## Characterization of the Blood Microbiome in Rheumatoid Arthritis Patients Compared to Healthy Control Subjects Using V4 Region 16S rRNA Sequencing

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Abstract: Rheumatoid arthritis (RA) is a disabling and common autoimmune disease during which the body's immune system attacks healthy tissues. This results in complicated and long-lasting actions being carried out by the immune system, which typically only occurs when the immune system encounters a foreign object. In the case of RA, the disease affects millions of people and causes joint inflammation, ultimately leading to the destruction of cartilage and bone. Interestingly, the disease mechanism still remains unclear. It is likely that RA occurs as a result of a complex interplay of genetic and environmental factors including an imbalance in the microorganism population inside our body. The human microbiome or microbiota is an extensive community of microorganisms in and on the bodies of animals, which comprises bacteria, fungi, viruses, and protozoa. Recently, the development of molecular techniques to characterize entire bacterial communities has renewed interest in the involvement of the microbiome in the development and progression of RA. We believe that an imbalance in some of the specific bacterial species in the gut, mouth and other sites may lead to atopobiosis; the translocation of these organisms into the blood, and that this may lead to changes in immune system status. The aim of this study was, therefore, to characterize the microbiome of RA serum samples in comparison to healthy control subjects using 16S rRNA gene amplification and sequencing. Serum samples were obtained from healthy control volunteers and from patients with RA both prior to, and following treatment. The bacterial community present in each sample was identified utilizing V4 region 16S rRNA amplification and sequencing. Bacterial identification, to the lowest taxonomic rank, was performed using a range of bioinformatics tools. Significantly, the proportions of the Lachnospiraceae, Ruminococcaceae, and Halmonadaceae families were significantly increased in the serum of RA patients compared with healthy control serum. Furthermore, the abundance of Bacteroides and Lachnospiraceae nk4a136 group, Lachnospiraceae UGC-001, RuminococcaceaeUCG-014, Rumnococcus-1, and Shewanella was also raised in the serum of RA patients relative to healthy control serum. These data support the notion of a blood microbiome and reveal RA-associated changes that may have significant implications for biomarker development and may present much-needed opportunities for novel therapeutic development.

Keywords: blood microbiome, gut and oral bacteria, Rheumatoid arthritis, 16S rRNA gene sequencing

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