Erythrocyte invasion by *Plasmodium falciparum* is a multi-step process mediated by specific receptor/ligand interactions. It is an attractive target for drugs or vaccine-mediated immunity for if blocked by drugs or vaccine-mediated immunity, merozoites would be eliminated and clinical malaria prevented. Most *P. falciparum* clones use the sialic acid residues on glycophorin-A and/or B as the receptor for invasion of erythrocytes. The parasite molecule that recognizes glycophorin A is a sialic acid dependent erythrocyte-binding antigen 175 (EBA-175) and is the best-characterized pathway of invasion of human erythrocytes. However, *in vitro* growth assays have demonstrated that some parasite strains may utilize alternative pathways based on other molecules present on the merozoite and/or receptors on the surface of RBCs. It is unclear what proportion of wild isolates in western Kenya are able to utilize both sialic acid-dependent and independent invasion mechanisms. I hypothesized that *P. falciparum* has develop alternative invasion pathways perhaps under immunological pressure by the host and that some strains utilize the sialic acid-dependent pathway, others use sialic acid-independent pathways, and yet others may be able to engage both. In order to test this hypothesis, this study investigated the invasion phenotypes of 20 *P. falciparum* wild isolates in the presence of normal, neuraminidase-treated, trypsin-treated or dual enzyme treated RBCs. Enzymatic treatment of human erythrocytes with trypsin or neuraminidase reduced the invasion efficiencies of some parasite isolates. Dual enzyme treatment of RBCs completely abolished the ability of *P. falciparum* to invade such cells.

These results suggest that the utilization of multiple pathways of RBCs invasion by *P. falciparum* is a common occurrence among the field isolates. Therefore, immunization with single antigens such as EBA-175 may not be effective against some *P. falciparum* isolates utilizing alternative RBCs invasion pathways. Further studies are required to identify the parasite molecules used in these alternative pathways for potential inclusion in a blood stage vaccine.