Systems biology to identify biomarkers of vaccine immune responses in newborns

More than 2 million infants die every year from infections, particularly in resource-poor settings. Moreover, due to distinct immunity compared to adults, neonates (newborns) are less able to mount protective immune responses following vaccination. Improvement of neonatal immunization, thus requires a better biological understanding of vaccine-induced immune responses that correspond to protection, which is difficult due to scarcity of vaccine-related research in neonates. This project proposes an innovative systems biological investigation to better understand vaccine-induced immunity in neonates. Novel advanced statistical and computational approaches will be used to analyze very large and unbiased datasets of molecular and cellular information measured from small samples of blood obtained from 720 neonates undergoing immunization with hepatitis B vaccine (HBV), given with or without the Bacille Calmette-Guérin (BCG) vaccine. The molecular datasets consist of precise measurements of tens of thousands of gene expression read-outs (gene transcripts [RNA] and proteins), generated using state-of-the-art methods and instruments, such as next generation sequencing (RNA-Seq) and mass spectrometry. Molecular response signatures and biomarker classifiers that predict subsequent immunogenicity, especially measurable signatures of immunity against infection (correlates of protection (CoP)), will be identified. Innovative bioinformatics-based and data-driven biomarker integration approaches will reveal patterns of gene expression, bionetworks, molecular pathways and biomarker classifiers associated with successful immunization, and/or sub-optimal immunogenicity. The knowledge gained from this project will provide fresh insights to improving current immunization protocols for neonates adopted by health organizations across the world.

The main objective of this research project is to identify blood transcriptomic and plasma proteomic signatures and biomarkers in human neonates that correlate with effective immunization, using pre- and post-vaccine whole blood RNA-Seq datasets. In this first phase of the study we aim to develop efficient visualization tools to better explore the high dimensional dataset available. In addition, we aim to use statistical and computational approaches to allow biomarker integration across the transcriptomic and proteomic datasets.