Antibody gene transfer for prophylaxis of respiratory syncytial virus (RSV) infection

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Respiratory syncytial virus (RSV) infection is the single most common cause of hospitalisation in infants under 1 year of age, with no currently licensed vaccine available. Prophylaxis with monoclonal antibody palivizumabis effective but costly due to the complexity of large-scale manufacture and is only offered to select vulnerable infant populations. We are developing gene delivery approaches to directly express palivizumab in patients as an alternative to parenteral administration. Recombinant adeno-associated virus (rAAV2/8) was used for intramuscular delivery in mice and recombinant simian immunodeficiency virus (SIV) pseudotyped with Sendai virus envelope proteins F and HN (rSIV.F/HN) was delivered to the murine lung via insufflation. When BALB/c mice were dosed with either vector configuration containing the secreted Gaussia luciferase (GLux) or palivizumab cDNA, dose-dependent, sustained, transgene expression was observed in the lung lumen and circulation for at least 12 months. When rAAV expressing palivizumab was delivered to mice, therapeutically relevant serum levels of the antibody (89.3 μg/mL; $p<0.001$) were observed for a minimum of 6 months postdelivery. Delivery of either vector to BALB/c mice 28 days prior to challenge with 7.5e5 pfu of RSV significantly reduced weight loss ($p<0.05$ and $P<0.0001$ for 1e8 TU rSIV.F/HN and 1e11 VG rAAV2/8, respectively). Translation of this approach could reduce the overall 'per dose treatment cost' allowing for wider use of prophylaxis against RSV infection in at risk human populations despite the continued absence of an effective vaccine.