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GUEST EDITORIAL

Understanding Dental Pulp Innate Immunity - A Basis for Identifying New Targets for Therapeutic Agents that Dampen Inflammation

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Innate immunity represents the first line of defence against infectious agents and is essential for the detection of pathogens invading the host. Unless adaptive immunity, innate immunity is considered as non-specific as it is antigen-independent and reacts similarly to a variety of micro-organisms. It is responsible for mounting potent inflammatory responses that bring to infected tissues a variety of blood-borne immune cells in charge of eliminating harmful pathogens.

During caries infection, oral bacteria degrade enamel and dentin and trigger an innate immune response in the dental pulp through the diffusion of bacterial by-products into dentin tubules. This response may eliminate the insult and block the route of infection when accompanied by dentin neoformation within tubules and/or at the pulp–dentin interface. Unchecked, pathogen invasion results in excessive and deleterious pulp immune response, irreversible acute inflammation, tissue necrosis, and microbe dissemination through blood vessels. Previous data have revealed that bioactive molecules, mostly of the Transforming Growth Factor-beta/Bone Morphogenetic Protein family, induce dentin formation at the pulp-dentin interface. However, this formation is greatly impaired by the increase of pulp inflammation. Understanding how dental pulp innate immunity is initiated and maintained appears thus a major challenge in conservative dentistry. It will help design therapeutic agents which effectively dampen the inflammatory process triggered by intradentinal pathogens and favor dentin formation, and, hopefully, will reduce the occurrence of pulp necroses.

Odontoblasts are organized as a densely packed cell layer at the pulp-dentin interface. They send long cytoplasm processes into dentin. During carious demineralization, bacteria and/or derived components can gain access to these processes. Odontoblasts are therefore the first cells encountered by bacteria entering dentin from the oral cavity and represent in the tooth the first line of defense for the host. Most studies that aim at elucidating the role of odontoblasts in pulp innate response have focused on Gram-positive bacteria as these largely dominate the carious microflora in initial and moderate dentin caries lesions. Over the last three years, several authors have shown that odontoblasts sense Gram-positive bacteria and may be involved in the initiation, development, maintenance and cessation of the dental pulp immune response. Pathogen sensing mainly occurs by means of the pattern recognition receptor Toll-like receptor (TLR) 2 which detects components from Gram-positive bacteria including lipoteichoic acid (LTA) and diacylated/triacylated lipopeptides. In vitro, engagement of odontoblast TLR2 by LTA triggers TLR2 up-regulation, NF-κB nuclear translocation, chemokine production and immature dendritic cell recruitment. All these events constitute as so many potential targets for interrupting the signaling cascade that ultimately leads to excessive pulp inflammation. Several strategies may be considered to achieve this goal. These include blocking of agonist recognition through TLR2 and inhibition of pro-inflammatory intracellular signal transduction and chemokine production by odontoblasts. Future studies will undoubtedly result in a better understanding of the initial events responsible for pulp innate immune response and will pave the way for designing effective therapeutic agents that modulate pulp cell behaviour to promote healing and repair.

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