



# HBM4EU project

science and policy  
for a healthy future

Extracellular vesicles as novel biomarkers  
for monitoring human disease

Metka Lenassi


1<sup>st</sup> HBM4EU Training School 2018

## *Presentation outline:*

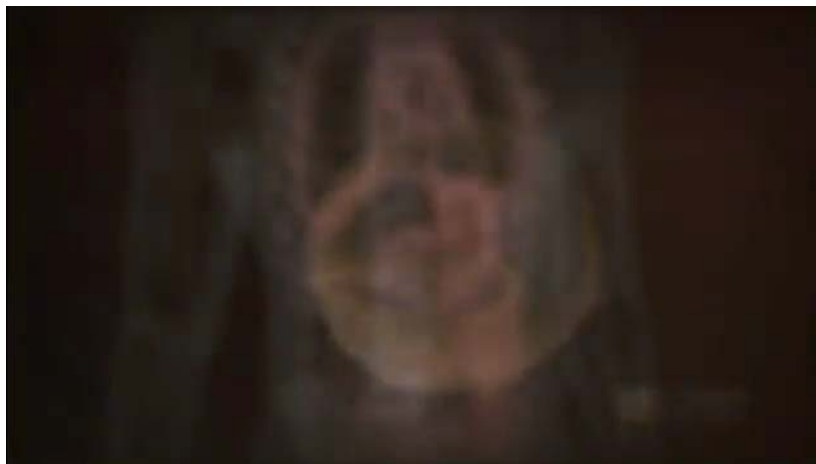
---

- *What are extracellular vesicles?*
- *What is the role of extracellular vesicles in the human body?*
- *Why are extracellular vesicles good source of disease biomarkers?*
- *Extracellular vesicles in the blood*
- *Conclusions*

1<sup>st</sup> HBM4EU Training School, Ljubljana, June 18-22, 2018



## What are extracellular vesicles (EVs)?

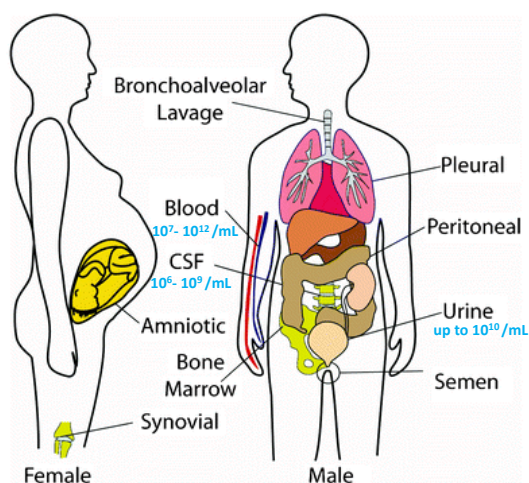


Adapted from CARIS Life Sciences video:  
[https://www.youtube.com/watch?v=og5\\_T\\_heSQY](https://www.youtube.com/watch?v=og5_T_heSQY)

1st HBM4EU Training School, Ljubljana, June 18-22, 2018



## EVs accumulate in all body fluids

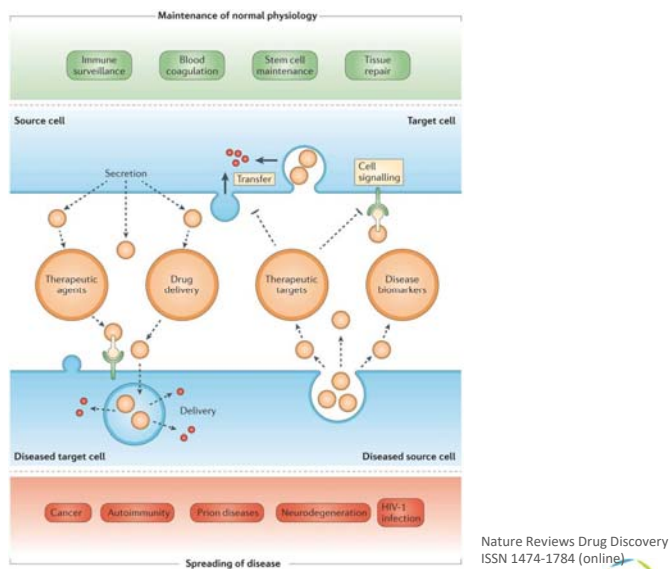


Lab Chip, 2013, 13, 1011

1st HBM4EU Training School, Ljubljana, June 18-22, 2018



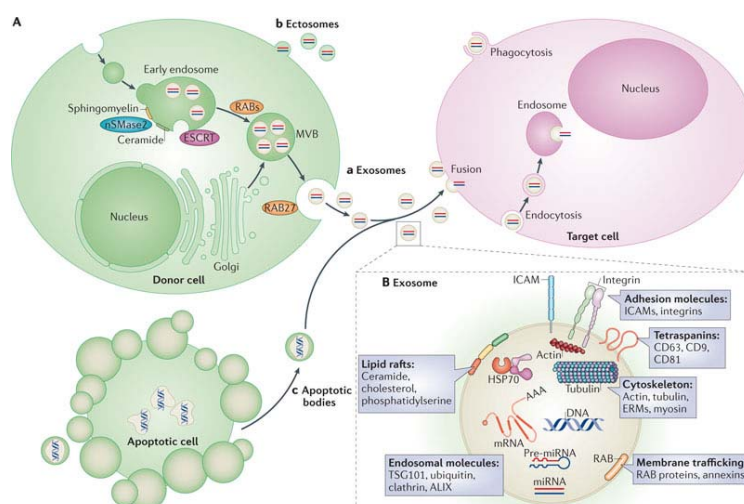
## EVs have diverse (patho)physiological roles



1st HBM4EU Training School, Ljubljana, June 18-22, 2018



## EVs are heterogeneous in subcellular origin

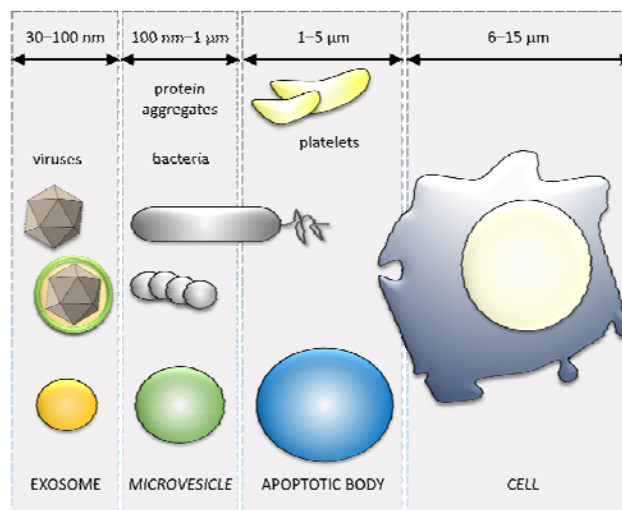


Nature Reviews Molecular Cell Biology ISSN 1471-0080 (online)

1st HBM4EU Training School, Ljubljana, June 18-22, 2018



## EVs are heterogeneous in size



Gyorgy et al., Cell Mol Life Sci, 2011, 68: 2667-88

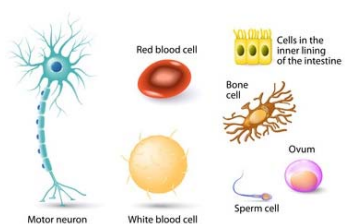
1st HBM4EU Training School, Ljubljana, June 18-22, 2018



## EVs are heterogeneous in molecular composition

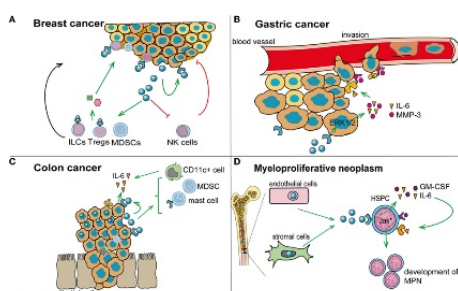
Defined by parental cell:

- type



from Dreamstime.com

- (patho)physiological state



Front. Immunol., 09 January 2017

1st HBM4EU Training School, Ljubljana, June 18-22, 2018

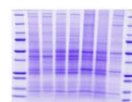


## We can identify those differences by:

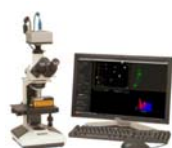
Electron microscopy: **morphology**



Western blotting (or ELISA): **proteins**



NTA (Nanoparticle tracking analysis):  
**size and concentration**



AF4-MALS  
(Asymmetrical flow field-flow fractionation  
combined with MALS detector):  
**size and concentration**



qPCR: **miRNAs**

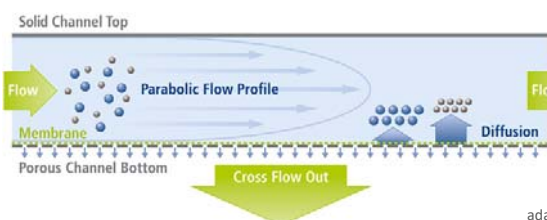


1st HBM4EU Training School, Ljubljana, June 18-22, 2018

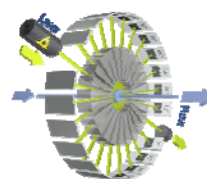
9

## Principles of EV analysis by AF4-MALS

Asymmetrical flow field-flow fractionation (AF4)

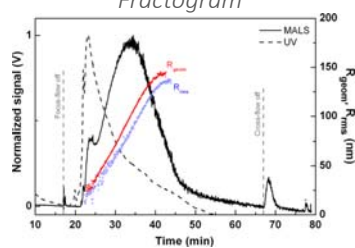


MALS detector



adapted from: Front Chem. 2015; 22(3):45

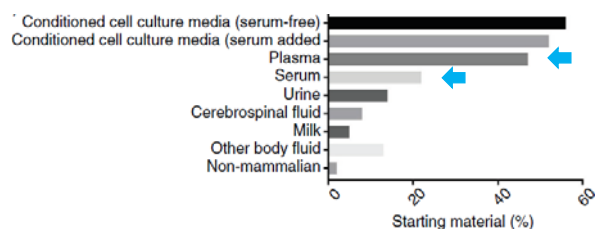
Fractogram



1st HBM4EU Training School, Ljubljana, June 18-22, 2018

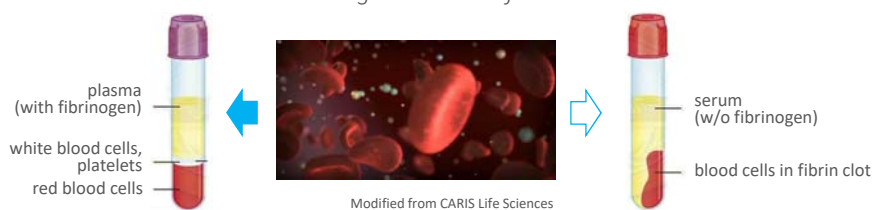
10

## EVs are a rich source of disease biomarkers



Gardiner et al., JEV, 2016, 5: 32945

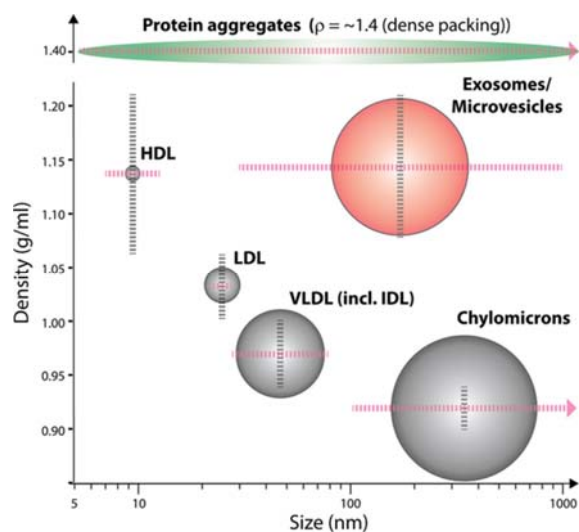
## Blood a good source of EVs



1st HBM4EU Training School, Ljubljana, June 18-22, 2018



## Nanoparticles found in the blood



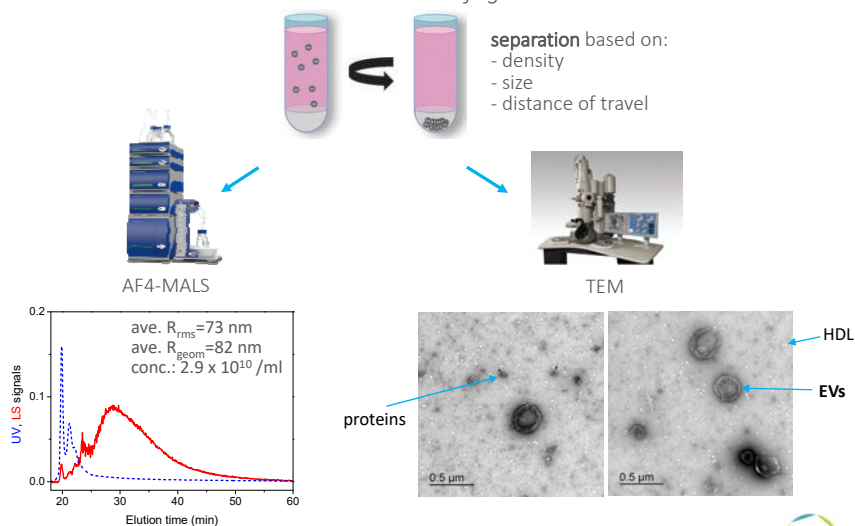
Circ Res. 2017 Sep 29;121(8):920-922

1st HBM4EU Training School, Ljubljana, June 18-22, 2018



## Isolation of EVs from blood plasma

sucrose cushion ultracentrifugation



## Conclusions

- EVs are messengers between cells.
- EVs are cell type specific.
- EVs morphology and composition is affected by disease.
- EVs are a rich source of disease biomarkers.
- Blood is a good source of disease-related EVs.

1st HBM4EU Training School, Ljubljana, June 18-22, 2018



Univerza v Ljubljani  
*Medicinska* Fakulteta

Assist. Prof. Metka Lenassi

University of Ljubljana,  
Faculty of Medicine,  
Institute of Biochemistry

[metka.lenassi@mf.uni-lj.si](mailto:metka.lenassi@mf.uni-lj.si)  
ORCID ID: <https://orcid.org/0000-0002-9488-6855>



This project has received funding  
from the European Union's  
Horizon 2020 research and  
innovation programme under  
grant agreement No 733032.