SCHOLARLY PUBLICATIONS
Kalinga Institute of Dental Sciences
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Journal Name: Rheumatology **IF: 5.5**

Title: 16s RNA-based metagenomics reveal previously unreported gut microbiota associated with reactive arthritis and undifferentiated peripheral spondyloarthritis

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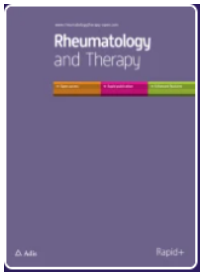
Details: 2024 MAR 15

Abstract: Objectives Reactive arthritis (ReA) provides a unique opportunity to comprehend how a mucosal infection leads to inflammatory arthritis at a distant site without the apparent invasion of the pathogen. Unfortunately, conventional stool cultures after ReA provide limited information, and there is a dearth of metagenomic studies in ReA. The objective of this study was to identify gut microbiota associated with the development of ReA.Methods Patients with ReA or undifferentiated peripheral spondyloarthritis (UpSpA) were included if they presented within 4 weeks of the onset of the current episode of arthritis. Metagenomic DNA was extracted from the stools of these patients and of 36 age- and sex-similar controls. Sequencing and analysis were done using a standard 16S ribosomal pipeline.Results Of 55 patients, there was no difference between the gut microbiota of postdiarrheal ReA (n = 20) and of upSpA (n = 35). Comparing the gut microbiota of patients vs healthy controls, the patients had significantly higher alpha and beta diversity measures. After stringency filters, Proteobacteria had high abundance while Firmicutes had lesser as compared with the controls. Six families were overexpressed in patients, while another five were overexpressed in controls. Sixteen genera and 18 species were significantly different between patients and controls. At the species level there was strong association of Staphylococcus aureus, Clostridium septicum Klebsiella pneumoniae, Escherichia coli, Empedobacter brevis, Roseburia hominis, Bacillus velezensis and Crassaminicella with ReA.Conclusion The microbiota of classical gut-associated ReA and upSpA is similar. Patients have higher diversities in their gut microbiota compared with healthy controls. Both known and previously unreported species associated with ReA/upSpA were identified.



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