Control of influenza virus pathogenicity by pkr inhibitor protein and its application

2001 Fiscal Year Final Research Report Summary

CONTROL OF INFLUENZA VIRUS PATHOGENICITY BY PKR INHIBITOR PROTEIN AND ITS APPLICATION

Research Project

Project/Area Number

12670279

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Virology

Research Institution

KANAZAWA UNIVERSITY

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Keywords

INFLUENZA VIRUS / PROTEIN KINESE R / NS1 PROTEIN / PHOSPHORYLATION / PATHOGENICITY

Research Abstract

The influenza virus nonstructural protein NS1 has been reported to have many functions. We previously demonstrated that it has an RNA binding activity, by which it inhibits the PKR activation in the infected cell. In addition, its RNA binding activity has been recently shown to participate in the resistance against interferon in influenza virus infection, underlining NS1 as a determinant for this virus pathogenicity. In this study, we analyzed the RNA binding ability of NS1 in more detail, and related it to the activation state of PKR, which is one of the indicators of this virus pathogenicity.
(1) Effect of C-terminal region of NS1 on its inhibition of PKR activation. The region of NS1 essential for its RNA binding was the N-terminal 82 araino acid sequence, which strongly inhibits the activation of PKR. This truncated NS1 in the presence of the following more than 60.araino acid sequence, and also the full-length NS1, attenuated this activity, and lost its poly A binding activity. It was newly disclosed that NS1'longer than N-terminal 82 amino acid,sequence has a binding ability to U clusters, and bound to the 5-6 U cluster at the 5'-terminal region of Vrna.
(2) Effect of phosphorylation of NS1 on its functions. We identified several Ser/Thr residues which are phosphorylated in the infected cells.
The effects of NS1 phosphorylation at each of these residues in vitro and in vivo are now investigated by constructing Ala or Asp substitution mutants of these residues. Phosphorylation of NS1 in vitro attenuated its RNA binding activity, but had little effect on its inhibition of the PKR activation. NS1 in the infected cells is distributed in the nucleus and the cytoplasm, and is associated with VRNP and ribosomes. The phosphorylation level of NS1 of these fractions were separately determined without appreciable difference among them.

Research Products (1 results)

All | Other

All | Publications (1 results)

[Publications] E.HATADA, R.FUKUDA: "(論文投稿中)"

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