Peran Penghambat Matriks Metaloproteinase-9 pada Replikasi Virus Hepatitis B: Kajian terhadap MMP-9, IFNAR1, IFN-, HBsAg, DNA VHB, dan cccDNA, Studi In Vitro pada Hepatosit Tupaia Javanica dan PBMC Manusia = The Role of Matrix Metalloproteinase-9 Inhibitor in Hepatitis B Virus Replication: Analysis of MMP-9, IFNAR1, IFN-Î², HBsAg, HBV DNA, and cccDNA, an In Vitro Study in Tupaia javanica Hepatocyte and Human PBMC

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Abstrak

Infeksi virus hepatitis B (VHB) merupakan masalah kesehatan global. Terapi yang ada saat ini hanya berdampak minimal terhadap covalently closed circular deoxyribonucleic acid (cccDNA), sehingga eradikasi sulit dicapai. Matriks Metaloproteinase-9 (MMP-9) berperan dalam meningkatkan replikasi VHB, namun belum ada penelitian yang mengevaluasi peran penghambat MMP-9 terhadap replikasi VHB. Kultur primer hepatosit diperoleh dari Tupaia javanica dan diinfeksi dengan VHB manusia, kemudian dibagi menjadi dua kelompok, yaitu kontrol dan intervensi. Kelompok intervensi diberikan penghambat MMP-9 dosis 1 nM, 3 nM, dan 7 nM. Peripheral blood mononuclear cells (PBMC) manusia diperoleh dari pasien hepatitis B kronik, kemudian dibagi menjadi dua kelompok, yaitu kontrol dan intervensi. Kelompok intervensi diberikan penghambat MMP-9 dosis 3 nM. Dilakukan pengukuran HBsAg, DNA VHB, cccDNA, MMP-9, type-1 IFN receptor 1 (IFNAR1), dan interferon- (IFN-) sebelum dan 72 jam setelah pemberian intervensi pada kedua kelompok. Pada kultur primer hepatosit T. javanica yang diinfeksi VHB manusia, pemberian penghambat MMP-9 dosis 1 nM, 3 nM, dan 7 nM secara konsisten menurunkan kadar HBsAg, DNA VHB, cccDNA, dan MMP-9. Dosis 3 nM meningkatkan kadar IFNAR1, sedangkan dosis 7 nM meningkatkan kadar IFN-. Dosis 3 nM menunjukkan efek yang lebih optimal dibandingkan dosis lainnya. Pada PBMC manusia dengan infeksi VHB, pemberian penghambat MMP- 9 dosis 3 nM menurunkan kadar HBsAg, DNA VHB, cccDNA, dan MMP- 9, serta meningkatkan kadar IFN-, namun menurunkan kadar IFNAR1. Studi ini menunjukkan bahwa pemberian penghambat MMP-9 dapat menurunkan kadar HBsAg, DNA VHB, cccDNA, dan MMP-9, serta meningkatkan kadar IFN- pada kultur primer hepatosit T. javanica dan PBMC manusia.

.....Hepatitis B virus (HBV) infection remains a significant global health concern. Current therapies have minimal impact on covalently closed circular deoxyribonucleic acid (cccDNA), making HBV eradication difficult. Matrix Metalloproteinase-9 (MMP-9) enhance HBV replication, but its inhibition has not been studied. Primary hepatocyte cultures were obtained from Tupaia javanica and infected with human HBV, then divided into control and intervention groups. The intervention groups were treated with MMP-9 inhibitors at doses of 1 nM, 3 nM, and 7 nM. Human peripheral blood mononuclear cells (PBMC) were isolated from chronic hepatitis B patients and divided into control and intervention groups. The intervention groups received MMP-9 inhibitors at dose of 3 nM. Measurements of HBsAg, HBV DNA, cccDNA, MMP-9, type-1 IFN receptor 1 (IFNAR1), and interferon- (IFN-) were performed before and 72 hours after intervention in both groups. In T. javanica primary hepatocyte culture infected with human HBV, MMP-9 inhibitors at doses of 1 nM, 3 nM, and 7 nM consistently decreased levels of HBsAg, HBV DNA, cccDNA,

and MMP-9. The 3 nM dose increased IFNAR1 levels, while the 7 nM dose increased IFN- levels. The 3 nM dose demonstrated the most optimal effects. In human PBMC with HBV infection, MMP-9 inhibitor at dose of 3 nM decreased levels of HBsAg, HBV DNA, cccDNA, MMP-9, increased IFN- levels, but reduced IFNAR1 levels. This study shows that administration of MMP-9 inhibitors reduced levels of HBsAg, HBV DNA, cccDNA, and MMP-9, while increased IFN- levels in T. javanica primary hepatocyte cultures and human PBMC.