Unveiling the life-cycles of malarial parasites to aid the routine validation of drugs and live vaccines

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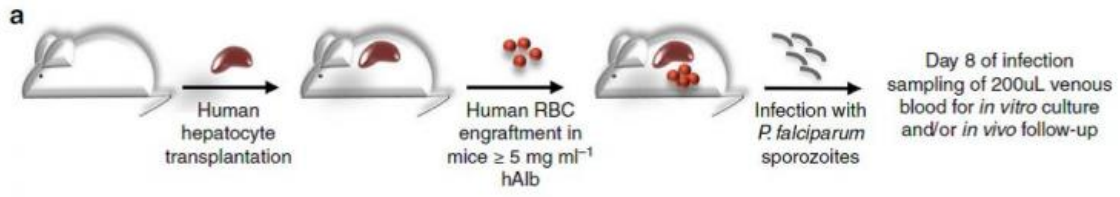

For the first time, researchers in France (with the help of the Central Institute for Experimental Animals, Kawasaki, Japan) have generated humanized mice engrafted with both human liver tissue and human red blood cells. The mice were then used to reveal the full life-cycle of Plasmodium falciparum, and liver stage life-cycle of Plasmodium ovale, two of the parasites that cause malaria.

Details of the life-cycles of P. falciparum and P.ovale, two of the parasites that cause malaria, are revealed by Hiroshi Suemizu at the Central Institute for Experimental Animals, Kawasaki and researchers affiliated with Kawasaki Innovation Gateway at Skyfront, Japan. The findings are published in *Nature Communications*. The researchers expect the use of humanized mice for malarial studies to aid the routine validation of drugs and live vaccines for the disease.

Unveiling the life-cycles of malarial parasites

Malaria is caused by variants of Plasmodium parasites carried by mosquitoes, and remains a leading cause death worldwide. The strain Plasmodium falciparum triggers a very severe form of malaria, accounting for the majority of deaths. Those people infected with less virulent strain P.ovale may also suffer serious illness, but a key difference is that this particular strain has the ability to 'lie dormant' in the body only to reappear months, or even years, later.

Due to the parasites behaving differently in different hosts, it has proven difficult to study the parasites inside the body to verify their precise life-cycle and replication.

Now, for the first time, Valerie Soulard and co-workers at Sorbonne University, Paris, France, with an international team of scientists including Hiroshi Suemizu at the Central Institute for Experimental Animals, Kawasaki, have successfully analyzed the complete life cycle of P.falciparum in the bodies of humanized mice. They also uncovered the stages P.ovale parasites follow inside humanized mice liver cells.

Soulard and her team engrafted mice with both human liver tissues and human red blood cells, to follow the complete development of the P.falciparum parasites from early stages in liver cells, through multiplication to the appearance of mature germ cells in the blood stream.

In addition, the team discovered that, unlike P.falciparum, P.ovale parasites are able to 'pause' their development in the liver, maturing weeks later to trigger a relapse of the disease in the patient.

The team hope the further use of humanized mice for malarial studies will aid the routine validation of drugs and live vaccines for the disease, together with further analysis of Plasmodium strains.

More information: Valérie Soulard et al. Plasmodium falciparum full life cycle and Plasmodium ovale liver stages in humanized mice, *Nature Communications* (2015). DOI: 10.1038/ncomms8690