

B型肝炎ウイルスX蛋白の機能

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2004 Fiscal Year Final Research Report Summary

Function of Hepatitis B Virus X protein

Research Project

Project/Area Number

12213050

Research Category

Grant-in-Aid for Scientific Research on Priority Areas

Allocation Type

Single-year Grants

Review Section

Biological Sciences

Research Institution

KANAZAWA UNIVERSITY

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Project Period (FY)

2000 - 2004

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HBv X protein / RNA polymerase / RPB5 / RMP / HBV replicon / Transcriptional modulation / Telomerase

Research Abstract

For better understanding molecular mechanism of transcriptional modulation by HBV X protein (HBx), we studied structure and function of RNA polymerase subunit 5 (RPB5) as a nuclear target of HBx, and contribution of HBx on immortalization and/or transformation process of human cells. In addition, subcellular localization and nuclear function of RMP which is a functional antagonist of HBx. The followings are main results of the project in this fiscal year.

1) By analyzing clustered alanine substitution mutant (Cm) and point mutant (Pm) libraries of the middle part of RPB5, we pinpointed 6 residueus

critical for HBx-binding and 6 residues for TFIIF subunit RAP30-binding. Among them, 4 residues - F76, 1104, T111 and S113, are critical both for the bindings. The former two residues are not solvent exposed and probably contributing to the structural integrity. T111 and S113 are exposed and is in near position to DNA in light of the Pol II crystal models. The 4 residues are also critical or important for DNA-binding ability of RPB5 (in preparation). Taken together, DNA-binding ability of RPB5 may be the target of HBx and RAP30.

2) Using the Cm library of HBx, we addressed the critical region(s) of HBx for augmentation ability on HBV replication in a HBV replicon system, which is defective in X-ORF. Two discontinuous regions in the coactivation domain of HBx are indispensable for the augmentation effect on HBV replication. In the same experiment, the same regions were required not only for increase in HBV DNA but also for increase in pregenomic (pg) RNA. The same regions were also critical for the coactivation function of HBx, suggesting that HBx coactivates pgRNA synthesis that resulted in increase in HBV DNA synthesis.

3) Recently it was found that RMP/URI, a functional antagonist of HBx, is localized with RPB5 in cytoplasm. Subcellular localization of RMP/URI can be modulated in the presence of DMAP1 and nuclear RMP/URI acts as a corepressor. From these results, RMP/URI is a regulatory protein in cytoplasm as well as nucleus.

4) We addressed whether HBx acts positively in immortalization and/or transformation process of human cells. In our preliminary results, immortalization of human primary cells is barely affected by HBx, but transformation frequency of immortalized human cells seems to be augmented by HBx in the presence of activated oncogenes. This facilitating role of HBx requires the coactivation domain of HBx.▲ Less

Research Products (46 results)

All	2005	2004	2003	2002	2001	2000
All Journal Article (46 results)						

- [Journal Article] Transcriptional transactivation function of HBx protein is important for the augmentation role in Hepatitis B Virus replication **2005** ▾
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- [Journal Article] Subcellular localization of RPB5-mediating protein and its putative functional partner **2004** ▾
- [Journal Article] Hepatitis B virus X protein induces angiogenesis by stabilizing hypoxia-inducible factor-1alpha **2004** ▾
- [Journal Article] Effect of interaction between Hepatitis C Virus NS5A and NS5B on the Hepatitis C Virus replicon **2004** ▾
- [Journal Article] Mutational analysis of Hepatitis C Virus NS5B in the subgenomic replicon cell culture **2004** ▾
- [Journal Article] Nucleolin interacts with telomerase **2004** ▾
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- [Journal Article] Interaction with general transcription factor TFIIF (TFIIIF) is required for the suppression of the activated transcription by RPB5-mediating protein RMP **2003** ▾
- [Journal Article] Significant of immunological detection of human telomerase reverse transcriptase : re-evaluation of expression and localization of human telomerase reverse transcriptase **2003** ▾
- [Journal Article] Direct interaction between nucleolin and Hepatitis C Virus NS5B **2003** ▾
- [Journal Article] Telomerase maintains telomere structure in normal human cells **2003** ▾

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