Identifying DNA Methylation Status In Oral Cancers Using CpG Island Microarray

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Purpose:

To investigate the DNA methylated status induced by areca nut and to find new detection biomarkers for patients with oral cancer.

Materials and Methods:

To find more specific genes which are aberrant methylated by arecoline, CpG island microarrays were used to analyze aberrant methylation in oral cancer tissues with different treatment and time schedule of the 4-NQO plus arecoline induced animals. Methylation-specific PCR (MS-PCR) assays were used to further confirm the gene methylation condition. Specific RNA expression levels were analyzed by real-time reverse transcription- polymerase chain reaction analysis.

Results:

Forty-two genes are hypermethylated and nine genes are hypomethylated in 4-NQO plus arecoline induced animal oral cancer tissues by CpG island microarray method. Five hyper-methylated genes and two hypo-methylated genes were further confirmed by MS-PCR. The gene methylated type in 4-NQO plus arecoline induced oral cancer tissue were also shown similar pattern in TW2.6 and OEC-M1 cells but not SCC-4 cells. An over-expressed pattern of a hypo-methylated gene was further detected in tumor part of the cancer tissues and OEC-M1 cells.

Conclusion:

In many Asia cultures chewing areca is known to be a strong risk factor for developing oral cancer. In this study, a 4-NQO plus arecoline induced animal model was used to confirm areca really increasing occurrence of oral cancer. In addition, our data show that DNA methylation status is associated with the areca-associated oral tumorigenesis. Several specific genes have been confirmed by MS-PCR and will be further checked in tissues from oral cancer patients. The mechanisms of specific hyper- or hypo-methylation genes involved in the modulation of oral cancer will be further investigated.