Pathways Deregulation in Oral Squamous Cell Carcinoma Using Methylation Profiling

Introduction: Analyses based on methylation profiling offers an understanding in the mechanisms of carcinogenesis. Single gene analysis is insufficient to describe the complex perturbations responsible for cancer onset, progression and invasion. Objective: To identify gene pathways of highly hypermethylated genes in oral squamous cell carcinoma (OSCC) using DNA microarray-based methylation profiling.

Methods: DNA methylation assay was carried out on bisulfite-converted DNA extracted from frozen section tissues of 3 normal subjects and 20 patients of OSCC, using Illumina Infinium Methylation assay. 20620 genes of raw data obtained were normalized and analyzed using Genome Studio software. Significantly methylated genes were generated by Gene Set Enrichment Analysis (GSEA), with less-than 25% false discovery rate and 0.05 of nominal p-value were applied in gene pathway analysis. Results: High quality bisulfite-converted DNA was obtained and the methylation array was successfully run on all samples. In unsupervised cluster analysis, the normal subject samples were cluster differently from OSCC cases with false discovery rate of p-value of less than 0.05 and fold change more than 2.0. 113 hypermethylated genes were generated by GSEA where 18 hypermethylated genes are involved in pancreatic cancers, 42 in cell cycle, 20 in apoptosis, 15 in chronic myeloid leukemia, 7 in bladder cancer and 9 in non-small cell lung cancer. Conclusions: Based on the data analysis, the hypermethylated genes found on these pathways are related to the cancer-causing mechanisms.

Keywords: Molecular biology, Pathology and methylation profiling