Identifying host receptors for *Plasmodium falciparum* infected erythrocytes binding to human brain microvascular endothelial cells

Nouhoum Diallo and J. Alexandra Rowe
Institute of Immunology and Infection Research, School of Biological Sciences, University of Edinburgh, Edinburgh EH9 3FL, United Kingdom

Abstract

Background: Sequestration of *Plasmodium falciparum* infected erythrocytes in human brain microvasculature is the hallmark of cerebral malaria. Sequestration is mediated by the molecular interaction between *Plasmodium falciparum* erythrocyte membrane protein 1 family member and receptor expressed on endothelial cells. Severe and cerebral malaria are associated with the expression of *Plasmodium falciparum* erythrocyte membrane protein 1 domain cassettes 8 and 13, but the endothelial receptor for parasites expressing these ligands remain unknown. Previous studies have identified Complement C1Q Binding Protein (C1QBP) as a potential receptor for cytoadhesion of *Plasmodium falciparum* infected erythrocytes on microvascular endothelial cells. However, despite this adhesive interaction being described, it has rarely been investigated and it is unknown whether infected erythrocyte adhesion to C1QBP plays a role in cerebral malaria. **Aims/methods**: In this study, we describe the cellular localization of C1QBP as well as other putative receptors on the human brain microvascular endothelial cell line hCMEC/D3 using immunofluorescence assays and fluorescence microscopy. **Results:** Resting and TNFα-activated endothelial cells showed intracellular staining for C1QBP, but cell surface staining was not observed. However, after incubation for 2 hours with soluble C1QBP, the endothelial cells did exhibit positive surface membrane expression of C1QBP in both resting and activated conditions. hCMEC/D3 cells also displayed positive surface membrane staining for other known *P. falciparum* adhesion receptors including ICAM1, VCAM1, PECAM1, CSA, EPCR and integrin αV in both conditions. Whereas other putative IE receptors such as CD36, NCAM, fractalkine, thrombospondin, CD62E and CD62P were not detected. **Conclusions:** These findings suggest that although C1QBP is not constitutively expressed on the surface of microvascular endothelial cells, it can become associated with the cell surface from human serum or if added exogenously. Future work will examine the concentration of soluble C1QBP in normal plasma and during malaria infection and determine whether human endothelial cell surface associated C1QBP can serve as a receptor for *Plasmodium falciparum* infected erythrocyte cytoadherence.