Exosomes from amniotic epithelial cells for the treatment of disease

Our team is developing a unique exosome therapy platform based on amniotic epithelial cells, with a first focus on idiopathic pulmonary fibrosis.

Researchers from Hudson Institute and Monash University have over a decade of studies showing that amniotic exosomes are immuno-modulatory, anti-fibrotic and have pro-regenerative effects.

Summary

Exosomes are nanosized vesicles released by all cell types, including stem cells. They contain 'cargo' such as proteins, RNA and cytokines which reflect the intracellular contents of their donor cell.

Our exosomes are derived from our proprietary bank of human placental amniotic epithelial stem cells (hAECs) and exhibit potent immuno-modulatory, anti-fibrotic and pro-regenerative effects.

In addition, our exosomes are highly effective over a range of conditions including idiopathic pulmonary fibrosis (IPF), bronchopulmonary dysplasia (BPD), asthma, stroke, liver and kidney fibrosis.

They also have unique production advantages and can be isolated, purified, frozen, lyophilized, packaged and distributed like a standard drug product. Our first product is being developed as a regenerative and anti-fibrotic therapy for IPF, with a second focus on BPD.

Immortalised cell lines have been created for reproducible exosome manufacturing.

Advantages and research strengths

- Proprietary exosome therapy with regenerative effects
- Pathway to scalable GMP manufacture
- Greater than 30-fold more exosomes from hAECs than MSCs
- Off-the-shelf, easy to use cell-derived product, administered like a standard drug
- Clinical trial capacity with experienced physicians
- Compelling biological validation in various fibrosis indications including IPF
- Strong expertise in hAEC biology and manufacturing
- Multi-disciplinary team – biology experts, clinicians
- Extensive tools (screens, models) and expertise to deliver
- Large market with recognised unmet needs
- IP protection

Key data

Our exosomes have been tested and show promising results in numerous models of disease including IPF, BPD, asthma, kidney, liver fibrosis, and stroke.

In vivo studies in a range of lung disease models show that a single intranasal dose of the exosomes reduces pulmonary fibrosis, has direct pro-regenerative effects by activation of bronchioalveolar stem cells and type 2 alveolar cells. They also perform better than pirfenidone in reducing myofibroblast deposition and lung fibroblast collagen production.

They also increase phagocytic activity of macrophages, suppress T cell proliferation and promote a predominant regulatory T cell phenotype.

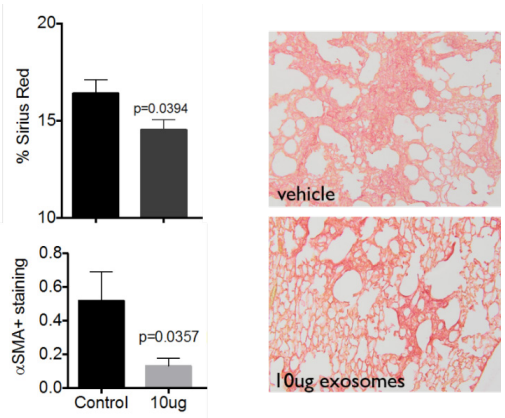

Figure 1. Amniotic exosomes reverse established lung inflammation and fibrosis in a mouse model of bleomycin-induced lung fibrosis, demonstrated by a reduction in activated myofibroblasts (αSMA positive) and reduction in collagen deposition in the lungs (Sirius Red).

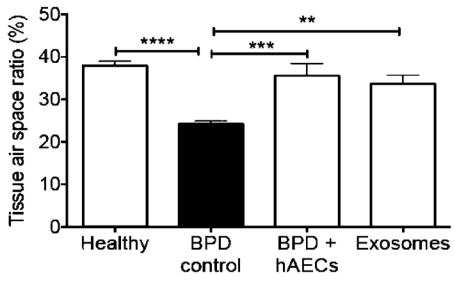

Figure 2. Amniotic exosomes reverse alveolar simplification in a bronchopulmonary dysplasia (BPD) mouse model, demonstrated by an improvement in the tissue: airspace ratio. In BPD the alveolarisation process, or final stage of lung development, is disrupted.

Development pathway

Therapy area: fibrotic and lung diseases such as idiopathic pulmonary fibrosis and bronchopulmonary dysplasia

Stage: late preclinical

Development plan: rapid human proof-of-concept: 2 years to end of phase 1

Manufacture: reproducible, low-cost, cell-free

Our team have access to animal and clinical facilities to undertake a defined research plan through phase 1 clinical trial, with a pathway to scalable GMP manufacture. We are now seeking a venture or commercial partner for continued product development through to Phase 1b dose-escalation clinical safety trial.

Market

Due to their utility for a range of indications, exosomes have the potential to be the next major biotech breakthrough. The global exosomes market size is expected to reach USD2.28 billion by 2030 exhibiting a CAGR of 18.8% (Grand View Research, Inc.). Idiopathic pulmonary fibrosis (IPF) is an incurable fatal disease with a mean survival of only 3-5 years. The global IPF treatment market is expected to reach USD4.6 billion by 2023. Worldwide, IPF affects 13 to 20 out of every 100 000 people.

Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease that develops in preterm neonates. In 2017 there was an estimated prevalence of 64 468 in the seven major markets, and market size of USD307 million (Research and Markets). However, a major challenge in managing BPD is that the life-saving interventions such as antenatal corticosteroids and assisted ventilation are also the very triggers for BPD itself. There is currently no treatment to reverse BPD once it is established.

IP position

Entered into National Phase in Australia, USA, Europe, China, Japan, South Korea, Singapore and Canada based on PCT/AU2016/050468.

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Team

The exosomes program at Hudson Institute is driven by Associate Professor Rebecca Lim, a world leading expert in exosome therapeutics. She has assembled a diverse and expert team of collaborators to develop this technology towards the clinic, including academic researchers and experienced clinicians.

This program leverages founder expertise in the clinical development of allogeneic hAEC stem cells, and strong clinical trial expertise in regenerative medicine, including first-in-world stem cell trials for BPD and stroke.

Related publications

Amnion Epithelial Cell-Derived Exosomes Restrict Lung Injury and Enhance Endogenous Lung Repair. Tan J *et al.*, 2018 *Sci Trans Med.*

To Protect and to Preserve: Novel Preservation Strategies for Extracellular Vesicles. Kusuma GD *et al.*, 2018 *Front Pharmacol.*

The Human Amnion Epithelial Cell Secretome Decreases Hepatic Fibrosis in Mice with Chronic Liver Fibrosis. Alhomrani M *et al.*, 2017 *Front Pharmacol.*

Hudson Institute of Medical Research

Hudson Institute of Medical Research is a leading Australian medical research institute recognised internationally for research into reproductive health and pregnancy, infant and child health, hormones and health, inflammation and cancer. Our research programs span discovery science and translational research, and clinical trials.

Our worldwide scientific and medical collaborations provide a foundation for transformative healthcare programs across the globe, with our researchers leading developments in cell therapies, women's health, microbiome research, diagnostics, and cancer.

Partnership opportunities include:

- Therapeutics, including oncology and gene therapy
- Reproductive, women's and children's health
- Regenerative medicine
- Inflammation and immunology
- Diagnostics and biomarkers