# *Plasmodium yoelii* infection modulates the expression of SIRPα-CD47 axis and associated cytokine response

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## Abstract

SIRPα/CD47 axis is a key immune checkpoint implicated in the regulation of several immunological processes, including phagocytosis, inflammation, and lymphocyte activation. In malaria, SIRPα-CD47 axis is believed to play a pathogenic role, since the blocking of its signaling protects against cerebral malaria and attenuates parasitemia in experimental models. However, knowledge about the role of the SIRPα-CD47 axis in malaria is still incipient. Thus, the present study investigated the dynamics of SIRPα and CD47 splenic expression during the lethal (*Py*17XL) and non-lethal (*Py*17XNL) infection of *Plasmodium yoelii* in BALB/c mice, and the impact of SIRPα-CD47 axis blockage in the induced immune response. As expected, *Py*17XL lethal infection was marked by hyperparasitemia, severe anemia, and intense hypothermia, all preceding mice death. Severe anemia was also observed in *Py*17XNL infection, which spontaneously resolved in parallel with parasitemia. Both strains negatively modulated SIRPα expression on splenocytes, with no significant effect on CD47, and a marked increase in the frequency of SIRPα+ cells was noted during non-lethal infection. Interestingly, *in vitro* antibody blockade of the SIRPα-CD47 pathway reduced cytokine secretion (IFN-γ, TNF, IL-17A and IL-10) by splenocytes obtained from non-lethal infection, while a prominent secretion was observed in lethal infection, especially of IL-6. In conclusion, our results suggest that the splenic expansion of SIRPα+ cells may be involved in the resistance to lethal malaria infection and that *P. yoelii* strains can differently impact the SIRPα-CD47 signaling, as observed under antibody blocking treatment. In light of these finds, additional investigations are necessary to define the cell populations expressing the CD47/SIRPα axis as well as the *in vivo* differential effect of the anti-CD47/SIRPα immunotherapy in lethal and non-lethal experimental malaria.