Science and Technology in Medicine

ResearchProjectProforma(SchoolofMedicine)

Research Title:	Functional-genomics and chemical-interference to reveal essential traits of human malaria asexual cycle
Keywords (up to 5)	Gene Drug Function Malaria
Supervisor: Job Title: **Department:** **Email Address:** **Telephone:** **Webpage link:**	Lecturer Faculty of Natural Sciences/School of Medicine i.russo@keele.ac.uk ---- ----
Type of projects offered	Intercalation and Studentship

(1) Outline the broad aims of your research and its medical relevance (150 words):

Malaria annually deprives humanity of ~600,000 individuals mostly aged 1-5 years. Unicellular parasites of the genus Plasmodium are the malaria causative agents. Current vaccination strategies are limited, while available drugs diminish their impact as resistance is expanding. New drugs and targets are urgently needed to treat this devastating disease.

Little is known of Plasmodium asexual cell cycle regulation in erythrocyte phases. My previous work identified and characterized Pf_Calpain and Plasmepsin V, two novel targets with ideal profiles for new anti-malaria interventions. These disclosed new unique pieces of parasite cell biology and are now been exploited for drug discovery as targets for inhibiting parasite asexual proliferation. In fact, the Plasmodium erythrocytic asexual cycle has a huge potential for drug treatments due to its peculiar and unusual traits, but how parasites regulate their asexual development is still largely unknown.

Collections of antimalarial compounds are available for studies aiming to identify their targets, but require and sensible strategies for their prioritization in drug development. However, these efforts are hindered by the scarceness of specific high-throughput (HT) phenotypic assays in P. falciparum and vivax.

Here, based on previous successes, we shall develop a novel and unbiased transversal analysis that, working simultaneously on both defined targets and chemical compounds, will provide high density information on functional genomics and chemical hits. To this end, we will generate innovative cellular assays focusing on cellular events related to the asexual parasite cell cycle; perform a chemical interference analysis using anti-malarial and fragment-based collections; and identify gene functions via my novel random mutagenesis system. This last shows high efficiency and a technical design that will revolutionize forward genomics.

Our concrete results will be state-of-the-art HT-cellular assays; creation of mutant collections; identification of novel antimalarial compounds and gene networks functionally related to selected cellular events; and identification of essential genes in parasite erythrocytic cell cycle.

The project will directly impact the high demand for novel targets and new chemical entities for novel anti-malaria therapeutic interventions, and the needs for a better understanding of parasite cell cycle biology and gene-function relationships.

(2) Indicate the skills/techniques the student will learn (100 words)

Bioinformatics,
Molecular biology,
microbiology techniques,
cell culture,
microscopy,
biochemistry
Flow cytometry
CRISPR/CAs9 techniques

Please submit this form electronically to Prof Divya Maitreyi Chari on d.chari@keele.ac.uk