



Karolinska
Institutet

ERC CoG DELIVER
In situ engineering of extracellular
vesicles

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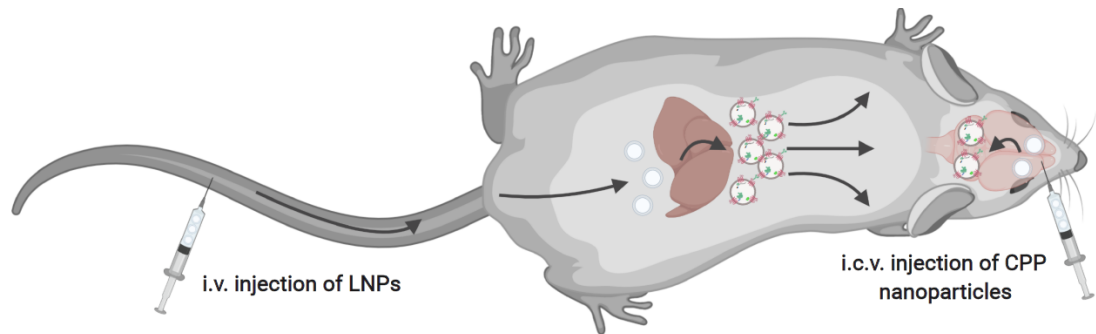
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Me before ERC

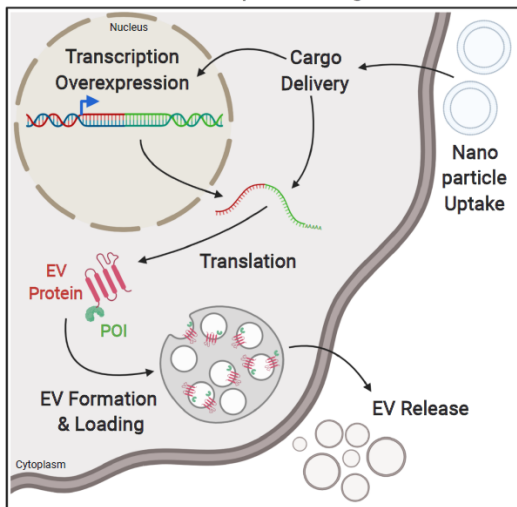
- PhD in Neurochemistry at Stockholm University in 2008.
- Postdoc at KI in 2010 and Oxford 2011–13 (SSMF postdoc).
- Established lab at KI in 2013 and Oxford 2013–18.
- VR and SSMF start-up grants in 2012.
- Very little success with Swedish Foundations (Söderberg, KAW etc).
- Founder of EVOX Therapeutics in 2016; employed 7 new FTEs.
- Multiple international meetings– expanded my collaborative network
- Applied for the ERC consolidator grant for the first and only time in 2020.

Developing a successful proposal

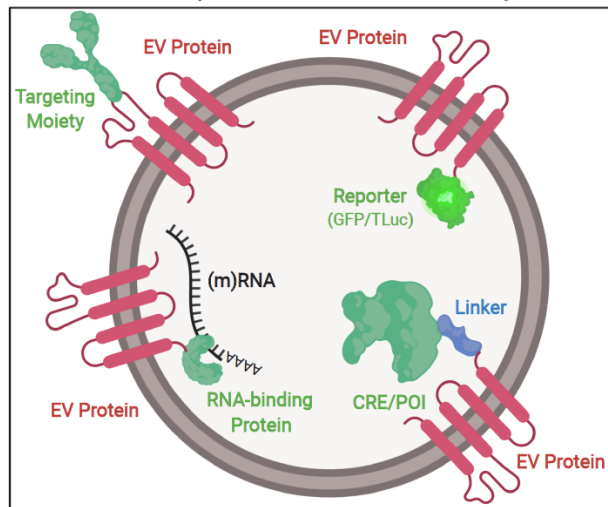
- Think carefully how to create a high risk/ high reward project– connect it to your current research activities BUT make it different!
- Why is the project important, why now and why you?
- Set time a side– I spent nearly 2 full months writing it. Be mindful about the small things! Transparency about risks– have solid risk mitigation plans.
- Use simple graphics to describe the project– reviewers need to grasp the project without too much reading!



in situ EV production from synthetic nanoparticle cargo



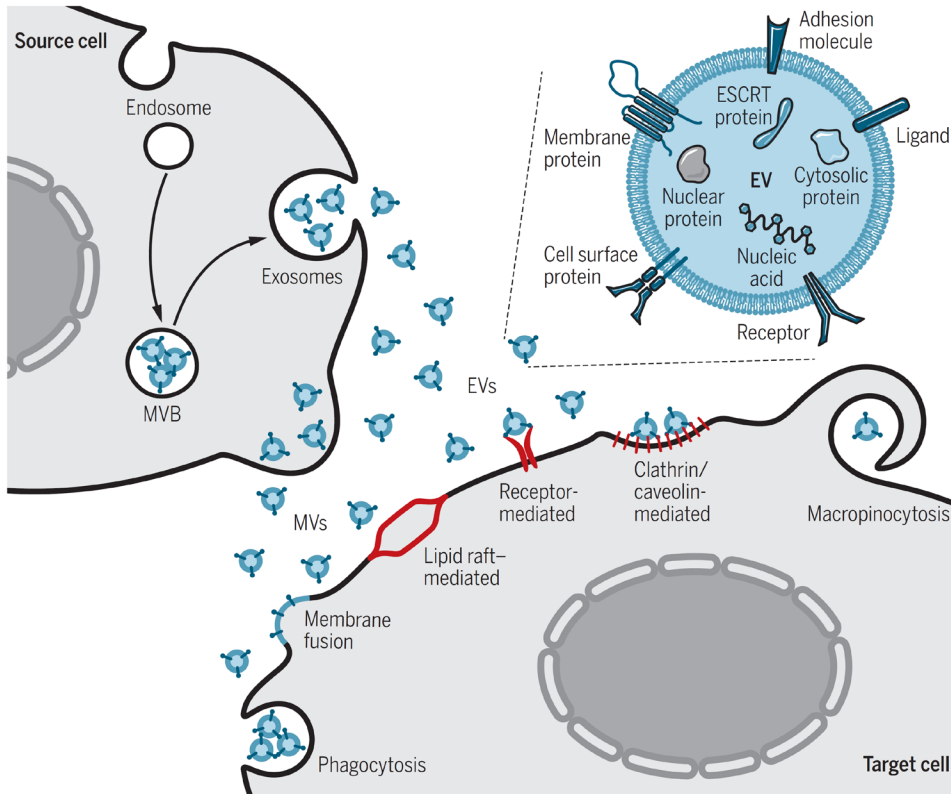
in situ engineered EVs for therapeutic CNS delivery or extrahepatic biodistribution and delivery



Developing a successful proposal

- Laser sharp abstract- catch the reviewers attention.
- Write concisely- excessive text is exhasutive.
- Describe collaborations- collaborative networks are important. Go to conferences and interact with other peers.
- Be detailed with budget descriptions and etical considerations. The "boring" parts of the application are important too!
- Promote yourself in the CV and on the interview.

Extracellular vesicles (EVs)

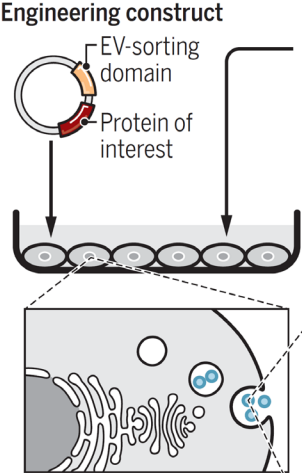


- Safe for repeated dosing
- Protection of RNA/protein
- Delivery across barriers
- Potent surface signalosome
- Amenable to engineering

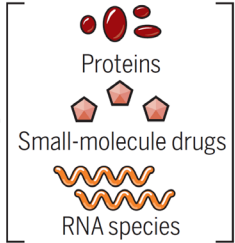
EV engineering strategies

Endogenous Loading

Genetic manipulation of source cells
BEFORE EV isolation



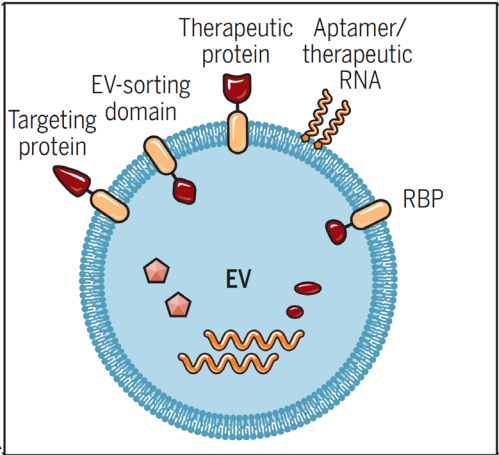
Endogenous loading



Exogenous loading

Exogenous Loading

Loading of EVs AFTER isolation





Identification of scaffold proteins for improved endogenous engineering of extracellular vesicles

Received: 19 October 2022

Accepted: 27 July 2023

Published online: 07 August 2023

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ARTICLES

<https://doi.org/10.1038/s41551-021-00792-z>nature
biomedical engineering

Amelioration of systemic inflammation via the display of two different decoy protein receptors on extracellular vesicles

Dhanu Gupta^{1,14}✉, Oscar P. B. Wiklander^{1,14}✉, André Görgens^{1,2}, Mariana Conceição³, Giulia Corso¹, Xiuming Liang¹, Yiqi Seow⁴, Sriram Balusu^{5,6}, Ulrika Feldin¹, Beklem Bostancioglu¹, Rim Jawad¹, Doste R. Mamand^{1,7}, Yi Xin Fiona Lee^{1,8}, Justin Hean⁹, Imre Mäger^{1,3}, Thomas C. Roberts^{1,10}, Manuela Gustafsson¹, Dara K. Mohammad^{1,11}, Helena Sork¹, Alexandra Backlund¹², Per Lundin⁹, Antonin de Fougères⁹, C. I. Edvard Smith^{1,13}, Matthew J. A. Wood^{1,10}, Roosmarijn E. Vandenbroucke^{1,5,6}, Joel Z. Nordin¹✉ and Samir EL Andaloussi¹✉

Antibody-displaying extracellular vesicles for targeted cancer therapy

Received: 20 March 2023

Accepted: 8 April 2024

Published online: 20 May 2024

Check for updates

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RESEARCH ARTICLE

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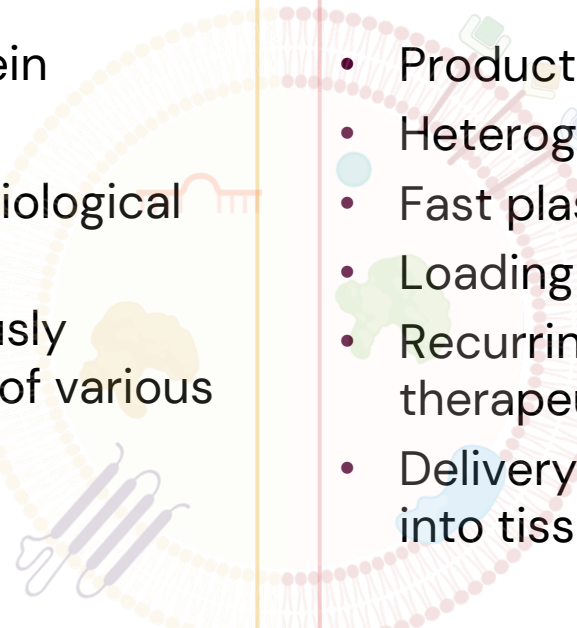
www.advancedscience.com

Novel Endogenous Engineering Platform for Robust Loading and Delivery of Functional mRNA by Extracellular Vesicles

Antje M. Zickler,* Xiuming Liang,* Dhanu Gupta, Doste R. Mamand, Mariacristina De Luca, Giulia Corso, Lorenzo Errichelli, Justin Hean, Titash Sen, Omnia M. Elsharkasy, Noriyasu Kamei, Zheyu Niu, Guannan Zhou, Houze Zhou, Samantha Roudi, Oscar P. B. Wiklander, André Görgens, Joel Z. Nordin, Virginia Castilla-Llorente, and Samir EL Andaloussi*

EVs as delivery vectors

Promises

- Protection of RNA/protein
 - Immune tolerance
 - Translocation through biological barriers
 - Ability to be endogenously engineered for delivery of various biotherapeutics
- 

Challenges

- Production and characterization
- Heterogeneity
- Fast plasma clearance
- Loading limitations
- Recurring dosing for sustained therapeutic effect
- Delivery of biotherapeutics deeper into tissue parenchyma

ERC project- in situ engineering!

Solution

1

Deliver gene therapy modality with information for the production of engineered EVs

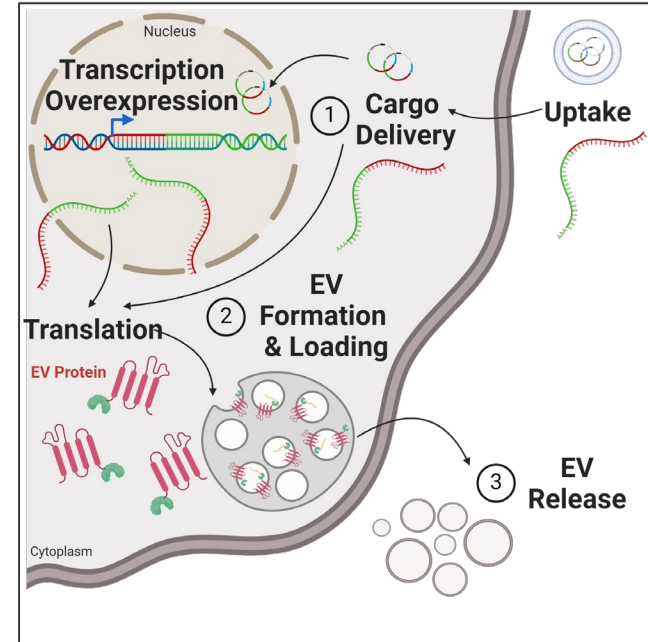
2

Endogenous production and secretion of engineered EVs systemically or in CNS

3

Distribution of EVs to hard-to-reach organs

In situ production of EVs



Final remarks

- Mind the details– never submit a proposal you are not happy with– especially to ERC
- Think big BUT be mindful about the feasibility of the project
- Let others read and comment multiple times before sending
- Be stubborn– grant failures are part of the scientific journey!
- Surround yourself with good people!!

The Team





European
Research
Council



Horizon2020
European Union Funding
for Research & Innovation

