Komi Gbedande, PhD
Postdoctoral Researcher
Internal Medicine

Continuous Generation of Effector T cells with Mouse Cytomegalovirus Vaccination to Prolong Malaria Immunity

Dr. Gbedande is an immunologist with several years' research focusing on malaria. His academic and professional accomplishments begin with a BSc degree in Biochemistry and M.Sc degree in cell biology and immunology. Then he earned his PhD in Immunology from Paris Descartes University in France and conducted intensive research on pregnant women and neonatal immunology, with a particular focus on malaria in pregnancy and clinical development of a vaccine to prevent malaria during pregnancy. Presently, he is a postdoc researcher at the University of Texas Medical Branch, where he is conducting research on malaria immunology focusing on vaccinology aspects investigating immune mechanisms associated with protection. His current research project aims to investigate mechanisms of development of effective and long-lived T cell responses to malaria using *P. chabaudi* infection.

Abstract: Immunity to *Plasmodium* infection or vaccination is known to decay. In mouse models, this decay correlates with loss of malaria-specific T cells, not antibody. Whole parasite vaccines, such as "infection and drug cure", protect. However, sterile protection from *P. chabaudi* lasts less than 200 days. Effector (Teff) and effector memory (Tem) T cells can contribute to prolonged protection. We recently identified effector T cells making IFN-□ as the immune component likely responsible for the protection provided by persistent *P. chabaudi* infection. Therefore, we have reverse-engineered a vaccine strategy that first induces a long-lived protective antibody response with live parasite vaccination, and then boosts the IFN-γ $CD4^+$ Teff and Tem response to prolong protection. We chose CMV as it is an excellent T cell-inducing vaccine vector with early promise against SIV, tuberculosis and liver-stage malaria. Therefore, we used chronic vaccination with MCMV to test our hypothesis that promoting generation of Teff for longer would be protective if maintained over longer periods of time. We observed that mice with chronic MCMV infection have strongly reduced parasite growth upon *P. chabaudi* infection. Persistent MCMV infection also induces non-specific protection to *Leishmania* and gamma-herpesvirus, suggesting a useful adjuvant effect. To promote continuous induction of *P. chabaudi*-specific Teff/Tem, we expressed the *P. chabaudi* MSP-1 epitope B5 as an MCMV immediate

early gene (MCMV-B5). Upon infection of mice with MCMV-B5, adoptively transferred B5 TCR Tg T cells and MCMV-specific $CD4^+$ T cells proliferated and maintained over 2.5 months. Importantly, we found that MCMV promotes the highly-differentiated Teff and Tem phenotypes that we have previously shown to be protective. We found that a prime-boost strategy using the MCMV vector worked to prolong protection generated by the “infection and drug cure vaccine”. In investigating the mechanisms of protection, we found that IFN-γ induced by MCMV prolongs the protection, potentially through promotion of IL-12 producing. Our findings suggest that chronic vaccination can play an important role in malaria immunity to redress the problem of short-lived protection to malaria infection and vaccines, which is known to be due to decay of CD4 T cell memory.