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Interim Report
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2018 Queenan Fellowships for Global Health Investigator-Initiated Research Project Award

"Maternal Histoblood Group Antigen Genotype as a Predictor for Rotavirus Vaccine Response in Breastfed Infants in Bangladesh."

I am pleased to report that our investigations into genetically-determined breast milk contributions to infant rotavirus vaccine response are progressing well. Our primary outcomes have returned with intriguing results, prompting new lines of inquiry.

Through the last academic year (completed last month), I have been able to characterize the maternal secretor (*FUT2*) genotype of our vaccinated cohort, while our collaborators in Dhaka have completed secretor and Lewis (*FUT3*) phenotypic analysis of breast milk samples. Preliminary analysis reveals an association between maternal secretor status and infant vaccine seroconversion, consistent with our hypothesis; to our surprise, the association runs in the opposite direction of our prediction. Both phenotypic and genotypic analysis of maternal secretor status shows that infants of nonsecretor mothers had higher rates of seroconversion. In bivariate regression modeling, maternal status outweighs that of the infant in infant vaccine take. Analysis of maternal Lewis phenotype showed no effect on infant seroconversion. These findings have been submitted as conference abstracts and a manuscript is currently in the final stages of preparation, with goal of submission before the end of the month.

Our results have led us to reconsider the mechanisms by which maternal secretor antigen in breast milk may influence infant vaccine response. New hypotheses include the antigen preventing infectivity by serving as a decoy receptor for the vaccine virus or the maternal antigen modulating the infant gut microbiome, altering efficiency of vaccine virus infection. Collaborators are currently working on characterizing microbiome data from our vaccinated cohort, which will allow us to describe the relationship between maternal secretor status and infant microbiota. Questions have also been opened regarding maternal secretor status on naturally occurring rotavirus infection, leading to our current project of genotyping 155 mothers of non-vaccinated infants to correlate their secretor status with infant diarrheal outcomes. Importantly, our findings have continued to unearth potential mechanisms for disparities in rotavirus vaccine response in Bangladesh.

In addition to research questions I have been able to address, the Queenan Fellowship has empowered me to develop wet lab skills in DNA extraction and polymerase chain reaction amplification, as well as building a growing foundation for sequence analysis. I was invited to present my findings at the University of Vermont's Translational Global Infectious Disease Center's Annual Meeting, and received direct feedback from the Center's External Advisory Board as a potential future candidate for funding. I am grateful for the support by the Queenan Fellowship for Global Health from the Foundation for SMFM.