



Latvian Biomedical
Research and Study Centre
research and education in biomedicine from genes to human



Oslo
University Hospital



**LATVIJAS
UNIVERSITĀTE**
ANNO 1919

NFI/R/2014/045

Cancer-derived extracellular vesicles: function and clinical applications in prostate cancer

Coordinator: Dr. Aija Linē



Latvijas Biomedicīnas
pētījumu un studiju centrs
biomedicīnas pētījumi un izglītība no gēniem līdz cilvēkam



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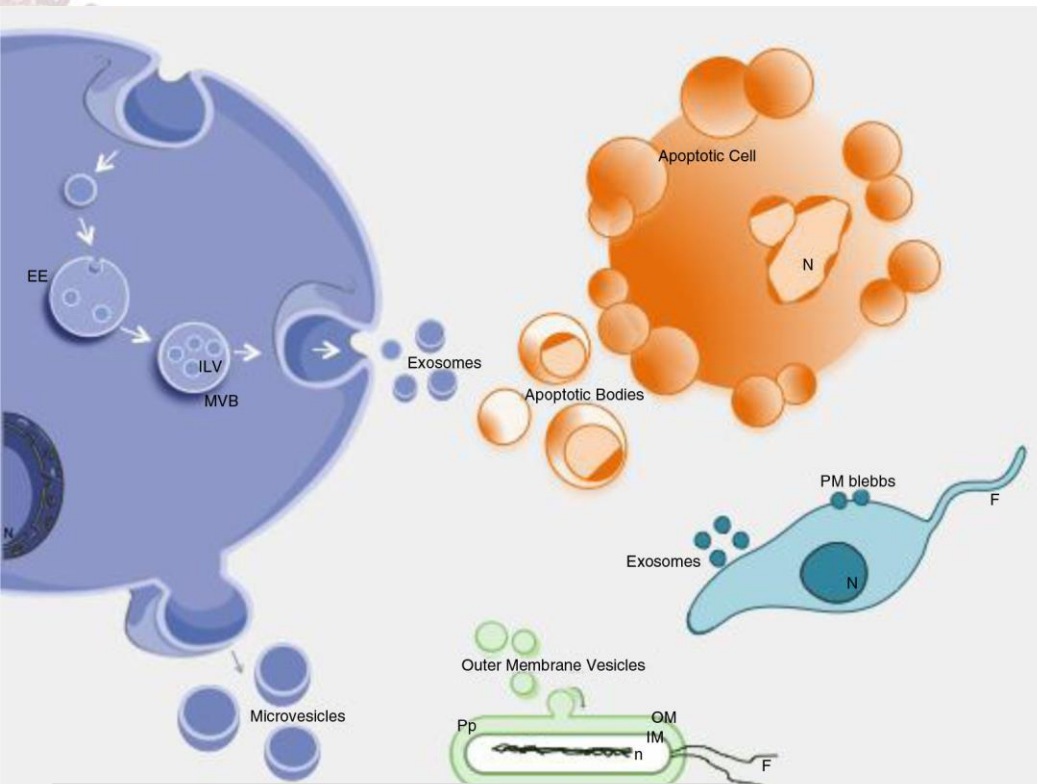
NFI/R/2014/051

Image-guided cancer gene therapy in combination with advanced chemotherapeutics

Coordinator: Dr. Anna Zajakina

Cancer-derived extracellular vesicles: function and clinical applications in prostate cancer

Extracellular vesicles (EVs)



Types of EVs:

- ✓ Exosomes
- ✓ Microvesicles
- ✓ Apoptotic bodies

- ✓ EVs are produced by many cell types
- ✓ EVs have been found in a variety of biofluids – blood, urine, saliva, milk etc.
- ✓ Mediate intercellular communication
- ✓ Increased in cancer patients



Journal of
Extracellular Vesicles

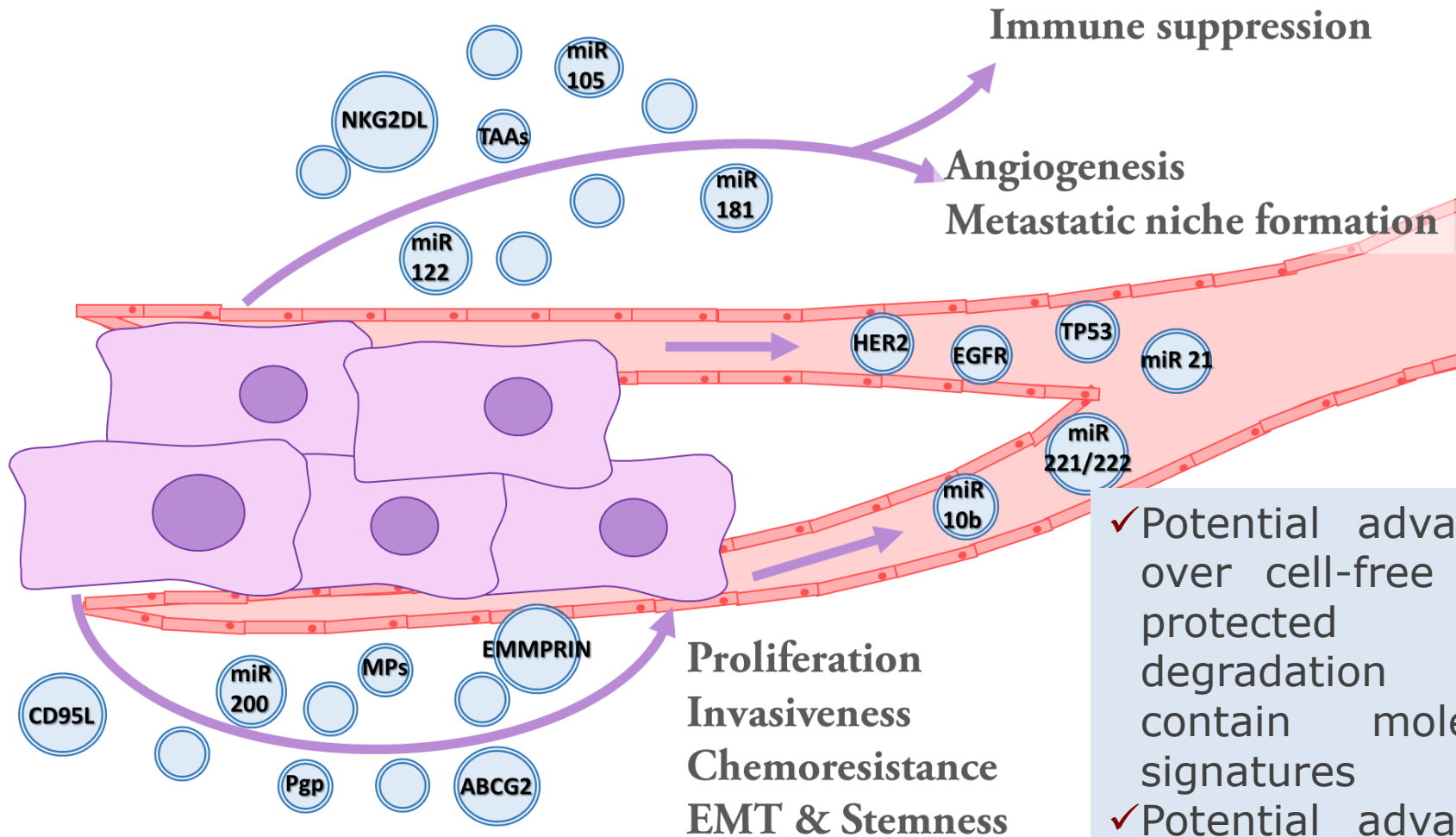
REVIEW ARTICLE

Biological properties of extracellular vesicles and their physiological functions

Maria Yanez-Mo et al, JEV, 2015



Cancer-derived EVs may serve as “liquid biopsies” and therapeutic targets



- ✓ Potential advantage over cell-free RNA: protected from degradation and contain molecular signatures
- ✓ Potential advantage over CTCs: abundant in plasma

Objectives

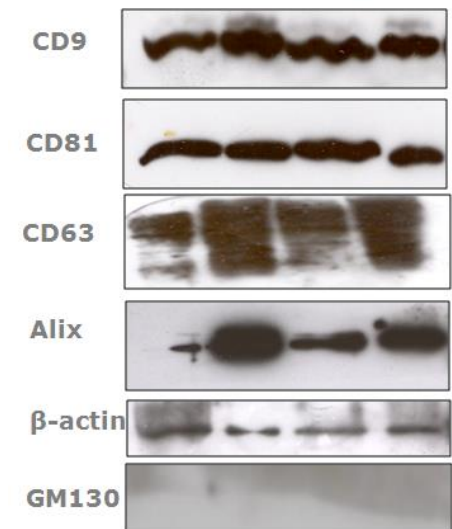
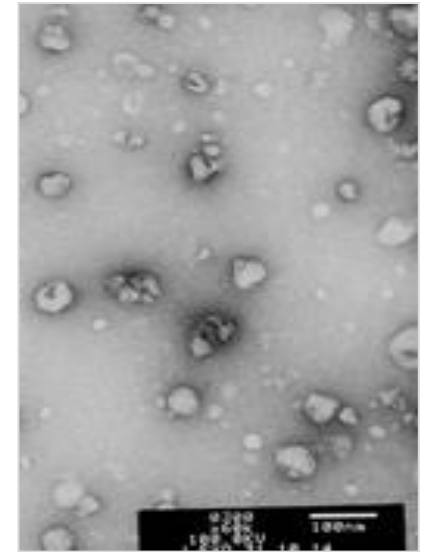
To delineate the role of cancer-derived EVs in the progression of prostate cancer and to identify EV-enclosed RNAs that can serve as potential therapeutic targets and/or prognostic biomarkers of prostate cancer.

Specific objectives:

- ✓ To characterise RNA content of EVs released by aggressive and indolent prostate cancer cells
- ✓ To study EV uptake mechanisms by recipient cells *in vitro*
- ✓ To study EV biodistribution and effects on tumour growth *in vivo*
- ✓ To establish prostate cancer biobank
- ✓ To analyse RNA biomarker candidates in biofluids of prostate cancer patients

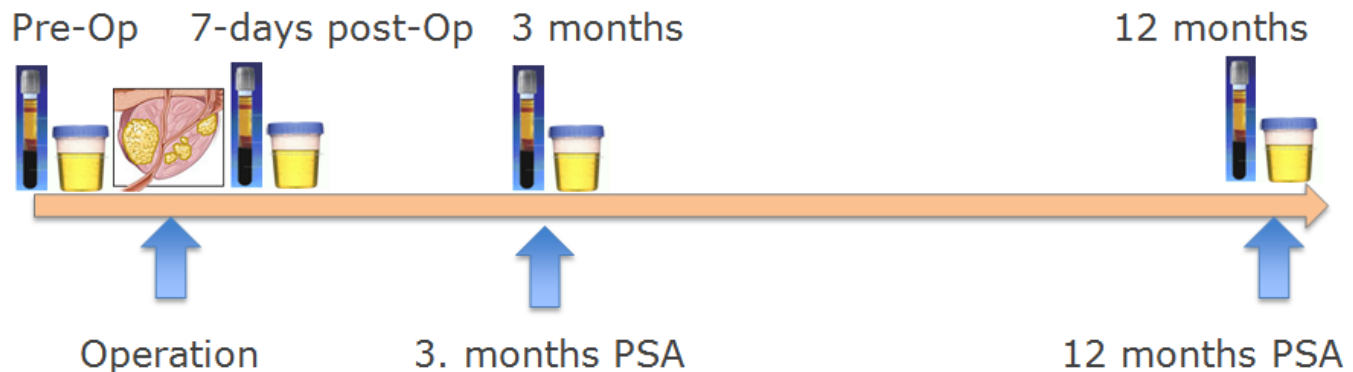
Results

- ✓ Established a robust method for the isolation of EVs from cell culture media, patients' plasma and urine. Novelty – urinary EVs.
- ✓ Established a methodology for the characterisation of EVs based on electron microscopy, Western blotting and NTA analysis.
- ✓ Acquired new data on the uptake mechanisms and functional effects in mesenchymal stem cells.
- ✓ Established a mouse model of prostate cancer for studying EV biodistribution.



Results

- ✓ Established two collections of clinical material from prostate cancer patients:
 - A retrospective cohort of ~200 PC, BPH and healthy controls – follow up and clinical info for 4-6 years: **prognostic value**
 - A longitudinal cohort of 50 PC patients: **dynamics of EV content**



- ✓ Performed RNA sequencing in two sample sets:
 - Urinary EVs from patients with high vs low Gleason score and healthy controls: **prognostic biomarker candidates**
 - Urinary and plasma EVs before and after surgery and tumour tissue from a PC patient: **comparison of RNA content in plasma and urinary EVs**

Outcomes: publications and MSc theses

Endzeliņš et al. *Molecular Cancer* (2016) 15:41
DOI 10.1186/s12943-016-0523-5

Molecular Cancer

REVIEW

Open Access

Diagnostic, prognostic and predictive value of cell-free miRNAs in prostate cancer: a systematic review



Edgars Endzeliņš^{1†}, Vita Melne^{1,2†}, Zane Kalniņa¹, Vilnis Lietuvietis^{1,2}, Una Riekstiņa³, Alicia Llorente⁴ and Aija Linē^{1*}

Regulation of exosome release by 2-hydroxyoleic acid and oleic acid

Dhakkshaginy Rajalingam



Department of Biosciences

The Faculty of Mathematics and Natural Sciences

UNIVERSITY OF OSLO

June 2016

LATVIJAS UNIVERSITĀTES RAKSTI. 2016, 812. sēj.
MEDICĪNA

85.–99. lpp.

Vēža šūnu līniju producēto eksosomu uzņemšana un funkcionālie efekti mezenhimālajās cīlmes šūnās

Uptake and functional effects of cancer cell line-produced exosomes in mesenchymal stem cells

Ineta Popēna,¹ Kaspars Jēkabsons,¹ Artūrs Ābols,² Līga Saulīte,¹
Una Čonka,¹ Inga Kozlovska,¹ Elīna Zandberga,² Juris Stefanovičs,²
Velta Ose-Klinklāva,² Ruta Muceniece,¹ Aija Linē,² Una Riekstiņa¹

LATVIJAS UNIVERSITĀTE
MEDICĪNAS FAKULTĀTE
FARMĀCIJAS MAĢISTRA STUDIJU PROGRAMMA

IN VITRO MODEĻA IZVEIDE
ĻAUNDABĪGĀ AUDZĒJA EKSTRACELULĀRO
VEZĪKULU ENDOCITOZES PĒTĪŠANAI
MEZENHIMĀLAJĀS CILMES ŠŪNĀS

MAĢISTRA DARBS

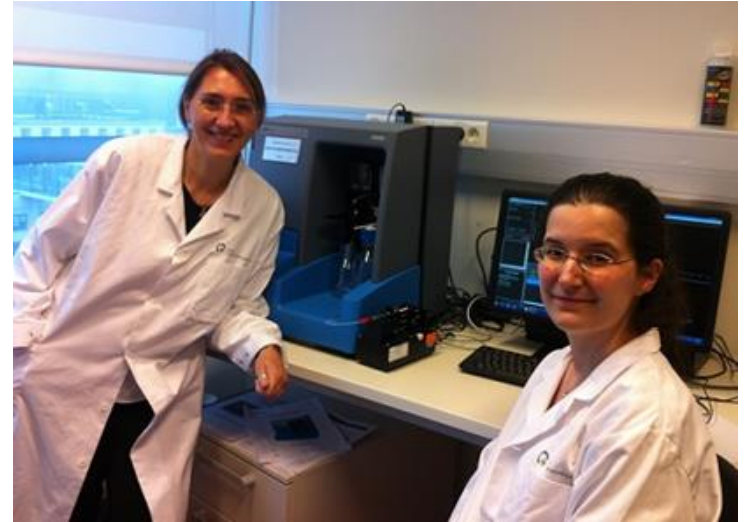
Autore: Inga Kozlovska
Studenta apliecības Nr.: ik11205
Darba vadītāja: asoc. prof. Dr. Biol. Una Riekstiņa



Added value of collaboration and synergy with the Fellowship activity



- ✓ Research training and mobility of PhD students
- ✓ Advanced courses in animal research, bioinformatics etc. at Oslo University
- ✓ Hands on training in the isolation of EVs, NTA analysis, generation of xenograft tumour models etc.
- ✓ Exchange of knowledge and standardisation of protocols
- ✓ Combing expertise in different areas of research
- ✓ Increased visibility and potential leadership in the Baltic region in the area of EV-derived cancer biomarkers



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