**Streptococcus gordonii antagonizes Porphyromonas gordonii-induced OLFM4 in epithelial cells**

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### Introduction

*Porphyromonas gingivalis* (Pg) is an oral obligate anaerobe that is considered a keystone pathogen in periodontal disease. Additionally, Pg has been strongly associated with oral squamous cell carcinoma (OSCC), which is the most common oral malignancy with roughly a 50% survival rate after 5 years. Pg has been shown to inhibit apoptosis, accelerate cell cycle progression, and induce epithelial-to-mesenchymal transition through ZEB1/ZEB2 in gingival epithelial cells. Interestingly, the oral commensal *Streptococcus gordonii* (Sg) can inhibit ZEB2 upregulation induced by Pg. OLFM4 is strongly associated with gastric cancer, and is primarily known for its role in inhibiting oncogenes. Interestingly, this antagonism is specific to certain commensal streptococci. Understanding this relationship, and the mechanism by which Pg activates and antagonizes OLFM4 is considered a keystone pathogen in periodontal disease.

Our lab has established Sg as a homeostatic commensal, and here we show an additional antagonism of Pg induced oncogenes. Interestingly, this antagonism is specific to certain commensal streptococci. Understanding this relationship, and the mechanism by which Pg activates and Sg inactivates oncogenic pathways will be valuable for understanding OSCC initiation and progression.

### Objective

To investigate OLFM4 regulation by Pg in gingival epithelial cells.

### Methods

Telomerase immortalized gingival keratinocytes (TIGKs) were grown to 80% confluence. Cells were challenged with bacteria for 3h, media was changed and RNA was harvested at 24h. RNA was reverse transcribed, then qPCR was performed and fold change calculated using ΔΔCT. siRNA transfection was performed 48h before bacterial challenge, and scrambled siRNA was used as a control. All qPCR data was normalized to GAPDH.

### Results

#### Figure 1: Schematic of Notch Signaling

- a) Schematic of Notch Signaling

#### Figure 2: Relative quantities of OLFM4 mRNA

- a) Relative quantities of OLFM4 mRNA
- b) Relative quantities of OLFM4 mRNA

#### Figure 3: Relative quantities of OLFM4 mRNA

- a) Relative quantities of OLFM4 mRNA
- b) Relative quantities of OLFM4 mRNA

#### Figure 4: Relative quantities of OLFM4 mRNA

- a) Relative quantities of OLFM4 mRNA
- b) Relative quantities of OLFM4 mRNA

### Conclusions

Our lab has established Sg as a homeostatic commensal, and here we show an additional antagonism of Pg induced oncogenes. Interestingly, this antagonism is specific to certain commensal streptococci. Understanding this relationship, and the mechanism by which Pg activates and Sg inactivates oncogenic pathways will be valuable for understanding OSCC initiation and progression.

### Acknowledgments

NCI R25-CA134283, NIDCR F3028166 (ZRF), NIDCR R0101111 (RJL), and R01012505 (RJL).