DEVELOPMENT OF DOWNSTREAM PROCESSING OPTIONS FOR THE COMMERCIAL SCALE PURIFICATION OF STEM CELL DERIVED EXOSOMES

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Exosomes (or extracellular vesicles) are rapidly gaining momentum as a novel type of regenerative medicine. Exosomes are nano-vesicles in the size range of 20-150nm that are secreted by mammalian cell types (including stem cells). They can induce potent biological functions in surrounding target cells to induce effects that mimic those of the producing cell. These functions can be regenerative, immunomodulatory, anti-scarring and even anti-cancer depending on the state of the producer cell. Consequently, there is enormous potential to develop a range of function-specific products across a wide variety of indications similar to macromolecular blockbusters, but which extend beyond symptom management to produce curative outcomes. However, current methods for purifying exosomes have been based on technologies grandfathered in from the viral industry which are not suitable for large scale, high purity production but are robust enough to perform preliminary characterisation of the exosome population composition.

The aim of this study was to develop a new platform technology/process for purification at commercially relevant scales to acceptable regulatory standards. A further aim of this work is to create processes which operate orthogonally to the commonly used exosome recovery steps which are predominantly physically based.

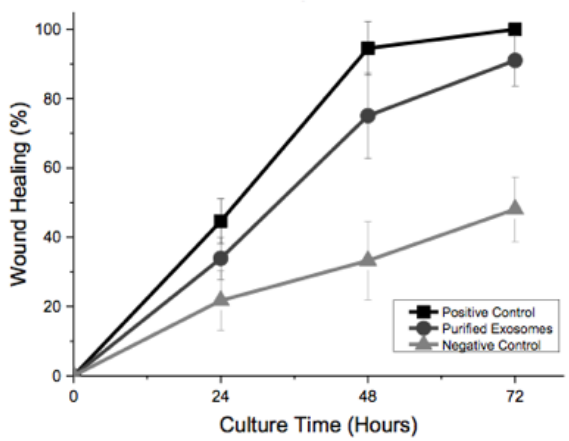

Fig. 1: Potency of purified exosomes in wound closure model

A commercial cell line that is in clinical development was used to generate exosomes. A wide variety of acceptance criteria were established (including particle concentration/size distributions, particle:protein ratios, host cell DNA/RNA clearance and exosomal specific markers such as CD63 and CD81) to ensure quality-driven process development that is scalable and removes cell-culture associated impurities. The monolithic options established in this project to date have shown that exosome material recovered via batch tangential flow filtration can be efficiently captured and recovered from both columns whilst removing key process contaminants and maintaining a product that retains both identity and potency (Figure 1).