Extracellular vesicles

Introduction to EVs

"Extracellular vesicles are **membrane-enclosed nanoscale particles** released from essentially all prokaryotic and

EVs present many different surface proteins, mainly **tetraspanins** (commonly used markers to identify them) but

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The cargo of an EV tends to reflect the state of the cell that produced it; this way EVs become a way to transport

Different types of EVs exist (different cargo, dimensions, genesis...). In older literature EVs were calssified based on

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Notice that size is not enough to subdivide them since there are overlaps. A way better way of classifying EVs is by

Exosomes originate from **multivesicular bodies**. Multivesicular bodies are organelles whose membrane buds inward cr

Microvesicles originate from outward budding of the plasmatic membrane.

Apoptotic bodies are generated from apoptotic cells through various mechanisms.

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The EV genesis defines the cargo and the surface markers, which define the target cell for the EV. Surface markers

EV uptake by target cells can occur through different modalities (depending on target cell, vesicle size and others):

Phagoytosis

Macropinocytosis

Clatrhrin dependent endocytosis

Receptor mediated endocytosis

Fusion with the plasmatic membrane

Medical applications of EVs

Due to the aforementioned facts that:

Almost all cells produce EVs, cancer and other diseased cells included

The cargo reflects the functional status of the secerning cell

EVs can convey signal through long distances

EVs are being studied more and more for clinical applications, mainly to understand disease pathogenesis (and eventual

One other significant advantage of EVs is the fact that they can be obtained through liquid biopsy, together with c

In order to use EVs in clinical applications, a consistent and reproducible way of extracting EVs from the liquid bio

Nickel-based isolation (NBI), which utilizes the fact that EVs are negatively charged, hence they are attracted by p

Size exclusion cromatography (SEC), which is a chromatographic technique in which the retention time of an obje

Ultracentrifugation (UCFG), meaning centrifugation at around 22000 RPM for some hours. EVs are too small to se

The total amount of RNA obtained from each extraction was measured using SMARTseq kit.

The result was that different isolation methods were highly reproducible on homogeneous samples (EVs from prosta

Another challenge, deriving from the use of EVs, is the fact that RNA signal deriving from multiple populations is

Supervised deconvolution, which means using known cell line signatures to split the signal and compute the fraction

Unsupervised deconvolution, which means using unsupervised clustering algorithms to subdivide the signals into po

Deconvolution approaches are therefore plausible but not well established.

EVs conference Notes from the conference *"Extracellular vesicles as diagnostic and therapeutic tools for kidney dise*

DISCLAIMER: they might not be perfect but they should suffice for a general idea of the concept

EVs are part of the secretome produced by stem cells in order to try and induce tissue regeneration after damage, s

One way to analyse EVs is MACSPlex, a cytofluorimetric tool with beads and detection antibodies for tetraspanins

Regarding the activity of EVs on kidney diseases, there have been different studies:

Renal damage markers in kidney injury model decrease overtime in presence of stem cells or just scdEVs; the responses

Repeated administrations of scdEVs to diabetic nephropaty models reduce inflammation and fibrosis

In healhy patients most vesicles reach liver and spleen, while in diseased patients one can find more EVs than usual in t

A phase 1 study has been conducted on the use of scdEVs in kidney diseases.

Urine derived EVs are comparable in potency with MSCs EVs. Urine derived EVs are all generated from kidney cells, s

Klotho, a recently discovered hormone, is produced mostly by the kidney both in a transmembrane and in a soluble forn

Autologous urinary EVs seem to have a beneficial effect in kidney injury model.

CD133+ is a marker for regenerative kidney cells in adult humans; studies have tried to test if its expression on urinary