Could this be malaria's Achilles heel?

08.11.2017 - Portuguese researchers at Instituto de Medicina Molecular (iMM) Lisboa have identified a defence mechanism by which the malaria parasite can survive inside its host's liver cells, a crucial stage where the parasite acquires the capacity to infect red blood cells causing the symptoms associated with this disease.

The *Plasmodium* parasite, responsible for malaria infection, replicates inside its host's liver cells involved by a membrane that protects it against threats present in the intracellular environment, namely autophagy, a process that is triggered upon infection and in which cells degrade materials that are no longer necessary. Importantly, this process is dependent on a protein named LC3.

Although autophagy is activated by host cells after infection the malaria parasite is resistant to this cellular defence mechanism, unlike other more susceptible pathogenic agents. However, researchers led by Maria Mota have now found the Achilles heel of the malaria parasite: a protein named UIS3 which binds to LC3 and forms a type of protective shield against autophagy. Without this protection the parasite becomes vulnerable and is rapidly eliminated by the host.

The study has revealed that parasites lacking the UIS3 protein cannot survive inside mice liver cells. However, if the host's autophagy capacity is compromised the parasite gains back its capacity to infect cells.

These results show that UIS3 protein could become a possible target for the development of novel targets against the malaria parasite, namely against the hepatics forms of this disease which, in some *Plasmodium* species, may persist in a dormant state and cause symptoms several years after the time of first infection.

It is particularly relevant to identify new therapeutic targets at a time where several cases of drug resistance begin to occur, specifically in Southeast Asia. In the future, the team wishes to identify compounds that can block the parasite's capacity to inhibit cellular autophagy and test its efficiency as novel drugs against malaria.