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Biomarker discovery using monoclonal VLR antibodies of the evolutionarily distinct sea lamprey

Monoclonal antibodies are widely used reagents in biomedical research as well as in clinical applications. However, tolerogenic and structural constraints limit the antibody repertoire. In contrast to conventional antibodies, the recently identified variable lymphocyte receptor (VLR) antibodies of the evolutionarily distant jawless vertebrates utilize the **β**-sheet forming leucine-rich repeat (LRR) as basic structural unit. We hypothesize that the unique origins and radically distinct protein architecture will allow VLR antibodies to bind antigens, which conventional antibodies cannot readily recognize for tolerogenic or structural constraints. Memory B cells (Bmem) and plasma cells (PC) are tasked with providing long lasting humoral protection to re-encountered pathogens. However, no conventional antibodies exist that specifically detect these cell populations. In an effort to identify novel biomarkers uniquely expressed on Bmem and PC, we developed a method to generate monoclonal VLR antibodies to cell surface antigens. We isolated panels of monoclonal VLR antibodies binding specifically to human Bmem and PC. Flow cytometric analysis of VLR antibody binding to cell lines and primary human cells from blood, tonsil, spleen and bone marrow revealed binding patterns that are inconsistent with those of any conventional antibody, suggesting that the monoclonal VLR antibodies recognize novel antigens. Interestingly, we observed greatly increased VLR antibody binding to memory B cell populations in blood of individuals diagnosed with the autoimmune disorders Systemic Lupus Erythematosus (SLE) and Multiple Sclerosis (MS). Our data indicate that monoclonal VLR antibodies hold promise as novel reagents with a wide range of application potential in basic and clinical research.

Speaker Biography

Goetz RA Ehrhardt has completed his PhD at the University of British Columbia and continued his training as Post-doctoral fellow in the laboratory of Dr. Max D Cooper at Emory University in Atlanta, GA. In 2011, he was recruited to the Department of Immunology at the University of Toronto. His laboratory focuses on mechanisms governing the regulation of human memory B cell responses and on the use of the non-conventional VLR antibody system of jawless vertebrates for biomarker discovery purposes.

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