

P043 Profiling antiviral response pathways following TLR stimulation of human blood

Deborah Hamilton, Tanya Parkinson, Hannah Perkins, Phil Brain, Marilyn Lewis and Carl Laxton

Pfizer, Ramsgate Road, Sandwich, Kent, CT13 9NJ

Toll-like receptor 7 (TLR7) is a pattern recognition receptor that initiates antiviral immune responses following interaction with viral RNA. This study set out to investigate the expression of certain canonical genes known to be involved in antiviral responses, following stimulation with the TLR7 agonist SM-360320, in human blood from a healthy volunteer. Briefly, blood was drawn and incubated in the presence of three concentrations of compound. The reaction was stopped at 4 time-points post incubation. RNA was extracted using a commercially available kit and gene expression profiled using Taqman Low Density Array technology (TLDA). Proteins were quantified from generated plasma samples, using a human multi-analyte profile (MAP). Two analyses were carried out. The first was ANOVA, which detected evidence of a dose vs. time interaction for most genes. The second modelled the results by fitting dose response curves, to see if there was a dose-related behaviour. This fit was significant at the 5% level for only a few genes. Examples of up and down regulation were observed. Mx1 and 2'5'-Oligoadenylate synthetase, well-characterised markers of a heightened immune antiviral state, were among those found to be induced. Findings here warrant further investigation to support progression of TLR7 agonists in the clinic.