Mucosal Autoimmunity in Rheumatoid Arthritis: Intestinal Microbial Dysbiosis

Authors: Austin Pan MS4[1], M. Kristen Demoruelle MD[1]

1: School of Medicine, University of Colorado, Aurora, CO, USA

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and in most cases, serum elevations of autoantibodies such as rheumatoid factor and anti-cyclic citrullinated peptide. Though inflammatory arthritis manifests in the clinical phase of RA, data suggests that production of autoantibodies occurs in mucosal sites before the clinical phase. One potential mucosal site linked to other systemic autoimmune diseases is the gut, with recent research suggesting gut microbiota are involved in autoimmune disease. This project aims to review and summarize findings on the relationship between gut microbiota and rheumatoid arthritis.

Methods: A comprehensive literature review was conducted using articles found on PubMed and Google Scholar. The inclusion criteria focused on studies that looked at dysbiosis in gut microbiota in rheumatoid arthritis patients, both in humans and mouse models, including studies that observed changes in gut microbiota as well as ones that attempted to explain possible mechanisms of pathogenesis. Clinical trials, qualitative and quantitative studies, and other reviews were included.

Results: The vast majority of literature suggests that the gut microbiota between rheumatoid arthritis patients and healthy patients are significantly different. Different studies highlighted different bacterial species as notable differences in rheumatoid arthritis, with *Prevotella copri*

and *Subdoligranulum* emerging as two potential arithrogenic bacterial species. Other studies noted differences in bacterial metabolites, particularly butyrate and tryptophan, and linked these metabolites to inflammation-modulating effects in the gut, providing another possible mechanism of pathogenesis.

Discussion: The findings from this review demonstrate that the gut microbiota likely plays an important role in the pathogenesis of rheumatoid arthritis, whether through direct activation of the immune system by the bacteria itself, or through changes in bacterial metabolites. Further research into this field, as well as how other mucosal sites are involved in rheumatoid arthritis, is necessary and could potentially uncover more mechanisms of pathogenesis. These could represent targets for medications that prevent rheumatoid arthritis from even progressing to a clinical stage, rather than current treatment regimens that are used after inflammation has occurred. It could also identify more specific risk markers that help predict which patients will develop rheumatoid arthritis.