Clinical Utilization of Exosomes As Biomarkers and Therapeutics Exosomes: Great Things Come in Small Packages

EXOSOME BIOLOGY AND IMPACT IN CELLULAR COMMUNICATION

IMPLICATIONS OF EXOSOMES IN VARIOUS DISEASE AREAS.

Cancer Immunosuppression PD-L1 on Cancer-derived exosomes thwarts immunotherapy Guo, Yaxin *et al*. Molecular Cancer 2019.

Memory & Learning Thomson lab & Shepherd labs, Cell 2019

Proteinopathies PrPSc is selectively targeted to exosomes Fang et al., PLoS Biol. 2007

Modified Tumor Microenvironment Nedawi et al. Nature Cell Biology 2008

Virus "cloaking" Santiana et al., Cell Host & Microbe 2018

transmembran

protein

UTILIZATION OF EXOSOMES IN CLINICAL APPROACHES

– exosome -

Multivesicular endosome (MVE)

Intraluminal Vesicles (ILV)

—

EXOSOMES AS BIOMARKERS

Invagination of II V

to generate MVEs

plasma membrane

- Monitor Response
- Patient Stratification
- Pharmacokinetic/Pharmacodynamic (PK/PD) Studies

EXOSOMES AS BIOMARKERS TO:

- Confirm Modification
- Indicate Response to Cell

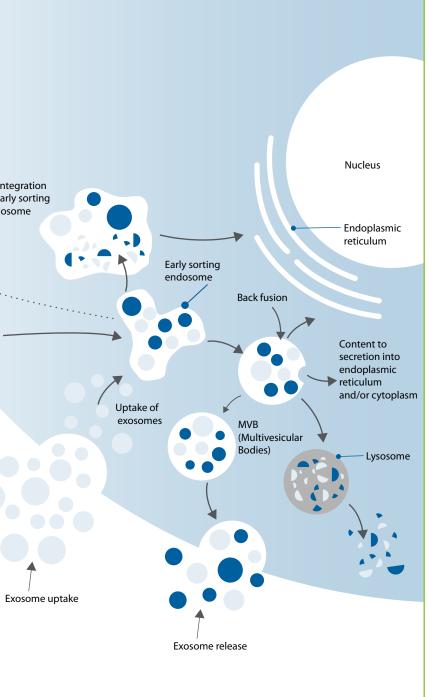
IMPLANTATION OF DONOR CELL OR DONOR EXOSOMES

Donor Cell

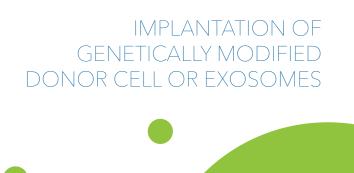
EXOSOMES IN CELL THERAPY APPLICATIONS:

Manipulation Donor cell for improved cargo loading or EV production/Targeting/Delivery

Manipulation of Cargo or surface of vesicles for improved recipient-cell targeting and delivery followed by injection



 ANALYZING EXOSOME HETEROGENEITY **Size** (E.g. 40-75nm, 75-100 nm, 100-160 nm,...) **Content** (E.g. CD63 or CD81 Expression) **Functional** (E.g. Imparts Pro-Survival or Pro-Apoptotic) **Source** (E.g. Brian vs Pancreas)



Genetically Modified **Donor Cell**

COMPONENTS OF EXOSOMES

Protein

Exosomes are critical in cellular signaling and several biological processes. Many of these proteins are of interest as biomarkers but below are some reasons to analyze exosome derived proteins:

- Enable enrichment from the tissue of origin
- Analyze protein expression
- Analyze post-translational modification like clevage, phosphorylation, glycosylation and methylation
- Analyze protein configurations

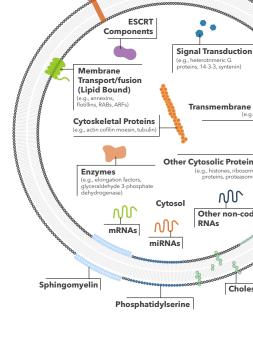
The majority of clinically actionable RNA biomarkers are currently mRNA. Some potential applications of ExoRNA are:

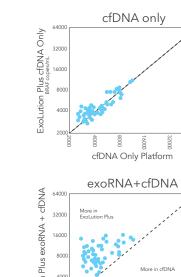
- Whole transcriptome analysis
- Rare mutations
- Splice variants
- RNA pathway analysis

DNA

Exosomes contain DNA that remains an area of focus for research to understand more. Some potential applications of ExoDNA include:

- Mutation and fusion analysis Methylation patterns
- Fragmentomics





32000 16000 8000

cfDNA Only Platforr

(Upper) ExoLution Plus extracts amounts of cfDNA as the gold standard cfDNA kit. (Lower) In a clinical cohort of 30 malignant melanoma patients, ExoLution Plus extracts MORE copies of BRAF by combining exoRNA with cfDNA. More copies equals enhanced sensitivity and accuracy in identifying mutations.

EXOSOMES AS BIOMARKERS IN CLINICAL APPLICATIONS AND THERAPEUTICS

Abundant



- Actively released by almost every living cell • More abundant than CTC & cfDNA
- Large density of exosomes in various biofluids
- Higher copies/ml of biofluid enables lower volume input

Actionable Biomarkers

- Snapshot of living process
- Contain patient's transcriptome & proteome • Actionable biomarkers including RNAs (IncRNA, miRNA, and more), proteins, & DNA



- Lipid bilayer protects from enzymatic degradation creating a stable environment
- Results in high quality RNA
- Amenable to frozen storage

Non-Invasive Liquid Biopsy 🛛 🖞 🗍 🥅

- Ideal for clinical trials
- Patient stratification insights • Wide range of clinical indications, including oncology, neurology, metabolic, cardiac and more

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EVOLUTION OF EXOSOMES	

2010

2000

1990

1980

2019

2016

2015

2012

2008

2007

2001

1983

of exosomes

Exosome based ExoDx[™] Prostate test

included in the National Comprehensive

Cancer Network (NCCN) guidelines for

early detection of prostate cancer

ExoDx[™] Prostate test is the first

to assess prostate cancer risk

Hishino *et al.* Integrins on EVs

Peinado et al. Tumour EVs (Extracellular

vesicles) influence recipient cells to

(Extracellular vesicles) direct

Nedawi *et al*. EVs modify cell

(tumor cell) responses in their

Valadi et al. EVs (Extracellular

vesicles) can transfer functional

nucleic acids between cells in vitro

Wolfers et al. Tumour cells release

Zitvogel et al. Dentritic cell derived

EVs (Extracellular vesicles) are a

potential cancer vaccine

Pan et al. First descriptions

EVs (Extracellular vesicles)

organ-specific metastasis

support metastasis

microenvironment

commercial exosome-based test

20	2	0	2	0
20				

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Exosome-based	
clinical trials for the	è
treatment of COVID-19)

2016 Morigi et al. Exosomes from Mesenchymal stem cells (MSC) improved the overall kidney function of patients with chronic kidney disease

2012 Peinado et al. Exosomes affect the pre-metastatic niche of non-tumor cells

2008 Skog et al. First discovery of tumor derived mutations in plasma exosomes (RNA). Tumour EVs (Extracellular vesicles) modulate the behaviour of recipient cells

> 2006 Baj-Krzyworzeka M et al. EVs (Extracellular vesicles) from cell cultures contain RNA

1996 Raposo et al. EVs (Extracellular vesicles) are capable of antigen presentation 1987

Johnstone *et al*. First descriptions of exosome functions and biology

> 1970 1967 Wolf et al. First reported 1960 observations of microvesicles



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Find out more about the commercial exosome platform with a flexible and customizable approach. Support from discovery to commercialization at Bio-Techne.

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