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Basic Science

Abstract Title
Fungal quorum sensing molecules mediated taste receptor desensitization in gingival epithelia

Background
Microbial dysbiosis is a major contributing factor in the development of oral diseases including caries, periodontitis and oral cancer. It is well established that high chemoattractant or agonist concentrations can reduce host cellular responses by a process termed G protein-coupled receptor (GPCR) desensitization. Desensitization is defined as the decrease in cellular signal upon repeated stimulation of agonists. GPCRs undergo receptor desensitization - a process that involves ligand and beta-arrestin dependent, selective phosphorylation by GPCR-kinases (GRKs). The sweet (T1Rs), umami (T1Rs) and bitter taste receptors (T2Rs) belong to the GPCR family. The 25 T2Rs in humans are regarded as immune sentinels with T2R14 playing a prominent role. Very little is known about the mechanism and physiological significance of taste desensitization by oral fungi.

Objective
The aim of the present study is to investigate: 1) whether fungal quorum sensing molecules (QSMs) could induce T2R14 desensitization in gingival epithelial cells (GEC), 2) if GRKs and beta-arrestins are involved in fungal QSM induced desensitization in GECs.

Methods
To evaluate the effect of fungal QSMs on T2R14 desensitization and innate immune responses, GEC cell lines OKF6 Wt and OKF6 T2R14 knock out (KO) cells were used as a model system. Cell based assays and biophysical studies were performed to measure activation, desensitization and protein-protein interactions of T2R14 with GRKs and beta-arrestins. Enzyme linked immunosorbent assay and immunofluorescence analysis were pursued to analyze T2R14 internalization in GECs after fungal QSM treatment.

Results
Our results suggest that stimulation of fungal QSMs to OKF6 cells leads to T2R14 activation and this response is T2R14-dependent. Next, repeated stimulus of fungal QSMs leads to T2R14 desensitization. This desensitization mechanism involved recruitment of both GRKs and beta-arrestins.

Conclusion
In conclusion, our study suggests that fungal QSMs leads to T2R14 desensitization and hyperinflammatory response in GEC.

Authors

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