

# 泌尿器科領域悪性腫瘍における癌関連遺伝子群の異常に関する研究

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# 1994 Fiscal Year Final Research Report Summary

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## MOLECULAR GENETICS OF UROLOGICAL TUMOURS

Research Project

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04670955

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### Allocation Type

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### Research Field

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泌尿器科学

### Research Institution

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### Project Period (FY)

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1992 - 1994

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

### Research Abstract

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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 suppressor 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 prostate 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<sup>-4</sup> mg RNA of LNCaP cells in 1 mg RNA of HEL cells was detected on the 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 prosthctic 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 bladder caryr cells in chick ambryos aeingthe plymerhcl chain reaetion feonmigne" Canur Chenvother Pharmacol.35. 84-87 (1994) ▼
- [Publications] Kazuto Kunimi et al.: "Point mutation of the 53 gene is an intregneht erent in untreated pnesthtic cancer" J.Caner Preventian and Petaetian. in press. (1995) ▼
- [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) ▼
- [Publications] Kazuto Kunimi et al.: "Nuclear deoxyribonucleic aeid contont in inverted papilloma of the wotholiua" Eur Uiol. 26. 149-152 (1994) ▼
- [Publications] Tadao Uchibayashi et al.: "Expression of interferon senas in cultured human cancer cells" Urol Res. (in press). (1995) ▼
- [Publications] Tadao Uchibayashi et al.: "Oncoganes and Moleanlar genetics of Urological Tumours" Olsson C.A., (1992) ▼
- [Publications] Kazuto Kunimi et al.: "Allelotype of urothelial and pnestatic cancers" Olsson C.A., (1992) ▼
- [Publications] Kazuto Kunimi, Ulf S R Bergerheim, Inga-Lisa Larsson, Peter Ekman, Peter Collins: "Allelotyping of human prostatic adenocarcinoma." Genomics. 11. 530-536 (1992) ▼
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- [Publications] Tadao Uchibayashi, Soo-Woong Lee, Kazuto kunimi, Mitsuo Ohkawa, Yoshio Endo, Mika Noguchi, Takuma Sasaki: "Studies of Effects of anticancer agents in combination with/without hyperthermia on metastasized human bladder cancer cells in chick embryos using the polymerase chain reaction teqnique." Cancer Chemother Pharmacol.35. S84-S87 (1994) ▼
- [Publications] Kazuto Kunimi, Toshiyasu Amano, Tadao Uchibayashi: "Point mutation of the p53 gene is an infrequent event in untreated prostate cancer." J Cancer Prevention and Detection.(in press). (1995) ▼

[Publications] Kazuto Kunimi, Tadao Uchibayashi, Tadahiro Kobayashi, Testuya Imao, Yoshio Endo, Takuma Sasaki: "Molecular detection of prostate cancer cells by prostate specific antigen-directed reverse transcriptase-polymerase chain reaction." J Cancer Prevention and Detection.(in press). (1995) ▼

[Publications] Tadao Uchibayashi, Tohru Hasegawa, Kazuto Kunimi, Yoshio Endo, Takuma Sasaki: "Expression of interferon genes in cultured human cancer cells." Urol.Res.(in press). (1995) ▼

[Publications] Tadao Uchibayashi, Haruo Hisazumi, kazuto Kunimi, Toru Hasegawa: Specific detection of metastasized human tumour cells in embryonic chicks by the polymerase chain reaction. In Oncogenes and Molecular genetics of Urological Tumours.eds by Olsson C.A.churchill Livingstone, London, 51-59 (1992) ▼

[Publications] Kazuto Kunimi, VP Collins, U S R Bergerheim, L Andersson, Tadao Uchibayashi, Haruo Hisazumi: Allelotype of urothelial and prostatic cancers. In Oncogenes and Molecular genetics of Urological Tumours.eds by Olsson C.A.Churchill Livingstone, London, 155-163 (1992) ▼

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