Human mast cell response to nanosurfaces: Balancing innate and adaptive immunity

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Located at mucosal surfaces and surrounding blood vessels and nerves, human mast cells are uniquely situated to regulate the function of the vasculature, to initiate the recruitment and activation of leukocytes into tissues and to trigger physiological responses that are mediated by the nervous system. Mast cells are primarily responsible for the acute allergic response to allergen exposure, including bronchoconstriction and edema. Mast cells and immunoglobulin E (IgE) are also felt to be important in the evolution of allergic late phase responses, which are largely responsible for the pathogenesis of chronic allergic diseases such as asthma, atopic dermatitis and rhinitis. Our recent research has shown that human mast cells respond to a vast array of proteins, each of which activates a unique signaling pathway through specific surface receptors. Our laboratory is interested in modulating human mast cell function using proteins, lipid nanoparticles and silver oxysalt nanofibers with the goal of producing hypoallergenic nanosurfaces. In one of our projects, we have focused on complement and specific complement protein receptors. The anaphylatoxin C5a regulates diverse innate and adaptive immune responses by chemoattracting and activating immune cells, such as mast cells (MC). It is postulated that C5a regulates human MC function by activating a G protein-coupled receptor (GPCR) However, C5a can bind to C5aR, a G protein-coupled receptor, or C5L2, not coupled to G proteins and thought to activate distinct signaling cascades. The presence and role of C5L2 in human MC remain unknown. Using a human mast cell model that expresses C5L2 but not C5aR, we have shown that C5L2 is a functional receptor, capable of modulating specific mast cell responses. C5a activates LAD2 cytokine and chemokine production and initiates adhesion and migration by human mast cells. Our research suggests that functionalizing surfaces with specific proteins may be an effective way of modulating human mast cell responses and regulating allergic inflammation.

Speaker Biography

Marianna Kulka is currently a Group Leader and Project Leader at the National Institute for Nanotechnology located at the University of Alberta, Edmonton, Canada. She is also an Adjunct Professor in the Department of Medical Microbiology and Immunology at the University of Alberta. Currently, she is investigating the role of G protein-coupled receptors in inflammatory disease and mast cell activation pathways. Her focus is on activation pathways of human mast cells and their regulation of human inflammatory diseases. Her work aims to use novel nano-packaging strategies to manipulate these pathways. She has published numerous articles in peer-reviewed journals and serves on several review panels, including national and international granting agencies.

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