Screening the MMV "Malaria Box" for rapid rate-of-kill

Imran Ullah, Raman Sharma, Giancarlo Biagini, Paul Horrocks

Institute for Science and Technology in Medicine, Keele University, Staffordshire ST5 5BG,UK and Research Centre for Drugs and Diagnostics, Liverpool School of Tropical Medicine, Liverpool L3 5QA, UK

Massive screens of chemical libraries for antimalarial activity have identified thousands of compounds that exhibit sub-micromolar potency against the blood stage of the malarial parasite *Plasmodium falciparum.* Triaging these compounds to establish priorities to take forward for development requires additional information regarding their activity. Key amongst their pharmacodynamics (PD) properties is the rate-of kill (RoK) – with a rapid RoK specifically identified as a key requirement for a Single Exposure Radical Cure and Prophylaxis (SERCaP) product. Compounds that kill quickly (fast RoK) rapidly reduce parasite burden to ameliorate the morbidity and mortality of disease. With the overall aim to accelerate drug screening by validating a rapid RoK, we describe here the validation of a novel, rapid (6hr) and a scalable BRoK assay that demonstrates a good correlation with *in vitro* recrudescence-based RoK data and available *in vivo* clinical findings. BRoK data for the Medicine for Malaria Venture's Malaria Box is presented here – highlighting leads with initial RoK as good as, and better than, artemisinin – reflecting their potential in meeting target candidate profile 1 for a future SERCaP.