IDA Highlight: What's New in anti-HIV humoral immunity.

Humoral immunity is one of the most studied aspects of anti-HIV immunity. This year IDA Symposium faculty members gave talks on various aspects of anti-HIV humoral immunity.

Richard Koup, from the National Instittute of Health, USA, began his talk highlighting why we currently don't have an HIV vaccine. He showed that HIV is heavily glycosylated compared to Influenza and respiratory syncytial virus (RSV), and influenza of which we have a vaccine for. He highlighted that VRC scientists have managed to identify conserved bNAb epitope called fusion peptide. They also isolated atypical bNAb called VRC34 which targets this highly conserved fusion peptide epitope. He further outlined that the VRC has done some NHP vaccinations with the fusion peptide immunogen and boosted with an HIV trimer, and this led to the elicitation of broad antibody responses in 4/5 NHPs tested. This brings optimism to the HIV vaccine field. Furthermore, the VRC is also perusing other avenues such as Lineage based vaccine strategy, whereby they are studying the development of bNAbs in a select individuals who develop these special antibodies. Through this approach they hope to identify the immunogens to use in vaccination that will elicit bNAbs.

The constant region of the Ab also known as the FC plays an important role in directing cellular mediate humoral immunity. Two faculty members Tony Moody (Duke University) and Simone Richardson (NICD, University of Witwatersrand, former IDA

scholar) gave talks on their research on humoral immunity. **Tony Moody**'s talk "**FcR Diversity–It's not just single polymorphisms anymore**", gave an overview of some of the factors that contribute to Ab-mediated protection against HIV-1, such as Fc-gamma receptor alleles, alternative splice variation and expression level. He also highlighted that there are many difference between rhesus macaque and human Fc-gamma receptors. Therefore, determining if any newly observed human and rhesus macaque Fc-gamma receptor alleles are functionally significant will be critical for bridging antibody mediated effector function across species. His take home message was that the Fc-gamma receptor biology is more complicated than single nucleotide polymorphisms.

Well know HIV associated Fc effector functions include Ab-dependent enhancement of infection, Ab-dependent cellular phagocytosis (ADCP) and Ab-dependent cellular cytotoxicity (ADCC). Ab-depedent trogocytosis is new in HIV. Trogocytosis is a process whereby lymphocytes conjugated to antigen-presenting cells extract surface molecules from these cells and express them on their own surface. Simone Richardson, presented some of her research findings in talk titled "**Simone Richardson –New Fc effector functions in vaccination (HIV)**". During her talk she showed showed that HIV tragocytosis is associated with IgG3, and is an area worth exploring.

Lastly talk by IDA Scholar, **Holly Spencer (University of Witwatersrand)** gave a talk on **"Functional Impact Of Ighg3 Genetic Variation In HIV-1 Infection."** She showed that IgG3 are polymorphic and polyfunctional Abs that play a critical role in infectious diseases clearance. Her research aimed at identifying genetic diversity in IgHG3 genes in Zulu speaking South African individuals and to functionally characterize IgG3 Abs, linking genetic diversity to functional diversity. During this study the research group identified 6 novel IgHG3 alleles (that were not in any database) in Zulu speaking south African individual using a novel PCR protocol. This indicate

that, the Southern African population are under represented in current databases. In future they will functionally characterise these novel mutants and the documented IgHG3 alleles linking genetic diversity with functional diversity in IgG3 Abs, which could potentially contribute to the arsenal of therapeutic Abs we have available.

Article by Abel Lissom, Tsegaye Yosef and Yanga Mdleleni