Neuroprotective Agents for Cerebral Malaria

PROJECT DESCRIPTION

Malaria is a leading cause of child mortality worldwide, accounting for an estimated 1.24 million deaths annually. Most deaths (86%) occur in children under 5 years of age. In addition, long-term neurocognitive disability occurs in 25% of pediatric survivors of cerebral malaria (CM). Blood-brain barrier (BBB) dysfunction is associated with CM. Modulating endothelial barrier function at the BBB may suggest new therapeutic approaches to improve outcomes in CM. We propose to study licensed pharmacologic modulators of vascular endothelial growth factor receptor-2 (VEGFR-2), a key regulator of endothelial barrier function, under infectious and inflammatory challenge. We will use two complementary lines of inquiry: (1) in vitro BBB model; and (2) in vivo murine model of experimental cerebral malaria (ECM). Pharmacologic agents of interest include pazopanib, sunitinib, and regorafenib. These are newly developed drugs for cancer treatment, which are known to modulate endothelial permeability via interaction with the VEGFR-2 receptor but have never been tested in malaria. In addition to their anti-angiogenic (and anti-cancer) properties, VEGFR-2 antagonists promote endothelial quiescence in mature vascular beds, motivating our hypothesis that they will be neuroprotective in cerebral malaria.

FACULTY-DEPARTMENT

Medicine-Pediatrics

DESIRED FIELD OF (STUDENT) STUDY

Biological sciences, including lab experience

INTERNSHIP LOCATION

University of Alberta Main Campus - Edmonton

NUMBER OF INTERNSHIP POSITIONS

1

INTERNSHIP START DATE

January 2, 2018
### INTERNSHIP END DATE

March 31, 2018 or 12 weeks after start date

### ARE THE DATES FLEXIBLE?

Yes