P173

Study of the Influence on the Carcinogenesis by Tandem Repeats Polymorphism Located on Intronic Region of Human *TERT* Gene

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The human telomerase reverse transcriptase (hTERT) gene includes four minisatellites (VNTR 2-1, VNTR 2-2, VNTR 6-1 and VNTR 6-2). The polymorphisms of the minisatellites were analyzed by PCR. The frequencies of rare alleles of the hTERT-VNTR (human telomerase reverse transcriptase-variable number of tandem repeats) 2-2 region in normal males and prostate cancer patients were examined. As a result, the frequencies were 0.26% and 2.14%, which are more than 8-fold different from each other. Such results were statistically analyzed and, as a result, in the case of having the rare allele of hTERT-VNTR 2-2, the risk (odds ratio, OR; risk ratio) of prostate cancer development was increased by 8.32 times at a 95% confidence interval (p=0.017, statistically very significant). This suggests that the hTERT-VNTR 2-2 region can be used to predict and diagnose prostate cancer. In addition, for the hTERT VNTR 2-2 region, genomic DNA was extracted from 381 normal persons and 368 prostate cancer patients and subjected to PCR compare haplotype patterns between the normal persons and the prostate cancer patients. As a result, in the prostate cancer patients, 7 alleles were found, which consisted of 28 repeats, 37 repeats, 39 repeats, 40 repeats, 42 repeats, 43 repeats and 44 repeats of a 61-bp repeat unit, respectively. Particularly, in the samples of the prostate cancer patients, prostate cancer-specific alleles consisting of 28 repeats, 37 repeats and 40 repeats, respectively, which did not appear in the normal persons were found. This suggests that the rare allele of hTERT VNTR 2-2 is related to prostate cancer.

P174

Analysis of Human SCK1/SLI that Show Unstable Repeat Polymorphism

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Some human DNA sequences, including unique genes, are also unstable and non-clonable in E. coli. In previous work, we demonstrated that closing the four gaps of the human chromosome 19 could be achieved through a combination of two strategies, i.e. screening of new BAC and cosmid libraries and selective TAR cloning in yeast. The opportunity to compare the clones isolated in different hosts allowed us to determine the structure of the missing genomic segments. Two gap regions contained large blocks of micro- and/or minisatellite repeats. Another gap region was highly enriched by Alu repeats. In the fourth clone, a large block of TGG trinucleotide repeats was detected. Analysis of the GAP1 sequences revealed that one of the regions includes an approximately 50-kb segment of the neuronal cell signaling SCK1/SLI gene. Further analysis of the GAP1 sequence revealed that it contained several abnormalities, including large blocks of tandem repeats that could result in instability in E. coli. To characterize these repeated regions, we evaluated the DNA composition, phylogenic tree, and pairwise distances of its minisatellites. Furthermore, we examined the cloning efficiency of each minisatellite into the TA vector and the instability of the minisatellites during propagation in E. coli. From these studies, we observed that seven minisatellite regions yielded 0-30% cloning frequency, while others were cloned efficiently (90-100%). The cloning frequency in bacteria is affected by the GC content and the length of the repeats; however, the maintenance of the clones was unaffected by minisatellites. We suggest that minisatellite rearrangement can occur in the early stage of plasmid construction and duplication, thus their instability is dependent on both their length and DNA composition.