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The BceABRS four-component system essential for bacitracin sensing and response is required for biofilm formation and virulence of *Streptococcus mutans*

Yung-Hua Li, David Ropson, Anton Dugandzic and **Xiao-Lin Tian**
Dalhousie University, Canada

Streptococcus mutans is a primary etiological agent of dental caries worldwide. Natural life of *S. mutans* in dental biofilms often faces life-threatening insults, such as killing by antibiotics or innate defense molecules produced by competing species or by the host. How such insults affect physiology and virulence of *S. mutans* is poorly understood. In this study, we explored this question by analyzing the effects of sub-MIC concentrations of bacitracin and ß-defensin 3 on S. mutans. Microarray analysis showed that both bacitracin and ß-defensin 3 induced differential expression of subsets of genes that were largely regulated by the BceABRS four-component system. The results were further confirmed by examining gene expression profiles of selected genes or genetic loci using qRT-PCR. We then examined the effects of gene deletion of *bceRS* on the peptide antibiotics and virulence. The results showed that a deletion of *bceRS* resulted in a mutant that was sensitive to bacitracin or ß-defensin 3. Introduction of a wild copy of *becRS* in trans (complementation) restored the wild type phenotype of the mutant. In particular, both peptide antibiotics at a sub-MIC induced biofilm formation in the parent but not in the mutant. A competitive fitness analysis showed that the mutant was unable to compete with the parent for co-existence in duel-strain mixed cultures in the presence of bacitracin. In conclusion, the BceABRS four-component system controls a regulon that is required for sensing, response and resistance to bacitracin and ß-defensin. This system may play an important role in adaptation and virulence expression of *S. mutans* in dental biofilms.

Speaker Biography

Yung-Hua Li received his Doctorate in Molecular Microbiology at University of Manitoba. Following his Post-doctoral fellowships in the University of British Columbia and University of Rochester, NY, he worked as a Scientist in the University of Toronto, with his research focus on molecular dissection of microbial biofilms. In 2004, he joined the Faculties of Dentistry and Medicine at Dalhousie University, where he has been directing a research team on genetic analyses of bacterial biofilms, biofilm ecology and pathogenesis.

e: yung-hua.li@dal.ca

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