Molecular genetics of urological tumours

1994 Fiscal Year Final Research Report Summary

MOLECULAR GENETICS OF UROLOGICAL TUMOURS

Research Project

Project/Area Number

04670955

Research Category

Grant-in-Aid for General Scientific Research (C)

Allocation Type

Single-year Grants

Research Field

泌尿器科学

Research Institution

KANAZAWA UNIVERSITY

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Project Period (FY)

1992 – 1994

Keywords

RFLP / RT-PCR / p53 / UROLOGICAL TUMOUR / ONCOGENE

Research Abstract

We applied restriction fragment length polymorphism (RFLP) analysis to 24 cases of renal cell carcinomas (RCC) , 18 cases of prostate adenocarcinoma (PC) , and 11 cases of transitional cell carcinomas (TCC) in renal pelvis to study the oncogene amplification and inactivation of tumor suppresor genes. All of the cases showed no amplification nor gross rearrangements of the Harvey ras, c-myc, c-fos, EGFR and PDGFR.In contrast, RFLP analyzes demonstrated allelic losses interpreted as inactivational events of TSGs among the tumor forms studied. RCC had allelic

losses on the short arm of chromosome 3 (3p) (68%) , the long arm of chromosome 18 (18q) (33%) , Y chromosome (29%) , and 17p (27%) at high frequencies. PC showed frequent allelic losses on 16q (67%) , 8p (50%) , 18q (43%) , 10p (40%) , and 10q (38%) . TCC had allelic losses on 17p (73%) , 11p (64%) , and 9q (40%) . It was likely that the cases with the more malignant grade tumor had the more allelic losses.
We tried to identify prost ate cancer cells by detecting messenger RNA (mRNA) of prostate specific antigen (PSA) amplified using reverse transcriptase-polymerase chain reaction (RT-PCR) assay. A panel of cell lines derived from diverse human neoplastic tumors were investigated, resulting that no cell lines tested were positive by the assay except for prostate cancer cell line, LNCaP cells. Sensitivity of the assay was tested using a serial dilution of PSA-positive LNCaP cells with PSA-negative human embryonic lung fibroblast (HEL) cells. Only 10^<-4> mg RNA of LNCaP cells in 1 mg RNA of HEL cells was detected on the a agarose gel under ultraviolet illumination. Therefore, the PSA-directed RT-PCR assay could be sensitive and specific molecular marker for prostate cancer cells.
The positivities of this assay in a spectrum of stages of prostate cancer patients were as follows ; 0 of 1 stage A1 : 0 of 2 stage A2 : 2 of 5 stage B : 2 of 8 stage C : 3 of 3 stage D0 : 1 of 4 stage D1 : 7 of 11 stage D2.totally, 16 of 36 patients with prostate cancer (44.4%) were positive. The clinical usefulness of the PSA-based RT-PCR assay is under assessment in terms of earlier staging diagnosis of prostate cancer in an individual case.
The p53 gene is known to be one of the frequently altered tumor suppressor genes, and involved in the oncogenesis of a wide spectrum of human malignant tumors. We investigated mutational event of the p53 gene in 18 clinically untreated prostate cancers. Direct sequencing analysis demonstrated that 1 of 18 cases harbored point mutation in the highly conserved transcript region. The case showed CAT at codon 273 instead of wild type CGT,substituting the encoded amino acid from histidine to arginine. The case had previously revealed homozygous loci on 17p, including the p53 locus, by restriction fragment length polymorphism analysis. Other 17 cases harbored no mutation nor small deletion. It is concluded that point mutation of the p53 gene is a infrequent event in the oncogenesis of untreated prostate cancer.▲ Less

Research Products (17 results)

All Other

All Publications (17 results)

[Publications] Kazuto Kunimi et.al.: "Allelotyping of human prosthtic adenocorunoma" Genomics. 11. 530-536 (1992)

[Publications] Tadao Uchibayashi et.al.: "Stndies of effeats of anticonor agents in combihation with/without typerthernia on metastasized human bledder caryr cells in chick ambryos aeingthe prlymerhcl chain reaetion feonmigne" Canur Chenvother Pharmacol.35. 84-87 (1994)

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[Publications] Javier S Castresana et al.: "Laek of mutation at udon 12 of the c-H-ras onwgene in 51 human sarcomasasseceaud by PCT-RFLP" Int.J.Oncol. 2. 823-825 (1993)

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