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New mathematical models for artemisinin-induced parasite killing and growth retardation in blood-stage Plasmodium falciparum

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Falciparum malaria is a major parasitic disease causing widespread morbidity and mortality globally. Artemisinin derivatives – the most effective and widely-used antimalarials that have helped reduce the burden of malaria by 60% in some areas over the past decade – have recently been found to induce growth retardation of blood-stage *Plasmodium falciparum* when applied at clinically relevant concentrations. Furthermore, novel in vitro experiments indicate a complex relationship between drug concentration, the duration of exposure, and the rate of parasite killing.

In this presentation I will discuss how extensions to the pharmacokinetic-pharmacodynamic (PK-PD) modelling paradigm are required to explain in vitro observations and discuss the implications for our understanding of drug action. Given the stage sensitivity of the parasite to drug and the short half-life of the artemisinin derivates in vivo, our model-based analyses suggest how drug resistance may manifest and how alternative dosing strategies, or alternative antimalarials with altered pharmacokinetic properties, may aid in maintaining clinical efficacy.

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