Timely Topics
In HIV Vaccines

Global HIV Vaccine Enterprise

Avenues for Further Exploration in Developing Durable Antibodies to HIV

Outcome of Antibody Durability Think Tank – 23 September 2013

At a think tank on Antibody Durability in HIV Vaccine Development organized by the Global HIV Vaccine Enterprise and held on 23 September 2013, participants agreed that the areas below are important steps to defining, understanding and addressing the challenges to developing a durable, protective HIV vaccine. An important piece of the discussion was also the need to endorse a definition of vaccine durability that allows direct comparison of HIV Env with other licensed or experimental vaccines, and emphasizes the most important features needed for long-term protection. In addition, the need to identify epitopes able to elicit high affinity antibodies against these epitopes and overcome the problem of virus variation (drift viruses), underlies all efforts to generate or improve the quality and durability of any HIV vaccine.

1. **Is HIV Env unique or similar to comparable immunogens used in successful vaccines?** Understanding if vaccine induced antibody responses to HIV-1 Env are of shorter duration than antibody responses to other licensed or experimental vaccine immunogens is critical. Such an analysis will reveal whether the problem is specific to HIV Env or general to vaccines targeting other viral glycoproteins. A head-to-head trial in NHP using trimeric Env and other comparable viral glycoproteins, like influenza HA or rabies virus glycoprotein, using different adjuvants and alternate dosing schedules and boosts would allow a proper evaluation of the magnitude, functionality, isotype, and decay rates after immunization. Boosting could give insights into whether the peak and plateau values can be re-set, as has been observed with certain other vaccines.
2. **Do different antibody populations have the same durability?** Perform longitudinal studies on antibody qualities and functions (isotype, subtype, neutralizing activity, ADCC, binding titer) during durability studies to show whether discrete populations of serum or mucosal antibodies decay with the same rates.
3. **What is the relationship of peak and plateau antibody levels?** Explore rigorously the relationship between peak and plateau antibody levels, comparing binding versus neutralizing antibody titers and including the expanded panel of tests for isotype, subtype, ADCC, etc.
4. **Can durability of antibody responses be modulated by the timing/spacing of prime boost doses?**
5. **Are there biomarkers of durable antibody responses?** Create a systematic effort to develop biomarkers of durable antibody responses that can be evaluated during the initial months of immunization.
6. Incorporate tools of systems biology, phenotyping studies, antibody characterization and peak to plateau measurements.
7. Incorporate studies of B and T cell memory and of potential T follicular helper T cells and/or their precursors for efforts to correlate phenotype with function during the development of surrogate markers.
8. **What is the role of long-lived plasma cells?** Characterize the impact of long-lived plasma cells on durability ofantibody responses to HIV Env and to a comparator viral glycoprotein antigen.
9. **Comparing durability studies in NHP and humans**. Studies in NHPs should also assess cells from secondary lymphoid tissues and bone marrow in parallel with blood to allow bridging to data obtainable in human volunteers. Strive to utilize common reagents and assays for comparative studies of vaccine durability done in NHP or man.