Title: CAN GUT BACTERIA PROMOTE ANTI-MALARIA VACCINE EFFICIENCY?

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Abstract: Malaria, caused by species of the parasite, Plasmodium, remains a major threat to human health. Despite many attempts to target this pathogen through chemical intervention, 219 million cases and 435,000 deaths are still attributed to malaria worldwide, highlighting a need for effective vaccination approaches. Only one vaccine, the RTS,S, vaccine, has been approved for use in the field, however its efficacy is relatively low and additional measures are required to promote the eradication of malaria.

We found that gut colonisation by the enteric bacterium, Escherichia coli O86:B7, protected mice against malaria transmission. Protection is due to a host antibody response raised against the bacterium that recognises one of its surface carbohydrate structures (or glycans), known as αGal (Galα1-3Galβ1-4Glc), which is also found on the surface of Plasmodium. These anti-αGal antibodies target Plasmodium sporozoites when inoculated into the skin, to block transmission and promote sterile protection against malaria in mice. Given that humans generate natural anti-αGal antibodies, we hypothesise that boosting this response, thought to arise following exposure to αGal-expressing members of the gut microbiota, may be of benefit in targeting Plasmodium and preventing malaria transmission.

With support from the Bill and Melinda Gates Foundation, our group is now working towards assessing whether anti-αGal antibodies effectively prevent malaria transmission either alone or in conjunction with other well-characterised anti-malarial antibodies. Alongside this study, we propose to investigate whether gut colonisation by αGal-expressing bacteria might similarly enhance vaccine functionality and Plasmodium targeting. In this project we will use a series of mutant strains of E. coli O86:B7 affected in the synthesis of αGal to investigate whether this bacterium modulates the expression of αGal in response to αGal immunity, how these processes affect bacterial colonisation of the gastrointestinal tract, and whether colonisation, αGal expression and the elicitation of a natural anti-αGal response can promote the efficacy of Plasmodium targeting and host protection by existing, characterised anti-Plasmodium antibodies.