
E-mail: igordo@igc.gulbenkian.pt
url: http://www.igc.pt/research/unit/61
http://eao.igc.gulbenkian.pt/EB/index.html

All natural populations are constantly subject to new mutations, and frequently face new environments, to which they adapt. Despite its extreme importance, the process of adaptation is far from being understood. For example: What is the rate and distribution of fitness effects of beneficial mutations? How does the shape of distribution of fitness effects of mutations depend on the environment? What is the importance of epistasis in evolution? These are still open questions. The major goal of the lab is to contribute to the understanding of the evolutionary forces responsible for the generation and maintenance of genetic diversity in populations. Because after life appeared on Earth it became populated with prokaryotes, and during that long time the most basic elements of life, as well as its most fundamental innovations appeared, in our lab we dedicate our studies to understanding genetic variation in microorganisms. We use essentially three approaches to achieve that major goal: experimental evolution, mathematical modeling and analysis of variation of natural microbial populations.

RATE AND EFFECTS OF MUTATIONS IN TETRAHYMENA

The aims of this project are to perform a MA experiment in the sexual species *Tetrahymena thermophila* and an adaptation experiment in the asexual species *Tetrahymena pyriformis*, with the aim of estimating rates and effects of mutations in two Tetrahymena species, therefore providing, for the first time, a direct estimate of these parameters in ciliates.
We have found a high rate of extinction of *Tetrahymena thermophila*, as opposed to *T. pyriformis*. We also found a slow rate of adaptation of *T. pyriformis* to a novel harsh environment when population sizes are large

DIVERSITY AND MOLECULAR EVOLUTION OF PATHOGEN POPULATIONS

This project entails the development of new modeling frameworks, which consider both epidemiology and population genetics of pathogen populations, and that can be directly applied to interpreting sequence variation in natural populations
We have developed and analysed a model for assessing the levels and patterns of genetic diversity in pathogen populations, whose epidemiology follows a susceptible-infected-recovered model (SIR). In our discrete time model the population of pathogens is a metapopulation composed of subpopulations (infected hosts), where pathogens replicate and mutate, and where hosts transmit pathogens to uninfected hosts. By analysing the patterns of genetic diversity in this framework, we identified the molecular signatures during the replacement of new strains and compared these with those observed in sequences of influenza A.

STUDY OF THE FITNESS EFFECTS OF ANTIBIOTIC RESISTANCE MUTATIONS OF PATHOGENS

The main aim of this research is to measure the cost of resistance mutations in conserved genes of bacterial species.
Unlike previous studies that found both positive and negative epistasis between transposon insertions in *E. coli*, with an average level of no epistasis (Elena and Lenski 1997), we have found a clear signature of positive epistasis between alleles that confer antibiotic resistance.

GROUP MEMBERS
Ana Margarida Sousa (Post-Doc)
Patricia Brito (Post-Doc)
Migla Miskinyte (PhD student)
Sandra Trindade (PhD student)
Tiana Gonçalves (PhD student)
João Batista (MSc student)
Joana Antunes (Technician)

THIS GROUP COLLABORATES WITH:
Helena Soares, Francisco Dionisio (Universidade de Lisboa, Portugal)
Paulo Campos (Universidade Federal Rural de Pernambuco, Brazil)
Karina Xavier, Miguel Godinho Ferreira (IGC)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal

ACTIN DYNAMICS

Florence Janody

PhD in Developmental Biology
Université de la Mediterranée, France
E-mail: fjanody@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/72

Actin is one of the most abundant and highly conserved proteins in Eukaryotes. Actin monomers can polymerise into filaments, forming the actin cytoskeleton, which controls numerous processes, including the generation and maintenance of cell morphology and polarity, endocytosis, intracellular trafficking, contractility and cell division.
The type of filamentous actin-based structures that will be formed can be dictated by the properties of actin protein itself, since multicellular organisms contain several actin proteins that show differences in term of their biophysical and biochemical properties. Moreover, specific actin-binding proteins (ABPs) that control the rate, extent and spatial pattern of actin polymerisation/depolymerisation or organise filaments into specific higher-order structures can pattern distinct actin-based structures. Conversely, arrangement of the actin web can dictate whether they can be use as a scaffold, as physical support or a track. This implies that particular actin-based structures exist in cells that have specialised functions.
Using Drosophila as a model system, which allows for relatively ease in manipulating gene expression, we aim to understand how cytoskeletal organisation is regulated in distinct epithelia and to characterise the role of specialised filamentous actin-based structures. Our project addresses a fundamental aspect of cell biology but also aims to broader our understanding of pathogenesis associated with actin dynamics. Indeed, cell division, cell shape and polarity, cell-cell and cell-matrix adhesions and cell migration are all aspects of cell behaviour controlled by the actin cytoskeleton and which often go awry during cancer progression.

USING DROSOPHILA TO UNDERSTAND THE MOLECULAR CONTROL OF ACTIN DYNAMICS IN ABERRANT ACTIVE CELL MIGRATION

The goal of this project is to get some insight on how the dynamics of the actin cycle is regulated to prevent tumour formation.
Our work demonstrates that the actin cytoskeleton acts as a Tumor Suppressor organelle. We found that the Ezrin/Radixin/Moesin (ERM) family members, Expanded, which lie upstream of the Hippo tumor suppressor kinase cassette, in addition to some actin cytoskeletal genes, including Capping Protein and Capulet, regulate an apical actin filament network, which restrict nuclear translocation of the Yorkie co-transcription factor, thus preventing excessive proliferation of epithelial tissues. Moreover, our results argue in favour of actin cytoskeletal integrity restricting signalling by the Src proto-oncogene and in this way controlling the balance between cell proliferation and cell death in restricted epithelia. This reveals the crucial function of filament actin-based structures to coordinate the behavior of multicellular organisms, in this way preventing conflicts among cells within cellular communities, and cancer progression.

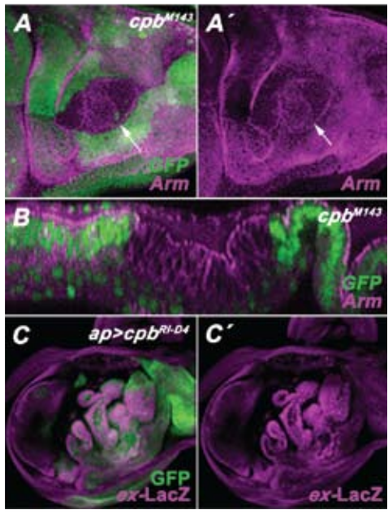
MOLECULAR CONTROL OF ACTIN DYNAMICS AND CHANGE IN CELL SHAPE IN THE MORPHOGENETIC FURROW DURING DROSOPHILA EYE DEVELOPMENT

The goal of this research project is to understand how the dynamics of the actin cycle is regulated to promote the change in cell shape in the morphogenetic furrow. Differentiation of the Drosophila eye imaginal disc starts with the formation of an indentation called the morphogenetic furrow (MF), which progresses from anterior to posterior across the disc epithelium, driving neuronal differentiation. The Hedgehog (Hh) signalling pathway regulates the change in cell shape in the MF. Conversely, we found that actin cytoskeletal genes involved in MF formation control intracellular signal transduction pathways involved in eye morphogenesis. Our results highlight the interesting feedback loop mechanism between signal transduction pathways and the actin microfilament system required to coordinate tissue morphogenesis.

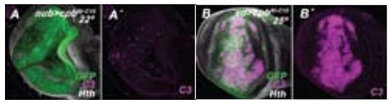
GROUP MEMBERS
Beatriz García Fernández (Post-doc)
Catarina Bras Pereira (Post-doc)
Barbara Jezowska (PhD Student)
Pedro Miguel Gaspar (PhD Student)
Claudia Mendes (External MSc Student)
João Félix (External MSc Student)
Ana Rita Amândio (Technician)

THIS GROUP COLLABORATES WITH:
Fernando Casares (Universidad pablo de Olavide, Spain)
Nicolas Tapon (Cancer Research, UK)
Helena Richardson (Peter MacCallum Cancer Institute, Australia)
Georg Halder (The University of Texas, USA)
Mark Peifer (University of North Carolina, United States)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



ACTIN CAPPING PROTEIN REGULATES F-ACTIN TO RESTRICT HIPPO DEPENDENT CELL PROLIFERATION.
A-B - cpbm143 mutant clones marked by the absence of GFP (green in A and B) and stained with anti-Arm (magenta) to outline apical cell membrane. **A-A'** - Standard confocal sections. **B** - Optical cross sections through the wing disk epithelium. Arrows in A and A' indicates the folds around and within the clone. **C** - ap-Gal4 driving UAS-cpbr1-d4 and UAS-GFP (green in C) and stained with anti-β -galactosidase to reveal ex-LacZ.



WEAK DECREASE OF CPB LEVEL INDUCES TISSUE OVERGROWTH, WHILE STRONG DECREASE LEADS TO CELL DEATH.
Standard confocal sections of third instar wing imaginal discs stained with anti-activated Caspase 3. **A-A'** - nub-Gal4 driving UAS-GFP (green in A) and UAS-cpbr1 at 22 degree. **B-B'** - sd-Gal4 driv ing UAS-GFP (green in B) and UAS-cpbr1 at 25 degree.

EPIGENETIC MECHANISMS

Lars E.T. Jansen

PhD in Molecular Genetics
Leiden University, The Netherlands
E-mail: ljansen@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/89

During human development a single zygote differentiates into approximately 200 different cell types that, despite being genetically identical, maintain their cellular identity through mitotic divisions. Therefore, in addition to the genomic information embedded in the primary DNA sequence, epigenetic information is propagated as well, that "memorises" gene activity states and specific chromatin structures across somatic division and sometimes even across generations. Epigenetic inheritance forms the basis for many aspects of biology that includes development, gene regulation and disease. Several molecular components such as histone proteins and modifications thereof have been implicated in this process but in most cases we don't understand the logic of how something other than DNA can be faithfully duplicated when a cell divides. We have a broad interest in how this works. We are using molecular genetic and cell biological tools with a focus on novel fluorescent labelling techniques, high-end microscopy and the latest tricks in genetic engineering of human cells to tackle a wide range of problems in this emerging and fascinating area of biology.

DETERMINING THE EPIGENETIC MECHANISM OF CENTROMERE PROPAGATION

The aims of this project include the determination of the cell cycle control mechanism of centromere assembly, and development of fluorescent pulse labelling to determine the turnover and dynamics of the centromere complex.
Earlier work suggested that mitosis may be an obligate prerequisite for assembly of nascent CENP-A in early G1 phase. In the initial stages of this project we have shown that mitotic passage is in fact, dispensable for CENP-A loading. Treatment of cells in G2 phase with cyclin dependent kinase (CDK) inhibitors induces rapid assembly of newly synthesised CENP-A at centromeres. Based on this and several other observations we are building a model that provides an important insight into the molecular coupling of cell cycle progression and centromeric chromatin propagation which forms the basis for the epigenetic nature of the centromere.

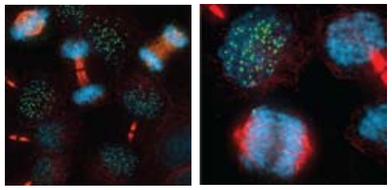
MOLECULAR MECHANIM OF EPIGENETIC INHERITANCE

This project aims at the identification of factors that control deposition of the histone H3 variant CENP-A into centromeric chromatin, and also the determination of the role of centromeric DNA and transcripts in centromere identity. Using SNAP-based pulse-chase imaging we have identified an epigenetic feedback loop that couples centromeric chromatin formation with the assembly of the functional centromere complex that drives chromosome segregation during mitosis. In addition we have successfully developed genome engineering tools for structure function analysis of CENP-A in the context of human cells.

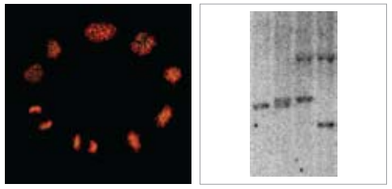
GROUP MEMBERS
Luis Valente (Post-doc)
Mariana Silva (PhD student)
Mariluz Gómez (PhD student)
Dani Bodor (MSc Student)
João Mata (Research Technician)
Nuno Martins (Trainee)

THIS GROUP COLLABORATES WITH:
Aaron F. Straight (Stanford University, USA)
Helfrid Hochegger
(Sussex Centre for Genome Damage and Stability, UK)
Don W. Cleveland (Ludwig Institute for Cancer Research, USA)

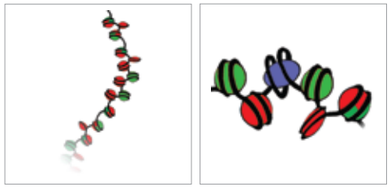
FUNDING
Marie Curie International Reintegration Grant, European Commission
European Molecular Biology Organization (EMBO) Installation Grant
Fundação para a Ciência e a Tecnologia (FCT), Portugal



Assembly of pulse-labelled fluorescent histones at human centromeres during mitosis.



Left - Genomic engineering of human cells with fluorescent centromere proteins. **Right** - Genetic analysis of genome engineered human cells.



MODEL OF CHROMATIN DISPLAYING VARIANT HISTONES.

TISSUE MORPHOGENESIS

Mathias Koeppen

PhD in Cellular and Molecular Biology
University of Wisconsin, USA
E-mail: koeppen@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/91

Our focus is the analysis of fundamental mechanisms of tissue morphogenesis in the zebrafish embryo, using high-resolution live microscopy in combination with genetic and embryological techniques. Specifically, we are interested in the morphogenetic behaviour of the embryonic surface epithelium, the enveloping layer. During the first few hours of zebrafish development, this tissue enwraps and seals the embryo in a process called epiboly. This process is of general interest, since it occurs in many developmental contexts and during the healing of wounded tissue. Interestingly, we recently found that the enveloping layer plays a central role during the formation of the first zebrafish organ, Kupffer's vesicle. The laboratory pursues two main lines of investigation:

1. Analysis of the cellular and molecular mechanisms that control the spreading and sealing of the enveloping layer;
2. Study of the origin and morphogenesis of Kupffer's vesicle.

CYTOSKELETAL DYNAMICS DURING ZEBRAFISH EPIBOLY

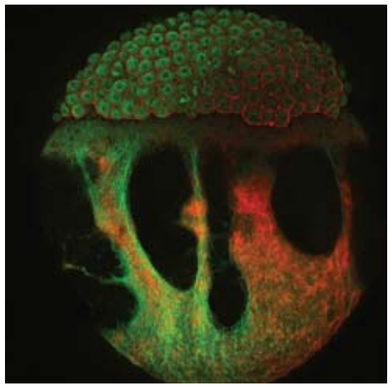
We are investigating the molecular control of enveloping layer epiboly, with a specific focus on the cytoskeleton. Past work suggested a mechanism by which a contractile actin "cable" drives the epiboly movement. Here we are addressing the mechanism that assembles this contractile structure, focusing specifically on the interaction between the actin and microtubule networks.
Live confocal imaging and functional analysis revealed that actin undergoes long-range streaming within the embryo towards the contraction zone, possibly facilitated by the microtubule network. Drug-based inhibition of the microtubule network impairs actin recruitment and slows the progression of epiboly. This highlights the importance of global cytoskeletal dynamics during embryo morphogenesis.

MODELLING APPROACHES TO TISSUE CLOSURE IN ZEBRAFISH

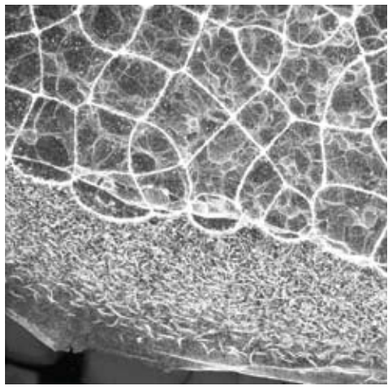
Tissue sealing occurs both during normal development and wound healing. Here, we are addressing the general principles of tissue sealing of the zebrafish enveloping layer. In collaboration with Luis Almeida, a mathematician at the University of Nice, we are working towards a theoretical model of enveloping layer closure. This work will make predictions about the nature of the contractile closure mechanism.
We have employed multi-photon live imaging of zebrafish embryos expressing the actin marker lifeact-GFP to obtain insight into actin dynamics and cell shape changes. The work revealed an intriguing pattern of cell shape changes at the tissue margin during closure, arguing against a simple purse-string model. Additional experiments, involving laser-based measurements of tension, will be required and will be followed by the development of a mathematical model.

GROUP MEMBERS
Ana Cristina Borges (Post-doc)
Inês Cristo (Research Technician/PhD Student)
Paulo Raimundo (Short Term Apprentice)
Pedro Almada (Visiting Undergraduate Student)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



Zebrafish embryo at 30% epiboly, stained for actina (red) and tubulin (green).



Zebrafish embryo ate 50% epiboly stained for actin.

ORGANOGENESIS

Joaquín Rodríguez León

PhD in Biological Sciences
University of Extremadura, Spain
E-mail: jleon@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/35

In our group we are focused on unveiling the mechanisms behind limb development and fin regeneration. Towards that end we use the chicken, zebrafish and mouse as models. We have divided our research into two main lines. The first involves the study of ion dynamics as a mechanism controlling different signaling pathways during development and regeneration. Also, we are examining the role of different stemness genes during limb bud formation and outgrowth, and fin regeneration.

ROLE OF ION CURRENTS DURING LIMB DEVELOPMENT AND FIN REGENERATION

The aims of this research programme are:

1. To map the spatial and temporal distribution of specific extracellular ion fluxes in the lateral plate mesoderm of chick embryos during limb bud initiation and in zebrafish embryos during fin regeneration;
2. To image the distribution of relevant ions *in vivo*, using genetic ratiometric sensors and ion indicators.

We have described potassium (K+) fluxes for zebrafish caudal fin regeneration. A strong outward K+ current was always detected in the first 30 minutes post amputation (mpa); after this, K+ returned to the no net flux situation also characteristic of the intact fins. This pattern points to a role for K+ currents in the first steps of regeneration, namely wound healing.
We have also detected an outward H+ current that is maintained during a time window of crucial regeneration events (blastema formation, regenerative outgrowth) and disappears when regeneration is complete. To confirm the data from the Affymetrix chips, we performed immunohistochemistry assays against V1E1 protein in 48hpa fin sections. V-ATPase V1E1 seems to be present in the epithelial layer of the regenerating tissue.

OCT4 ACTIVITY IN THE FORMATION AND MAINTENANCE OF THE AER DURING VERTEBRATE LIMB BUD DEVELOPMENT

In this project we aim to:

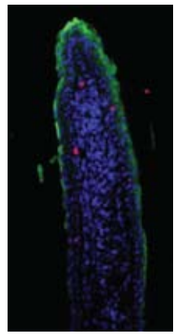
1. Elucidate the role of different stemness genes (namely oct4) during limb development;
2. Characterise the behaviour of AER cells from their cell biology point of view (study of proliferation versus apoptosis, ratios of cell division, etc).

During limb development, the limb bud grows and the ectoderm condenses to form the Apical Ectodermal Ridge at its tip. We have found oct4 expression in the ectoderm and in the forming AER in a "two stripe" pattern running along the anterior-posterior axis of the limb, dorsally and ventrally to the AER, suggesting a role for oct4 in the maintenance of AER during limb development. We then analysed the imunostaining data for Phospho-Histone H3, which marks proliferating cells. Those cells were located on the base, both ventral and dorsal to the AER. We did not find mitotic cells in the center apical part of the AER. We can then assume that in the developing AER there are two pools of cells at the base of the structure that are responsible for the renewal of the AER, and that, as cells lose contact with the extracellular matrix and die at the tip of the AER, a new batch of cells are dividing at the base and moving towards the top. These areas of proliferation at the base of the AER and running through the anterior-posterior axis of the limb coincide with oct4 expressing areas.
Upon oct4 overexpression, AER cell dynamics is altered. We analysed whether the expansion of the AER and consequent enlargement of the limb upon oct4 overexpression was due to an alteration on the cell balance towards an increase of the proliferation rate, or a decrease in the cell death ratio.
Cell death ratio is not altered in the AER, 48h and 72h post-electroporation. However, we observe an increase in the proliferation rate at the AER, and consequently in the mesechyme, induced by the increased levels of oct4.

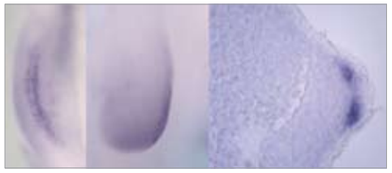
GROUP MEMBERS
Ana Catarina Afonso (Post-doc)
Ana Raquel Viegas Tomá (PhD Student)
Joana Freire Monteiro (PhD Student)
Frederico (MSc Student)
Rita Aires (MSc Student)

THIS GROUP COLLABORATES WITH:
Yasuhiko Kawakami (Stem Cell Institute and Department of Genetics, University of Minnesota, USA)

FUNDING
Fundação para a Ciência e a Tecnologia (FCT), Portugal



Immunohistochemistry of 48 hpa fin sections using an anti-V1E1 antibody (in green): V-ATPase E subunit is present in the epithelial layer and seems to be located in the cell membrane. In blue: cells nuclei stained with DAPI; In red: proliferating cells marked with Histone 3.



As the limb bud grows and the ectoderm condenses to form the Apical Ectodermal Ridge at its tip, oct4 expression can be observed in the ectoderm and in the forming AER in a "two stripe" pattern running along the anterior-posterior axis of the limb .

SYSTEMS NEUROSCIENCE

Zachary Mainen

PhD in Neurosciences
University of California, USA
E-mail: zmainen@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/85
http://pgcn.igc.gulbenkian.pt/doku.php/cnp-research:zach_mainen:start

THIS GROUP IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

OPTOGENETIC IDENTIFICATION AND CONTROL OF SEROTONIN NEURONS IN BEHAVING ANIMALS

Serotonin (5-HT) is implicated in a wide spectrum of brain functions and disorders. However, its functions remain controversial and enigmatic due to limitations in the temporal and molecular specificity of conventional pharmacological and electrophysiological techniques. The objectives of this project are to:

1. Record;
2. Stimulate;
3. Silence the activity of 5-HT neurons with high molecular selectivity and temporal precision by using genetically-encoded sensors, activators and inhibitors of neural function.

This year we demonstrated specific expression of exogenous proteins in 5-HT neurons using adeno-associated virus vectors using the PET-1 promoter (in collaboration with S. Lima). We initiated development of a virus production facility to facilitate the development of viral vectors. We established *in vivo* recording in anesthetised animals and in vitro recording in dorsal raphe brain slices and began to use them to validate the potency of PET1-channelrhodopsin to activate 5-HT neurons.

OLFACTORY OBJECTS AND DECISIONS: FROM PSYCHOPHYSICS TO NEURAL COMPUTATION

Neural computations within the olfactory system enable faithful recognition and tracking of meaningful odor sources, even when they comprise complex chemical blends embedded in a sea of background odors. The overall aim of this line of work is to understand the neural computations that make olfactory object recognition possible.
In 2009, we developed theoretical models of olfactory recognition based on probabilistic population coding (in collaboration with A. Pouget, University of Rochester, USA) and developed quantitative behavioural paradigms and equipment for quantifying odor recognition.

EVALUATING THE RELIABILITY OF KNOWLEDGE: NEURAL MECHANISMS OF CONFIDENCE ESTIMATION

We hypothesise that a sense of confidence or uncertainty is not the product of a higher cognitive faculty, but a reflection of the fundamentally probabilistic nature of neural representation and computation. The aim of this project is to elucidate the biological mechanisms by which organisms evaluate the reliability of their knowledge (predictions, beliefs, memories, etc) about the world.
Studies this year using transient pharmacological inactivation show that OFC is required for animals to selectively abort waiting for uncertain rewards (in collaboration with A. Kepecs, Cold Spring Harbor Laboratory, USA).

FRONTAL CORTEX AND THE CONTROL OF IMPULSIVE ACTION

Inhibition of behaviour is often as important as its generation and failure to inhibit inappropriate actions-impulsivity is a central feature of pathologies including attention deficit hyperactivity disorder, drug addiction and obsessive compulsive disorder. The aim of this work is to understand how neural circuits within the frontal cortex operate to inhibit impulsive actions. Previously, we showed that frontal cortex neuron firing can predict a subject's willingness to wait. This year, we tested whether such waiting-predictive neurons were general to waiting or specific to the action involved in waiting. We found that only a small fraction of neurons are predictive in two different types of waiting tasks.

GROUP MEMBERS
Guillaume Dugué (Post-doc)
Hope Johnson (Post-doc)
Magor Lorincz (Post-doc)
Masayoshi Murakami (Post-doc)
Ana Rita Fonseca (PhD Student)
André Mendonça (PhD Student)
Maria Inês Vicente (PhD Student)
Gil Costa (PhD Student)
Sara Matias (PhD Student)
Niccolò Bonacchi (MSc Student, left September 2009)
Pedro Garcia Da Silva (Research Technician, left September 2009)

THIS GROUP COLLABORATES WITH:
Susana Lima (IGC)
Alex Pouget (University of Rochester, USA)
Adam Kepecs (Cold Spring Harbor Laboratory, USA)

FUNDING
Marie Curie Intra-European Fellowship (IEF)
Champalimaud Foundation, Portugal
Bial Foundation, Portugal
ERC Starting Grant/Advanced Grant, European Research Council, Belgium

PATTERNING AND MORPHOGENESIS

Moises Mallo

PhD in Biochemistry and Molecular Biology
Universidade de Santiago de Compostela, Spain
E-mail: mallo@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/48

Our group is interested in several aspects of vertebrate embryonic development. The ultimate goal of our research is to understand the molecular mechanisms that translate patterning information into morphogenetic processes during formation of the vertebrate embryo. For a number of years, we have explored different developmental processes, including ear formation, neural crest induction/migration and differentiation of branchial arches. Our most recent work is focused on the role that Hox genes play during formation of the vertebrate axial skeleton.

THE ROLE OF HOX GENES IN GLOBAL PATTERNING OF THE AXIAL SKELETON

This project aims at understanding how Hox genes control development of global domains in the vertebral column of the mouse.
We had previously shown that Hoxa10 and Hoxb6 control formation of ribs is by modulation of the expression of two myogenic genes, Myf5 and Myf6, specifically in the hypaxial myotome. Now, we have shown that this regulation is exerted through direct interaction with a specific enhancer that controls expression of these genes. In addition, we have now demonstrated that Myf5 and Myf6 then act in a redundant fashion in the rib inducing process, and presented genetic proof for the hypothesis that Myf5/Myf6 are indeed a major component of the network regulated by Hox genes to control rib formation with the rescue of the ribless phenotpe of Hoxa10 transgenics, with the expression of Myf6 in the hypaxial myotome using an enhancer not modulated by Hox genes.

HOX GENES IN CONTROL OF AXIAL VERTEBRATE ELONGATION

With this project we want to understand how Hox genes of group 13 modulate the axial extension of the vertebrate body.
We have shown that premature expression of Hoxc13 in the presomitic mesoderm of transgenic embryos results in truncations in the axial skeleton of the resulting embryos. We have provided evidence that this is due to inactivation of Wnt signaling in this region. These results suggest that the activity of Hox genes of group 13 are part of the stop signal for axial elongation and, therefore, can have a big impact on the evolution of the vertebrate body plan.

TISSUE REQUIREMENTS OF UDP-N-ACETYL GLUCOSAMINE (GNE) ACTIVITY FOR PROPER HOMEOSTASIS OF SKELETAL MUSCLE

Mutations in the GNE gene are responsible for the human syndrome Heterologous Inclusion Body Myopathy (HIBM), a progressive muscle-wasting disease. We want to determine in which tissue GNE is required for normal homeostasis of the muscle.
We have produced embryonic stem cells carrying a modification in the GNE locus in which exon 3 has been flanked by LoxP sites. Chimeric mice were generated from these cells and are now been bred to determine if the stem cells contributed to the germ line. We have also established mouse lines expressing cre recombinase in the muscle or the liver, so we can then cross them to the mice carrying the LoxP-modified GNE allele to determine in which tissue GNE is required for normal muscle function.

GROUP MEMBERS
Jennifer Rowland (Post-doc)
Filipa Moraes (PhD Student)
Tânia Vinagre (PhD Student)
Arnon Jurberg (PhD Student)
Ana Nóvoa (Research Technician)
Isabel Guerreiro (Trainee)
Sofia Pereira (Trainee)

THIS GROUP COLLABORATES WITH:
Jacqueline Deschamps (Hubrecht Institute, Holland)

FUNDING
Advancement of Research for Myopathies (ARM), USA
Fundação para a Ciência e Tecnologia (FCT), Portugal

EARLY FLY DEVELOPMENT

Rui Gonçalo Martinho

PhD in Biology
University of Sussex, UK
E-mail: rmartinho@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/70

Drosophila early embryonic development is rapid and temporally coordinated, with a series of fast syncytial nuclear divisions, posterior segregation of the primordial germ cells, *de novo* activation of the zygotic genome, synchronous formation of thousands of epithelial cells (blastoderm cellularisation), and ultimately, gastrulation and germ-band extension. Remarkably, although most of these events are functionally interdependent, some are incompatible with each other. For example, cell division is incompatible with gastrulation. Our long-term research goals are to better understand tissue morphogenesis, germ-line development, and how an embryo is capable of coordinating development and resist perturbations.

ANALYSIS OF EARLY TRANSCRIPTIONAL ACTIVATION AND GERM-LINE SEGREGATION IN *DROSOPHILA MELANOGASTER*

The aim is to study the development of the germ-line in the Drosophila embryo. We identified a functional antagonism between pgc and tor that was important for the correct specification of germ-line and somatic properties. We also observed that during oogenesis establishment of the follicular epithelium is extremely sensitive to reduced levels of apkc activity (when compared to a fully mature follicular epithelium) and concluded that epithelial tissues respond differently to sub-optimal levels of apkc activity given their maturity and morphogenetic status. Furthermore, we identified a novel NAT related to San, whose mitotic activity might explain the differential requirements of san within the female germ-line stem cells.

CHARACTERISATION OF THE TRANSCRIPTIONAL ACTIVATION OF THE QUIESCENT ZYGOTIC GENOME AFTER OOCYTE FERTILISATION

This project aims to study early transcriptional regulation in the Drosophila embryo. Complementation group 7 was defective for early zygotic transcription. We named this mutant fandango based on its blastoderm cellularisation phenotype. We identified the affected gene and we are currently defining the function of this gene during transcriptional activation of the quiescence zygotic genome.

GROUP MEMBERS
Ema Alves (Post-doc, left in 2009)
Leonardo Gaston Guilgur (Post-doc)
Denisa Liszekova (Post-doc)
Ana Rita Pimenta Marques (PhD Student)
Tânia Ferreira (PhD Student)
Pedro Prudêncio (Laboratory manager/ MSc student)

THIS GROUP COLLABORATES WITH:
Susana Lima, Florence Janody, Jorg Becker (IGC)
Alex Pouget (University of Rochester, USA)
Adam Kepecs (Cold Spring Harbor, USA)
Thomas Arnesen (University of Bergen, Norway)
Kris Gevaert (University of Gent, Belgium)
Buzz Baum (University College of London, UK)
Jordi Casanova (University of Barcelona, Spain)
Claudio Gomes (ITQB, Universidade Nova de Lisboa, Portugal)

FUNDING
Fundação para a Ciência e a Tecnologia (FCT), Portugal

BEHAVIOURAL NEUROSCIENCE

Marta Moita

PhD in Neuroscience
University of Porto, Portugal
E-mail: moita@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/64

THIS GROUP IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

We are interested in understanding the neural mechanisms underlying behavioural plasticity using a combination of behavioural, pharmacological, molecular and electrophysiological tools. In particular, we are studying how prior experience and how social interactions shape behaviour. To this end, we are studying fear; both how animals learn to fear cues that are predictive of aversive events or threats, and how fear can be socially transmitted, i.e. how animal respond to the distress of con-specifics. We chose fear learning since it is conserved across species, entailing fast robust learning and very long lasting memories. We are also studying decision-making in the context of social interactions, using game theory to test how rats learn and evaluate the payoffs that result from the interaction with another individual.

NEURAL MECHANISMS OF TRACE AUDITORY FEAR CONDITIONING

This project focuses on the role of different memory systems in trace auditory fear conditioning (tAFC). We hypothesised that the mechanism underlying the association between a tone and a shock depends on the length of the trace interval between the two stimuli, where in the case of a short interval rats rely on working memory and in the case of long intervals they rely on episodic memory.
We found that temporary inactivation of the hippocampus, involved in episodic memory, affects tAFC only when long trace intervals are used. In contrast, inactivation of either the medial prefrontal cortex (mPFC), thought to be important for working memory, or the amygdala, important for fear learning, disrupts learning irrespective of interval length.

NEURAL MECHANISMS OF DISCRIMINATIVE AUDITORY FEAR CONDITIONING

This project aims at elucidating the role of the different auditory input pathways to the amygdala in the acquisition of auditory fear conditioning. To this end we performed lesions to each pathway, the lemniscal and non-lemniscal, and tested their role in the acquisition and expression of discriminative auditory fear.
We found that a selective fear response requires cooperation between lemniscal and non-lemniscal auditory projections to the amygdala. In contrast, expression of previously learned discriminative fear responses relies only on the non-lemniscal thalamus. Finally, the non-lemniscal, but not the lemniscal, thalamus is important for the recall of extinction. Our findings suggest that the lemniscal pathway is important for discriminative learning, whereas the non-lemniscal is important for negatively regulating fear responses.

COOPERATION IN SOCIAL DILEMMAS IN RATS

Game theory has constituted a powerful tool in the study of the mechanisms of reciprocity. Having shown that, in a Prisoner's Dilemma game, rats shape their behaviour according to the opponent's strategy and the relative size of the payoff resulting from cooperative or defective moves, we now aim at dissecting the mechanisms underlying the decision-making process during such social dilemma games.
We have designed and set-up an automated maze to study the behavior of rats in different social dilemma games, such as the Stag Hunt and the Snow drift game, which allow for dissection of the factors that govern cooperation between two rats.

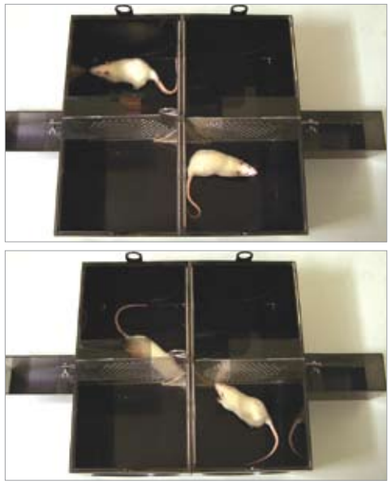
MECHANISM OF VICARIOUS FEAR

This project aims at investigating the mechanisms underlying vicarious fear in rats, i.e. how rats respond to the distress of a con-specific. In collaboration with Dr. Christian Keysers, we have developed a paradigm for studying vicarious fear in rats.
We have found that a rat will show vicarious fear, when observing a con-specific being shocked, provided that it has had himself prior experience with shock. This finding suggests that in rats vicarious freezing is empathic in nature.

GROUP MEMBERS
Marta Guimarães (PhD Student)
Raquel Antunes (PhD Student)
Ana Pereira (PhD Student)
Scott Rennie (PhD Student)
Andreia Cruz (MSc Student, left September 2009)
Alexandre Lucas (MSc Student, left August 2009)
Ana Gregório (Technician)

THIS GROUP COLLABORATES WITH:
Hugh Blair (University of California, Los Angeles, USA)
Christina Keysers (University of Groeningen, Holand)
Glenn Schaffe (Yale University, USA)
Roian Egnorr (Howard Hughes Medical Institute, Janelia Farm, USA)
Susana Lima (Champalimaud Neuroscience Programme at IGC)
Elio Sucena (IGC)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



Experimental setup used to study neural mechanisms underlying learning of and social transmission of fear, in mice.

ANIMAL BEHAVIOUR

Rui Oliveira

PhD in Biology
University of Lisbon, Portugal
E-mail: roliveira@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/83

The main research aim of our group is the understanding of the inter-relationship between neuroendocrine mechanisms and social behaviour, using an integrative approach (i.e. by integrating ecological/evolutionary analysis with physiological analysis of behaviour). With our studies we hope to contribute to the understanding of how complex social environmental processes interact with biological systems. I have been developing two main research lines:

1. To understand how the social environment modulates hormones and gene expression in order to affect the expression of subsequent behaviours;
2. The study of the neuroendocrine mechanisms underlying behavioural plasticity.

Both research lines have been mainly focused in teleost fish as study models (tilapia, pecock blenny and zebrafish) but I have also expanded my research to other vertebrate groups, including humans. In these research lines we combine neuroendocrinology and molecular biology techniques with behavioural observations and we conduct studies both in the lab and in free-living subjects.

WINNERS AND LOSERS: SOCIAL MODULATION OF HORMONES, BRAIN AND BEHAVIOUR

The aims of this project are to investigate how social interactions influence brain function (i.e. patterns of gene expression in areas of interest in the brain using qPCR and gene microarrays), and how socially driven hormonal changes influence subsequent behaviour. Two fish model species are used: zebrafish *(Danio rerio)* and the Mozambique tilapia *(Oreochromis mossambicus)*.
In 2009 we completed the development of the molecular tools needed for some of the tasks with tilapia (cloning, sequencing and developing primers for qPCR and probes for in *situ* hybridisation), and we started some behavioural experiments both with tilapia and with zebrafish. In both species we have investigated how social information is translated into neuroendocrine signals. First results using unsolved social interactions (mirror fights) suggest that individuals need to assess the outcome of social interactions before they trigger a physiological response suggesting a cognitive activation of these responses.

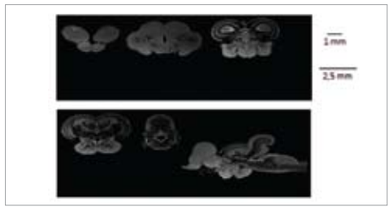
NEUROENDOCRINE CONTROL OF REPRODUCTIVE BEHAVIOUR IN THE MOZAMBIQUE TILAPIA: MECHANISMS AND EFFECTS OF THE SOCIAL ENVIRONMENT

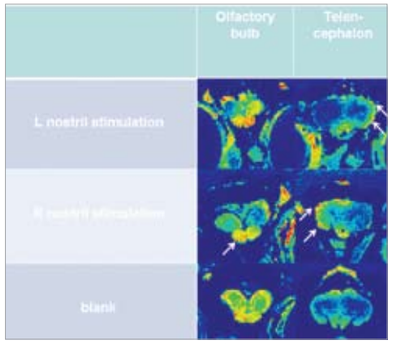
This projects aims to investigate the neuroendocrine mechanisms involved in the control of social (territorial and courting) behaviour in the Mozambique tilapia. Using the expression of immediate early genes (egr-1, c-fos) we aim to map the patterns of brain activation associated with the expression of different types of social behaviour. We also aim to assess the effects of sex steroids (androgens in particular) and neuropeptides (vasotocin and isotocin) in the modulation of social behaviours.
In 2009 we developed molecular and analytical tools needed for the behavioural tasks. We cloned, sequenced and developed primers for qPCR and probes for in situ hybridisation for immediate early genes (egr-1, c-fos) and we validated the quantification of vasotocin and isotocin from brain tissue using HPLC. Preliminary HPLC results indicate that subordinate males have higher levels of vasotocin in the olfactory bulbs and the pituitary gland, suggesting a modulaton of chemical communication by vasotocin in this species (vasotocin is an anti-diuretic hormone and urine is stored in dominants, but not in subordinates, to be actively released during social interactions). Castration, that was intended to manipulate the levels of sex steroids, failed to reduced androgen concentrations (within 10d post-surgery) suggesting either the existence of a steroid binding globulin that is extending the half-life of the hormone in circulation or a non-gonadal source of androgens in this species (e.g. neurosteroids? inter-renal tissue?). These possibilities are being investigated.

GROUP MEMBERS
Magda Teles (PhD Student)
José Miguel Simões (PhD Student)
Joana Ferreira da Silva (MSc student, left November 2009)
Ana Catarina Oliveira (Research technician)

THIS GROUP COLLABORATES WITH:
Gunther Zupanc (Northeastern University, Boston, USA)
Hans Hofmann (University of Texas at Austin, USA)
Ewa Kulczykowska (Oceanology Institute of the Polish Academy of Sciences, Poland)
Svante Winberg (Uppsala University, Sweden)
Adelino Canário (Universidade do Algarve, Portugal)

FUNDING
Fundação para a Ciência e a Tecnologia (FCT), Portugal





Top - Magnetic resonance imaging (MRI) for tilapia brains. Our lab is developing in collaboration with the BioImage Lab from Univ. Antwerp a 3D MRI stereotaxic atlas for the tilapia brain. **Bottom** - and a manganese enhanced MRI technique to study patterns of brain activation in response to social stimuli.

Mirror elicited fights fail to trigger an endocrine response despite the expression of aggressive behavior. This contrasts with what happens when fighting a real intruder, suggesting that the assessment of fight outcome is needed to activate a physiological response.

INFECTION AND IMMUNITY

Michael Parkhouse

PhD in Biochemistry
University of London, UK
E-mail: parkhous@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/42

The theme of the group is the reciprocal adaptation between an infectious organism and its host. The ability to recognise and destroy invading pathogens has played a crucial role in the evolution of the immune system of both vertebrates and invertebrates. At the same time, pathogens, in particular viruses, have evolved reciprocal strategies to manipulate the immune system. As there are a range of pathogen life styles an efficient immune system must select the immune effector mechanism most appropriate to the biology of the pathogen. Equally important, the immune response, once selected, must be terminated. Failure to switch off both appropriate and inappropriate immune response is the cause of many un-infectious diseases, such as autoimmunity and inflammation. Thus the study of how pathogens control immune responses will offer novel approaches for the manipulation of the immune responses in health and disease, with novel vaccines being the most obvious outcome in our laboratory. Therefore, we are identifying and characterising virus host evasion genes directed towards subversion of cell biology and innate immunity. The two viruses that we have selected are Herpesvirus and the African Swine Fever Virus. There is a small, but socially relevant project, focusing on control, through diagnosis and vaccine development, of the human tapeworm parasite.

EVALUATING AND CONTROLLING THE RISK OF AFRICAN SWINE FEVER (ASF) IN THE EU

The aim is to provide new tools and strategies for the control of ASF in Africa and reduce the risk of importation and/or spread of the disease in EU member states.
Four proteins (B602L, p54, A104R and K205R) were identified as potential target antigens in sensitivity and specificity tests. These recombinant proteins were produced and will be used as antigens to test field ASFV isolates in new recombinant ELISAs by Dr Carmina Gallardo, CISA-INIA. As the K205R protein revealed high IgM titres, it has been produced and sent to Dr Carmen Vela, INGENASA, to develop a new commercial kit able to detect recently ASFV infected animals.

MECHANISM OF CELL CYCLE ARREST INDUCED BY A HOST MODIFICATION GENE OF THE HUMAN BETA HERPESVIRUS HCMV

This application will define the mechanism of the conserved, "non-assigned", non-homologous UL76 gene of HCMV, which we have shown to induce host cell cycle arrest and apoptosis, and which is therefore likely to play a critical role in the pathogenesis of herpesvirus infections.
A UL24 deletion mutant of HCMV was constructed and characterised. After the first passage, a severe deficiency in the mutant virus replication was evident. This observed phenotype clearly revealed that the UL24 homologue from HCMV is an important gene for viral replication. Microarray analysis of transcription profiles of cells transduced with control and UL24-recombinant retroviruses revealed an up-regulation of IL-8 in cells expressing the HCMV viral gene. Luciferase assays using deletion mutant reporters indicated that UL24 induction of IL-8 is NF-kB-dependent.

GROUP MEMBERS
Rute Nascimento (Post-doc)
Sílvia Correia (Post-doc)
Helena Costa (PhD student)
Sónia Ventura (PhD student)
João Dias (Technician)

THIS GROUP COLLABORATES WITH:
Sun Huaichang (Yangzhou University, China)
Alexandre Leitão (Universidade Técnica de Lisboa, Portugal)
John Sinclair (Cambridge University, UK)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal
Marie Curie International Reintegration Grants, European Commision

DISEASE GENETICS

Carlos Penha Gonçalves

PhD in Immunology
Umea University, Sweden
E-mail: cpenha@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/30

Our laboratory started by adopting forward genetics approaches to identify genetic factors related to disease, both in mice and humans. Two diseases are the focus of our work: Malaria and Type 1 diabetes (T1D). In the past years the lab evolved to explore the pathogenesis of these diseases by combining cell and molecular biology methodologies with classic genetics techniques. A good part of our research is converging on searching for correlations of the response to different innate immune system stimuli (e.g TLR signals) and specific outcomes of the immediate inflammatory reaction and of the long-term adaptive response. The emerging picture is that specific cell types that are located in defined sites in the body (e.g. placental macrophages, peritoneal B cells) respond to innate stimuli and condition the adaptive immune system response in a PAMP-specific fashion. This is leading us to see such innate responses as promising targets to deviate the immune response and halt disease progression.
In coming years a strong theme in the lab will be to investigate particular cell types (and functions) of the innate immune system and to decipher their role:

1. In mediating pathogen-induced pathology (in pregnancy malaria);
2. In conferring infection resistance (in malaria liver stage);
3. In conditioning long term adapative responses (in human chronic and actue malaria);
4. In shaping the response to auto-antigens (in T1D).

PREGNANCY-ASSOCIATED MALARIA

The main aim of this project is to investigate the mechanisms of placenta malaria pathogenesis, namely: to study the adhesion of the parasite to the placenta tissue, *in vivo*, and the role of local innate immunity molecular and celular components provided by the fetal tissues.
Two mouse models of pregnancy-associated malaria were constructed and characterised at the immuno-pathological and parasitological levels.

PLASMODIUM DEVELOPMENT IN HEPATOCYTES

This project aims to identify key hepatocyte pathways and molecules that are targeted by the parasite during liver stages, at the level of the individual infected hepatocytes.
We have obtained evidence that the Fas pathway is involved in apoptosis-resistance of infected hepatocytes.

HUMAN GENETICS OF MALARIA

We aim to identify antigenic determinants of cerebral malaria pathogenesis and natural decay of immunological memory to the malaria parasite.
We have identified HMOX1 and TGFB2 genes as risk factors for cerebral malaria in Angolan children.

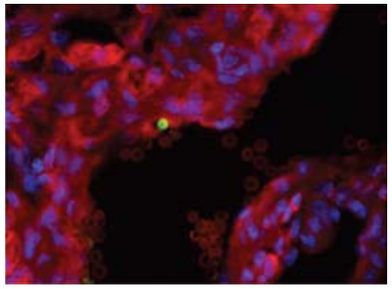
B1 CELLS AND NATURAL ANTIBODIES IN TYPE 1 DIABETES (T1D) PATHOGENESIS

The main aims are to correlate alterations in the development and functional activation of autoreactive B1 cells with T1D pathogenesis, and to determine the role of auto-antibodies in the autoimmune attack of pancreatic Beta-cells.
We have identified abnormal phenotypes in B1 cells of the NOD mouse and found a genetic assocation of human T1D and multiple autoreactivity to the IgH locus.

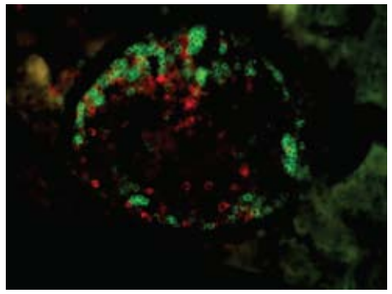
GROUP MEMBERS
Nadia Duarte (Post-doc)
Luciana Moraes (Post-doc)
Maria de Jesus Trovoada (Post-doc)
Liz Ball (PhD student)
Lurdes Duarte (PhD student)
Joana Corte-Real (PhD student)
Joana Rodo (PhD student)
Ligia Deus (PhD student)
Rosario Sambo (PhD student)
Rita Neres (PhD student)

THIS GROUP COLLABORATES WITH:
Lars Hviid, Dan Holmberg (University of Copenhagen, Denmark)
Chris Jansen (Leiden University Medical Center, The Netherlands)
Maria Mota (Instituto de Medicina Molecular, Portugal)
Jon Clardy (Harvard Medical School, USA)
Peter Crompton (National Institute of Health, USA)
Taane Clark (London School of Hygiene and Tropical Medicine, UK)
Miguel Soares (IGC)
Linda Wicker (University of Cambridge, UK)
Kristina Lejon (University of Umea, Sweden)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal
Fundação Luso-Americana (FLAD), Portugal



PREGNANCY MALARIA.
an adherent red blood cell infected with malaria parasite (green) in a mouse placenta. The placental cell nuclei were stained with DAPI (blue) and counterstained with rhodamine (red).



TYPE 1 DIABETES.
Mouse pancreas showing an islet of Langerhans surrounded and infiltrated by T-cells (red staining) and B-cells (green staining).

COMPUTATIONAL GENOMICS

Jose Pereira Leal

PhD in Biomedical Sciences
University of Porto, Portugal
E-mail: jleal@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/75
http://evocell.org/

We are interested in the evolutionary mechanisms underlying the origins and evolution of cellular life and the complex structures within the cell, the transitions to multi-cellularity, and the medical applications of evolutionary genomics. Our research encompasses themes that are broadly classified as evolutionary cell biology, systems biology, pathogenomics, and translational or medical bioinformatics.

EVOLUTIONARY CELL BIOLOGY

The aims of this project are to study the origins of cellular structures, and to develop the methods and resources that enable evolutionary studies in cell biology.
We developed three data integration platforms: TrafficDB, CentrioleDB and SporeDB, where automated methods for sequence classification are integrated with morphological information, described by image data and novel controlled vocabularies.

EVOLUTION OF PROTEIN INTERACTIONS

Within this project we aim to study the evolution of protein interactions, with an emphasis on transient interactions.
We studied the evolution of Rab: effector interactions and discovered that they are poorly conserved accross species and across paralogues, contrasting with the high conservation of protein trafficking (Submitted for publication).

GROUP MEMBERS
Ana Abecasis (Post-doc, left December 2009)
Luisa Rodrigues (Post-doc)
Sofia Braga (PhD student)
Yoan Diekmman (PhD student)
Renato Alves (Research Student)
Marc Gouw (Research Student)

THIS GROUP COLLABORATES WITH:
Monica Bettencourt-Dias , Miguel Seabra (IGC)
Juliette Azimzadeth (UCSF, USA)
Keith Gull (Oxford University, UK)
Adriano Henriques (ITQB, Portugal)
Carlos Caldas (Cambridge University, UK)
José Luis Passos Coelho (IPO, Portugal)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal

BEHAVIOUR AND METABOLISM

Carlos Ribeiro

PhD in Cell Biology
University of Basel, Switzerland
E-mail: cribeiro@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/101

THIS GROUP WAS ESTABLISHED AT THE IGC IN JUNE 2009 AND IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

We are interested in understanding how molecular and cellular mechanisms control complex biological processes at the level of the whole organism. For this we are focusing on how the internal metabolic state of the fruit fly *Drosophila melanogaster* affects its behavioural decisions. Starting from novel behavioural paradigms, we use molecular genetic techniques to identify and characterise genes and neuronal populations involved in producing the appropriate behavioural response to a specific metabolic need of the fly. We use tissue specific whole genome behavioural RNAi screens to identify molecular processes. Neuronal substrates are identified by screening for fly lines marking neuronal populations necessary to produce correct behavioural outputs. The identified molecular mechanisms and circuits are then analysed using quantitative behavioural observations, state of the art genetic and molecular techniques, as well as imaging approaches.

MOLECULAR AND NEURONAL MECHANISMS OF NUTRIENT CHOICE

We want to understand how Drosophila knows what type of nutrients it needs and what molecular and neuronal mechanisms are used by the nervous system to change the behaviour of the animal to allow it to find and eat the required nutrients.
We have started to analyse genes identified as being required for nutrient choice in a neuronal whole-genome RNAi screen. Contemporaneously we have used genetic approaches to identify neuronal populations which are required for the same nutrient choices. The knowledge of molecular and neuronal players will be an entry point for studying neuronal mechanisms of nutrient balancing at the molecular, cellular and circuit levels.

QUANTITATIVE ANALYSIS OF FEEDING BEHAVIOUR IN DROSOPHILA

This project aims at using automated video analysis to quantitatively link genetics to feeding behaviour in the fruit fly.
In collaboration with the laboratory of Aldo Faisal at Imperial College London we have started devising strategies and approaches for using automated video analysis to quantitatively link genetics to feeding behaviour in the fruit fly.

GROUP MEMBERS
Laura Napal Belmonte (Post-doc)
Teresa Montez (Post-doc)
Ana Carolina Doran (Research assistant)
Ana Paula Elias (Lab Manager and Research Assistant)

THIS GROUP COLLABORATES WITH:
Aldo Faisal (Imperial College London, UK)

FUNDING
Champalimaud Foundation, Portugal

FOOD CHOICE ASSAY
Left - Setup used for studying food choice in Drosophila. Flies can choose to eat two different nutrients mixed with two different colors. **Right** - The food choices are assessed by inspecting the color of the abdomen of the flies: if their bellies are blue they preferred the nutrient mixed with the blue color, if they are red they preferred the nutrient mixed with the red color.

MEMBRANE TRAFFIC IN DISEASE AND NOVEL THERAPIES

Miguel Seabra

PhD in Biochemistry and Molecular Biology
University of Texas, USA
E-mail: mseabra@igc.gulbenkian.pt
url: //www.igc.gulbenkian.pt/research/unit/78

One of the most important challenges for the Biomedical Sciences this century is to develop a comprehensive knowledge of the fundamental unit of life, the cell. One main question in Molecular Cell Biology is focused on understanding how cells achieve their highly sophisticated internal compartmentalisation. Each organelle is individualised by membranes, which contain specific proteins and lipids to execute specific functions. How are proteins and lipids sorted and retained to different locations, or in other words, how are organelles made, maintained (identified) and how do they communicate with each other? Our work in the last 15 years has dealt with this problem and our approach has been to study both normal cells and disease processes. We are currently working in a variety of diseases with different phenotypes whose common feature is dysfunction of intracellular membrane trafficking pathways. We also wish to apply the fundamental knowledge to develop new therapeutic approaches to these diseases.

MOLECULAR MECHANISMS OF PARASITOPHORUS VACULE FORMATION IN MALARIA INFECTION

The aim of this project is to carry out a comprehensive study of the localisation of all the Rab proteins during Plasmodium infection in liver cells.
There seems to be some association between certain specific host Rabs and the parasite, such as Rab3b, Rab3d, Rab6a, Rab8a, Rab9a, Rab 15 and Rab11b, which have all in some way been descrived as golgi or/and secretory Rabs.

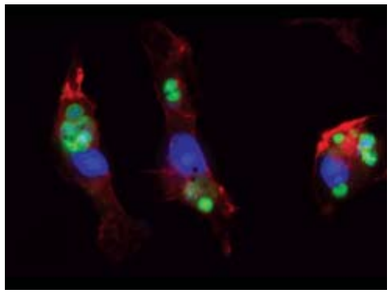
MOLECULAR MECHANISMS OF ORGANELLE MOTILITY

This project aims to study the role of the Rab27/Mlph/MyoVa complex in melanosome trafficking and the role of the Mypt phosphatase in this process.
We proposed that Mlph is targeted to and/or stabilised on melanosomes by Rab27a, and then recruits MyoVa, which provides additional stability to the complex and allows melanosomes to transfer from MT to actin-based transport and achieve peripheral distribution.

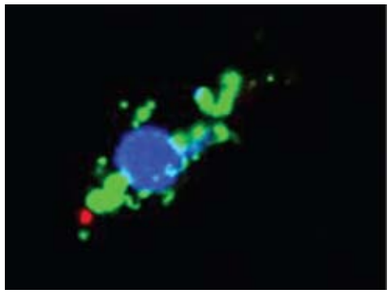
GROUP MEMBERS
Elsa Seixas (Post-Doc)
Laura Santos (Post-Doc)
Carolina Matos (PhD Student)
Maria Inês Patrício (PhD Student)
Mafalda Silva (PhD Student)
Marta Pedro (Trainee)
Maria Margarida Silva (Trainee)

THIS GROUP COLLABORATES WITH:
Tanya Tolmachova, Robert Sinden, Alistair Hume (Imperial College London, UK)
Sebastien Amigorena, Graça Raposo (Institut Curie, France)
Clare Futter (Institute of Ophtalmology, UK)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



PHAGOCYTOSIS OF PLASMODIUM BERGHEI-GFP BY MOUSE BONE-MARROW DERIVED MACROPHAGES.
Blue - Nucleus. Geen - P. berghei. Red - Phalloidin.



PLASMODIUM BERGHEI EXOERYTHROCYTIC FORM SURROUNDED BY LC3 POSITIVE VESICLES AND WITH DEGRADATIVE VESICLE IN CLOSE PROXIMITY AT 20 HPI.
Blue - parasite. Geen - LC3 (autophagosome marker). Red - Degradative compartment.

INFLAMMATION

Miguel Che Parreira Soares

PhD in Science
University of Louvain, Belgium
E-mail: mpsoares@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/43

Our objective is to gain further understanding of the cellular and molecular mechanisms regulating inflammatory reactions as to prevent the pathogenesis of immune mediated inflammatory diseases. The projects developed by our group address essentially the mechanisms via which the expression of "protective genes" and in particular heme oxygenase 1 (HO-1 encoded by Hmox1) re-establish homeostasis after a wide range of inflammatory conditions with diverse and multifarious underlying pathogenesis. Briefly, HO-1 is a stress responsive enzyme that degrades free heme into equimolar amounts of three products: the gas carbon monoxide (CO), iron (Fe, which induces the expression of H chain ferritin, an iron-sequestering protein) and biliverdin (which is rapidly converted to the anti-oxidant bilirubin by biliverdin reductase). These different "arms" of the HO-1 system can each alone act in a salubrious manner. We aim to understand further the cellular and molecular bases underlying the salutary effects of these molecules.

CROSSTALK BETWEEN NITRIC AND CARBON MONOXIDE IN SUPPRESSING THE PATHOGENESIS OF CEREBRAL MALARIA

This project addresses three hypotheses:

1. That NO suppresses the pathogenesis of Experimental Cerebral Malaria (ECM) via CO;
2. That CO suppresses the pathogenesis of ECM via NO;
3. That the combination of NO and CO inhalation might afford maximal therapeutic effect in preventing the onset of ECM.

We have shown that the protective effect of nitric oxide against the onset of cerebral malaria is mediated via the induction of heme oxygenase-1 and the production of carbon monoxide.

CARBON MONOXIDE GENERATED BY HEME OXYGENASE-1 SUPPRESSES THE PATHOGENESIS OF CEREBRAL MALARIA: MECHANISM OF ACTION

Within this project we are researching the following hypotheses:

1. That HO-1 derived CO suppresses the generation of free heme associated with the oxidation of ferrous Hb into MtHb;
2. That heme contributes to the pathogenesis of ECM;
3. That heme triggers blood brain barrier dysfunction leading to the development of CM.

All the aims specified within this project have been achieved.

ENGINEERING OF THE PORCINE GENOME FOR XENOTRANSPLANTATION STUDIES IN PRIMATES: A STEP TOWARDS CLINICAL APPLICATION

The aim of this research programme is to identify protective genes controlled via activation of the trascription factor Nrf2.
Work is ongoing.

HEME OXYGENASE-1 UNDERLIES THE "PROTECTIVE TRAIT" AFFORDED BY SICKLE CELL DISEASE AGAINST SEVERE ACUTE MALARIA

The main hypothesis to be tested under this proposal is that up-regulation of heme oxygenase-1 (Hmox1/HO-1) during sickle cell disease (SCD) ameliorates the pathological outcome of this condition and underlies the protective trait afforded by the sickle genotype against the development of cerebral malaria (CM). Presumably, the generation of carbon monoxide (CO) mediates these effects.
We have shown that mutations in the beta chain of human hemoglobin afford protection against severe forms of malaria via the induction of heme oxygenase-1 and the production of carbon monoxide.

GROUP MEMBERS
Ana Margarida Ferreira (Post-doc)
Rasmus Larsen (Post-doc)
Raffaella Gozzelino (Post-doc)
Viktoria Jeney (Post-doc)
Andreia Cunha (PhD student)
Ivo Marguti (PhD student)
Nadja Pejanovic (PhD student)
Zélia Gouveia (PhD student)
Virginia Marques (Post-doc)
Josina Filipe (Post-doc)
Silvia Cardoso (Laboratory Assistant)
Sofia Rebelo (Laboratory Manager)

THIS GROUP COLLABORATES WITH:
József Balla (Medical and Health Science Center, University of Debrecen, Hungary)
Yves Beuzard and Ingo Bechman (Hospital Saint Louis, Paris, France and Institute for Clinical Neuroanatomy, Johann Wolfgang Goethe-University, Frankfurt/Main, Germany)

FUNDING
Fundação para a Ciência e a Tecnologia (FCT), Portugal
European Comission Framework Programme 7 (FP7) – Marie Curie Actions
GEMI fund Lind Healthcare

IN VIVO DELIVERY OF ANTI-INFLAMMATORY CHIMERIC PROTEINS: ASSESSMENT OF THERAPEUTIC APPLICATION

Three hypotheses are under study:

1. That PTDs can be used to deliver HO-1 *in vivo* and prevent the development of atherosclerosis in mice;
2. That live lactic acid bacteria can be used as therapeutic "vehicles" for systemic delivery of active PTD-fused proteins in mice;
3. That live lactic acid bacteria can be used to deliver PTD-HO-1 *in vivo* and prevent the development of atherosclerosis in mice.

We showed that, when fused to a TAT domain HO-1 can prevent the pathogenesis of a variety of immune mediated inflammatory diseases.

STRESS AND CYTOSKELETON

Helena Soares

PhD in Biomedical Sciences
University of Porto, Portugal
E-mail: mhsoares@fc.ul.pt & msoares@igc.gulbenkian.pt
url: http://www.igc.pt/research/unit/33

Microtubules are polarised and dynamic polymers of tubulin that participate in a wide range of crucial cell functions. The maturation of tubulin heterodimers is a complex process involving the interaction of tubulins with several proteins: molecular chaperones (CCT) and the tubulin cofactors (TBCA-TBCE). The main goal of the Stress and Cytoskeleton group is to understand how the components of the tubulin folding pathway control tubulin synthesis, flux, transport and heterodimer recycling and therefore are putative targets for regulation of the assembly of specialised Microtubule structures (i.e cilia) and Microtubule dynamics in eukaryotic cells.

STUDY OF THE NEW CENTROSOMAL PROTEIN TBCCD1

The main aim is to characterise TBCCD1: a centrosomal protein related to RP2 and tubulin cofactor C. We reported the first characterisation of human TBCCD1, a protein related to tubulin cofactor C. TBCCD1 localises at the centrosome and at the spindle midzone, midbody and basal bodies of primary and motile cilia. Knockdown of TBCCD1 in RPE-1 cells caused the dissociation of the centrosome from the nucleus and disorganisation of the Golgi apparatus. TBCCD1-depleted cells are larger, less efficient in primary cilia assembly and their migration is slower in wound healing assays. We propose that TBCCD1 is a key regulator of centrosome positioning and consequently of internal cell organisation.

RATE AND EFFECTS OF MUTATIONS IN THE PROTOZOA *TETRAHYMENA THERMOPHILA*

See IGC Evolutionary Biology Group for details on this collaborative project.

STUDY OF THE CCT CHAPERONIN SUBUNITS IN CILIA ASSEMBLY AND MAINTENANCE IN TETRAHYMENA

The main aim is to investigate the role of the Cytosolic chaperonin CCT-subunits in cilia biogenesis and function. Tetrahymena cells lacking the zygotic expression of either CCTα or CCTd, failed to assemble new cilia, show shorter axonemes and splaying of cilia tips. An epitope-tagged CCTα rescued the gene knockout phenotype and localised primarily to cilia tips. A mutation in CCTα, G346E, at a residue also present in the related protein implicated in the Bardet Biedel Syndrome, BBS6, also caused defects in cilia and impaired CCTα localisation in cilia. In conclusion CCT subunits are essential for ciliary assembly and maintenance of axoneme structure, especially at the tips of cilia.

STUDY OF PHYSICAL PROPERTIES OF MICROTUBULES BY AFM TECHNIQUES

The main aim is to control and manipulate microtubules in order to produce new MEMS (microelectromechanical systems) for use in medical and biological applications. Microtubules are powerful spatial organisers in vivo and the possibility of using them to control the position and movement of other molecules makes these polymers attractive candidates for bionanotechnological applications. Using AFM we observed the successful alignment of microtubules on a custom-made chip by the application of fields up to 1 MV/m. To go further, we have produced a simplified glass chip to be used with an optical microscope in order to further characterise microtubule alignment and interaction with associated proteins.

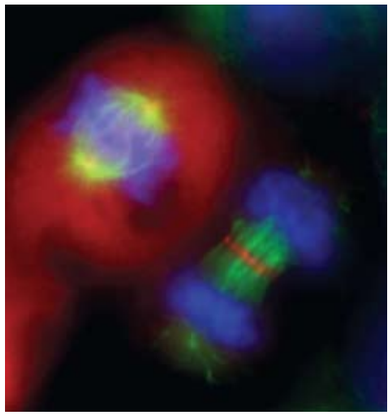
ROLE OF *BESNOITIA BESNOITI* CYTOSOLIC CHAPERONIN IN HOST CELL INVASION

The main aim is to study the molecular mechanisms underlying the cross-talk between the Besnoitia and host microtubule cytoskeletons. *Besnoitia besnoiti* is a coccidian tissue cyst-forming protozoan of the phylum Apicomplexa responsible for bovine besnoitiosis, an emerging cattle disease in Europe. Proliferation of these organisms occurs by invasion of a host cell followed by the replication. We have focused on the study of the microtubule cytoskeleton and in the role of the chaperonin CCT in isolated tachyzoites *B. besnoiti* and its characterisation during the first steps of host cell invasion. Additionally we have been studying how tubulin post-translational modifications could be affected during the invasion event.

GROUP MEMBERS
Sofia Nolasco (Post-doc)
João Gonçalves (PhD Student)
Rita Cardoso (PhD Student)
Rúben Ramalho (PhD Student)
Alexandra Tavares (Trainee)

THIS GROUP COLLABORATES WITH:
Alexandre Leitão, Helder Cortes (Instituto de Investigação Científica Tropical and Laboratório de Parasitologia-Universidade de Évora, Portugal)
Isabel Gordo (IGC)
Luis Viseu Melo (Instituto Superior Técnico, Portugal)
Juan Carlos zabala (Universidad de Cantabria, Spain)
Jacek Gaertig (University of Georgia, USA)

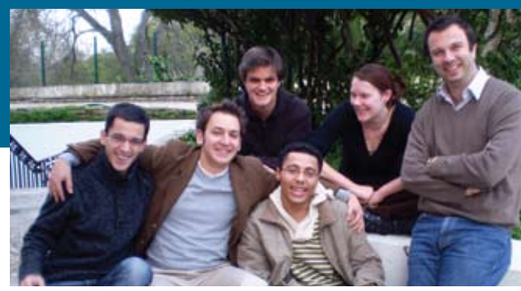
FUNDING
Fundação para a Ciência e a Tecnologia (FCT), Portugal



MITOSIS.
293T cells expressing TBCCD1-RFP and stained with an α-tubulin antibody (green) and DAPI (blue). This picture shows the localization of human TBCCD1 tagged with the fluorescent protein RFP (red) at the centrosomes in the spindle poles during metaphase and also at the spindle midzone during anaphase.

The ciliate Tetrahymena during cell division stained with an antibody against centrin. Rows of basal bodies and the old and the new oral apparatus are visible.

EVOLUTION AND DEVELOPMENT



Élio Sucena

PhD in Evolution & Development
University of Cambridge, UK
E-mail: esucena@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/57

In recent years, research in my lab has focused on evolutionary novelties. We have been approaching this concept experimentally at different levels and with diverse methodologies. Specifically, we have looked into novelty at:

1. The genetic level, namely looking at gene function evolution on gene duplication;
2. The cellular level, approaching immune cell function diversity in Drosophila;
3. The morphological level, by studying the evolutionary origin of dorsal appendage formation in the Drosophila clade;
4. The behavioural level, through the study of cooperation in rats;
5. The conceptual level by looking into the mechanisms that may underlie the origins of endosymbiosis.

THE BASIS OF MORPHOLOGICAL NOVELTY: DORSAL APPENDAGE FORMATION IN THE DROSOPHILA CLADE

Using the described developmental genetics of *D. melanogaster* egg dorsal appendage formation as a comparative model, we wish to determine the developmental mechanisms operating during oogenesis of a species without such structures *(C. capitata)* as a representatitve of the ancestral state. Ultimately, we expect this comparison to point to the genetic basis for the emergence of this morphological novelty and test it functionally using the powerful toolkit available in the *D. melanogaster* system.
We have shown that in the ancestral state represented by *C. capitata*, both the initial triggering event, grk expression and nuclear migration as well as dpp signaling are conserved accross higher dipterans. Also, at the end of oogenesis the first genetic elements that determine the dorso-ventral axis (twist, sog, dpp) have expression patterns in the medfly that are reminiscent of those described for Drosophila. These observations are consistent with our hypothesis that the novel programme which determines the dorsal appendages in Drosophila may result from the co-option of an ancient DV patterning cascade without deleterious pleiotropic effects.

FUNCTIONAL EVOLUTION UPON GENE DUPLICATION

The recently described TFD gene family of Drosophila provides a unique setup to approach the generation of novelty, particularly at the cis-regulatory level, upon gene duplication. We wish to establish the functional differences between paralogue genes within this family in order to establish clear instances of functional novelty and its corresponding genetic (nucleotidic) bases.
We have determined that TFD gene family members of clusters III and V are expressed in specific subsets of glial cells and neurons during eye disc differentiation. Our preliminary results suggest that homo- and heterophylic interactions mediated by TFD proteins could play a central role in the differentiation, migration and wrapping of neurons by glial cells in the developing eye disc. Clearly, the functional analysis of this protein family in Drosophila, *per se*, will provide important insights into nervous system development and function.

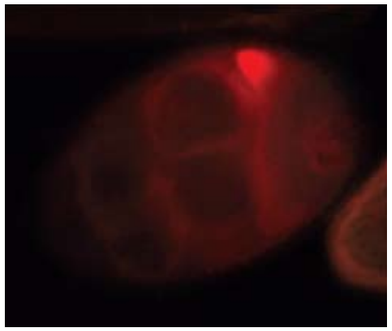
IMMUNE CELL FUNCTION DIVERSITY IN DROSOPHILA

In this project we aim at further characterising cellular immunity in Drosophila. In particular, we want to explore the putative heterogeneity of hemocyte types and their functional specificities with a view to establish their relationship with analogous functions in the (jawed) vertebrate adaptive immune system.
We have shown that, contrary to the current view, Drosophila plasmatocytes (the functional analogues of vertebrate macrophages) constitute a heterogeneous population. For this we have established a novel protocol for hemocyte purification using a combination of GFP lines, specific staining and FACS analysis.

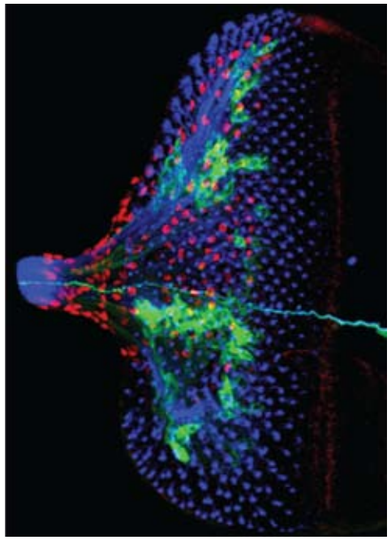
GROUP MEMBERS
Barbara Vreede (PhD Student)
Vítor Faria (Msc Student)
Alexandre Leitão (MSc Student, left October 2009)
Alexis Hazbun (MSc Student)

THIS GROUP COLLABORATES WITH:
Siegfried Roth (University of Koeln, Germany)
Fernando Roch (Centre de Biologie du Développement, France)
Jocelyne Demengeot, Thiago Carvalho, Luis Teixeira (IGC)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal
Marie Curie International Reintegration Grant, European Commission



Fluorescent in situ hybridisation for Gurken gene product in a *Ceratitis capitata* egg chamber.



Expression pattern of a TFD gene in the developing eye disc of D. melanogaster. (blue- photoreceptors, red- glial cell nuclei, green- TFD gene).

MITOSIS

Álvaro Tavares

PhD in Molecular Biology
University of Porto, Portugal
E-mail: tavares@igc.gulbenkian.pt

We are interested in understanding the mechanisms responsible for proper cell division and chromosome segregation. An increasing number of cell cycle regulatory molecules are found at the centrosomes and on the kinetochores. The inactivation or amplification of their activity has been associated with genomic instability and oncogenesis. We believe that knowledge of the basic processes of centrosome cycle and mitotic spindle dynamics will contribute to understanding the biology of cancer cells and will point the way towards novel therapeutic approaches. Towards this goal we have developed a method of identifying new kinetochore and spindle checkpoint proteins and we are elucidating their function in the regulation of chromosome segregation, by a combined approach of genetics and biochemistry. We are equally interested in determining the role of centrosomes in the regulation of cytokinesis, for which we have been analysing the function of human and Drosophila Mob-like proteins.

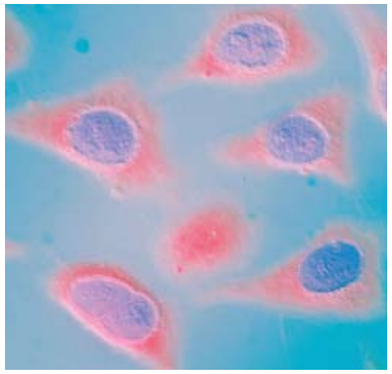
STUDY OF THE ROLE OF VERTEBRATE ADTK1, A NOVEL DUAL-SPECIFICITY SER/THR/TYR KINASE GENE FAMILY
The aim of this project is to determine the role of the gene ADTK1 in heart development

MOLECULAR DETERMINANTS OF BRAIN SIZE
Within this project we aim to determine which genes are determinant for brain size in higher eukaryotes (namely humans). In particular we will address the function of the gene Asp and why mutations in this cell cycle gene cause microcephaly.

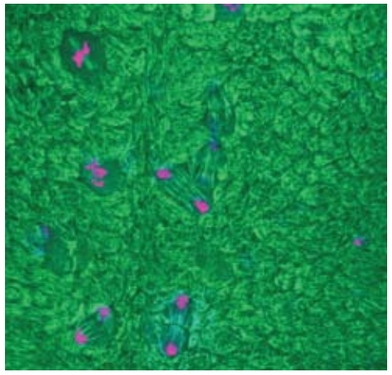
GROUP MEMBERS
Claudia Florindo (Post-Doc)
Sara Esteves (MSc Student, left September 2009)
Nuno Amaral (MSc Student)

THIS GROUP COLLABORATES WITH:
José António Belo (IBB/CBME, Universidade do Algarve, Portugal)
Maria do Carmo Avides Moreira (Universidade de Braga, Portugal)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal

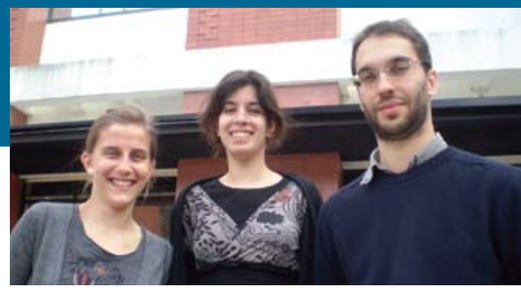


Human cells after a failed cell division resulting in the formation of a binucleated cell and of a cytoplast (cell without nucleus).



Mitosis in a Drosophila embryo.

HOST MICROORGANISM INTERACTIONS



Luis Teixeira

PhD in Biomedical Sciences
University of Lisbon, Portugal/European Molecular Biology Laboratory
E-mail: lteixeira@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/100

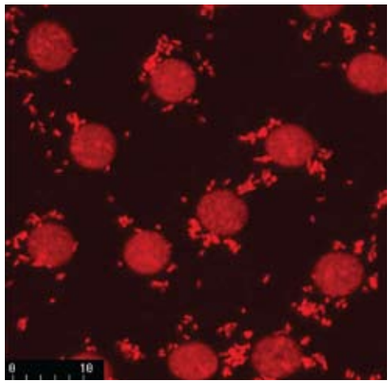
THIS GROUP WAS ESTABLISHED AT THE IGC IN JANUARY 2009

Multicellular organisms and microorganisms are continuously interacting. Many of these interactions are mutually beneficial. However, multicellular organisms have to actively thwart invasion by opportunistic or overtly pathogenic microbes. We are studying the interaction of the model organism *Drosophila melanogaster* with different microorganisms, in particular intracellular ones. *D. melanogaster* has been successfully used as a model system to study innate immunity against many pathogens. Recently it has been shown that several innate immunity pathways against viruses are conserved between insects and mammals. We are investigating mechanisms of resistance to viruses in the fruit fly. Interestingly, we have found that the intracellular bacteria Wolbachia confer resistance to RNA viruses in *D. melanogaster*. We want to understand the molecular basis of this induced resistance. Finally, we are interested in the interplay between Drosophila and Wolbachia itself. These endosymbionts are one of the most widespread intracellular bacteria in the world but little is known, at the molecular level, on how the hosts control Wolbachia or Wolbachia manipulate the hosts.

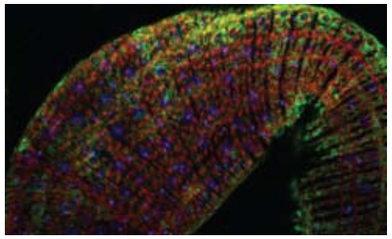
GROUP MEMBERS
Sabine Patot (Post-doc)
Pamela Raposo (Technical assistant)
Sara Esteves (Technical assistant)

THIS GROUP COLLABORATES WITH:
Michael Ashburner (University of Cambridge, UK)

FUNDING
Fundação para a Ciência e a Tecnologia (FCT), Portugal



DNA STAINING, WITH PROPIDIUM IODIDE, OF EARLY DROSOPHILA EMBRYOS. Large circles correspond to nuclei, smaller dots to the endosymbiotic bacteria Wolbachia.



DROSOPHILA ADULT GUT INFECTED WITH DROSOPHILA C VIRUS. Actin in red, DNA in blue, virus in green.

EVOLUTIONARY GENETICS

Henrique Teotónio

PhD in Evolutionary Biology
University of Lisbon, Portugal
E-mail: teotonio@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/56

The main objective of the Evolutionary Genetics group is to study the genetics of adaptation using experimental evolution, by testing current evolutionary theory. Adaptation and the study of natural selection and its consequences are central to any understanding of biology because they provide a comprehensive framework for the origin, divergence and maintenance of diversity. We use experimental evolution to integrate the study of variation at the phenotype level with the study of variation at the genotype level.
Since setting up at the IGC, we have established experimental evolution populations of *Caenorhabditis elegans*, whose ecology is described by discrete non-overlapping generations at constant 10^4 census sizes, under benign resource conditions. These populations were manipulated to initially have levels of outcrossing and genetic diversity. Phenotyping is carried out at the level of fitness-proxies, life-history and RNA expression. Genome-wide linkage disequilibrium association mapping is carried out to determine the number and relative effects of the loci underlying adaptation. Numerical simulations are used to obtain the expected distributions of relevant statistics under the conditions of experimental evolution.
Our work with *Drosophila melanogaster* similarly addresses the genetic basis of adaptation by correlating the observed patterns of DNA sequence diversity with the phenotype distributions. In Drosophila we are particularly interested in understanding the process by which populations can revert to ancestral phenotype and genotype states, from standing genetic variation.
Prelimiminary conclusions from our work with both model systems are that evolution from standing genetic variation may involve the non-linear interaction among large genomic regions (10-50kb), encompassing several functional ORFs, through within generation negative frequency dependence among them. In *C. elegans*, we have been able to observe the evolution of male function, indicative of their role promoting adaptation to novel environments, through increased outcrossing rates. Inbreeding depression does not *per se* explain the maintenance of androdioecy in this organism. Future avenues of research include the explicit modelling of adaptation in the laboratory from the details of population genetics.

DROSOPHILA MOLECULAR POPULATION GENETICS

The aim of this project is to determine patterns of DNA sequence evolution during Drosophila reverse experimental evolution.
In 2009 we have achieved: 1) Genotyping of > 40 populations at ~80SNPs, at several time points during experimental evolution; 2) Performed the statistical analysis of the data obtained.

C. ELEGANS LABORATORY ADAPTATION

This project aims to 1) Determine patterns of DNA sequence evolution during laboratory adaptation; 2) Determine selective costs of androdioecy versus diocy under conditions of standing genetic variation.
During 2009 we were able to carry out 1) Genotyping of ~10 populations and >300 inbred lines derived from them at ~50SNPs; 2) competition experiments between dioecious and androdioecious lab adapted populations.

GROUP MEMBERS
Ivo Chelo (Post-doc)
Sara Carvalho (PhD student)

THIS GROUP COLLABORATES WITH:
Anthony D. Long (University California, USA)
Patrick Phillips (University of Oregon, USA)

FUNDING
European Research Council (ERC)
Fundação Calouste Gulbenkian (FCG)-IGC, Portugal

INNATE BEHAVIOUR

Maria Luisa Vasconcelos

PhD in Neuroscience
Universidade Nova de Lisboa, Portugal
E-mail: vasconcelos@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/93

THIS GROUP IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

Animals exhibit behavioural repertoires that are often innate and result in stereotyped sexual and social responses to their environment. Innate behaviors do not require learning or experience and are likely to reflect the activation of developmentally programmed neural circuits. We are interested in the nature of defined neural circuits: how activation of circuits elicits specific behaviours. In complex organisms it has been extremely difficult to study a circuit beyond the early stages of sensory processing. *Drosophila melanogaster* is an attractive model system to understand a circuit because flies exhibit complex behaviours that are controlled by a nervous system that is numerically five orders of magnitude simpler than that of vertebrates. We use a combined behavioural, genetic, imaging and electrophysiological approach to determine how defined neural circuits and their activation elicit specific behaviours.

FEMALE RECEPTIVITY

Genetic studies have elucidated how Drosophila male courtship behaviour is specified and its circuit components are being dissected at a surprising speed. The circuit of female behavior on the other hand has been largely uncharacterised.
We have setup a behavioural protocol that allows us to selectively inactivate subsets of neurons in the adult flies only. We have tested lines of flies with different subsets of inactivated neurons and isolated lines that have a behavioural phenotype.

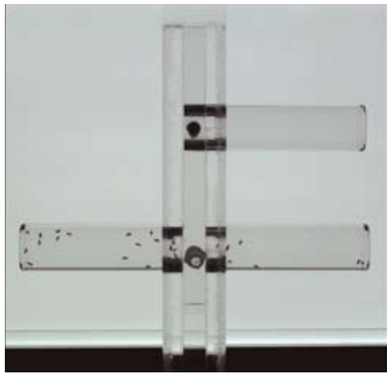
ACROSS-SPECIES STRESS ODOUR RESPONSE

Stressed *Drosophila melanogaster* release an aversive odorant that elicits a robust avoidance response in test flies. We wish to test this response in closely related species with different feeding habits.
Our data indicate that stress odour avoidance is not common to all Drosophilids. The response index to the odour of stressed *D. melanogaster* is similar for *D. melanogaster*, *D. simulans* and *D. mauritiana* but switches from repulsion to attraction for *D. sechellia* and *D. erecta*. This behavioural difference between melanogaster and some of its sister-species provides a powerful framework, amenable to genetic, developmental and anatomical dissection, to investigate how evolution has shaped distinct responses to an environmental cue.

GROUP MEMBERS
Dennis Hermann (PhD student)
Nuno Martins (MSc Student)
Sophie Dias (Research Technician)
Joao Afonso (Research Technician)

FUNDING
IGC start-up fund
Oeiras City Council Professor António Xavier Young Scientist's Installation Award, Portugal
Marie Curie International Reintegration Grant, European Comission
Fundação para a Ciência e Tecnologia (FCT), Portugal

FEMALE RECEPTIVITY.
Single couples are placed in an arena. The females have subsets of neurons inactivated.



STRESS ODOR RESPONSE.
When allowed to choose between a vial with the odor of stressed vials and a empty vial, flies choose the empty vial (left side).

BACTERIAL SIGNALLING

Karina B. Xavier

PhD in Biochemistry
Universidade Nova de Lisboa, Portugal
E-mail: kxavier@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/73

Bacteria use small chemical molecules called autoinducers to communicate with one another by a process called quorum sensing. This process enables a population of bacteria to regulate behaviours which are only productive when many bacteria act in concert as a group, similarly to what happens with multi-cellular organisms. Behaviours regulated by quorum sensing are often crucial for successful bacterial-host relationships whether symbiotic or pathogenic. In our laboratory, biochemical and genetic approaches are used to study the molecular mechanisms underlying quorum sensing, with an emphasis on systems promoting bacterial inter-species communication. This research includes an integrated study involving elucidation of the chemical molecules that are used as signals, the network components involved in detecting the signals and processing information inside individual cells, and finally characterisation of the behaviour of the bacterial community in multi-species bacterial consortia. Our ultimate goal is to understand how bacteria use inter-species cell-cell communication to coordinate population-wide behaviours in consortia and in microbial-host interactions.

IDENTIFICATION AND CHARACTERISATION OF QUORUM SENSING SYSTEMS INVOLVED IN BACTERIAL INTER-SPECIES COMMUNICATION

The possible role of autoinducer-2 in regulating inter-species communication has been accompanied with great enthusiasm by the scientific community. However, the molecular mechanisms involved in autoinducer-2 recognition and signal transduction are poorly understood. In this project we will identify novel autoinducer-2 signal transduction pathways and use this knowledge to study the role of these signals in bacterial-bacterial, and bacterial-host interactions.

We used sequence analysis and structure prediction to establish a set of criteria for identifying functional autoinducer-2 receptors in bacteria with complete genome sequences. We tested these predictions experimentally in key bacterial species and we were able to demonstrate the presence of functional autoinducer-2 receptors in the families Enterobacteriaceae, Rhizobiaceae, and Bacillaceae. Our experimental results strongly supported our ability to identify functional autoinducer-2 receptors.

We expect that our method may be widely applicable in identifying novel autoinducer-2 receptors as new genome sequences become available. This will further elucidate the widespread use of this signal in the bacterial world.

GROUP MEMBERS
Michal Bejerano-Sagie (Post-doc)
Catarina S. Pereira (PhD student)
Rita Valente (PhD student)
Bruno A. C. Afonso (MSc Student, left September 2009)
Daniel Marques (MSc Student, left September 2009)
Andreia Correia (Research Technician, left June 2009)

THIS GROUP COLLABORATES WITH:
Stephen Miller (Swarthmore College, USA)
Pedro Lamosa (ITQB, Portugal)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal

BIOLUMINESCENCE OF *VIBRIO HARVEYI* CULTURE.
Vibrio harveyi is the model bacteria we use in our laboratory to study the response to inter-species quorum sensing signals. This organism is a marine bacterium which regulates its own light production by sensing and responding to autoinducer signal molecules. *V. harveyi* produces species-specific autoinducers and also the universal bacterial signal, AI-2. By integrating the response to these two signals this bacterium is capable of counting its own cell numbers and also the bacteria cells from all the species present in its vicinity.

COMPLEX ADAPTIVE SYSTEMS AND COMPUTATIONAL BIOLOGY

Luis Mateus Rocha

PhD in Systems Science
State University of New York, USA
E-mail: rocha@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/76
http://cnets.indiana.edu/groups/casci3

We are interested in the informational properties of natural and artificial systems which enable them to adapt and evolve. This means both producing computational models of biological systems to understand the evolutionary role of information, as well as abstracting principles from biology to produce adaptive information technology. Our current research projects are on complex dynamics in biological networks (gene regulation, cell signaling, and metabolic networks), text and literature mining (in proteomics, protein-protein interaction and pharmokinetics), computational models of RNA editing, artificial immune systems, genomic multivariate analysis, evolutionary systems, artificial life, cognitive science, and biosemiotics.

BIOMEDICAL LITERATURE MINING

The aims are to carry out literature-based automatic discovery, classification and annotation of protein-protein and gene-disease interactions, pharmokinetic data, protein sequence family and structure prediction, functional annotation of trancription data, enzyme annotation publications, etc. Top team in the Article Classification task of the Biocreative II.5 challenge-topic was protein-protein-interaction. We developed our binary classification method to be applicable to full-text documents and developed a novel citation network classifier. We were also successful in showing that literature mining can be used to automatically obtain drug-specific pharmokinetic numerical data for human and animal experiments.

COLLECTIVE DYNAMICS IN COMPLEX BIOCHEMICAL NETWORKS

The dynamics of complex biochemical networks, to identify control, modularity, robustness and collective computation. We are currently working with models of genetic regulation in yeast, body segmentation in Drosophila, intracellular signal transduction in fibroblasts, a genome-scale transcriptional and metabolic network for E-Coli, and others. Our EU ERA Complexity programme proposal was one of the 28 (out of 117) that passed to the full-proposal stage. We also submitted proposals to FCT, NSF and the John McDonnell Foundation which are under evaluation. Our work entails collaborations with Marta Cascante (Barcelona), Jim Crutchfield (UC Davis), Santiago Schnell (Michigan), Luis Amaral (Northwestern), George Kampis (Budapest), and Miguel Rocha (U Minho). We are also collaborating with Claudine Chaouiya and Filipa Alves at IGC.

COMPUTATIONAL MODELS OF RNA EDITING

Models to study the evolutionary implications of genotype editing in the living organisation. Our goal is twofold: (1) to study the role of RNA Editing regulation in the evolutionary process, and (2) to investigate the conditions under which genotype edition improves the optimisation performance of evolutionary algorithms. We developed an entirely new code on Python for more expansive simulations, and initiated a collaboration with Alekos Athanasiadis (IGC) and Stefan Mas (Lehigh).

ARTIFICIAL MODELS OF T-CELL CROSS-REGULATION

We use Carneiro's Model of Cross-regulation in T-Cell dynamics to produce bio-inspired algorithms for binary classification. The goal is to gain further insights about T-Cell Cross-regulation in the vertebrate Immune System, and produce useful bio-inspired algorithms for text mining and spam detection. We have developed new simulations to model the effects of: presentation sequence of self and nonself antigens, rates of apoptosis, and dependence on initial conditions. Integrated part of this research in FCT-funded project on "Insitutional Robotics" with Pedro Lima and Jorge Carneiro.

STOCHASTIC MODELS OF TOPOLOGY CONSTRAINTS ON COMPLEX NETWORKS

This porject aims at the study of transitive properties of complex networks modeled as weighted graphs. Studying the impact of alternative distance measures on scale free and small-World behaviour, and developing stochastic models of vertex aging in networks, to better predict network growth. Ongoing analysis of large-scale wikipedia data, networks of neuronal activity, etc. Started collaboration with Nuno Crato (ISEG) to model decision-tree searches.

GROUP MEMBERS
Manuel Marques-Pita (Post-doc)
Artemy Kolchinsky (PhD Student)
Azadeh Nematzadeh (PhD Student)
Tiago Simas (PhD Student)
Alaa Abi-Haidar (PhD Student)

THIS GROUP COLLABORATES WITH:
Anália Lourenço and Miguel Rocha (Universidade do Minho, Portugal)
Hagit Shatkay (Queen's University, Canada)
Marta Cascante (University of Barcelona, Spain)
Jim Crutchfield (University of California, Davis, USA)
Santiago Schnell (Michigan University, USA)
Luis Amaral (Northwestern University, USA)
George Kampis (University of Budapest, Hungary)
Claudine Chaouiya, Filipa Alves, Alekos Athanasiadis and Jorge Carneiro (IGC)
Stefan Mass (Lehigh University, USA)
Pedro Lima and Porfirio Silva (Instituto Superior Técnico, Portugal)
Nuno Crato (Instituto Superior de Economia e Gestão, Portugal)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal
Programa de Bolsas Científicas de Oeiras - Professor António Xavier, Câmara Municipal de Oeiras, Portugal
FLAD Computational Biology Collaboratorium

Control modules in the Drosophila Segment Polarity network. The essential regulation is shown as a bipartite graph, where round nodes correspond to genes or proteins in specific states (1 expressed, 0 not expressed); diamond-shaped nodes are state-transition patterns.

RESEARCH FELLOWS

PLANT GENOMICS

Jörg Becker

PhD in Biology
University of Bielefeld, Germany
E-mail: jbecker@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/102

Our group is interested in the mechanisms underlying sexual reproduction and early embryogenesis with a particular focus on the role of the male gametes. Contrary to previous assumptions, recent studies have shown that male gametes both in the plant and animal kingdom carry complex sets of RNA molecules, including not only mRNAs but also small RNAs. We are particularly interested in the role of these two RNA classes before, during and after double fertilisation as it occurs in higher plants. Using *Arabidopsis thaliana* as our primary experimental model we are addressing specific questions like:

1. What are the functions of small RNA and DNA methylation pathways in sperm cells?
2. Do sperm cell-derived RNAs play a role after fertilisation?
3. Do conserved core sets of genetic modules underlie common characteristics of male gametes across kingdoms?

In a second research line we are analysing the symbiotic transcriptome of the model legume *Medicago truncatula*.

THE ROLE OF SPERM DERIVED SMALL RNAS DURING SEXUAL REPRODUCTION IN ARABIDOPSIS

Deep sequencing of small RNAs from FACS-isolated sperm cells of *Arabidopsis thaliana* has shown that they contain numerous siRNAs and miRNAs. We are analysing the potential role of these small RNAs for sperm cell viability and, if being delivered to the female gametes upon fertilisation, for the regulation of early embryogenesis and endosperm development.
A novel class of 21nt siRNAs deriving from the reactivation of Athila retrotransposons in the vegetative nucleus of pollen was identified. The siRNAs accumulate in the adjacent sperm cells where these transposable elements (TEs) are silenced. On a broader scale the results suggest that the reactivation of TEs in germline companion cells reveals intact TEs in the genome in order to effectively silence these TEs in the gametes (details in Slotkin et al, Cell 136(3): 461-72, 2009). In addition we identified dozens of miRNA families, with a number of them showing higher expression levels in sperm cells than in whole pollen.

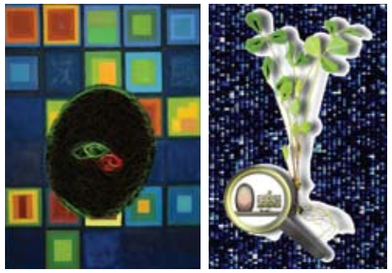
IDENTIFICATION OF CONSERVED GERM CELL-SPECIFIC MODULES AS POTENTIAL PRECURSORS OF TOTIPOTENCY

Despite the variety of mechanisms distinguishing germ cell differentiation and fertilisation strategies in plants and animals, the molecular pathways towards totipotency are likely to remain conserved. This project focuses on the identification of a conserved core set underlying the totipotent potential of the gametes through the functional analysis of transcripts encoding orthologue gene products in male gametes of plant, human and fly.
We have obtained the transcriptional profiles of human and fly sperm, and initiated the combined comparison with our plant sperm cell data.

GROUP MEMBERS
Filipe Borges (PhD student)
Patrícia Pereira (Trainee)

THIS GROUP COLLABORATES WITH:
Rob Martienssen (Cold Spring Harbor Laboratory, USA)
Keith Slotkin (Ohio State University, USA)
Rui Gardner, Rui Martinho (IGC)
Ji He (The Samuel Roberts Noble Foundation, USA)
Carlos Plancha (Cemeare Lda, Portugal)
Helge Küster (Leibniz University Hanover, Germany)
Helena Carvalho (Instituto de Biologia Molecular e Celular, Portugal)
Leonilde Moreira (Instituto Superior Técnico, Portugal)

FUNDING
Fundação Calouste Gulbenkian (FCG)-IGC, Portugal



Left – Genetic and epigenetic mechanisms of the male germline in Arabidopsis highlighted by genome-wide transcriptomics. An artist's impression showing a mature pollen grain of Arabidopsis enclosing the two gametes (sperm cells) and the companion vegetative nucleus, overlaid on an oil painting representing a DNA microarray. **Right** – A gene expression map of *Medicago truncatula* root symbioses. Schematic representation of root nodule and mycorrhizal symbiosis formed by the model legume plant Medicago, superimposed on unprocessed expression data as obtained by DNA microarray analysis.

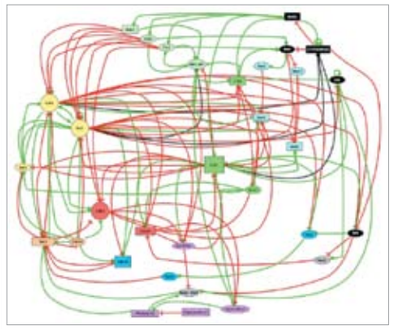
NETWORK MODELLING

Claudine Chaouiya

PhD in Computer Science
University of Nice-Sophia Antipolis, France
E-mail: chaouiya@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/108

Advances in molecular biology, genomics and functional genomics open the way for a better understanding of regulatory mechanisms. These mechanisms interplay and operate at diverse levels (transcription and translation of the genetic material, protein modifications, etc.). They define large and complex networks, which in turn constitute a relevant functional framework to integratively study the control of cellular processes. To assess the behaviors induced by such networks, dedicated mathematical and computational tools are arguably needed. In this context, our goal is to develop generic tools for the modelling and analysis of large molecular networks. For this purpose, we mainly rely on qualitative modelling approaches combining the generalised logical formalism and Petri nets. In close collaboration with biologists, methodological developments are systematically challenged with real case applications, specifying and analysing models for the control of cell proliferation and differentiation.

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal



Cell cycle control in yeast (A. Faur et al (2009) Molecular BioSystems, 5:1787-96)

LUPUS AND AUTOREACTIVE IMMUNE REPERTOIRES

Constantin Fesel

PhD in Immunology
Université Paris VI / Institut Pasteur, France
E-mail: cfesel@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/98

Systemic Lupus Erythematosus (SLE) is an autoimmune disease where an altered immune physiology and self-reactive repertoires of both B- and T-cells are intimately connected. In this context it is now known that autoreactive IgG antibodies, the diagnostic hallmark of SLE, diversify many years before the disease becomes clinically manifest. Furthermore, bearers of SLE-associated autoantibodies are far from always developing overt pathology: we and others have documented that particularly unaffected relatives of SLE patients frequently show enhanced autoreactivity, the pathologic potential of which, however, appears under efficient control. Based on our finding that the autoreactivity in this group, other than in SLE patients, was throughout positively correlated with regulatory T-cell activity, we are now following the aim to characterise this T-cell regulation and to explore the possibility to make use of it in novel therapeutic approaches to SLE.

LUPUS AND ITS COMPENSATION IN UNAFFECTED RELATIVES BY T-CELL REGULATION

The aim os this study is to study the hypothesised compensation of potentially pathogenic effects of lupus-associated autoantibodies, by regulatory T-cells, in first-degree relatives of Systemic Lupus Erythematosus patients, in comparison with the patients themselves and unrelated control subjects.
In collaboration with various clinical centers and the ICBAS in Porto, we are following an integrated approach to assess specific and broad-scale autantibody profiles, cytometric characterisations of T-cells, B-cells and antigen-presenting cells with and without stimulation, functional immune parameters as well as relevant genotypes and some other parameters, all strictly in parallel. Laboratory procedures have been established since the beginning of this project in 2009. Regular sample collections and systematic data acquisition are currently underway.

GROUP MEMBERS
Nuno Costa (Trainee)

THIS GROUP COLLABORATES WITH:
Maria Berta Silva Martins
(Instituto de Ciências Biomédicas Abel Salazar, Portugal)
Carlos Vasconcelos, Margarida Lima
(Hospital Geral de Santo Antonio, Portugal)
Cristina João, Ana Elisabete Pires
(Centro de Investigação de Patologia Molecular, Portugal)
Carlos Ferreira, Maria Francisca Fontes
(Hospital de Santa Maria, Portugal)
Jorge Martins and colleagues (Hospital dos Marmeleiros, Portugal)

FUNDING
Fundação Calouste Gulbenkian (FCG)-IGC, Portugal

NEURONAL STRUCTURE AND FUNCTION

Inbal Israely

PhD in Molecular and Medical Pharmacology
University of California, Los Angeles
E-mail: iisraely@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/105

THIS GROUP WAS ESTABLISHED AT THE IGC IN JULY 2009 AND IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

We are interested in understanding how activity can lead to specific structural changes in neurons which may be important for learning, and how such changes affect connectivity within neural circuits. We would also like to understand how the structural diversity among neurons contributes to connectivity in the brain. The current focus is on single neurons, even single spines, to understand the cellular mechanisms that are important for synaptic plasticity and learning. By combining molecular and genetic tools together with imaging and electrophysiological methodologies, we investigate how information is physically stored in the brain.

DENDRITIC COMPARTMENTALISATION OF PROTEIN SYNTHESIS-DEPENDENT SYNAPTIC PLASTICITY

The ability to alter synaptic strengths is believed to be a cellular mechanism by which memories can be encoded and retained. We utilise 2-photon microscopy to stimulate individual synapses and to visualise the changes that occur in living spines in response to this activity. We look at how local protein synthesis plays a role in these changes, and how activity at one site can lead to either cooperation or competition at nearby locations.
We have set up a 2-photon microscopy system that allows us to stimulate individual spines of neurons, to visualise structural changes at those spines, and to measure the electrophysiological changes related to these stimulations. We find that strong stimulation at one spine facilitates plasticity at neighbouring spines; furthermore, this facilitative effect decreases with increasing time and distance between spines. Paradoxically, stimulated spines can also compete for cellular resources if stimulated too closely together in time. These findings help define the rules that govern changes in synaptic plasticity and structure, and can elucidate how stable memory engrams are stored at synapses of a neuron.

STRUCTURAL CORRELATES OF BIDIRECTIONAL CHANGES IN SYNAPTIC EFFICACY

While there is growing evidence demonstrating that potentiation can drive spine enlargement at individual synapses, it is unclear whether the wide variety of synaptic inputs experienced by a neuron can be structurally differentiated or graded in relation to experience. We aim to determine what are the structural changes correlated with various forms of long lasting synaptic depression. We will examine whether the structural changes in response to long term synaptic depression are akin to those observed during long term potentiation, or if they lead to opposite changes.
We are establishing several paradigms by which to induce long lasting synaptic depression at individual synaptic sites. This involves various methods which activate metabotropic glutamate receptors (mGluRs). We are recording electrophysiological responses from neurons following such stimulations in addition to visually monitoring any related structural changes. We are also examining whether dendritically synthesised proteins generated as a result of mGluR mediated synaptic depression at specific spines localise to the site at which plasticity is induced.

GROUP MEMBERS
Yazmín Ramiro Cortés (Post-doc)

FUNDING
Fundação Champalimaud, Portugal

NEUROETHOLOGY LABORATORY

Susana Lima

PhD in Neuroscience
University of Lisbon, Portugal
E-mail: slima@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/92

THIS GROUP IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

Mate choice is a decision-making process observed throughout the animal kingdom. The outcome of this behaviour has deep evolutionary consequences, if we consider that only the genes of animals that can successfully mate will pass to the next generation. To advertise themselves, prospective mates display a variety of signals and cues that are picked up by the sense organs of choosers. A lot of effort has been dedicated to elucidating the nature of the cues employed to broadcast attractiveness, but very little is known about the mechanistic basis for mate preference, how the decision to select a better mate based on the animal´s preferences is taken and how it is used to trigger the appropriate behaviour. Using mice as a model system, our laboratory is interested in obtaining a mechanistic understanding of how the brain implements the necessary computations to achieve this goal.

BEHAVIOURAL PARADIGMS AND NEURAL MECHANISMS UNDERLYING MATE PREFERENCE AND SELECTION IN MICE

How the decision to select a better mate based on the animal´s preferences is taken and how it is used to trigger the appropriate behaviour is the aim of our research. Using mice as model system, our laboratory is interested in obtaining a mechanistic understanding of how the brain implements the necessary computations to achieve this goal.

We have performed experiments to test if females of the strain PWD prefer to interact with males of their own strain or of the PWK strain. Preliminary data suggests that PWD females prefer to stay near a PWK male when compared to a male of their own strain. The experiments were performed in a Y-maze apparatus and we have measured the time spent near each male during a period of 15 minutes. The results indicate that PWD prefer to interact with males from the other strain, which means that they might prefer to mate with males that are genotypically different from them. This is, they seem to be doing inbreeding avoidance.

GROUP MEMBERS
Léa Zinck (Post-doc)
Vanessa Urbano (Research Technician)

THIS GROUP COLLABORATES WITH:
Zack Mainen, Rui Costa, Marta Moita
(IGC/Champalimaud Foundation, Portugal)

FUNDING
Marie Curie International Reintegration Grant, European Comission
Champalimaud Foundation, Portugal

ANTIGEN PRESENTATION AND T CELL ACTIVATION

Elisabetta Padovan

PhD in Immunology
University of Padova, Italy
E-mail: epadovan@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/97

T cells are central actors of antigen-specific immune responses and their function is strongly influenced by signaling through Pattern Recognition Receptors (PRR). While the instructive role of PRR in the cell fate decisions of naïve T lymphocytes has been largely investigated, a careful analysis of how PRR agonists modulate effector T cell function is still missing and is the topic of our research.

Our specific goals are:

1. To dissect how cooperation among different Antigen Presenting Cells (APC) and PRR signaling influences the expansion and function of effector T cells;
2. To study the biological outcome of the interaction between effector T cells with different types of APC;
3. To characterise the molecular dynamics occurring at the interface of APC/T cell conjugates.

HOW PATTERN RECOGNITION RECEPTORS SIGNALING CONTROLS T LYMPHOCYTES ACTIVATION

Classically, CD4+ T cell responses result from the triggering of T cell receptors (TCR) expressed on T cells by specific MHC-II/peptide complexes on Antigen Presenting Cells (APC), and the outcome of this process is influenced by the engagement of Pattern Recognition Receptors (PRR). Cooperation between different APC types and PRR signaling is likely to influence CD4+ T cell activation with both positive and detrimental consequences.

By employing human T cell clones producing IFN-γ and/or IL-17 we aim to assess how signaling through PRR modulates effector CD4+ T cell activation and how these cytokine-polarised effector T cells communicate with APC.

During 2009, we have:

1. isolated and characterised T cell clones from healthy individuals producing IFN-γ or IL-17, named Th1 and Th17 respectively (Fig. 1);
2. generated different APC types (Fig. 2);
3. begun to assess the biological consequences of the crosstalk between APC and effector T cells.

We find that, although Th1 and Th17 clones are equally activated by different APC types (Fig. 3A and B), the cytokine pattern elicited in APC/T cell co-cultures during antigen presentation depends on the type of APC responding to the activated T cell (Fig. 3C and D). We are currently dissecting the molecular basis of this APC/T cell crosstalk, how signaling through PRR modulates this crosstalk and its consequences on cognate and bystander cell activation.

THIS GROUP COLLABORATES WITH:
Jorge Carneiro (IGC)
Markus Simon (Max Planck Institute for Immunebiology, Germany)

FUNDING
Fundação para a Ciência e Tecnologia (FCT), Portugal

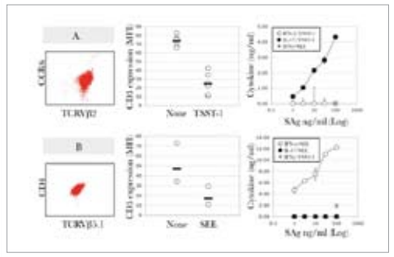


Fig. 1.
T cell clones. (A) A Th17 clone expressing TCRVβ2 and responding to the model antigen TSST-1. (B) A Th1 clone expressing TCRVβ5.1 and responding to the model antigen SEE.

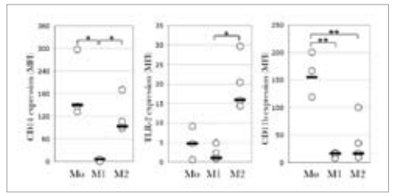


Fig. 2.
APC phenotype. Expression of CD14 (left panel), TLR-2 (central panel) and CD11b (right panel) in freshly isolated peripheral blood monocytes (Mo) and monocyte-derived macrophages upon culture in GM-CSF (M1) or M-CSF (M2). *P<0.05; **P<0.005.

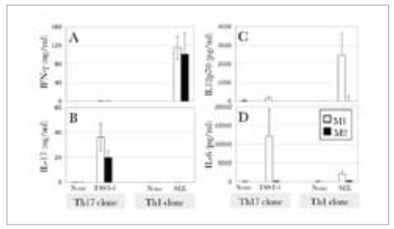


Fig. 3.
APC/T cell crosstalk. Cytokine patternhs of macrophages/Th co-cultures. (A, B) Th17 and Th1 clones express their respective signature cytokine in response to the specific enterotoxin-pulsed M1 and M2 macrophages. (C, D) IL12p70 and IL-6 characterize the response of M1/Th1 and M1/Th17 co-cultures, respectively.

DOPAMINE IN ACTION LEARNING

Joseph Paton

PhD in Neurobiology and Behavior
Columbia University, USA
E-mail: jpaton@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/87

THIS GROUP IS A MEMBER OF THE CHAMPALIMAUD NEUROSCIENCE PROGRAMME AT THE IGC

The film director Elia Kazan once said that directing is "turning psychology into behaviour". Your brain is charged with the same task every moment you are awake. Aside from reflexes, actions are almost always, at least initially, directed in nature. Disease states such as Parkinson's disease, where voluntary action is inhibited, and obsessive compulsive disorder and drug addiction, where actions cannot be terminated, highlight the importance of proper direction of action for normal functioning. The core of my laboratory's research is to study the neural mechanisms by which the actions that make up adaptive behaviour are learned and generated. Taking a cue from Mr. Kazan, we begin by developing well-controlled behavioural tasks, using rodents as models systems. We are currently focusing on how the neurotransmitter dopamine (DA) modulates neural functioning within the basal ganglia, an evolutionarily aged collection of structures historically thought of as being important for movement. Among other things, DA appears important for normal timing of behavioural responses. Thus, we have started by developing cognitive tasks in which rodents must learn to time intervals. Our approach employs multi-site neurophysiological recordings, as well as theoretical, pharmacological, and molecular biological techniques.

NEUROPHYSIOLOGY OF TIME ENCODING IN THE RODENT STRIATUM

We aim to identify neural correlates of time intervals that rats estimate during performance of a novel timing task.
In 2009, we succeeded in training rats to press a lever in order to gain rewards at defined intervals, classically called operant conditioning on a Fixed Interval (FI) reinforcement schedule. We have adapted the classical FI schedule such that in blocks of 30 trials, on average, we shift the fixed interval over a range of about one minute. We call this schedule a Serial Fixed Interval (SFI) schedule of reinforcement and have analysed rats' behaviour and initiated neurophysiological recordings during this task. Rats begin responding after the midpoint of the reinforcement interval. We then shift the interval of reinforcement in blocks of trials to a different interval and animals shift the time at which they begin to respond, giving us a behavioural readout that reflects the animals changing knowledge about time until reward. Animals learn the interval associated with each block quickly, adapting their response times within five or fewer cycles of reward. This allows us to test animals on as many as ten intervals across a range of about one minute during single sessions. This wide range of variation in estimated interval gives us statistical power when searching for neural correlates of timing behaviour.

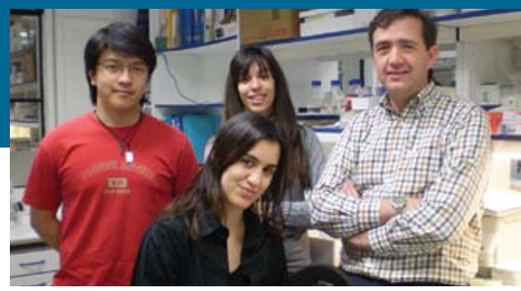
OPTOGENETIC MANIPULATION OF TIMING BEHAVIOUR

We aim to test the hypothesis that direct and indirect pathways within the basal ganglia exert opponent effects on timing behaviour.
In the past year, we have initiated a parallel set of timing studies in mice in order to take advantage the increased molecular power of the mouse relative to the rat. We have trained mice on a classic temporal reproduction task, called the peak interval task, and are currently training mice on the SFI task mentioned above. By combining viruses dependent on CRE recombinase activity for expression of transgenes, with mouse lines expressing CRE in specific basal ganglia cell types, we plan to express light sensitive channels and pumps in targeted locations within the basal ganglia circuit. Stimulating these proteins with light during experiments will provide us with two potentially powerful pieces of data. First, we will be able to ask what type of cell we are recording from *in vivo* much more easily and in higher volume than was available with older techniques. Second, we can test hypotheses about the role of activity in specific populations of neurons for timing behaviour.

GROUP MEMBERS
Rui Azevedo (PhD student)
Sofia Soares (MSc student)
Gustavo Mello (MSc student)

THIS GROUP COLLABORATES WITH:
Joshua T. Dudman (Janelia Farm Research Campus, Howard Hughes Medical Institute, USA)

CARDIAC REGENERATION



Luís Brás Rosário

PhD in Medicine and Physiology
University of Lisbon, Portugal
E-mail: lrosario@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/99

Our main areas of research are:

1. The determination by invasive and noninvasive parameters of left ventricular function;
2. Autonomic cardiovascular control, in particular the central angiotensin system in acute myocardial infart;
3. Cardiac imaging for quantification of left ventricular function and determination of indexes of severity of valvular disease, clinical research in heart failure and coronary syndromes.

MODULATION OF CARDIOVASCULAR ADAPTATION TO DISEASE: IMPACT OF STEM CELL TRANSPLANTATION ON POST MYOCARDIAL INFARCT REMODELLING AND ARRHYTHMIAS

The aim of this project is to determine the factors responsible for the control of proliferation and differentiation of cardiac stem cells.
In 2009 we were able to identify the main proteins in the cellular membrane of the cardiac stem cells. We also isolated the differentially expressed micro RNA in these cells. Together these two approaches give us the data to isolate the receptors and membrane proteins involved in the cellular interactions that may control proliferation and differentiation, as well as information on one of the mechanisms involved in transcription control, micro RNA. These data will be used in current research protocols of differentiation and proliferation control mechanisms.

GROUP MEMBERS
Alex Jun Matsuda (Trainee)
Laura Rodrigues (Trainee, left December 2009)

THIS GROUP COLLABORATES WITH:
Carlos Cordeiro, Margarida Gama-Carvalho (University of Lisbon, Portugal)
Adélia Sequeira (Instituto Superior Técnico, Portugal)
José António Bello (University of Algarve, Portugal)
Piero Anversa (Harvard Medical School, USA)
Miguel Soares (IGC)

FUNDING
Fundação Calouste Gulbenkian (FCG), Portugal
Quadro de Referência Estratégico Nacional, Portugal

EXTERNAL GROUPS

THE FOLLOWING GROUPS DEVELOP THEIR RESEARCH AT EXTERNAL ASSOCIATED LABORATORIES:

GASTRULATION – José Belo
University of Algarve, Portugal
url: http://www.cbme.ualg.pt/jbelo_cbme.html

NEOANGIOGENESIS – Sérgio Dias
Instituto Português de Oncologia, Lisbon, Portugal
url: http://www.igc.gulbenkian.pt/research/unit/54

EVOLUTIONARY ECOLOGY OF MICROORGANISMS – Francisco Dionísio
University of Lisbon, Portugal
url: http://webpages.fc.ul.pt/fadionisio/

ANTÓNIO DUARTE – Vascular Development
Technical University of Lisbon, Portugal
url: http://pt.embnet.org/research/unit/68

SYSTEMS IMMUNOLOGY – José Faro
University of Vigo, Spain
url: http://eao.igc.gulbenkian.pt/SI/index.html

CELLULAR IMMUNOLOGY – Luis Graça
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.imm.fm.ul.pt/web/imm/cellularimmunology

NEURAL DEVELOPMENT – Domingos Henrique
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.imm.fm.ul.pt/web/imm/developmentalbiology

MORPHOGENESIS – António Jacinto
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.imm.fm.ul.pt/web/imm/umo

MALARIA CELL BIOLOGY – Maria Mota
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.imm.fm.ul.pt/web/imm/malaria

AZORES GENETICS – Luísa Mota Vieira
Divino Espírito Santo Hospital, Azores, Portugal
url: http://pt.embnet.org/research/unit/53

HUMAN GENETICS – Sofia Oliveira
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.igc.gulbenkian.pt/sites/soliveira/

HAEMATOPOIESIS – Leonor Parreira
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.igc.gulbenkian.pt/research/unit/52

SYMMETRY AND DEVELOPMENT – Leonor Saúde
Instituto de Medicina Molecular, Lisbon, Portugal
url:http://www.imm.fm.ul.pt/web/imm/embryonicdevelopmentofvertebrates

MOLECULAR IMMUNOLOGY – Bruno Silva Santos
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.imm.fm.ul.pt/web/imm/molecularimmunology

VIRAL PATHOGENESIS – João Pedro Simas
Instituto de Medicina Molecular, Lisbon, Portugal
url: http://www.imm.fm.ul.pt/web/imm/viralpathogenesis

EXTRACELLULAR MATRIX – Solveig Thorsteinsdóttir
University of Lisbon, Portugal
url: http://cba.fc.ul.pt/research/developmentevolutionarymorphogenesis.php

GENETIC EPIDEMIOLOGY – Astrid Vicente
Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisbon, Portugal
url: http://biofig.fc.ul.pt/groups/human-molecular-genetics-and-functional-analysis-unit

FACILITIES AND SERVICES

ANIMAL FACILITIES

Head: **Jocelyne Demengeot**
Group Leader
E-mail: jocelyne@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/services/static/animals

The Animal Facility provides services to researchers using mouse, rat, fish and fly as experimental models. Its infrastructure is split into several areas, corresponding to each model organism.

THE RODENT FACILITY

The rodent facility is composed of four independent maintenance units serving six areas of specified levels of biocontainment. These are:

- The production area (SPF, restricted to Facility personnel);
- Three experimental zones;
- An importation area;
- And a germ free service corresponding in 2009 to a total of 4500 cages and about 12 000 animals (95% mice, 5% rats).

The facility hosted more than 130 mouse and two rat strains maintained on shelves. Of those, 40 were bred by the Production Unit.
Beyond housing, health monitoring and animal production, the rodent facility offers several services to the IGC community:

- Rederivation of mouse lines into Specific Pathogen Free (SPF) conditions;
- *In vitro* fertilization;
- Cryopreservation of mouse germplasm and germ free conversion.

An important activity of the Rodent Facility is the importation of genetically modified models. In 2009, 41 new strains were imported. Among those, 25 required cleansing performed in-house by embryo transfer while eight were received as frozen embryos and revitalized in-house. To ensure a turnover of strains maintained on shelves according to the development of IGC research projects, the archiving of 52 strains was initiated during 2009. The total number of mouse lines safely embryo-cryopreserved and validated was 42.
The Germfree Service is part of the European Mouse Mutant Archive (EMMA) consortium. In 2009, four requests were initiated and two brought to conclusion. Together the rodent facility served 20 research groups.

THE RODENT FACILITY IS EQUIPPED WITH:

- 7 autoclaves;
- 15 IVCs (Isolated Ventilated Cages) rack system;
- 6 Germ-Free Isolators;
- 1 osmosis reverse system;
- 1 vapor-phase hydrogen peroxide decontamination system;
- 1 transfer and decontamination chamber;
- 1 animal transfer chamber.

THE FISH FACILITY

The fish facility underwent a major renovation. It is composed of a quarantine and an independent production/experimental zone. It includes a behaviour room and a microinjection room. All fish imported to the IGC are hosted in the quarantine and only eggs are introduced into the production/experimental zone. It hosted two fish species and served 3 research groups.

THE FISH FACILITY IS EQUIPPED WITH:

- 1 ZebTEC system with 6 racks, with a total capacity of 300 tanks (3.5L);
- 1 zebrafish system for Quarantine, with capacity for 126 tanks (3.5L);
- 2 microinjectors;
- 2 microscopes;
- 2 incubators 28C.

FACILITY STAFF
Manuel Rebelo (Manager of the Facilities)
Ana Mena (Animal Research - Project Officer)
Joana Bom (Technician)
Rubina Caldeira (Technician)
Ana Sofia Leocádio (Technician)
Paulo Raimundo (Technician)
Carina Brilha (Administrative Assistant, left March 2009)
Ana Bernardino (Administrative Assistant, left December 2009)
Carlos Pires (Caretaker responsible for E0 Unit)
João Lopes (Caretaker responsible for Production Unit)
Graça Ramalho (Caretaker responsible for Quarantine Unit)
Eusébia Varela (Caretaker responsible for E1 Unit)
Samira Varela (Caretaker)
Cláudia Gafaniz (Caretaker)
Autelinda Costa (Caretaker)
Rogério Silva (Caretaker, left December 2009)
Olinda Queirós (Caretaker)
Luís Arroja (Caretaker)

Mouse, Drosophila and zebrafish are some of the animal models used at the IGC, under supervision of the Animal Facilities Unit.

THE FLY FACILITY

The fly facility is composed of several walk-in chambers, a preparation room and a procedure lab. In addition, a quarantine is set outside the facility. The fly facility served 7 research groups in 2009. Centralised common strains and stocks as well as a strain data-base are being implemented.

THE FLY FACILITY IS EQUIPPED WITH:

- 18 work stations with CO2 output pedal system;
- 2 working stations with CO2 output flow buddy system;
- 1 microinjector;
- 1 boiling pan for food preparation, 80L capacity;
- 1 food dispenser;
- 2 heat shock baths;

INCUBATORS:

- 1 room 25C,
- 1 room 18C;
- 1 behaviour room 25C;
- 3 incubators 25C.

TRANSGENICS FACILITY

Head: **Moisés Mallo**
Group Leader
E-mail: mallo@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/services/static/ut

The Transgenics Unit is the gene manipulation unit. The unit provides transgenic services to the research staff. Both classic transgenics, by pronuclear microinjection, and gene targeting, by blastocyst injection of embryonic ES cells, are offered as a service. The unit also offers the cryopreservation of embryos for long-term storage.

THE FACILITY IS EQUIPPED WITH:

- A Microinjection set up with Nikon inverted microscope, DIC optics, and three dimensional Narishige micromanipulators;
- A Microinjection set up with Leica inverted microscope, DIC optics, and three dimensional, power assisted, Narishige micromanipulators;
- Two FemtoJet pumps.
- A Zeiss SV 6 Stereomicroscope with training head;
- two additional Zeiss SV 6 Stereomicroscopes;
- Sutter P-87 Flaming/Brown micropipette puller.
- A CO2 incubator;
- A Ultrasonic Cleaning Device.

FACILITY SERVICES

The Unit performed both pronuclear DNA injections and blastocyst injections of ES cells. A total of 91 DNA injections were performed during 2009, using 34 different DNA constructs, which produced 121 transgenic embryos or founders. Most transgenics were produced by microinjection into the FVB/N background. In addition, injections were also performed into the C57BL/6 background mostly to produce founders directly in this background, to better fit the experimental requirements of the requesting groups, which prefer this genetic strain for immunology-related projects. In most of the cases of FVB/N injections the phenotypes were not dependent on the strain and most of the times led to embryonic lethality, which implied that the studies had to be performed using a transient transgenic approach. Therefore, the use of this strain for the experiments increased the production of transgenic embryos. The overall transgenic efficiency was 26%. In the case of blastocyst microinjections, during 2009, 6 different ES cell clones (129sv background) were injected, which produced 11 chimeras.

FACILITY STAFF
Ana Nóvoa (Research Technician)

TWO CELL MOUSE EMBRYOS.

PLANT FACILITY

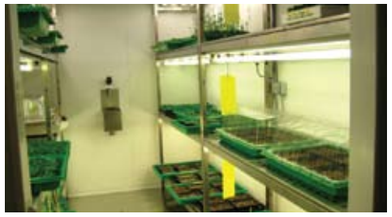
Users: **Elena Baena-González, Paula Duque, José Feijó / Jorg Becker**
Group Leaders/ Research Fellow
E-mail: duquep@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/research/unit/94

The Plant Facility at the IGC ensures the growth and maintenance of *Arabidopsis thaliana* plants, the model organism used by the four plant research groups hosted at the Institute. The facility consists of a custom-built greenhouse with lighting control and temperature regulation and three custom-made fully-controlled growth chambers with short day, long day and continuous light settings. In addition, in 2009, the institute acquired a walk-in plant growth room and a small reach-in chamber (Aralab 10.000 EH 2009 and S600PLH, respectively) that allow the performance of cell-based assays and more precise phenotypic analyses.

Four research groups make use of the IGC Plant Facility, as all use *Arabidopsis thaliana* as a model system in their research work. The Plant Development group focuses on developing integrated models of cellular growth and morphogenesis using the pollen tube as a biological model, ion dynamics as an experimental paradigm and theoretical modeling as an integrative tool. The Plant Molecular Biology group investigates how plants perceive and respond to environmental signals and endogenous developmental cues at the molecular level, focusing on the role of pre-mRNA splicing in the regulation of gene expression. The Plant Stress Signaling group is interested in the mechanisms underlying tolerance to multiple types of stress and on how these signaling cascades interact with other physiological and hormonal cues to orchestrate growth and development. Finally, the Plant Genomics group focuses on the role of male gametes during double fertilisation.

FACILITY STAFF
Vera Nunes (Technician)

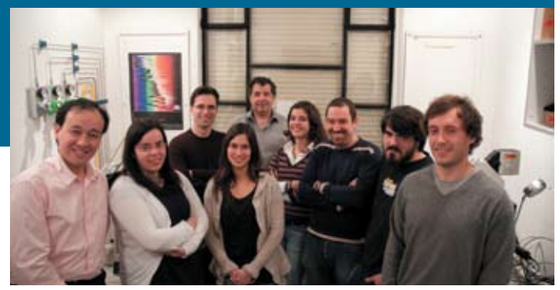
Reach-in chamber for cell-based assays and phenotypic analyses.



Walk-in plant growth room with *Arabidopsis thaliana* cultures.

One of the three custom-built fully-controlled growth chambers.

CELL IMAGING UNIT



Head: **José Feijó**
Group Leader
E-mail: jfeijo@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/41
http://uic.igc.gulbenkian.pt/

The cell imaging unit's main goal is to provide access to high-end technology and cutting-edge technical support for biosciences research. We provide a unique facility that allows ready access to a wide range of technologies and expertise in an integrated manner that can help drive research forward efficiently. The unit currently stands as an international reference laboratory for confocal and multi-photon microscopy, as well as for high-throughput cell sorting. We currently run two cell sorters, two confocal microscopes, a DeltaVision deconvolution microscope system and two multi-photon microscopes. Researchers are trained through regular workshops on basic and advanced light microscopy techniques as well as in flow cytometry, and image acquisition software themselves, with technical assistance when necessary to ensure collection of high quality images and analysis of their data. All users receive basic training in the systems in use, in troubleshooting, and advice on experimental design. We have developed a strong and broad base of users and continue to train new users. Because microscopy is currently in high demand and new systems and techniques are continuously being developed to meet increasing scientific need, we try to expand the facilities to keep accessibility problems low and to introduce the latest innovations (in microscopy and flow cytometry) to the research community.

FACILITY STAFF
Nuno Moreno (General Coordinator)
Rui Gardner (Graduate Technician, Cell Sorting Applications)
Carlos Tadokoro (Graduate Technician, Two-Photon Excitation applications)
Bárbara Fekete Beltrame (Technician, Imaging, left September 2009)
Telma Lopes (Technician, Sorting)

THE FACILITY HAS AT ITS DISPOSAL THE FOLLOWING EQUIPMENT:

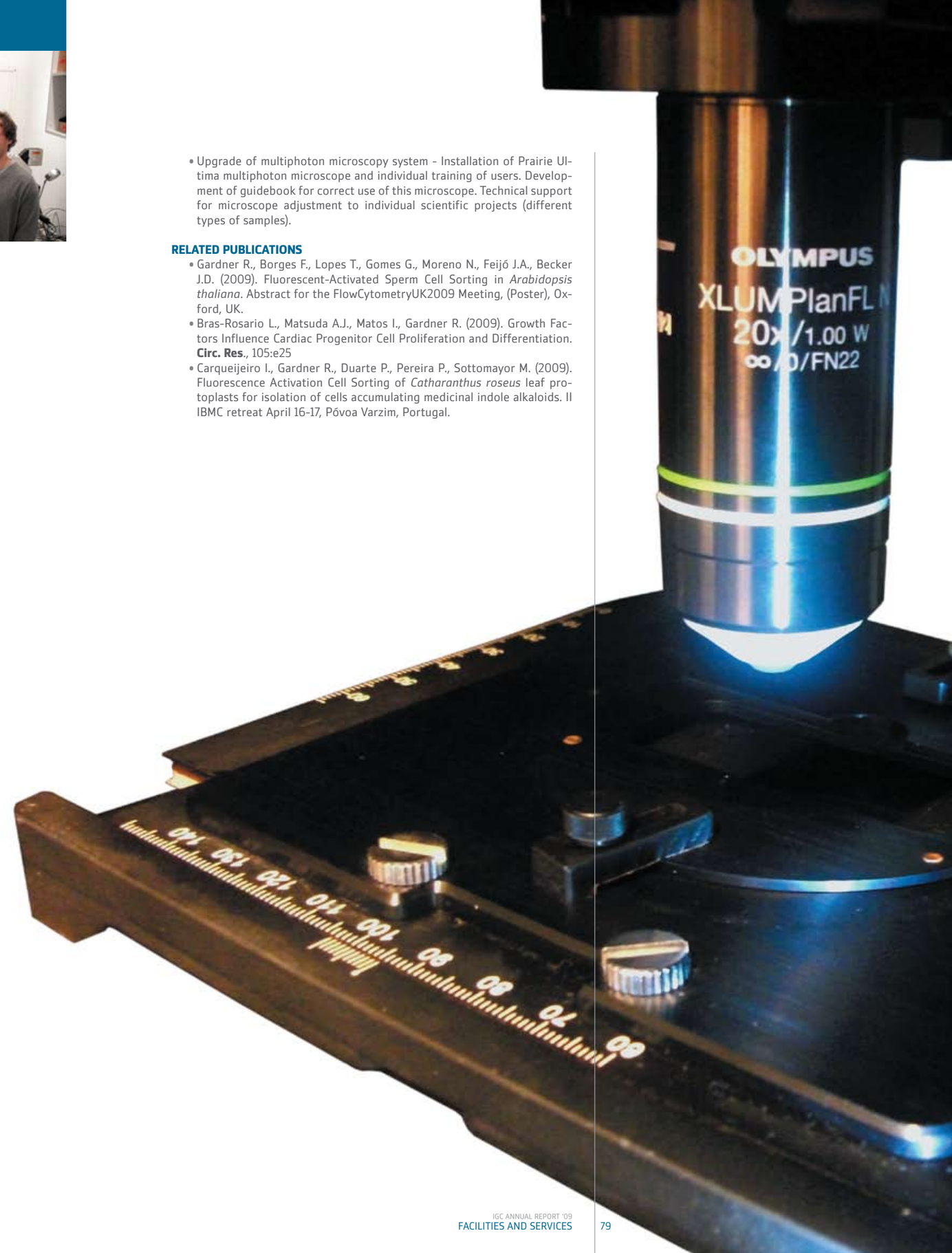
- Inspection Widefield light Microscopes: Olympus BH2, Olympus IMT-2, Leica DMLB2;
- Research Widefield light Microscopes: Leica inverted DMIRE2; Leica upright DMRA2; Zeiss AxioImager M1.
- Confocal microscopes: Leica SP5 (with resonant fast scanhead); Zeiss LSM 510 (with Meta detector); Condor Spinning disk (with EM-CCD intensified camera).
- Multiphoton: Bio-Rad MRC 1024 with Coherent Mira-Verdi laser system; Prairie TPE microscope with Coherent Chameleon laser system (with double scanhead, can take the two lasers for simultaneous excitation/imaging)
- DeltaVision - Deconvolution microscope system from Applied Precision, Inc. (full featured system with EM-CCD intensified camera)
- Flow Cytometry:
  - Cell Sorters: MoFlo; FACSAria
  - Analyzers: FACSCan; FACSCalibur; CyAn ADP (3 lasers, 9 fluo-detectors) Beckman Coulter

THE FACILITY CARRIES OUT SEVERAL TECHNOLOGY DEVELOPMENT PROJECTS:

- Integration of a screening microscope - This microscope is fully automated and works with open source software, being a good platform for on-the-fly analysis. The equipments uses fast filter wheels and shutters which, together with a sensitive CCD camera, enables 3 color images in a 96 well plate in few minutes. For now, it has been used for automatic stitching, producing images of full brain mice or fish slices.
- New scheduling system - The UIC has developed a new resource scheduling system. With this new system, a single equipment reservation can hold a waiting list: in case the user deletes the entry, the following user is automatically entitled to the slot, being warned by SMS or e-mail. Another interesting feature is that users have to register entry onto the equipment and during usage period. This procedure aims to ensure that scheduled bookings are indeed used, thus avoiding no-use periods and risk of the equipment being left on overnight.
- Upgrade of multiphoton microscopy system - Installation of Prairie Ultima multiphoton microscope and individual training of users. Development of guidebook for correct use of this microscope. Technical support for microscope adjustment to individual scientific projects (different types of samples).

RELATED PUBLICATIONS

- Gardner R., Borges F., Lopes T., Gomes G., Moreno N., Feijó J.A., Becker J.D. (2009). Fluorescent-Activated Sperm Cell Sorting in *Arabidopsis thaliana*. Abstract for the FlowCytometryUK2009 Meeting, (Poster), Oxford, UK.
- Bras-Rosario L., Matsuda A.J., Matos I., Gardner R. (2009). Growth Factors Influence Cardiac Progenitor Cell Proliferation and Differentiation. **Circ. Res**., 105:e25
- Carqueijeiro I., Gardner R., Duarte P., Pereira P., Sottomayor M. (2009). Fluorescence Activation Cell Sorting of *Catharanthus roseus* leaf protoplasts for isolation of cells accumulating medicinal indole alkaloids. II IBMC retreat April 16-17, Póvoa Varzim, Portugal.



GENOMICS UNIT

Head: **Carlos Penha-Gonçalves**
Group Leader
E-mail: cpenha@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/48

The Genomics Unit provides technological support and expertise for research at the genome scale. It is composed of the Genotyping and DNA Sequencing services:

- The Sequencing Service offers DNA sequencing and fragment analysis using both multicapillary and slab-gel electrophoresis with automatic sequencer ABI 3130XL. Taqman® Technology in a 384-well format is also available to users both for SNP genotyping and Real-Time PCR gene expression with 7900 HT Fast Real-Time PCR System.
- The Genotyping Service offers the Sequenom iPLEX technology, allowing rapid SNP genotyping assays with up to forty SNPs assayed simultaneously. The facility collaborates with researchers on: SNP choice and SNP Assay Design, Sequenom Procedure and Data Management for Genetic Studies, providing access to the BC/GENE interface software.

THE UNIT IS EQUIPPED WITH:

- Two robotic pippeting devices, Robot PlateMate 2×2 (Matrix) *;
- Five thermocycling machines - ABI 9700 equipped with 2×384 blocks *;
- Chip spotting robot (MassARRAY Nanodispenser) *;
- SNP detection, MALDI-TOF technology-MassARRAY Compact (Sequenom) *;
- ABI 3130XL and ABI 377 Automatic Sequencers;
- 7900 HT Fast Real-Time PCR.

* Financed by Fundação para a Ciência e Tecnologia (Programa Nacional de Re-Equipamento Científico).

SEQUENCING SERVICE

DNA Sequencing

Thirty three internal and six external groups used the ABI 3130XL Sequencing Service from January 2009 until February 2010. A total of 10 834 samples were sequenced:

INTERNAL GROUPS
Actin Dynamics; Bacterial Signalling; Behavior and Metabolism; Cell Cycle Regulation; Development and Selection; Disease Genetics; Early Fly Development; Epigenetic Mechanisms; Epigenetics and Soma; Evolution and Development; Evolutionary Biology; Evolutionary Genetics; Host-Microorganism Interactions; Infections & Immunity; Inflammation; Innate behavior; Lymphocyte; Membrane Traffic in Disease and Novel Therapies; Mitose; Neurobiology of Action; Neuroethology lab; Organogenesis; Patterning and Morphogenesis; Plant Development; Plant Genomics; Plant Molecular Biology; Plant Stress Signaling; Population and Conservation Genetics; Protein-Nucleic Acids Interactions; Stress & Cytoskeleton; Telomeres and Genome Stability; Tissue Morphogenesis; Yeast Stress.

EXTERNAL GROUPS
Human Genetics, Morphogenesis, Neural Development, Symmetry & Development and Viral Pathogenesis groups at the Institute for Molecular Medicine (IMM), in Lisbon; and Vascular Development group at the Faculdade de Medicina Veterinária (FMV), in Lisbon.

Fragment Analysis/MIRUS

Six internal groups used the ABI 3130XL Sequencing Service, on a total of 3604 samples, from January 2009 to February 2010:
Disease Genetics; Evolution and Development; Population and Conservation Genetics; Epigenetics and Soma; Evolutionary Biology; Collective Dynamics.

FACILITY STAFF
Isabel Marques (Senior Laboratory manager)
Jaqueline Garcia (Research assistant, left September 2009)
Susana Ladeiro (Research assistant)
João Costa (Research assistant)

PUBLICATIONS TO WHICH THE GENOMICS UNIT CONTRIBUTED IN 2009 (INCLUDES PAPERS PUBLISHED AND/OR SUBMITTED):

- Marinho C.R., Neres R., Epiphanio S., Gonçalves L.A., Catarino M.B., Penha-Gonçalves C. (2009). Recrudescent Plasmodium berghei from pregnant mice displays enhanced binding to the placenta and induces protection in multigravida. **PLoS ONE**, 20: 4(5).
- Côrte-Real J., Rodo J., Almeida P., Garcia J., Coutinho A., Demengeot J., Penha-Gonçalves C. (2009) Irf4 is a positional and functional candidate gene for the control of serum IgM levels in the mouse. **Genes Immun**, 10(1): 93.
- Krug T., Manso H., Gouveia L., Sobral J., Xavier J.M., Albergaria I., Gaspar G., Correia M., Viana-Baptista M., Simões R.M., Pinto A.N., Taipa R., Ferreira C., Fontes J.R., Silva M.R., Gabriel J.P., Matos I., Lopes G., Ferro J.M., Vicente A.M., Oliveira S.A. Kalirin: A novel genetic risk factor for ischemic stroke. **Human Genetics** (Epub ahead of print).
- Manso H., Krug T., Sobral J., Albergaria I., Gaspar G., Ferro J.M., Oliveira S.A., Vicente A.M. Variants of the Matrix Metalloproteinase-2 but not the Matrix Metalloproteinase-9 genes significantly influence functional outcome after stroke. **BMC Medical Genetics**, 11: 40 (Epub ahead of print).
- Domingues-Montanari S., Fernández-Cadenas I., Rio-Espinola A., Krug T., Manso H., Gouveia L., Sobral J., Mendioroz M., Fernandez-Morales J., Ribó M., Rubiera M., Obach V., Martí J., Freijo M., Serena J., Ferro J.M., Vicente A.M., Oliveira S.A., Montaner J. Association of a genetic variant in the ALOX5AP gene with higher risk of Ischemic Stroke. Meta-analysis and case-control study. **Cerebrovascular Diseases**, in press.
- Krug T., Xavier J.M., Fonseca B.V., Jesus G., Barcelos F., Vedes J., Salgado M., Patto J.V., Crespo J., Oliveira S.A. (2009). Signature genes for Behcet's disease: Blood genomic expression profile. **Cellular Oncology**, 31: 143.
- Weiss L.A., Arking D.E. (2009). Gene Discovery Project of Johns Hopkins & the Autism Consortium, Daly MJ, Chakravarti A. A genome-wide linkage and association scan reveals novel loci for autism. **Nature**, 461(7265): 802-8.
- Correia C., Coutinho A.M., Silva S., Sousa I., Lourenço L., Almeida J., Lontro R., Lobo C., Miguel T., Gallagher L., Gill M., Ennis S., Oliveira G., Vicente A.M. Increased BDNF levels and association with the NTRK2 gene suggest a disruption of the BDNF/TRKB signalling pathway in autism (Submitted).
- Teotónio, H., Chelo, I.M., Bradic, M., Rose, M.R., Long, A.D. (2009). Reverse evolution reveals natural selection on standing genetic variation. **Nat Genet**, 41, 251-257.
- Sambo R., Trovoada M.J., Benchimol C., Quinhentos V., Gonçalves L., Velosa R., Marques M.I., Sepúlveda N., Clark T.G., Mustafa S., Wagner O., Coutinho A., Penha-Gonçalves C. Transforming Growth Factor Beta 2 and Heme Oxygenase 1 genes are risk factors for the cerebral malaria syndrome in Angolan children. **PlosOne**, RA 16469).

Fast Real-Time PCR System

Nine internal, four external and two non-IGC groups (corresponding to 17 different projects) used 7900 HT on a regular basis, to detect gene expression of several genes:

INTERNAL GROUPS
Animal House - Service Unit; Bacterial Signalling; Disease Genetics; Epigenetics and Soma; Host-Microorganism Interactions; Inflammation; Membrane Traffic in Disease and Novel Therapies; Plant Genomics; Population and Conservation Genetics.

EXTERNAL GROUPS
- Neoangiogenesis and Immune Reconstitution groups, both at the Instituto Português de Oncologia (IPO), in Lisbon;
- Animal Behaviour group at the Instituto Superior de Psicologia Aplicada (ISPA), in Lisbon;
- Genetic Epidemiology group at the National Health Institute Doutor Ricardo Jorge (INSA), in Lisbon.

NON-IGC GROUPS
- Haematology Unit at the Instituto Português de Oncologia (IPO), in Lisbon;
- Grapevine functional genomics group at the Instituto Superior de Agronomia (ISA), in Lisbon.

GENOTYPING SERVICE

Seven internal and five external IGC groups used the Genotyping Service on the following projects:

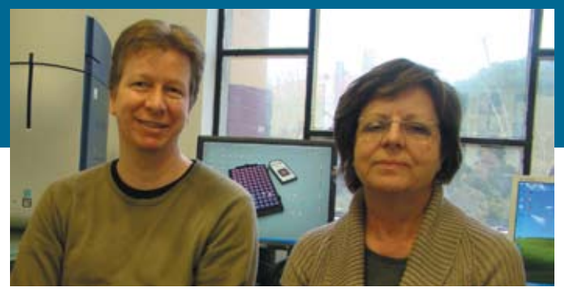
INTERNAL GROUPS
- Epigenetics and Soma - Project: *Mouse genetic quality control*;
- Lymphocyte Physiology - Project: *Mouse genetic quality control*;
- Disease Genetics - Projects: a) *Genetics of Malaria in the Príncipe Population*; b) *Genetic Susceptibility to Cerebral Malaria in Angolan Children*; c) *Type 1 Diabetes*: *Genetic susceptibility*; d) *Mouse genetic quality control*;
- Evolutionary Genetics - Project: a) *Population genetics of adaptation in C. elegans*; b) *Analysis of candidate genes involved in adaptation of reversed evolved populations of Drosophila melanogasters*;
- Evolutionary Genetics & Cave Biology Research Group (NYU, USA) - Collaborative Project: *Genetic basis of morphological change in natural population - Identifying candidate genes behind convergent evolution in blind cave fish Astyanax mexicanus*;
- Disease Genetics & Faculté de Médecine de Sfax (Tunisia) - Laboratoire d'Immunologie - Collaborative Project: *Genetic predisposition to chronic inflammatory bowel disease and polyendocrinophaties in Tunisia*;
- Lupus and Autoreactive Immune Repertoires - Project: *Autoantibody repertoires and regulatory T-cells in human and murine lupus*;
- Collective Dynamics - Project: *Tuberculosis molecular epidemiology*.

EXTERNAL GROUPS:
- Genetic Epidemiology (INSA, Lisbon) - Projects: a) *Genetic Epidemiology of Autism*; b) *Genetic factors involved in susceptibility to stroke and in outcome after 3 and 12 months*; c) *Alzheimer*;
- Human Genetics, PI: Sofia Oliveira (IMM, Lisbon) - Projects: a) *Genetic epidemiology of stroke in the post-genomic era*; b) *BEDGET: deciphering Behçet's Disease Genetics*.

NON IGC GROUPS:
- Center of Metabolism and Endocrinology (IMM, Lisbon) - Project: *Genetic Screening of Cardiomyopathies*;
- Genetics, Evolution and Pathology (IPATIMUP, Porto) - Project: *On the edge of the Bantu expansions: inferring recent African population history with independently evolving haplotypic systems*;
- Genética Populacional, Hibridização e Especiação (CIBIO-Universidade do Porto) - Project: *Evaluating the importance of the X-chromosome "large effect" in the initial stages of reproductive isolation between two pairs of divergent lagomorph taxa*.

A total number of 2 600 000 SNP genotypes were produced from January 2009 to February 2010.

GENE EXPRESSION UNIT



Head: **Jörg Becker**
Research Fellow
E-mail: jbecker@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/131

The Gene Expression Unit provides DNA microarray services, ranging from experimental design over complete sample processing to expert advice on data analysis. We are an Affymetrix Core Lab with reference status for GeneChip technology in Portugal since 2002. Running a total of 270 microarrays we have contributed to 23 in-house, national and international projects in 2009.

SERVICES PROVIDED INCLUDE:

- Gene Expression Profiling (3' IVT, Gene, Exon and Tiling arrays);
- Genotyping, CNV (500K array set and SNP 6.0 array);
- Cytogenetics (Whole-genome 2.7M array);
- MicroRNA Profiling (miRNA array);
- ChIP-on-Chip (Tiling arrays);
- Custom array projects;
- RNA and DNA quality analyses (Bioanalzyer).

THE FACILITY IS EQUIPPED WITH:

- a Scanner 3000 7G with Autoloader *;
- a Fluidics Station 450 *;
- a Hybridization Oven 640;
- a Bioanalyzer 2100;
- Affymetrix and Partek Genomics Suite software.

* Financed by Fundação para a Ciência e Tecnologia (Programa Nacional de Re-Equipamento Científico), Portugal.

THE FOLLOWING IGC GROUPS HAVE USED THE FACILITY, IN 2009:

- Early Fly Development - Processing of 8 fly arrays;
- Inflammation - Processing of 8 human arrays;
- Bacterial signaling - Processing of 6 Sinorhizobium meliloti arrays;
- Plant Genomics - Processing of 78 Medicago truncatula arrays and of 6 Arabidopsis tiling arrays;
- Malaria Cell Biology (IGC external group) - Processing of 12 mouse arrays;
- Animal behaviour (IGC external group) - Processing of 25 zebra fish arrays.

External users, in 2009, include the Instituto de Tecnologia Química e Biológica (ITQB), the Instituto for Molecular Medicine (IMM), the Instituto Superior Técnico, the Instituto Superior de Agronomia, the National Institute of Health Dr. Ricardo Jorge, in Lisbon; the University of Minho, in Braga; the University of Freiburg, in Germany; and, the Institute National de la Recherche Agronomique (INRA), in France.

FACILITY STAFF
Júlia Lobato (Technician)

PUBLICATIONS TO WHICH THE FACILITY CONTRIBUTED IN 2009:

- Albuquerque S.S., Carret C., Grosso A.R., Tarun A.S., Peng X., Kappe S.H.I., Prudêncio M., Mota M.M. (2009). Host cell transcriptional profiling during malaria liver stage infection reveals a coordinated and sequential set of biological events. **BMC Genomics**, 10: 270.
- Nobre L.S., Al-Shahrour F., Dopazo J., Saraiva L.M. (2009). Exploring the antimicrobial action of a carbon monoxide-releasing compound through whole-genome transcription profiling of *Escherichia coli*. **Microbiology**, 155: 813–824.
- Mira N.P., Lourenço A.B., Fernandes A.R., Becker J.D., Sá-Correia I. (2009). The RIM101 pathway has a role in *Saccharomyces cerevisiae* adaptive response and resistance to propionic acid and other weak acids. **FEMS Yeast Research**, 9: 202-216.

HISTOLOGY UNIT

Head: **Susana Lima**
Research Fellow
E-mail: slima@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/42

The Histology Unit provides a wide range of services related to tissue preparation. These include collection, fixation, processing, embedding, sectioning and staining of animal tissue samples. The unit also provides microscopy assistance as well as training to new users in sample preparation and sectioning.

THE FACILITY HAS AT ITS DISPOSAL:

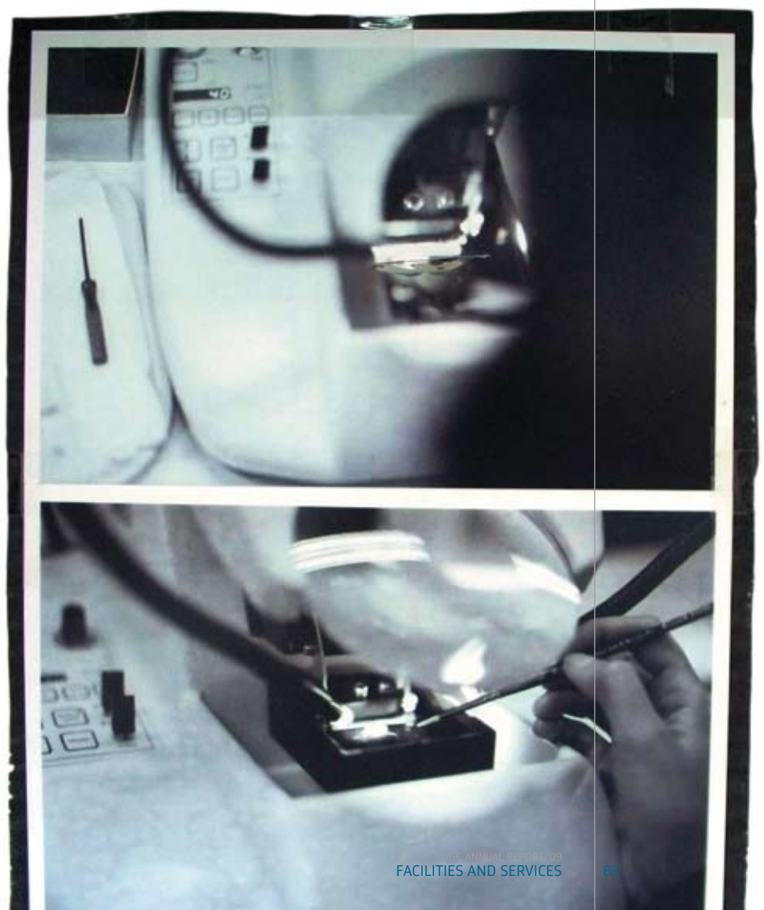
- Equipment for chemical and cold fixation of animal and plant tissue;
- Equipment for processing fixed tissue for light microscopy;
- Equipment to embedding (paraffin, etc);
- Cryostat, vibratome and microtome apparatus;
- Equipments for Histochemistry, immunohistochemistry and immunofluorescence staining of tissues.

THE FOLLOWING IGC GROUPS HAVE USED THE HISTOLOGY UNIT IN 2009:

- Patterning and Morphogenesis, Inflammation, Lymphocyte Physiology - Histological Preparation of Animal and Plant Tissues.

External users, in 2009, include the Institute for Molecular Medicine (IMM), in Lisbon.

FACILITY STAFF
Ana Santos (Technician)
Ana Gaspar (Technician)
Marisa Pardal (Technician, left March 2009)



BIOINFORMATICS AND COMPUTATIONAL BIOLOGY UNIT

Head: **José Pereira Leal**
Group Leader
E-mail: jleal@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/services/static/bioinfo

Our unit's mission is to promote the use of computational methods in biological research, through training and development of resources and materials; to support the graduate programmes of the Associated Laboratory of Oeiras (LAO); to provide direct user support in biological data analysis using computational methods; to conduct research and development in bioinformatics, in particular in data-flow, data warehousing and data analysis, supporting the LAO.

The Bioinformatics Unit is equipped with several workstations and data servers.

THE UNIT IS INVOLVED IN THE FOLLOWING PROJECTS:

- Data warehousing environment for flow cytometry experiments - We have developed and implemented the whole system;
- Data warehousing for microscopy data - Open Microscopy Consortium (UK, USA, Fance) - We are a test site, and the unit maintains servers and helps users test the data environment;
- Direct user support was provided to 11 IGC internal groups - Lymphocyte Physiology, Bacterial Signalling, Population and Conservation Genetics, Cardiac Regeneration, Plant Molecular Biology, Disease Genetics, Collective Dynamics, Organogenesis, Computational Genomics, Stress & Cystoskeleton - and to 7 external groups - Genetic Epidemiology (INSA, Lisbon), Gastrulation (University of Algarve), Symmetry and Development (IMM , Lisbon), Heamatology (IPO, Lisbon), CIPM (IPO, Lisbon), Filomena Caeiro (FCUL, Lisbon), Francisca Fontes (Hosp. Sta Maria, Lisbon).

DIRECT USER SUPPORT INCLUDES:

- Finding mutations, mapping orthologues, identifying transcription factors and regulatory signals, assembly, primer design, protein family assignment, sequence alignment, gene structure identification, SNP identification, phylogenetic analyses, genetic analyses. The unit maintains workstations with software that several groups resort to for their research projects.
- Bioinformatics in high schools - Directed at Portuguese high schools, this projects entails the development of a inquiry-based learning tool based on bioinformatics for high schools; teatcher training and interaction with students.

FACILITY STAFF
Isabel Marques (Senior Specialist)
Paulo Almeida (Systems Administrator and Programmer)

HIGH PERFORMANCE COMPUTING RESOURCE FOR BIOINFORMATICS

Head: **Pedro Fernandes**
E-mail: pfern@igc.gulbenkian.pt
url: http://hermes.igc.gulbenkian.pt

This is a national facility created by the FCT Re-Equipment Programme in 2005. It is hosted by the Instituto Gulbenkian de Ciência, where service in this area is regularly provided since 1991 as the portuguese node of EMBnet. The High Performance Computing Centre (HPCC) has been built around a medium size cluster of Linux machines. Its biggest attractiveness is that it is dedicated to Bioinformatics, and users can expect a fast response and in spite of the simplicity of the user interface. Usage is monitored and accounted for reporting purposes only. Access to our services requires opening an individual account. Hermes provides the storage of registered user results in a private folder for 90 days, allowing for continued work. More than 250 users have opened this kind of account, so far. No charges are applied until maintenance costs rise above a level that cannot be supported institutionally.

The HPCC is a 60 node computer cluster based on high density IBM Power PC JS20 dual processor, single core Blades. The aggregate computing power of these 120 CPUs, served by a high availability storage of 4.2 TeraByte, is a giant step in delivering high speed Bioinformatics applications to the portuguese users community. We use the iNquiry suite in which there is a mixture of open access, licensed and locally added programmes. Some of them use the cluster's high availability feature (many "free" processors), others take a great deal of advantage of the parallel architecture by breaking complex tasks into subtasks that can execute simultaneously. We also hold a fairly large collection of Molecular Biology databases with regular updates. Hermes' hardware was built on IBM's e-server Blade Center technology that provides high compactness and added reliability/maintainability, and runs the Novell Suse Linux SLES9 operating system on all the nodes.

The facility has supported the computational needs of several IGC groups: Population Genetics and Conservation, Evolutionary Biology, Computational Genomics, Protein - Nucleic Acids Interactions.
The facility also provided support to the University of Lisbon and Instituto Superior Técnico, both in Lisbon.

RESEARCH STRUCTURES

RESEARCH STRUCTURES

Laboratório Associado de Oeiras (LAO)

Director: José Artur Martinho Simões (ITQB Director)
url: http://www.igc.gulbenkian.pt
http://www.itqb.unl.pt
http://www.ibet.pt

The Laboratório Associado de Oeiras (LAO) brings together the Instituto de Tecnologia Química (ITQB), the Instituto Gulbenkian de Ciência (IGC), and the Instituto de Biologia Experimental e Tecnológica (IBET), in one of the first Associated Laboratories set up by the Ministry of Science and Technology, in 2001. The three institutes aim to carry out a collaborative research programme, underpinned by a strong communication network and sharing of infrastructures, namely libraries, scientific facilities, academic services, and administrative support.

LAO research encompasses the following areas: biologically active molecules; complex disease genetics; developmental biology in animals and plants; evolutionary genetics; biological risk; plant and forest improvement; computational and theoretical biology.

In 2009, research at the LAO involved 166 scientists (post-docs, group leaders), 173 PhD students, and a further 62 graduates. Of these, 17 group leaders (and group members), two research fellows and 6 staff scientists are IGC researchers.

Genetics and Development of Natural Tolerance Unit of the Fundação para a Ciência e a Tecnologia (Portugal)

Head: António Coutinho (IGC Director)
E-mail: coutinho@igc.gulbenkian.pt

This Unit was created in 1999, and has been operating since 2000, during which time it has repeatedly been awarded the official rating of "Excellent" by the national Foundation for Science and Tecnology (FCT). The research programme of the Unit, involving just over 40 scientists at the IGC and several collaborations with other institutions, concerns physiopathology, genetics and evolution of the immune system, immunity to viruses, bacteria and parasites, host interactions with pathogenic and commensal microbes, inflammation, genetics of autoimmune diseases, and epidemiology. The scientists in the Unit explore the experimental systems of flies and mice, while also addressing relevant questions in humans. The Unit has worked closely with several Portuguese patient groups, and maintains active collaborations with a variety of research groups and institutions, both in Portugal and abroad.

The following IGC research groups belong to this Unit:

- Alekos Athanasiadis (Protein-Nucleic Acids Interactions)
- Vasco Barreto (Epigenetics and Soma)
- Jorge Carneiro (Quantitative Organism Biology)
- Jocelyne Demengeot (Lymphocyte Physiology)
- Gabriela Gomes (Collective Dynamics)
- Isabel Gordo (Evolutionary Biology)
- Michael Parkhouse (Infection and Immunity)
- Carlos Penha Gonçalves (Disease Genetics)
- Miguel Soares (Inflammation)

The following IGC Research Fellows also belong to this Unit:

- Claudine Chaouiya (Network Modelling)
- Elisabetta Padovan (Antigen Presentation and T Cell Activation)
- Luis Rosário (Cardiac Regeneration)

Centre for Developmental Biology of the Fundação para a Ciência e a Tecnologia (Portugal)

Head: Moisés Mallo
E-mail: mallo@igc.gulbenkian.pt

The Center for Developmental Biology was created in August 2003. The research programme currently involves more than 60 researchers, including 31 postdoctoral scientists, and integrates different research projects in the area of Developmental Biology within the IGC. The goal of this research Center is to understand the mechanisms that govern tissue and organ formation during normal embryonic development, their role in the origin of a variety of malformations and their possible applications for the design of novel therapeutic approaches. The research activities of the Unit cover a wide spectrum of biological processes in Arabidopsis, Drosophila, Xenopus, chicken and mouse. The Unit has collaborative projects with several Portuguese and foreign laboratories.

The following IGC research groups belong to this Unit:

- Elena Baena-González (Plant Stress Signaling)
- Patricia Beldade (Variation: Development and Selection)
- Monica Bettencourt Dias (Cell Cycle Regulation)
- Paula Duque (Plant Molecular Biology)
- José Feijó (Plant Development)
- Miguel Godinho Ferreira (Telomeres and Genome Stability)
- Florence Janody (Actin Dynamics)
- Lars Jansen (Epigenetic Mechanisms)
- Mathias Koeppen (Tissue Morphogenesis)
- Moisés Mallo (Patterning and Morphogenesis)
- Rui Martinho (Early Fly Development)
- Joaquín Rodríguez León (Organogenesis)
- Elio Sucena (Evolution and Development)

Champalimaud Foundation Neuroscience Programme at the IGC

Head: Zachary Mainen
E-mail: zmainen@igc.gulbenkian.pt
url: http://pgcn.igc.gulbenkian.pt/doku.php/start

The Champalimaud Neuroscience Programme (CNP) is a basic research team with the broad aim of understanding brain function through integrative biological approaches. CNP laboratories are using advanced molecular, physiological and imaging techniques to elucidate the function of neural circuits and systems in behaviour using animal models including Drosophila, mouse, rat and zebrafish. As of December 2009 the CNP comprises 10 independent research groups, including 5 in-house PIs, 3 Research Fellows and 2 associated External PIs. The CNP also organises the International Neuroscience Doctoral Programme (INDP). The CNP was created in 2007 through a collaborative agreement between the Fundação Champalimaud and the Fundação Calouste Gulbenkian.

In-house Principal Investigators:

- Rui Costa (Neurobiology of Action)
- Zach Mainen (Systems Neuroscience)
- Marta Moita (Behavioural Neuroscience)
- Carlos Ribeiro (Behaviour and Metabolism)
- Luísa Vasconcelos (Innate behaviour)

Research Fellows:

- Inbal Israely (Neuronal Structure and Function)
- Susana Lima (Neuroethology)
- Joe Paton (Dopamine in Action learning)

External Principal Investigators:

- Domingos Henrique (Developmental Biology)
- Rui Oliveira (Animal behaviour)

FLAD Computational Biology Collaboratorium

Head: Luis Rocha
E-mail: rocha@igc.gulbenkian.pt
url: http://bc.igc.gulbenkian.pt/collaboratorium/

The chief aim of the FLAD Computational Biology Collaboratorium is to establish, enable, and foster an international, collaborative network of associated institutions and scientists. It is an open host organisation designed to

enable intense cooperation amongst researchers from national and international institutions, aiming to provide suitable facilities for visiting scientists, and hosting informatics technology to enable continuing off-site collaboration and research in Mathematical and Computational Biology. The Collaboratorium operates in close synergy with the PhD Programme in Computational Biology: faculty are encouraged to stay longer periods of time to participate in work groups and collaborative projects hosted by the collaboratorium. Likewise, visitors to the collaboratorium are encouraged to give seminars and interact with students and faculty of the PhD Programme. Furthermore, the PhD programme will help identify research areas in Mathematical and Computational Biology that are not yet sufficiently developed in Portugal. Reciprocally, the growing collaboration network fostered by the collaboratorium, will facilitate the insertion of the newly formed Computational Biology PhDs within the Portuguese research and technology communities.

In 2009, the Collaboratorium hosted the following researchers:

José Fortes (University of Florida, USA)
2 March-10 May

Michel Bornens (CNRS at Institut Curie, Paris, France)
1-15 June

Ruy Ribeiro (Los Alamos National Laboratory, USA)
1-25 June

Stefan Mass (Lehigh University, USA)
7-13 June

Luis Amaral (Northwestern University, USA)
25 June-7 July

Santiago Schnell (Michigan University, USA)
28 June-5 July

Gabriel Marais (University of Lyon, France)
1 July-30 September

Hagit Shatkay (Queen's University, Canada)
12 July-9 August

Paulo Campos (Universidade Federal Rural de Pernambuco, Brasil)
19-26 July

Anália Lourenço (Universidade do Minho, Portugal)
10-11 September

James Crutchfield (University of California, Davis, USA)
12-19 September

Vitaly Selivanov (University of Barcelona, Spain)
4-7 November

George Kampis (University of Budapest, Hungary)
4-7 November

The European Mouse Mutant Archive (EMMA)

IGC Head: Jocelyne Demengeot
E-mail: jocelyne@igc.gulbenkian.pt
url: http://www.emmanet.org/index.php

Mouse mutants offer the opportunity to decipher the molecular mechanisms of disease, and provide a basis for the development of diagnostic, prognostic and therapeutic approaches. The European Mouse Mutant Archive (EMMA) is a resource centre for the deposition and distribution of mouse disease models and research tools. EMMA draws on the expertise of 11 leading research institutes across Europe, including the Instituto Gulbenkian de Ciência (IGC), in Portugal.

The IGC offers the crucial Germ-Free Service that generates, breeds and houses mice that are free of all microorganisms. These germ-free animals are crucial in studies aimed at understanding the effects of microorganisms on a host, or dissecting the molecular mechanisms underlying the function of the immune system.

To date, the germ-free facility of the IGC has generated 11 different strains of germ-free mice, requested by researchers from Portugal, Germany, USA, France and the UK. The facility has the capacity to temporarily host scientists wishing to carry out their own research with the mice at the IGC itself.

PUBLICATIONS

PUBLICATIONS

Abecasis, A.B., Vandamme, A.M., Lemey, P. (2009). Quantifying differences in the tempo of Human Immunodeficiency Virus Type 1 Subtype evolution. **Journal of Virology** 83(24): 12917-12924.

Águas R., Lourenço J.M.L., Gomes M.G.M., White L.J. (2009). The impact of IPTi on malaria clinical burden - in silico perspectives. **PLoS ONE** 4: e6627.

Aguiar, M., Stollenwerk, N., Kooi, B. (2009) Torus bifurcations, isolas and chaotic attractors in a simple dengue fever model with ADE and temporary cross immunity. **International Journal of Computer Mathematics** 86: 1867-1877.

Amorim, M.C.P., Vasconcelos, R.O., Parreira, B. (2009). Variability in the sonic muscles of the Lusitanian toadfish (*Halobatrachus didactylus*): acoustic signals may reflect individual quality. **Canadian Journal of Zoology** 87 (8): 718-725.

Anderson, C., Thorsteinsdottir, S., Borycki, A.G. (2009). Sonic hedgehog-dependent synthesis of laminin alpha 1 controls basement membrane assembly in the myotome. **Development** 136 (20): 3495-3504.

Antunes, R.A., Oliveira, R.F. (2009). Hormonal anticipation of territorial challenges in cichlid fish. **PNAS** 106 (37): 15985-15989.

Arikkath, J., Peng, I.F., Ng, Y.G., Israely, I., Liu, X., Ullian, E.M., Reichardt, L.F. (2009). Delta-catenin regulates spine and synapse morphogenesis and function in hippocampal neurons during development. **Journal of Neuroscience** 29(17): 5435-42.

Bacaëra, N., Gomes, M.G.M. (2009). On the final size of epidemics with seasonality. **Bulletin of Mathematical Biology** 71: 1954–1966.

Bansal, D., Herbert, F., Lim, P., Deshpande, P., Becavin, C., Guiyedi, V., de Maria, I., Rousselle, J.C., Namane, A., Jain, R., Cazenave, P.A., Mishra, G.C., Ferlini, C., Fesel C., Benecke, A., Pied, S. (2009). IgG autoantibody to brain Beta Tubulin III associated with Cytokine Cluster-II discriminate cerebral malaria in central India. **Plos One** 4(12): 38245.

Baron, R.A., Tavare, R., Figueiredo, A.C., Blazewska, K.M., Kashemirov, B.A., McKenna, C.E., Ebetino, F.H., Taylor, A., Rogers, M.J., Coxon, F.P., Seabra, M.C. (2009). Phosphonocarboxylates inhibit the second Geranylgeranyl addition by Rab Geranylgeranyl Transferase. **Journal of Biological Chemistry** 284(11): 6861-6868.

Barreto, M., Ferreira, RC., Lourenco, L., Moraes-Fontes, M.F., Santos, E., Alves, M., Carvalho, C., Martins, B., Andreia, R., Viana, J.F., Vasconcelos, C., Mota-Vieira, L., Ferreira, C., Demengeot, J., Vicente, A.M. (2009). Low frequency of CD4(+)CD25(+) Treg in SLE patients: a heritable trait associated with CTLA4 and TGF gene variants. **BMC Immunology** 10(5).

Batista-Brito, R., Rossignol, E., Hjerling-Leffler, J., Denaxa, M., Wegner, M., Lefebvre, V., Pachnis, V., Fishell, G. (2009). The cell-intrinsic requirement of Sox6 for cortical interneuron development. **Neuron** 63 (4): 466-481.

Batista-Brito, R., Fishell, G. (2009). The developmental integration of cortical interneurons into a functional network. **Current Topics in Developmental Biology, Development of Neural Circuitry** 87: 81-118.

Beldade, P., Saenko, S.V., Pul, N., Long, A.D. (2009). A gene-based linkage map for Bicyclus anyana butterflies allows for a comprehensive analysis of synteny with the Lepidopteran reference genome. **Plos Genetics** 5(2): e1000366.

Beldade, P., Van't Hof, Arjèn E., Jerónimo, M.A., Long, A.D. (2009). Microsatellite markers associated with genes expressed in developing wings of Bicyclus anynana butterflies. **Molecular Ecology Resources** 9 (6): 1487 – 149.

Bettencourt-Dias, M. and D. M. Glover (2009). SnapShot: centriole biogenesis. **Cell** 136(1): 188-U1.

Bettencourt-Dias, M., Goshima, G. (2009). RNAi in Drosophila S2 cells as a tool for studying cell cycle progression. **Methods in Molecular Biology** 545: 39-6.

Black, A.J., McKane, A.J., Nunes, A., Parisi, A. (2009) Stochastic Fluctuations in the SIR model with distributed infectious periods. **Physical Review** E 80: 021922.

Branco, C.C., Pacheco, P.R., Cabrol, E., Cabral, R., Vicente, A.M., Mota-Vieira, L. (2009). Linkage disequilibrium and diversity for three genomic regions in Azoreans and mainland Portuguese. **Genetics and Molecular Biology** 32(2): 220-226.

Branco, C.C., Pereirinha, T., Cabral, R., Oacheco, P.R., Mota-Vieria, L. (2009). Thrombotic genetic risk factors and warfarin pharmacogenetic variants in São Miguel's healthy population (Azores). **Thrombosis Journal** 7: 9.

Bras-Rosario L., Matsuda A., Matos I., Gardner R. (2009) Growth factors influence cardiac progenitor cell proliferation and differentiation. **Circulation Research** 105; e25.

Bray, T.C., Chikhi, L., Sheppy, A.J., Bruford, M.W. (2009). The population genetic effects of ancestry and admixture in a subdivided cattle breed. **Animal Genetics** 40 (4): 393-400.

Bray, T.C., Sousa, V., Parreira, B., Bruford, M.W., Chikhi, L. (2009). 2BAD: an application to estimate the parental contributions during two independent admixture events. **Molecular Ecology Resources**, doi: 10.1111/j.1755-0998.2009.02766.x.

Brito, P.H., Edwards, S.V. (2009). Multilocus phylogeography and phylogenetics using sequence-based markers. **Genetica** 135 (3): 439-455.

Burkhardt, J.M., Jin, X, and Costa R.M. (2009). Dissociable effects of dopamine on the firing rate and synchrony of striatal ensembles. **Frontiers in Integrative Neuroscience** 3:28. doi:10.3389/neuro.07.028.2009.

Cabrito, T.R., Teixeira, M.C., Duarte, A.A., Duque, P., Sá-Correia, I. (2009). Heterologous expression of a Tpo1 homolog from *Arabidopsis thaliana* confers resistance to the herbicide 2,4-D and other chemical stresses in yeast. **Applied Microbiology and Biotechnology** 84(5): 927-36.

Caetano-Lopes, J., Nery, A.M., Henriques, R., Canhao, H., Duarte, J., Amaral, P.M., Vale, M., Moura,R.A., Pereira, P.A., Weinmann, P., Abdulghani, S., Souto-Carneiro, M. , Rego, P., Monteiro, J., Sakagushi, S., Queiroz, M.V., Konttinen, Y.T., Graca, L., Vaz, M.F., Fonseca, J.E. (2009). Chronic arthritis directly induces quantitative and qualitative bone disturbances leading to compromised biomechanical properties. **Clinical and Experimental Rheumatology** 27 (3): 475-482.

Carneiro, J., Duarte, L., Padovan, E. (2009) Limiting dilution analysis of antigen-specific T cells. **Methods in Molecular Biology** 514:95-105.

Carneiro, J., Duarte, L., Padovan, E. (2009). Limiting dilution analysis of antigen-specific T cells. **Methods in Molecular Biology** 514: 95-105.

Carroll, C., Silva, M., Godek, K., Jansen, L., Straight, A. (2009). Centromere assembly requires the direct recognition of CENP-A nucleosomes by CENP-N. **Nature Cell Biology** 11(7): 896-902.

Carvalho, T.P., Buonamano, D.V. (2009). Differential effects of excitatory and inhibitory plasticity on synaptically driven neuronal input-output functions. **Neuron** 61(5): 774-785.

Charlesworth, B., Betancourt A.J., Kaiser V.B., Gordo I. (2009). Genetic Recombination and Molecular Evolution. **Cold Spring Harbor Symposia on Quantitative Biology**. [Epub ahead of print]

Chelo, I.M., Zé-Zé, L., Tenreiro, R. (2009). Genome diversity in *Fructobacillus, Leuconostoc* and *Weissella genera* through physical and genetic mapping. **Microbiology**. [Epub ahead of print]

Cheng, C., Noordeloos, A.M., Jeney, V., Soares, M.P. Moll, F., Pasterkamp, G., Serruys, P.W., Duckers, H.J. (2009). Heme Oxygenase 1 determines atherosclerotic progression into a vulnerable plaque. **Circulation** 119(23): 3017-A9.

Chikhi, L. (2009). Genetic data and story-telling: from Archeogenetics to Astrologenetics? An update to "Clinal variation in the nuclear DNA of Europeans" By Chikhi, L., Destro-Bisol, G., Pascali, V., Baravelli V., Dobosz, M., Barbujani, G. Published in 1998 in Human Biology. **Human Biology** 81, (5-6), 639-643.

Claycomb, J.M., Batista, P.J., Pang, K.M., Gu, W.F., Vasale, J.J., van Wolfswinkel, J.C., Chaves, D.A., Shirayama, M., Mitani, S., Ketting, R.F., Conte, D., Jr., Mello, C.C. (2009). The argonaute CSR-1 and Its 22G-RNA cofactors are required for holocentric chromosome segregation. **Cell** 139 (1): 123-134.

Coelho, F.C., Codeço, C.T. (2009). Dynamic modeling of vaccinating behavior as a function of individual beliefs. **PLoS Computational Biology** 5(7): e1000425.

Correia, C., Coutinho, A.M., Almeida, J., Lontro, R., Lobo, C., Miguel, T.S., Martins, M., Gallagher, L., Conroy, J., Gill, M., Oliveira, G., Vicente, A.M. (2009). Association of the 4 integrin subunit gene (ITGA4) with autism. **Neuropsychiatric Genetics** 150B (8): 1147-1151.

Correia, C.T., Almeida, J.P., Santos, P.E., Sequeira, A.F., Marques, C.E., Miguel, T.S., Abreu, R.L., Oliveira, G.G., Vicente, A.M. (2009). Pharmacogenetics of risperidone therapy in autism: association analysis of eight candidate genes with drug efficacy and adverse drug reactions. **Pharmacogenomics Journal**. [Epub ahead of print]

Correia, C., Coutinho, A.M., Almeida, J., Lontro, R., Lobo, C., Miguel, T.S., Martins, M., Gallagher, L., Conroy, J., Gill, M., Oliveira, G., Vicente, A.M. (2009). Association of the alpha4 integrin subunit gene (ITGA4) with autism. **American Journal of Medical Genetics Part B: Neuropsychiatric Genetics** 150B (8): 1147-51.

Correia, C., Santos, P., Coutinho, A.M., Vicente, A.M. (2009). Characterization of pharmacogenetically relevant CYP2D6 and ABCB1 gene polymorphisms in a Portuguese population sample. **Cell Biochemistry and Function** 27(4): 251-5.

Côrte-Real, J., Duarte, N.A, Tavares, L.B., Penha-Gonçalves, C. (2009). Autoimmunity triggers in the NOD mouse: a role for natural auto-antibody reactivities in Type 1 Diabetes. **Annals of the New York Academy of Sciences**. 1173 (Issue Contemporary Challenges in Autoimmunity): 442 - 448.

Côrte-Real, J., Rodo, J., Almeida, P., Garcia, J., Coutinho, A., Demengeot, J., Penha-Gonçalves, C. (2009). Irf4 is a positional and functional candidate gene for the control of serum IgM levels in the mouse. **Genes and Immunity** 10(1): 93-99.

Craul, M., Chikhi, L., Sousa, V., Olivieri, G.L., Rabesandratana, A., Zimmermann. E., Radespiel, U. (2009). Influence of forest fragmentation on an endangered large-bodied lemur in northwestern Madagascar. **Biological Conservation**. 142 (12): 2862-2871.

Cruz, A.V., Mallet, N., Magill, P.J., Brown, P., Averbeck, B.B. (2009). Effects of dopamine depletion on network entropy in the external globus pallidus. **Journal of Neurophysiology** 102 (2): 1092-1102.

Cunha-Ferreira, I., Rodrigues-Martins, A., Bento, I., Riparbelli, M., Zhang, W., Laue, E., Callaini, G., Glover, D.M., Bettencourt-Dias, M. (2009). The SCF/Slimb Ubiquitin Ligase limits centrosome amplification through degradation of SAK/PLK4. **Current Biology** 19(1): 43-49.

Cunha-Ferreira, I., Bento, I., Bettencourt-Dias, M. (2009) From zero to many: control of centriole number in development and disease. **Traffic** 10(5): 482-498.

Darwich, L., Coma G., Pena R., Bellido R., Blanco E.J.J., Este J.A., Borras F.E., Clotet B., Ruiz L., Rosell A., Andreo F., Parkhouse R.M.E., Bofill M. (2009). Secretion of interferon-gamma by human macrophages demonstrated at the single-cell level after costimulation with interleukin (IL)-12 plus IL-18. (2009). **Immunology** 126 (3): 386-393.

de las Heras, J.M., Martinho, R.C., Lehmann, R., Casanova, J . (2009). A functional antagonism between the pgc germline repressor and torso in the development of somatic cells. **Embo Reports** 10 (9): 1059-1065.

Dias-Ferreira, E., Sousa, J.C., Melo, I., Morgado, P., Mesquita, A.R., Cerqueira, J.J., Costa, R.M. , Sousa, N. (2009). Chronic stress causes frontostriatal reorganization and affects decision-making. **Science** 325 (5940): 621-625.

Diaza Z., Xavier K.B., Miller S.T. (2009). The crystal structure of the Escherichia coli autoinducer-2 processing protein LsrF. **PLoS One** 4(8):e6820.

Dos Santos S.C., Tenreira S., Palma M., Becker J., Sá-Correia I. (2009). Transcriptomic profiling of the yeast response to quinine evidenced a glucose limitation response attributable to drug-induced inhibition of glucose uptake. **Antimicrobial Agents and Chemotherapy** 53 (12), 5213–5223.

Duarte, J.H., Zelenay, S., Bergman, M.L., Martins, A.C., Demengeot, J. (2009). Natural Treg cells spontaneously differentiate into pathogenic helper cells in lymphopenic conditions. **European Journal of Immunology** 39(4): 948-955.

Dugué G.P., Mainen Z.F. (2009). How serotonin gates olfactory information flow. **Nature Neuroscience** 12(6): 673-5.

Faure, A., Naldi, A., Lopez, F., Chaouiya, C., Ciliberto, A., Thieffry, D. (2009). Modular logical modelling of the budding yeast cell cycle. **Molecular Biosystems** 5(12): 1787-1796.

Ferrer, E., Martínez-Escribano, J.A., González Barderas, M.A., González, L.M., Cortéz, M.M., Dávila, I., Harrisonf, L.J.S., Parkhouse, R.M.E. , Gárate. T. (2009). Peptide epitopes of the *Taenia solium* antigen Ts8B2 are immunodominant in human and porcine cysticercosis. **Molecular and Biochemical Parasitology** 168 (2): 168-171.

Figueiredo, L.F.de, Podhorski, A., Rubio, A., Kaleta, C., Beasley, J.E., Schuster, S., Planes, F.J. (2009). Computing the shortest elementary flux modes in genome-scale metabolic networks. **Bioinformatics** 25 (23): 3158-3165.

Foltz, D.R., Jansen, L.E.T., Bailey, A.O., Yates J.R.III., Bassett, E.A., Wood, S., Black, B.E., Cleveland, D.W. (2009). Centromere-specific assembly of CENP-A nucleosomes is mediated by HJURP. **Cell** 137: 472–84.

Fournier-Thibault, C., Blavet, C., Jarov, A., Bajanca, F., Thorsteinsdottir, S., Duband, J.L. (2009). Sonic Hedgehog regulates integrin activity, cadherin contacts, and cell polarity to orchestrate neural tube morphogenesis. **Journal of Neuroscience** 29 (40): 12506-12520.

Friesema, I.H.M., Koppeschaar, C.E., Donker, G.A., Dijkstra, F., van Noort, S.P., Smallenburg, R., van der Hoek, W., van der Sande, M.A.B. (2009). Internet-based monitoring of influenza-like illness in the general population: Experience of five influenza seasons in the Netherlands". **Vaccine** 27 (45): Sp. Iss. SI: 6353.

Gallardo, C, Reis A.L., Kalema-Zikusoka, G., Malta, J., Soler, A., Blanco, E., Parkhouse, R.M., Leitá, A. (2009). Recombinant antigen targets for serodiagnosis of African swine fever. **Clinical Vaccine Immunology** 16(7): 1012-1020.

Galhardo, L., Almeida, O., Oliveira, R.F. (2009). Preference for the presence of substrate in male cichlid fish: Effects of social dominance and context. **Applied Animal Behaviour Science** 120 (3-4): 224-230.

Gardner, A., Arce, A., Alpedrinha, J. (2009). Budding dispersal and the sex ratio. **Journal of Evolutionary Biology** 22(5): 1036-1045.

Gates, J., Nowotarski, S.H., Yin, H., Mahaffey, J.P., Bridges, T., Herrera, C., Homem, C.C.F., Janody, F., Montell, D.J., Peifer, M. (2009). Enabled and capping protein play important roles in shaping cell behavior during Drosophila oogenesis. **Developmental Biology** 333(1): 90-107.

Giovannini, A., Zanghirati, G., Beaumont, M.A., et al. (2009). A novel parallel approach to the likelihood-based estimation of admixture in population genetics. **Bioinformatics** 25(11): 1440-1441.

Gordo, I., Gomes, M.G.M., Reis, D.G., Campos, P.R.A. (2009). Genetic diversity in the SIR model of pathogen evolution. **PLoS One** 4(3): e4876.

Gu, W.F., Shirayama, M., Conte, D., Vasale, J., Batista, P.J., Claycomb, J.M., Moresco, J.J., Youngman, E.M., Keys, J., Stoltz, M.J., Chen, C.C.G., Chaves, D.A., Duan, S.H., Kasschau, K.D., Fahlgren, N., Yates, J.R., Mitani, S., Carrington, J.C., Mello, C.C. (2009). Distinct argonaute-mediated 22G-RNA pathways direct genome surveillance in the C. elegans germline. **Molecular Cell** 36 (2): 231-244.

Hume, A.N., Buttgereit, J., Al-Awadhi, A.M., Al-Suwaidi, S.S., John, A., Bader, M., Seabra, M.C., Al-Gazali, L., Ali, B.R. (2009), Defective cellular trafficking of missense NPR-B mutants is the major mechanism underlying Acromesomelic Dysplasia type Maroteaux. **Human Molecular Genetics** 18(2): 267-77.

Jurberg, A.D., Gonçalves, T., Costa, T.A., de Mattos, A.C., Pascarelli, B.M., de Manso P.P., Ribeiro-Alves M, Pelajo-Machado M, Peralta JM, Coelho PM, Lenzi HL. (2009). The embryonic development of *Schistosoma mansoni* eggs: proposal for a new staging system. **Development Genes and Evolution** 219(5): 219-34.

Kinderlerer A.R., Gregoire I.P., Hamdulay S.S., Ali F., Steinberg R., Silva G., Ali N., Wang B.F., Haskard D.O., Soares M.P., Mason J.C. (2009). Heme oxygenase-1 expression enhances vascular endothelial resistance to complement-mediated injury through induction of decay-accelerating factor: a role for increased bilirubin and ferritin. **BLOOD** 113 (7): 1598-1607.

Kuriyama, R., Bettencourt-Dias, M., Hoffman, I., Arnold, M., Sandvig, L. (2009). gamma-Tubulin-containing abnormal centrioles are induced by insufficient Plk4 in human HCT116 colorectal cancer cells. **Journal of Cell Science** 122(12): 2014-2023.

Leong, H., Ros, A.F.H., Oliveira, R.F. (2009). Effects of putative stressors in public aquaria on locomotor activity, metabolic rate and cortisol levels in the Mozambique tilapia *Oreochromis mossambicus*. **Journal of Fish Biology** 74(7): 1549-1561.

Lima, P.T., Faria, V.G., Patraquim, P., Ramos, A.C., Feijo, J.A., Sucena, E. (2009). Plant-microbe symbioses: new insights into common roots. **Bioessays** 31 (11): 1233-1244.

Lima SQ., Hromádka T., Znamenskiy P., Zador A.M. (2009). PINP: a new method of tagging neuronal populations for identification during *In Vivo* electrophysiological recording. **PLoS ONE** 4(7): e6099.

Lince-Faria, M., Maffini, S., Orr, B., Ding, Y., Florindo, C., Sunkel, C.E., Tavares, A., Johansen, J., Johansen, K.M., Maiato, H. (2009). Spatiotemporal control of mitosis by the conserved spindle matrix protein Megator. **Journal of Cell Biology** 184(5): 647-657.

Mainen, Z.F., Kepecs A. (2009). Neural representation of behavioral outcomes in the orbitofrontal cortex. **Current Opinion in Neurobiology** 19 (1): 84-91.

Mallo, M., Vinagre,T., Carapuço, M. (2009). The road to the vertebral formula. **The International Journal of Developmental Biology** 53: 1469-1481.

Malta-Vacas, J., Nolasco, S., Monteiro, Soares, H., Brito, M. (2009). Translation termination and protein folding pathway genes are not correlated in gastric cancer. **Clinical Chemistry and Laboratory Medicine** 47(4): 427-431.

Mantilla-Beniers, N.B., Gomes, M.G.M. (2009). Mycobacterial ecology as a modulator of tuberculosis vaccine success. **Theoretical Population Biology** 75(2-3): 142-152.

Lince-Faria M., Maffini S., Orr B., Ding Y., Florindo C., Sunkel C.E., Tavares Á., Johansen J., Johansen K.M., and Maiato H.. (2009). Spatio-temporal control of mitosis by the conserved spindle matrix protein Megator. **Journal of Cell Biology** 184:647-657.

Marinho C.R., Neres R., Epiphanio S., Gonçalves L.A., Catarino M.B., Penha-Gonçalves C. (2009). Recrudescent *Plasmodium berghei* from pregnant mice displays enhanced binding to the placenta and induces protection in multigravida. **PLoS ONE** 4(5): e5630.

Marques, J.M., Alonso, I., Santos, C., et al. (2009). The spatial learning phenotype of heterozygous leaner mice is robust to systematic variation of the housing environment. **Comparative Medicine** 59(2): 129-138.

Martins, J., Pinto, A., Stollenwerk, N. (2009). A scaling analysis in the SIRI epidemiological model. **Journal of Biological Dynamics** 3(5): 479-496.

Mateus, A.M., Gorfinkiel, N., Martinez Arias, A. (2009). Origin and function of fluctuations in cell behaviour and the emergence of patterns. **Seminars in Cell & Developmental Biology** 20 (7): 877-884.

Maude, R.J., Pontavornpinyo, W., Saralamba, S., Aguas, R., Yeung, S., Dondorp, A.M., Day, N.P.J., White, N.J., White, L.J. (2009). The last man standing is the most resistant: eliminating artemisinin-resistant malaria in Cambodia. **Malaria Journal** 8(31).

Michard, E., Alves, F., Feijó, J.A. (2009). The role of ion fluxes in polarized cell growth and morphogenesis: the pollen tube as an experimental paradigm. **International Journal of Developmental Biology** 53: 1609-1622.

Mira, N.P., Lourenço, A.B., Fernandes, A.R., Becker, J.D., Isabel Sá-Correia, I. (2009). The RIM101 pathway has a role in *Saccharomyces cerevisiae* adaptive response and resistance to propionic acid and other weak acids. **FEMS Yeast Research** 9(2): 202-216.

Moosajee, M., Tulloch, M., Baon, R.A., Gregory-Evans, C.Y., Pereira-Leal, J.B., Seabra, M.C. (2009). Single choroideremia gene in nonmammalian vertebrates explains early embryonic lethality of the Zebrafish model of Choroideremia. **Investigative Ophthalmology & Visual Science** 50(6): 3009-3016.

Moraes-Fontes, M.F., Rebelo, M., Caramalho I., Zelenay, S., Bergman, M.L., Coutinho, A., Demengeot, J. (2009). Steroid treatment in mice do not alter the number and function of regulatory T cells, but amplify cyclophosphamide-induced autoimmune disease, **Journal of Autoimmunity** 33(2): 109-120.

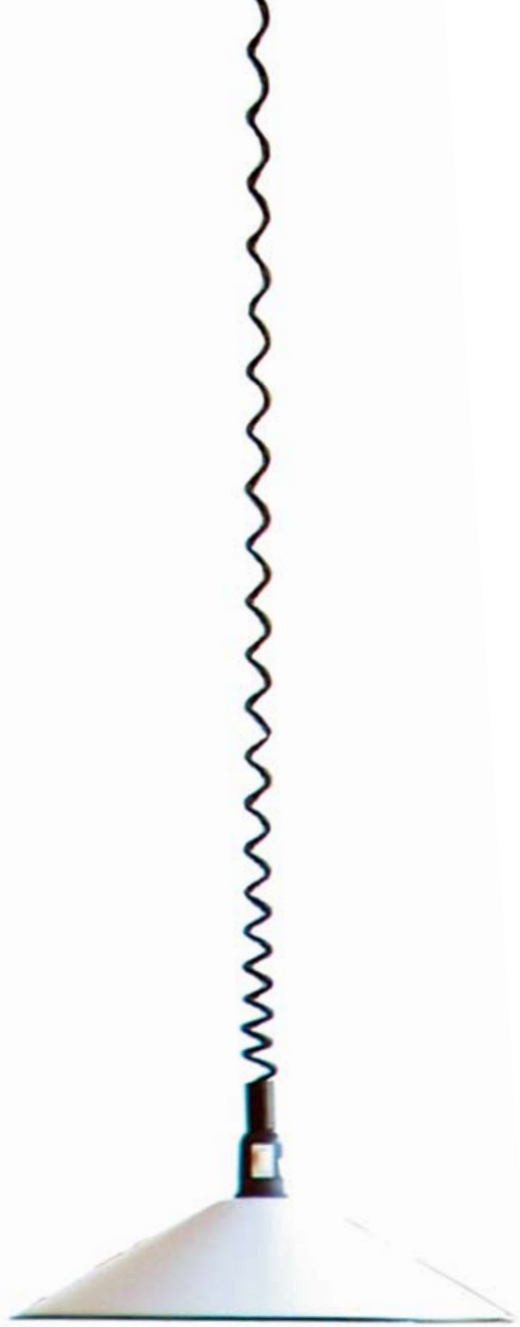
Moosajee M., Tulloch M., Baron R.A., Gregory-Evans C.Y., Pereira-Leal, J.B., Seabra M.C. (2009). Single Rab Escort Protein gene in non-mammalian vertebrates explains early embryonic lethality of a zebrafish model of Choroideremia. **Investigative Ophthalmology and Visual Science** 50(6): 3009-16.

Naldi A., Berenguier D., Fauré A., Lopez F., Thieffry D., Chaouiya C. (2009). Logical modelling of regulatory networks with GINsim 2.3. **Biosystems** 97(2): 134-9.

Naldi A., Remy, E., Thieffry, D., Chaouiya, C. (2009) A reduction of logical regulatory graphs preserving essential dynamical properties. **LCS/Lecture Notes in Bioinformatics** 5688: 266-80.

Nascimento R., Dias, J.D.,Parkhouse, R.M.E. (2009). The conserved UL24 family of human alpha, beta and gamma herpesviruses induces cell cycle arrest and inactivation of the cyclinB/cdc2 complex. **Archives of Virology** 154(7): 1143-1149.

Nightingale T.D., Pattni K., Hume A.N., Seabra M.C., Cutler D.F. (2009) Rab27a and MyRIP regulate the amount and multimeric state of VWF released from endothelial cells. **Blood** 113(20): 5010-8.



Oki, S., Kitajima, K., Marques, S., Belo, J.A., Yokoyama, T., Hamada, H., Meno, C. (2009). Reversal of left-right asymmetry induced by aberrant Nodal signaling in the node of mouse embryos. **Development** 136 (23): 3917-3925.

Oliveira, N.M., Hilker, F.M. (2009). Modelling disease introduction as biological control of invasive predators to preserve endangered prey. **Bulletin of Mathematical Biology**. [Epub ahead of print]

Oliveira, R.F. (2009). Social behavior in context: Hormonal modulation of behavioral plasticity and social competence. **Integrative and Comparative Biology** 49(4): 423-440.

Oliveira, T., Gouveia, M.J., Oliveira, R.F. (2009). Testosterone responsiveness to winning and losing experiences in female soccer players. **Psychoneuroendocrinology** 34 (7): 1056-1064.

Oliveira, R.F., Silva, A., Canário, A.V.M. (2009). Why do winners keep winning? Androgen mediation of winner but not loser effects in cichlid fish. **Proceedings of The Royal Society: Biological Sciences** 276(1665): 2249-56.

Pacheco, P.R., Brilhante, M.J., Ballart, C., Sigalat, F., Polena, H., Cabral, R., Branco, C.C., Mota-Vieira, L. (2009). UGT1A1, UGT1A6 and UGT1A7 genetic analysis repercussion for Irinotecan: Pharmacogenetics in the Sao Miguel Island Population (Azores, Portugal). **Molecular Diagnosis & Therapy** 13(4): 261-268.

Pamplona, A., Hanscheid, T., Epiphanio, S., Mota, M.M., Vigário, A.M. (2009). Cerebral malaria and the hemolysis/methemoglobin/heme hypothesis: Shedding new light on an old disease. **The International Journal of Biochemistry & Cell Biology** 41 (4): 711-716.

Parker, M.J., Gomes, M.G.M., Stewart, I.N. (2009). Examples of forced symmetry-breaking to heteroclinic cycles and networks in three dimensional Euclidean-Ivariant systems. **International Journal of Bifurcation and Chaos** 19 (15): 1655-1678.

Parreira, B., Trussart, M., Sousa, V., et al. (2009). SPAms: A user-friendly software to simulate population genetics data under complex demographic models. **Molecular Ecology Resources** 9(3): 749-753.

Pereira, C.S., de Regt, A.K., Brito, P.H., Miller, S.T., Xavier, K.B. (2009). Identification of functional LsrB-like autoinducer-2 receptors. **Journal of Bacteriology** 191 (22): 6975-6987.

Quéméré, E., Louis, E., Ribéron, A., Chikhi, L. Crouau-Roy, B. (2009). Non-invasive conservation genetics of the critically endangered golden-crowned sifaka (*Propithecus tattersalli*): high diversity and significant genetic differentiation over a small range. **Conservation Genetics** Doi 10.1007/s10592-009-9837-9.

Quirk M.C., Sosulski D.L., Feierstein C.E., Uchida N., Mainen Z.F. (2009) A defined network of fast-spiking interneurons in orbitofrontal cortex: responses to behavioral contingencies and ketamine administration. **Frontiers in Systems Neuroscience** 3: 13.

Ramalho J.S., Lopes V.S., Tarafder A.K., Seabra M.C., Hume A.N. (2009). Myrip uses distinct domains in the cellular activation of myosin VA and myosin VIIA in melanosome transport. **Pigment Cell and Melanoma Research** 22(4):461-73.

Ramos A.C., Martins M.A., Okorokova-Façanha A.L., Olivares F.L., Okorokov L.A., Sepúlveda N., Feijó J.A., Façanha A.R. (2009). Arbuscular mycorrhizal fungi induce differential activation of the plasma membrane and vacuolar H+ pumps in maize roots. **Mycorrhiza** 19(2): 69-80.

Ramos, A.C., Lima, P.T., Dias, P.N., Kasuya, M.C.M., Feijó, J. A. (2009). A pH signaling mechanism involved in the spatial distribution of calcium and anion fluxes in ectomycorrhizal roots. **New Phytologist** 181(2): 448-462.

Ranade, S.P., Mainen, Z.F. Transient firing of dorsal Raphe neurons encodes diverse and specific sensory, motor, and reward events. **Journal of Neurophysiology** 102 (5): 3026-3037.

Rangan P., DeGennaro M., Jaime-Bustamante K., Coux R.X., Martinho R.G., Lehmann R. (2009). Temporal and spatial control of germ-plasm RNAs. **Current Biology** 19(1): 72-77.

Rasteiro R., Chikhi L. (2009). Revisiting the peopling of Japan: an admixture perspective. **Journal of Human Genetics** 54: 349-354.

Ribot, J.C., deBarros, A., Pang, D.J., Neves, J.F., Peperzak, V., Roberts, S.J., Girardi, M., Borst, J., Hayday, A.C., Pennington, D.J., Silva-Santos, B. (2009). CD27 is a thymic determinant of the balance between interferon-gamma-and interleukin 17-producing gamma delta T cell subsets. **Nature Immunology** 10(4): 427-436.

Rocha, S.F., Lopes, S.S., Gossler, A., Henrique, D. (2009). Dll1 and Dll4 function sequentially in the retina and pV2 domain of the spinal cord to regulate neurogenesis and create cell diversity. **Developmental Biology** 328(1): 54-65.

Rodrigues, L., Filipe, J., Seldon, M.P., Fonseca, L., Anrather, J., Soares, M.P., Simas, J.P. (2009). Termination of NF-kappaB activity through a gammaherpesvirus protein that assembles an EC(5)S ubiquitin-ligase. **EMBO Journal** 28: 1283-1295.

Rodrigues, P., Gomes, M.G., Margheri, A., Rebelo, C. (2009). Heterogeneity in susceptibility to infection can explain high reinfection rates. **Journal of Theoretical Biology** 259(2): 280-290.

Rog, O., Miller, K.M., Ferreira, M.G., Cooper, J.P. (2009). Sumoylation of RecQ Helicase Controls the Fate of Dysfunctional Telomeres. **Molecular Cell** 33(5): 559-569.

Ros A.F.H., Fagundes T., Oliveira R.F. (2009). Adjustment of brood size and androgen levels in a teleost species with exclusive male parental care. **Animal Behaviour** 78: 25-33.

Ros, A.F.H., Oliveira, R.F. (2009). Androgens and immune function in male alternative reproductive morphotypes of the Peacock Blenny Salaria pavo. **Ethology** 115(6): 555-565.

Sa-Leao, R., Nunes, S., Brito-Avo, A., Frazao, N., Simoes, A.S., Crisostomo, M.I., Paulo, A.C.S., Saldanha, J., Santos-Sanches, I., de Lencastre, H. (2009). Changes in pneumococcal serotypes and antibiotypes carried by vaccinated and unvaccinated day-care centre attendees in Portugal, a country with widespread use of the seven-valent pneumococcal conjugate vaccine. **Clinical Microbiology and Infection** 15 (11): 1002-1007.

Samoshkin, A., Arnaoutov, A., Jansen, L.E.T, Ouspenski, I., Dye L., Karpova, T., McNally, J., Dasso, M., Don, W., Strunnikov, C., Strunnikov, A. (2009). Human condensin function is essential for centromeric chromatin assembly and proper sister kinetochore orientation. **PLoS One** 4 :e6831.

Santos, S.C.dos, Tenreiro, S., Palma, M., Becker, J., Sá-Correia, I. (2009). Transcriptomic profiling of the *Saccharomyces cerevisiae* response to quinine reveals a glucose limitation response attributable to drug-induced inhibition of Glucose uptake. **Antimicrobial Agents Chemotherapy** 53: 5213-5223.

Seixas E., Moura Nunes J.F., Matos I., Coutinho A. (2009). The interaction between DC and *Plasmodium berghei*/chabaudi-infected erythrocytes in mice involves direct cell-to-cell contact, internalization and TLR. **European Journal of Immunology** 39(7): 1850-63.

Seixas, E., Gozzelino, R., Chora, A., Ferreira, A., Silva, G., Larsen, R., Rebelo, S., Penido, C., Smith, N.R., Coutinho, A., Soares ,M.P. (2009). Heme oxygenase-1 affords protection against noncerebral forms of severe malaria. **PNAS** 106 (37): 15837-15842.

Sepúlveda, N., Paulino, C.D., Penha-Gonçalves, C. (2009). Bayesian analysis of allelic penetrnace models for complex binary traits. **Computational Statistics and Data Analysis** 53: 1271-1283.

Sepúlveda, N., Paulino, C.D., Carneiro, J. (2009). Estimation of T-cell repertoire diversity and clonal size distribution by Poisson abundance models. **Journal of Immunological Methods**. [Epub ahead of print]

Silva, M.C., Jansen, L.E. (2009). At the right place at the right time: novel CENP-A binding proteins shed light on centromere assembly. **Chromosoma** 118: 567-574.

Silva, G., Jeney, V., Chora, A., Larsen, R., Balla, J., Soares, M.P. (2009). Oxidized hemoglobin is an endogenous proinflammatory agonist that targets vascular endothelial cells. **Journal of Biological Chemistry** 284 (43): 29582-29595.

Slotkin, R.K., Vaughn, M., Borges, F., Tanurdzic, M., Becker, J.D., Martienssen, R.A. (2009). Epigenetic reprogramming and small RNA silencing of transposable elements in pollen. **Cell** 136 (3): 461-472.

Slotkin R.K., Vaughn M., Tanurdžić M., Borges F.S., Becker J.D., Feijó J.A., Martienssen R.A. (2009). Reactivation of transposable elements in the vegetative nucleus of pollen. **Cell** 136:461-472.

Soares, M.P., Marguti, I., Cunha, A., Larsen, R. (2009). Immunoregulatory effects of HO-1: how does it work?. Current **Opinion in Pharmacology** 9 (4): 482-489.

Soares, M.P. and Bach F.H. (2009). Heme oxygenase-1: from biology to therapeutic potential. **Trends in Molecular Medicine** 15(2): 50-58.

Sousa V.M., Fritz M., Beaumont M.A., Chikhi L. (2009). Approximate Bayesian Computation (ABC) without summary statistics: the case of admixture. **Genetics** 181 (4): 1507-1519.

Sousa, V., Penha, F., Pala, I., Chikhi, L. Coelho, M.M. (2009). Conservation genetics of a critically endangered Iberian minnow: evidence of population decline and extirpations. **Animal Conservation** 10.1111/j.1469-1795.2009.00317.x.

Teotónio H., Chelo I.M., Bradić M., Rose M.R., Long A.D. (2009). Experimental evolution reveals natural selection on standing genetic variation. **Nature Genetics** 41(2): 251-257.

Thorsteinsdóttir S., Rodrigues G., Crespo E.G. (2009). Teaching and research on Developmental Biology in Portugal. **International Journal of Developmental Biology** 53 (8-10): 1235-43.

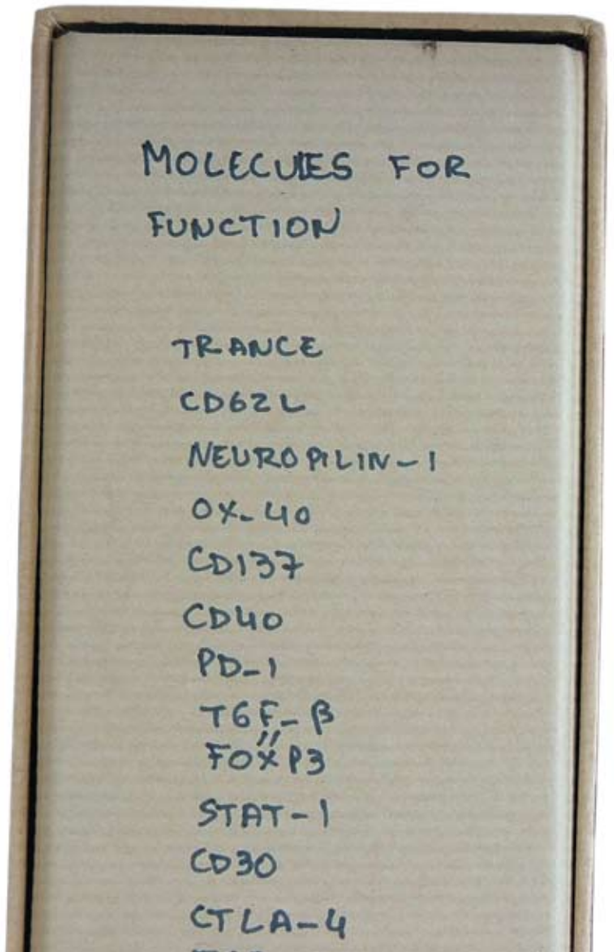
Trindade, S., Sousa, A., Xavier, K.B., Dionisio, F., Ferreira, M.G., Gordo, I. (2009). Positive epistasis drives the acquisition of multidrug resistance. **PLoS Genetics** 5 (7): e1000578.

Wang, Z.P., Kim S., Quinney, S.K., Guo, Y.Y., Hall, S.D., Rocha, L.M., Li, L. (2009). Literature mining on pharmacokinetics numerical data: A feasibility study. **Journal of Biomedical Informatics** 42 (4): 726-735.

Wittkopp, P.J., Beldade, P. Development and evolution of insect pigmentation: genetic mechanisms and the potential consequences of pleiotropy. (2009). **Seminars in Cell & Developmental Biology** 20, 65-71.

White, N.J., Pongtavornpinyo, W., Maude, R.J., Saralamba, S., Aguas, R., Stepniewska, K., Lee, S.J., Dondorp, A.M., White, L.J., and Day, N.P.J. (2009). Hyperparasitaemia and low dosing are an important source of anti-malarial drug resistance. **Malaria Journal** 8: 253.

White, L.J., Maude, R.J., Pongtavornpinyo, W., Saralamba, S., Aguas, R., Van Effelterre, T., Day, N.P.J., White, N.J. (2009). The role of simple mathematical models in malaria elimination strategy design. **Malaria Journal** 8: 212.



Yates, J.R., Mitani, S., Carrington, J.C., Mello, C.C. (2009). Distinct argonaute-mediated 22G-RNA pathways direct genome surveillance in the C. elegans Germline. **Molecular Cell** 36 (2): 231-244.

Yin, H.H., Prasad-Mulcare, S., Hilario, M.R.F., Clouse, E., Davis, M. I., Lovinger, D.M., Costa, R.M. (2009). Dynamic reorganization of striatal circuits during the acquisition and consolidation of a skill. **Nature Neuroscience** 12:3.

Young, T., Rowland, J.E., van de Ven, C., Bialecka, M., Novoa, A., Carapuco, M., van Nes, J., de Graaff, W., Duluc, I., Freund, J.N., Beck, F., Mallo, M., Deschamps, J. (2009). Cdx and Hox Genes differentially regulate posterior axial growth in mammalian embryos. **Developmental Cell** 17 (4): 516-526.

OTHER ARTICLES

Chikhi, L. (2009). Diversité génétique et évolution humaine. Journal de l'UPS.

Prado, A.M. (2009). Targeting Cancer Stems: How to switch off Immortality. **Recent Patents on Endocrine, Metabolic & Immune Drug Discovery** 3 (3): 225-232.

CHAPTERS IN BOOKS

Beldade, P, & Saenko, S.V. (2009). Conserved developmental processes and the evolution of novel traits: wounds, embryos, veins, and butterfly eyespots. In Animal Evolution. Telford, M. & Littlewood T. (eds). Novartis Foundation.

Beldade, P, & Saenko, S.V. (2009). Evolutionary and developmental genetics of butterfly wing patterns: focus on *Bicyclus anynana* eyespots. In Molecular Biology and Genetics of the Lepidoptera (Contemporary Topics in Entomology). Goldsmith, M. & Marec, F. (eds).

Brakefield, P.M., Beldade, P., Zwaan, B.J. (2009). The African Butterfly Bicyclus anynana: A Model for Evolutionary Genetics and Evolutionary Developmental Biology. In Emerging Model Organisms: A Laboratory Manual, Volume 1, RR Behringer. Johnson, A.D. & Krumlauf, R.E. (eds). Cold Spring Harbor Laboratory Press.

Champeau, J.B., Rasolondraibe, A., Quéméré, E., Rabarivola, E., Crouau-Roy C., Chikhi, L. (2009). In: Le propithèque de Tattersall : conservation d'une espèce de lémurien menacée. CEPA Magazine, 19-20, 27-29.

Cruz, C., Ramos, A.C., Façanha, A., Feijó, J.A., Martins-Loução, M.A. (2009). Enzyme activity modulated by AMF colonization: the urea cycle and membrane-bound phosphatase activities. In: Microbes for human life. Varma, A., Verma, E. (eds.) Springer-Verlag, ch25, 10 pp.

Estes, S. and H. Teotónio. (2009). The experimental study of reverse evolution. In: Experimental Evolution. Garland, T. and Rose, M.R. (eds.). University of California Press, LA, USA.

Goossens, B., Chikhi, L. Jalil, F., James, S., Lackman-Ancrenaz, I., Bruford, M.W. (2009). Taxonomy, geographic variation and population genetics of the Bornean and Sumatran orangutans. In: Orangutans: geographic variation in behavioural ecology and conservation. Wich, S., Atmoko, S.S.U., Setia T.M., Schaik, C. van (Ed.). Oxford University Press. Chapter 1, 1-14.

Prado, M.P., Feijó, J.A., Porterfield, M.D. (2009-10). Calcium dependent NO signaling in plant cell polarity and sexual reproduction. In: Nitric Oxide in Plant Physiology. Hayat, S., Mori, M., Pichtel J., Ahmad, I. (eds.). WILEY-VCH Verlag GmbH & Co. KGaA, Weinheimin. pp. 31-50.

Rocha, L.M. (2009). The Logical Mechanisms of Life. In: Complex Biological Systems. Icfai University Press, India.

Rocha, L.M. (2009). Reality is Stranger than Fiction: What can Artificial Life do about Advances in Biology?. In: Complex Biological Systems. Icfai University Press, India.

Teotónio H., Rose M.R., Proulx, S. (2009). Phenotypic plasticity and evolvability: an empirical test with experimental evolution. In: Phenotypic Plasticity in Insects. Whitman, D., Ananthakrishnan, T.N. (eds.). Science Publishers, Inc. Plymouth, UK.

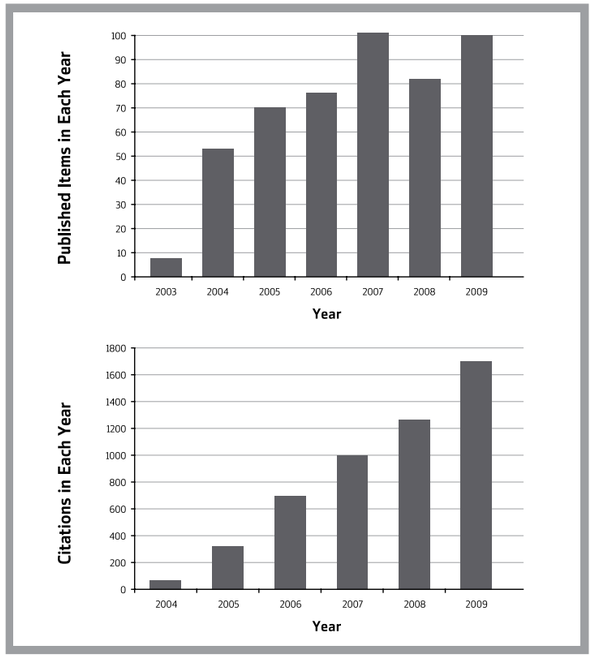
PROCEEDINGS

Kolchinsky, A., Abi-Haidar, A., Kaur, J., Hamed, A.A. and Rocha, L.M. (2009). Classification of protein-protein interaction documents using text and citation network features. **Proceedings of the BioCreative II.5 Workshop 2009: Special Session on Digital Annotations**, Madrid, Spain, October 7-9, 2009. pp 34.

Lourenço, A., Carneiro, S., Ferreira, E.C., Carreira, R., Rocha, L.M., Glez-Peña, D., Méndez, J.R., Fdez-Riverola, F., Diaz, F., Rocha I. and Rocha, L.M. (2009). Biomedical Text Mining Applied To Document Retrieval and Semantic Indexing. In: **Proceedings of the 3rd International Workshop on Practical Applications of Computational Biology & Bioinformatics** (IWPACBB'09). Lecture Notes in Computer Science Series. Springer-Verlag, 5518: 954-963.

Seabra Lopes, L.; Lau, N.; Mariano, P.; Rocha, L.M. (Eds.) (2009). Progress in Artificial Intelligence. **Proceedings of the 14th Portuguese Conference on Artificial Intelligence** (EPIA 2009). Lecture Notes in Artificial Intelligence (LNAI) Series, 5816. Springer-Verlag.

SUMMARY OF IGC PUBLICATIONS AND CITATION REPORT FOR THE LAST FIVE YEARS (2004-2009)



Source: ISI Web of Knowledge (2009)

AWARDS

AWARDS

Elena Baena-González
EMBO Installation Grant
EMBO (European Molecular Biology Organisation)
December 2009

Vasco Barreto
'Apoio à investigação em onco-hematologia' Award
Associação Portuguesa Contra a Leucemia, Portugal
February 2009

Vasco Barreto
'Bolsa Terry Fox' Award
Canadian Embassy and Núcleo Regional do Sul da L.P.C.C. - Terry Fox, Portugal
March 2009

Mónica Bettencourt-Dias
Young Investigator Award
EMBO (European Molecular Biology Organisation)
November 2009

Catarina Certal and Joaquin Leon
'FACC - Fundo de Apoio à Comunidade Científica' Meeting Support Award
Fundação para a Ciência e a Tecnologia (FCT), Portugal
July 2009

Rui Costa
European Research Council Starting Grant
European Research Council
November 2009

Francisco Freixo
OPtimusAlive!09 Oeiras - IGC Research Fellowships in Biodiversity
Everything is New, Portugal
December 2009

Gabriela Gomes
Bilateral Cooperation Agreement - Travel Award
Fundação para a Ciência e a Tecnologia (FCT), Portugal

Lars Jansen
EMBO Installation Grant
EMBO (European Molecular Biology Organisation), Fundação para a Ciência e a Tecnologia (FCT) and Calouste Gulbenkian Foundation (FCG)
July 2009

Lars Jansen
Prémio Crioestaminal
Associação Viver a Ciência and Crioestaminal, Portugal
November 2009

Margarida Prado
Rede UTEN - Travel Allowance
Fundação para a Ciência e a Tecnologia (FCT), Portugal

Henrique Teotónio
European Research Council Starting Grant
European Research Council
December 2009

Sam Viana
OPtimusAlive!09 Oeiras - IGC Research Fellowships in Biodiversity
Everything is New, Portugal
December 2009

PRIZES

Marie Louise Bergman
Prémio de Excelência em Imunologia – Mário Arala Chaves
Sociedade Portuguesa de Imunologia, Portugal

António Coutinho
Medalha Mérito Municipal Grau Ouro
Câmara Municipal de Oeiras (Oeiras City Council)
April 2009

José Feijó
Fellow of the Linnean Society (FLS)
Linnean Society, UK

Gripenet
Best Practices Award for Gripenet
Agência para a Modernização Administrativa - Rede Comum de Conhecimento, Portugal
May 2009

Inflammation Group
Prémio Pfizer em Investigação Básica (ex-aequo)
Pfizer Laboratories and Sociedade das Ciências Médicas de Lisboa, Portugal
November 2009

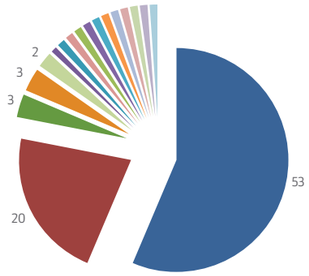
Maria Francisca Morais-Fontes
Prémio NEDAI de Investigação em Auto-imunidade 2009
NEDAI - Núcleo de Estudos de Doenças Auto-imunes da Sociedade Portuguesa de Medicina Interna, Portugal
November 2009

Telomere and Genome Stability Group
Prémio Pfizer em Investigação Básica (ex-aequo)
Pfizer Laboratories and Sociedade das Ciências Médicas de Lisboa, Portugal
June 2009

RESEARCH FUNDING

RESEARCH FUNDING

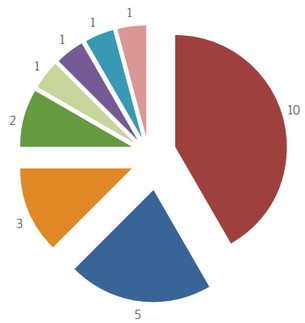
In 2009, a total of 93 research grants were running at the IGC, awarded by the following agencies and organisations:



Total nº 93 (includes new awarded grants)

- Fundação para a Ciência e Tecnologia (Portugal)
- European Commission
- Fundação Bial (Portugal)
- Câmara Municipal de Oeiras (Portugal)
- EMBO + FCT + FCG
- APCL - Associação Portuguesa contra a Leucemia (Portugal)
- Fondation pour la Recherche Médicale / FS (France)
- Embaixada do Canadá e NRS-LPCC (Portugal)
- Advancement of Research for Myopathies (USA)
- Associação Viver a Ciência + Criostaminal (Portugal)
- Association for International Cancer Research (UK)
- Autism Speaks (USA)
- Consortium USA, UK, Canada and Ireland agencies
- Fundação Astra Zeneca (Portugal)
- GEMI FUND (USA)
- L'Oreal (FCT)
- Wellcome Trust (UK)

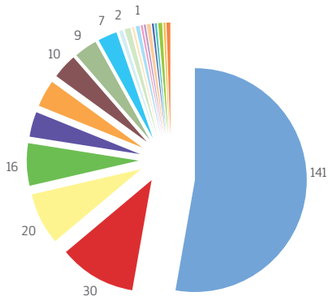
In 2009, 24 new research grants and awards were secured by IGC researchers, from the following funders:



New grants and awards for 2009
Total nº 24

- European Commission
- Fundação para a Ciência e Tecnologia (Portugal)
- Câmara Municipal de Oeiras (Portugal)
- Fundação Bial (Portugal)
- EMBO + FCT + FCG
- APCL - Associação Portuguesa contra a Leucemia (Portugal)
- Fondation pour la Recherche Médicale / FS (France)
- Embaixada do Canadá e NRS-LPCC (Portugal)

The agencies and organisations below provided support for research careers at the IGC, in 2009. The listing includes laboratory, technical and animal facilities staff. It does not include secretarial and administrative staff.



Breakdown of career funding sources in 2009

- Fundação para a Ciência e Tecnologia (Portugal)
- IGC (Portugal)
- Progrma Ciência- FCT-MCTES (Portugal)
- European Commission
- Universities / Hospitals
- IEFP Trainee Programme (Portugal)
- Champalimaud Foundation (Portugal)
- Laboratório Associado de Oeiras - FCT (Portugal)
- Calouste Gulbenkian Foundation (Portugal))
- Everything is New
- Association for International Cancer Research (UK)
- Siemens (Portugal)
- Schlumberger
- Others
- MNRT (France)
- Harvard Medical School-Portugal Programme (Portugal, USA)
- Fond. Rech. Biodiv. (France)
- European Research Council
- European Molecular Biology Organisation

GRADUATE TRAINING AND EDUCATION

PHD PROGRAMME IN INTEGRATIVE BIOMEDICAL SCIENCES

Head: **Thiago Carvalho**
E-mail: tcarvalho@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/32

The PhD Programme in Integrative Biomedical Sciences (PIBS) is the continuation of a strong investment in graduate education at the IGC that dates back to 1993. IGC alumni as a group have not only been personally sucessful, over the past decade those who stayed or returned to Portugal have dramatically reshaped the country's research landscape.
The PIBS programme is supported by the Fundação para Ciência e Tecnologia (FCT) and the Calouste Gulbenkian Foundation, selects students to develop their own research projects at the IGC. PIBS students are selected by a committee from a large pool of applicants from all over the world, and with very diverse backgrounds, not restricted to life sciences. After 4 months of courses taught by a mixture of IGC faculty and invited guest lecturers, students are given time to design their research programmes. PIBS students are strongly encouraged to engage in projects that involve more than one research group at the IGC.
Student life at the IGC is a learning experience not restricted to the course modules, with several workshops and courses available throughout the year, an abundance of guest seminar speakers who are asked to spend time with graduate students, as well as meetings students themselves organise, like their annual retreat.

STUDENTS IN 2009

Alexandre Castanho Barata Leitão	Biology
Bruno Alexandre Caetano Afonso	Evolutionary Development Biology
Francisca Ferreira Vasconcelos	Biochemistry
Leila Teruko Shirai	Genetics and Evolutionary Biology
Pedro Raimundo Teixeira Lima	Plant Molecular Biology
Raquel Alexandra Martinho dos Santos	Plant Molecular Physiology
Bahtiyar Yilmaz	Molecular Biology
Inês Gomes de Noronha Trancoso	Human Molecular Biology
Marisa Mateus de Oliveira	Biomedical Engineering
Rafaela Lacerda Santos	Biological and Celular Biotechnology
Rui Alexandre Ferreira Castanhinha	Biology

COURSES IN 2009

Welcome and Orientation Week
14 - 18 September, 2009
Thiago Carvalho, Zach Mainen (IGC, Portugal)

History of Biological Concepts
21 - 25 September, 2009
Thiago Carvalho, Antonio Coutinho, Jorge Carneiro, Lars Jansen, Joe Paton, Vitor Barbosa and Luis Rosario (IGC, Portugal), Anthony Dean (University of Minnesota, USA), Juliette Azimzadeh (UCSF, USA)

Statistics
28 September - 9 October, 2009
Jorge Carneiro (IGC, Portugal)

Genetic Models
12 - 16 October, 2009
Elio Sucena, Thiago Carvalho, Joaquin Rodriguez Leon, Vitor Barbosa, Moises Mallo, Vasco Barreto, Miguel Godinho, Henrique Teotonio and Matthias Koeppen (IGC, Portugal), Isabel Abreu (IBMC, Portugal), Miodrag Grbic (University of Western Ontario, Canada), Fernando Roch (Université de Toulouse, France)

Hypothesis Driven Research
19 - 30 October, 2009
Rui Martinho, Vasco Barreto, Thiago Carvalho, Filipe Barbosa and Miguel Soares (IGC, Portugal), Diogo Lucena (FCG, Portugal), Fernando Carvalho (Universidade Federal do Rio de Janeiro, Brazil), Ruth Lehmann (New York University, USA), Antonio Giraldez (Yale, USA), Luis Murci (Institut Pasteur, France), Helder Maiato (IBMC, Portugal)

Evolution
2 - 13 November, 2009
Isabel Gordo, Henrique Teotónio, Patrícia Brito, Ivo Chelo, Margarida Sousa, Élio Sucena, Sandra Trindade and José Pereira Leal (IGC, Portugal), Anthony Dean (University of Minnesota, USA), Francisco Dionisio (FCUL, POrtugal), Christian Schloetterer (Vienna University, Austria), Carlos Marques Silva (FCUL, Portugal), Phillip Gerrish (University of New Mexico, USA), Guillaume Dugue (University de Lausanne, Switzerland)

A Day of Structural Biology
16 November, 2009
Alekos Athanasiadis (IGC, Portugal), Alexander Rich (MIT, USA)

Ecology
17- 20 November, 2009
Thiago Carvalho, Lounes Chikhi, Karina Xavier, Isabel Gordo, Jocelyne Demengeot and Susana Lima (IGC, Portugal), John Thompson (University of California Santa Cruz, USA)

Inside the Cell
23 - 27 November, 2009
Miguel Godinho, Elena Baena Gonzalez, José Leal, Lars Jansen, Mónica Dias and Vitor Barbosa (IGC, Portugal), Rafael Carazo-Salas (ETH-Zurich, Switzerland), Ana Costa-Pereira (Imperial College London, UK), Domingos Henrique (IMM, Portugal)

In Between Cells
30 November - 4 December, 2009
Florence Janody, Matthias Koeppen, Susana Lima, Joaquin Rodriguez Leon, Karina Xavier and Catarina Certal (IGC, Portugal), Antonio Jacinto, Soren Prag, Susana Lopes Leonor Saude and Rita Fior (IMM, Portugal), Will Wood (Bath University, UK), Shane Hutson (Vanderbilt University, USA), Carl Phillip Heisenberg (MPI Dresden, Germany), Luis Almeida (Université de Nice, France)

Immunology
7 - 11 December, 2009
Thiago Carvalho, Jocelyne Demengeot, Vasco Barreto, Miguel Soares, Luis Teixeira (IGC, Portugal), Marc Dionne (King's College London, UK), Louis Du Pasquier (Basel University, Switzerland), Luca Imeri (University of Milan, Italy)

Research Presentations by IGC, Portugal Groups
14 - 18 December, 2009
Thiago Carvalho (IGC, Portugal)

SUPPORT STAFF
Manuela Cordeiro (Administrative Assistant)

PHD PROGRAMME IN COMPUTATIONAL BIOLOGY

Director: **Jorge Carneiro**
Group Leader
E-mail: jcarneir@igc.gulbenkian.pt
url: http://bc.igc.gulbenkian.pt/pdbc/

The PhD Programme in Computational Biology (PDBC) is a pilot graduate programme that aims to create a critical mass of researchers in computational biology, who will act as the future leaders in the field. To this end it operates in close association with its twin initiative, the Collaboratorium in Computational Biology, and is promoted by the Portuguese Ministry for Science and Technology, the Calouste Gulbenkian Foundation, and Siemens SA, and co-sponsored by several institutions including the PT Foundation, FCCN (Fundação para a Computação Científica Nacional) and FLAD (Luso-American Development Foundation). The PDBC has a definitive lifespan and was planned to educate 4 generations of 12 students per year, from 2005 onwards. Education is organised as a four-year programme divided into a first year of full-time courses, workshops and projects, covering the main aspects of computational biology from the biological, computational, mathematical, chemical and physical points of view, and three years of research training in a recognised laboratory anywhere in the world, including Portugal. Non-national citizens were accepted under the condition that their research training be carried out in a Portuguese research laboratory. The choice of laboratory was left to the student but needed to meet the standards set by the Programme Direction. The PDBC has come of age, and all 45 students are doing their research training in laboratories in Europe and beyond.

2008/2009 STUDENTS

António Miranda	Biology
António Rodrigues	Computer Science
Bruno Santos	Biochemistry
Carlos Afonso	Physical Engineering
Daniel Damineli	Biology
Jose Lourenço	Software Engineering
Miguel Proa	Biology
Sylvie Estrela	Biochemistry
Yoan Diechmann	Bioinformatics
Tiago Macedo	Biomedical Engineering
Tiana Gonçalves	Biology

2009 COURSES

Biomolecular simulation and Structural Bioinformatics
5 - 9 January, 2009
Claudio M. Soares (ITQB, Portugal), António Baptista (ITQB, Portugal)

Fundamental graph algorithms
12 - 16 January, 2009
Claudine Chaouiya (TAGC, Université de Marseille, France and IGC)

Nucleic acid structure and function
19 - 23 January, 2009
Eric Westhof (IBMC/CNRS, Strasbourg, France) and Jose Cruz (PDBC and IBMC/CNRS, Strasbourg, France)

Combinatorial Pattern Matching Algorithms in Computational Biology
26 - 31 January, 2009
Gabriel Valiente (Technical University of Catalonia, Spain)

Sequence Alignment
2 - 7 February, 2009
Burkhard Morgenstern (Institut for Mikrobiologie und genetik, Universitat Gottingen, Gottingen, Germany)

SUPPORT STAFF
Claudine Chaouiya (Coordinator)
Manuela Cordeiro (Administrative Assistant)

Organisation and dynamics of prokaryotic genomes
9 - 13 February, 2009
Eduardo Rocha (Université Pierre et Marie Curie-Paris 6 and Institut Pasteur, Paris, France) and Sara Silva(PDBC and Université Pierre et Marie Curie-Paris 6, France)

Phylogenetics
9 - 13 February, 2009
Vincent Moulton and Katharina Huber (University of East Anglia, UK)

Integrative Genomics
16 - 20 February, 2009
Jotun Hein and Rune Lyngso (University of Oxford, UK)

Chromosome Organisation
23 - 27 February, 2009
Benjamin Audit (Ecole Normale Supérieure de Lyon)

MicroRNA genomics
2 - 6 March, 2009
Anton Enright (Wellcome Trust Sanger Institute, Cambridge, UK)

Analysis of DNA expression microarrays
11 - 12 March, 2009
Nuno Barbosa Morais (Cancer Research UK Cambridge Research Institute, UK)

Principles of Bayesian inference and statistics
16 - 20 March, 2009
Jose M. Bernardo (Facultad de Matematicas, Valencia, Spain)

Protein interaction networks
23 - 28 March, 2009
Jose Pereira Leal (IGC, Portugal)

Introduction to Dynamic Systems
30 March - 3 April, 2009
Tiago Paixão (University of Houston, USA)

Transcriptional Networks
2 March - 3 April, 2009
Sarah Teichmann and Sarath Chandra Janga (MRC Laboratory of Molecular Biology, Cambridge, UK)

Proteomics
6 - 10 April, 2009
Nuno Bandeira (UC San Diego, USA)

Bifurcation theory
6 - 10 April, 2009
Frank Hilker (University of Alberta, Canada)

Metabolic network modeling
20 - 24 April, 2009
Rui Alves (University of Lleida, Spain)

Logical modeling
24 April, 2009
Rene Thomas (Université Libre de Bruxelles, Belgium)

Petri nets in molecular network modeling
27 April - 2 May, 2009
Claudine Chaouiya (TAGC, Universite de Marseille, France and IGC) and Ina Koch (Technical University of Applied Sciences Berlin, Germany)

Computational approaches to cell cycle
27 - 30 April, 2009
Attila Csikasz-Nagy (University of Trento, Italy)

Metabolic and genetic network modelling
4 - 8 May, 2009
Hidde de Jong, Delphine Ropers (INRIA, Rhône-Alpes, France), Pedro Monteiro (PDBC and INRIA, Rhône-Alpes, France)

Stochastic dynamics of biomolecular networks
11 - 16 May, 2009
Andrzej Kierzek (University of Surrey, UK)

Stochastic resonance and coherence in dynamic systems
11 - 15 May, 2009
Andreas Bohn (ITQB, Portugal)

Reverse engineering of regulatory networks
18 - 23 May, 2009
Reinhard Laubenbacher (Virginia Bioinformatics Institute, USA)

Population biology, epidemiology and immune systems 1
28 - 30 May, 2009
Ruy Ribeiro (LANL, New Mexico, USA)

Drosophila segmentation
1 - 4 June, 2009
Denis Thieffry (Université de Marseille, France) and Filipa Alves (IGC, Portugal)

Pattern formation in development
30 May - 1 June, 2009
Hans Meinhardt (MPI Entwicklungsbiologie, Tubingen, Germany)

Epidemiology of infectious diseases
5 - 10 June, 2009
Gabriela Gomes (IGC, Portugal)

Cell-based models of development
9 - 11 June, 2009
Stan Maree (University of Utrecht, Netherlands)

Computational Neurosciences
22 - 26 June, 2009
Konrad Kording (Northwestern University, USA), Dan Goldreich (McMaster Univ, USA), Wei Ji Ma (Rocherster Univ, USA), Alan Stocker (NYU, USA), Jonathan Pillow (Univ. of Texas at Austin, USA)

Medical Bioinformatics and System Biology
29 June - 1 July, 2009
Jose Pereira-Leal (IGC, Portugal), Nuria Lopez-Bigas (Univ. Pompeu Fabra, Spain), Sofia Braga (IGC, Portugal), Nuria Domedel (Univ. Politecnica de Catalunya, Spain), Pablo Villoslada (Univ. Gottenburg, Sweden), Julio Saez-Rodriguez (MIT, USA)

INTERNATIONAL NEUROSCIENCE DOCTORAL PROGRAMME

Director: **Zachary Mainen**
Group Leader of the Champalimaud Neuroscience Programme at the IGC
E-mail: zmainen@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/89
http://www.fchampalimaud.org/care-research/cf-neuroscience-programme/doctoral-programme/

The International Neuroscience Doctoral Programme (INDP) aims to train students to perform innovative and integrative research into the biological bases of behaviour. During the first year, students attend courses organised by a combination of internal faculty and invited international researchers. This initial training phase aims at providing students with a broad background and common language in biology and neuroscience. The curriculum emphasises active participation, discussion and practical exercises. The goal is to develop critical and creative thought and to gain exposure to a variety of perspectives on the biology of the nervous system.
Autumn courses, organised in conjunction with the in-house PIBS programme, focus on general biological principles. Spring courses concentrate on neuroscience, including physiology, development, sensory and motor systems, learning, social behaviour and cognition. There is a strong quantitative component to the curriculum, including programming, data analysis and modeling. At the end of the first year, students choose a thesis laboratory guided by faculty the programme director and neuroscience core faculty.
In 2009, the INDP entered its third year. A total of 32 students were enrolled, including eleven performing thesis research abroad, nine performing their research in CNP laboratories at the IGC, and twelve new students, including six from abroad and six from Portugal.

FACILITY STAFF
Joe Paton (Coordinator)
Alexandra Piedade (Assistant)

STUDENTS IN 2009

Ali Ozgur Argunsah	Biomedical engineering
Andreia Cruz	Marine Biology - (Biology applied to the animal resources)
Anna Hobbiss	Natural Sciences and Genetics
Diogo Peixoto	Physics
Elizabeth Rickenbacher	Psychology and Neuroscience
David Raposo	Computer Science
Niccolò Bonacchi	Rehabilitation and Social Inclusion
Sevinç Mutlu	Physics
Raquel Abreu	Biochemistry
Thiago Gouvêa	Biomedicine

2009 COURSES

Introduction
5 - 16 January, 2009
Joe Paton (IGC)
Zach Mainen, Rui Costa, Marta Moita and Susana Lima (IGC); Chris Braun (CUNY, USA)

History & Philosophy
19 - 23 January, 2009
Brian Keeley (Pitzer, USA)
Dorothée Legrand (CREA, CNRS)

Approaches
26 - 30 January, 2009
Luísa Vasconcelos (IGC)
Martha Constantine-Paton (MIT, USA)

Cellular physiology
2 - 6 February, 2009
Josh Dudman (JFRC)
Thomas Nevian (Bern), Mike Berry (Princeton), Michael Hausser (UCL)

Structure and function of circuits
9 - 13 February, 2009
Josh Dudman (JFRC), Alex Reyes (NYU)
Mike Berry (Princeton, USA), Dean Buonomono (UCLA, USA), Loren Frank (UCSF, USA)

Neural systems & behaviour
16 - 20 February, 2009
Brian Lau (Columbia, USA), Kenway Louie (NYU, USA)
Jim DiCarlo (MIT, USA), Tony Movshon (NYU, USA)

Cognition, perception, consciousness
23 - 27 February, 2009
Greg Corrado (Stanford, USA), Leo Sugrue (Stanford, USA)
Kacey Ballard (Stanford, USA), Mickey Goldberg (Columbia, USA), Yonatan Loewenstein (Hebrew Univ, Israel)

Neural development
9 - 13 March, 2009
Luísa Vasconcelos (IGC)
Joshua Corbin (CNR, USA), Ana Godinho (IGC, Portugal) and Luísa Vasconcelos (IGC, Portugal)

Evolution & development
16 - 20 March, 2009
Élio Sucena (IGC, Portugal) and Luísa Vasconcelos (IGC, Portugal)
Georg Striedter (UC Irvine, USA), Elio Sucena (IGC, Portugal) and Luísa Vasconcelos (IGC, Portugal)

Developmental plasticity
23 - 27 March, 2009
Dan Feldman (Berkeley, USA) and Marla Feller (Berkeley, USA)
Ken Harris (Rutgers, USA), Ed Ruthazer (McGill Univ, Canada), Mark Huebener (Max-Planck-Institute of Neurobiology, Germany)

Synaptic plasticity and learning
30 March - 3 April, 2009
Inbal Israely (IGC, Portugal), Marta Moita (IGC, Portugal) and Simon Rumpel (IMP, Austria)
Steven Kushner (UCLA, USA)

Metabolism, energetics, foraging, food selection
13 - 17 April, 2009
Carlos Ribeiro (IGC, Portugal)
John Pospisilik (Univ. British Columbia, Canada), Giorgio Gilestro (Wisonsin-Madison, USA)

Basal ganglia, reinforcement, reward
20 - 24 April, 2009
Joe Paton (IGC, Portugal) and Rui Costa (IGC, Portugal)
Yael Niv (Princeton, USA), Peter Redgrave (Univ. Sheffield, UK), Nathaniel Daw (NYU, USA) and Daniel Salzman (Columbia, USA)

Sequences
27 - 29 April, 2009
Rui Costa (IGC, Portugal) and Joe Paton (IGC, Portugal)
Rui Costa (IGC, Portugal) and Joe Paton (IGC, Portugal)

Moving into action
4 - 7 May, 2009
Rui Costa (IGC, Portugal) and José Carmena (Berkeley, USA)
Matthew Tresch (Northwestern, USA) and Joe McIntyre (Univ. Paris 5, France)

Timing
12 - 16 May, 2009
Rui Costa (IGC, Portugal) and Joe Paton (IGC, Portugal)
Randy Gallistel (Rutgers, USA), Carlos Brody (Princeton, USA)

Sensorimotor integration (neuroethological perspective)
18 - 29 May, 2009
Florian Engert (Harvard, USA), Adam Kampff (Harvard, USA)
Curtis Bell (Portland Univ., USA), Michael Orger (Harvard, USA) and Michael Reiser (JFRC, USA)

Cooperation, competition, morality
1 - 5 June, 2009
Rui Oliveira (IGC, Porugal/ISPA, Portugal)
Ed Kravitz (Harvard, USA), Hans Hofmann (Univ. Texas Austin, USA), Sarah Certel (Harvard, USA), Jill Penn (Harvard, USA), Magda Teles (ISPA, Portugal) and Miguel Simões (ISPA, Portugal)

Sleep and Dreaming
8 - 12 June, 2009
Zach Mainen (IGC, Portugal)
Allan Hobson (Harvard, USA)

Bayesian approaches to brain & behavior
22 - 26 June, 2009
Konrad Koerding (Northwestern Univ., USA)
Wei Ji Ma (Baylor College, USA), Daniel Goldreich (Univ. Pennsylvania, USA), Alan Stocker (Univ. Pennsylvania, USA), Jonathan Pillow (Univ. Texas Austin, USA)

PROGRAMME FOR ADVANCED MEDICAL RESEARCH - DOCTORAL PROGRAMME FOR PHYSICIANS

Director: **Leonor Parreira**
Professor of Histology and Developmental Biology (Faculdade de Medicina da Universidade de Lisboa, Portugal) and Associate Investigator at IGC
E-mail: lparreira@igc.gulbenkian.pt
url: http://www.gulbenkian.pt/index.php?section=53&artId=299

The Programme for Advanced Medical Education is a Doctoral Programmme for physicians, supported by the Gulbenkian (FCG) and Champalimaud (FC) Foundations, the Ministry of Health and the Foundation for Science and Technology (FCT).
The Programme is targeted at highly motivated clinicians who, as a complement to their clinical practice, wish to acquire a strong scientific background as a basis for excellence in medical research and clinical practice. The Programme selects 10 students per year, five on a full time-basis (Specialists and Interns), fully supported by a FCG or FC three year fellowship, five on a part-time basis (Interns). Part-timers receive a six months FCG fellowship for full-time attendance of graduate courses, after which they return to the internship supported by FCT and the Ministry of Health.
Students receive six months graduate courses by an international Faculty, followed by doctoral thesis work at national or international institutions. Graduate courses take place at leading Portuguese Biomedical research Institutions: Instituto Gulbenkian de Ciência; Institute for Molecular Medicine (IMM)/Faculty of Medicine, in Lisbon; IPATIMUP, in Lisbon, in Porto; Faculdade de Ciência Médicas, Universidade Nova de Lisboa; Faculdade de Medicina da Universidade do Porto.

STUDENTS IN 2009

FULL-TIME:

Alexandra Borges	Specialist in Radiology	Instituto Português de Oncologia, Lisboa
Sandra Jacinto	Specialist in Pediatrics	Hospital D. Estefânia, Lisboa
Alexandra Santos	Intern in Immunoallergology	Hospitais da Universidade de Coimbra
Susana Vacas	Intern in Anesthesiology	Hospital de Santarém
Inês Pires da Silva	Intern in Medical Oncology	Instituto Português de Oncologia, Lisboa

PART-TIME:

Nuno Cortez-Dias	Intern in Cardiology	Hospital Santa Maria, Lisboa
Catarina R. dos Santos	Intern in General Surgery	Instituto Português de Oncologia, Lisboa
Diogo Bogalhão do Casal	Intern in Plastic Surgery	Hospital S. José, Lisboa
Cláudia Faria	Intern in Neurosurgery	Hospital Santa Maria, Lisboa
Jaime Almeida	Intern in Pshychiatry	Hospital S. Francisco Xavier, Lisboa

2009 MODULES

Gene Expression
1 - 16 October, 2009
João Ferreira (Organizer, IMM/FML, Lisbon, Portugal), Luis F. Moita, Maria Mota and Leonor Saúde (FML/IMM, Lisbon, Portugal), Margarida Carvalho (FML/FCUL, University of Lisbon, Portugal), Carlos Farinha (FCUL, University of Lisbon, Portugal), Jamal Tazi (Institut Génétique Moleculaire, Montpellier, France), Christèle Maison (Institut Curie, Paris, France), Ron Hay (University of Dundee, Scotland)

Structural Biology
26 - 30 October, 2009
Anna Tramontano (Organiser, University La Sapienza, Rome), Domenico Raimondo and Paolo Marcatili (University La Sapienza, Rome), Antony Dean (University Minnesota)

Cell cycle, Cytoskeleton & Disease
2 - 6 November, 2009
Mónica Bettencourt-Dias (Organiser, IGC, Oeiras, Portugal), Dyche Mullins (University of California, San Francisco, USA), Marcus Malumbres (Spanish National Cancer Research Center, Madrid, Spain), Carla Martins (University of Cambridge, Cambridge, UK), Alexey Khodjakov (Wadsworth Center, Albany, NY,USA), Philip Beales (Institute Child Health, University College, London, UK), Helder Maiato (IBMC, Porto, Portugal), Florence Janody, Lars Jansen, Rui Martinho and Vitor Barbosa (IGC, Oeiras, Portugal)

Biostatistics
9 - 14 November, 2009
Armando Teixeira Pinto (Organiser, Faculty of Medicine, Universidade do Porto, Portugal), A. Teixeira-Pinto (Faculty of Medicine, Universidade do Porto, Portugal), Jaroslaw Harezlak (University of Indiana, USA)

Introduction to clinical investigation
16 - 18 November, 2009
Luis Filipe Azevedo (Faculty of Medicine, Universidade do Porto, Portugal)

Integrative Epidemiology
23 - 27 November, 2009
Gabriela Gomes (Organiser, IGC, Oeiras, Portugal), Laura Rodrigues and Isabel Silva (London School Hygiene & Tropical Medicine)

Computational Biology & Medicine
30 November - 4 December, 2009
José Leal (Organiser, IGC, Oeiras, Portugal), Jorge Carneiro and Isabel Gordo (IGC, Oeiras, Portugal), Patrícia Figueiredo (Instituto Superior Técnico, Lisbon, Portugal), James Brenton (University of Cambridge, UK), Alfonso Valência (Centro Nacional Investigaciones Oncologicas, Spain), Jonas Almeida (M.D. Anderson, USA), Karen Nelson (The Craig Venter Institute, USA)

Genetics
7 - 11 December, 2009
Carlos Penha Gonçalves (Organizer, IGC, Oeiras, Portugal), Susana Campino and Taane Clark (Wellcome Trust Sanger Genomic Campus, Hinxton, UK), Lounes Chikhi (IGC, Oeiras, Portugal), Jan Korbel (EMBL, Heidelberg, Germany), Isabel Marques (IGC, Oeiras, Portugal)

GTPB - THE GULBENKIAN TRAINING PROGRAMME IN BIOINFORMATICS

Head: **Pedro Fernandes**
E-mail: pfern@igc.gulbenkian.pt
url: http://gtpb.igc.gulbenkian.pt

The GTPB has been running at the IGC since 1999. It aims at providing a fair degreee of independence in the usage of Bioinformatics tools and resources. This is acheived by combining a series of methods that maximise the rate of acqusition of skills, while keeping the attendees interested in the conceptual framework of each course theme. The courses are exclusively taught in English, and completely documented in electronic form (CDROM; DVD). Tracking of self-assessment questionnaires allows for a continued improvement in the organisation and methods. Periodical poling for expressions of interest allows us to probe new subjects for adequacy to the interests of audiences that are constantly being renewed. The attendees span from bench biologists to full-fledged computational biologists. IGC, ITQB and IBET members have equalt access to GTPB courses, due to a specific protocol. GTPB courses range very widely in level, from introductory to professionally specialized.

In 2009, a total of 181 students attended the GTPB training programme: 143 are Portuguese students and 38 are from several countries in Europe and America.

INDIVIDUAL MODULES / COURSES

MEPA09 - Molecular Evolution, Phylogenetics and Adaptation
2 - 6 March, 2009
Hernan Dopazo, François Serra (Centro de Investigacion Principe Felipe, Spain)

IB09 - Introductory Bioinformatics (1st course)"
16 - 20 March, 2009
David Judge (University of Cambridge, UK)
Phillip Cunningham (King's College London, UK)
Pedro Fernandes (IGC)

ENSGEN09 - ENSEMBL: Browsing on genes and genomes, mining with BIOMART
31 March - 1 April, 2009
Bert Overduin (European Bioinformatics Institute, UK)

ENSAPI09 - ENSEMBL Developers workshop: CORE AND COMPARA
2- 3 April, 2009
Javier Herrero (European Bioinformatics Institute, UK)

MDAGB09 - Microarray Data Analysis using GEPAS and BABELOMICS
6 - 8 May, 2009
Joaquin Dopazo, Ignacio Medina, Francisco Garcia (Centro de Investigacion Principe Felipe, Spain)

MMPG09 - Molecular Markers and Population Genetics (1st Course)
15 - 19 June, 2009
Mark Beaumont (University of Reading, UK)
Lounès Chikhi, Vitor Sousa (IGC)

PHYLOINF09-ComputationalPhyloinformatics-aGTPB-NESCentCollaboration
9 - 19 July, 2009
Hilmar Lapp (NESCENT, USA)
Darin London (Duke University, USA)
William Piel (Yale University, USA)
Rutger Vos (University of British Columbia, Canada)

SG09 - Structural Genomics
27 - 31 July, 2009
Marc Marti-Renom, Antonio Pineda-Lucena (Centro de Investigacion Principe Felipe, Spain)

IB09 - Introductory Bioinformatics (2nd course)
7 - 11 September, 2009
David Judge (University of Cambridge, UK)
Phillip Cunningham (King's College London, UK)
Pedro Fernandes (IGC)

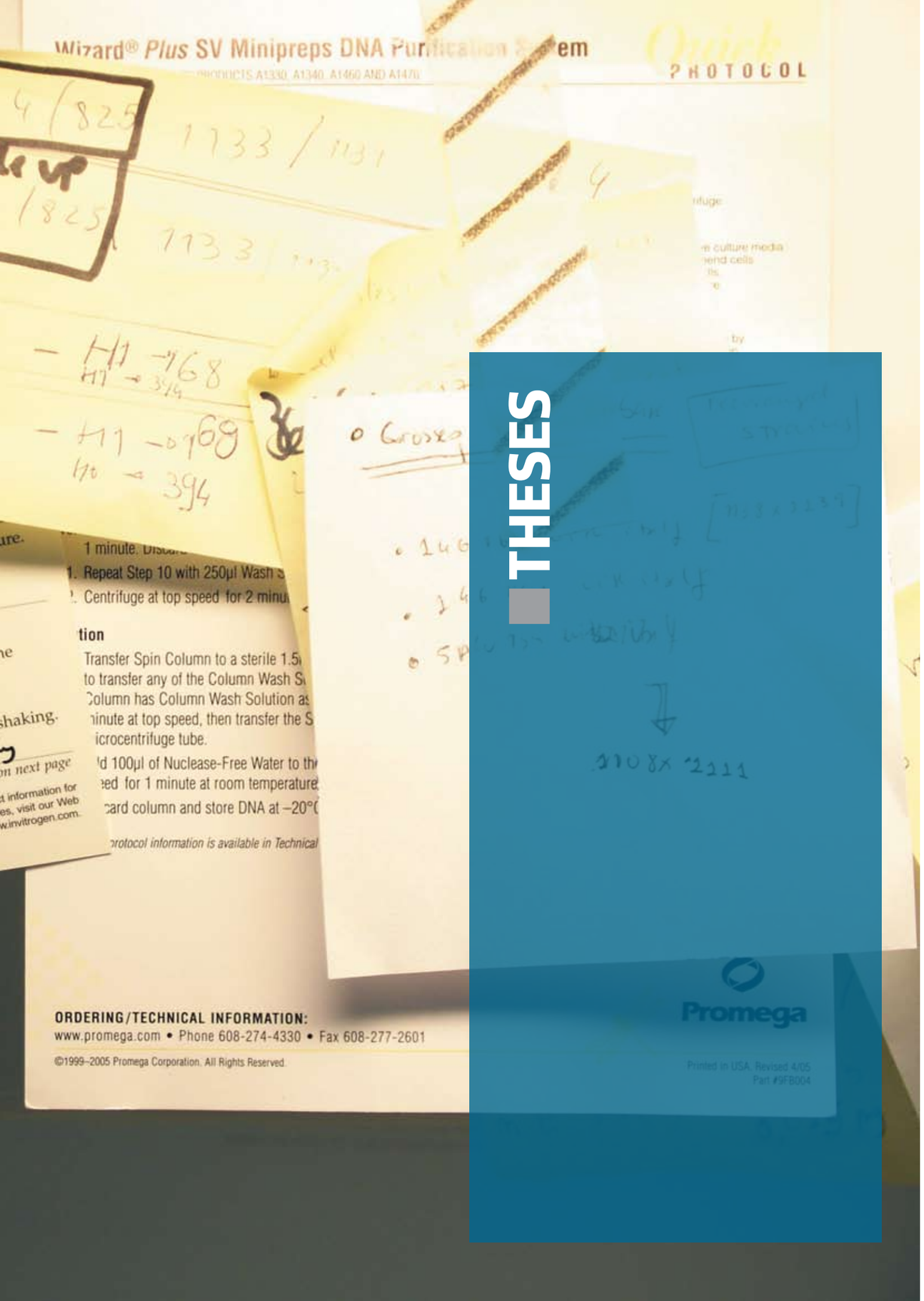
MDARB09
Microarray Data Analysis using R and Bioconductor
14 - 19 September, 2009
Nuno Barbosa-Morais, Rosalyn Russel (University of Cambridge, UK)

PA09 - Pathway Biology: How to analyse transcriptomics, ChIP-chip/seq and proteomics data
12 - 13 October, 2009
Alexander Kel, Olga Kel-Margoulis (Biobase GmbH, Germany)
(Biobase GmbH, Germany)
Christophe Wierling (Max Plank Institut Berlin, Germany)
Bijay Jassal (European Bioinformatics Institute, UK)
Roman Zubarev (Karolinska Institutet, Sweden)

WPAT09 - Workflows and Programatically Accessible Tools
16 - 17 November, 2009
Katherine Wolstencroft (University of Manchester, UK)

GACT09 - Genetic Architecture of Complex Traits
9 - 11 December 2009
Arcadi Navarro, Hafid Laayouni (Universitat Pompeu Fabra, Spain)

MMPG09A - Molecular Markers and Population Genetics (2nd Course)
14 - 18 December, 2009
Mark Beaumont (University of Reading, UK)
Lounès Chikhi, Vitor Sousa, Barbara Pereira (IGC)



THESES

PHD THESES

Erwan Quéméré. Génétique du paysage de populations fragmentées de lémuriens à Madagascar. Université Paul Sabatier, France. June 2009.

Paula Rodrigues. Modeling tuberculosis: a compromise between biological realism and mathematical tractability. Universidade de Lisboa, Portugal. October 2009.

Maria Francisca Fontes. Modulation of Regulatory T cells in autoimmune disease. Faculdade de Medicina da Universidade de Lisboa, Portugal. May 2009.

Joao Duarte. The transcription factor Foxp3 and regulatory T cell physiology. Universidade de Coimbra, Portugal. 9 October 2009.

Nuno Moreno. Oscillatory behavior in pollen tubes: the biophysical and biochemical fundamental basis of cell growth and morphogenesis. Instituto de Tecnologia Química e Biológica/Universidade Nova de Lisboa, Portugal. July 2009.

Laura Cabrita dos Santos. Molecular regulation of Plasmodium sporozoites exocytosis and infection. Faculdade de Medicina da Universidade de Lisboa, Portugal. October, 2009.

Rita Neres. Experimental Pregnancy-Associated Malaria: Immunopathological components. Universidade de Lisboa, Portugal. October 2009.

Ana Rodrigues Martins. Centriole architecture, biogenesis and function in *Drosophila melanogaster*. University of Cambridge, United Kingdom. August 2009.

Nuno Sepúlveda. How is the T cell repertoire shaped?. Universidade do Porto, Portugal. October 2009.

MSC THESES

Rita Aires. Analisis of the role of V-ATPases during caudal fin egenration in zebrafish. Faculty of Sciences, Universidade de Lisboa, Portugal. October 2009.

Ana Mafalda de Almeida Cavaleiro. Transcriptional activation in *Saccharomyces ceerevisiae* gim mutantes (Activação transcricional em mutantes gim de Saccharomyces cerevisie). Faculdade de Ciências da Universidade de Lisboa, Portugal. December 2009.

Filipe Cadete. CentrioleDB and the Rabifier: Two bioinformatic tools for the cell biology community. Faculdade de Ciências da Universidade de Lisboa, Portugal. September 2009.

Bruno Alexandre Caetano Afonso. The effect of inter-species communication in the mutational rate of *Escherichia coli*. Faculdade de Ciências da Universidade de Lisboa, Portugal. December 2009.

Sara Catita. Give to receive: Private Funding of Science and Corporate Social Responsibility. Instituto Superior de Clências do Trabalho e da Empresa da Universidade Nova de Lisboa, Portugal. 1 May 2009.

Andreia Cruz. The role of the amygdala in trace fear conditioning. Faculdade de Ciências da Universidade de Lisboa, Portugal. Novembro 2009.

Daniel Espadinha. Directed Evolution of Activation Induced Cytidine Deaminase. Faculdade de Ciências da Universidade de Lisboa, Portugal. December 2009.

Sara Esteves. Regulation of mitotic exit in higher eukaryotes: Drosophila mob genes. Faculdade de Ciências da Universidade de Lisboa, Portugal. September 2009.

Vítor Faria. Mecanismos de transmissão vertical e horizontal do endossimbionte Wolbachia. Faculdade de Ciências da Universidade de Lisboa, Portugal. December 2009.

Francisco Freixo. Centrosome biogenesis and number: mechanisms of control - Determination of SAK/PLK4 interactors. Faculdade de Ciências da Universidade de Lisboa, Portugal. October 2009.

Alexandre Leitão. Towards the characterization of plasmatocyte heterogeneity in *Drosophila melanogaster*. Faculdade de Ciências da Universidade de Lisboa, Portugal. December 2009.

Pedro Lima. Cell to cell communication in plants: ions take charge. Universidade do Minho, Braga, Portugal.

Daniel Marques. The role of AI-2 quorum sensing in *Escherichia coli* colonization of the mammalians intestines. Faculdade de Ciências da Universidade de Lisboa, Portugal. December 2009.

Frederico Matos. Analysis of the flrt2 and flrt3 genes during pectoral fin development in zebrafish. Faculdade de Ciências da Universidade de Lisboa, Portugal. October 2009.

Inês Gomes de Noronha Trancoso. Screening for RAG activity in haematopoietic tumours using a novel reporter strategy. Faculdade de Ciências da Universidade de Lisboa, Portugal. November 2009.

Marisa Oliveira. Pattern formation and wound healing: experimental and theoretical approaches. Instituto Superior Técnico, Lisbon, Portugal. 15 October 2009.

Matteo Villa. Heme, a double edged sword linking sickle cell disease and cerebral malaria. Facoltà di Medicina e Chirurgia - Universita degli studi di Milano Bicocca, Italy.

Maurícia Vinhas. Role of the different actin genes during extrusion of capping Protein mutant cells in the Drosophila wing blade epithelium. Universidade do Algarve, Portugal. June 2009.

BSC THESES

Isabel Guerreiro. Analysis of Hoxa10 specific peptide motifs in their patterning functions of the axial skeleton. Faculdade de Ciências da Universidade de Lisboa, Portugal. November 2009.

SEMINARS, WORKSHOPS, AND MEETINGS

SEMINARS AT THE IGC

JANUARY 2009

05-01-2009
Sónia Rocha
Wellcome Trust Center for Gene Regulation and Expression, School of Life Sciences, Dundee, UK
Mechanisms controlling gene expression in Hypoxia

06-01-2009
Elisabetta Padovan
IGC
Human Immunology

09-01-2009
Sara Ricardo
Skirball Institute for Biomolecular Medicine, NYU School of Medicine, NY, USA
An ABC transporter controls the export of a Drosophila germ cell attractant

13-01-2009
Elena Baena-González
IGC
Integration of stress signals into plant growth and development

15-01-2009
Jill Scott
Institute Cultural Studies, University of the Arts, Zurich, Switzerland
Neuromedia

15-01-2009
Ana Sofia Pires
Instituto de Tecnologia Química e Biológica (ITQB), Oeiras, Portugal
Plant cell cultures as an alternative production system for recombinant proteins

16-01-2009
Jaime Mota
Instituto de Tecnologia Química e Biológica (ITQB), Oeiras, Portugal
Interaction between intracellular Salmonella and post-Golgi trafficking

20-01-2009
Erwan Michard
IGC
Plant ionotropic amino-acid receptors: calcium channels involved in pollen tube growth and orientation

23-01-2009
Jorge M. Pacheco
Centro de Física Teórica e Computacional, University of Lisbon, Portugal
Modeling the architecture and dynamics of hematopoiesis

26-01-2009
Fabrizio d'Adda di Fagagna
FIRC Institute of Molecular Oncology Foundation, Milan, Italy
Molecular mechanisms of cellular senescence

27-01-2009
Jorge Carneiro
IGC
Set a thief to catch a thief: towards fully automated image analysis based on morphodynamic cell models

30-01-2009
Martha Constantine-Paton
McGovern Institute for Brain Research at MIT, Cambridge, MA, USA
Changes in glutamate receptor trafficking, scaffolding, and LTP upon eye opening in the developing rodent

FEBRUARY 2009

02-02-2009
Jan Hoejimakers
Erasmus Medical Center, Rotterdam, The Netherlands
DNA damage, cancer, ageing and the survival response that promotes longevity

03-02-2009
Filipa Alves
IGC
Three-dimensional models for cell polarization in pollen tubes

03-02-2009
Kai Konrad
IGC
Usefulness of voltage-sensitive dyes and reporter proteins to monitor the membrane potential of pollen tubes, a plant model cell system to study polar

04-02-2009
Tony Dean
University of Minnesota, Minneapolis-St. Paul, USA
The structure of an ancient adaptive landscape

04-02-2009
Thomas Nevian
University of Bern, Switzerland
Signaling mechanisms in spike-timing dependent plasticity

05-02-2009
Michael Hausser
University College London, UK
Dendritic computation of direction and velocity

06-02-2009
Michael Berry
Department of Molecular Biology, Princeton University, USA
Reading out a correlated population code

10-02-2009
Florence Janody
IGC
Proper regulation of cytoskeletal genes is essential to prevent aberrant growth of Drosophila epithelia

10-02-2009
Dean Buonomano
University of California-Los Angeles (UCLA), USA
Temporal processing and neural dynamics

12-02-2009
Alex Reyes
New York University (NYU), USA
Input-dependent modulation of functional inhibition in neural networks

12-02-2009
Alexander Dammermann
Ludwig Institute for Cancer Research, University of California, San Diego, USA
Molecular analysis of centriole assembly and function

13-02-2009
Crisanto Gutierrez
Consejo Superior de Investigaciones Cientificas, Universidad Autonoma de Madrid, Spain
Cell division, chromatin and differentiation during Arabidopsis development

13-02-2009
Loren Frank
University of California-San Francisco (UCSF), USA
Learning and memory reactivation in the Hippocampus

17-02-2009
Henrique Teotónio
IGC
Experimental evolution of C. elegans populations

18-02-2009
Marcelo Urbano Ferreira
Instituto de Ciências Biomédicas da Universidade de São Paulo, Brazil
Antigenic diversity and evolution in Plasmodium falciparum

20-02-2009
Jonathan Pines
Wellcome/CR UK Gurdon Institute, University of Cambridge, UK
The Ins and Outs of cell division

27-02-2009
Susana Valente
Columbia University, NY, USA
Human cellular factors that restrict HIV-1 activity

MARCH 2009

03-03-2009
Jocelyne Demengeot
IGC
Immune tolerance to genetically self and non-self components: striving for harmony

06-03-2009
Conly Rieder
Wadsworth Center, New York State Department of Health, Albany, USA
Live cell studies on the mitotic checkpoint in humans

10-03-2009
Miguel Godinho-Ferreira
IGC
How telomeres prevent checkpoints

13-03-2009
Ron DePinho
Harvard Medical School, Dana Farber Cancer Institute, USA
Mining and modeling cancer genomes

13-03-2009
Jon Van Rood
Europdonor Foundation, Leiden, The Netherlands
Consequences of bidirectional microchimaerism between mother and fetus on transplant survival and genetic predisposition for Rheumatoid Arthritis

18-03-2009
Matthias Haury
EMBL International Centre for Advanced Training (EICAT), Heidelberg, Germany
The EMBL International Centre of Advanced Training

19-03-2009
Roberto Araújo
Aberdeen University, NY, USA
Mechanotransduction- a novel 3D perspective

20-03-2009
Cláudia Codeço
Fundação Oswaldo Cruz, Rio de Janeiro, Brazil
Ecological thinking and vector borne diseases

23-03-2009
Dan Weinreich
Brown University, Providence, USA
Predicting molecular evolutionary trajectories in principle and in practice

24-03-2009
Michael Parkhouse
IGC
Host versus Pathogen: The game is drawn but the fight goes on

26-03-2009
Rafal Butowt
Institute of Biology, University of Tromso, Norway
Long-distance trafficking of neurotrophins in the nervous system: the concept of "trophic currencies"

27-03-2009
Alex Pouget
Department of Brain and Cognitive Sciences and Center for Visual Science, University of Rochester, NY, USA
Probabilistic inference and decision making in neural circuits

30-03-2009
Bert Overduin
EMBL - European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, UK
An overview of the ENSEMBL project

31-03-2009
Gabriela Gomes
IGC
Modeling and remodeling in population biology

APRIL 2009

01-04-2009
Brian Trench
Dublin City University, Ireland
Benefits and risks for scientists in public communication of research

03-04-2009
Keith Slotkin
Cold Spring Harbor Laboratory, NY, USA
Germ cell-specific epigenetic activation and silencing of transposable elements in plants

03-04-2009
Sarah Teichmann
MRC Laboratory of Molecular Biology, Cambridge University, UK
Transcriptional regulatory network dynamics

06-04-2009
Thomas M. Lewinsohn
Universidade Estadual de Campinas, Brazil
Diversity of species and of interactions among plants and herbivores

07-04-2009
Luis Rosário
IGC
Cardiac regeneration: first footsteps

08-04-2009
Bill Earnshaw
Wellcome Trust Centre for Cell Biology, University of Edinburgh, Scotland, UK
Multidimensional proteomics and genetic analysis reveal condensin's function in vertebrate mitotic chromosomes

14-04-2009
Ana Paula Godinho
IGC
Science Communication, Outreach and Fundraising at the IGC - an 18 month review

15-04-2009
Giorgio Gilestro
University of Wisconsin, Madison, USA
Synaptic homeostasis and sleep in Drosophila

16-04-2009
Tagny Duff
Practicing Artist Going Viral

17-04-2009
Michael Richardson
Institute of Biology, Leiden University, The Netherlands
Evolution and development in reptiles

20-04-2009
Aldo Faisal
University of Cambridge, UK
Variability and the nervous system - from molecules to behaviour

21-04-2009
Miguel Soares
IGC
Regulation of immune mediated inflammatory disorders by the Heme oxygenase-1 enzymatic system: from biology to therapeutic applications

24-04-2009
Anthony Hyman
Max Planck Institute, Dresden, Germany
Systems approaches to cell division

28-04-2009
Claire Wyart
University of California, Berkeley, USA
Optogenetic dissection of behavioral modules that drive locomotion

28-04-2009
José Pereira Leal
IGC
Towards an evolutionary cell biology

30-04-2009
Alain Debec
Institut Jacques Monod, CNRS - Université Paris, France
Cellular and molecular analysis of acentriolar division in Drosophila cells

MAY 2009

05-05-2009
Moisés Mallo
IGC
Of ribs and embryonic arteries: two stories from the lab

05-05-2009
Dan Holmberg
University of Umea and University of Copenhagen, Sweden and Denmark
Cellular and molecular events in autoimmune induced inflammation

08-05-2009
Andrew Fry
Department of Biochemistry, University of Leicester, UK
NIMA-related kinases in cell cycle control and human disease

12-05-2009
Élio Sucena
IGC
Approaching the basis for evolutionary novelty: from genes to networks

14-05-2009
Enrique Martin-Blanco
Instituto de Biologia Molecular de Barcelona (IBMB), Spain
Signaling mechanisms controlling cell proliferation and invasiveness during morphogenesis

15-05-2009
Carlos Brody
Department of Molecular Biology Princeton, Princeton Neuroscience Institute, Princeton University, USA
Functional separation between "what" and "when" in prefrontal cortex

19-05-2009
Patrícia Beldade
IGC
Genetic and developmental mechanisms of morphological diversification

23-05-2009
Jean-Pierre Changeux
Pasteur Institute, France
The nicotinic receptor: an authentic allosteric protein engaged in synaptic transmission

23-05-2009
Susumu Tonegawa
Massachusetts Institute of Technology, USA
Molecular and circuit mechanisms for Hippocampal memory

23-05-2009
Terry Sejnowski
The Salk Institute, USA
Ectopic synaptic transmission: truth and consequences

23-05-2009
Sydney Brenner
The Salk Institute, USA
The future of neuroscience

26-05-2009
Michael Levin
Forsyth Center for Regenerative and Developmental Biology, Boston, USA
Endogenous bioelectrical signals as morphogenetic cues in embryonic development, regeneration, and cancer: molecular techniques and applications

28-05-2009
Álvaro Tavares
IGC
10 years with the Mob – the bitter splitting of MOBless cells

28-05-2009
Nicolas Borghi
Stanford University, California, USA
Regulation of epithelial cell motile behavior through crosstalk between extracellular matrix- and cell-cell adhesions

29-05-2009
Decio Eizirik
Université Libre de Bruxelles, Belgium
Using functional genomics to understand pancreatic beta-cell apoptosis in diabetes

JUNE 2009

02-06-2009
Helena Soares
IGC
The other side of tubulin cofactors: two stories

04-06-2009
Keith Gull
Sir William Dunn School of Pathology, Oxford, UK
Building the microtubule cytoskeleton and centriole during the cell cycle: insights from trypanosomes to man

04-06-2009
Hans Hofmann
University of Texas, Austin, USA
Genes, hormones and neurons in social decision making

05-06-2009
Ed Kravitz
Harvard Medical School, Boston, MA, USA
How does behavior happen?

08-06-2009
Michel Bornens
Institut Curie, Paris, France
The Centrosome-Golgi connection: an evolutionary survey combined with functional approaches

09-06-2009
Rasmus Larsen
IGC
Heme Oxygenase-1 protects against severe sepsis via inhibition of Heme-mediated sensitization to cell death and Hmgb1 release

09-06-2009
Susana Lopes
IGC
A novel role for Notch signalling In Left-Right determination through ciliary length control

11-06-2009
Allan Hobson
Harvard Medical School, Boston, USA

12-06-2009
Stefan Mass
Lehigh University, USA
Molecular complexity and gene regulation through A-to-I RNA editing

15-06-2009
Jean-Michel
Department of Zoology and Animal Biology, University of Geneva, Switzerland
Chromatin regulator network variation: phenotypic plasticity, local adaptation and evolvability

16-06-2009
Karina Xavier
IGC
Recognition and signal transduction of the inter-species quorum sensing signal AI-2

19-06-2009
Susana Montenegro Gouveia
Erasmus Medical Center, Rotterdam, The Netherlands
Regulation of microtubule dynamics by microtubule plus end tracking proteins

23-06-2009
Marta Moita
IGC
How do we learn to associate stimuli separate in time?

24-06-2009
Ana Magalhães
Sloan-Kettering Institute, NY, USA
Cellular functions of the PRK/PKN family of proteins

25-06-2009
Ana Carvalho
Ludwig Institute for Cancer Research, San Diego, USA
Cytokinesis in C. elegans: structural memory in the contractile ring

25-06-2009
Reto Gassmann
Ludwig Institute for Cancer Research, San Diego, USA
Elucidating the mechanisms coordinating chromosome alignment and checkpoint signaling during cell division

26-06-2009
Konrad Kording
Northwestern University, Chicago, IL, USA
Normative models of brain function

29-06-2009
Luis Amaral
Northwestern University, Chicago, IL, USA
Systems biology: a personal perspective

30-06-2009
Paula Duque
IGC
Resistance to herbicides and other xenobiotics in Arabidopsis-role of multiple drug resistance transporters

JULY 2009

02-07-2009
Santiago Schnell
Medical School CCMB, University of Michigan, USA
How is protein load sensed in the endoplasmic reticulum?

03-07-2009
Joachim Hermisson
Max F. Perutz Laboratories, Vienna, Austria
The genetic basis of phenotypic adaptation

07-07-2009
Rui Martinho
IGC
Epithelial morphogenesis: living on the edge!

09-07-2009
Martyn Goulding
Molecular Neurobiology Laboratory, Salk Institute, San Diego, USA
Genes, circuits and behavior: new insights into the spinal networks that control locomotion

10-07-2009
Gage Crump
USC Keck School of Medicine, Los Angeles, USA
How to make a face: lessons from zebrafish genetics

14-07-2009
Tiago Carneiro
IGC
Counteracting checkpoints at damaged fission yeast telomeres: the clue is in the pot

14-07-2009
Clara Reis
IGC
Requirement of the MRN complex in repairing unprotected telomeres

16-07-2009
Hagit Shatkay
Queen's University, Canada
Life by the book: pragmatically using text in large scale-omics

16-07-2009
Manuela Ferreira
Cambridge Research Institute, UK
Activating Beta-1 Integrin mutation in skin tumours

20-07-2009
Pedro Carvalho
Harvard Medical School, Boston, USA
Molecular mechanisms of ER-associated protein degradation

21-07-2009
Mónica Bettencourt-Dias
IGC
Centriole biogenesis and evolution

22-07-2009
Luis Almeida
University of Nice, CNRS, France
A mechanical model for dorsal closure and embryonic wound healing

24-07-2009
Paloma Más
Instituto de Biologia Molecular de Barcelona, Spain
Mechanisms of clock progression in Arabidopsis thaliana

28-07-2009
Lisete Fernandes
IGC
Differential contribution of Gim subunits for stress response

29-07-2009
Elodie Mohr
Institute of Biomedical Research, University of Birmingham, UK
Functional microenvironments influencing antibody responses

31-07-2009
Mike Blatt
Faculty of Biomedical & Life Sciences, University of Glasgow, UK
SNAREs at the traffic junction of signalling, transport and nutrition

AUGUST 2009

03-08-2009
Marie Bonnet
Centre d 'Immunologie de Marseille Luminy (CIML), France
Dynamical models of early T-cell differentiation: theoretical and molecular data

28-08-2009
Botond Roska
Friedrich Miescher Institute (FMI), Basel, Switzerland
Seeing with and without classical photoreceptors

SEPTEMBER 2009

01-09-2009
Zachary Mainen
IGC
On the neural origins of behavioral variability

04-09-2009
David Schneider
Department of Microbiology and Immunology, Stanford University, California, USA
Defining tolerance and resistance mechanisms to infections using the fruit fly as a model

07-09-2009
Gohta Goshima
Nagoya University, Japan
Microtubule generation within the mitotic spindle

08-09-2009
Maria João Leão
IGC
Fundraising for science-new approaches for research funding in Portugal

11-09-2009
Joe Lewis
Chemical Biology Core Facility, EMBL, Heidelberg, Germany
Finding needles in chemical haystacks: small molecule screening in academia and beyond

15-09-2009
Anthony Leonardo
Janelia Farm, Howard Hughes Medical Institute (IHMI), USA
Dynamics of prey capture in the salamander and the dragonfly

18-09-2009
Isabel Gordo
IGC
Predation, compensation and immortality in the world of microbes

22-09-2009
Christen Mirth
IGC
The development and evolution of foraging behaviour in the genus Drosophila

24-09-2009
Dinis Calado
Immune Disease Institute, Harvard Medical School, Boston, USA
The role of NF-κB signaling and c-Myc in mature B-cell lymphomagenesis

25-09-2009
Mónica Sousa
Instituto Biologia Molecular e Celular (IBMC), Porto, Portugal
Nerve Regeneration: growing axons in inhibitory milieus

29-09-2009
Luisa Vasconcelos
IGC
On repulsion and receptivity

OCTOBER 2009

01-10-2009
Brigitta Stockinger
MRC Institute for Medical Research, Mill Hill, London, UK
Modulation of innate and adaptive IL-17 mediated immunosurveillance and autoimmunity by environmental stimuli

02-10-2009
Hanno Pijl
Leiden University, The Netherlands
Obesity: evolution of a symptom of affluence

06-10-2009
Lars Jansen
IGC
The remarkable epigenetic centromere

09-10-2009
Helena Vieira
Instituto de Biologia Experimental e Tecnológica (IBET), Oeiras, Portugal
ROS signalling in neural cells: impact on preconditioning, apoptosis and stem cell differentiation

09-10-2009
Larry Zipursky
Howard Hughes Institute, University of California, Los Angeles, USA
Dscam proteins and neural circuit assembly

12-10-2009
Alfonso Martinez-Arias
Department of Genetics, University of Cambridge, UK
Origin, control and function of dynamic heterogeneities in mouse ES cells

13-10-2009
Joaquin Leon
IGC
Limb outgrowth and control of tissue renewal in the apical ectodermal ridge

15-10-2009
Patrick Heun
Max-Planck Institute of Immunobiology, Freiburg, Germany
Neocentromere formation in Drosophila melanogaster

16-10-2009
Miodrag Grbic
University of Western Ontario, Canada
Evolution of arthropod development: from an ancestral developmental program to developmental novelties and biotechnology applications

20-10-2009
Bioinformatics Service
IGC
Taking your research that extra (computational) step - how the bioinformatics unit can help you

23-10-2009
Antonio Giraldez
Yale Department of Genetics, USA
The role of microRNAs in vertebrate development

26-10-2009
Ruth Lehmann
Kimmel Center for Biology and Medicine, Skirball Institute, NY University, USA
Germ line stem cell development

27-10-2009
Vasco Barreto
IGC
Random autosomal monoallelic expression

30-10-2009
Helder Maiato
Instituto de Biologia Molecular e Celular (IBMC), Porto, Portugal
Spatiotemporal control of chromosome segregation

NOVEMBER 2009

02-11-2009
Dyche Mullins
A little larger than the entire cytoskeleton: the role of actin in prokaryotes

02-11-2009
Thomas Arnesen
University of Bergen, Norway
Protein N-terminal acetylation: basic concepts and biological relevance

03-11-2009
Mathias Koeppen
IGC
Cytoskeletal dynamics during Zebrafish embryogenesis

03-11-2009
Marcos Malumbres
Spanish National Cancer Research Center (CNIO), Madrid, Spain
Modelling the functional relevance of mitotic regulators in vivo

05-11-2009
Philip Beales
Institute of Child Health, University College, London, UK
From James Bond to Donny Osmond: cilia in development and disease

06-11-2009
Alexey Khodjakov
Wadsworth Center, Albany, NY, USA
Of kinetochores and centrosomes: Who is the top dog in spindle assembly?

10-11-2009
Luis Teixeira
IGC
Drosophila, viruses, and Wolbachia: from single interactions to a household of three

13-11-2009
Christian Schlotterer
Institut für Populations genetik, Vienna, Austria
Using NGS for the analysis of natural populations

17-11-2009
Henrique Teotónio
IGC
Adaptation from standing genetic variation

18-11-2009
Juan Lafaille
Skirball Institute, New York University, USA
Generation of Foxp3-positive Regulatory T cells

19-11-2009
Diane Mathis
Harvard Medical School, Boston, USA
Molecular Mechanism of AIRE

20-11-2009
John N. Thompson
University of California, Santa Barbara, USA
Coevolution across changing environments

23-11-2009
Caetano Reis e Sousa
Lincoln's Inn Fields Laboratory, Cancer Research, London Research Institute, UK
Innate regulation of adaptive immunity by dendritic cells

24-11-2009
Vítor Barbosa
IGC
The response to endogenous DNA damage during meiosis modulates Drosophila oocyte polarity

25-11-2009
Lucien Aarden
Sanquin Blood Supply Foundation, The Netherlands
Serum factors involved in the disposal of apoptotic and necrotic cells

27-11-2009
Rafael Carazo-Salas
ETH Zürich, Switzerland
Systemic regulation of microtubule organization and its role in the establishment of cellular coordinate

30-11-2009
Carl Philipp Heisenberg
Max Planck Institute for Molecular Cell Biology and Genetics, Dresden, Germany
Cell and tissue mechanics in zebrafish gastrulation

DECEMBER 2009

01-12-2009
Shane Hutson
Department of Physics & Astronomy, Vanderbilt University, USA
The mechanics of morphogenesis

03-12-2009
Susana Lima
IGC
Neural mechanisms underlying mate choice and sexual behavior

03-12-2009
Martin Häsemyer
Research Institute of Molecular Pathology, Vienna, Austria
Sensory neurons in the Drosophila genital tract regulate female reproductive behavior

04-12-2009
Will Wood
Department of Biology and Biochemistry, University of Bath, UK
Cell battles: Drosophila embryos as model systems for monitoring bacterial infection in real time

09-12-2009
Elena Baena-González
IGC
Early signaling events in the convergent stress response

11-12-2009
Luca Imeri
Medical School, University of Milan, Italy
Neuroimmune regulation of sleep

11-12-2009
Yves Coppens
College de France, Paris, France
The emergence of man: the (H)Omo event

15-12-2009
Florence Janody
IGC
The actin cytoskeleton: a tumor suppressor organelle

18-12-2009
Diogo Castro
National Institute for Medical Research, London, UK
Transcriptional control of neuronal differentiation by vertebrate proneural factors

PRESENTATIONS BY IGC RESEARCHERS

ALEKOS ATHANASIADIS
Modeling A to I RNA editing: Understanding The Role of RNA Sequence Variation In Gene Evolution
Estudos Avançados de Oeiras, Oeiras, Portugal
1 November, 2009

ELENA BAENA-GONZÁLEZ
Convergencia de señales energéticas y de estrés
XXXII SEBBM (Sociedad Española de Bioquímica y Biología Molecular) Meeting
Oviedo, Spain
26 September, 2009

Convergent stress and energy signaling
8th Plant Genomics European Meeting (Plant GEM)
Lisbon, Portugal
7 October, 2009

FILIPA BARBOSA*
*Godinho, A.
The 'Resistant!' Kits
Communicating Darwin's ideas: richness and opportunity Symposium
York, United Kingdom
28 October, 2009

VASCO BARRETO
Ig loci hallmarks
IGC - IMM Immunology meeting
Oeiras, Portugal
April, 2009

JÖRG D. BECKER
Genetic and Epigenetic Basis of Sexual Reproduction in Higher Plants: A Focus on the Male Gametes
Institut de Biologie Moléculaire des Plantes du CNRS
Strasbourg, France
16 January, 2009

Microarray technology and its applications in plant genomics
Instituto Superior de Agronomia (ISA)
Lisbon, Portugal
15 May, 2009

PATRÍCIA BELDADE
Genetic and developmental mechanisms of morphological diversification
Departamento de Zoologia, Faculdade de Ciênicas da Universidade de Lisboa
Lisbon, Portugal
8 October, 2009

Evo-devo: getting at the mechanisms behind morphological diversification
15th Annual European Meeting of PhD Students in Evolutionary Biology
Schoorl, Netherlands
14 August, 2009

Evolution, Development, and the genes behind morphological diversity
Ciência 2009 meeting promoted by Fundação para a Ciência e a Tecnologia (FCT)
Lisbon, Portugal
29 July, 2009

Evo-devo, uma nova disciplina que explica a diversificação evolutiva (Evo-devo, a new discipline to explain evolutionary diversity)
Public Lecture in Darwin Series, Science Museum of the University of Coimbra
Coimbra, Portugal
14 May, 2009

Evolução e Desenvolvimento: transformações a dois tempos (Evolution and Development: transformations at different time scales)
Public Lecture in 'Café de Ciência' Series, Ciência Viva
Bragança, Portugal
9 May, 2009

Evolução e Desenvolvimento: mudanças em compasso binário (Evolution and Development: changes at two different time scales)
Public Lecture in 'Biologia da Noite' Series, Centro Cultural e de Congressos de Aveiro
Aveiro, Portugal
5 May, 2009

Genetic and developmental basis of morphological diversification
Evolutionary Biology Department of the Zoological, Institute of the University of Basle
Basle, Switzerland
23 March, 2009

Genetic and developmental basis of morphological diversification
Andalucia Center for Developmental Biology
Seville, Spain
13 March, 2009

INES BENTO
Young Investigator PhD Course, EMBO
Heidelberg, Germany
14 - 20 September, 2009

The European Molecular Biology Laboratory (EMBL)*
*Bettencourt-Dias, M.
10 - 20 March, 2009

Portuguese Drosophila Meeting*
*Cunha-Ferreira, I. and Carvalho-Rodrigues, Z.
Porto, Portugal
18 December, 2009

JOANA BOM
Instituto Gulbenkian de Ciência: who we are and what we do (Instituto Gulbenkian de Ciência: Quem somos e o que fazemos)
Centro de Bioterismo, Faculty of Medicine, University of São Paulo, Brazil
9 March, 2009

MARIE LOUISE BERGMAN
Novel role for TEC in Treg selection: TEC present self antigens through a mechanism of cross-presentation
IGC - IMM Immunology meeting
IGC, Oeiras, Portugal
14 January, 2009

MÓNICA BETTENCOURT-DIAS
Institute for Research in Immunology and Cancer (IRIC)
Montreal, Canada
14 December, 2009

London Cancer Institute
London, UK
6 October, 2009

Young Investigator PhD Course, EMBO
Heidelberg, Germany
17 September, 2009

Institute for Research in Biomedicine (IRB)
Barcelona, Spain
9 July, 2009

Institute of Zoology, University of Zurich
Zurich, Switzerland
12 June, 2009

Young Investigator Programme Meeting
Istambul, Turkey
13 - 15 May, 2009

MPI-CBG-Dresden PhD Retreat
25 - 28 April, 2009

Centro Nacional de Investigaciones Oncológicas (CNIO)
Madrid, Spain
14 April, 2009

University of Siena
Siena, Italy
27 February, 2009

Cilia and Mucus-Ciliary Interactions
Gordon Conference on Mucus
El Ciocco, Italy
22 - 27 February, 2009

Minisymposia on Cilia and Centrosomes
American Society for Cell Biology Meeting
San Diego, USA
5 December, 2009

The European Molecular Biology Laboratory (EMBL)*
*Bento, I.
10 - 20 March, 2009

HBIGS Summer school 2009 on Cell cycle regulation*
*Cunha-Ferreira, I.
Bopard, Germany
18 - 21 May, 2009

MARIA DO ROSÁRIO BRAGANÇA SAMBO
Haplotypes of Transforming growth factor beta 2 and Heme oxygenase 1 genes control Cerebral Malaria in Angolan population
Malaria 2009 - A Collaborative Solution for Tropical Diseases: The Luso-American Response
Lisbon, Portugal
8 - 10 July, 2009

JORGE CARNEIRO
Set a thief to catch a thief: towards fully automated image analysis based on morphodynamic cell models Imaging Immunity
Satellite Meeting of the 2nd European Congress of Immunology, ECI 2009
Berlin, Germany
12-13 September, 2009

How to tame a transposon: lessons from a stochastic model of V(D)J recombination
XXXV Reunião Anual da Sociedade Portuguesa de Imunologia
Lisbon, Portugal
29 September, 2009

Biologia computacional: desafios e oportunidades (Computational Biology: challenges and opportunities)
1as Jornadas de Bioengenharia, FEUP
Porto, Portugal
27 November, 2009

How to tame a transposon: lessons from a model of V(D)J recombination
CIML
Luminy, France
12 June, 2009

Dynamics and selection of regulatory T cell repertoire
Tolerance and Development Symposium
Les Treilles, France
19 April, 2009

TIAGO CARNEIRO
Counteracting checkpoints at damaged fission yeast telomeres
Pombe 2009
Tokyo, Japan
26 October, 2009

ZITA CARVALHO RODRIGUES
Masters in Evolution and Developmental Biology*
*Rodrigues-Martins, A.
University of Lisbon, Lisbon, Portugal
18 May, 2009

*Mitosis: Spindle Assembly and Function**
*Rodrigues-Martins, A.
FASEB Meeting
El Ciocco,Italy
30 July - 4 August, 2009

Portuguese Drosophila Meeting*
*Cunha Ferreira, I. and Bento, I.
Porto, Portugal
18 December, 2009

SÍLVIA CASTRO
'Communication' is the word
Post-doctoral Retreat of Instituto Gulbenkian de Ciência
Sesimbra, Portugal
October, 2009

How to write a press release and have it on the news
Programa doutoral GABBA
Universidade do Porto
Porto, Portugal
April, 2009

LOUNES CHIKHI
Les peuplements humains vus par la génétique... une belle histoire?
Public Lecture - Institut Franco-Portugais
Lisbon, Portugal
12 March, 2009

Conservation genetics at the Population and Conservation Genetics group
Boumerdes University
Algiers, Algeria
19 April, 2009
Can population structure explain genetic bottlenecks detected in orang-utans and other endangered species?
CIBIO
Porto, Portugal
23 June, 2009

Can population structure explain genetic bottlenecks detected in orang-utans and other endangered species?
Christian Schlötterrer Laboratory
Vienna, Austria
10 June, 2009

Back to the Neolithic: is DNA mytho-chondrial?
Darwin's legacy: new insights into human evolution
French Genetics Society and Human Genetics Society Joint Meeting
Paris, France
22 - 23 October, 2009

RUI COSTA
Erasmus University
Rotterdam, Holland
December, 2009

150 years of Darwin
Public Lecture - Museu Soares dos Reis
Porto, Portugal
November, 2009

Institute for Molecular Medicine
Lisbon, Portugal
October, 2009

Gallo Center
UCSF
San Francisco, USA
September, 2009

150 years of Darwin
Fundação Calouste Gulbenkian
Lisbon, Portugal
May, 2009

Gladstone Institute of Neurological Disease,UCSF
San Francisco, USA
March, 2009

HELENA COSTA
Induction of Interleukin-8 expression by Human Cytomegalovirus UL76 protein
IGC-IMM Immunology Meeting,
IGC, Oeiras, Portugal
7 January, 2009

INÊS CUNHA-FERREIRA
HBIGS Summer school 2009 on Cell cycle regulation*
*Bettencourt-Dias, M.
Bopard, Germany
18 – 21 May, 2009

Portuguese Drosophila Meeting*
*Bento, I. and Carvalho-Rodrigues, Z.
Porto, Portugal
18 December, 2009

JOCELYNE DEMENGEOT
Central tolerance to peripheral antigen
Workshop: Tolerance and Development
Les Treilles, France
19 April, 2009

Experimental Models of autoimmune diseases
XV Annual meeting NEDAI/ 1st national congress of autoimmunity
Portugal
25 April, 2009

Promoting regulatory T cells differentiation and function: precursors, location and environmental factors
NAIMIT kick off meeting
Leuven, Belgium
2 November, 2009

Striving for Harmony
Mucosal Immunity workshop of SPI
Institute for Molecular Medicine
Lisbon, Portugal
11 December, 2009

SARA ESTEVES
A screen for Drosophila genes interacting with Wolbachia
Portuguese Drosophila meeting, IBMC Porto, Portugal
December, 2009

JOSÉ FEIJÓ
Pollen tube growth: of male gametophytes and their urges for models
Department of Plant Sciences, University of Cambridge
Cambridge, United Kingdom
January, 2009

Excitement in sexual plant reproduction: the remarkable biology of pollen tubes and their urges for models
Biomechanics of Growth in Plant Biology, University of York
York, United Kingdom
March, 2009

Modelling pollen growth under the view of ion dynamics
Keynote speaker at Pollen Tube Growth session
Plant Molecular Biology, St. Louis
Missouri, USA
October, 2009

The perfect tool for the right experiment
EMBO - Live Cell Imaging
IGC, Oeiras, Portugal
May, 2009

The biophysics of pollen tube growth
Biophysical Basis of Development
IGC, Oeiras, Portugal
May, 2009

Modelling pollen growth under the view of ion dynamics
Congresso Iberico Fisiologia Vegetal
Zaragoza, Spain
September, 2009

PEDRO FERNANDES
Origins and applications of Bioinformatics (Origens e aplicações da Bioinformática)
Leiria Polytechnic
Leiria, Portugal
26 May, 2009

CONSTANTIN FESEL
How does the healthy immune system prevent lupus-type autoimmunity?
Annual Meeting Sociedade Portuguesa de Imunologia
Lisbon, Portugal
29 September, 2009

ANA GODINHO
Science Communication
Career Paths Workshop,
IGC, Oeiras, Portugal
6 July, 2009

Presenting research to policy-makers
European Science Communication Network (ESCONET) Training Workshop
Dubrovnik, Croatia
15 July, 2009

Science in Dialogue
European Science Communication Network (ESCONET) Training Workshop
Dubrovnik, Croatia
17 July, 2009

Media writing: making news from science
European Science Communication Network (ESCONET) Training Workshop
Dubrovnik, Croatia
19 July 2009

Public science on the web
European Science Communication Network (ESCONET) Training Workshop
Dubrovnik, Croatia
20 July 09

Science Communication at the IGC
Welcome to PIBS students
IGC, Oeiras, Portugal
16 September 2009

*The 'Resistant!' Kits**
*Barbosa, F.
Communicating Darwin's ideas: richness and opportunity Symposium
York, United Kingdom
28 October, 2009

MIGUEL GODINHO FERREIRA
Living dangerously at the edge of the chromosome: how telomeres prevent DNA repair and checkpoints
IBMC
Porto, Portugal
24 September, 2009

Living at the edge of the chromosome - how telomeres protect chromosome-ends
The Genetics Society's Pombe Club, Paterson Institute
Manchester, UK
26 June, 2009

Dysfunctional telomeres prevent checkpoints in spite of ongoing DNA repair
Telomeres and Telomerase Meeting, Cold Spring Harbour
New York, USA
28 April, 2009

GABRIELA GOMES
High rates of reinfection tuberculosis: The selection hypothesis
Mathematical Modelling of Epidemics, University of Bristol,
Bristol, UK
September, 2009

Influenzanet
Design and Analysis of Infectious Disease Studies
Oberwolfach, Germany
November, 2009

Interpreting genetic variation in pathogen populations
Modelling, Computation, and Measurement of Multiple Carriage
Saariselkä, Finland
December, 2009

LÍGIA GONÇALVES DEUS
Identification of murine host factors that control P.berghei sporozoite infection
5th Annual BioMalPar Conference
Heidelberg, Germany
20 May, 2009

P.berghei expansion in hepatocytes is controlled by the Fas pathway and modulated by HGF signaling
5th MIM Pan-African Malaria Conference 2009 Nairobi, Kenya
2-6 November, 2009

ISABEL GORDO
Mutation, selection and epistasis in Escherichia coli
IPATIMUP
Porto, Portugal
19 March, 2009

Adaptation and epistasis in bacteria
Centre d'Ecologie Fonctionnelle et Evolutive (CEFE) Montpellier, France
02 November, 2009

Adaptation of Escherichia coli to macrophages
V Encontro Nacional de Biologia Evolutiva
21 December, 2009

Evolução experimental em bactérias
Public Lecture - Museu da Ciência de Coimbra
Coimbra, Portugal
21 November, 2009

Genomes and Evolution
Fundação Calouste Gulbenkian
Lisbon, Portugal
29 July, 2009

INBAL ISRAELY
Cooperativity and competition at the level of individual dendritic inputs
Department of Neuroscience, Erasmus University
Rotterdam, Netherlands
1 December, 2009

FLORENCE JANODY
Actin Capping Protein restricts cell proliferation through the Hippo Tumor suppressor pathway
Ecole Normale Supérieure-Lyon
Lyon, France
22 June, 2009

Actin Capping Protein restricts cell proliferation through the Hippo Tumor suppressor pathway
University of Cambridge
Cambridge, United Kingdom
24 June, 2009

Actin Capping Protein promotes activation of the Hippo Tumor suppressor pathway.
Barcelona BioMed Conferences - Modelling Cancer in Drosophila
Barcelona, Spain
14 September, 2009

Actin Capping Protein restricts cell proliferation through the Hippo Tumor suppressor pathway.
Nice - European Drosophila Research Conference
Nice, France
15 November, 2009

LARS JANSEN
Histone assembly and stability in centromeric chromatin
Institute Curie
Paris, France
23 April, 2009

Assembly and maintenance of centromeric chromatin
Dynamic kinetochore workshop
Marie Curie Research Institute
London, United Kingdom
17 May, 2009

MATHIAS KOEPPEN
Global Dynamics During Tissue Movement in the Zebrafish Embryo
Zebrafish Meeting
Rome, Italy
16 June, 2009

SUSANA LIMA
Can New Tools Revolutionise Understanding of Hypothalamic Neural Circuits?
Howard Hughes Medical Institute at Janelia Farm
Virginia, USA
October, 2009

Communicating in Neural Circuits
Pan Iberian Systems Neuroscience Meeting
Lisbon, Portugal
November, 2009

ANDREIA LINO
B cells regulate CD4 T cell phenotype and number
IGC - IMM Immunology meeting
IGC, Oeiras, Portugal
24 June, 2009

B cells regulate CD4 T cell phenotype and number
RCAI international Summer Program 2009
Japan
10 July, 2009

B cells regulate CD4 T cell phenotype and number
Shiga Medical Center Research Institute
Shiga, Japan
14 July, 2009

B cells regulate CD4 T cell phenotype and number
SPI annual meeting
Lisbon, Portugal
29 September, 2009

ZACHARY MAINEN
From cognition to neurons
PENS/Hartie Winter School: Structure and Function of Neural Circuits
Obergurgle, Austria
January, 2009

From cognition to neurons
Instituto de Biologia Molecular e Celular (IBMC)
Porto, Portugal
February, 2009

Neural mechanisms of decision confidence: From cognition to neurons
Department of Neurobiology, Duke University
Durham, Virginia, USA
March, 2009

Neural mechanisms of olfactory-guided decisions in rodents
2009 Keystone Symposium on Chemical Senses: Receptors and Circuits
Tahoe City, California, USA
March, 2009

Understanding mind and behaviour through the brain
Frontiers in Biology Symposium
IGC, Oeiras, Portugal
April, 2009

How the brain computes and uses subjective confidence
Simpósio "Psicologia e Neurociências" at Instituto Superior de Psicologia
Lisbon, Portugal
April, 2009

Neural mechanisms underlying odor-guided decisions in the rat
Friedrich Miescher Institute for Biomedical Research
Basel, Switzerland
May, 2009

Neural mechanisms underlying odor-guided decisions in the rat
Simpósio Luso Brasileiro-Neurociência
Braga, Portugal
June 2009

Neural mechanisms underlying odor-guided decisions in the rat
Okinawa Computational Neuroscience Course
Okinawa, Japan
July, 2009

Neural mechanisms underlying odor-guided decisions in the rat
Computational Neuroscience Meeting: Quantitative Models of Behaviour Workshop
Berlin, Germany
July, 2009

Neural mechanisms underlying odor-guided decisions in the rat
Interdisziplinaeres Zentrum fuer Neurowissenschaften,
University of Heidelberg, Heidelberg, Germany
July, 2009

Neural mechanisms underlying odor-guided decisions in the rat
Lemanic European Neuroscience Institute Network Meeting
Geneva, Switzerland
September, 2009

Neural circuits underlying odor-guided decisions in the rat
EMBO Conference Series: The Assembly and Function of Neuronal Circuits
Ascona, Switzerland
October, 2009

Neural mechanisms underlying odor-guided decisions in the rat
Pan-Iberian Systems Neuroscience Meeting: Communicating in Neural Circuits
Lisbon, Portugal
November 2009

Neural mechanisms underlying odor-guided decisions in the rat
CNRS Université Claude Bernard
Lyon, France
November, 2009

MOISES MALLO
Ribs or no ribs: Hox genes are the answer
College of Medicine, University of Illinois at Chicago
Chicago, USA
1 April, 2009

Specifying domains in the vertebrate axial skeleton: Hox genes at work
Workshop on Hox and TALE homeodomain proteins in development and disease
Carmona, Spain
1 May, 2009

Transgenics and Knock outs: General Principles
Post-graduate course, Laboratory Animal Science
Braga, Portugal
16 November, 2009

ISABEL MARQUES
Genoma Humano
Escola Secundária José Afonso
Loures, Portugal
January, 2009

Aplicações de Bioinformática em Biologia Molecular
Instituto de Higiéne e Medicina Tropical
Lisbon, Portugal
April, 2009

*Detectives de DNA**
*Almeida, P., Pereira-Leal J.
Comemoração do bicentenário de Darwin, Fundação Calouste Gulbenkian
Lisbon, Portugal
May, 2009

MARTA MOITA
Spring Hippocampus Research Conference
Verona, Italy
14-19 June, 2009

Goettingen Neurobiology Conference
25-29 March, 2009

Pan-Iberian Systems Neuroscience Meeting
Lisbon, Portugal
29 November – 2 December, 2009

APPE Annual Meeting: Symposium "Psicologia e Neurociências"
Lisbon, Portugal
18 April, 2009

Rodent Social Behaviour Workshop
Cascais, Portugal
17-21 September, 2009

JOANA MONTEIRO
The role of ion dynamics in zebrafish fin regeneration
7th European Biophysics Congress
Genova, Italy
11-15 July, 2009

Proton fluxes during zebrafish fin regeneration
Biophysical Mechanisms of Development - Instituto Gulbenkian de Ciência Workshop Series
IGC, Oeiras, Portugal
25-27 May, 2009

LUCIANA MORAES
Parasite sequestration in murine model for pregnancy associated malaria
5th MIM Pan-African Malaria Conference 2009
Nairobi, Kenya
2-6 Nov 2009

MARIA FRANCISCA MORAES-FONTES
Why do we have autoimmune diseases?
7th International Medinterna Meeting
Porto, Portugal
January, 2009

Terapêuticas em Doenças Auto-imunes. Imunoterapia com Células T-reguladoras
1st Congresso Nacional de Auto-imunidade
Torres Vedras, Portugal
April, 2009

A susceptibilidade genética no Lupus Eritematoso Sistémico
1st Reunião do Núcleo de Doenças Auto-Imunes das Clínicas Universitárias das Medicinas I e II / Hospital de Santa Maria
Lisbon, Portugal
October, 2009

RUTE NASCIMENTO
A single conversed herpesvirus gene with dual evasion strategies
Society for General Microbiology Spring Meeting: Delivering modern microbial science
Harrogate, United Kingdom
30 March-2 April, 2009

RUI OLIVEIRA
Social behaviour in context: how animals adjust their behaviour to the social environment
2009 Annual Meeting of the Society for Integrative and Comparative Biology
3 January, 2009

RICARDO PAIVA
Maturation Stage Conditions T cell Susceptibility to Acquire Foxp3 Expression
4th ENII-MUGEN Summer School in Advanced Immunology
Sardinia, Italy
17 - 24 May, 2009

Control of Lymphopenia Induced Proliferation by Foxp3 Regulatory T Cells Differentiated in Peripheral Organs
XXXV Reunião Anual da Sociedade Portuguesa de Imunologia "Desenvolvimento do Sistema Imunitário na Saúde e na Doença"
Lisbon, Portugal
28 - 30 September, 2009

MICHAEL PARKHOUSE
Control of African Swine Fever Virus
Inspection and Quarantine of Jiangsu Province
Nanjing, China
5 April, 2009

Host pathogen interaction: a reciprocal two edged sword
College of Veterinary Medicine
Yangzhou University, China
9 April, 2009

Virus non-homologous genes as a source of novel tools for the manipulation of host cell biology and immune responses
College of Veterinary Medicine
Yangzhou University, China
11 April, 2009

Control of African Swine Fever Virus
Chinese Academy of Agricultural Sciences
Beijing, China
13 April, 2009

Identification of non-homologous, non-assigned host evasion genes of ASFV
Wellcome Trust Meeting
Pretoria, South Africa
24 April 2009

Control of African Swine Fever Virus
AFRISK Full Consortium Meeting
Madrid, Spain
21 May 2009

Cisticercosis: una enfermedad tropical abandonada (Cysticercosis: a neglected tropical disease)
Curso international "La lucha frente a las enfermedades de los pobres"
Madrid, Spain
15 October, 2009

Host pathogen interaction: lessons from viruses and parasites
Faculdade de Biociências da PUCRS, Porto Alegre, Brazil
23 October, 2009

Cisticercosis: una enfermedad tropical desatendida (Cysticercosis: a neglected tropical disease)
XXI Congresso Brasileiro de Parasitologia
Foz do Iguaçu, Brazil
26 - 30 October, 2009

Host pathogen interaction: a reciprocal two edged sword
XXI Congresso Brasileiro de Parasitologia
Foz do Iguaçu, Brazil
26 - 30 October, 2009

JOSEPH PATON
Time and learning in the rodent striatum
Pan-Iberian Systems Neuroscience Meeting
Lisbon, Portugal
December, 2009

CARLOS PENHA GONÇALVES
Pregnancy induces malaria recrudescence in immunised mice
5th MIM Pan-African Malaria Conference 2009
Nairobi, Kenya
2 - 6 November, 2009

JOSÉ PEREIRA-LEAL
Modularity, gene gain and loss
Instituto Superior de Agronomia (ISA)
Lisbon, Portugal
17 February, 2009

Gene loss in intracellular parasites and endosymbiontes
Portugalia Genetica
Porto, Portugal
20 March, 2009

Gene loss in intracellular parasites and endosymbiontes
University of Dundee
Dundee, United Kingdom
20 May, 2009

The evolution of protein interactions
Barcelona, Spain
6 July, 2009

Bioinformatics in Medical Research
National meeting of the "Laboratórios Associados"
Lisbon, Portugal
30 July, 2009

Towards an evolutionary cell biology
EMBL Alumni meeting
Porto, Portugal
02 September, 2009

The evolution of protein interactions
Dresden, Germany
04 September, 2009

CLARA PEREIRA
The epigenetic nature of Ig gene allelic exclusion
XXXV Reuniao Anual da SPI
Lisbon, Portugal
September, 2009

ESTELLE REMY
Resistance to herbicides and other chemical stresses of agricultural interest: role of plant Major Facilitator Superfamily transporters
MicroBiotec09
Vilamoura, Portugal
28 - 30 November, 2009

CARLOS RIBEIRO
Sex peptide receptor and neuronal TOR/S6K signaling modulate value-based nutritional decisions in Drosophila
The 11th European Symposium on Insect Taste and Olfaction (ESITO XI)
Villasimius, Italy
22 September, 2009

Sex peptide receptor and neuronal TOR/S6K signaling modulate value-based nutritional decisions in Drosophila
EMBO conference series on The Assembly and Function of Neuronal Circuits
Mont Versita, Ascona, Switzerland
7 October, 2009

Nutritional value-based decision in Drosophila
Pan-Iberian Systems Neuroscience Workshop
Lisbon, Portugal
30 November, 2009

Sex peptide receptor and neuronal TOR/S6K signaling modulate value-based nutritional decisions in Drosophila
Portuguese Drosophila Meeting, IBMC
Porto, Portugal
18 December, 2009

LUÍS ROCHA
Bibliome Informatics and Complex Networks in Proteomics and Systems Biology
School of Informatics
Indiana University Purdue University Indianapolis, USA
23 January, 2009

Darwinian Natural Selection and self-organization in biological and social heterarchies
"Das Sociedades Humanas às Sociedades Artificiais" Series
Instituto Superior Técnico (IST), Portugal
3 March, 2009

Bibliome Informatics in Computational Biology
Data and Search Institute
Indiana University, USA
25 March, 2009

Computation and Control in Complex Networks
Networks and Complex Systems Talk Series
Indiana University, USA
20 April, 2009

Dynamics in Complex Networks: Preserving robustness in a hyper-connected World
Everything Is Connected Conference
Estoril, Portugal
18 September, 2009

Classification of protein-protein interaction documents using text and citation network features
BioCreative II.5 Workshop 2009
Madrid, Spain
8 October, 2009

ANA RODRIGUES MARTINS*
*Carvalho-Santos, Z.
Masters in Evolution and Developmental Biology
Unversidade de Lisboa
Lisbon, Portugal
18 May, 2009

*Mitosis: Spindle Assembly and Function**
*Carvalho-Santos, Z.

FASEB Meeting
El Ciocco, Italy
30 August - 4 September, 2009

MIGUEL SEABRA
Correction of the Prenylation Defect in Choroideremia by Viral Delivery of the Choroideremia Gene
ARVO Annual Meeting Fort Lauderdale
Florida, USA
3 - 7 May, 2009

Rab 27 and Myosin V in organelle transport
EMBO II International School of Biochemistry, Molecular & Cell Biology
Rio de Janeiro, Brazil
4 - 14 August, 2009

Mechanisms of melosome transfer and keratinocyte processing
15th Meeting of the European Society for Pigment Cell Research
Münster, Germany
20 - 23 September, 2009

Molecular Vision: New models for new challenges
1st Annual Meeting of IBILI
Faculdade de Medicina da Universidade de Coimbra
Coimbra, Portugal
11 - 13 December, 2009

Rab GTPases, membrane traffic and disease
Co-organiser FASEB Summer Conference on Protein Lipidation, Signalling and Membrane Domains, Saxtons River
Vermont, USA
26 - 31 July, 2009

NUNO SEPÚLVEDA
Biodiversity estimation: quantifying the immune repertoire in the body's cellular ecosystem
16th European Young Statisticians Meeting
Bucharest, Romenia
24 - 28 August, 2009

Mapeamento bayesiano de BTL com comparação de métodos de calculo de factores de Bayes (Bayesian BTL mapping comparing Bayes factor calculating methods)
XVII Congress of the Portuguese Society for Statistics
Sesimbra, Portugal
30 September - 3 October, 2009

Quantificação de repertórios de linfócitos T através do modelo Poisson-lognormal (Quantification of T cell reportoire through the Poisson-lognormal model)
XVII Congress of the Portuguese Society for Statistics
Sesimbra, Portugal
30 September - 3 October, 2009

REETA SHARMA
Molecular genetic analysis of Bengal tiger (Panthera tigris tigris) populations and its implications in conservation and wildlife forensics
Integrating Population Genetics and Conservation Biology Conference
Trondheim, Norway
26 May, 2009

Demographic and genetic responses to habitat fragmentation and habitat loss in large forest mammals
IGC Post-Doc Retreat
Sesimbra, Portugal
10 October, 2009

HELENA SOARES
The Other Side of Tubulin Cofactors: Two Stories
Centro de Química e Bioquímica Seminars
Faculdade de Ciências, Universidade de Lisboa
Lisbon, Portugal
26 June, 2009

MIGUEL SOARES
Heme oxygenase-1: From biology to therapeutic potential
IMDEMI Symposium - Immune deficient animals: Mouse models of Immunological diseases
11 - 12 May, 2009

Heme oxygenase-1: a cytoprotective gene with broad therapeutic potential in xenotransplantation and other inflammatory diseases
11th Minisymposium Xenotransplantation of the German Working Group Xenotransplantation, Robert Koch Institute
Berlin, Germany
5 - 6 June, 2009

Regulation of cell death by free heme
6th International Conference on Heme Oxygenases: Heme Oxygenases in Biology and Medicine
Miami Beach, Florida
30 September - 4 October, 2009

Heme oxygenase-1: A cytoprotective gene that regulates the pathogenesis of immune mediated inflammatory diseases
XXXIV Congresso Brasileiro de Imunologia
Salvador, Brazil
23 - 26 September, 2009

Is heme at the center stage of immune mediated inflammatory diseases?
Fourth European Workshop on Immune-Mediated Inflammatory Diseases
Cascais, Portugal
18 - 20 November, 2009

A central role for free heme in the pathogenesis of severe malaria
Iberian Malaria Platform or PIM: 1st Scientific Meeting - GSK-Diseases of the Developing World Research Centre
Tres Cantos, Madrid
17 - 18 December, 2009

ÉLIO SUCENA
Cognitive and Motivational Requirements for the Emergence of Cooperation in a Rat Social Game
Rodent Social Behaviour Symposium
Cascais, Portugal
20 September, 2009

TATIANA TEIXEIRA
Presentation of the project: Demographic and Genetic Responses to Habitat Fragmentation and Habitat Loss in Large Forest Mammals
European Science Foundation Summer School Ecological Genomics
Bertinoro, Italy
October, 2009

LUIS TEIXEIRA
Drosophila, Wolbachia and viruses
Frontiers in Life Science Symposium
IGC, Oeiras, Portugal
April, 2009

Wolbachia induces protection to viruses in Drosophila melanogaster
Immunity and Symbiosis
Aussois, France
May, 2009

Wolbachia induces protection to viruses in Drosophila melanogaster
Insect Immunity in Action
Aussois, France
May, 2009

Drosophila, Wolbachia and viruses
Instituto de Medicina Molecular
Lisbon, Portugal
May, 2009

Wolbachia induces protection to viruses in Drosophila melanogaster
European Drosophila Research Conference
Nice, France
November, 2009

HENRIQUE TEOTÓNIO
Genetic Constraints in Evolutionary Theory
Darwin's impact on science, society and culture
Catholic University
Braga, Portugal
October, 2009

The role of natural selection and recombination in shaping patterns of DNA sequence diversity
SPGH annual meeting
Porto, Portugal
November, 2009

RAQUEL TOMÁS
AER activity and Stemness genes
6th plenary meeting of "Cells into Organs" European Network of Excellence
Fundação Calouste Gulbenkian
Lisbon, Portugal
3 - 6 February, 2009

SANDER VAN NOORT
Influenzanet: Ongoing analysis and problems
Annual Meeting of the Influenza Surveillance Network in Europe, ECDC
Stockholm, Sweden
June, 2009

LUISA VASCONCELOS
The circuits of innate behaviors
Pan-Iberian systems neuroscience workshop
Lisbon, Portugal
30 November, 2009

Neuronal circuits of innate behavior
Max-Plank Institute of Neurobiology
Martinsried, Germany
09 December, 2009

Neuronal circuits of innate behavior
Portuguese Drosophila Meeting, IBMC
Porto, Portugal
18 December, 2009

BARBARA VREEDE
The origin of evolutionary novelties: what we can learn from Drosophila oogenesis
Universität zu Köln, Institut für Entwicklungsbiologie
Cologne, Germany
12 December, 2009

The origin of evolutionary novelties: what we can learn from Drosophila oogenesis
5th Annual European Meeting of PhD Students in Evolutionary Biology
16 July, 2009

KARINA XAVIER
Quorum Sensing and Inter-Species Communication in Bacteria
Instituto de Biologia Molecular e Cellular, Universidade do Porto
Porto, Portugal
20 March, 2009

Quorum Sensing: The chemical language of bacteria
Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa
Lisbon, Portugal
22 April, 2009

Interference with bacterial communication
Department of Chemistry and Biochemistry, Universidade de LisboaLisbon, Portugal
17 June, 2009

WORKSHOPS, COURSES AND MEETINGS HELD AT THE IGC

Social Modulation of Hormones, Brain and Behaviour
5 June, 2009
Organisers: Rui Oliveira (IGC/ISPA), K. Hirschenhauser (Max Planck Institute, Seewiesen, Germany) and G. Tervo (Howard Hughes Medical Institute, Janelia Farm, USA)
The purpose of this workshop was to bring together researchers from different backgrounds to exchange ideas on the function and mechanisms involved in the social feedback on neuroendocrine mechanisms underlying social behaviour. The main topics addressed during the workshop were the following: How social interactions are shaped by the social milieu in which the individuals interact (i.e. effects of prior experience and social context)? What is the ecological function of this social modulation of behaviour? What are the mechanisms that translate social information into neuroendocrine signals? How socially-driven neuroendocrine signals modulate brain function and subsequent behaviour?

IMMxIGC Immunology worshop series
14 January, 4 March, 8 April, 20 May, 24 June, 18 November, 2009 (6 per year)
Organisers: Marie Louise Bergman, Iris Caramalho and Andreia Lino (IGC)
This meeting aims to create a space for immunologists of the Lisbon area to present their work, exchange experiences and set collaborations. The meeting is held at IGC during a morning, every 2 months. There are 4 talks of 30 minutes with 15 minutes discussion/each.

Pan-Iberian Systems Neuroscience Meeting: Communicating in Neural Circuits
30 November - 2 December, 2009
Organisers: Z. Mainen (Champalimaud Neuroscience Programme at IGC) and Miguel Maravall (Instituto Neurociencias de Alicante, Spain)
Recent technical advances are making it possible to analyse neural circuit organisation and communication with unprecedented specificity. A number of centres in the Iberian Peninsula have begun to apply these powerful new approaches toward addressing the neural bases of behaviour. The purpose of this workshop was to provide a forum for interaction between these groups and to foster the growth of a virtual community of neuroscientists working in the Iberian Peninsula.

EMBO - Live Cell Imaging
May, 2009
Organisers: Nuno Moreno and José Feijó (IGC)
To expose, train and discuss the cutting-edge of live cell microscopy. This course was aimed at advanced students and user-facility managers.

Rodent Social Behaviour
17 - 21 September, 2009
Organisers: Susana Lima and Marta Moita (Champalimaud Neuroscience Programme at IGC)
The workshop on rodent social behaviour aimed to create a more cohesive view of the mechanisms underlying social interactions in these species. It covered a broad range of social behaviours, such as parental care, sexual behaviour, communication, cooperation and perception of others. Furthermore, it brought together investigators whose research addresses social behaviour using several different approaches, while keeping an ethological perspective.

Postgraduate Course on Cardiometabolic Syndrome and Atherosclerosis
Organiser: Luís Rosário (IGC)
A course for physicians and researchers, to foster cooperation and research, with 200 attendees, and participation of major cardiovascular clinical centres from Portugal. It was co Sponsored by Harvard Medical School, Faculdade de Medicina de Lisboa and Sociedade de Ciências Médicas de Lisboa.

Biophysical Mechanisms of Development
25 - 27 May, 2009
Organisers: Ana Teresa Tavares, Catarina Certal, Susana Lopes, Beatriz Fernandez, Filipa Alves and Sofia Rodrigues (IGC)
This event brought together twelve outstanding invited speakers and more than sixty other participants from seven different countries. The aim of the workshop was to encourage discussion among different scientists and to promote future collaborations. This was definitely achieved as many new collaborative projects were streamlined between IGC scientists, IMM and FCUL and various speakers of this workshop. Developmental processes such as dorsal closure, tissue regeneration, collective cell migration and left-right determination were discussed.

4th European Workshop on Immune mediated inflammatory diseases
18 - 20 November, 2009
Organisers: Miguel Soares and João Eurico Fonseca (Workshop chairs), Dominique Baeten and Martin van Hagen (Workshop organising committee)
The 4th European Workshop on Immune Mediated Inflammatory Diseases (IMID) held in Lisbon (Cascais), Portugal used as a guideline the intrinsic biologic processes involved in recognition, signaling, effector function and regulation of innate and adaptive immunity and how these processes impact on the pathogenesis and outcome of IMID. Scientific sessions included, in a balanced manner, recent advances on basic, translational and clinical research related to the understanding and potential therapeutic intervention on IMID. Each session included two keynote speakers covering basic, translational and/or clinical implications of the biologic process under each scientific session.

Career Paths Workshop
6 - 9 July, 2009
Organisers: Margarida Prado, David Cristina and Jorge Carneiro (IGC)
The Career Paths Workshop promoted an open discussion amongst PhD students, post-docs, and several internationally successful professionals with very different and exciting career paths. It offered insights into a broad array of careers ranging from science communication to technology entrepreneurship. It was organised as part of the PhD Programme in Computational Biology.

GAMeets - Gulbenkian Alumni Meetings, 5th Edition
28 December, 2009
Organisers: Maria João Leão and Greta Martins (IGC)
GAMeets is the annual meeting of Gulbenkian Alumni, aimed at discussing key issues in research and science policy, and at being a forum for the Gulbenkian Alumni to meet regularly and network amongst themselves and with current IGC graduate students and researchers. The 2009 meeting was dedicated to the Role of Private Foundations in Science Funding. Representatives of Portuguese foundations that have been playing a crucial role in funding science in Portugal - the Gulbenkian Foundation and the Champalimaud Foundation - and of the Volkswagen Foundation in Germany presented and discussed experiences, strategies and the special role of foundations in funding research and innovating in this funding.

Introduction to Flow Cytometry
23 - 26 March, 4-8 May, 15-18 June, 9-12 November, 15-18 December, 2009
Organisers: Cell Imaging Unit at the IGC
Bi-monthly internal basic courses for widefield and confocal microscopy

Embo Course on Light microscopy in Living Cells
June, 2009
Organisers: Cell Imaging Unit at the IGC

Basic Techniques in Multiphoton & Confocal Laser Scanning Microscopy
July, 2009
Organisers: Cell Imaging Unit at the IGC

Advanced Optical Sectioning Microscopy Course
September, 2009
Organisers: Cell Imaging Unit at the IGC

Introduction to the SOLID sequencing system
28 April 2009
Organisers: Genomics Unit at the IGC
A series of presentations on the application of a massive sequencing platform.

Introduction to the GS FLX Roche pyrosequencing
28 May 2009
Organisers: Genomics Unit at the IGC
A series of presentations on the application of a massive sequence platform

IGC Practical Course on Animal Handling and Experimentation on Rodents and Fish
22 - 24 June, 2009
Organisers: Ana Mena and Jocelyne Demengeot (Animal House Facility at the IGC)
The aim of this course was to train researchers that carry out experiments with animals in basic procedures, following FELASA's recommendations. Education in laboratory animal sciences is mandatory by the Portuguese and European Law in order for researchers be considered competent to work with animals. This 20 hour course was structured to cover all vertebrate models in use at the IGC, namely mouse, rat and zebrafish, providing awareness on the three animal models most in use.

PathProt-II
14 - 16 October, 2009
Organiser: Pedro Fernandes (High Performance Computing Resource for Bioinformatics at the IGC)
PathProt is the international forum for Pathway Analysis in Proteomics. We are an informal discussion group that holds periodic brainstorming meetings. http://gtpb.igc.gulbenkian.pt/PathProt/
Sponsors: ENFIN - Enabling Systems Biology, Thermo Fisher Scientific Inc, BIOBASE GmbH, Dias de Sousa SA.

JB2009 - Jornadas de Bioinformática
3 - 6 November, 2009
Organiser: Pedro Fernandes (High Performance Computing Resource for Bioinformatics at the IGC)
The aim of this meeting, that follows on from a series of Spanish Bioinformatics Conferences (Jornadas de Bioinformática), was to provide a forum to present and discuss recent research developments in the broad field of Bioinformatics. In 2009 the conference was co-organised by the Spanish and Portuguese Bioinformatics Networks, with the aim of strengthening the cooperation links between researchers in the two countries.
http://www.bioinformatics-portugal.org/jb2009/
Sponsors: Fundação Calouste Gulbenkian, Universidade de Aveiro, Faculdade de Ciências da Universidade de Lisboa, INESC-ID, Fundação Luso-Americana, Instituto Nacional de Bioinformática, Medicwave

PUBLIC ENGAGEMENT IN SCIENCE

SCIENCE COMMUNICATION AND OUTREACH

Head: **Ana Godinho**
PhD in Developmental Neurobiology (University of London, UK)
E-mail: agodinho@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/112

The IGC runs a dedicated in-house science communication and outreach programme, centred around two main aims: raising the profile of IGC research, both nationally and internationally, and promoting public engagement in science. Approaches are based on two-way, dialogue-based interactions between IGC researchers, students and staff, and a range of audiences including the media, students, teachers, the general public, other research and science communication organisations.

MEDIA RELATIONS

During 2009 we consolidated our database of national and international journalists, from print, broadcast and online media, including the two major science news agencies - Eurekalert (USA) and Alphagalileo (Europe) – thus reaching a population of over 6,600 and 7,000 reporters, respectively, in over 60 countries.
We put out 26 media releases, covering publications (8), awards and prizes (11), outreach (6) and a call for the PhD programme (1).
A total of 369 IGC news clippings, in print, broadcast and online outlets were monitored, in Portuguese (75% of total) and international (25% of total) media outlets. Coverage in Portuguese media included the major broadsheets, national television and radio. On average, each press release generated 14.2 news items.

	PORTUGUESE	INTERNATIONAL	TOTAL
Print	81	1	82
Broadcast	11	0	11
Online	183	93	276
TOTAL	**275**	**94**	**369**

SCHOOL VISITS TO THE IGC

The IGC programme of structured school visits is targetted at students in the last four years of school and undergraduates. Visits are structured around a general introduction to the IGC, by a science communication and outreach team member, followed by guided visits to research laboratories or facilities. The aims of these visits are to engage students and teachers with cutting-edge research questions and approaches, through direct contact with research labs and reseachers. In 2009, a total of 971 students visited the IGC, on 29 separate visits, throughout the year. The largest number of visits took place in March, April and May. The majority of students were in the two final years of high school (16-18 year olds). In all, 38 different IGC research groups and/or facilities took part in the school visit programme; on average, each group/facility hosted two visits during the year. The school visit programme was temporarily suspended at the start of the 2009/10 school year, and replaced by a more focused schools project-support programme, targeted at students and/or teachers developing science-based projects."

OUTREACH TO SCHOOLS

During 2009, IGC researchers and the Science Communication and Outreach team carried out several outreach activities at schools, upon invitation from teachers and students:

DNA Extraction from Strawberry and the Gene Game
February, 2009
Escola Vieira da Silva (secondary school)
Participants: Filipa Barbosa (Science Communication and Outreach) and Carla Rodrigues (Equipment Management Unit)

TEAM MEMBERS
Sílvia Castro (Post-doc)
Filipa Barbosa (Post-doc)
Sandra Moreira (Project Officer)
Catarina Júlio (Trainee)

Theatre and performing arts by scientists, across four cities - Lisbon, Porto, Coimbra and Olhão - during the Setting the Stage project for Researchers' Night 2009.

DNA Extraction from Strawberry and Play-dough cells
February, 2009
Agrupamento de Escolas da Charneca da Caparica (primary and secondary schools)
Participants: Filipa Barbosa (Science Communication and Outreach), Maria João Leão (Science Communication and Outreach)

Science week in Azores - activities for students and teachers (see Fundraising section for more details on this activity)
March, 2009
Escola Santa Maria, Azores (primary and secondary schools)
Participants: Filipa Barbosa (Science Communication and Outreach), Maria João Leão (Science Communication and Outreach); Silvia Castro (Science Communication and Outreach)
This project was supported by the Oeiras City Council

Speed-dating with IGC Scientists
June, 2009
Escola Gama Barros, Queluz (secondary school)
Participants: Ana Godinho (Science Communication and Outreach); Sílvia Castro (Science Communication and Outreach); Rui Gardner (Flow Cytometry Facility Manager)

Science Day Activities - DNA Extraction from Strawberry
June, 2009
Escola Nº3 dos Olivais, Lisbon (primary and secondary)
Participating scientists: Catarina Júlio (Science Communication and Outreach); Sílvia Castro (Science Communication and Outreach)

Sequencing and Genotyping methods: Applications
February, 2009
Escola Secundária de Abrantes (secondary school)
October, 2009
Escola Secundária de Silves (secondary school)
Participating scientists: Isabel Marques (Genotyping and Sequencing Unit)

BRAGANÇA-IGC HOLIDAY PLACEMENTS FOR SECONDARY-SCHOOL STUDENTS

As part of an agreement established between the IGC and the City Council of Bragança, six secondary school students carried out 2-week research projects at IGC labs, during the Easter holidays. The students were selected by their teachers, based on their academic achievements, and were place din the following IGC groups: Telomeres and genome Stability, Evolutionary Biology, Actin Dynamics, Organogenesis and Disease Genetics. This agreement was extended to three more city councils in the northeast of Portugal.

DARWIN-INSPIRED EXPERIMENTAL KITS FOR SCHOOLS

To mark Charles Darwin's 200th birthday, we developed a kit for high schools, in association with the Darwin's Evolution exhibiton at the Gulbenkian Foundation. The 'Resistent!' kit was based on the X-Bacteria activities developed by the Wellcome Trust, and entailed a conjugation experiment between two E.coli strains, carrying resistance to different antibiotics. Between March and May 2009, a total of 131 kits were sent out to 68 teachers. In all, 41 student reports were sent back to the IGC and evaluated by IGC scientists. The six shortlisted reports were presented at the IGC and were all awarded a 2-week project placement at the IGC, to take place in September 2010. Acknowledgementss to the Wellcome Trust and the National Centre for Biotechnology Education (NCBE), UK, the Evolution and Bacterial Signalling Groups of the IGC, Ana Homem and Carla Rodrigues (IGC).

RESEARCHERS' NIGHT 2009

25 September, 2009
Oporto, Coimbra, Lisbon, Olhão
The IGC coordinated the project 'Setting the Stage: Researchers and the Public come together through Theatre', for the 2009 edition of Researchers' Night. The proposal was ranked amongst the top ten applications in 2009. Through the medium of theatre and interactive activities, SettingTheStage brought together nine partners and several collaborating organisations (research centres, universities, a small-medium enterprise, a science museum

and theatre groups), across four major cities in Portugal, to create multiple spaces where scientists (350 researchers, across the natural and social sciences) and the public (12800 people) actively engaged in the reality of being a scientist, through a series of purposely-created theatre performances - puppet show, forum theatre, physical theatre, stand-up comedy - and interactive activities. SettingTheStage produced science communication tools and material that has outlived Researchers' Night itself, being available to project partners and other institutions to use in their science communication activities.

2009 IGC OPEN DAY

21 November, 2009

The 4th edition of the annual IGC open day, brought close to 700 visitors to the IGC. Over 100 IGC researchers and staff took part in the 2009 edition, facilitating discussion, debate and hands-on experiments to illustrate the research programmes of the IGC. In an effort to attract different audiences, the 2009 Open Day extended into an Open Night, with dinner, a 'find-the-scientist-with-the-answer-to-your-question' game, and after-dinner activities (an informal conversation with Antonio Coutinho and stand-up scientists of the SettingThe Stage project).

PUBLIC EVENTS

Darwin Extravaganza

8 May, Calouste Gulbenkian Foundation

To mark the closing of the Darwin's Evolution exhibition, a range of discussion events, performances and hands-on activities ran through the day.

Oeiras 250th Anniversary Festival

20 June, Oeiras Public Park

We organised a series of hands-on activities (DNA extraction and play-dough cells), for families, and stand-up comedy by the SettingTheStage scientists.

INSTITUTIONAL COMMUNICATIONS - PUBLICATIONS

IGC Newsletter 'Quinta Grande' - Four issues were published. Print - 400 copies for internal and external distribution and available online.

The Parliaments' Magazine Research Review, Issue 9, May 2009 - feature 'Stimulated students - Portugal's Instituto Gulbenkian de Ciencia is an entrance hall for high-impact biomedical research' and two half-page articles on the European Mouse Mutant Archive (EMMA) and Epiwork projects (both funded by the Framework Programmes of the European Commisison). Research review was read by MEPs, Commissioners, European R&D institutions and academic research institutions.

Lab Times, Issue 5, September 2009 - the IGC was included in a feature article on research in Portugal ('Career strategies for young European scientists (XVIII): Doing a PhD (or more) in Portugal). The feature article included an interview with IGC Group Leader, Lars Jansen. Lab Times is a popular European Life Science journal, targeted mainly at the life science research community, and described as a 'grass roots magazine produced by scientists for scientists'.

SOCIAL NETWORKS AND NEW MEDIA

In 2009 the IGC pages on Facebook and on Twitter were launched, as well as an IGC site on YouTube. The aim of this use of new media and social networking is to allow for discussion and debate, and reach a wider and non-self-selected audience.

- url Facebook: http://www.facebook.com/pages/Instituto-Gulbenkian-de-Ciencia/58041555823
- url Twitter: https://twitter.com/IGCiencia
- url Youtube: http://www.youtube.com/user/IGCiencia

INSTITUTIONAL VISITS

The IGC hosted several institutional visits in 2009, including:

Wellcome Trust (UK)

15 April, 2009

Visitors: Sir William Castell (Chariman), Clarie Matterson (Director, Medical Humanities and Engagement); Ken Arnold (Head, Public Programmes, Wellcome Collection)

Hosts: Miguel Soares (Inflammation Group), Thiago Carvalho (Graduate Studies), Ana Godinho (Science Communication and Outreach)

Gulbenkian Foundation UK Branch

1 May, 2009

Visitors: Andrew Barnett (Director), Siân Ede (Deputy Director), Felicity Luard (Head of Communications), Annabel Knight (Social Change Officer)

Hosts: José Feijó (Plant Development), Thiago Carvalho (Graduate Studies), Ana Godinho (Science Communication and Outreach).

Local election candidates

September 2009

A visit to the IGC was requested by a delegation of candidates for the Oeiras City Council from the two main political parties - Socialist Party (PS) and Social Democrat Party (PSD).

Hosts: José Pereira Leal (Computational Genomics); Ana Godinho (Science Communication and Outreach).

During the 2009 Open Day, close to 700 visitors met and discussed science with IGC researchers.

FUNDRAISING

Head: **Maria João Leão**
PhD in Cancer and Virology (Imperial College, University of London, UK)
E-mail: mjleao@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/100

This page describes the public fundraising activities aimed at involving the scientific community, the private sector and the general public in funding science.

TEAM MEMBERS
Sara Catita (MSc Student, left March 2009)
Sandra Moreira (Trainee, left May 2009)

SCIENCE AT "MUNDO MIX"

29 - 31 May 2009

The IGC participated in "Mundo Mix", a cultural event at the S. Jorge Castle, in Lisbon, with Associação viver a Ciência (VaC) and Cooking Lab.
Through the purchasing of the IGC "Science" Calendar and postcards from the VaC exhibition "Laboratório de Imagens", the public could contribute to scientific research in Portugal.

SOLIDÁRIOS ATÉ À MEDULA

June - July 2009

A major fundraising event on Portuguese television, "Solidários até à Medula", was developed by "Associação Portuguesa Contra a Leucemia" (APCL), a Portuguese Leukaemia Association, together with Instituto Gulbenkian de Ciência (IGC) and the public television channel, RTP1. This 12 hour television Marathon, that took place on 2nd of July 2009, included the APCL fundraising concert and other musical varieties, a call centre for donations, an auction, and testimonials from celebrities, scientists, medical doctors and patients.
Other initiatives within this project included:

- "Mexa-se na Marginal" a sports event organised by Oeiras Council;
- The football game "Sporting Solidário" between scientists from different scientific institutions and celebrities, organised by "Sporting Clube de Portugal".

THE IGC - EVERYTHING IS NEW PARTNERSHIP AND OPTIMUS ALIVE!09 OEIRAS

9 - 11 July, 2009

Science, Music and Art came together for the second year during OptimusAlive! Oeiras09. The main activities in the IGC corner were speed-dating with scientists, DNA extraction, and the "Champimóvel", run by the Fundação Champalimaud. Around 70 IGC volunteers were present and 1000 people visited the IGC space.
For the second time, the promoters of this festival, Everything is New, funded two research fellowships for recent graduates. The call for the 2009 fellowships received 120 applications, 46more than in the previous year.

FUNDRAISING ACTIVITIES ORGANISED BY THE 2009/2010 IGC PHD DELEGATES

November - December 2009

Several fundraising activities were organised in 2009 to raise funds for the 3rd PhD AMeeGuS meeting:

- The Alley Cat Race 4 Science, a bicycle race organised in partnership with the bicycle shop Ciclone;
- The Science Party at Fragil Bar in Lisbon;
- The Table-football Tournament at the IGC;
- The IGC Christmas Party at the IGC.

SCHOOL FUNDRAISING ACTIVITIES IN SCHOOLS

During 2009 several fundraising projects were developed with schools across the country:

- IGC calendar fundraising project - IGC calendars were sent to different schools from North to South of Portugal and used by the school staff to raise funds for scientific research.

Collection of Vista Alegre IGC Mugs.

Football Game - Sporting Solidario.

Theatre and performing arts by scientists, across four cities - Lisbon, Porto, Coimbra and Olhão - during the Setting the Stage project for Researchers' Night 2009.

- Science week at Santa Maria School island in Azores, a project supported by Oeiras Council (2-6 March 2009) - the IGC was invited to develop and present a series of hands-on and fundraising activities for the schools's Science week. Funds raised by selling IGC products amongst school staff and the general public sponsored the visits of two students to IGC;
- "More awareness, less cancer/ More research, less leukaemia" project developed by final year students of Escola Secundária de José Afonso (in Loures), April-May 2009 - Funds were raised by selling IGC calendars and delivered to APCL, a Portuguese charity that support leukaemia research.

IGC MERCHANDISING PRODUCTS

THE IGC CALENDAR FOR 2010

A fundraising partnership between IGC and Bayer was established to produce the IGC calendar for 2010.

THE IGC MUGS AND PINS

A second collection of seven IGC mugs produced by porcelain manufactureres Vista Alegre and IGC Pins were designed with images obtained by researchers at the IGC (Design by Designways).

PARTNERS AND SPONSORS

Several partnerships and sponsorships were established to support scientific research, education and science communication and outreach activities at IGC, either financially or in kind:

Academia Siemens, Alfagene, Alpha Centauri, Alto Patrocínio de Sua Excelência O Presidente da República, Associação de Beneficiários de Lezíria Grande e Vila Nova de Chira, AJISM, Associação Portuguesa contra a Leucemia (APCL), Associação Viver a Ciência (VaC), Bar Frágil, Bayer, Bio-Rad, BIOBASE, Biognóstica, BIOPORTUGAL, Bragança City Council, Castanheira, CBD, Centro de Informação Europeia Jaques Delors, Ciclone, Ciência Viva, Clara.net, Clarkemodet, Comissão Europeia, Cooking Lab, Criatividade e Inovação Ano Europeu 2009, CV, DEFESA, DELTA, Dias de Sousa, ENFIM, ESMAE/Politécnico do Porto, Everything is New, Évora City Council, FCCN, FDTI, Flores do Seu Desejo, FNAC, Frilabo, Fundação Champalimaud, Fundação da, Juventude, Fundação Luso-Americana, Fundação PT, Grupo TAPER ,ILLC, IMM, ITQB, INB, Inesc id Lisboa, IPJ, ISDB, IZASA, Leica, Lisboa City Council, Lisboa Fórum, Máfia, Medicwave, National Geographic Channel, Natura Algarve, NzyTech, Oeiras City Council, Olhão City Council, OptimusAlive!Oeiras09, Parlamento Europeu, Pavilhão do Conhecimento, Pedras, Porto City Council, Portugal Telecom (PT), Público , Ria Shopping Olhão, Roche, RTP1, RTP2, SAPO, SATA, Sesimbra City Council, Science4You, Sociedade Portuguesa de Biologia do Desenvolvimento, Sporting Clube de Portugal, Super Bock, Take the Wind, THERMO Scientific, TMB, UMIC, Unicer, Universidade de Aveiro, Universidade de Lisboa, Universidade do Porto, Vitalis, Werfen Group, ZEISS.

OTHER SERVICES

RESEARCH FUNDING AFFAIRS
HEAD: SHEILA VIDAL
PhD in Drosophila Immunity (Université Paris Sud XI, France)
E-mail: svidal@igc.gulbenkian.pt
Staff
INÊS CRISÓSTOMO (Project Officer, left July 2009)
ANDREIA REIS (Assistant)

INNOVATION AND TECHNOLOGY OFFICE
HEADS: ANA MARGARIDA PRADO
PhD in Cell Biology (University of Lisbon, Portugal)
E-mail: aprado@igc.gulbenkian.pt
DAVID CRISTINA
PhD in Genetics of Ageing (Universidade Nova de Lisboa, Portugal)
E-mail: davidc@igc.gulbenkian.pt

INFORMATICS
HEAD: JOÃO SOUSA
PhD in Theoretical Immunology (University of Lisbon, Portugal)
E-mail: jsousa@igc.gulbenkian.pt
url: http://www.igc.gulbenkian.pt/node/view/46
Staff
ANA MAYA (Informatics Technician)
MANUEL Carvalho (Informatics Technician)
JOÃO GARCIA (Systems and Database Administrator)
GIL NETO (Informatics Technician)

EQUIPMENT PURCHASING AND MANAGEMENT
ANA HOMEM
CARLA RODRIGUES
FRANCISCO HENRIQUES
NUNO MORENO
PEDRO ANACLETO

LIBRARY
MARGARIDA MEIRA (Librarian)
url: http://www.igc.gulbenkian.pt/node/view/40

ADMINISTRATION AND ACCOUNTS
ANA LÍCIA PIRES
ANA MARIA SANTOS
FÁTIMA MATEUS
JOÃO NUNES
JORGE COSTA
VITOR SANTOS
ANTÓNIO BRETANHA

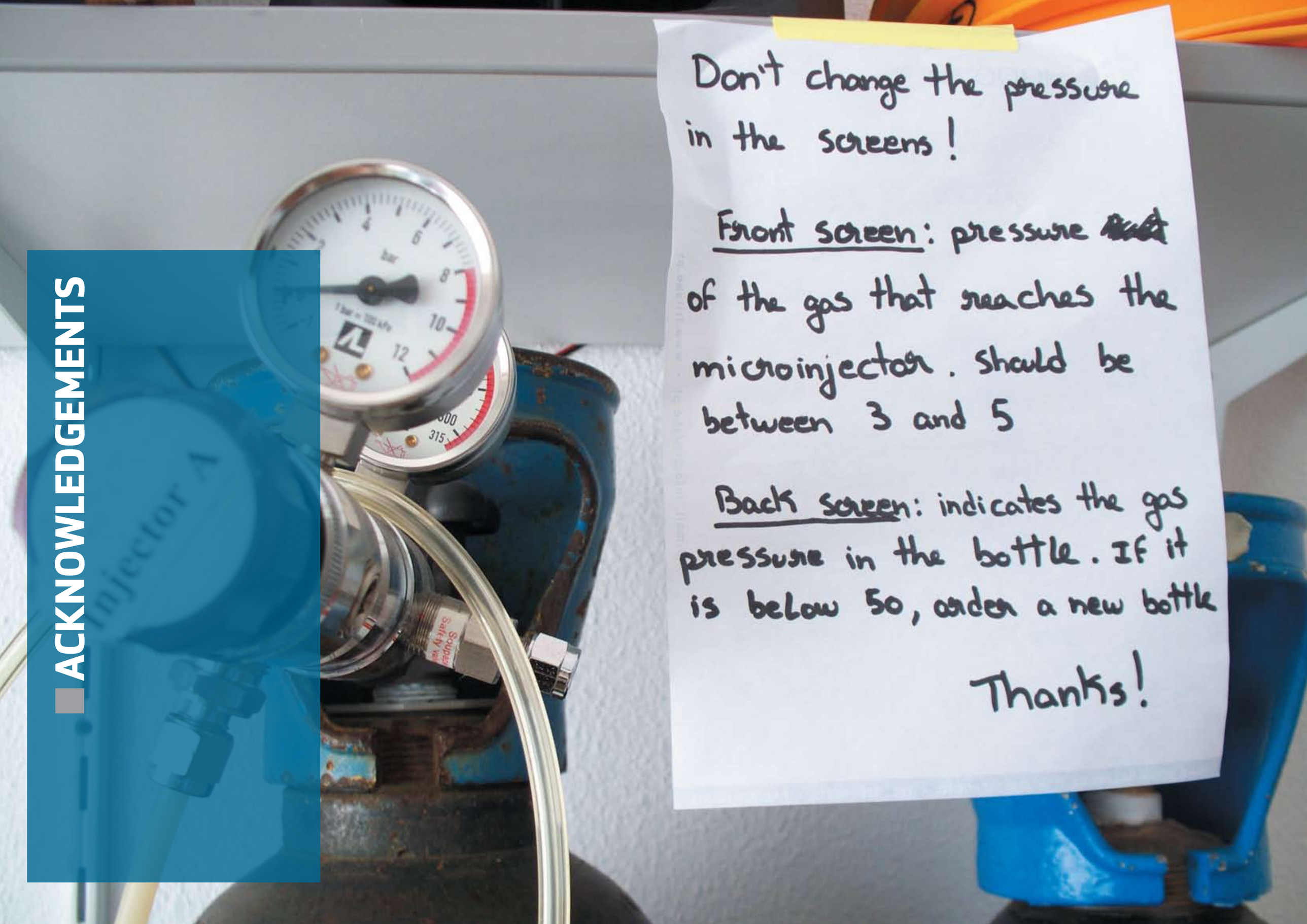
ASSISTANT TO THE DIRECTOR
GRETA MARTINS

DIRECTION SECRETARIES
TERESA MEIRA
ANA PAULA PIRES (left January 2009)

LABORATORY TECHNICAL STAFF
TATIANA ROCHA
PAULO DUARTE
TERESA GOMES

SUPPORT STAFF
ANTÓNIO SOUSA (Maintenance)
CARLOS NUNES (Driver)
TERESA SOUSA (Reception)
ABÍLIO SIMÕES (Stores)

ACKNOWLEDGEMENTS



'09 ANNUAL REPORT

INSTITUTO GULBENKIAN DE CIÊNCIA IGC

We are grateful to everyone at the IGC, researchers, students and staff, who supplied information, text and images used in this report. A special thank you to Greta Martins, for proofreading the report.

PROJECT MANAGER
ANA GODINHO

PROJECT OFFICER
CATARINA JÚLIO

LAYOUT AND DESIGN
DESIGNWAYS - WWW.DESIGNWAYS.PT

PRINTING
TEXTYPE

The Instituto Gulbenkian de Ciência Annual (IGC) Report is also available to download from the IGC website at www.igc.gulbenkian.pt.

If you would like to receive a print copy of this report, please contact:

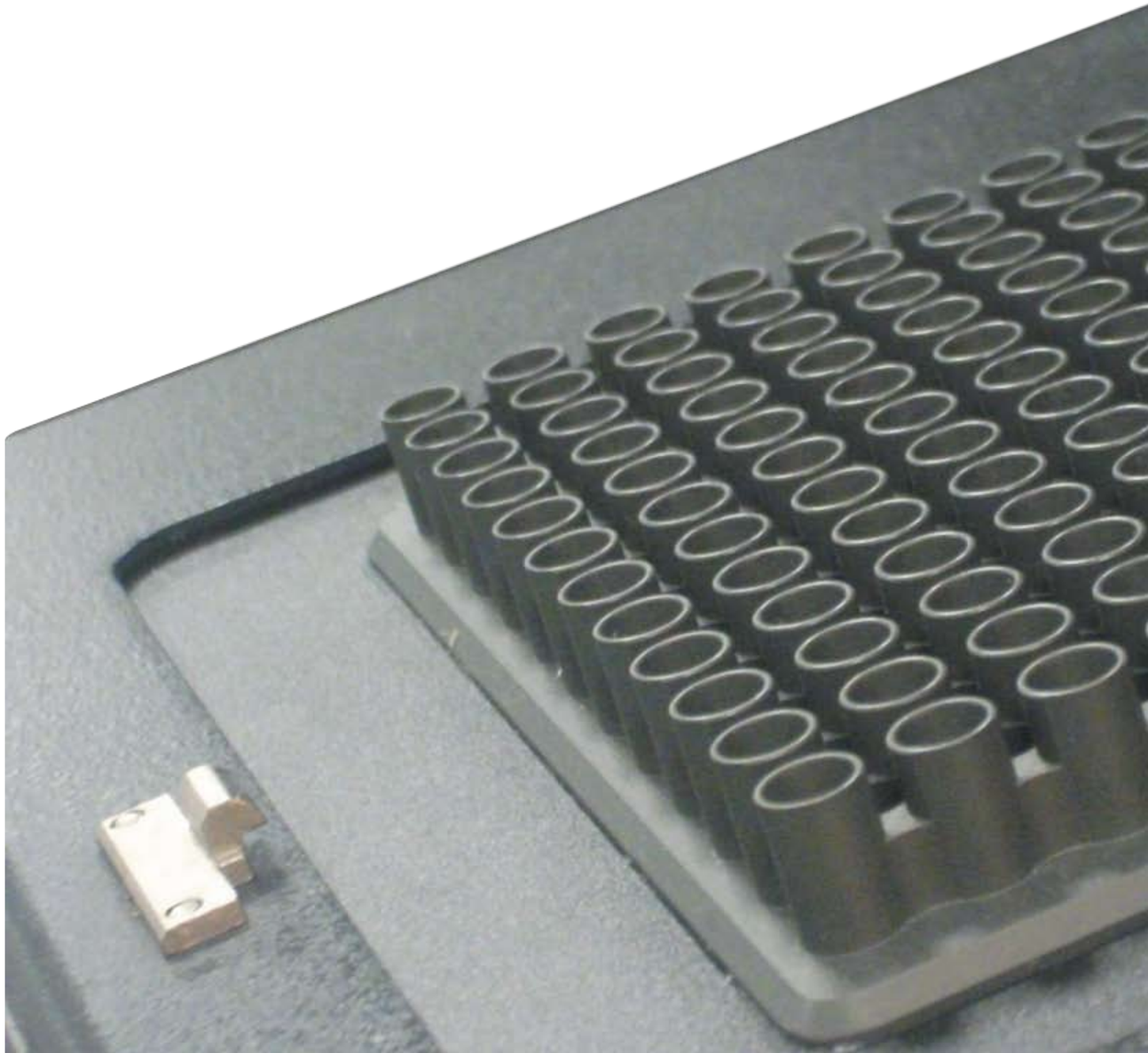
Science Communication and Outreach
Instituto Gulbenkian de Ciência
Rua da Quinta Grande, 6
2781-156 Oeiras
Portugal
Tel: +351 440 7959
Fax: +351 440 7970
E-mail: info@igc.gulbenkian.pt

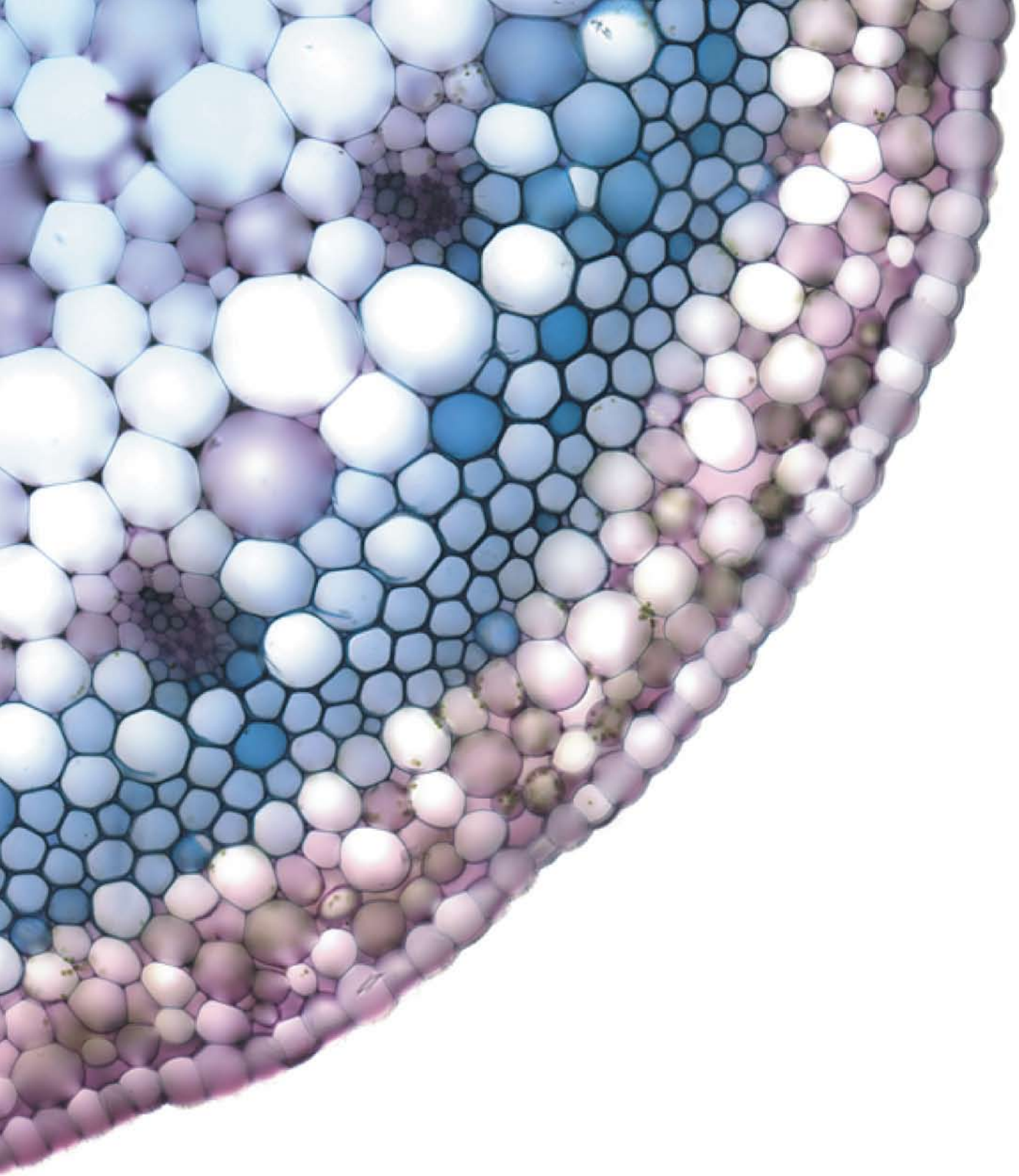
This is an open access publication, and with the exception of images and illustrations, the content may, unless otherwise stated, be reproduced free of charge in any format or medium, subject to the following conditions: content must not be used in a misleading context, the IGC must be credited as the original author and the title of the document specified in the attribution.

The IGC was founded by the Calouste Gulbenkian Foundation, a Portuguese private institution of public utility whose statutory aims are in the fields of arts, charity, education and science. Created by a clause in Calouste Sarkis Gulbenkian's will, the Foundation's statutes were approved in 1956. The head-office is located in Lisbon.

First published by the Instituto Gulbenkian de Ciência, 2010

© Copyright Fundação Calouste Gulbenkian 2010





Instituto Gulbenkian de Ciência

ADD Rua da Quinta Grande, 6
2780-156 Oeiras, Portugal

TEL +351 21 440 7900 FAX +351 21 440 7970

EMAIL info@igc.gulbenkian.pt

WEB www.igc.gulbenkian.pt