The chemistry and biology of the unique plastid organelle, the apicoplast, in malaria parasites

Malaria caused by Plasmodium spp parasites has an enormous disease burden that disproportionately affects the world’s poorest and youngest. New anti-malarials with novel drug mechanisms are desperately needed in the face of existing or emerging drug resistance to all available therapies. Investigation of Plasmodium biology offers...
both the potential for important biomedical impact and an opportunity to explore fascinating eukaryotic biology. Given the challenges of genetic and other approaches to studying this complex organism, the development of chemical tools will be especially critical in pushing forward basic research.

My research focuses on the apicoplast, a prokaryotically-derived plastid organelle unique to Plasmodium (and other pathogenic Apicomplexa parasites) and a key anti-malarial drug target. My laboratory's goal is to elucidate apicoplast biology, function, and role in pathogenesis with the ultimate goal of realizing the potential of the apicoplast as a therapeutic target. In a major step toward this goal, my previous work has demonstrated that the sole essential function of the apicoplast in blood-stage P. falciparum parasites is the biosynthesis of isoprenoid precursors. As such, I was able to generate parasites completely devoid of this essential organelle but chemically rescued by supplementation of the growth media with isopentenyl pyrophosphate (IPP), the pathway product. Chemical rescue and "apicoplast(-)" parasites are innovative tools for investigating apicoplast biology and for advancing apicoplast-directed drug and vaccine development. Our research takes advantage of these new tools and our newfound understanding of apicoplast function to explore a variety of topics, including protein trafficking to the apicoplast and the protein "prenylome" in Plasmodium. We employ a variety of methods but have a particular focus on the use of chemical tools to overcome the current challenges in studying this organelle. Our exploration of the Plasmodium apicoplast are likely to reveal both unique biology and targets for anti-malarial drug development.

Teaching

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GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biochemistry (Phd Program)
- Infectious Diseases (Fellowship Program)
- Microbiology and Immunology (Phd Program)

Publications

PUBLICATIONS

- **A mutagenesis screen for essential plastid biogenesis genes in human malaria parasites.** *PLoS biology*  
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- **Host Cell Metabolism Contributes to Delayed-Death Kinetics of Apicoplast Inhibitors in Toxoplasma gondii** *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*  
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- **Disruption of Apicoplast Biogenesis by Chemical Stabilization of an Imported Protein Evades the Delayed-Death Phenotype in Malaria Parasites.** *mSphere*  
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