

婦人科癌におけるテロメラーゼをターゲットにした遺伝子治療

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雑誌名	平成11(1999)年度 科学研究費補助金 基盤研究(B) 研究成果報告書概要
巻	1997 1999
ページ	3p.
発行年	2001-10-22
URL	http://doi.org/10.24517/00065989



1999 Fiscal Year Final Research Report Summary

Gene therapy against gynecologic cancers targeting telomerase

Research Project

Project/Area Number

09470354

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Obstetrics and gynecology

Research Institution

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Project Period (FY)

1997 - 1999

Keywords

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

Research Abstract

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) ▼
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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) ▼
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- [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) ▼

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URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-09470354/094703541999kenkyu_seika_hokoku_

Published: 2001-10-22