

LIPOPEPTIDE NANOPARTICLE GENE DELIVERY SYSTEM

Novel lipopeptide-polymer nanoparticle carriers for intracellular delivery of nucleic acid therapeutics. This non-viral gene delivery system offers assembly in aqueous solution for ease of manufacture and potential clinical advantages, including enhanced tissue distribution, improved tolerability and suitability for chronic administration. The system has potential applications in delivery of nucleic acids for vaccination, gene silencing or protein expression.

- **Composed of biodegradable materials that are well tolerated and likely to be suitable for chronic administration**
- **Low molecular weight, self-cross-linking lipopeptides allow nanoparticle assembly in a single step in aqueous solution**
- **Small size and neutral or negative charge maximise tissue distribution**
- ***In vivo* studies show DNA or mRNA delivery results in adequate gene expression and immune responses after IM injection in animals**

THE CHALLENGE

Non-viral methods of delivering genes have been disappointing. Complexes that effectively transfect cells *in vitro* have inappropriate physicochemical properties for *in vivo* use.

For transfection of cells in culture, DNA is condensed to form cationic particles. These are effective *in vitro* because they aggregate in culture media to form disorganised complexes, often larger than 1µm in diameter. These aggregates sediment, then bind to negatively-charged cell surfaces, and are subsequently taken up into cells by non-specific processes.

DNA or RNA complexes for *in vivo* use should be small (25-100nm), electrically neutral or negative, and should resist aggregation in biological media. Small size and neutral charge have the effect of maximising tissue distribution, for example after intramuscular injection of a DNA or mRNA vaccine. Methods for production of small, neutral particles containing DNA or RNA have been elusive, with few encouraging advances. Lipids are typically water-insoluble which implies the use of organic solvents at some stage of particle assembly, leading to manufacturing and safety concerns.

THE TECHNOLOGY

Researchers at the Monash Institute of Pharmaceutical Sciences have developed a means of assembling neutral or negative DNA particles without requiring non-aqueous solvents. This is achieved by mixing nucleic acid (DNA or RNA), lipopeptides and a neutralising and steric stabilisation component in a single mixing step, producing particles of 50-100nm which resist aggregation. Suitable steric stabilisation components include block polymers (e.g. polyGlutamate- PEG or acrylate block polymers such as poly(acrylic acid)-poly(HPMA)) or lipopolymers (e.g. phosphatidyl-ethanolamine-PEG (PE-PEG)). The common features of the steric stabilisation component is that they comprise an anionic polymer or lipid, covalently linked to a neutral hydrophilic polymer.

The technology has been evaluated in animal studies to deliver either DNA or RNA to express reporter genes after intramuscular injection. In addition, proof of concept studies using ovalbumin expression showed successful induction of humoral and cell-mediated adaptive immune responses (Figure 1).

The Monash lipopeptide-polymer nanoparticle carrier technology has potential applications in delivery of DNA or RNA for vaccination, gene silencing and gene expression. The system offers potential clinical and manufacturing benefits over available gene delivery systems.

Intellectual property: AU provisional patent application 2017902238 filed, claiming composition of matter of agents and methods for gene delivery or transfer for applications such as gene therapy for diseases, medical disorders or vaccination.

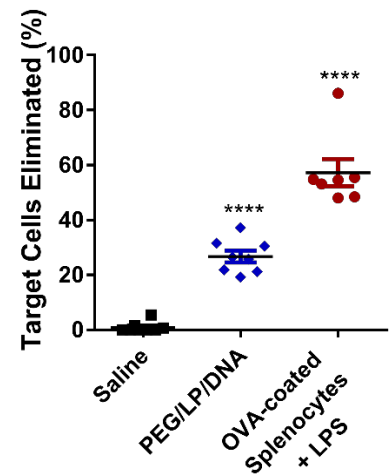


Figure 1. Killing of target cells by cytotoxic T cells *in vivo* after IM vaccination with formulated DNA vaccine (PEG/LP/DNA) expressing ovalbumin. OVA-coated splenocytes + the adjuvant LPS (lipopolysaccharide) represent a highly potent positive experimental control.

THE OPPORTUNITY

Monash is now seeking partners to progress the development of its novel non-viral gene delivery system.

CONTACT US

Monash Innovation
T: +61 3 9905 9910
E: innovation@monash.edu
Monash.edu/industry