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## Career Profiles

# Choosing the Less Traveled Road

Lars Jansen was halfway through his Ph.D. at **Leiden University** (<http://www.leiden.edu/>) in his native Holland when he

presented his work in a plenary session at the 1999 American Society for Microbiology conference on DNA repair and mutagenesis at Hilton Head Island in South Carolina. The talk won Jansen accolades and postdoc offers, but the most valuable thing it gave him was "a chance to talk to even senior scientists that would normally never talk to a Ph.D. student," Jansen says. It was, he says, "a turning point" in his scientific career. From then on, "I knew that I was actually made to do this."

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*He was "tenacious in [the] pursuit of his goals ... and uniformly upbeat--always seeing the glass as half full." --Don Cleveland.*

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But "this" turned out to be something other than the field of DNA repair. By the time he finished his Ph.D., Jansen didn't see many more exciting questions to solve, so he decided to move to the emerging area of epigenetics, where he cracked another long-standing problem during a postdoc at the **Ludwig Institute for Cancer Research** (<http://www.licr.org/>). Today, Jansen, at 36, heads his own **Laboratory for Epigenetic Mechanisms** (<http://www.igc.gulbenkian.pt/research/unit/89>) at the Instituto Gulbenkian de Ciência in Portugal, a move he supported with a **Marie Curie International Reintegration Grant** ([http://ec.europa.eu/research/fp7/understanding/marie-curieinbrief/back-europe\\_en.html](http://ec.europa.eu/research/fp7/understanding/marie-curieinbrief/back-europe_en.html)) from the **European Commission** (<http://ec.europa.eu/research/index.cfm?lg=en>) and an **Installation Grant** (<http://www.embo.org/programmes/installation-grants.html>) from the **European Molecular Biology Organization** (<http://www.embo.org/>) (EMBO). His desire and courage to change fields even when he had succeeded in one, combined with the tenacity to keep going in the face of failure in the new field, have got him off to a promising start.

## Finding his vocation

Jansen developed an interest in science-related things as a child but discovered science as a career option much later. "I grew up in a small town, and ... there is nobody in my family that went to do a science or even had a university degree," he says. At 16, Jansen, fascinated by DNA experiments he saw during demonstrations at a professional school, enrolled and trained as a lab technician. It was that training that first showed him how "incredibly exciting" science is and "really motivated me to ... go on to university."

Jansen then enrolled in another, more advanced professional degree program, in biochemistry, at the Polytechnic University of Etten-Leur. As part of this training, he did an internship in the lab of molecular geneticist Jaap Brouwer at Leiden University. During his internship, Jansen displayed an "early, recognizable drive to do science and be a scientist," Brouwer tells *Science Careers* in an e-mail. Brouwer invited him to stay on for a Ph.D. Setting aside some doubts about his own abilities, Jansen took extra classes to meet the university's entry requirements and accepted the offer.

Starting in 1997, Jansen worked to elucidate DNA-repair mechanisms using yeast as a model organism. All the major genes and proteins involved in DNA repair were already known, Jansen says. But "one thing ... was always enigmatic: The types of damages to the DNA were very broad, [yet] they were all being repaired by the same group of enzymes." After a rough start--"the whole 1st year went down the sink," Jansen says--he solved the problem. Just one protein, he found, was responsible for binding errant DNA and initiating repair events. "The answer in the end was that this system is ... simply very sloppy. It just recognizes anything that's out of the ordinary and then repairs it." It was just the 2nd year of his Ph.D.



Jansen then turned to another problem: why the DNA strands that serve as templates for proteins are repaired much more efficiently than other strands are. Jansen had a hand in answering this question, too: With help from other lab members, he screened yeasts for genetic mutations and identified several genes involved in this repair process.

Jansen's strengths--"his commitment, enthusiasm, and his experimental abilities combined with a very clear mind," Brouwer says--put him on his way to making a name for himself while he was still a doctoral student. But Jansen felt that most of the important problems in the field had been solved already. "I made a really conscious decision to get out of the DNA-repair fields, get away from anybody that I knew, and basically start something completely different."

## Entering a new field

Jansen finished his degree in 2002 and then decided to study epigenetics, how changes in gene expression can be inherited via mechanisms other than DNA changes. At the time, epigenetic phenomena had "started to become more known in molecular terms, ... and I felt like ... there were many very exciting things to be done there," Jansen says.

Jansen did a postdoc with Kevin Sullivan at **The Scripps Research Institute** ([http://www.scripps.edu/e\\_index.html](http://www.scripps.edu/e_index.html)) in San Diego, California. Sullivan had identified a DNA-packaging protein whose role is to help chromosomes segregate into two identical lots during cell division by labeling the DNA regions--called centromeres--where the individual chromatids (the identical "sister" chromosome copies) join together to be split. The protein was believed to carry the memory of where those centromeres should be localized on new chromosomes. Jansen hypothesized that if so, the protein should remain attached to centromeres during cell division. He set out to find out if this was true.

He encountered some difficulties. "I knew what people were doing with microscopy, ... but you don't see the limitations when you read those papers," Jansen says. After a year of failed experiments, with Sullivan considering leaving Scripps, Jansen arranged to continue working under the supervision of Sullivan's former postdoc adviser, Don Cleveland, at the nearby **San Diego, California, branch** (<http://sandiego.licr.org/>) of the Ludwig Institute for Cancer Research.

The project kept failing for another 2 years. But Jansen was "tenacious ... and uniformly upbeat--always seeing the glass as half full," Cleveland writes in an e-mail. The easiest thing for him would have been to start another project using a new technique called RNA interference, which makes it possible to deplete genes from their products, Jansen says. But Jansen was stubborn. Everyone was using RNAi back then, which "doesn't really [help you] distinguish yourself," Jansen says.

His luck turned one day when he spotted a paper about a new fluorescent tag. He used it to develop a new fluorescence technique, which validated his hypothesis. "Jansen developed an approach for visualizing only those [proteins] that were synthesized at a chosen time. This allowed him to follow the fate of those molecules over time," Cleveland says. "This uncovered a highly surprising and redirecting insight about how the epigenetic mark that defines the centromere is replicated."

## A lab of his own

After 4 years in Cleveland's lab, Jansen and his wife--a lab technician who as a teenager had immigrated to Holland from Mozambique, a former Portuguese colony--decided to return to Europe to raise their two small children closer to home. Jansen secured several job offers in the Netherlands. His family already spoke some Portuguese, so he decided to apply for jobs in Portugal as well.

Jansen saw many reasons to join the **Instituto Gulbenkian de Ciência (<http://www.igc.pt/>)** (IGC), a private research institute near Lisbon. When visiting for the interview, Jansen was struck by the "can-do" spirit of the place, he says. The 5-year position at IGC guaranteed him immediate independence, allowing him to set up his own group, seek funding, and publish papers on his own--"something that's not usual in many universities" in Europe, he says. IGC also gave him access to excellent core facilities and lab space. All he needed was some bench-top equipment to get his research up and running.

When 1st-year IGC Ph.D. student Mariana Silva expressed an interest in doing her research in his lab, Jansen arranged for her to come and work with him in Cleveland's lab for 3 months while he wrapped things up there. This allowed Silva "to learn all the things for her project in a place where everything was running" already, Jansen says. And because she already knew IGC, Silva was able to guide Jansen in his new working environment. Together, "we really hit the ground running," says Jansen, whose lab now employs two Ph.D. students (including Silva), two master's degree students, a technician, and, starting in the fall, a postdoc.

The early, self-doubting days are long gone for Jansen. The funding he has secured--including a 3-year **EMBO Installation Grant (<http://www.embo.org/programmes/installation-grants.html>)**--will keep his lab running for his whole term at IGC. Jansen has identified an important scientific question and "set about tackling the problem in a logical but imaginative fashion that requires setting up a novel and sophisticated methodology," writes Jonathon Pines, a cell-division researcher at the University of **Cambridge (<http://www.cam.ac.uk/>)** in the United Kingdom, who sat on the EMBO evaluation committee, in an e-mail. And while Jansen "is taking what some might consider to be a risk in his career" by setting up his lab in Portugal instead of in a country with a higher scientific profile, he "thinks that he can both succeed personally and contribute to the science community and effort in Portugal," Pines says.

"Jansen has assembled a brilliant tool chest of approaches to dissect the mechanisms of centromere replication and to determine what really is the epigenetic mark ... that defines the position of those centromeres," Cleveland writes. "He is poised for independent success." Yet, with the lab growing and the centromere field becoming increasingly competitive, Jansen is already planning to steer his research into new directions, though perhaps not so drastically this time. His next target: other DNA-packaging proteins, Jansen says, which "have nothing to do with centromeres but ... have also roles in epigenetics."

Photo (top): **Nicholas T ([http://www.flickr.com/photos/nicholas\\_t/361161401/](http://www.flickr.com/photos/nicholas_t/361161401/))**

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