Investigation of *Plasmodium* kinase inhibitors & ubiquitin signaling pathways

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Muser
Summer 2021 & Fall 2021 positions
Malaria is a major global health burden

229 million new malaria infections in 2019

409,000 people died of malaria in 2019

Malaria parasite *P. falciparum* undergoes a complex lifecycle

There is a continual and pressing need to study *Plasmodium* biology to inform malaria drug discovery.
Aim: validate potential targets of Plasmodium kinase inhibitors and propose mechanisms of binding through computational models

Methods:
- PyMol + AutoDock Vina plugin
- Schrödinger Glide

Future directions:
- Experimental validation
- Binding studies


Project 1: Background

**Relevant literature:**


**Project 2:**

**Biochemical interrogation of *Plasmodium* ubiquitin signaling**

**Aim:** identify protein-protein interactions in *P. falciparum* ubiquitination pathways and small molecules as chemical probes

**Methods:**
- Molecular cloning
- Protein expression & purification
- Assay development

**Future directions:**
- Binding studies
- Proteomic analyses

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**Ubiquitin roles in *Plasmodium* blood stage:**

- Unknown/other: 25%
- Translation: 11%
- Transcription: 4%
- DNA repair & metabolism: 4%
- Chromatin structure: 6%
- Redox metabolism: 4%
- Chaperonin/protein folding: 12%
- Phosphorylation: 4%
- Ubiquitin-dependent processes: 11%
- RNA metabolism: 11%
- Parasite-specific processes: 8%

**Biochemical assay**

- *P*PK9 binding screen
- SAR
- Inhibition


**Project 2: Background**

**Relevant literature:**