

# Large-Scale Exosome Production Stirred-Tank Bioreactors

## Researchers' affiliations

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## Background

Cytotoxic drugs for cancer therapy cause several side effects due to toxicities in non-targeted organs. Loading drugs into purified exosomes as vehicles is a promising approach for a more targeted delivery and consequently for minimizing side effects and maximizing drug dosage. Genetic engineering to display tumor-penetrating and -targeting peptides on the exosome surface could further increase the delivery efficiency.

## Challenge

**The aim of this study was to analyze the ability of exosomes to deliver cytotoxic doxorubicin (Dox) to breast cancer cell lines *in vitro*.**

Exosomes were isolated from wild type HEK293F cells and from three different engineered HEK293F cell lines, expressing one or two tumor-homing peptides, respectively. These peptides were displayed on the exosomes surface. The study included:

- > The characterization of purified exosomes by western blotting, electron microscopy, and size distribution analysis
- > The optimization of exosome loading with Dox
- > Functional assays to compare the uptake of the different exosome types by different breast cancer cell lines and the cytotoxic effect of Dox-loaded exosomes.


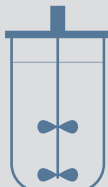

**A large number of exosomes was needed to perform these experiments.**

## Equipment

> [BioFlo® 120 bioreactor control station](#)

## Strategy

For large-scale exosome production HEK293F cells were cultured in a bioreactor in a culture volume of 1–2 L.

Cell maintenance	Large-scale exosome production	Exosome purification and storage
		
<ul style="list-style-type: none"> <li>&gt; Cell maintenance in cell culture flasks in a CO<sub>2</sub> incubator</li> </ul>	<ul style="list-style-type: none"> <li>&gt; Bioreactor culture (1–2 L)</li> <li>&gt; Inoculation density: 1–2 × 10<sup>5</sup> cells/mL</li> <li>&gt; Final cell density: 2 × 10<sup>6</sup> cells/mL</li> </ul>	<ul style="list-style-type: none"> <li>&gt; Differential centrifugation and tangential flow filtration followed by ultracentrifugation</li> <li>&gt; Exosome storage at –80 °C</li> </ul>

## Results

- > Bioreactor culture resulted in 2 × 10<sup>9</sup> cells per liter.
- > Average exosome yield was 3.43 mg per liter of culture, corresponding to 1 × 10<sup>13</sup> particles/liter.
- > The exosomes produced were suitable for investigating their ability to deliver Dox to breast cancer cells *in vitro*.
- > Harboring two peptides on the exosome surface improved the delivery of cytotoxic Dox.

## Conclusion

Engineered exosomes displaying tumor-homing peptides are a promising tool for the targeted delivery of cytotoxic drugs. With the help of a bioreactor, the large quantities of exosomes required for characterization and functional tests could be produced.

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## Read the full story

[Nam HB Tran, et al. Dual-targeting exosomes for improved drug delivery in breast cancer. \*Nanomedicine \(Lond.\)\* 2023](#)

