



2012-2013 Research Synopses

Infection and Immunity

Microbes are involved in many common oral diseases, some of which are also implicated in diseases and disorders affecting the rest of the body. However, the mouth contains thousands of different microbial species, and the precise mechanisms underlying the balance between oral health and disease are extremely complex. The **Infection and Immunity Research Group** of the HKU Faculty of Dentistry aims to study such topics in a comprehensive manner by using biomedical, clinical, and translational approaches. Below is a selection of summaries of research findings published by the Infection and Immunity Research Group, with online links to abstracts or full papers in *Medline*.

Dr Rory Watt, rmwatt@hku.hk, is the convenor of the Infection and Immunity Research Group at the HKU Faculty of Dentistry. A list of the group's members can be found at: <http://facdent.hku.hk/index.php/discovery/research-groups/infection-and-immunity>

You M, Mo S, Watt RM, Leung WK.

Prevalence and diversity of *Synergistetes taxa* in periodontal health and disease.

J Periodontol Res 2013;48:159-68. <http://www.ncbi.nlm.nih.gov/pubmed/22881378>

■ How oral microbes differ in people with and without long-term gum disease (periodontitis) is still unclear, and new types of oral bacteria are being detected, such as *Synergistetes*. These researchers performed genetic tests on microbes in dental plaque from 20 Chinese people and found that *Synergistetes* bacteria were more common in the 10 people with periodontitis than in the 10 without: in 25.4% versus 5.9% of each group, and with 29 subtypes versus 8 subtypes identified. Five subtypes were associated with periodontitis, suggesting “a role in the occurrence or pathogenesis of periodontal disease”.

Mo S, You M, Su YC, Lacap-Bugler DC, Huo YB, Smith GJ, Leung WK, Watt RM.

Multilocus sequence analysis of *Treponema denticola* strains of diverse origin.

BMC Microbiol 2013;13:24. <http://www.ncbi.nlm.nih.gov/pubmed/23379917>

■ *Treponema denticola* is a species of spiral-shaped bacteria that is linked to gum diseases. This study used a new method, called multilocus sequence analysis, to study different strains of bacteria belonging to this species. By comparing the DNA sequences of the same 7 genes in each strain, the researchers were able to draw a “family tree” for 20 *Treponema denticola* strains that had been isolated from the dental plaque of people with gum

disease living in North America, Europe, and Asia. In future, this method may help in the research of how the genetic material of this and related bacteria varies around the world, in people with and without different types of oral diseases.

Seneviratne CJ, Wang Y, Jin LJ, Wong SS, Herath TDK, Samaranayake LP.

Unraveling the resistance of microbial biofilms: has proteomics been helpful?

Proteomics 2012;12:651-65. <http://www.ncbi.nlm.nih.gov/pubmed/22246638>

■ These researchers reviewed the available literature on the study of whole-system protein expression (proteomics) to investigate how attached microbial communities (biofilms) become resistant to antimicrobial drugs.

Choi MY, Wang Y, Wong LL, Lu BT, Chen WY, Huang JD, Tanner JA, Watt RM.

The two PPX-GppA homologues from Mycobacterium tuberculosis have distinct biochemical activities.

PLoS One 2012;7:e42561. <http://www.ncbi.nlm.nih.gov/pubmed/22880033>

■ Some bacteria make polyphosphate molecules to increase their infectivity, so understanding how they control polyphosphate levels is important. This team conducted laboratory tests on two relevant enzymes from the bacterium *Mycobacterium tuberculosis*, which causes tuberculosis through persistent infection. Although the two enzymes had similar compositions, only one of them was able to break down polyphosphates. The results suggest that the two enzymes “may play distinct biochemical roles” in polyphosphate metabolism.

Li JP, Li FY, Xu A, Cheng B, Tsao SW, Fung ML, Leung WK.

Lipopolysaccharide and hypoxia-induced HIF-1 activation in human gingival fibroblasts.

J Periodontol 2012;83:816-24. <http://www.ncbi.nlm.nih.gov/pubmed/22087807>

■ Fibroblasts are cells that help maintain the structure of soft tissues in the gum. However, during long-term gum disease (periodontitis) caused by certain bacteria collecting below the gum-line, fibroblast activities become altered, leading to tissue loss. In this laboratory study, a surface component from bacteria (lipopolysaccharide) caused cultured fibroblasts from human gums to produce a certain molecule (HIF-1 α peptide) when the oxygen level was either normal or low (hypoxia). The researchers suggest that during periodontitis, the fibroblasts’ response to lipopolysaccharide on bacteria “may prepare the tissues to adapt to hypoxia caused by the bacterial infection”.

Herath TDK, Darveau RP, Seneviratne CJ, Wang CY, Wang Y, Jin LJ.

Tetra- and penta-acylated lipid A structures of Porphyromonas gingivalis LPS differentially activate TLR4-mediated NF- κ B signal transduction cascade and immuno-inflammatory response in human gingival fibroblasts.

PLoS One 2013;8:e58496. <http://www.ncbi.nlm.nih.gov/pubmed/23554896>

Herath TDK, Wang Y, Seneviratne CJ, Darveau RP, Wang CY, Jin LJ.

The expression and regulation of matrix metalloproteinase-3 is critically modulated by *Porphyromonas gingivalis* lipopolysaccharide with heterogeneous lipid A structures in human gingival fibroblasts.

BMC Microbiol 2013;13:73. <http://www.ncbi.nlm.nih.gov/pubmed/23548063>

■ In these two studies, two purified types of lipopolysaccharide (LPS) from the surface of the bacterium *Porphyromonas gingivalis* had different effects on cultured cells (fibroblasts) from human gums. The two LPS types differed in a component containing either four fatty-acid chains (tetra-acylated lipid A LPS) or five fatty-acid chains (penta-acylated lipid A LPS). In the first study, the expression of certain genes encoding factors favouring inflammation was increased by tetra-acylated lipid A LPS, but decreased by penta-acylated lipid A LPS. In the second study, the expression of matrix metalloproteinase-3—an enzyme involved in the destruction of gum tissue—was increased by penta-acylated lipid A LPS. The researchers conclude that *Porphyromonas gingivalis* may contribute to gum disease through its different LPS structures.

Ding PH, Wang CY, Darveau RP, Jin LJ.

***Porphyromonas gingivalis* LPS stimulates the expression of LPS-binding protein in human oral keratinocytes in vitro.**

Innate Immun 2013;19:66-75. <http://www.ncbi.nlm.nih.gov/pubmed/22736337>

Ding PH, Wang CY, Darveau RP, Jin LJ.

Nuclear factor- κ B and p38 mitogen-activated protein kinase signaling pathways are critically involved in *Porphyromonas gingivalis* lipopolysaccharide induction of lipopolysaccharide-binding protein expression in human oral keratinocytes.

Mol Oral Microbiol 2013;28:129-41. <http://www.ncbi.nlm.nih.gov/pubmed/23194012>

■ These researchers investigated the effects of exposing cultured cells (keratinocytes) from the human mouth lining to a lipopolysaccharide containing five fatty-acid chains (penta-acylated lipid A LPS) from the surface of the bacterium *Porphyromonas gingivalis*, which is implicated in gum disease. The first study showed that the LPS increased the expression of LPS binding protein—a molecule linked to gum health and disease. The second study showed that this effect involved certain signalling pathways within the cell (NF- κ B and p38 MPAK pathways). These findings may be relevant to defence mechanisms in the gum.

Luo W, Wang CY, Jin LJ.

Baicalin downregulates *Porphyromonas gingivalis* lipopolysaccharide-upregulated IL-6 and IL-8 expression in human oral keratinocytes by negative regulation of TLR signaling.

PLoS One 2012;7:e51008. <http://www.ncbi.nlm.nih.gov/pubmed/23239998>

■ In this study, cells from the human mouth lining (keratinocytes) were grown in the laboratory and challenged with lipopolysaccharide (LPS) from the surface of the bacterium *Porphyromonas gingivalis*, which is implicated in gum disease. LPS triggered the expression of two inflammatory factors (IL-6 and IL-8), but

expression was reduced when cells were treated with baicalin—a chemical extracted from a herb used in traditional Chinese medicine to treat inflammation. The researchers call for clinical studies on the possible use of baicalin “as a potential adjunct” in gum disease treatment.

Tsang PWK, Bandara HMHN, Fong WP.

Purpurin suppresses Candida albicans biofilm formation and hyphal development.

PLOS One 2012;11:e50866. <http://www.ncbi.nlm.nih.gov/pubmed/23226409>

■ This laboratory study showed that purpurin, a red pigment extracted from madder root and used as a traditional Chinese medicine and as a food colouring, had dose-dependent antifungal activity against *Candida albicans*. The pigment’s effect on growing and mature layers of cells, or biofilms, was due to reduced expression of genes needed for the growth of filaments (hyphae), which are needed in biofilm development and fungal virulence. Purpurin was also non-toxic to cultured human cells, so it “may have clinical relevance as a new method to treat candidiasis”, the researchers suggest.

Li X, Tse HF, Yiu KH, Zhang CF, Jin LJ.

Periodontal therapy decreases serum levels of adipocyte fatty acid-binding protein in systemically healthy subjects: a pilot clinical trial.

J Periodontal Res 2013;48:308-14. <http://www.ncbi.nlm.nih.gov/pubmed/23057990>

■ A molecule called adipocyte fatty acid-binding protein (A-FABP) is involved in fat transport within certain cells and has been linked to diseases such as diabetes and heart and blood vessel disease. In this study, non-surgical treatment of long-term gum disease (periodontitis) was given to 12 of 24 patients. At 3 months, the treated group showed significantly lower levels of A-FABP in the blood than the untreated group. Longer and larger studies are needed to confirm this effect and to explore clinical implications, the researchers note.

Li X, Lan HY, Huang XR, Zhang CF, Jin LJ.

Expression profile of macrophage migration-inhibitory factor in human gingiva and reconstituted human gingival epithelia stimulated by Porphyromonas gingivalis lipopolysaccharide.

J Periodontal Res 2013;48:527-32. <http://www.ncbi.nlm.nih.gov/pubmed/23298274>

■ In 22 people showing long-term gum disease (periodontitis), affected parts of the gum showed lower expression of a gene involved in fighting bacteria (macrophage migration-inhibitory factor; MIF) than healthy parts of the gum. In addition, a laboratory study on gum cells showed that expression of the MIF gene was reduced by lipopolysaccharide from the surface of the bacterium *Porphyromonas gingivalis*, which is implicated in gum disease. The MIF gene may thus be important in gum disease, the researchers suggest.

Lam OLT, McGrath CPJ, Bandara HMHN, Li LSW, Samaranayake LP.

Oral health promotion interventions on oral reservoirs of *Staphylococcus aureus*: a systematic review.

Oral Dis 2012;18:244-54. <http://www.ncbi.nlm.nih.gov/pubmed/22126675>

■ Methods of improving oral hygiene are important, especially because the mouth and throat are sources of *Staphylococcus aureus*—a bacterium that is a leading cause of infectious disease and is also becoming increasingly resistant to antibiotics. However, this review of the literature on mouth cleaning and antiseptic use found “a wide gap in knowledge” on the effectiveness of methods of removing *Staphylococcus aureus*. Some chemicals are active in the laboratory, but high-quality studies are still needed to show their effectiveness in people.

Perera RAPM, Tsang PCS, Samaranayake LP, Lee MP, Li P.

Prevalence of oral mucosal lesions in adults undergoing highly active antiretroviral therapy in Hong Kong.

J Investig Clin Dent 2012;3:208-14. <http://www.ncbi.nlm.nih.gov/pubmed/22573355>

■ Using the European Community–Clearinghouse classification system, these researchers found that a quarter of 101 ethnic Chinese adults in Hong Kong with human immunodeficiency virus (HIV) infection had lesions inside their mouths. All had received long-term highly active antiretroviral therapy (HAART) for more than 2 years, and the prevalence of oral lesions was lower after treatment than before. However, when compared with a group of 83 HIV-negative people, the study group had significantly lower flow rates of saliva, which is a risk factor for tooth decay. Hence, to check for and manage all oral conditions, including possible malignant tumours, the researchers recommend “regular systematic oral screening” during HAART.

Zhu XF, Yin XZ, Chang JWW, Yu W, Cheung GSP, Zhang CF.

Comparison of the antibacterial effect and smear layer removal using photon-initiated photoacoustic streaming aided irrigation versus a conventional irrigation in single-rooted canals: an in vitro study.

Photomed Laser Surg 2013;31:371-7. <http://www.ncbi.nlm.nih.gov/pubmed/23863104>

■ By simulating root-canal treatment on single-rooted human teeth that had already been extracted, this team compared a conventional method of root preparation and a newer method using laser light (photon-initiated photoacoustic streaming). They found that adding disinfectant followed by either conventional syringe-irrigation or laser light treatment led to root disinfection and a similar extent of cleaning (removal of the smear layer to the middle third of the root). Future studies could further improve cleaning with the laser technique, such as by placing the laser tip deeper, the researchers suggest.