Clinical scale production of exosomes, a novel therapeutic platform for the delivery of biomolecules

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ABSTRACT

Exosomes are vesicles comprised of lipids, proteins, carbohydrates, and nucleic acids that are produced by cells. These complex nanoparticles transit the body and are taken up by cells, thereby altering the recipient cell biology. We seek to harness the therapeutic potential of exosomes by loading pharmacological biomolecules into exosomes to co-opt the natural trafficking and uptake of exosomes.

Current state of the art technology for purifying exosomes requires unit operations such as gradient ultracentrifugation that do not have a clear path to scalability in manufacturing. We have developed an exosome purification process that utilizes unit operations that are rapidly scalable from bench to pilot to clinical scale production in a GMP environment. Here we present data from our proprietary manufacturing process at the clinical scale. We show that process performance, product quality, and product yield are consistent from the bench scale to the clinical scale. The ability to produce exosomes at a clinical scale removes a significant bottleneck in the development of exosomes for therapeutics.

INTRODUCTION

Exosome Biology

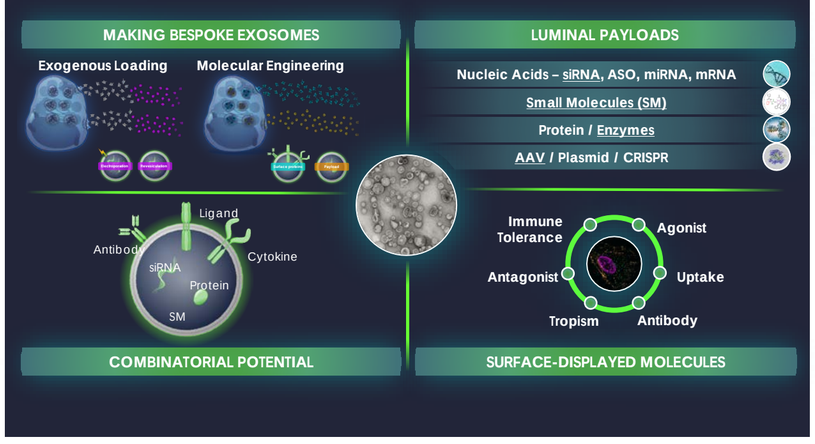
- Lipid bilayers containing nucleic acids, proteins, and carbohydrates
- Subclass of extracellular vesicles
- Produced by all living cells
- Native information carrier between tissues
- Deliver complex pharmacologic payloads and alter biology of recipient cells
- Protected from the immune system

Exosome Attributes

- 30-200 nm in diameter
- Canonical proteins: CD9, CD47, CD63, CD81, etc.
- Relevant functional assays include uptake, potency, biodistribution

We are exosomes
A typical human contains:
10^{13} Cells
10^{14} Bacteria
10^{16} Extracellular vesicles

Codiak's Proprietary Engineered Exosomes (engEx™)



A Typical Process in the Literature

Upstream

- Adherent cells
- Primary cell lines
- Serum-containing media
- Small scale production in T-flasks, cell factories, etc.

Downstream

- Ultracentrifugation with density gradients
- Small scale chromatography kits – difficult to scale
- No viral clearance

Analytics

- Limited
- Various instruments utilized to count particles (includes exosomes but also apoptotic bodies, microvesicles, aggregates, etc.)

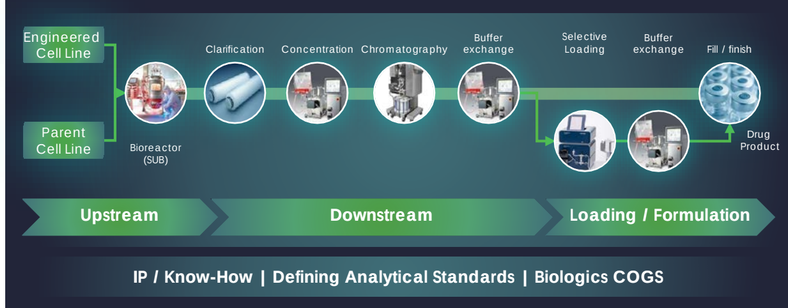
Loading/Formulation

- PBS as default, sometimes include cryo-preservative
- Limited data on storage conditions and stability
- Small scale techniques to load payload

Modality Attributes

	Exosome	Mammalian Protein	Polysaccharide	Conjugate Vaccine	Viral Vector	Cell Therapy
Polydisperse	X		X	X		X
Repeating Structure		-/X	X		X	
Multi-component	X			X	X	X
Particle	X			X	X	X
Exterior Not Well-characterized	X			X	X	X
Interior Not Well-characterized	X			X	X	X
Enveloped	X				-/X	X

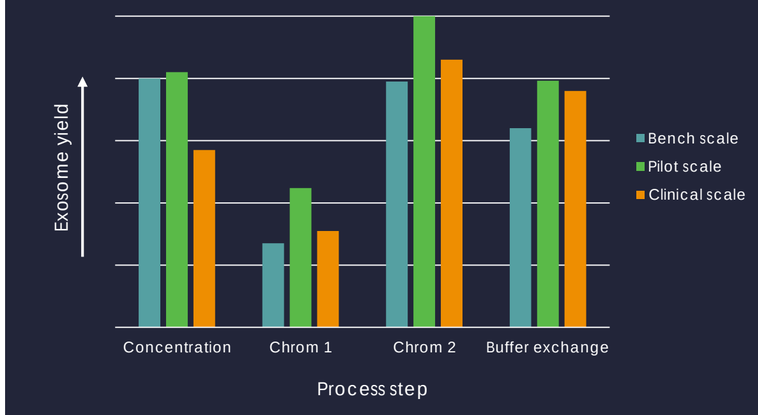
Proprietary Manufacturing Process Established



PROCESS PERFORMANCE

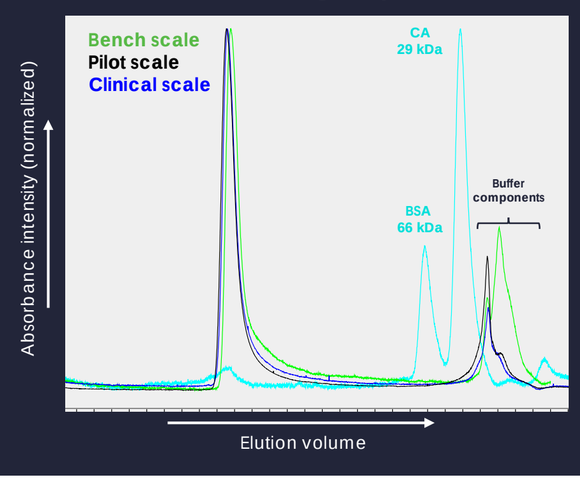
Bioreactor Performance

Exosome Yield during Purification

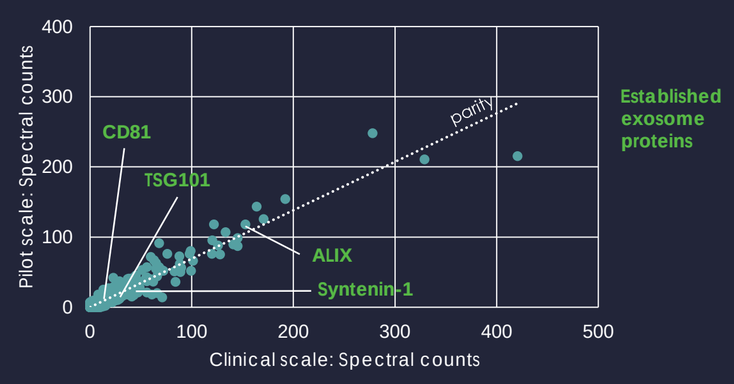


PRODUCT QUALITY

Exosome Chromatographic Profiles



Exosome Proteomic Profiles



SUMMARY

Codiak has developed a manufacturing process that enables clinical scale production of exosomes, thereby removing a significant bottleneck in the development of exosomes for therapeutics.

Process performance, product quality, and product yield are consistent from bench to clinical scale.

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