O34-PATHOGEN SENSING BY HUMAN ODONTOBLASTS

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Key words
Human odontoblasts, Dendritic cells, Innate immunity, Gram-positive bacteria, Pathogen recognition receptors, Chemokines.

Abstract
Human odontoblasts are neural crest-derived, dentin-producing mesenchymal cells aligned at the periphery of the dental pulp. They become exposed to cariogenic oral bacteria as these progressively demineralise enamel then dentin to gain access to the pulp. Due to their situation at the dentin-pulp interface, odontoblasts are the first cells encountered by invading pathogens and/or their released components, and represent, in the tooth, the first line of defence for the host. Previous studies have shown that odontoblasts are able to sense pathogens and elicit innate immunity. In particular, they express several pathogen recognition receptors of the Toll-like receptor (TLR) and nucleotide-binding oligomerisation domain (NOD) families, which allow them to recognize specific bacterial and viral components. So far, most studies aiming at elucidating the role of odontoblasts in the dental pulp innate response have focused on Gram-positive bacteria, as these largely dominate the carious microflora in initial and moderate dentin caries lesions. In vitro, odontoblasts were found to be sensitive to Gram-positive bacteria-derived components, mainly lipoteichoic acid which is recognized through cell membrane TLR2. Our studies have shown that engagement of odontoblast TLR2 by LTA triggers TLR2 and NOD2 up-regulation, NF-□B nuclear translocation, production of various chemokines including CCL2, CXCL1, CXCL2, CXCL8 and CXCL10, while promoting immature dendritic cell recruitment. Conversely, LTA down-regulates major dentin matrix components, including collagen type I and dentin sialophosphoprotein, as well as TGF-β1, a known inducer of dentin formation. We provide here additional data showing the fine localization of NOD2 in healthy dental pulps, as well as differential regulation of TLR2, TLR4, NOD2, CCL2 and CXCL8 genes by LTA and the synthetic TLR2 agonists Pam2CSK4 and Pam3CSK4.
It appears from the aforementioned data that odontoblast-triggered immune events constitute potential targets for interrupting the signaling cascades which lead to excessive immune response and necrosis in the dental pulp tissue challenged with cariogenic bacteria. In particular, preventing Gram-positive bacteria recognition or signal transduction by pattern recognition receptors may represent a valuable strategy to achieve this goal. Future studies in the field will pave the way for designing novel therapeutic agents which modulate odontoblast behaviour to promote pulp healing and repair.

Acknowledgements
This work was supported by University Lyon 1, CNRS, IFRO and Région Rhone-Alpes. TAK acknowledges support from the Deutsche Forschungsgemeinschaft (DFG), SFB670.

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