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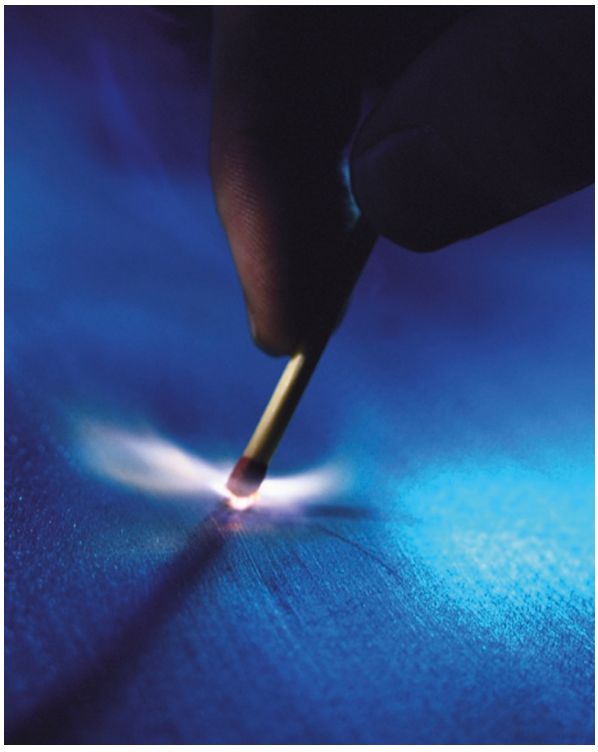
MICROBIOME

Pro-inflammatory *Prevotella*?

> *P. copri* thrives in a pro-inflammatory environment and might even increase inflammation

Changes in the gut microbiota have been linked to the development of autoimmune diseases but causality is difficult to prove. A study now identifies a potential role for the intestinal bacterium *Prevotella copri* in the pathogenesis of rheumatoid arthritis, which is one of the most common autoimmune diseases.

Rheumatoid arthritis is characterized by joint inflammation, and arthritis animal models have indicated that the gut microbiota can trigger this inflammation in the context of pre-existing autoimmunity. To investigate the role of gut microbiota in disease development, Scher *et al.* used 16S rRNA sequencing to analyse the faecal microbiota of untreated patients who had new-onset rheumatoid arthritis (NORA) and compared these data with sequencing data from patients who had chronic, treated disease and healthy subjects. Compared with the other groups, patients with NORA had an overabundance of *Prevotella* spp., whereas the abundance of other bacteria that are thought to be important for the maintenance of intestinal homeostasis (such as *Bacteroides* and cluster XIV Clostridia) was reduced.



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Further analysis indicated that *Prevotella* OTU4 was the most prevalent taxon in patients with NORA, and whole-genome sequencing identified *Prevotella* OTU4 as *P. copri*. Interestingly, the NORA-associated *P. copri* genomes contained several ORFs that were observed far less often in previously sequenced *P. copri* genomes from healthy individuals; two of these ORFs encode components of an iron transporter, which is a known virulence factor in other bacteria. Furthermore, unlike bacteria that dominate the healthy microbiota (such as *Bacteroides*), *P. copri* encodes a superoxide reductase and a phosphoadenosine phosphosulphate reductase. These two genes might favour the development and maintenance of intestinal inflammation by increasing *P. copri* resistance to host-derived reactive oxygen species and by producing the redox protein thioredoxin, which has been previously described as a pathogenic factor in rheumatoid arthritis. A colitis mouse model further supported the pro-inflammatory role of *P. copri*: mice that were colonized with *P. copri* showed increased epithelial inflammation and weight loss compared with mice that were colonized with the commensal *Bacteroides thetaiotaomicron*.

Together, these data suggest that *P. copri* thrives in a pro-inflammatory environment and might even increase inflammation for its own advantage, but more work is needed to determine whether *P. copri* causally contributes to the development of rheumatoid arthritis. Interestingly, patients with NORA who lacked known risk alleles for rheumatoid arthritis had a higher relative abundance of *P. copri* than those who had these genes, which could indicate that fewer bacteria are sufficient to trigger disease in individuals who have a genetic risk.

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ORIGINAL RESEARCH PAPER Scher, J. U. *et al.* Expansion of intestinal *Prevotella copri* correlates with enhanced susceptibility to arthritis. *eLife* **2**, e01202 (2013)