Toll-like Receptors in Salivary Glands

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Stone formation

Sialoadenitis and sialolithiasis are two common disorders of the salivary glands. They can be caused by stones in the salivary glands or the in the ducts of those and may cause great discomfort and need treatment. But how do the stones form? Why are some people more prone to form stones in their salivary glands?

We believe that TLRs and innate immunity might play a key role in this process.

Salivary glands in the first line of defence

The oral cavity is constantly exposed to inhaled and digested microbes. To keep the micro flora in balance the salivary glands can release antimicrobial agents into the saliva. Of these, cystatins, mucins and defensins have both antibacterial and antiviral effects. The salivary glands also produce significant quantities of proteins like nerve growth factor (NGF), epidermal growth factor (EGF), transforming growth factor (TGF)-β, renin and kallikreins as well as numerous cytokines, like interleukin (IL)-1α/β, tumour necrosis factors (TNFs), and interferon (IFN)-γ, that all contribute to the regulation of the immune/inflammatory response in the mucosal tissue, and participate in regeneration or healing of wound tissue. The salivary glands therefore appear to interact with the mucosal and systemic compartments of the immune system via its secretion, saliva.

Toll-like receptors

The Toll-like receptors (TLRs) constitute a family of receptors involved in pathogen recognition. They identify structural motifs located on microorganisms. Ten different TLRs, TLR1-10, have so far been found in humans. They are all known to participate in host responses to injury and infection, indicating their strong linkage with the antimicrobial proteins and cytokines mentioned above. Each TLR recognises specific microbial components, so called pathogen-associated molecular patterns (PAMPs), including bacterial lipoproteins and lipoteichoic acids (TLR2), double-stranded viral RNA (dsRNA; TLR3), lipopolysaccharides (LPS; TLR4), flagellin (TLR5), imidazoquinolines and single-stranded viral RNA (ssRNA; TLR7 and TLR8) and unmethylated CpG oligodeoxynucleotides (ODNs; TLR9). The ligand for TLR10 is yet unknown.

Methods

10 patients undergoing surgical extirpation of the submandibular gland due to chronic inflammation were included. A piece of the submandibular gland close to the centre of the inflammation was harvested, split into two and placed in formaldehyde and in RNA-later, respectively for later analysis. The former was used for histopathology and the later for mRNA quantification of TLR 1-10 with RT-PCR.

10 patients undergoing superficial parotid surgery because of pleomorf adenoma (a benign tumor) was used as control. A normal piece of the gland far away from the tumor handles as mentioned above. 2 children with cerebral palsy undergoing removal of the submandibular gland due to hypersalivation-problems were used as alternative controls.

Results

A constant mRNA expression for TLR 1, 2, 3 and 5 were seen in all specimens and an up-regulation of TLR2 was seen in gland tissues from patients with chronic sialoadenitis. The immunohistochemistry revealed moderate expression of TLR 3, 5, 6 and 9 in serous glands and an intense TLR 2 expression in mucous acini.

Conclusion

Our results suggest that a TLR-mediated inflammatory component might be involved in the development of sialoadenitis, perpetuating lymphocytic infiltration and cytokine production.

Aims

Although the oral cavity is one of the first barriers to the entry of bacteria and viruses into the body and most saliva is secreted by the submandibular as well as the parotid glands, our knowledge of TLR in these glands is scarce. Hence, the present study was designed to examine the presence of TLRs in human salivary glands and to investigate if ongoing chronic sialoadenitis affects their expression.

TLR2 TLR3 TLR6 TLR9

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