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The Role of Bitter Taste Receptors in Oral Innate Immunity

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Background:

Early childhood caries (ECC) has become a major public health concern posing a significant socioeconomic burden worldwide. The causes of ECC are multifactorial and host immunity has been shown to play a major role in its development. *Streptococcus mutans* a key etiological pathogen has been shown to secrete Competence Stimulating Peptides (CSPs) during caries pathogenesis. However the mechanism by which these CSPs influence host immunity is not well understood. In this study we propose that bitter taste receptors (T2Rs) interact with *S. mutans* CSPs and generate immune responses.

Objective:

[1] Pharmacological characterization of CSPs with select T2Rs using heterologous HEK293T expression system. [2] Characterize the expression and function of select T2Rs in Gingival Epithelial Cells (GECs).

Methods:

Intracellular calcium levels were measured using Ca^{2+} binding dye (Fluo NW) after addition of CSPs to GECs and HEK293T expressing different T2Rs. Real-time PCR was carried out for T2R4, 14, and 20 in GECs. IL-1 α and IL-8 quantification in GEC supernatants by ELISA.

Results:

(i) CSP-1, 2 and 3 were able to mobilize intracellular calcium at 50 μM (** $p < 0.01$, * $p < 0.05$) concentration. These calcium responses were blocked by T2R signaling inhibitors U-73122 and gallein (** $p < 0.001$). We observed a dose-dependent calcium mobilization upon CSP-1 treatment on individual T2Rs. The EC_{50} values for CSP-1 treated cells were as follows T2R4 ($4.2 \pm 1 \mu\text{M}$), T2R20 ($5.2 \pm 1.2 \mu\text{M}$), T2R14 ($5.8 \pm 1.8 \mu\text{M}$) (ii) qPCR analysis revealed moderate expression of T2R4, and T2R14 in GECs. (iii) GECs treated with CSP-1 showed T2R mediated secretion of IL-1 α and IL-8 (* $p < 0.05$).

Conclusion:

CSPs are identified as potent T2R agonists. These results suggest that T2Rs are involved in innate immunity and may be protective in function. Currently we are quantifying anti-microbial peptides (AMPs) secreted by T2R activation and the role of T2Rs involved in caries innate immunity.