COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

Potential Vaccine Correlates Of Protection: Evaluation Of B Cell And T Cell Receptors Generated Using Different Vaccine Platforms.

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The immune system responds to and produces immune memory that can recognize a plethora of different pathogens. Immune memory functions through B cells (antibodies) and T cells (cell meditated) responses. These cells utilize highly diverse B cell and T cell receptors that can recognize foreign pathogen antigens and epitopes. The receptors are composed of two chains that undergo gene segment rearrangement, junctional diversity and in the case of B cells, hypersomatic mutation. This process can generate up to 1015 unique receptors depending on the immune cell type, which vastly outnumbers the number of cells possible in a single individual. We investigated the B and T cell receptor diversity after vaccination to determine if it correlates with protection from challenge. Through the RAPTER consortium, mice were vaccinated with the glycoprotein from Ebola virus and the Hcp1 and CPS antigens from Burkholderia pseudomallei (melioidosis). We received spleen RNA samples from mice vaccinated with the different vaccine platforms and generated T cell receptor (TCR) and B cell receptor (BCR) libraries and sequences. Common receptor allotypes were compared between the vaccinated mice within a platform or between platforms. Similar receptor allotypes generated during vaccination were also identified using receptor clustering approaches (TCRdist and CoNGA). Using this data, diversity estimates were determined for each vaccine and compared. These diversity estimates will be compared to mouse survival after challenge with the goal of identifying correlates of protection. These data will further be used by the RAPTER consortium to predict the preferable vaccine planform for different viral and bacterial infectious diseases.

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