Development of lung and muscle protein factories to deliver therapeutic monoclonal antibodies

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Recombinant therapeutic proteins, of which monoclonal antibodies (mAbs) represent the largest market, are used to treat diseases including cancer, blood and immune disorders. The cost and complexity of large-scale production and purification of mAbs translates to high cost of therapy. We hypothesise that our rSIV.F/HN lentiviral lung gene delivery platform, currently undergoing preclinical evaluation for cystic fibrosis gene therapy, could be used to establish protein factories within patients' lungs. This approach is being evaluated using two model mAbs, infliximab and palivizumab, for delivery to the lung lumen and circulatory system, respectively. The efficiency of mAb-secreting lung protein factories using rSIV.F/HN lung gene transfer is being compared with conventional muscle protein factories using rAAV2/8. Preliminary *in vivo* studies using vectors expressing secretory reporter protein *Gaussia* luciferase (GLux) delivered 10^7 and 10^8 transducing units (TU) of rSIV.F/HN to the mouse lung and 10^{10} and 10^{11} genome copies (GC) of rAAV2/8 delivered intramuscularly. Each resulted in robust and sustained secretion of GLux into the circulation ($p<0.001$ at 9 and 4 months post-delivery, respectively), supporting progression to experiments using mAb-encoding vectors. We have developed rSIV.F/HN and rAAV2/8 vectors encoding infliximab and palivizumab, which direct detectable antibody expression in cell culture (46-350 ng/mL), and are currently conducting *in vivo* studies with these vectors to determine whether therapeutically relevant levels of mAb expression can be achieved in serum and lung lumen. If successful, this approach could translate into reduced patient burden and treatment costs.