Investigating the effects of Methylseleninic Acid on anti-HIV immunity.

Authors:
Kirsten E Amos[1], Rory A Shepherd[1], Hannah King[1], Sharon R Lewin[1,2,3], Michael Roche[1,4]

Affiliations: 1 University of Melbourne/Peter Doherty Institute Department of Infectious Diseases; 2 Monash University/Alfred Hospital, Department of Infectious Diseases; 3 Victorian Infectious Diseases Service, Royal Melbourne Hospital at the Peter Doherty Institute; 4 Royal Melbourne Institute of Technology (RMIT), School of Health and Biomedical Sciences

Background:
HIV can mask immune recognition of infected cells through viral Nef mediated downregulation of the host cell major histocompatibility complex-1 (MHC-1). Previous studies have shown that MSA can have immunomodulatory properties including upregulating MHC-1 expression. We hypothesised that MSA may be able to counteract Nef mediated MHC-1 downregulation.

Methods:
HEK-293T cells were transfected with a Nef expression plasmid and treated for 24-48hrs with MSA (2.5, 5μM). MHC-1 and Nef expression was measured by flow cytometry. Total peripheral blood mononuclear cells (PBMCs) from people not living with HIV were cultured for 24hrs with MSA (2.5, 5, 10μM) and stained for activation/cytotoxicity (CD69, CD57) or exhaustion (PD-1, PD-L1, TIM-3, TIGIT), and analysed by CD4+ (CD3+, CD4+), CD8+ (CD3+, CD8+) and NK (CD3-, CD56+) cell subsets. Alternatively, PBMCs were pre-treated with MSA (2.5, 5μM) for 24hrs before stimulation with a CEF (Cytomegalovirus, Epstein-Barr virus, Influenza) peptide pool or SEB (Staphylococcal Enterotoxin B) for a further 6hrs then stained for markers of degranulation (LAMP-1, perforin, TNF, IFNγ, GranzymeB) and analysed by CD4+ and CD8+ subsets.

Results:
In 293T cells whereby Nef downregulated MHC-1 expression, we observed partial restoration with a 1.2-fold ($p=0.027$) increase in MHC-1 expression after 2.5μM MSA treatment for 48hrs. Additional experiments in PBMCs demonstrated minimal effect of MSA treatment on cell activation and degranulation.

Conclusion:
Our data suggests that MSA may be able to partially overcome Nef mediated downregulation of MHC-1, without interfering with broad immune cell function, potentially helping to reveal HIV infected cells to the immune system.

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