Role of gut microbiota dysbiosis and metabolic endotoxemia in pathogenic mechanisms of Rheumatoid Arthritis (RA)

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RA is an autoimmune disease manifested by chronic inflammation of synovial joints that leads to bone and cartilage damage, systemic complications, and disability. RA affects approximately 0.5% to 1% of the population worldwide. Epidemiological studies show that RA has a complex genetic background. The heritability of RA is estimated to be about 60%. A strong association between certain human leukocyte antigens (HLAs) and predisposition to RA was shown in multiple studies. However, genetic factors are not alone in determining the risk and outcomes of RA development. It was demonstrated that environmental and lifestyle-related factors such as microbial burden and diet may also contribute to RA susceptibility in genetically predisposed individuals. Emerging evidence suggests the existence of a relationship between changes in gut microbiota and development of RA, although the precise role of microbial dysbiosis in the pathogenic mechanisms of RA is still to be fully defined. The autoimmune nature of RA is confirmed by the presence of anti-citrullinated protein antibodies (ACPA) and autoantigen-specific CD4+ T cells in RA patients. Mounting experimental and clinical evidence also suggest a key role of synovial macrophages (Mϕ in joint health and disease. In healthy joints, synovial M exhibit relatively quiescent M2 phenotype characterized by anti-inflammatory properties. In RA, inflammatory M are reprogrammed into M1 phenotype and serve as the major source of pro-inflammatory cytokines and other mediators implemented into synovial tissue inflammation, bone erosion, and ultimate destruction of joints. In our search for environmental triggers involved in early development of autoimmune diseases, we identified gut-derived endotoxin as a putative causative factor in the onset of RA. Here, we will review the emerging clinical and experimental evidence suggesting an important role of gut microbiota and metabolic endotoxemia in modulation of M1/M2 phenotypic responses of synovial M relevant to the pathogenic mechanisms of RA.

Speaker Biography

Alex Shnyra (born January 05, 1956) received his Doctor of Medicine in 1979 and Doctor of Philosophy in 1985 at Moscow, Russia. Dr. Shnyra was a senior scientist at All-Union Cardiology Research Center at Moscow, a visiting scientist at Dept. of Clinical Bacteriology, Karolinska Institute, Stockholm, Sweden, and he hold Faculty Positions at several medical schools in the U.A.E. and U.S.A. Since 2007, he is an Associate Professor of immunology at Kansas City University of Medicine and Biosciences. Dr. Shnyra is an expert immunologist with extensive experience in cell biology, immunology, molecular biology and biochemistry. He has developed several funded research projects in Russia, Sweden, and UAE and at NIH, USA. Dr. Shnyra is a receiver of International and Nationals awards and honors. His research is cited in more than 800 scientific publications. His current research is focused on the link between autoimmune diseases and the gastrointestinal microbiome..

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