HIV AND HEPATITIS B VIRUS CO-INFECTION LEADS TO INCREASES IN INTRACELLULAR HEPATITIS B SURFACE ANTIGEN, HBV DNA AND TRANSCRIPTION FACTORS IN HEPATOCYTES: A POTENTIAL MECHANISM FOR ADVERSE LIVER OUTCOMES

Zhao W[1], Singh KP[123], Sozzi V[3], Revill PA[14], Lewin SR[1,3]

[1] The Peter Doherty Institute for Infection and Immunity, University of Melbourne and Royal Melbourne Hospital, 792 Elizabeth St, Melbourne, VIC 3000, Australia, [2] Victorian Infectious Diseases Service, Royal Melbourne Hospital, [3] Department of Infectious Diseases, Alfred Hospital and Monash University, Melbourne Australia, [4] Victorian Infectious Diseases Reference Laboratory, Royal Melbourne Hospital at the Peter Doherty Institute of Infection and Immunity,

Background: HIV infection significantly alters the natural history of chronic hepatitis B (HBV). Compared to HBV mono-infection, HIV-HBV infected individuals experience accelerated progression of liver disease and increased liver-related mortality. HBV-active antiretroviral therapy (ART) including tenofovir has improved rates of virological control, however liver related mortality and morbidity remains increased. We hypothesized that direct interactions between HIV and HBV in the hepatocyte, in the presence and absence of HBV-active ART, drives adverse liver outcomes.

Methods: The hepatocyte cell lines HepG2.2.15 and AD38 (expressing HBV) or HepG2 cells (not expressing HBV) were infected with laboratory strains of wild-type (WT) HIV (NL4-3) or vesicular stomatitis virus (VSV)-pseudotyped HIV expressing EGFP. NTCP-expressing HepG2 cells were infected with HBV inoculum derived from AD38 first and subsequently with HIV. EGFP expression was quantified by flow cytometry; integrated HIV DNA and mRNA level of HBV-related transcription factors by qPCR; intracellular HBsAg by western blotting; and HBV DNA/cccDNA by southern blotting. Comparisons between conditions were made using a student T test.

Results: High-level HIV infection was achieved following infection with VSV-pseudotyped HIV with 70% of cells expressing EGFP after 4 days while no EGFP was observed following WT infection. When infections were performed in the presence of raltegravir, EGFP expression was reduced but not eliminated while integrated DNA was not detected. In the presence of HIV infection, there was a significant increase in intracellular HBsAg and HBV DNA, Moreover, the mRNA levels of transcription factors involved in HBsAg production either specific or non-specific to liver were also up-regulated after HIV co-infection.

Conclusion: HIV-HBV co-infection of hepatocytes significantly increased intracellular HBsAg, HBV DNA and transcription factors that bind to HBsAg promotor region. Such increase in HBsAg may contribute to accelerated liver disease in patients with HIV-HBV co-infection. The effects of antiviral therapy on this interaction are now being evaluated.

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