

葉酸受容体の組織特異的遺伝子発現に関する転写因子の同定とcDNAクローニング

メタデータ	言語: Japanese 出版者: 公開日: 2022-05-20 キーワード (Ja): キーワード (En): 作成者: メールアドレス: 所属:
URL	https://doi.org/10.24517/00056959

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1998 Fiscal Year Final Research Report Summary

Identification and cDNA cloning of the transcriptional factors regulating the tissue-specific expression of human alpha-folate receptor gene

Research Project

Project/Area Number

09670793

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Pediatrics

Research Institution

Kanazawa University

Principal Investigator

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Project Period (FY)

1997 - 1998

Keywords

alpha human folate receptor gene / tissue specific expression of the gene / drug resistance / transcriptional factor

Research Abstract

1. I-identification of the nuclear DNA-binding proteins involving the specific expression of alpha human folate receptor (hFR) gene : we have identified two promoters which are independently active in a tissue-specific manner in regulation of the alpha hFR gene expression. To further characterize the regulation of these promoters, the transcriptional elements involved in the promoter located upstream of exon 1 were investigated in the transport-defective methotrexate-resistant KB cells (02) by sequence analysis of the promoter, gel shift assays, nuclear run-on assays, and RNase protection assays.

Compared to wtKB cells grown in physiologic concentrations of folate, we demonstrate that (1) the O2 cells expressed 2% of a hFR protein and its mRNA ; (2) the transcription rate of a hFR gene was reduced 7 fold in the O2 cells relative to wtKB cells ; (3) the nuclear protein(s) that forms a complex with a -352/-461 (109 bp) DNA fragment located approximately 400 bp upstream of the transcription start site was demonstrated in wtKB cells and was significantly reduced in the C2 cells ; (4) based on competitive gel shift assays using several synthetic oligonucleotides corresponding - 426/-461 DNA sequences, a -4391-452 DNA fragment contained the specific binding sites of this nuclear protein(s). This sequence contains potential binding sites of CCAAT-enhancer binding protein beta, GATA-2, and Ets-1. The supershift assays using antibodies against these proteins will be performed to characterize the factor(s) to this region.

2. Tissue specific expression of the nuclear factor(s) : the binding of nuclear protein(s) to this DNA fragment was also decreased in MCF-7, MDCK, ACHN, SN12C, and TK- 10 celllines in which expression of the alpha hFR is not detectable. These results suggest that this factor may be involved in the tissue-specific expression of alpha hFR gene and in the modulation of receptor expression in antifolate resistant KB cells.

Research Products (18 results)

All Other

All Publications (18 results)

[Publications] Elwood,P.C.: "The divergent 5' termini of the a human folate receptor (hFR) mRNAs originate from two tissue-specific promoters and alternative splicing: characterization of the a hFR gene structure." *Biochemistry*. 36 · 6. 1467-1478 (1997) ▼

[Publications] Nishimura,R: "Microsatellite analysis of childhood leukemia and lymphoma: 9p and 12p abnormalities and expression of related genes." *Proc Am Soc Clin Oncol*. 17. 545a (1998) ▼

[Publications] Nishimura,R: "Microsatellite analysis of B-ALL:9p and 12p abnormalities and expression of related genes." *International Journal of Hematology*.67suppl. 90 (1998) ▼

[Publications] Saikawa,Y.: "Alteration of the transcriptinal factors involved in the human folate receptor gene expression in transport-defective methotrexate-resistant KB cells." *International Journal of Hematology*. 67suppl. 107 (1998) ▼

[Publications] Saikawa,Y.: "Alteration of the transcriptinal factors involved in the human folate receptor gene expression in transport-defective methotrexate-resistant KB cells." *Blood*. 92suppl. 1946 (1998) ▼

[Publications] Wada,H: "Overexpression of multidrug resistance-associated protein (MRP) gene in refractory B-cell non-Hodgkin's lymphoma." *International Journal of Pediatric Hematology Oncology*. 5 · 5. 303-312 (1998) ▼

[Publications] Sakakibara,M: "Membrane-type matrix metalloproteinase-1 expression and activation of gelatinase A as prognostic markers in advanced pediatric neuroblastomas." *Cancer*. 85 · 1. 231-239 (1999) ▼

[Publications] Wada,H.: "Selectively induced high MRP gene expression in multidrug resistant human HL60 leukemia ce" *Experimental Hematology*. 27. 99-109 (1999) ▼

[Publications] Nishimura,R: "Inactivated p16 gene in relapsed childhood acute leukemias as a prognostic determinant." *Proc Am Soc Clin Oncol*. in press. (1999) ▼

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[Publications] Saikawa, Y.: "Alteration of the transcriptinal factors involved in the alpha human folate receptor gene expression in transport-defective methotrexate-resistant KB cells." *International Journal of Hematology*. 67, suppl.107 (1998) ▼

[Publications] Saikawa, Y.: "Alteration of the transcriptinal factors involved in the alpha human folate receptor gene expression in transport-defective methotrexate-resistant KB cells." *Blood*. 92, suppl.194b (1998) ▼

[Publications] Wada, H.: "Overexpression of multidrug resistance-associated protein (MRP) gene in refractory B-cell non-Hodgkin's lymphoma." *International Journal of Pediatric Hematology Oncology*. 5. 303-312 (1998) ▼

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URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-09670793/096707931998kenkyu_seika_hokoku

Published: 1999-12-07