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Global metabolomics profiles and antimalarial drug therapy

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Since Trager and Jensen established intraerythrocytic culture of *Plasmodium falciparum*, biochemical characterization of essential nucleotide, carbohydrate, amino acid and lipid requirements have yielded drug targets and corresponding mechanistic studies. At the level of transcription, in *P. falciparum* few changes occur in response to antimalarial drugs. Global mass spectrometry analysis of hundreds of metabolites identifies stage dependent profiles, novel plant-like pathways and responses to drugs. Insights into the unique hemoglobin degradation pathway and hemozoin formation by targeted and nontargeted analysis revealed a role for neutral lipids in heme crystal formation.Published work from the group Manuel Llineas demonstrates accumulation of dipeptides in chloroquine resistant parasites. Comparison of metabolite changes with the antimalarial drugs identifies reproducible global patterns readily distinct for chloroquine, pyrimethamine and artemisinin. This unbiased approach is identifying discrete metablomic profiles and individual metabolites in *P. falciparum* by developmental stage and in response to antimalarial drugs.

Biography

David J Sullivan completed his MD at the University of Alabama at Birmingham and trained in Internal Medicine and Infectious Diseases at Washington University/ Barnes Hospital. He is an Associate Professor at the Johns Hopkins Malaria Research Institute. His research work communicated in over 100 publications has explored mechanisms of quinoline action and resistance related to hemozoin formation in *Plasmodium*, developed novel malaria diagnostic techniques, contributed to understanding of pathogenesis of disease, initiated ongoing malaria epidemiologic studies in Bangladesh and contributed an evidence base for new uses of existing drugs.

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