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Preterm Birth International Collaborative Australasia Workshop

21 March 2023

Enabling EV-based Biomarker Discovery and Diagnostics

Extracellular vesicles have long been a part of placentology and perinatology.

Jones and Fox (1980)

An Ultrastructural and Ultrahistochemical Study of the Human Placenta in Maternal Pre-eclampsia **Placenta** 1, 61-7

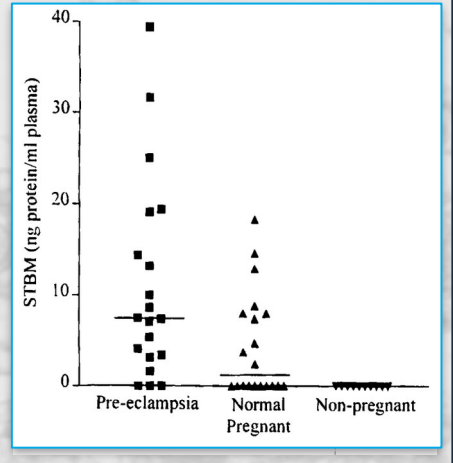
Figure 4. Free surface of the villous syncytiotrophoblast in a placenta from a woman with pre-eclampsia.

There is a marked loss of microvilli and those remaining are deformed. A cytoplasmic protrusion into the intervillous space is present. (x 10000).

Smárason, Sargent, Starkey, Redman (1993)

The effect of placental syncytio-trophoblast microvillous membranes from normal and pre-eclamptic women on the growth of endothelial cells in vitro. **Br J Obstet Gynaecol** 100 943-949

"It is therefore possible that syncytiotrophoblast microvillous membranes could be shed into the maternal circulation from the hypoxic placenta in pre-eclampsia."

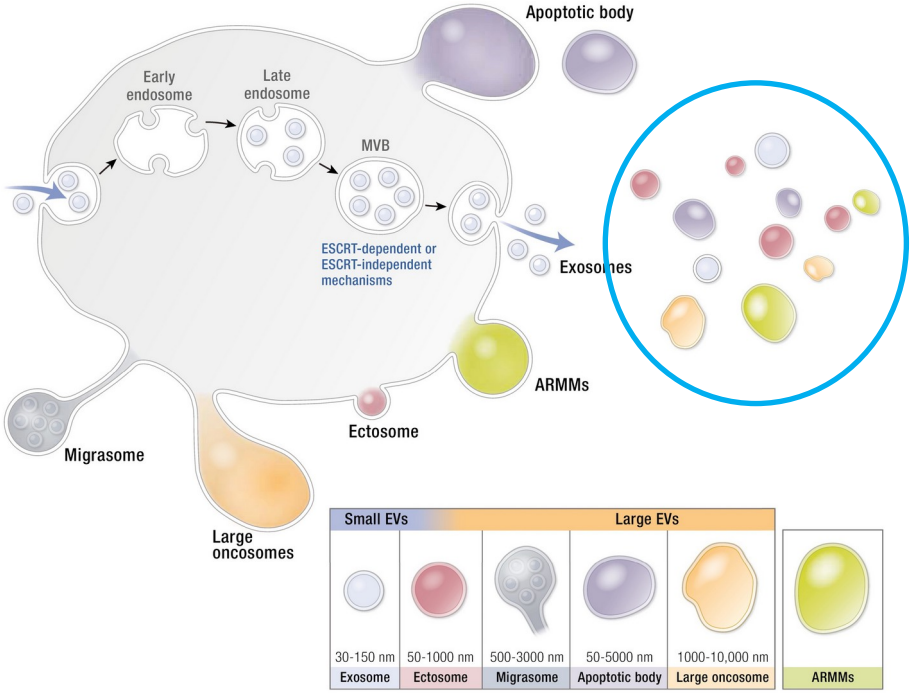


Knight Redman, Linton, Sargent (1998)

Shedding of syncytiotrophoblast microvilli into the maternal circulation in pre-eclamptic pregnancies **Br J Obstet Gynaecol** 105:632-40.

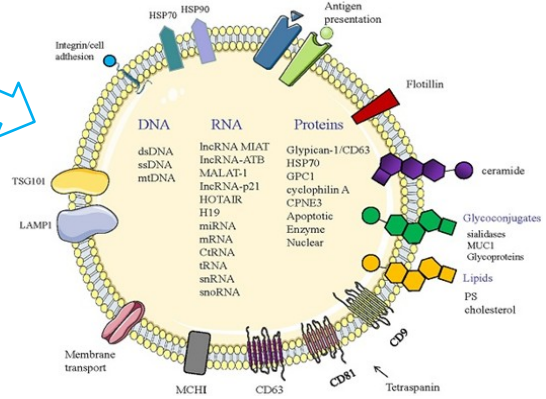
STBM are shed into the maternal circulation and are present in significantly increased amounts in pre-eclamptic women. They may contribute to the endothelial dysfunction underlying the maternal syndrome of pre-eclampsia

Extracellular Vesicle Biogenesis, Function and Heterogeneity



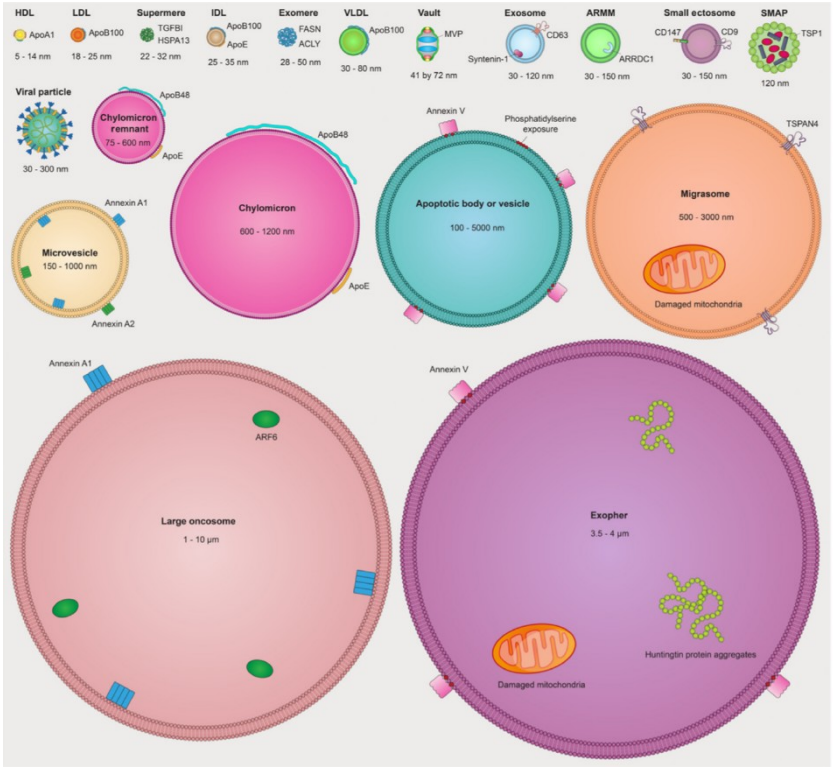
Cells continuously release a diverse population of vesicles (EVs) and nanoparticles in the maintenance of homoeostasis

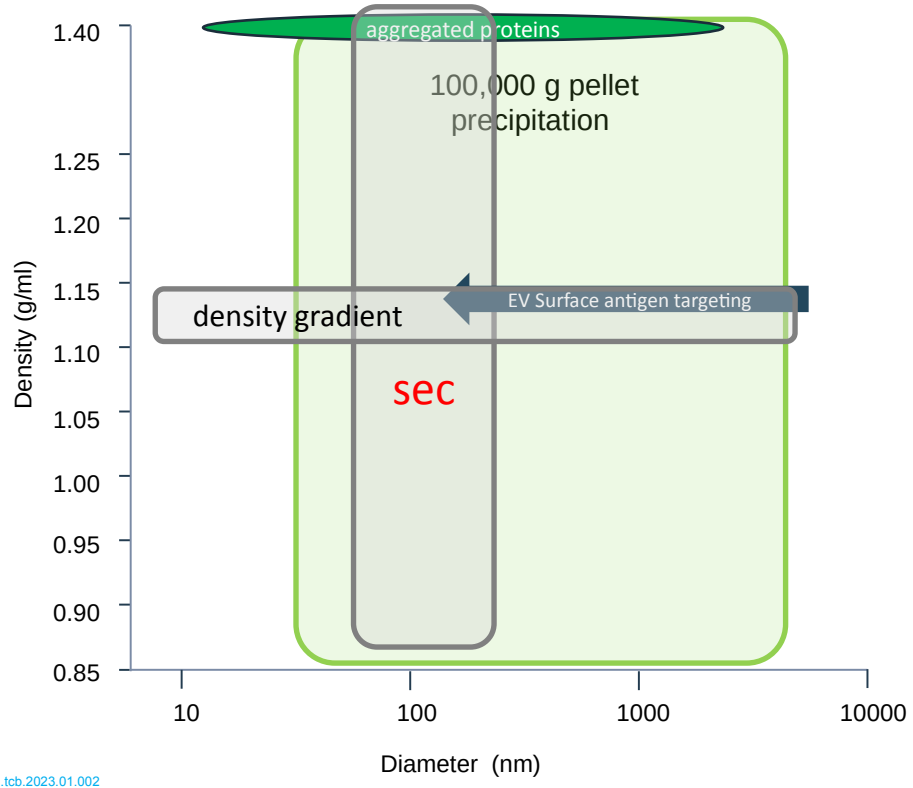
EVs can be captured from biofluids and their messages “read” to determine the disease or health status of a cell.



Salomon *et al.,* (2022) Extracellular Vesicles and Their Emerging Roles as Cellular Messengers in Endocrinology: An Endocrine Society Scientific Stateme

EVs | Multiple Type – non-specific methods of isolation confound data interpretion





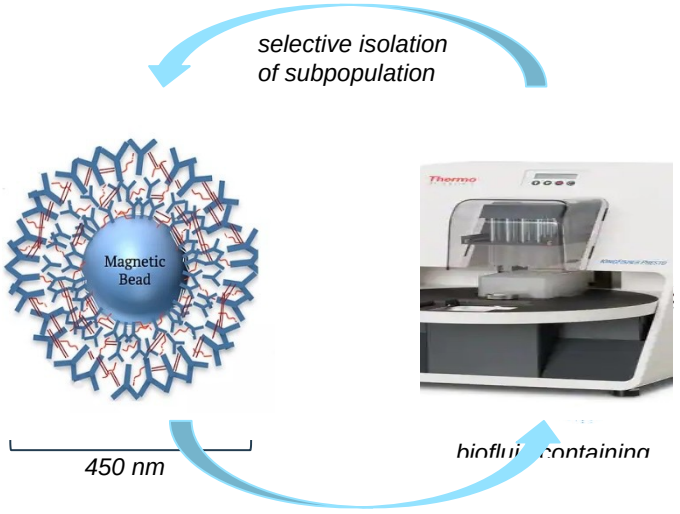
Jeppesen *et al.,* (2023) Extracellular vesicle and nanoparticles: emerging complexities, Trends in Cell Biology DOI:https://doi.org/10.1016/j.tcb.2023.01.002

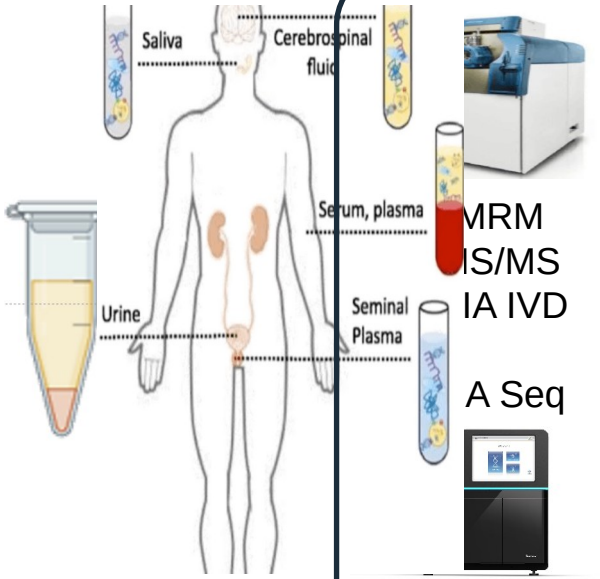
EXO-NET

Isolates a specific well-defined subpopulation of EVs for biomarker discovery

EXO-NET

- Magnetic bead-based immunoaffinity EV capture system (10 epitopes)
- On-Bead analysis or On-Bead lysis for downstream RNA, Protein or Lipid analysis
- Manual or Fully automated high-throughput isolation





Discovery

MRM
IS/MS
IA IVD

A Seq

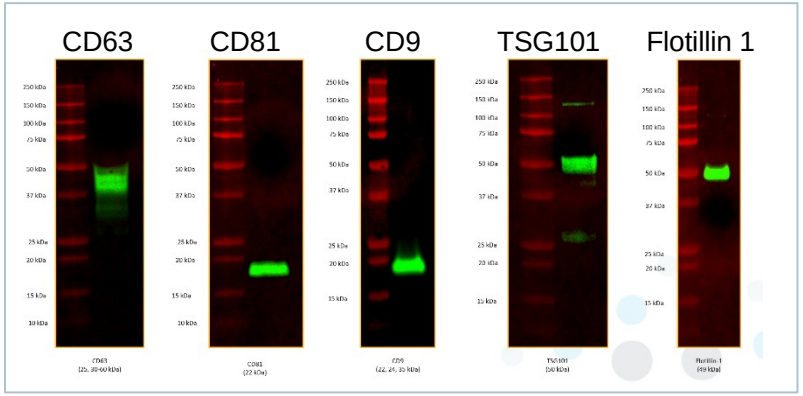
Delivery

BioPlex 2200

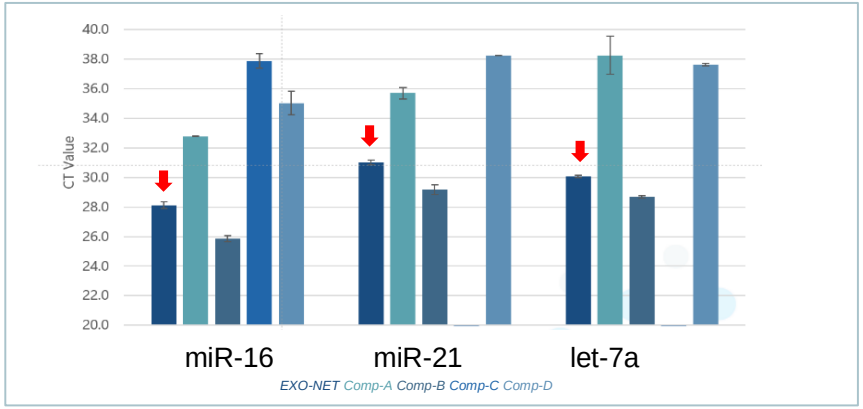
Digital PCR

EXO-NET | Characterization & Comparisons

EXO-NET plasma lysate contains canonical EV proteins



EXO-NET plasma lysate contains canonical EV miRNAs



EXO-NET ■ Commercial Kits ■ ■ ■

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EVDx | EXO-Ovarian Cancer Classification Model for Early Stage Disease

Samples: ovarian cancer and control plasma

EVs isolated from 0.1 - 0.5 ml plasma using EXO-NET

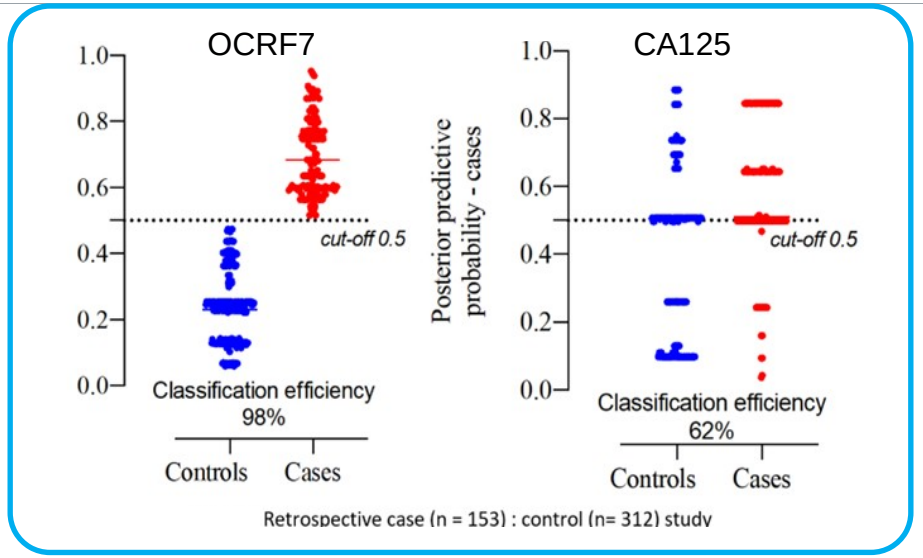
On bead lysis for downstream analysis

LC MS/MS

RT qPCR

Model training and validation: Lasso Linear Regression

Independent Test Set



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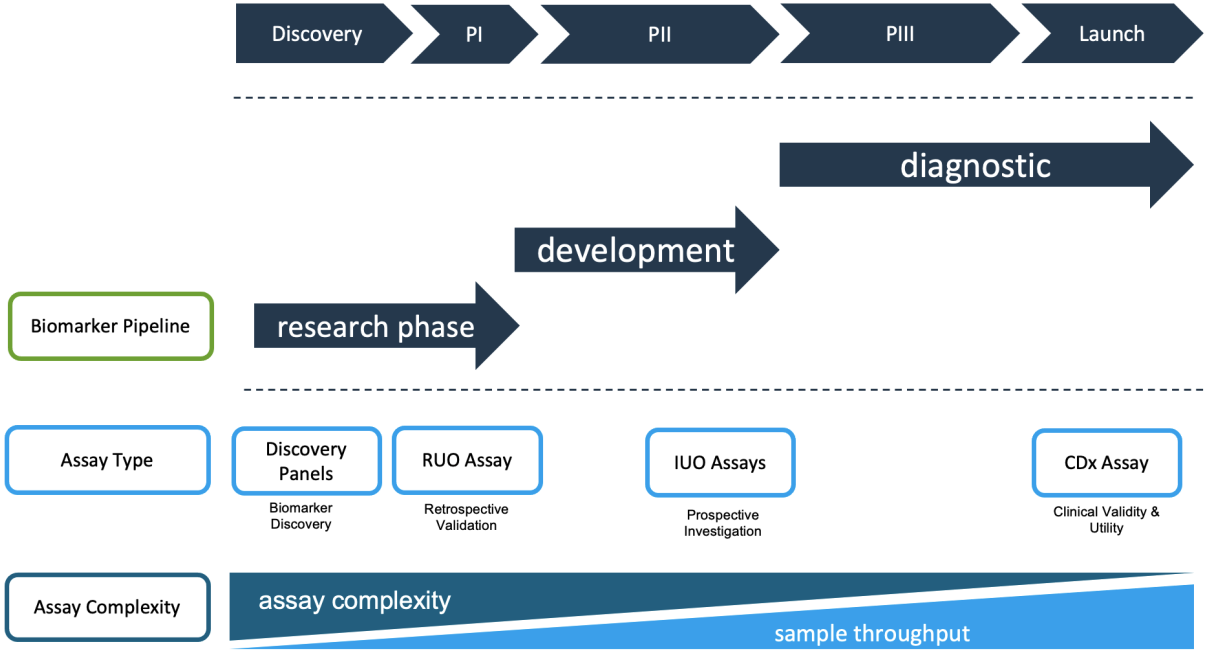
Enabling EV-based diagnostics - CTA, CDx & Dx



EXO-NET	manual	48 per batch	96 per batch	HT automation
samples/day	40	240	480	1000

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EXO-NET ENABLING YOUR EV RESEARCH

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