OMICS Group Conferences
Accelerating Scientific Discovery

International Conference on
Clinical & Cellular Immunology

October 22-24, 2012 DoubleTree by Hilton Chicago-Northshore, USA

Modulation of immune-mediated inflammation by cationic innate defence regulator peptides

Neeloffer Mookherjee
University of Manitoba, Canada

Immune-mediated chronic inflammatory diseases include rheumatoid arthritis (RA) and inflammatory bowel disease. Many therapies for these diseases compromise efficient immune function resulting in increased risk of infections and neoplasms. We have previously demonstrated that cationic host defence (antimicrobial) peptides, and their synthetic derivatives known as innate defence regulator (IDR) peptides, can selectively suppress pathogen-induced inflammation without compromising immune responses required for resolution of infections. In this study we investigated the potential of IDR-peptides in immune-mediated 'sterile' inflammation using RA as a disease model.

We have demonstrated that cathelicidin-derived IDR-peptides can significantly suppress inflammatory cytokines e.g. TNF, IL-1 and IL-6, and enzymes e.g. MMP-3 that mediate cartilage and bone destruction, in synovial fibroblasts (critical cell type in inflammatory arthritis). In contrast, IDR-peptides enhance anti-inflammatory proteins e.g. IL-RA, while differentially modulating chemokine responses required for resolution of infections. Quantitative proteomic analysis and computational interrogation of immunity-related proteins demonstrated that several members of the inflammatory NF-B and MAPK pathways are altered by IDR-peptides. Using various immunochemical assays we showed that the IDR-peptides interfere with the activation of NF-B/Rel family of transcription factors and signaling pathways e.g. MAPK ERK1/2 and JNK, in synovial fibroblasts isolated from patients with inflammatory arthritis ex-vivo. We further examined the impact these peptides in a murine model of collagen-induced arthritis, and established their ability to prevent inflammatory arthritis in-vivo. Overall, our results suggest that IDR-peptides may be valuable in controlling the destructive effects of inflammatory arthritis without abrogating immune functions required for resolution of infections.

Biography

Neeloffer Mookherjee completed her Ph.D from University of Victoria, Canada, and postdoctoral training at Vaccine & Infectious Diseases Org, and University of British Columbia, Canada. Mookherjee is Assistant Professor, Departments of Internal Medicine & Immunology, at the University of Manitoba, Canada. Her research is aimed at understanding the underlying molecular mechanisms of chronic inflammatory and autoimmune diseases, and investigating the impact of cationic host defence (antimicrobial) peptides in immune-mediated inflammation. She is also involved in a collaborative initiative focused on innate immunity & vitamin D-host defence peptide axis. She has published more than 25 papers and book chapters.

mookherj@cc.umanitoba.ca