Infectious Diseases Labs

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Dr Olivier Silvie

INSERM
Centre d'Immunologie et des Maladies Infectieuses
Paris, France

Date: Tuesday, 13 December 2022
Time: 5:00pm to 6:00pm

Join Zoom Meeting **here**
Meeting ID: 923 4332 9182
Passcode: 837289

Plasmodium sporozoite micronemal proteins and host cell invasion

Malaria is caused by Plasmodium, a protozoan of the phylum of Apicomplexa. Infection begins with the inoculation of invasive forms called sporozoites by a female Anopheles mosquito during blood feeding. Sporozoites traffic to the liver and invade hepatocytes for an initial and obligatory round of replication, before the release of merozoites into the blood circulation, which invade and replicate inside red blood cells, causing the disease. Merozoite invasion of erythrocytes has been well characterized at the molecular and structural levels. In sharp contrast, the molecular mechanisms underlying invasion of hepatocytes by sporozoites are poorly characterized, due in part to technical limitations and to the complexity of sporozoite biology. After an infectious mosquito bite, sporozoites migrate extensively to leave the injection site in the skin and reach the liver parenchyma, before ultimately switching to productive invasion of hepatocytes. Host cell invasion by apicomplexan parasites involves the secretion of apical organelles, called micronemes and rhoptries, and the formation of a unique structure known as the moving junction that leads to the internalization of the parasite within a replicative niche, the parasitophorous vacuole, which is essential for its development. Apical secretory organelles contain proteins specifically expressed in sporozoites, including 6-Cys proteins, and proteins shared between sporozoites and merozoites, such as AMA1 and RONs, which are involved in the formation of the moving junction. Our recent work based on conventional reverse genetics identified a new 6-Cys protein that is essential for sporozoite invasion of hepatocytes. Using a conditional mutagenesis strategy based on dimerisable Cre, we also demonstrated the role of AMA1 and RONs in sporozoites, not only for hepatocyte invasion in the mammalian host but also for salivary gland colonization in the mosquito. Our results support the hypothesis of a functional compartmentalization of microneme proteins in Plasmodium sporozoites, which may represent potential targets to block the early stages of malaria infection.

Dr Olivier Silvie is Deputy Director and Team leader at the "Centre d'Immunologie et des Maladies Infectieuses" (Sorbonne Université/INSERM), in Paris, France. He received a Medical Doctorate from Université René Descartes in 2003, and a Ph.D. in Biochemistry and Molecular Biology from Université Pierre et Marie Curie in 2006. After a 4-years postdoctoral stay in Heidelberg and Berlin in Germany, he was appointed by INSERM in 2010 as a tenure track researcher. Dr Silvie's research focuses on the malaria pre-erythrocytic stages, investigating the mechanisms of Plasmodium sporozoite invasion to identify novel vaccine targets. His work makes extensive use of genetic engineering and relies on cellular models for both human and rodent malaria parasites.

Seminar is open to all . No registration required

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