Editorial

DNA Methylation Induced Epigenetic Silencing: A Potential Biomarker and Therapeutic Target for Head and Neck Squamous Cell Carcinoma

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DNA methylation is a physiologic process in which the dinucleotides outside the CpG islands are methylated while the CpG islands with promoter regions remain non-methylated. This specific pattern of DNA methylation is called "methylotype" or the basic genomic methylation pattern. The process is catalyzed by a group of enzymes called DNA methyltransferases (DNMTs: DNMT1, DNMT3A and DNMT3B). DNMTs 3A and 3B are responsible for *de novo* methylation and DNMT1 for the maintenance of the methylation pattern of the template strand. Variation from "methylotype" represents an epigenetic aberration, causing an altered gene expression without changing the actual DNA sequence.[1] A shift in the methylation pattern may follow one of the following paths: Increased methylation of the promoter regions of CpG islands causing repression of genes involved in DNA repair, apoptosis, tumor suppression and cell cycle regulation (or) loss of methylation of oncogenes causing its overexpresion. A shift in the "methylotype" may lead to genetic instability and initiate carcinogenesis. Kozaki *et al*. observed that the epigenetic silencing of tumor suppressive miRNA including miR-34b, miR-137, miR-193a, and miR-203 was a common event in oral cancer.[2] Recent studies have found more than 30 altered miRNA genes due to aberrant DNA methylation patterns.[2-5] Baba *et al*. demonstrated that the CHFR gene, responsible for providing checkpoint at the G2-M transition, is significantly repressed following promoter hypermethylation.[6,7] It was noticed that aberrations in the DNA methylation pattern were not consistent among the subgroups of head and neck squamous cell carcinoma (HNSCC). There was a consistent variation in the degree and specificity of DNA methylation. This variation may be responsible for the heterogeneity seen in head & neck squamous cell carcinoma at the clinical and histopathological level. Thus, profiling HNSCC based on DNA methylation may provide us with a basic understanding of its molecular biology and enable us in establishing specific biomarkers for early diagnosis and treatment. A majority of these altered methylated patterns can be reverted, by using demethylation agents (chemotherapeutic agents).[1] It is necessary to identify such methylated tumor suppressor genes by sequential expression and methylation analyses. Several studies have elicited the various techniques for determining DNA methylation pattern. These include, use of restriction enzymes, microarray-based methylation analysis, genomic bisulfite sequencing, microarray-based methylation analysis and methylation-specific polymerase chain reaction (PCR) following bisulfite treatment (methylation-specific PCR).[8] Pyrosequencing of OSCC samples has shown that only a subgroup of HNSCC has epigenetic alterations like DNA methylation, whereas the rest have genetic alterations like deletions and mutations. Further, evaluation of large scale HNSCC samples may aid in validating such a segregation based on genetic or epigenetic alteration (hypermethylation), of which the later is reversible and may serve as therapeutic targets.[8]

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