Type I IFN response of human brain endothelial cells to extracellular particles from *Plasmodium falciparum*-infected RBC

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Cerebral malaria (CM) results from dysfunction of the brain's microvasculature and disruption of the blood–brain barrier (BBB), driven by *Plasmodium falciparum*–infected red blood cells (iRBCs). Their interaction with brain endothelial cells (BEC) triggers a cascade of inflammatory and pro-coagulant responses that may lead to death or neurologic deficits even after anti-malarial treatment.
In a murine CM model, we showed early activation of a type I IFN response in the brain. We found that this response is driven by activation of the innate immune receptor "Stimulator of interferon genes" (STING) in BECs, which increases CXCL10 production. This chemokine recruits leukocytes to the brain contributing to the immunopathology of CM. Importantly, we identified that extracellular particles (EP) from RBC infected with the rodent malaria parasite *Plasmodium berghei* contain STING agonists that induce type I IFN in BEC cultures.
We are now investigating whether a similar mechanism underlies human CM. Using a IFNβ-reporter human brain endothelial cell line and the human malaria parasite *P. falciparum*, we aim to identify the mechanisms of type I IFN activation in the human brain endothelium and the innate immune activators within EP derived from *P. falciparum*–iRBC.