Virus hepatitis A sampai E di Indonesia

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Hepatitis B Virus X Protein Upregulates mTOR Signaling through IKKβ to Increase Cell Proliferation and VEGF Production in Hepatocellular Carcinoma

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Abstract

Hepatocellular carcinoma (HCC), a major cause of cancer-related death in Southeast Asia, is frequently associated with hepatitis B virus (HBV) infection. HBV X protein (HBx), encoded by a viral non-structural gene, is a multifunctional regulator in HBV-associated tumor development. We investigated novel signaling pathways underlying HBx-induced liver tumorigenesis and found that the signaling pathway involving IκB kinase β (IKKβ), tuberous sclerosis complex 1 (TSC1), and mammalian target of rapamycin (mTOR) downstream effector S6 kinase (S6K1), was upregulated when HBx was overexpressed in hepatoma cells. HBx-induced S6K1 activation was reversed by IKKβ inhibitor Bay 11-7082 or silencing IKKβ expression using siRNA. HBx upregulated cell proliferation and vascular endothelial growth factor (VEGF) production, and these HBx-upregulated phenotypes were abolished by treatment with IKKβ inhibitor Bay 11-7082 or mTOR inhibitor rapamycin. The association of HBx-modulated IKKβ/mTOR/S6K1 signaling with liver tumorigenesis was verified in a HBx transgenic mouse model in which pIKKβ, pS6K1, and VEGF expression was found to be higher in cancerous than non-cancerous liver tissues. Furthermore, we also found that pIKKβ levels were strongly correlated with pTSC1 and pS6K1 levels in HBV-associated hepatoma tissue specimens taken from 95 patients, and that higher pIKKβ, pTSC1, and pS6K1 levels were correlated with a poor prognosis in these patients. Taken together, our findings demonstrate that HBx deregulates TSC1/mTOR signaling through IKKβ, which is crucially linked to HBV-associated HCC development.

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Introduction

Hepatocellular carcinoma (HCC), which occurs frequently in Southeast Asia, is one of the most important causes of cancer-related death in the world [1,2,3]. According to epidemiological studies [4,5,6,7], there is a strong correlation between chronic hepatitis B virus (HBV) infection and the occurrence of HCC. HBV X protein (HBx) is a well-known viral non-structural gene that operates as a multifunctional regulator by modulating activity of host cellular genes such as p53 [11,12,13] and transactivating some transcription factors including AP-1, NF-κB, CREB, and TBP [14,15]. Moreover, HBx is involved in the activation of multiple signaling pathways linked to cell proliferation and survival, such as RAS/RAF/MAPK, MEKK1/JNK, and PI3K/Akt [16,17,18]. Chronic inflammation is one of the key conditions of persistent HBV infection and has been implicated in tumor development [19,20,21]. The proinflammatory cytokines and chemokines, such as tumor necrosis factor α (TNF-α), IL-1, IL-6, and IL-8, produced in microenvironments, have been known to promote tumor development [22,23]. TNF-α is considered one of the most important factors involved in inflammation-mediated tumorigenesis [24,25,26], and the transcription factor NF-κB, a downstream signaling transducer of TNF-α, has been implicated in oncogenesis by promoting expression of genes related to cell proliferation and survival [27]. Activation of the inhibitor of nuclear factor κB (IκB) kinase (IKK) by TNF-α phosphorylates IκBs and promotes degradation of IκBs, resulting in nuclear translocation of NF-κB and induction of NF-κB downstream genes [28,29]. The involvement of the IKK/NF-κB pathway in HBV-induced hepatitis and HCC is well documented [30,31,32], whereas effects of IKKs independent of NF-κB on tumorigenesis have also been found [33,34,35]. It was recently reported that IKKβ increased tumor development and tumor angiogenesis by

Available in the National Library of Australia collection. Author: Sulaiman, H. Ali, ; Format: Book; ii, p.: ill. ; 25 cm.Infeksi virus oleh virus hepatitis B (HBV) menyebabkan banyak perubahan hepatosit yang disebabkan oleh aksi langsung dari protein yang dikodekan virus, .The Hepatitis B virus (HBV) can cause acute and chronic liver infections. It is transmitted through infected blood products, unprotected sex.Blood samples were collected from healthy volunteer blood donors from 21 of the 27 Indonesian provinces, and tested for antibodies to hepatitis C virus.A nationwide molecular epidemiological study on hepatitis B virus in Indonesia: Identification of two novel subgenotypes, B8 and C7. Article (PDF Available) in.H. Ali Sulaiman is the author of Virus Hepatitis A Sampai E Di Indonesia (avg rating, 1 rating, 0 reviews).Hepatitis B virus (HBV) infection is a major public health problem. Eijkman Institute for Molecular Biology, Jakarta, Republic of Indonesia; Faculty of Medicine.Hepatitis B virus subtypes and hepatitis C virus genotypes in patients with chronic liver disease or on maintenance hemodialysis in Indonesia. J. Med. Virol.Molecular Epidemiology of Hepatitis B Virus in Minangkabau Ethnic Group of. West Sumatera, Indonesia. Marlinang D. Siburian,1 Mariana D.B.A survey was performed to investigate HBV and HCV infection in Ujung Pandang . The total number of subjects was ; blood donors, 78 cases of acute.Background The Minangkabau is one of the major ethnic groups in Indonesia. Previous studies with a limited number of samples have shown a different.Hepatitis B virus pre-S2 start codon mutations in Indonesian liver disease Indonesia has a moderate to high endemnicity of HBV infection[2].Indonesia; Department of Microbiology, Cenderawasih University School of Medicine hepatitis B virus (HBV) have been identified worldwide.Human immunodeficiency virus, hepatitis B and hepatitis C in an Indonesian prison: prevalence, risk factors and implications of HIV screening. Erni J. Nelwan1,2.Hepatitis A, hepatitis B dan hepatitis C adalah virus yang berlainan yang Sampai saat ini di Australia masih beresiko, demikian juga di negara anda dilahirkan Jika Anda ingin menghubungi pelayanan tersebut dalam bahasa Indonesia.