PHILIPS

Characterisation of the subgingival microbiome in patients with Rheumatoid Arthritis

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Background: Chronic periodontitis is a ubiquitous human inflammatory disease and is a major cause of tooth loss. Chronic periodontitis has been associated with rheumatoid arthritis (RA)1,2. RA is characterized by inflammation in the joints ultimately leading to joint destruction and deformity, and consequently functional impairment and disability. In addition, patients with RA are more likely to develop cardiovascular disease premature death. Several studies now indicate that chronic periodontitis may initiate and/or aggravate inflammation in RA. A limited number of small clinical studies in patients with RA have indicated that periodontal therapy aimed at reducing the periodontal biofilm and associated inflammation can reduce joint and systemic inflammation in patients with RA2. Periodontitis is a polymicrobial disease, indeed there may be some 1200 microbial species associated with differing levels of oral health3. Great strides are being made in the phylogenetic and functional typing of microbial biofilms from the oral cavity. However, as yet, few studies have examined differences in the biofilm in patients with co-morbidity. It is hypothesized4 that Porphyomonas gingivalis, a well-established contributor to periodontal disease, may additionally contribute to the break in immune tolerance seen in patients with RA who possess antibodies to citrullinated proteins. Uniquely in the microbial world, P. gingivalis expresses an enzyme peptidyl-arginine deiminase (PPAD) that can citrullinate proteins. P. gingivalis has been shown to be present in the subgingival plaque of RA patients5 and the presence of the bacterium may be associated with greater RA severity6. Treatment of periodontitis decreases antibodies to P. gingivalis7, however neither the entire periodontal microbiome composition, nor the effect of treatment upon it, has yet been investigated. Widening our view of the role that the microbiome plays in interactions between periodontitis and RA will improve understanding of this association and help to develop novel therapeutic approaches based upon biofilm manipulation.

Aim: Using next generation sequencing methods, this study aims to phylotype the microbiome from patients with RA and healthy controls, with and without periodontitis. Such knowledge will help to define the role of the oral microbiome in the pathobiology of RA.

Methods: This study will make use of plaque samples that have been ethically biobanked from the Outcomes of PEriodontal Therapy in Rheumatoid Arthritis 'OPERA' study and prospectively collected from patients with RA with and without chronic periodontitis and unaffected systemically healthy controls. Clinical examinations and sample collection were performed by a trained and calibrated examiner at the University of Birmingham School of Dentistry and Dental Hospital. Microbial samples (n=180) will be prepared by established methods8 and 454-pyrosequencing of the V1–V3 region of 16S rRNA genes will be used to establish phylotypes for all samples. Sequencing will be carried out by the Cambridge DNA Sequencing Facility (http://www.bioc.cam.ac.uk/dnasequencing). 454 sequencing remains the best method for the required depth of analysis required to tease apart the multitude of microorganisms present in the oral cavity. MiSeq technology shows promise but established methods are not yet reliably available. Until such time that they are mainstream, precious clinical samples will be examined using established and reliable techniques.