Methods. Plasma viral RNA was sequenced from a convenience sample of 90 SM cohort samples, and then analyzed for polymorphisms associated with HLA class I and KIR genotypes. An ADCC assay was employed to detect responses to Env and Vpu peptides. An ELISA-based approach was optimized to identify potential Vpu epitopes. Finally, responders from the ADCC assay were assessed in an ADCV assay.

Results. In keeping with the lack of CTL targets in infants, no HLA class I associated polymorphisms were identified in Vpu. KIR analysis, however revealed evidence of a strong association between KIR2DS1 and a single amino acid at position 14 of Vpu. 59% of HIV-1 sequences derived from KIR2DS1+ individuals encoded a valine (V) at this position whereas the corresponding amino acid (A) was found in this position in the majority (76%) of KIR2DS1-individuals. ADCC responses to Env were found in 37% of the SM cohort, with only five subjects also showing responses to Vpu peptides. Plasma from all five Env/vpu responders showed potent inhibition of virus replication, nearing 95%, in the ADCV assay.

Conclusion. We demonstrate a significant association between an activating KIR, KIR2DS1, and a polymorphism at amino acid position 14 of HIV-1 Vpu, which is consistent with selection by Natural Killer (NK) cells expressing this KIR. We also demonstrate Vpu and Env ADCC responses that are associated with potent virus inhibition in vitro in responders. These data help to shed light upon the immune selection pressures exerted on the HIV-1 vpu gene and may provide insights into the role of this protein in immune evasion.

Disclosures. All authors: No reported disclosures.

634. Transcriptional Stimulation of Antiviral Response Components by the Structural and Accessory Human coronavirus OC43 Proteins

Widad Widad, PhD; Ali-Nakhaie, Ph.D; Hana, MSc; Elsayed, MD; and Wassim Chehadeh, PhD. Microbiology, Faculty of Medicine, Kuwait University, Kuwait, Kuwait. Microbiology, Kuwait University, Kuwait, Kuwait. Virology Unit, Faculty of Medicine, Kuwait, Kuwait

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Background. In Kuwait, human coronavirus OC43 (HCoV-OC43) causes 25–30% of common cold, and 8.8% of respiratory infections in hospitalised patients. It is also associated with severe respiratory symptoms in infants, elderly, and immunocompromised patients. Our previous results showed that the expression of antiviral genes in human embryonic kidney (HEK) 293 cells is downregulated in the presence of HCoV-OC43 proteins. To understand the role of HCoV-OC43 proteins in antagonising antiviral responses of the host, we investigated the effect of HCoV-OC43 structural and accessory proteins on the transcriptional activation of interferon-stimulated response element (ISRE), interferon-beta (IFN-β) promoter, and nuclear factor kappa B response element (NF-kappaB-RE).

Methods. HCoV-OC43 ns2a, ns5a, membrane (M), and nucleocapsid (N) mRNA were translated and cloned into the pAcGFP1-3 N expression vector, followed by transfection in HEK-293 cells. Two days post-transfection, the cells were co-transfected with a reporter vector containing firefly luciferase under the control of ISRE, IFN-β promoter, or NF-kappaB-RE. Renilla luciferase vector was used as an internal control for transfection efficiency. Following 24 hours of incubation, the cells were treated with either IFN or tumour necrosis factor (TNF) for 6 hours. Thereafter, promoter activity was assayed using the dual-luciferase reporter assay system. Infection NS1 protein was used as positive control for antagonism.

Results. The transcriptional activity of ISRE, IFN-β promoter, and NF-kappaB-RE was downregulated in the presence of ns2a, ns5a, M, or N protein as there was a sharp fall in firefly luciferase levels. Overall, HCoV-OC43 proteins reduced firefly luciferase levels for ISRE and IFN-β promoter by at least ten fold, whereas for NF-kappaB-RE the firefly luciferase levels were reduced by at least five fold.

Conclusion. HCoV-OC43 has the ability to block the activation of different anti-viral signaling pathways.

Disclosures. All authors: No reported disclosures.

635. In HIV-Infected Patients Killing of Latently HIV-Infected CD4 T Cells by Autologous CD8 T Cells Is Modulated by Nef

Yasuyoshi Aoki, MD, PhD; Yuuki Ohshima, MD, PhD; and Hiroshi Takada, MD, PhD

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Background. HIV-1 infection is characterized by persistence of the virus in the human body despite effective antiretroviral therapy (ART). This persistence is due to the formation of latently infected CD4 T cells. These cells acquire the ability to produce virus and can act as an infective source in the host. Therefore, the development of a strategy to eliminate these cells is a key component of strategies to cure HIV-1 infection.

Methods. We isolated CD4 T cells from HIV-1 infected patients and used an anti-CD8 T cell antibody to block CD8 T cell-mediated killing of CD4 T cells. We then used an antibody to block the Nef protein, which is known to downregulate cellular CD8 T cell-mediated killing. Finally, we used an antibody to block the CD8 T cell receptor (CD8-TCR) to determine the role of the TCR in killing CD4 T cells.

Results. We observed a significant increase in the killing of CD4 T cells by CD8 T cells in the presence of the anti-Nef antibody. This increase was further enhanced by the anti-CD8-TCR antibody. These results suggest that the Nef protein downregulates CD8 T cell-mediated killing of CD4 T cells, and that this downregulation is mediated by the CD8-TCR.

Conclusion. The Nef protein downregulates CD8 T cell-mediated killing of CD4 T cells, and this downregulation is mediated by the CD8-TCR. This suggests that strategies to block the Nef protein may be effective in eliminating latently infected CD4 T cells.