Pre-existing immunity to human parainfluenza virus (hPIV) does not affect rSIV.F/HN-mediated transduction efficiency.

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Lentiviral vector pseudotyped with the Sendai virus envelope proteins F and HN (rSIV.F/HN) transduces lungs efficiently, and can be repeatedly administered. These features make the virus a suitable vector for a range of diseases including cystic fibrosis (CF). Sendai virus has significant sequence homology with hPIV1 and ~80% of adults carry anti-hPIV1 antibodies. In preparation for a first-in-man CF trial we assessed whether hPIV1 antibodies inhibit rSIV.F/HN transduction efficiency. We passively immunised mice with human immunoglobulins (IVIg) administered either intraperitoneally (400 µl) or intranasally (100 µl) and showed that, using these doses, the concentration of hPIV1 antibodies in mouse serum and broncho-alveolar lavage fluid (BALF) was as high as or higher than in human serum and BALF. Next we transduced mice with rSIV.F/HN-lux intranasally 24 hrs after immunisation and showed that transduction efficiency was not affected by the presence of hPIV1 antibodies. To confirm results in human samples we performed in vitro transduction inhibition assays in serum positive or negative (n = 4/group) for hPIV1 antibodies and showed that both groups inhibited rSIV.F/HN transduction, whereas rSIV.VSVG control virus was significantly (p < 0.01) less affected. Subsequently we quantified hPIV1 IgG and IgA antibodies in BALF, grouped them into positive and negative cohorts and performed a transduction inhibition assay to address whether hPIV1 antibodies in epithelial lining fluid (ELF) inhibit rSIV.F/HN efficiency. There was no significant difference between the groups, suggesting that hPIV1 antibodies in ELF do not inhibit rSIV-F/HN transduction. The data suggest that hPIV1 antibodies will not inhibit rSIV.F/HN transduction in human lung.