

The Oral Microbiome Signature of Oral Cancer Transition

Research Abstract

The 5-year survival rates for oral cancer have not improved significantly over the last decade, underscoring the need for novel treatment and diagnostics approaches¹. Understanding the potential mediators and mechanisms of conversion from healthy to malignancy in early lesions, like oral epithelial dysplasia, is important to enhance oral cancer outcomes. Smoking, alcohol consumption, and HPV infection contribute to the pathogenesis of oral cancer^{2,3}. Although the oral microbiome and its dysbiosis have been implicated in the pathogenesis of oral cancer, oral microbes at the species level (except for *C. concisus*) that are associated with premalignant oral cancer tissues have not been identified or functionally tested in carcinogenesis; its contributions and bacterially-mediated mechanisms that promote cancer are not completely known or have not been well explored³. Although it has been determined that pathogenic oral bacteria, associated with periodontal disease *Porphyromonas gingivalis* (*P. gingivalis*), *Treponema denticola* (*T. denticola*), and *Fusobacterium nucleatum* (*F. nucleatum*) enhance cancer cell migration, invasion, stemness and tumorigenesis in vivo, our workgroup have previously demonstrated that specific oral microbial shifts are associated with transitions from health to carcinogenesis (oral/head and neck squamous cell carcinoma; OSCC)⁴; where carcinogenesis is specifically defined by a high Fusobacterium to low Streptococcus ratio.

We hypothesize that specific oral bacteria define the transition from health to oral dysplasia and to carcinogenesis. Therefore, the goal of the current proposal is to determine which microbes are associated with premalignant oral cancer. Our hypothesis will be tested by the **Specific Aim: Define the oral microbiome signature that characterizes the transition from health to oral dysplasia and to carcinogenesis in OSCC using shotgun metagenomic sequencing of patient tissues. Then, validate and test the top differential species found in the metagenomic test in functional carcinogenesis assays.**

References

1. Münscher, A. *et al.* Survivin expression in head and neck squamous cell carcinomas is frequent and correlates with clinical parameters and treatment outcomes. *Clin Oral Investig* **23**, 361–367 (2019).
2. Healy, C. M. & Moran, G. P. The microbiome and oral cancer: More questions than answers. *Oral Oncol.* **89**, 30–33 (2019).
3. Ganly, I. *et al.* Periodontal pathogens are a risk factor of oral cavity squamous cell carcinoma, independent of tobacco and alcohol and human papillomavirus. *Int. J. Cancer* **107**, 283 (2019).
4. Shin, J. M. *et al.* Microbial Communities Associated with Primary and Metastatic Head and Neck Squamous Cell Carcinoma - A High Fusobacterial and Low Streptococcal Signature. *Sci Rep* **7**, (2017).