

The microbiome in tumor tissue and oral rinses are associated with the triple negative oral cavity squamous cell carcinoma

Marco J.W. LI¹, Zigui Chen^{2,3}, Po Yee Wong³, Cherrie W K Ng,¹ Linlin Lan¹, Sherwood Fung,^{4,5,6} Pu Lei,³ Liuyang Cai,² Sunny H Wong^{2,4,7,8,9}, Eric H L Lau¹, Zenon Yeung¹, Allen K C Chan^{4,5,6}, Eddy W Y Wong¹, Jun Yu^{2,4,7,8,9}, Paul K S Chan^{2,3} and Jason Y K Chan¹

Introduction

- Traditional risk factor of oral cavity squamous cell carcinoma (OSCC) include smoking, alcohol drinking, HPV infection.
- incidence of OSCC without traditional risk factors is in increasing trend.
- Emerging data implicates the human microbiome as a risk factor for a variety of cancers.

Objective

- We elucidated the bacterial microbiome across both OSCC tissues and oral rinses to elucidate the role of microbiome in OSCC.

Methods

- Prospective case-control study: 54 patients with tumour, adjacent normal tissue and pre-operative oral rinses compared with oral rinses from 93 healthy volunteers. High-throughput 16S rRNA gene sequencing defined a set of microbial biomarkers associated with OSCC (**Figure 1**)
- Machine learning on such biomarkers was applied to classify OSCC.

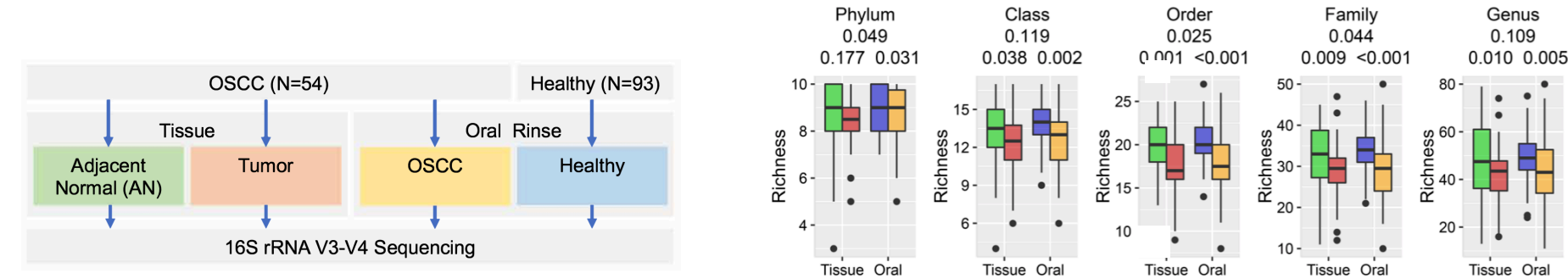


Figure 1: Workflow of the study design and sample collection

Figure 2: Comparison of oral microbiota diversity. Statistically significant using Mann-Whitney U-test

Conclusions

- OSCC has an associated microbial environment that might have clinical biomarker applications

Results

- Reduced bacterial diversity in tumour tissues w.r.t. adjacent normal tissues. (**Figure 2**)
- Significant enrichment of *Fusobacterium* in OSCC non-smokers compared to smokers and depletion of *Streptococcus* in OSCC non-drinkers.
- Core bacterial genera are altered in abundance in OSCCs across both tissues and oral rinses compared to controls (**Figure 3**)
- Machine learning on biomarkers abundance classified OSCC in tissue and oral rinse with an AUC of 0.885 (95% CI 0.819 – 0.951) and 0.886 (95% CI 0.824 – 0.948) (**Figure 4**)

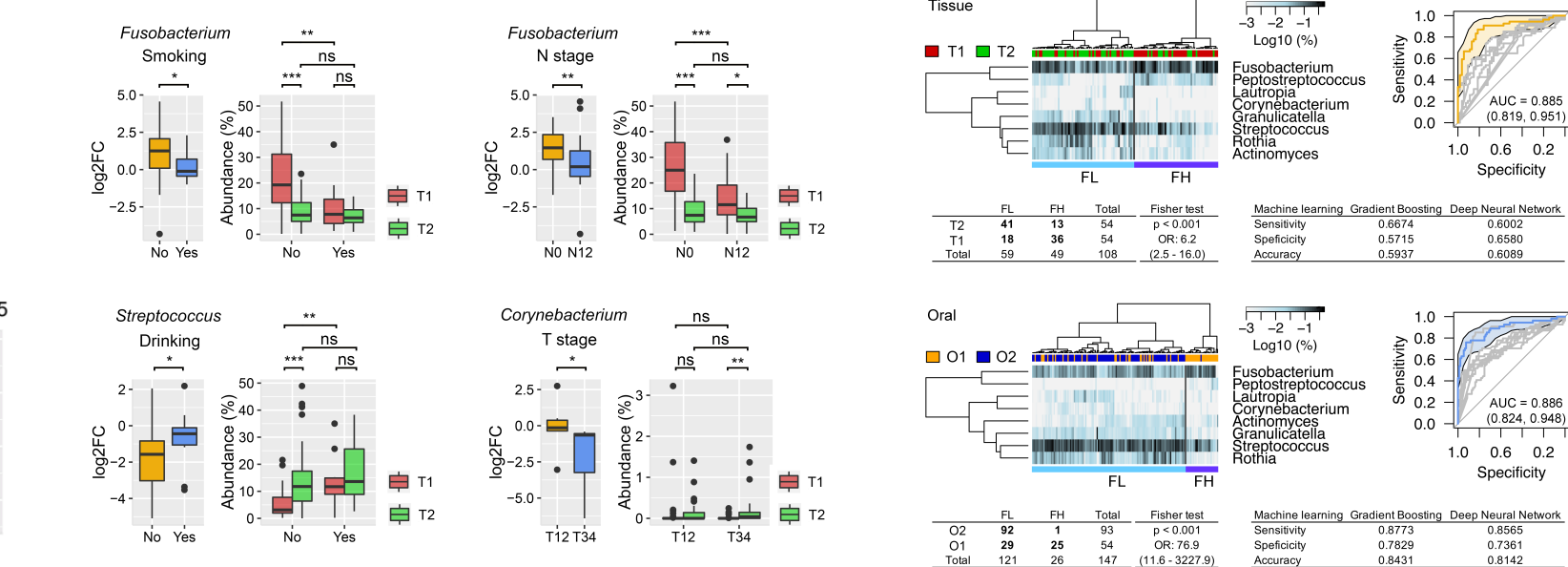


Figure 3: Fold-change analysis in paired OSCC tumor tissues and the adjacent normal controls demonstrating significant increase of *Fusobacterium* in non-smokers and lower N classification, decrease of *Streptococcus* in non-drinker

Figure 4: *Fusobacterium* and *Peptostreptococcus* are enriched while *Streptococcus* is depleted in OSCC cases across both tissues and oral rinses. ROC analysis of combined eight genera achieved an AUC of 0.885 and 0.996 respectively

Affiliations

¹ Department of Otorhinolaryngology, Head and Neck Surgery, The Chinese University of Hong Kong, Hong Kong SAR, China
² Centre for Gut Microbiota Research, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China
³ Department of Microbiology, The Chinese University of Hong Kong, Hong Kong SAR, China
⁴ Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong, Hong Kong SAR, China
⁵ Department of Chemical Pathology, Hong Kong SAR, China
⁶ State Key Laboratory of Translational Oncology, Sir Y.K. Pao Centre for Cancer, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China
⁷ Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR, China
⁸ Institute of Digestive Disease, State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong SAR, China
⁹ CUHK Shenzhen Research Institute, Shenzhen, China