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Genetic Susceptibility of Polymorphic Minisatellites Alleles in the *MUC5B* Gene to Cancer Development

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The mucus that covers delicate epithelial surfaces of the respiratory, gastrointestinal and reproductive tracts functions in a protective capacity to prevent desiccation and provide lubrication and defence from environmental bacteria and internal enzymes. The major glycoproteins of the mucus are the mucins. In normal state, mucins are secreted to protect tracheas or intestines, while in abnormal state of gene regulation or gene mutation, mucins might be excessively. Mucin genes can be classified into two main subfamilies: secreted mucins and membrane-associated mucins. Several secreted mucins (*MUC2*, *MUC5AC*, *MUC5B* and *MUC6*), whose genes are clustered on chromosome 11p15.5, these structural characters effected on gene expressions. In this study, we focused on the allelic variation in minisatellies-6 of *MUC5B* gene as candidates for susceptibility to cancer. Seven alleles of *MUC5B-MS6* were identified by PCR using specific primers from satellite-flanking sequences. The number of repeats varied from 3 to 10 with 7 repeats in the most common allele. Furthermore, case-control study was performed on DNA from cancer-free controls and cancer cases with gastro-intestinal cancer, colon cancer, rectal cancer, lung cancer, bladder cancer and breast cancer. Interestingly, long rare alleles (9 and 10 repeats) at MUC5B -MS6 were increased the susceptibility of gastric cancer and bladder cancer.

Key words: Polymorphic, minisatellite, mucin, common allele, rare allele

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Characterization of *CTCFL/BORIS* Gene Promoter and Analysis of the Influence of VNTR Located on Upstream Region to Epigenetic Control

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CTCFL/BORIS for CTCF-like/Brother of the Regulator of Imprinted Sites was previously uncharacterized testis-specific gene and regulated by site-specific epigenetic events in the male germ line. The sibling referred to is CTCF, the 11-ZF protein well known for its many roles in gene regulation including functional switching of allele-specific methylation marks. Indeed, CTCFL/BORIS activates abnormally in various human cancers, including both primary tumors and cancer cell lines. Therefore, BORIS can be classified as a unique cancer-testis (CT) gene and epigenetic alterations including aberrant promoter demethylation is also implicated in testis cancer cell line. But analysis of expression mechanism of CTCFL/BORIS is not carried out very well. Accordingly, we characterized promoter region of CTCFL/BORIS and found distinctive features. CTCFL/BORIS has CpG island in the promoter region rightly and two tandem repeats (BORIS-MS1 and BORIS-MS2). Each minisatellite has a 16-bp and 56-bp repetitive unit. Among them BORIS-MS2 showed the polymorphism pattern and the at least six alleles containing a different number of the repetitive unit in normal unrelated individuals and located nearby CpG island. A series of luciferase constructs that contain various fragment of the CTCFL/BORIS 5-genomic region were transfected into human lung cancer cells for promoter transactivation analysis. A 700-bp region that contains CpG island and GATA element maintained activity 29-fold. And we demonstrated that BORIS-MS2 sequence significantly decreases the transcription activity of 700-bp region in the promoter of CTCFL/BORIS (1.5-2.2 fold). Thus, our studies not only provide molecular basis of CTCFL/BORIS transcription regulation, but also define the influence of repeat sequence to decreases the transcription activity.