Instituto de Medicina Molecular

Master Project Proposal

Title: Unraveling the Role of Viperin Induction During *Plasmodium* Hepatic Infection

Synopsis:

Growing evidence shows that most intracellular pathogens can exploit the host cell to create a more hospitable environment. Not only do pathogens scavenge the host for nutrients, but they also evolved strategies for evasion and counterattack to face the well-equipped vertebrate immune system.

Plasmodium sporozoites, the infectious agents of malaria, are deposited in the skin of the mammalian host and travel to the liver, invading hepatocytes to produce thousands of merozoites. To support its massive development and replication in an immunoprivileged organ as the liver, *Plasmodium* has potentially evolved strategies to face a dual challenge: being able to forage all the nutrients it requires from the host, while avoiding the highly likely possibility of being recognized by its immune system.

There is now substantial evidence that *Plasmodium* specifically induces a TYPE-I IFN response during the liver stage of its life cycle, which has a strong impact on infection. Microarray studies investigating *Plasmodium* infection-mediated transcriptional changes in the liver further revealed that VIPERIN (virus inhibitory protein endoplasmatic reticulum associated, interferon-inducible), a key antiviral molecule, is one of the most transcriptionally induced genes within the *Plasmodium*-induced TYPE-I IFN response. Recent studies demonstrated that Viperin can have a dual antiviral or proviral role: besides being able to directly suppress viral replication by interfering with replication mechanisms, it can also interfere with signal mediators critical for an innate response. Indeed, viperin is now considered one of the major targets for evolutionary strategies to counteract antiviral effects and is an established key molecular link between lipid metabolism and immune defense / evasion. In this context, Viperin induction upon *Plasmodium* infection assumes enhanced relevance because *Plasmodium* infection strongly alters lipid metabolism in the liver.

In the present project, we propose to EXPLORE THE UNKNOWN ROLE OF VIPERIN DURING *PLASMODIUM* LIVER INFECTION AND ITS RELATIONSHIP WITH CELLULAR METABOLISM.

In order to achieve this aim, we will employ state-of-the-art methodologies, including immunofluorescence confocal microscopy, quantitative real-time PCR (qRT-PCR), among others.

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