Abstracts, 4th DICID

Free Paper Presentation 1: HCV & HIV
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PL-001 USP18 stimulates HCV production and blunts the antiviral effect of IFNα independent of its protease activity
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Background: Combination therapy with pegylated interferon and ribavirin is the best treatment for patients infected with hepatitis C virus (HCV), but it is only effective in half of patients. We recently demonstrated that USP18, the ISG15-specific protease, is important to HCV responses: it is one of the 18 gene signature predictive of response to therapy (Chen et al Gastroenterology 2005, 2010), and knockdown of USP18 increases the anti-HCV effect of IFNα (Randall et al Gastroenterology 2006). In this study we investigated how USP18 protease activity modulates HCV replication with and without IFNα.

Methods: USP18 wild type (wt) and a protease-inactive mutant (USP18 C64S, mUSP18) expression constructs were cloned with an N-terminal GFP tag. Enzymatic activity of the expressed USP18 was confirmed by co-transfecting wtUSP18 or mUSP18 with plasmid DNA expressing ISG15-GST fusion protein. The effect of over-expression of wtUSP18 or mUSP18 on HCV RNA replication/viral particle secretion with or without IFNα was tested in the J6/JFH1 infectious culture system.

Results: Over-expression of wtUSP18 in Huh7.5 cells led to decreased ISGylation in the presence of IFNα, an effect not seen with overexpression of mUSP18. Overexpression of both wtUSP18 and mUSP18 increased baseline HCV RNA replication and production of infectious virus by 4–5 fold; overexpression of both also blunted the anti-HCV effect of IFNα. Neither wtUSP18 nor mUSP18 inhibited the expression of common ISGs (MxA, ISG15, OAS2, Viperin) after exposure of Huh7.5 cells to IFNα.

Conclusions: USP18 modulates HCV replication and the anti-HCV activity of IFNα independent of its protease activity and without disrupting IFNα signaling. These studies reveal that increased USP18 expression may be one way that HCV shelters itself from the host response, and should be considered a target for new anti-HCV therapies.
The clinical features in HIV/AIDS complicated with cytomegalovirus infection

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To promote the diagnostic rate of HIV/AIDS complicated with CMV viremia, enhance curative effects and improve the prognosis, the clinical data in 249 cases of HIV/AIDS patients hospitalized from Oct.2008 to Nov.2009 have been collected and studied retrospectively, in which we found that 43 HIV/AIDS patients have infected CMV. Pathological detections have been analyzed from specimen taken with gastroscope, fibercoloscope, bronchoscope and bronchoalveolar lavage fluid (BALF). We also analyzed association between cellular immunity and CMV-DNA levels. We found that 43 HIV/AIDS patients have infected CMV. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients. We also found the positive association between low level of CD4+ T lymphocytes and CMV-DNA levels. No CMV esophagitis or colitis has been diagnosed in these 43 patients.

Figure 1. Retinitis.