The eye as a window to investigate the CNS microvasculature during a dynamic malarial infection

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Severe malaria, including cerebral malaria (CM), results in the deaths of nearly a million children each year in Africa and at present there are no effective adjunctive therapies to treat CM. Clearly the development of such therapies would benefit from a better understanding of the cellular and molecular mechanisms underlying CM. The eye provides a window to visualize important mechanisms in the brain microvasculature, as the retina is an extension of the optic nerve. For the first time, we used high resolution fundoscopy (HRF) and optical coherence tomography (OCT) to view the course of a *Plasmodium berghei* ANKA infection in mice, an experimental model of CM. As measured by OCT, the *in vivo* retinal cross-sections of infected mice do not seem to be enlarged or edematous in comparison to uninfected mice ($p = 0.81$). Additionally, with bright field fundoscopy we have identified hyper-reflective — yet unidentified — clumps that are confined to the retinal vasculature and seem to be correlated with parasitemia, increasing in number as the infection progresses. While the nature of these clumps is unknown, their size and behavior may be correlated with disease severity. Their presence however, is not; mice infected with *P. berghei* NK65, a strain which does not cause cerebral malaria, also have these clumps in their retinal vasculature. Infected mice are easily distinguished from uninfected controls based on the presence of hyper-reflective clumps, which suggests that HRF shows diagnostic promise to determine an individual's infection status. Using fundoscopy, we also detect a CM-specific increase in the number of GFP-positive immune cells (monocytes, macrophages, granulocytes) in the retina of LysM-GFP mice as the infection progresses. These preliminary data suggest that the eye can serve as a diagnostic window for malarial infection, or used to visualize and understand the development of cerebral malaria.