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Prospects for treatment of *Porphyromonas gingivalis*-mediated disease – immune-based therapy

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Chronic periodontitis is an inflammatory disease of the supporting tissues of the teeth associated with a polymicrobial biofilm (subgingival plaque) accreted to the tooth which results in destruction of the tooth's supporting tissues. A characteristic feature of the disease-associated plaque is the emergence of proteolytic species. One of these species, *Porphyromonas gingivalis* has recently been described as a keystone pathogen as it dysregulates the host immune response to favour the polymicrobial biofilm disrupting homeostasis to cause dysbiosis and disease. The level of *P. gingivalis* in subgingival plaque above threshold levels (~10% of total bacterial cell load) has been demonstrated to predict imminent clinical attachment loss (disease progression) in humans. *Porphyromonas gingivalis* is found as microcolonies in the superficial layers of subgingival plaque adjacent to the periodontal pocket epithelium which helps explain the strong association with underlying tissue inflammation and disease at relatively low proportions (10%) of the total bacterial cell load of the plaque. The mouse periodontitis model has been used to show that inflammation is essential to allow establishment of *P. gingivalis* at the levels in plaque (10% or greater of total bacterial cell load) necessary to produce dysbiosis and disease. The extracellular proteinases "gingipains" (RgpA/B and Kgp) of *P. gingivalis* have been implicated as major virulence factors that are critical for dysbiosis and disease. This has resulted in the strategy of targeting the gingipains by vaccination. We have produced a recombinant immunogen which induces an immune response in mice that neutralises the proteolytic and host/bacterial binding functions of the gingipains. Using this immunogen as a therapeutic vaccine in mice already infected with *P. gingivalis*, we have shown that inflammation and alveolar bone loss can be substantially reduced. The protection was characterised by a predominant Th2 cytokine and antibody (IgG1) response and shown to be mediated by the gingipain neutralising antibodies using adoptive transfer and systemic/topical passive antibody experiments. Vaccination may be a useful adjunct to scaling and root planing in the treatment of *P. gingivalis*-mediated chronic periodontitis.