



EVscale™ - New Perspectives for Regenerative Medicines

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Executive Summary



Many complex disease conditions are still lacking (good) treatment options (Unmet Medical Need)
Extracellular Vesicles (EV) e.g, from Stem Cells, offer exciting biological activities but are notoriously difficult to manufacture

Phoenestra has recently solved the manufacturing problems for Stem Cell-derived EV (EVscale™) and is characterizing these EV in depth

Functional characterization by selected in vitro model systems reveals mixtures of intrinsic biological activities for these EV preparations

It is tempting to believe that these biologically active EV preparations might play a beneficial role in complex disease conditions with unmet medical need as mentioned above

Phoenestra – together with a world-class network of collaborators - is therefore extremely well positioned to become a significant player in the field of EV therapeutics

EVscale™ has been developed in collaboration with



There is huge unmet medical need in many degenerative and acute/chronic disease conditions



The Problem

Degenerative and chronic diseases are frequently characterized by:

- Acute or chronic inflammation
- Activated immune cells
- Lack of blood vessel formation
- Fibrosis of tissues and organs
- Tissue damage

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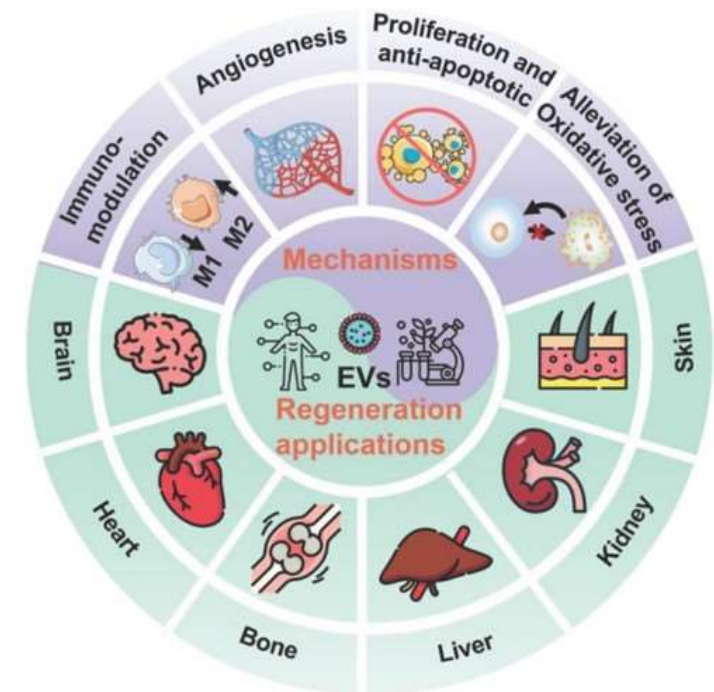
The Solution

Extracellular Vesicles (EV) from human cells address these disease characteristics naturally:

- Anti-inflammation
- Immune-modulation
- Blood vessel formation
- Anti-fibrosis
- Cell fitness and proliferation

The Case for Extracellular Vesicles (EV) from human cells and the state of EV as therapeutics

- Why EV and not stem cells or differentiated cells?
 - Proven biological activities
 - Non-immunogenic
 - No potential safety concerns e.g., no teratogenicity
 - Adventitious virus clearance possible
 - Sterile filtration possible
 - Engineering/loading potential
 - Categorized as biologics by regulators
- BUT: the status of therapeutic EV technology
 - Highly variable manufacturing and quality
 - Lack of scalability and supply issues
 - Complex mixtures
 - Clinical studies and product approvals for/of cell-based therapies are hampered by manufacturing issues



From: Li M, Fang F, Sun M, Zhang Y, Hu M, Zhang J. Extracellular vesicles as bioactive nanotherapeutics: An emerging paradigm for regenerative medicine. *Theranostics*. 2022 Jun 21;12(11):4879-4903. doi: 10.7150/thno.72812. PMID:35836815; PMCID: PMC9274746.

Phoenestra is ideally positioned to harvest the potentials of EV in many therapeutic areas



With *EVscale™*, Phoenestra has solved the manufacturing and quality issues hampering the EV field so far, opening up wide opportunities for novel therapeutic products

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EVscale™ is the solution

Extracellular Vesicles (EV) with scalability and consistency:

- Anti-inflammation
- Immune-modulation
- Vascular network formation
- Anti-fibrosis
- Cell proliferation

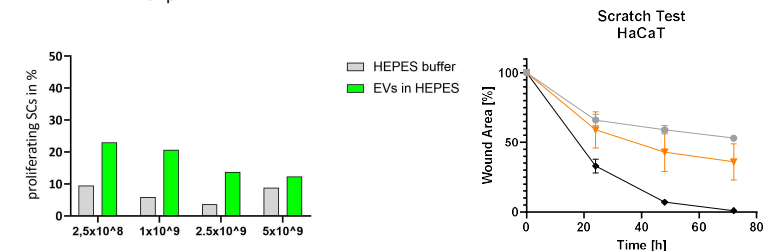
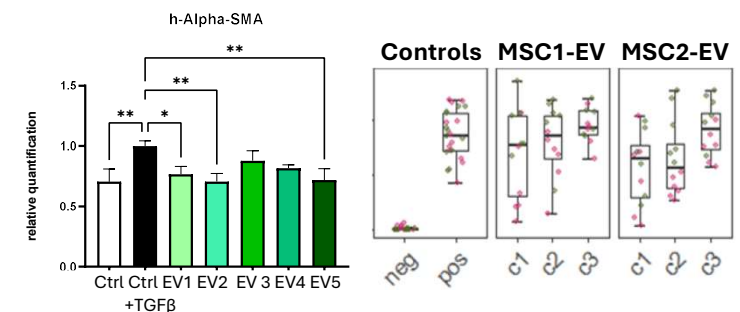
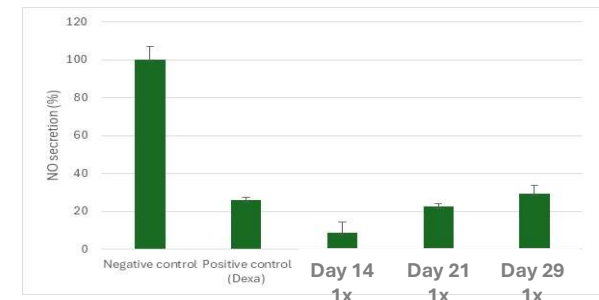
**Complex, multi-faceted diseases require therapeutic interventions at several levels
Depending on their cell source, EV offer combinations of biological functions**

EV from Phoenestra's EVscale™ platform display combinations of biological activities



Relevant biological activities of EVscale™ preparations are being tested in *in vitro* model systems where they show:

- Dexamethasone-like **anti-inflammatory activity** and **Macrophage polarization**
- **Anti-fibrosis activity** in a 2D-skin fibroblast and 3D-liver organoid model
- **Vascular network formation** in a 2D and a 3D- model
- EV-enhanced **proliferation of human Schwann cells** in a peripheral nerve regeneration model
- Excellent **wound healing** potential in a 2D scratch assay (the 3D wound healing model is underway)
- ... and more is to come!



The Value Proposition of EVscale™ - Summary



- **Extracellular Vesicles (EV) are exciting new therapeutic modalities – one of the next ‘big things’**
- **They are difficult to manufacture and Phoenestra has developed a first-in-class solution**
- **EVscale™ combines scalability, productivity, analytical excellence and cost leadership**
- **Manufactured EV preparations consistently display combinations of biological functions**
- **With a holistic approach we are very well positioned to move into EV product development**

EVscale™ has been developed in collaboration with

