Protection against inflammatory diseases by rodent malaria is due to a virus that cripples DC function in a IFN-I-dependent manner

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Introduction:
Exposure to malaria parasites likely influences the host immune status, leading to detrimental or beneficial consequences on the development of inflammatory diseases. The clinical evolution of malaria itself is influenced by co-infection with concurrent Plasmodium species. Moreover, malaria plays a beneficial role in a mouse model of multiple sclerosis, the Experimental Autoimmune Encephalomyelitis (EAE). The underlying protective mechanisms are largely unknown.

Materials and methods:
We studied the impact of the rodent malaria strain Plasmodium berghei K173 (PbK) on the T cell and DC compartments and on the clinical evolution of experimental cerebral malaria (ECM), a Th1-mediated complication of malaria, and on EAE.

Results:
We show that blood parasitized by PbK confers full protection against Pb ANKA (PbA)-induced ECM, as well as against MOG/CFA-induced EAE. The fact that such protective effect is associated with a strong IFN-I signature and is transmissible to new mice independently from the parasites, suggested the presence of a virus. We detected the presence of an RNA virus called Lactate Dehydrogenase-elevating Virus (LDV) in PbK stabilates, as well as in other stocks of the community. LDV elicits lifelong asymptomatic infection with persisting circulating viremia.
The modulatory effects of PbK are entirely recapitulated by infection with this virus. Protection against ECM is due to an IFN-I-mediated drop in the number of splenic cDC and their impaired ability to produce IL-12p70. Disruption of the cDC compartment is accompanied by a decrease in the pathogenic CD4+ Th1 responses. Protection against EAE conferred by LDV is also linked to the blunted differentiation of CD4+ T cells into IFN-γ-, IL-17- and GM-CSF-producing encephalitogenic cells in EAE.

Conclusion:
Our results identify the presence of a virus co-hosted in several Plasmodium stabilates across the community, that has major consequences on the host immune system. They show that this virus evokes a massive type I IFN response, which results in quantitative and qualitative defects of cDC that are no longer able to drive the pathogenic CD4+ T cell responses underlying ECM and EAE.

Keywords : Plasmodium - inlammation - LDV - CD4 T cells - cDC
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