Overview:

- The UK Cystic Fibrosis Gene Therapy Consortium is committed to the testing and development of gene therapy vectors for CF clinical trials.
- Successful lung gene therapy vectors will require topical administration to the airway epithelium via aerosol delivery.
- The cationic polymer 25kDa polyethylenimine (PEI) has demonstrated successful gene expression following aerosol administration to the mouse lung.
- Viability of PEI formulations for clinical applications is currently limited by low maximal pDNA concentrations of <0.5mg/ml.

Results:

- We have utilised ultrafiltration to generate concentrated PEI (cPEI) formulations containing >8mg/ml pDNA and we have examined gene expression and toxicity following administration of these formulations to the mouse lung.

Conclusions:

- Concentrated pDNA/PEI formulations can be generated by ultrafiltration of standard low concentration formulations.
- Aerosol administration of cPEI formulations is associated with high levels of gene expression and low levels of vector toxicity in the mouse lung model.
- Delivery method is an important determinant for lung toxicity following cPEI delivery.
- Concentrated pDNA/PEI formulations demonstrate improved viability for lung gene therapy applications.