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Imaging of CD8+ T cells in the malaria infected liver reveals key processes for effective protection

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CD8+ T cells can kill *Plasmodium* parasites in the liver of the mammalian host; a protective effect that can be harnessed for malaria vaccination. We have previously used intra-vital imaging to measure the interaction of CD8+ T cells in the liver and *Plasmodium* infected hepatocytes. We have previously observed that CD8+ T cells in the liver undertake LFA-1 dependent crawling motility in the allowing them to scan the liver and find infected hepatocytes. Subsequently we have observed that clusters of CD8+ T cells form around the infected hepatocyte, which may potentiate parasite killing. Key questions are how do these clusters form? And how are the parasites killed? Mathematical modelling suggested that clusters could form by at least two different processes. In the first process clusters form as a result of a positive feedback loop in which cells in the cluster recruit further effectors. Another model posits that clusters may form because it becomes harder for cells to leave the vicinity of an infected hepatocyte as clusters increase in size. To distinguish these possibilities we have imaged the behaviour of T cells in the liver to determine if they show evidence of directed migration towards infected hepatocytes. Moreover using Pertussis toxin mediated inhibition of chemokine receptors, chemokine receptor knockout mice and mice lacking key effector molecules we aim to understand the molecular processes underlying T cell clustering and parasite killing.

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