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Plasmodium falciparum cytoadherence to ICAM-1 is associated with cerebral malaria

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The pathology of sever malaria is in part related to the pro-inflammatory nature of the host response but a number of other factors are also thought to be involved, including the interaction between infected erythrocytes and endothelium. This phenotype involves a range of host receptors and the parasite-derived variant antigen PfEMP1, which is expressed on the surface of the infected erythrocyte membrane. Previous studies have suggested a role for ICAM-1 in the pathology of cerebral malaria, although these were inconclusive. In this study we measured the binding to CD36 and ICAM-1 of patient isolates from varying clinical syndromes under static and flow conditions. We also used mutant ICAM-1 proteins to characterise the key contact residues on ICAM-1 and produce a detailed binding phenotype. Our results show that increased binding to CD36 is associated with uncomplicated malaria while ICAM-1 adhesion under flow conditions is raised in parasites from cerebral malaria cases. The pattern of ICAM-1 binding has also been investigated using mutant ICAM-1 proteins and indicates that isolates from severe malaria are biased towards a binding signature also seen with ITO4, a laboratory isolate selected for binding on human endothelium with similar receptor expression to that seen in the brain.

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