

**Project title: The Second CRC of Excellence of MOHW- China Medical University Hospital
Program title: Reduction of Incidence and Mortality of Oral Cancer
Individualized Risk Assessments for Oral Pre-cancer Risk Stratification using
Genetic Biomarkers Panels**

Chia-Min Chung^{1,2}, Chung-Chieh Hung^{2,3}, Ying-Chin Ko¹
鍾加明，洪崇傑，葛應欽

¹Environment-Omics-Disease Research Center, China Medical University Hospital, Taichung, Taiwan, ²Graduate Institute of Clinical Medical Science, China Medical University, Taichung, Taiwan, ³Department of Psychiatry, China Medical University Hospital, Taichung, Taiwan

Objective: Genetic SNPs from pathological association might be helpful for treatment planning and optimizing the timing and cost of screening phases. This appears to be feasible, as rapid and low-cost genotyping methods are becoming increasingly available. The aim of this study was to identify high risk groups for oral precancerous subjects. The genetic biomarkers panels may give the rationale to the individualized risk assessments as well as risk stratification at the customized basis.

METHODS: This study included 167 subjects recruited from cancer screen center from China Medical Hospital. A total of 4 validated oral cancer risk SNPs were successfully genotyped. Genetic risk score was calculated by four tag SNPs found in NOTCH1, BRCA1, COL9A1, and HSPA13 genes. Several environmental variables and regression model were applied to identify a set of SNPs that together improve the prediction for oral pre-cancer.

RESULTS: Among all cases, 44.8% were high risk group, 50.6% were moderate risk group and 7.6% were low risk group. 10.1% had oral precancer. The median age of subjects was 46.5 years (range, 18-77 years). The areas under the ROC curves (AUROC) were 0.86 for combined GRS, BQ chewing, cigarette smoking and age with sensitivity of 81.6% and specificity of 78.6% ($P < 0.0001$). The moderate risk group and high risk group were associated with precancer with hazards ratio (HR) of 4.65 (95% C = 2.10-10.31, $P = 0.0002$), HR=5.92 (2.49-14.08, $P < 0.0001$), respectively .

CONCLUSION: The prediction panel stratifies oral precancer risk according to genetic risk score and environmental exposure status. The observed level of risk discrimination could inform targeted screening and prevention strategies. The risk stratification model may be useful as a clinical marker for oral cancer detection and risk assessment.