Function of Hepatitis B Virus X protein

2004 Fiscal Year Final Research Report Summary

Function of Hepatitis B Virus X protein

Research Project

Project/Area Number

12213050

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Grant-in-Aid for Scientific Research on Priority Areas

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Biological Sciences

Research Institution

KANAZAWA UNIVERSITY

Principal Investigator

MURAKAMI Seishi Dept of Mol. Oncology, Cancer Res. Inst., Professor, がん研究所, 教授 (90019878)

Co-Investigator(Kenkyū-buntansha)

HAYASHI Naoyuki Dept of Mol. Oncology, Cancer Res. Inst., Research Associate, がん研究所, 助手 (50253456)

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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 resideus

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 impor tant 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 abgiogenesis by stabilizing hypoxia-Inducible factor-lalfa 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 subgenomis replicon cell culture 2004

[Journal Article] Nucleolin interacts with telomerase 2004

[Journal Article] Hepatitis B virus X protein induces angiogenesis by stabilizing hypoxia-inducible factor-lalpha 2004

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[Journal Article] Nucleolin interacts with telomerase 2004

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[Journal Article] Significant of immunological detection of human telomerase reverseranscriptase : 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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[Journal Article] Direct interaction between Nucleoin and Hepatitis C Virus NS5B 2003

[Journal Article] STM1, a gene which encodes a guanine quadruplex binding protein interacts with CDC13 in Saccharomycec cerevisiae 2002

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[Journal Article] Direct interaction between the submit RAP30 of TFIIF and RNA polymerase subunit5(RPB5) which contributes to the association between TFIIF and RNA polymerase II 2001

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