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Needle in the haystack: combining intravital imaging and mathematical modeling to understand how vaccine-induced T cells find malaria-infected cells in murine livers

Vitaly V. Ganusov
University of Tennessee, vitaly.ganusov@gmail.com

Ian Cockburn
Australian National University, ian.cockburn@anu.edu.au

Reka Kelemen
Vienna Graduate School, rkelem@gmail.com

After Plasmodium-infected mosquito transmits the malaria parasite to the mammalian host, parasites (called sporozoites) travel to the liver and infect hepatocytes. Within several days, sporozoites replicate and differentiate into merozoites which are then able to re-enter circulation and infect red blood cells. Removal of sporozoites while they travel to the liver or during their replication in the liver prevents clinical symptoms of malaria, and this is why sporozoites have been considered as a good target for malaria vaccines. Using intravital imaging we recently discovered that vaccine-induced CD8 T cells form clusters around sporozoite-infected hepatocytes in murine livers, and that these clusters are associated with parasite removal. Here I extend our previous studies and demonstrate that formation of these clusters cannot be driven solely by differences in parasite's attractiveness for T cells, while the model in which T cells attract other T cells to the site of infection is best at describing our data. Additional analyses also suggest that formation of such clusters occurs rather rapidly after initial recognition of the infected cell.