STOCKBYTE

MICROBIOME

Tipping the balance

A recent *Cell Host & Microbe* paper reveals that *Porphyromonas gingivalis*, the key bacterial trigger for periodontitis, disrupts the homeostasis between the host and the commensal oral microbiota, thereby tipping the balance towards inflammatory disease.

Periodontitis is characterized by inflammatory periodontal bone loss and is the most common cause of tooth loss worldwide. *P. gingivalis* was known to have a key role in this complex polymicrobial infection, but its precise contribution to the disease state was unclear. Previous data had suggested that the host complement system is also involved, but whether complement activation has a protective or destructive effect was uncertain.

Hajishengallis and colleagues investigated the role of *P. gingivalis* in periodontitis using a mouse model. Inoculation of SPF (specific pathogen-free) mice, which harbour commensal bacteria but are free of specific mouse pathogens, with *P. gingivalis* induced periodontal bone loss. No bone loss was seen in control SPF mice nor, interestingly, in *P. gingivalis*-treated germ-free (GF) mice, which are completely free of bacteria. Moreover, in the *P. gingivalis*-treated SPF mice, the overall load of the commensal oral microbiota increased and its composition was altered, as determined by 16S ribosomal RNA analysis.

One of the major classes of *P. gingivalis* virulence factors is the gingipains, cysteine proteases that cleave complement component C5, generating C5a and thus promoting the activation of C5a receptor (C5aR). This allows *P. gingivalis* to manipulate the local inflammatory response. The authors found that *C5aR*$^{-/-}$ mice did not develop bone loss or show any changes in the composition of the oral microbiota following *P. gingivalis* inoculation. A gingipain-deficient strain of *P. gingivalis* caused no change in the oral bacterial load. Administration of a C5aR antagonist led to the effective elimination of *P. gingivalis* from periodontal tissues, along with a significant reduction in the oral bacterial load, an effect that was *P. gingivalis* dependent. Previously, the authors had found that *P. gingivalis* downregulates chemokine production by gingival epithelial cells, in turn reducing neutrophil infiltration. Analysis of mice with a genetic deficiency in neutrophil infiltration showed that disrupting leukocyte recruitment increased the amount of oral commensal bacteria and bone loss.

The authors argue that, analogous to the concept of a keystone species, *P. gingivalis* can be viewed as a keystone pathogen owing to its disproportionately large impact on a microbial community relative to its abundance. This is in contrast to most pathogenic bacteria, which usually cause inflammatory disease while outgrowing the commensal microbiota.

Sheilagh Molloy

ORIGINAL RESEARCH PAPER Hajishengallis, G. *et al.* Low-abundance biofilm species orchestrates inflammatory periodontal disease through the commensal microbiota and complement. *Cell Host Microbe* **10**, 497–506 (2011)
FURTHER READING Darveau, R. P. Periodontitis: a polymicrobial disruption of host homeostasis. *Nature Rev. Microbiol.* **8**, 481–490 (2010)