Deciphering HoxA9 function in multipotential progenitor biology and B cell development

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Common Variable Immunodeficiency (CVID) is a primary immunodeficiency disease characterized by low serum immunoglobulin, impaired antibody responses, and recurrent bacterial infections. Furthermore, many CVID patients develop autoimmune disease and malignancies. Together, these immune sequelae suggest that a subset of patients harbor genetic perturbations that impact innate and humoral immune function. Dendritic cells (DCs) play an essential role in bridging the innate and adaptive immune responses. Importantly, these cells play an important role in the maturation, differentiation, survival, and immune function of peripheral B, T, and NK cells. A subset of CVID patients exhibit DC deficiencies and impaired DC function has been linked to the pathophysiology of the disease. The Flt3 signaling pathway is critical in DC biology. Therefore, alterations in serum levels of Flt3-ligand and surface expression of the Flt3 receptor on residual DCs were evaluated to determine if defects in the Flt3 signaling pathway represent a novel genetic variable and possible prognostic indicator for impaired immunity in some CVID patients. Variations in serum FL were documented but did not segregate patients with DC deficiencies. However, patients with increased serum FL had increased incidence of autoimmune cytopenias, autoimmune disease, and malignancies, and DCs are known to play a critical role in the detection of neoplastic lesions and maintenance of peripheral tolerance. The identification of underlying genetic causes or contributors to the pathophysiology of CVID is critical for accurate diagnosis and design of treatment strategies, particularly stem cell transplantation. Therefore, identifying defects in the Flt3 signaling pathway as the basis of the DC defect will aid in disease diagnosis and management.

Biography

Kay L Medina completed her PhD at the University of Oklahoma Health Sciences Center and post-doctoral training at the University of Chicago as a Fellow of the Irvington Institute for Immunological Research. In 2005, Dr. Medina joined the Department of Immunology at the Mayo Clinic College of Medicine where she is currently an Associate Professor. She has over 60 peer reviewed journal publications and currently serves as Associate Editor for the Journal of Immunology and Frontiers in B Cell Biology. Dr. Medina’s research is focused on the generation and function of B lymphocytes in health and disease.