ISSN 0972-3757
INTERNATIONAL JOURNALOF HUMAN GENETICS

Int J Hum Genet, 1(2): 157-163 (2001)
PRINT: ISSN 0972-3757 ONLINE: ISSN 2456-6330
DOI: 10.31901/24566330.2001/01.02.15

Allelic Imbalance and Loss of Heterozygosity at 5q11 in Human Prostate Cancer: A Novel Region for a Tumor Suppressor Gene

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KEY WORDS Prostate cancer genetics; LOH; allelic imbalance; tumor suppressor gene; micro-satellite instability.

ABSTRACT Loss of heterozygosity (LOH) and allelic imbalance (AI) are widely recognized ways of localizing tumor suppressor genes. We have demonstrated structural alterations of chromosome 5 in 12 human prostate cancer cell lines. After mapping the breakpoints involved in translocations and deletions in chromosome 5, the 5q11 region was found to be the most consistent breakpoint. In this study, we further analyzed the 5q11 region in several prostate cancer cell lines as well as tumor samples from prostate cancer patients. Five different polymorphic sequence tagged sites (STSs) (D5S430, D5S822, D5S664, D5S645, and D5S2068) from this region were evaluated for LOH in order to discern the specific breakpoint in chromosome 5. A breakpoint was shown between the markers D5S2068 and D5S407 in the PC-3M human prostate cancer cell line. Allelotyping of prostate tumor samples revealed LOH in 6 (65%) of 9 tumor samples in at least one of the markers tested. In addition, in three cell lines (DU-145, MDAPCa2b and C4-2) microsatellite instability (MSI), shown as gain of alleles, was observed, suggesting RER^{+} phenotype. These results implicated 5q11 and specifically the region surrounding markers D5S2068 as a region of interest for locating a tumor suppressor gene in human prostate cancer.

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