

Polymorphism of thymidylate synthase gene in human gastrointestinal carcinoma cells and its regulational role in protein expression

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2000 Fiscal Year Final Research Report Summary

Polymorphism of thymidylate synthase gene in human gastrointestinal carcinoma cells and its regulational role in protein expression

Research Project

Project/Area Number

11671216

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Digestive surgery

Research Institution

Kanazawa University

Principal Investigator

OMURA Kenji Dept.of Surg (1).Kanazawa Univ. Associate Professor, 医学部・附属病院, 講師 (30194301)

Co-Investigator(Kenkyū-buntansha)

KAWAKAMI Kazuyuki Dept.of Surg (1). Kanazawa Univ. Research Assistant, 医学部・附属病院, 助手 (00293358)

KANEHIRA Eiji Dept.of Surg (1). Kanazawa Univ. Research Assistant, 医学部・附属病院, 助手 (10251951)

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Keywords

thymidylate synthase / gene polymorphism / translational activity / posttranscriptional regulation / tandem repeat sequence / complementary repeat sequence / 5-fluorouracil / chemosensitivity predictor

Research Abstract

We performed cloning of thymidylate synthase (TS) genes with various tandem repeat sequence (2, 3, 4, 5 and 6 repeats) in the 5' untranslated region (5'UTR). Furthermore, we observed translational activity of each genotype TS mRNA with or without complementary reverse sequence in the upstream of the repeat sequence by reticulocyte lysate translation assay. The translational activity of full-length TS mRNAs, which included both of the tandem repeat sequence and complementary reverse sequence, were quirk lowirrespective of the number of the repeat sequence. However, obvious elevation of translational activity was observed when the number of the

repeat sequence was increased. Translational activity increased markedly in the TS mRNAs without the complementary reverse sequence compared with the full-length TS mRNAs. The elevation of translational activity with increment of number of the repeat sequence disappeared in the TS mRNAs without the complementary reverse sequence. Capped TS mRNAs, both with and without complementary reverse sequence, showed increase of its translational activity. The products of reticulocyte lysate translation assay were confirmed as TS protein by Western blotting using polyclonal TS anti-body. The stem-loop structure, formed by repeat sequence and complementary reverse sequence, should inhibitively control the translational activity of TS mRNA. Further, some protein supposed to bind the stem-loop structure and regulate its inhibitory action. Further studies are required to look for the protein which binds to the stem-loop structure formed in 5'UTR of TS mRNA and its influence on the translational activity of TS mRNA.

Research Products (12 results)

All Other

All Publications

- [Publications] Kenji Omura, et al: "Quantification of thymidylate synthase gene expression in human gastrointestinal carcinoma tissue using competitive PCR."Hepato-Gastroenterology. 46. 985-990 (1999) ▼
- [Publications] Kazuyuki Kawakami et al: "Polymorphic tandem repeats in the thymidylate synthase gene is associated with its protein expression in human gastrointestinal cancers"Anticancer Research. 19. 3249-3252 (1999) ▼
- [Publications] Kenji Omura, et al: "Expression of thymidylate synthase in human gastric and colorectal adenocarcinoma is upregulated by p16/INK4."Hepato-Gastroenterology. 47. 742-745 (2000) ▼
- [Publications] Kazuyuki Kawakami et al: "Methylenetetrahydrofolate reductase polymorphism is associated with folate pool in gastro intestinal cancer tissue"Anticancer Research. 21. 285-289 (2001) ▼
- [Publications] 大村健二 ほか: "進行・再発消化器癌に対する化学療法戦略の理論的構築"癌と化学療法. 28. 63-68 (2001) ▼
- [Publications] 大村健二 ほか: "Thymidylate synthaseを介する感受性機構"Oncology & Chemotherapy. 16. 222-225 (2000) ▼
- [Publications] Kenji Omura, Minoru Morishita, Kazuyuki Kawakami, Eiji Kanehira, Yoshinori Ishida, Yoh Watanabe: "Quantification of thymidylate synthase gene expression in human gastrointestinal carcinoma tissues using competitive PCR."Hepato-Gastroenterol.. 46(26). 985-990 (1999) ▼
- [Publications] Kazuyuki Kawakami, Kenji Omura, Eiji Kanehira, Yoh Watanabe: "Polymorphic tandem repeats in the thymidylate synthase gene is associated with its protein expression in human gastrointestinal cancers."Anticancer Res.. 19(4B). 3249-3252 (1999) ▼
- [Publications] Kenji Omura, Yusuke Uno, Kazuyuki Kawakami, Eiji Kanehira, Kanae Tawaraya, Masaichi Tsukayama, Chikashi Hiranuma, Yoh Watanabe: "Expression of thymidylate synthase in human gastric and colorectal adenocarcinomas is upregulated by p16/INK4."Hepato-Gastroenterol.. 47(33). 742-745 (2000) ▼
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- [Publications] Kenji Omura, Kazuyuki Kawakami, Eiji Kanehira: "Theoretical construction of chemotherapeutic tactics for advanced or recurrent gastrointestinal carcinoma."Gan To Kagaku Ryoho. 28(1). 63-68 (2001) ▼
- [Publications] Kenji Omura, Kazuyuki Kawakami, Eiji Kanehira.: "Chemosensitivity related to expression of thymidylate synthase."Oncology & Chemotherapy. 16(3). 222-225 (2000) ▼

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