Summary
6. Summary

All the clinical symptoms of malaria are attributed to the blood stage of the parasite life cycle during which Plasmodium merozoites invade and multiply within host erythrocytes. Invasion by Plasmodium merozoites is a complex process that requires multiple molecular interactions between the invading parasite and target erythrocyte. Parasite proteins that bind erythrocyte receptors during invasion are localized in apical organelles called micronemes and rhoptries. The regulated secretion of microneme and rhoptry proteins to the merozoite surface to enable receptor binding is a critical step in the invasion process. Here, we have developed flow cytometry based methods to measure relative levels of cytosolic calcium and study surface expression of apical organelle proteins in \textit{P. falciparum} merozoites in response to different external signals. We describe the identification of physiologically relevant external signals that trigger the sequential release of microneme and rhoptry proteins. Exposure of \textit{P. falciparum} merozoites to low potassium ion concentrations as found in blood plasma leads to a rise in cytosolic calcium levels through a phospholipase C mediated pathway. Rise in cytosolic calcium triggers secretion of microneme proteins such as the 175 kDa erythrocyte binding antigen (EBA175) and apical membrane antigen1 (AMA1) to the merozoite surface. Subsequently, interaction of EBA175 with glycophorin A (glyA), its receptor on erythrocytes, restores basal cytosolic calcium levels and triggers release of rhoptry proteins. Our results identify for the first time the external signals responsible for the sequential release of microneme and rhoptry proteins during erythrocyte invasion and provide a starting point for the dissection of signal transduction pathways involved in regulated exocytosis of these key apical organelles. Signaling pathway components involved in apical organelle discharge may serve as novel targets for drug development since inhibition of microneme and rhoptry secretion can block invasion and limit blood-stage parasite growth.