

Innovating extracellular vesicles for cardiac repair

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Extracellular vesicles (EVs) function as a mode of intercellular communication and molecular transfer to elicit diverse biological/functional response. As therapeutic modalities EVs hold great promise due to their endogenous characteristics in transport and transfer of functional components to target cells¹; however, further bioengineering refinement is required to address clinical and commercial limitations^{2,3}. EVs are important components of paracrine signaling in stem/progenitor cell-based therapies, are employed as standalone therapies, and can be used as a drug delivery system³. Despite remarkable utility of native/biological EVs, they can be improved using bio/engineering approaches to further therapeutic potential. Our research program involves understanding and harnessing native EVs and integration of mass spectrometry-based proteomics with the goal of identifying new deliverable therapeutic targets. Here, we present insights into development of scalable approach to generate functional nanovesicles for cell-dependent cardiac repair⁴. We highlight the capacity of nanovesicles to improve three-dimensional cardiac organoid function in a post-injury/hypoxic model and induce organoid proteome reprogramming of cardiac-/angiogenic-related proteins to support repair functions. Our results indicate that stem cell-derived nanovesicles are a promising functional and potent therapeutic surrogate for native EVs for tissue repair.

¹ Rai A, et al., 2021. *J Extracell Vesicles*. 10(13):e12164. Proteomic dissection of large extracellular vesicle surfaceome unravels interactive surface platform.

² Claridge, B., et al., 2021. *Front Cell Dev Biol*. **9**, 734720. Development of Extracellular Vesicle Therapeutics: Challenges, Considerations, and Opportunities.

³ Xu R, et al., 2018. *Nature Rev Clin Oncol*. 15(10):617-638. Extracellular vesicles in cancer - implications for future improvements in cancer care.

⁴ Greening DW et al., 2023. *Semin Cancer Biol*. S1044-579X(23)00017-2. Extracellular Vesicles as Next Generation Immunotherapeutics.

⁵ Lozano J, et al., 2022. *Int J Mol Sci*. 23(22):14334. Scalable Generation of Nanovesicles from Human-Induced Pluripotent Stem Cells for Cardiac Repair.