Role of lipocalin 2, an innate immune protein, during immune-complex mediated inflammation

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Abstract

Lipocalin-2 (Lcn2), an innate immune protein, predominantly secreted by neutrophils is upregulated by several logs during inflammatory conditions including autoimmune diseases. However, the defined role of Lcn2 in autoimmune diseases is largely unknown. We investigated the role of Lcn2 in an acute model IC-mediated inflammation using Lcn2 knock out (Lcn2KO) and their wild type (WT) littermates. In an acute skin inflammation model, Lcn2KO mice demonstrated a 50% reduction in inflammation as evidenced by histopathological analysis which revealed strikingly reduced immune cell infiltration compared to WT mice. Administration of recombinant Lcn2 to Lcn2KO mice restored inflammation to levels observed in WT mice. Neutralization of Lcn2 using a monoclonal antibody significantly reduced inflammation in WT mice. In contrast, Lcn2KO mice developed more severe serum-induced arthritis compared to WT mice. Histological analysis revealed extensive tissue and bone destruction with significantly reduced neutrophil infiltration but considerably more macrophage migration in Lcn2KO mice when compared to WT. Moreover, we also observed a 16 fold increase of Lcn2 upregulation in lupus prone chronic autoimmune disease mice. Collectively, our studies demonstrate that targeting Lcn2 may be a promising approach for treating autoimmune inflammatory disorders.

Biography

Shashidharamurthy has completed his Ph.D from University of Mysore, Karnataka, India and postdoctoral studies from Vanderbilt and Emory University. He is Assistant Professor of Department of Pharmaceutical Sciences, PCOM-School of Pharmacy, Georgia campus. He has published more than 28 papers in peer reviewed journals and also serving as an external reviewer for many of the international peer reviewed journals. Dr. Shashidharamurthy research interest is in investigating the pathogenesis of chronic autoimmune/inflammatory disorders such as vasculitis and arthritis.