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 lack of CTL targets, no XLA class 1 associated polymorphisms were identified in Vpu. KIR analysis, however revealed evidence of a strong association between KIRDS1 and a single amino acid at position 14 of Vpu. 59% of HIV-1 sequences derived from KIRDS1+ individuals encoded a valine (V) at this position whereas the conservative amino acid (A) was found at this position in the majority (76%) of KIRDS1-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, KIRDS1, 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 Env and 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.

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

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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-β (IFN-β) promoter, and nuclear factor kappa B response element (NF-kB-RE).

Methods. HCoV-OC43 n2a, n2a, membrane (M), and nucleocapsid (N) mRNA were transfected and cloned into the pACGFP-1-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-kB-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. Insulin NS1 protein was used as positive control for antagonism.

Results. The transcriptional activity of ISRE, IFN-β promoter, and NF-kB-RE was downregulated in the presence of n2a, n2a, M, or N protein as there was a sharp fall in firely luciferase levels. Overall, HCoV-OC43 proteins reduced firefly luciferase levels for ISRE and IFN-β promoter by at least ten fold, whereas for NF-kB-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 signalling 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

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Background. In HIV-infected patients, the CD4 T cells are critically important in the control of the reservoir of latently infected cells. Recent clinical studies have shown that killing of latently infected CD4 T cells contributes to immune restoration in the context of ART. However, the precise mechanism(s) of killing of latently infected CD4 T cells by CD8 T cells remains poorly understood.

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 lack of CTL targets, no XLA class 1 associated polymorphisms were identified in Vpu. KIR analysis, however revealed evidence of a strong association between KIRDS1 and a single amino acid at position 14 of Vpu. 59% of HIV-1 sequences derived from KIRDS1+ individuals encoded a valine (V) at this position whereas the conservative amino acid (A) was found at this position in the majority (76%) of KIRDS1-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, KIRDS1, 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 Env and 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.

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