Malaria against malaria: Pre-existing malaria infection can prevent second infection

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A team of researchers have found that pre-existing malaria prevents secondary infection by another Plasmodium strain, the parasite responsible for malaria, by restricting iron availability in the liver of the host. This discovery will be published this Sunday, May 15, in *Nature Medicine* and has important implications for the management and prevention of malaria, a condition which affects millions of individuals worldwide.

The study was developed by the team led by researcher Maria M. Mota at Instituto de Medicina Molecular in Lisbon, Portugal, in collaboration with researchers at the Weatherall Institute of Molecular Medicine and Oxford University; and was funded by the Portuguese Fundacao para a Ciencia e Tecnologia, European Science Foundation and Medical Research Council, UK.

In this current study, the researchers focused at how malaria parasites developed in both the liver and in red blood cells and analysed patterns of infection in mice, looking in particular at cases of 'superinfection', in which an individual already infected with malaria is later bitten by a second infected mosquito. An individual in a high risk area can be bitten by hundreds of malaria-infected mosquitoes per year, making the issue of superinfection highly relevant. The study reveals for the first time the crucial role of iron in the development of multiple malarial infections, which has strong implications for iron supplementation used to combat

anaemia in malaria-endemic regions.

After a mosquito bite, malaria parasites first travel to the liver, multiply, then escape and invade red blood cells. It was previously understood that parasites in both the liver and in blood need iron in order to grow. This new study shows that a second mosquito bite of an individual, already carrying blood parasites, does not lead to a full-blown second infection. The superinfection is blocked in the liver by the first infection. This protective effect is due to the blood parasites causing the parasites in the liver to be starved of iron, so that they cannot grow. In that respect, the results challenge the biological concept that infection of distinct host cells (liver hepatocytes or red blood cells) occur independently from each other, which may also have impact in the research area of infection (beyond malaria).

Dr Silvia Portugal, first author of the study says: "I am very happy that we were able to find such an interesting interaction occurring between different malaria parasite stages in a single host, and that this might contribute for future control of malaria."

Dr Maria Mota, who led the study at Instituto de Medicina Molecular in Lisbon says: "Our findings help explaining the differences in infection risk and complexity of infections in young individuals observed in endemic-malaria regions that have hitherto required speculative explanations. Also, they challenge the idea that infection in distinct cell types is independent, which may have an impact in future research in the field of infectious diseases as a whole. "

Dr Hal Drakesmith who co-led the study at the Weatherall Institute of Molecular Medicine adds: "'Now that we understand how malaria parasites protect their territory in the body from competitor parasites, we may be able to enhance this natural defence mechanism to combat the risk of malaria infections. At the same time we may need to look again

at the advisability of iron supplementation programmes in malaria-endemic regions, as possible increased risk of infection may need to be weighed against benefits - more data is needed on this issue."

Malaria is a devastating disease that affects extensive areas of Africa, Asia, South and Central America, causing several thousands of deaths per year in children under the age of five. Malaria is caused by the infection of the protozoan parasite Plasmodium, which belongs to the phylum Apicomplexa. Attempts to eradicate malaria have so far been unsuccessful. Their failure can be attributed to increasing resistance to insecticides in the mosquito vector and to anti-malarial drugs in the parasite. There is an urgent need of developing novel strategies against malaria.

Provided by Instituto de Medicina Molecular

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