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High-throughput Identification of Biomarkers for Early Detection and Diagnosis of Oral Cancer by Integrating Metagenomics and Metabolomics Approaches, Immunological and Bioinformatics Analysis

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Oral squamous cell carcinoma (OSCC) is the most common malignant neoplasm of the oral cavity and the fourth leading malignancy and cause of cancer-related death in the male population of Taiwan. Most cases are detected at advanced stages, resulting in poor prognosis. Therefore, improved detection of early oral health disorders is indispensable. The involvement of oral bacteria in inflammation and their association with OSCC progression provide a feasible target for diagnosis. Due to the nature of oral neoplasms, the diagnosis of epithelial precursor lesions is relatively easy compared with that of other types of cancer. However, the transition from an epithelial precursor lesion to cancer is slow and requires further and continuous follow-up. Although some bacterial species are correlated with oral cancer, the complexity of the cancer-driving conditions associated with the microbiome remains unexplained by a single pathogen. High-throughput assays such as next-generation sequencing (NGS) offer comprehensive culture-free techniques for surveying human microbiome composition and biomolecular activity at the transcriptional level. In this study, we investigated microbiota differences between normal individuals, epithelial precursor lesion patients, and cancer patients with different lifestyle habits, such as betel chewing and smoking, using next-generation sequencing. Overall, the oral microbiome compositions of five genera, *Bacillus, Enterococcus, Parvimonas*, *Peptostreptococcus*, and *Slackia*, revealed significant differences between epithelial precursor lesion and cancer patients and correlated with their classification into two clusters. These composition changes might have the potential to constitute a biomarker to help in monitoring the oral carcinogenesis transition from epithelial precursor lesion to cancer.