

**P047** Diversity of human immune responses in blood to IFN $\alpha$  and a TLR7 agonist  
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Toll-like receptors (TLRs) recognise pathogen associated molecular patterns which leads to the induction of IFNs and various cytokines. The TLR7 agonist, Isatoribine, reduced Hepatitis C (HCV) viral load as short term monotherapy in infected patients through induction of IFN $\alpha$ , clinically validating TLR7 as an antiviral target. The aim of this study was to determine *in vitro* the immune responses to the TLR7 agonist, SM-360320, and IFN $\alpha$ . Blood samples, collected on 3 occasions from 80 healthy donors, were treated with compound and the induction of antiviral and inflammatory biomarkers were monitored. Results show significant variation in responses between donors and treatments with no consistent non-responder identified. Induction of the interferon inducible gene, 2'5'-oligoadenylate synthetase (2'5'OAS) was negatively correlated with baseline expression and higher overall with SM-360320 (4 to 31 fold for IFN $\alpha$ , 8 to 39 fold for SM-360320). SM-360320 induced >10 fold induction of 2'5'OAS in 97.5% of donors, whereas IFN $\alpha$  induced this level in 78.75%. IL-6, IP-10 and TNF $\alpha$  were induced to higher levels with SM-360320 whereas IL-2, IL-12p70, IL-8 and IL-10 were induced similarly for both compounds. TLR7 agonists therefore induce an immune response in most of the human population. Pre-screening patients prior to therapy using a method similar to that described here could provide a way to predict immune response.