Harnessing Human Milk B Cells for Antibody-Based Strategies to Combat Bacterial Pathogens

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The misuse of antibiotics has led to a critical antibiotic resistance crisis. Consequently, there is an urgent need for new approaches for precise diagnostics and treatment of bacterial infections. B cells in human milk originates from gut-associated lymphoid tissues (GALT) thus, they are primed against bacterial pathogens. This B cell population may further be supplemented by B cells that are *in-situ* activated by bacteria introduced by retrograde flow from infant's oral cavity. Regardless of B cell origin, I hypothesize that they can serve as a valuable source for the development of anti-bacterial monoclonal antibody (mAb) screening platform.

Here, I propose to characterize the interactions between the infants' oral cavity microbiota and human milk B cells and demonstrate that retrograde induces *in-situ* human milk B cell response. Additionally, I propose to develop a unique yeast surface display (YSD) library based on human milk B cells and integrate next-generation sequencing for library characterization and mAbs discovery enhancement. To this end, I have established an ethical approval where paired human milk and infant saliva samples will be collected. I have also demonstrated the validity of a unique library design using a single chain variable fragment (scFv) model system. Moreover, I designed and applied a primer-set for the amplification of the variable regions of the human milk B cells antibody heavy and light chains to be used for library construction. Overall, achieving the aims will both open new research avenues and provide a screening platform with enhanced potential for the discovery of anti-bacterial mAbs.