A breath of fresh air for cystic fibrosis- using nanotechnology to increase efficacy of gene therapy

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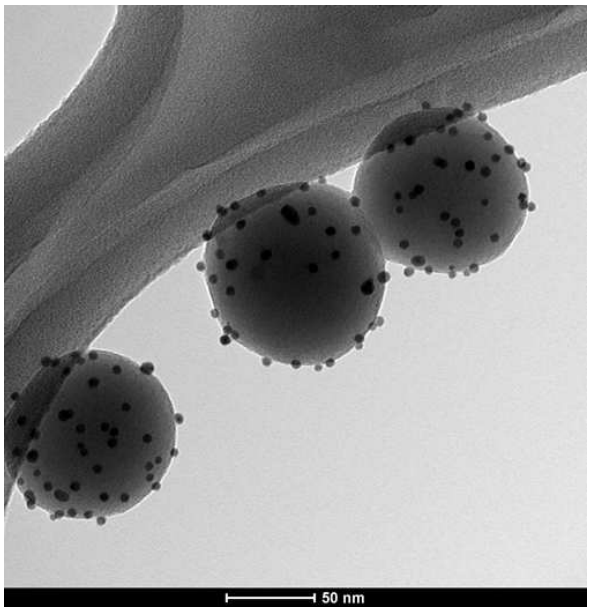
With Cystic Fibrosis (CF) currently being the leading life-threatening autosomal recessive disease in Australia, gene therapy has gained momentum as a possible treatment option. The Cystic Fibrosis Transmembrane Regulator (CFTR) gene is missing or deformed in CF patients and it is required for normalized airway function (Burney *et al*. 2008). Previous attempts at using aerosolised gene therapy have been inefficient due in-part to damage caused to the lentiviral vector (LV) delivery vehicle during the aerosolisation process. In order to protect the LV and increase efficacy of CFTR gene delivery, a protective coating for the LV has been developed. This coating consists of 5nm polyelectrolyte coated gold nanoparticles attached to the LV surface. The LV being used is a phenotype of HIV which has a glycoprotein 120 coat around its surface, allowing easy attachment for the gold nanoparticles.

The polyelectrolyte gold nanoparticles are formed through a layer-by-layer approach of the polymers *Poly(diallyldimethylammonium chloride)* (PDADMAC) and *Poly(sodium 4-styrenesulfonate)* (PSS) as described by Gole and Murphy (2005). They have been analysed though dynamic light scattering (DLS) and zeta potential measurements. Due to the biohazards associated with using HIV, models have been devolved using silica nanoparticles to mimic the HIV virus for faster testing of the protective coating. Gold nanoparticles have then been attached to the surface and the model systems have been aerosolised to determine if the gold nanoparticle coating has protected the surface of the model. The figure shows a TEM image of the silica nanoparticle model which has a coating of (3-Aminopropyl)triethoxysilane APTES on its surface (80nm) and is decorated with 5nm gold nanoparticles.



Protection efficiency was determined for the model system using electron microscopy of the model system before and after aerosolisation. The gold nanoparticles acted as a protective coating as they remained on the surface of the model LV after nebulisation. The polyelectrolyte coated gold nanoparticles will be attached to the surface of the HIV phenotype and tested on cells where gene delivery efficacy can be measured. This allows quantification on how many biologically active viruses survive the aerosolisation process.

If the gold nanoparticles show that they considerably improve the gene delivery efficacy, the treatment will then be tested on animal models. This treatment could lead to longer life expectancy and quality of life, especially if given this treatment at birth where the infant diagnosed with CF can breathe in the aerosol and ultimately never develop the onset of any CF symptoms in the lungs.

Burney TJ & Davies JC. (2012). Gene therapy for the treatment of cystic fibrosis. *Appl Clin Gen* **5**, 29-36.

Gole A & Murphy C. (2005). Polyelectrolyte-coated gold nanorods: Synthesis, characterization and immobilization. *Chem Mater*, 17, 1325-1330.