

Exosome therapy

A cell-free approach to regenerative medicine.

Exosome therapeutics is an emerging field that provides an alternative to stem cell therapy. Hudson Institute researchers, in partnership with Monash University, have over a decade of studies showing that amniotic exosomes are immunomodulatory, anti-fibrotic and have pro-regenerative effects.

Summary

Exosomes are 100-200nm sized vesicles released by all cell types, including stem cells. They are loaded with cell-specific proteins, lipids, and genetic material that they transport to other cells, where they can affect function and physiology.

These vesicles demonstrate similar characteristics as their producer cells. Thus, exosomes derived from stem cells show a remarkable regenerative capacity. However, by contrast to stem cells, exosomes are safer, less expensive, and more easily scaled for commercialisation. Exosomes are therefore emerging as an attractive therapeutic and commercial alternative for regenerative medicine. Exosomes provide the potential for an 'off-the-shelf', easy to use cell-derived product.

Our team – led by Dr Rebecca Lim, PhD, at Hudson Institute and Professor Euan Wallace, AM MBChB MD, at Monash University – have found that exosome treatment is highly effective in numerous fibrotic disease models. Using exosomes derived from human placental amniotic epithelial stem cells (hAECs), which exhibit immunomodulatory, anti-fibrotic, and pro-regenerative effects, they have demonstrated that amniotic exosomes can reverse established lung inflammation and fibrosis in preclinical models.

Both stem cells and exosomes demonstrate therapeutic efficacy, but in a number of measures exosomes are superior:

ideal product	stem cells	exosomes	benefit
safety / tumor risk eliminated	✗	✓	exosomes are non-cellular and unable to form a tumor
readily available source tissue	✗	✓	amniotic exosomes are sourced from placental donor tissue (otherwise often discarded)
simple, quick and consistent production	✗	✓	exosome collection does not require cell passaging or expansion
"off-the-shelf" storage	✗	✓	exosomes can be lyophilised for storage and shipping
easy administration, outpatient vs hospital	✗	✓	exosomes are more robust, so multiple routes to treatment delivery are possible (i.v., topical, nebulized, nasal spray, inhaler)

Applications

Our team are initially focussing on the therapeutic potential of amniotic exosomes for treatment of idiopathic pulmonary fibrosis (IPF).

IPF is a progressive and debilitating fatal lung disease. It is characterised by inflammation and scarring of lung tissue (fibrosis) and decreased lung function. The mean survival time for patients diagnosed with IPF is 3-5 years, with a five-year survival rate of 20-30%.

There is no complete cure available for IPF. Lung transplants are provided to a small number of patients (5%), however, outcomes are poor. The focus of current treatments is on the relief of symptoms and slowing of disease progression. Currently available treatments are not able to halt the progression of disease.

Our exosome therapy could be used an adjunct to currently approved IPF treatments, with their regenerative benefit to halt further deterioration.

Market

IPF typically occurs in middle-aged to older adults. The increasing aging population worldwide, alongside improvements in diagnostics, are expected to contribute to increased incidence rates of IPF.

The IPF market was valued at over \$900 million in 2015 and is expected to rise to \$3.2 billion by 2025, with a compound annual growth rate (CAGR) of 13.6%.

A number of exosome companies with strong financial backing strengthen the commercial confidence of exosomes to improve human health. Recent examples of preclinical R&D companies include Capricor (\$10M in 2015); ReNeuron (GBP68M in 2015); EvOx (GBP10 in 2016); Codiak Biosciences (Series A raised \$90M+ in 2015; total \$168.5M since founding).

Key data

Our proprietary amniotic exosome treatment is as effective as, or better than, their producer hAEC stem cells in preclinical models of fibrotic conditions.

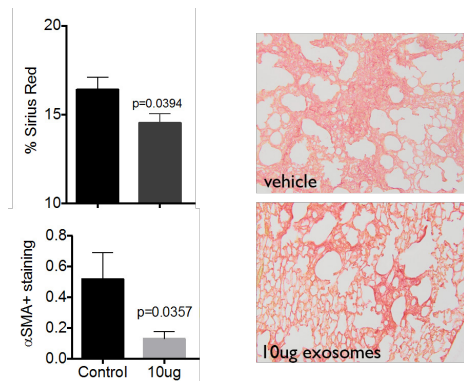


Figure 1. Amniotic exosomes reverse established lung inflammation and fibrosis in a mouse model of bleomycin-induced lung fibrosis, demonstrated by a reduction in activated myofibroblasts (αSMA positive) and reduction in collagen deposition in the lungs (Sirius Red).

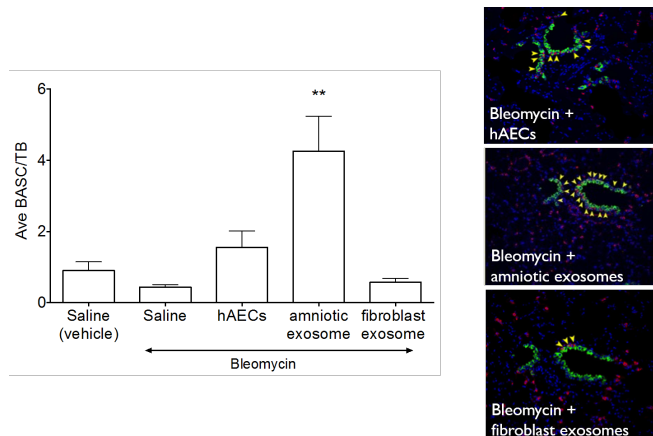


Figure 2. Amniotic exosomes demonstrate a pro-regenerative effect. They trigger an endogenous stem cell response in the lungs, which is significantly greater than that induced by human placental amniotic epithelial stem cells (hAECs). Fibroblast exosomes do not induce this same response.

Development pathway

To date we have completed preclinical assessments using our proprietary exosomes produced at a small scale. Our team have full access to animal and clinical facilities to undertake a defined research plan through 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 1 clinical safety trial.

IP position

We are developing a patent portfolio covering the development, manufacture and use of amniotic exosomes in the therapeutic setting, including:

PCT/AU2016/050468 'A method of treatment' filed June 2016

PCT/AU2017/050821 'A method of treatment' filed August 2017

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Hudson Institute of Medical Research

Hudson Institute is a leading independent Australian medical research institute located in the heart of the Monash Health Translation Precinct in Clayton, Victoria. Our specialist centres bring together the finest professionals in Australian science and medicine to conduct basic and translational research in the areas of:

- Cancer
- Endocrinology and metabolism
- Fetal, infant and child health
- Immunology and infectious diseases
- Reproductive health and biology
- Women's health

Opportunities for collaboration and partnership

Partnership opportunities include:

- Therapeutics, including oncology and gene therapy
- Reproductive, women's and children's health

- Regenerative medicine
- Infectious disease, inflammation and immunology
- Diagnostics and biomarkers

Hudson can facilitate access to:

- Unique pre-clinical models and research tools
- Platform technologies and clinical trials centre
- A Research Service Provider – Hudson is registered with AusIndustry to provide contract R&D services

Key Indicators

- 230 research staff trained nationally and internationally
- 51 research laboratories
- > 275 publications annually
- 140 HDR students
- 2 start-up companies