

# Gene therapy against gynecologic cancers targeting telomerase

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# 1999 Fiscal Year Final Research Report Summary

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## Gene therapy against gynecologic cancers targeting telomerase

Research Project

### Project/Area Number

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09470354

### Research Category

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Grant-in-Aid for Scientific Research (B)

### Allocation Type

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Single-year Grants

### Section

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一般

### Research Field

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Obstetrics and gynecology

### Research Institution

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Kanazawa University

### Principal Investigator

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### Project Period (FY)

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1997 - 1999

### Keywords

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Gynecologic tumors / Telomere / Telomerase / hTERT / hTERT-promoter / Gene therapy

### Research Abstract

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Human telomerase is composed of three main subunit components, human telomerase RNA (hTR), telomerase-associated protein (TP1) and telomerase reverse transcriptase (hTERT). RT-PCR analyses demonstrated that expression of hTERT was observed in cancer tissues and cell lines, while hTR or TP1

was broadly expressed not only in cancers but also in normal tissues. Thus, hTERT expression was well correlated with telomerase activity. We succeeded to clone promoter sequences of hTERT gene. Of particular importance is identification of transcription factors interacting with such regions and regulate hTERT express in utilizing it for gene therapy. C-Myc has been shown to be a direct transactivator of hTERT gene. Antisense strategy against c-Myc has been in success to inhibit telomerase activity in cancer cells and suppress the tumor growth. As another strategy, we have applied hTERT promoter to plasmid or virus vectors for gene therapy. We have constructed a chimeric vector in which hTERT promoter is cloned upstream of apoptosis-inducing genes inhibiting cell growth and introduced of these vectors into cervical cancer cells. We have confirmed the specific inhibition of tumor growth in cell lines and animal models by these gene therapies.

## Research Products (19 results)

All Other

All Publications (19 results)

- [Publications] Kyo S, Takakura M, et al.: "Estrogen activates telomerase"Cancer Res.. 59. 5917-5921 (1999) ▼
- [Publications] Takakura M, Kyo S, et al.: "Cloning of human telomerase catalytic subunit (hTERT) gene promoter"Cancer Res.. 59. 551-557 (1999) ▼
- [Publications] Segawa T, Sasagawa T: "Fragile histidine triad transcription abnormalities"Cancer. 85. 2001-2010 (1999) ▼
- [Publications] Kyo S, Kanaya T: "Human telomerase reverse transcriptase as a critical determinant of telomerase activity"Int J Cancer. 80. 60-63 (1999) ▼
- [Publications] "Spl cooperates with c-myc to activate transcription of human telomerase reverse transcriptase (hTERT) gene"Nucleic Acid Res.. (In press). (2000) ▼
- [Publications] Kyo S, Takakura M, Inoue M.: "telomerase activity in cancer as a diagnostic and therapeutic target"Histology and Histopathology. (In press). (2000) ▼
- [Publications] Kyo S, Takakura M, Kanaya T, Taira T, Ithoh H, Yutsudo M, Ariga H, Inoue M.: "Sp1 cooperates with c-myc to activate transcription of human telomerase reverse transcriptase (hTERT) gene."Nucleic Acid Res.. (In press.). (2000) ▼
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- [Publications] Kanaya T, Kyo S, Hamada K, Takakura M, Kitagawa Y, Harada H, Inoue M.: "Adenoviral expression of p53 represses telomerase activity through the transcriptional down regulation of hTERT."Clin Cancer Res.. (In press.). (2000) ▼
- [Publications] Sasagawa T Shimakage M, Nakamura M, Sakaike J, Ishikawa H, Inoue M.: "Epstein-barr virus (EBV) genes expression in cervical intraepithelial neoplasia and invasive cervical cancer ; a comparative study with human papillomavirus infection."Human Pathol.. (In press.). (2000) ▼
- [Publications] Ninomiya I, Endo Y, Sasagawa T, Miwa K, Inoue M.: "Bata-catenin expression in esophageal cancer."Int J cancer.. (In press.). (2000) ▼
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- [Publications] Kyo S, Takakura M, Kanaya T, Wang Z, Fujimoto K, Orio A, Inoue M.: "Estrogen activates telomerase."Cancer Res.. 59. 5917-5921 (1999) ▼
- [Publications] Nakashima R, Fujita M, Enomoto T, Haba T, Yoshino K, Wada H, Kurachi H, Inoue M, Burzard O, Murata Y.: "Alteration of p16 and p15 genes in human uterine tumors."Brit J Cancer. 80. 458-467 (1999) ▼
- [Publications] Takakura M, Kyo S, Kanaya T, Hirano H, Takeda J, Yutsudo M, Inoue, M.: "Cloning of human telomerase catalytic subunit (hTERT) gene promoter identification of proximal core promoter sequences essential for transcriptional activation in immortalized and cancer cells."Cancer Res.. 59. 551-557 (1999) ▼
- [Publications] Segawa T, Sasagawa T, Inoue M.: "Fragile histidine triad transcription abnormalities and human papillomavirus E6-E7 mRNA expression in the development of cervical carcinoma."Cancer. 85. 2001-2010 (1999) ▼
- [Publications] Kyo S, Kanaya T, Takakura M, Tanaka M, Inoue M.: "Human telomerase reverse transcriptase as a critical determinant of telomerase activity in normal and malignant endometrial tissues."Int J Cancer. 80. 60-63 (1999) ▼

[Publications] Kyo S, Kanaya T, Takakura M, Tanaka M, Yamashita A, Inoue H, Inoue M.: "Expression of human telomerase subunits in ovarian malignant borderline and benign tumors."Int J Cancer. 80. 804-809 (1999) ▼

[Publications] Ueno H, Yamashita K, Azumano I, Inoue M, Okada Y.: "Enhanced production and activation of metalloproteinase-7 in human endometrial carcinomas."Int J Cancer. 84. 470-477 (1999) ▼

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