Exploring the diversity of *Plasmodium falciparum* hypervariable RIFINs and their interactions with human immunomodulatory receptors

During the intra-erythrocytic replication cycle, *Plasmodium* parasites express members of highly variable, multi-gene families which are exported and displayed upon the surface of the infected erythrocyte. These proteins are thus available to directly interact with and down-modulate the human immune system to promote survival of erythrocytes infected with parasites. With ~150 members, the RIFINs are one of the largest hypervariable multi-gene families in *Plasmodium falciparum* and certain RIFINs have been shown to directly interact with human immunoinhibitory receptors such as LAIR1 and LILRB1. The full immunomodulatory potential of the RIFIN family however is unknown. To directly explore the extent of RIFIN interactions with human immune receptors we have constructed a library of >3,000 unique RIFIN hypervariable domain sequences from *Plasmodium falciparum* lab strains and field isolates. Initial experiments demonstrated that RIFIN hypervariable domains could be expressed and purified from HEK 293 cell supernatants. By also using sf21 insect cells, we could further expand the repertoire of expressed RIFINs. Expressed RIFINs will be systematically tested for direct binding against a panel of ~750 soluble ectodomains representing the human immune receptor repertoire. Interactions detected between our RIFIN library and human immune receptors will provide important molecular insights into how *Plasmodium falciparum* modulates host immunity during malaria progression.