Göteborg, 2025

Engineered extracellular vesicles for targeting and treating inflammation

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i sal Europa, Konferenscenter Wallenberg, Medicinaregatan 20A, den 4 december 2025, klockan 9.00

av

Markus Bergqvist

Fakultetsopponent:
Professor Lucia Languino
Jefferson University, Philadelphia, USA

Avhandlingen baseras på följande delarbeten

I. **M. Bergqvist**, K-S. Park, N. Karimi, L. Yu, C. Lässer, and J. Lötvall.
Extracellular vesicle surface engineering with integrins (ITGAL & ITGB2) to specifically target ICAM-1-expressing endothelial cells.
Journal of Nanobiotechnology, 2025; 23:64.

II. B. İ. Abas, **M. Bergqvist**, L. Yu, Y. Wang, M. Gimona, K-S. Park, and J. Lötvall.
An anti-Myd88 peptide synergistically enhances the anti-inflammatory effects of extracellular vesicles from naïve umbilical cord MSC or HEK293F CD24 overexpressing cells.
Advanced Materials Interfaces, 2025; e00252.

III. **M. Bergqvist**, K-S. Park, E. Åkesson, N. Ordouzadeh, Y. Wang, M. Rådinger, C. Lässer, and J. Lötvall.
Syndecan-expressing extracellular vesicles function as anti-inflammatory agents.
In Manuscript, 2025.

IV. **M. Bergqvist**, C. Lässer, R. Crescitelli, K-S. Park, and J. Lötvall.
A non-centrifugation method to concentrate and purify extracellular vesicles using superabsorbent polymer followed by size exclusion chromatography.
Journal of Extracellular Vesicles, 2025; 14(1):e70037.

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN

GÖTEBORGS UNIVERSITET

Göteborg, 2025

Engineered extracellular vesicles for targeting and treating inflammation

Markus Bergqvist
Avdelningen för invärtesmedicin och klinisk nutrition, Institutionen för medicin, Sahlgrenska akademin, Göteborgs universitet, Göteborg, Sverige, 2025.

ABSTRACT

Extracellular vesicles (EVs) are nano-sized particles released by human and mammalian cells. They are emerging as therapeutic platforms due to their ability to facilitate intercellular communication and their immunomodulatory potential. Their broad clinical translation remains limited by challenges in precise cell targeting, therapeutic efficacy, and scalable manufacturing. This thesis examines various EV engineering strategies designed to enhance targeting and induce immunomodulatory functions, while improving the scalability of isolation.

To address these challenges, engineered HEK293F cells were utilized to generate EV-based therapeutics for targeting and treating inflammation. EVs expressing LFA-1 were generated to enable selective targeting of ICAM-1-positive endothelial cells, providing a strategy for treating endothelial inflammation. Overexpression of CD24 and syndecans was introduced to produce EVs with intrinsic anti-inflammatory properties. These vesicles were further loaded with an anti-inflammatory peptide to potentially augment their therapeutic effects. In addition, a combined workflow employing superabsorbent polymer (SAP) concentration and size exclusion chromatography (SEC) purification was tested to isolate EVs using a non-ultracentrifugation approach.

This thesis successfully developed LFA-1-expressing EVs with enhanced targeting capacity to ICAM-1-positive endothelial cells, which enhanced delivery and efficacy of an EV-loaded anti-inflammatory peptide, resulting in synergistic effects (**Paper I**). Further, expression of either CD24 or Syndecans (1, 2, and 4) in EVs induced an anti-inflammatory function, evident both in vitro (**Papers II and III**) and in vivo (**Paper III**). Lastly, combining SAP with SEC enabled the isolation and purification of EVs in a possibly scalable manner, retaining their functionality and EV markers (**Paper IV**).

This thesis developed engineered EVs from HEK293F cells to improve targeting, immunomodulation, and scalable production, ultimately generating EV-based drug candidates for treating inflammation. Through surface modifications (LFA-1, CD24, syndecans), therapeutic peptide loading, and a robust SAP-SEC isolation workflow, it supports the development of EV therapeutics with intrinsic anti-inflammatory properties and synergistic efficacy, as well as scalable manufacturing.

Keywords: Exosomes, engineering, LFA-1, ICAM-1, targeting, peptide loading, CD24, syndecans, immunomodulation, EV isolation

ISBN: 978-91-8115-489-4 (TRYCK)
ISBN: 978-91-8115-490-0 (PDF)

http://hdl.handle.net/2077/89228