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Validation of a new high throughput *in vitro* Luciferase based assay to identify fast acting antimalarial compounds

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Aim: To validate a new high throughput in vitro Luciferase based assay to identify fast acting antimalarial compounds.

Rational: In partnership with Medicines for Malaria Venture, Novartis Institute for Tropical Diseases (NITD) research efforts focused on finding new drugs with diverse modes of action to combat resistance, block transmission, prevent infection, and reduce relapse. One approach in antimalarial drug development is to identify novel chemical lead series for fast acting, blood stage anti-malarial with novel mode of action, which will potentially lead to rapid parasite reduction and fever clearance in patients.

Approach: Leveraging the Cas9 technology, we integrated a luciferase reporter gene under the control of the Plasmodium calmodulin promoter into a non-essential locus (Elo1). Using this luciferase expressing parasites line (3D7), we developed a robust in vitro assay to evaluate the inhibitory effect of a compound on the growth of ring-stage malarial parasite at 6 hour, thus enabling distinction of fast from slow acting compounds in vitro. Assay was validated with marketed anti-malarial compounds and further miniaturized to 384-well microplates, so as to facilitate high throughput screening, where 4000 compounds from Novartis collection were screened in dose response format.

Conclusion: Promising novel scaffolds were identified and are currently being profiled. The readout of the assay allowed us to rank compounds according to their in vitro activity and the classification of fast versus slow correlated well with available in vivo data. Incorporation of this new high throughput robust assay in phenotypic screening allowed prioritization and evaluation of compounds, as well as an opportunity to gain insights into the possible mode of action of the compound.

Biography

Yi Hua Katherine Chan has Six years biomedical research experience in Novartis Institute of Tropical Diseases. Specializes in high throughput drug screening in tropical neglected diseases. Expertise includes Malaria, Human African Trypanosomiasis, Cryptosporidium and Dengue cell-based assays. Proficient in assay development, robotics automation and the use of High Content Imaging platform. Led and managed successful high throughput screening (HTS) projects with innovative cutting edge technology. Leadership skills include lab management and mentoring associates. An effective bilingual who enjoys working in a fast-paced, dynamic and interactive globalized environment. Proactive and willing to learn attitude. Driven and willing to make continuous improvements towards becoming a versatile professional in biotechnology and public health care industry.

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