Detecting Early-Stage Oral Cancer from Clinically Diagnosed Oral Potentially Malignant Disorders by DNA Methylation Profile

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Abstract: Clinically, early-stage oral cancers are difficult to distinguish from oral potentially malignant disorders (OPMDs), and invasive tissue biopsy should be performed to determine a treatment strategy. Previously, we focused on gargle fluid as a noninvasive testing method and reported aberrant methylation in gargle fluid in patients with oral cancer. This study aimed to distinguish early-stage oral cancer from clinically diagnosed OPMDs using gargle fluid samples. We collected gargle fluid samples from 40 patients who were clinically diagnosed with OPMDs in the training set; among them, 9 patients were pathologically diagnosed with oral cancer. Methylation levels of 25 tumor suppressor genes were analyzed using the methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) method. We found that a combination of six genes (TP73, CASP8, RARB, KLLN, GSTP1, and CHFR) could distinguish oral cancer from clinically diagnosed OPMDs with high diagnostic performance (area under the curve [AUC], 0.885; sensitivity, 77.8%; and specificity, 87.1%). Additionally, the panel comprised of the six methylated genes was validated in the test set. Furthermore, when compared with cytology testing, the panel could accurately detect oral cancer.