Project Title: **Relationship of proteomic profiles of anogenital secretions of P5 recipients with mucosal HIV envelope-specific antibody responses**

Preferred Scholar On-Site Project Dates: Long-Term Project, on site between September 2024-May 2025.

Project Site: Rochester, New York (University of Rochester)

Project Overview: Antibody intrinsic features (e.g. specificity, Fc) alone may not regulate their protective potential. Soluble factors in anogenital secretions likely directly and indirectly impact the protective activity of mucosal antibodies. We propose a retrospective analysis with the goal of identifying novel innate factors in the mucosal environment that impact local adaptive humoral immunity through the comprehensive proteomic profiling of this compartment.

Project Summary: The global epidemic of HIV continues to pose a major world health threat with more than 1.5 million new infections diagnosed in 2021. Although significant efforts have been underway for more than 30 years to develop a vaccine to prevent HIV infection, to date, only one trial has shown any significant efficacy at infection prevention. Here we propose a retrospective analysis with the goal of identifying novel innate factors in the mucosal environment that impact local adaptive humoral immunity through the comprehensive proteomic profiling of this compartment. This work is a part of previously accepted concept proposal. Specifically, we will perform untargeted proteomics and microbiomics on cervical secretion samples from HVTN 100 Part B and HVTN 111. We will then determine mucosal milieu defined by signatures of proteomics and micobiomics and evaluate their association with serum envelop specific antibody response.

RAMP scholar involvement: The RAMP scholar will be involved in the lab work, data analysis, community activities and clinical shadowing. We anticipate the scholar will spend 70% times learning lab assays, programming and performing analysis. The 30% of efforts will be spent in community and clinical shadowing activities. The scholar will work closely with physician-scientist post-doctoral fellow in the Thakar lab who is working with Rochester CTU. The post-doctoral fellow is performing data analysis/bioinformatics/ systems biology research and clinical work. Thus shadowing her will provide an exposure to the scholar on how to perform data intensive clinical research.

Regulatory requirements for the project and plans for completing them: This concept has already been approved by the HVTN and has been reviewed by the University of Rochester Medical center review board (IRB).

Expected Deliverables:

1. Identification of proteomic signatures correlated with HIV vaccine specific antibody response
2. Proteomic and micriobiome profiling of weck-cel rectal secretion samples collected

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