A screen of a transposon-mutagenized library identifies a Plasmodium falciparum RING domain-containing protein likely involved in sexual commitment

Presenter: Ilana Goldowitz, BSc, Harvard School of Public Health

The malaria parasite *Plasmodium falciparum* moves between multiple microenvironments within its human host and mosquito vector during its complex life cycle. This requires it to make dramatic changes in its physiology and gene expression. To become transmissible to mosquitoes, a small proportion of asexual parasites replicating in human erythrocytes first transform into a non-replicating sexual stage called the gametocyte. It is hypothesized that asexual parasites become committed to producing offspring which will either undergo sexual development or continue asexual replication. Recent studies have identified an epigenetic component in the developmental switch to the sexual pathway. Detailed understanding of this mechanism is of great interest because of its importance in malaria transmission and the spread of drug resistance. To identify components of the gametocyte conversion pathway, we performed a genetic screen of a transposon-mutagenized *Plasmodium falciparum* library constructed in the gametocyte-producing parental strain NF54 (Balu et al. 2009, 2010). We identified two disrupted lines with significantly increased gametocyte conversion rates and two with reduced conversion rates. One of these mutant parasite lines contains a promoter disruption leading to reduced expression of a gene coding for a RING domain-containing protein of unknown function. In addition to constitutively increased gametocyte production, this mutant line displays an impaired growth phenotype, likely due in part to an increased cell cycle length. Ongoing experiments aim to understand this protein's role and position in the sexual commitment pathway relative to other recently identified commitment-related proteins and environmental triggers.