The oral microbiome's relationship to oral innate defense

Darveau Laboratory
School of Dentistry
University of Washington
Seattle, WA
Periodontal Health and Disease both involve microbial communities.
Porphyromonas gingivalis

- Gram negative oral pathogen
- Etiologic agent of periodontitis
- Major cause of tooth loss
We propose that *P. gingivalis* manipulation of innate host responses is a component of a “keystone” phenotype.

A major periopathogen manipulated innate host defense to alter the entire community.

A keystone species can be defined as one that ‘serves an essential function for the entire community, similar to a differentiated cell serving a function for an entire tissue.'


P. gingivalis causes periodontal bone loss by elevation and alteration of the commensal bacterial load

Provided in vivo data for keystone hypothesis

A Low-Abundance Biofilm Species Orchestrates Inflammatory Periodontal Disease through the Commensal Microbiota and the Complement Pathway

A Low-Abundance Biofilm Species Orchestrates Inflammatory Periodontal Disease through the Commensal Microbiota and the Complement Pathway

**P. gingivalis gavage model for periodontitis in SPF and GF mice**

A Low-Abundance Biofilm Species Orchestrates Inflammatory Periodontal Disease through the Commensal Microbiota and the Complement Pathway

**P. gingivalis causes periodontal bone loss creating a commensal dysbiosis**

*P. gingivalis* can contribute to polymicrobial community-associated disease

Darveau R et al. J DENT RES 2012;91:816-820
Oral microbiome communities also contribute to periodontal health

Healthy plaque
(mostly gram positive bacteria)

Periopathogenic plaque
(mostly gram negative anaerobes)

Innate host response results in tissue protection

Innate host response results in tissue and bone destruction
Neutrophils migrate to where the bacteria are

Do all members contribute or not and how do they do it

Distribution of neutrophils across tooth surface is NOT uniform

Number of neutrophils varies with species added back
Oral commensals naturally cause bone loss

Two independent investigations demonstrate oral bone loss with commensals

1. Co-cage study (London)

Transmission of the commensal oral microbiota to co-caged GF mice and development of periodontal bone loss after an extended period.

2. Longitudinal study (South Carolina)

Natural periodontal bone loss by commensals occurs over time with induction of inflammatory mediators.

Oral commensals contribute to bone and collagen remodeling in clinically healthy tissue


When oral commensal bacteria contribute to normal tissue turnover processes.

Bone and collagen matrix
Acknowledgements

Directly involved in the work

Thao T. To, Department of Microbiology, University of Washington
Koichiro Irie, Okayama University Graduate School of Medicine, Okayama, Japan
Ara Greer, Department of Oral Health Sciences, University of Washington
Xiao Long Luo, Department of Stomatology, Shanghai Hospital, The Second Military Medical University, Shanghai
Chad Novice, (Univ. of Washington Resident) (now College of Dental Medicine, Medical University of South Carolina)
Nurcan Buduneli, Department of Periodontology, School of Dentistry, Ege University, İzmir, Turkey

Collaborators

Camille Zenobia, Department of Microbiology, University of Washington (now Colgate Palmalive)
Ahmed Hashim, Centre for Immunology and Infectious Disease, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London
George Hajishengallis, University of Pennsylvania School of Dental Medicine, Philadelphia
Mike A. Curtis, Centre for Immunology and Infectious Disease, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London