Hunter College of the City University of New York
Department of Biological Sciences
Fall 2023 Inga Richter Seminar Series

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Single-cell RNA-Seq provides new insights on immune evasion of the malaria parasite *Plasmodium falciparum*

The most severe form of malaria is caused by infection with the protozoan parasite Plasmodium falciparum. These organisms reside within red blood cells where they modify the host cell membrane through the placement of the variant antigen PfEMP1 on the cell surface, enabling adherence to the vascular endothelium and thereby avoiding splenic clearance. To evade immune recognition, *P. falciparum* can vary between isoforms of PfEMP1 in a process called antigenic variation. The different isoforms are encoded by the *var* multicopy gene family. *var* expression is thought to be mutually exclusive, ensuring the presentation of an individual PfEMP1 at any given time. The body of work so far, however, has analyzed populations of parasites, missing the contribution of individual parasites to the cumulative *var* expression.

Using parallel single cell RNA-seq approaches in combination with targeted-capture probes, we examined *var* gene expression in individual parasites. We discovered that contrary to standard models of monoallelic activation, *var* gene expression is much more heterogenous than previously thought. We observed that in addition to expressing a single *var* gene at a high level, individual parasites can instead co-express more than one *var* gene or display low level expression of many *var* genes. We hypothesize that these different expression states reflect the molecular mechanisms that underlie *var* gene switching and monoallelic choice. Our data also support the existence of immunologically silent parasites that are able to survive undetected and maintain chronic, asymptomatic infections. Furthermore, we showed that reduced methyl donor availability interferes with mutually exclusive expression, causing individual parasites to stably express several *var* genes at the same time.

Monday, Oct. 23, 2023 @12:30pm
Hunter North Room 926
Host: Jayne Raper