婦人科癌をターゲットにした新たな遺伝子治療の戦略

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2002 Fiscal Year Final Research Report Summary

Establishment of novel gene therapy targeting gynecologic tumors

Research Project

Project/Area Number

13557138

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

展開研究

Research Field

Obstetrics and gynecology

Research Institution

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Project Period (FY)

2001 – 2002

Keywords

Telomerase / Gene therapy / hTERT / hTR / Gynecologic tumors

Research Abstract

We established novel methods that inhibit telomerase activity in cancer cells using 2-5Adenylate-linked antisense DNA against human telomerase RNA component (hTR). This antisense DNA effectively blocked telomerase activity in cervical cancer ME180 cells. Growth of ME180 cells in vitro was significantly inhibited by the treatment with 2-5A anti-hTR. Surprisingly, inhibition of cell growth was observed in 24-48 hr after treatment, quite earlier than expected. Telomere length was not shortened in this short period. These findings suggest that blockade of telomerase led to cell growth inhibition via telomere-independent mechanisms. We confirmed that growth inhibition of cells by the treatment with 2-5A anti-hTR was due to induction of apoptosis. The further anaylsis of mechanisms how 2-5A anti-hTR induces apoptosis is on going.
We also established novel vector system for cancer gene therapy. We previously cloned promoter of human telomerase reverse transcriptase (hTERT), which is highly specific to cancer cells. We thus used this promoter for cancer-specific gene expression in gene delivery system. Various apoptosis-inducible genes, such as caspase-8 and

FADD, were combined with hTERT promoter and used as vectors for cancer gene therapy. Introduction of these vectors effectively induced apoptosis of cancer cells but of surrounding normal tissues.

Research Products (12 results)

All | Other

All | Publications

[Publications] Kyo S, Masutomi K, Maida M, et al.: "Significance of immunological detection of hTERT : re-evaluation of expression and localization of hTERT"Am.J.Pathol.. (印刷中).

[Publications] Tanaka M, Kyo S, Kanaya T, et al.: "Evidence of monoclonal composition of human endometrial epithelial glands and mosaic pattern of clonal distribution in luminal epithelium"Am.J.Pathol.. (印刷中).

[Publications] Kyo S, Inoue M.: "Complex regulatory mechanisms of telomerase activity in normal and cancer cells : How can we apply them for cancer therapy?"Oncogene. 21. 688-697 (2002)

[Publications] Maida Y, Kyo S, Kanaya T, et al.: "Is the telomerase assay useful for screening of endometrial lesions"Int.J.Cancer. 100. 714-718 (2002)

[Publications] Yatabe N, Kyo S, Kondo S., et al.: "2-5A antisense therapy directed against human telomerase RNA inhibits telomerase activity and induces apoptosis without telomere impairement in cervical cancer cells"Cancer Gene Ther.. 9. 624-630 (2002)

[Publications] Maida M, Kyo S, Kanaya T., et al.: "Direct activation of telomerase by EGF through Ets-mediated transactivation of TERT via MAP kinase signaling pathway"Oncogene. 21. 4071-4079 (2002)

[Publications] Kyo S., Masutomi K., Maida M., et al.: "Significance of immunological detection of hTERT: re-evaluation of expression and localization of hTERT"Am. J. Pathol. in press (2003)

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