

## **“Long-term DENV immunity in a human cohort”**

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Dengue virus (DENV) is the most important words). insect-borne viral pathogen of humans worldwide and a significant threat to global public health, with ~1/3 of the world's population at risk of DENV infection. There are four serotypes, DENV-1 through DENV-4. First infection with one induces short-term cross-protective immunity that wanes to a long-term serotype-specific immunity. Subsequent second infection with a different serotype confers broader immunity but also carries an increased risk of severe dengue disease - dengue hemorrhagic fever. Neither DENV vaccine nor antivirals are available to protect against DENV infection. To design effective dengue vaccines, the determinants of long-term serotype-specific protection, which are as yet unknown, must be defined. Despite this knowledge deficit, there have been no comprehensive studies of long-term DENV immunity in human cohorts, nor is there a central DENV immune sera or cell repository required to identify the critical determinants of long-term DENV immunity. To address this deficit, over the next year (July 1/2014-June 30/2015) we propose to: 1) recruit a cohort of local DENV immune individuals with the intent to 2) use cohort sera and immune cells to characterize the determinants and correlates of natural long-term DENV immunity in humans. This cohort will enable us to prospectively study DENV immunity over time, including developing a human dengue challenge model, and will serve as a reference repository for samples and data to be utilized by OHSU researchers and the larger DENV research community, providing high value correlates of DENV immunity, leading to more effective development of DENV vaccines.