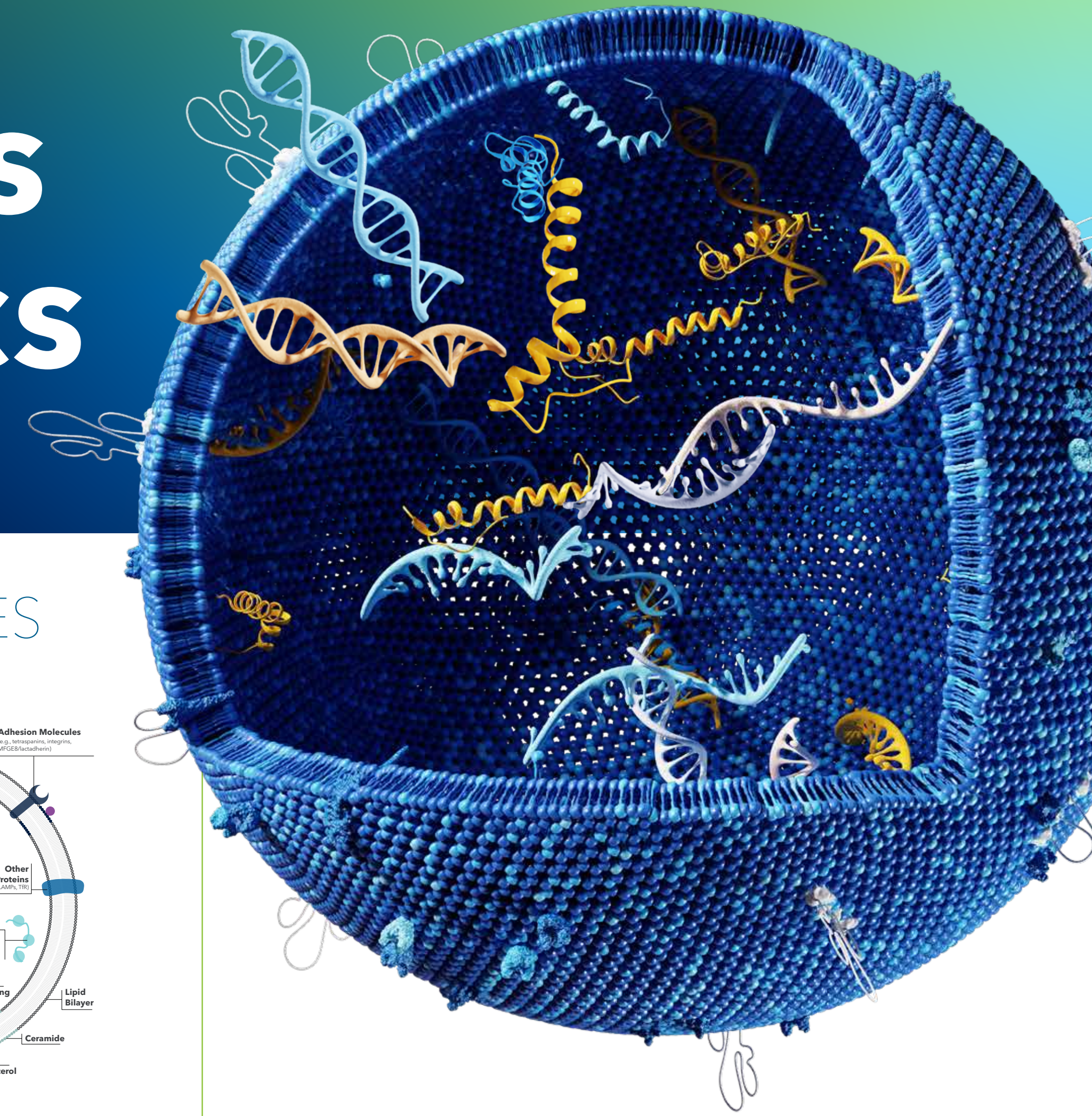


# Clinical Utilization of Exosomes As Biomarkers and Therapeutics

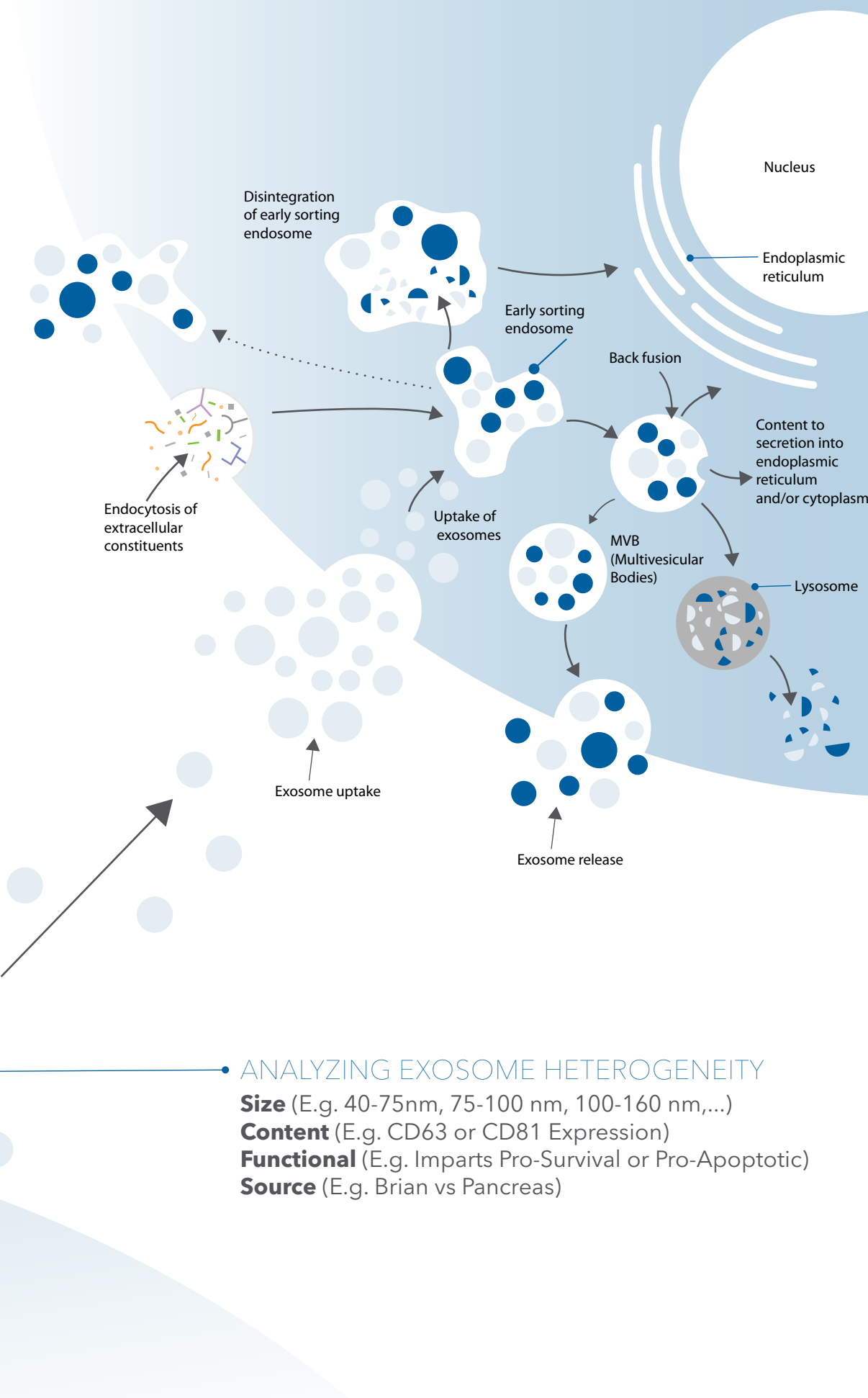
## Exosomes: Great Things Come in Small Packages



### 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

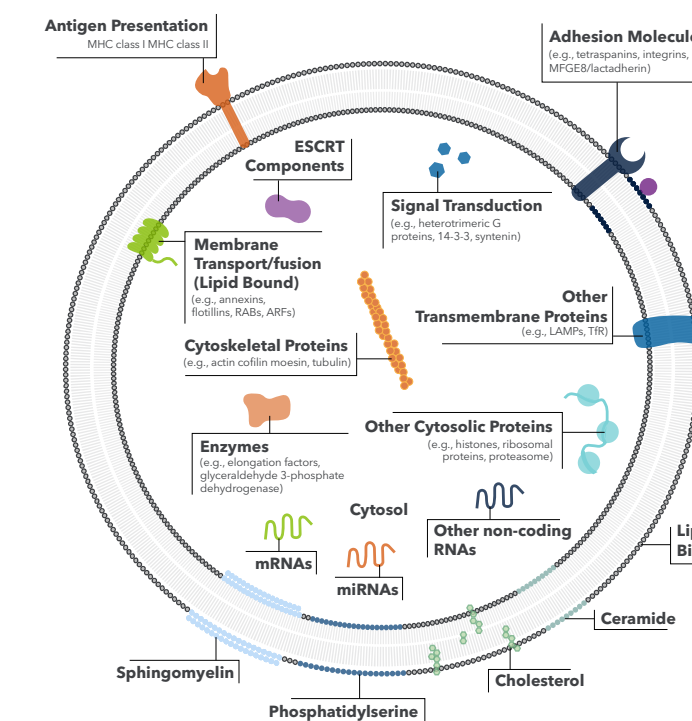


**ANALYZING EXOSOME HETEROGENEITY**  
**Size** (E.g. 40-75nm, 75-100 nm, 100-160 nm,...)  
**Content** (E.g. CD63 or CD81 Expression)  
**Functional** (E.g. Imparts Pro-Survival or Pro-Apoptotic)  
**Source** (E.g. Brain vs Pancreas)

### COMPONENTS OF EXOSOMES

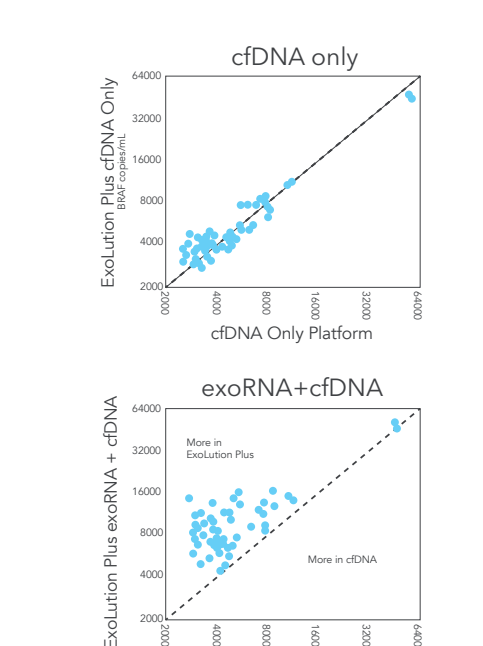
**Protein**  
Exosomes are critical in cellular signaling and several biological processes. Many of these proteins are of interest as biomarkers but below are some reasons to analyze exosome derived proteins:

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



**RNA**  
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

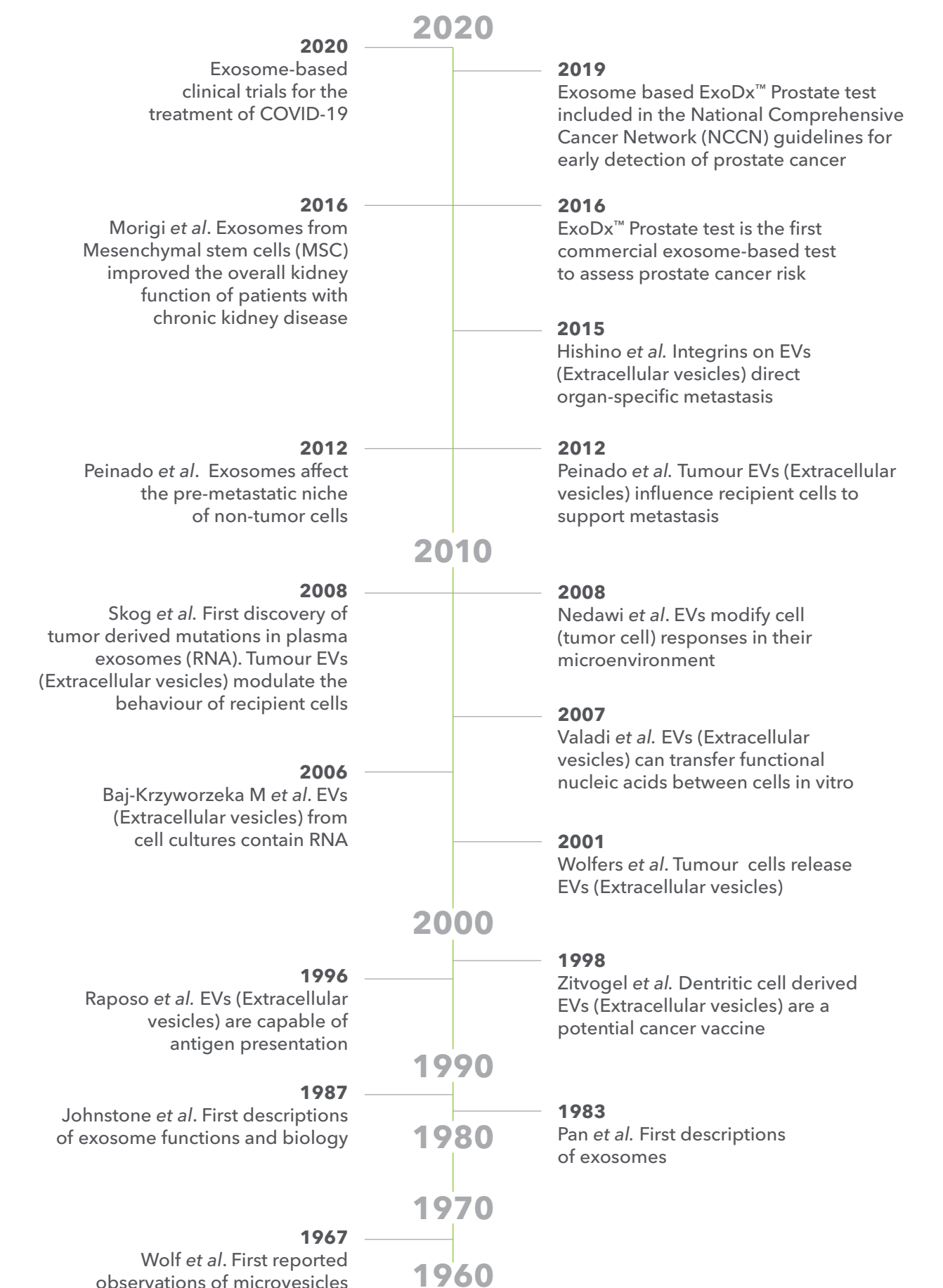


(Upper) Evolution Plus extracts amounts of cfDNA as the gold standard cfDNA kit. (Lower) In a clinical cohort of 30 malignant melanoma patients, ExoLution Plus extracts MORE copies of BRAF by combining exoRNA with cfDNA. More copies equals enhanced sensitivity and accuracy in identifying mutations.

**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

### EVOLUTION OF EXOSOMES



### UTILIZATION OF EXOSOMES IN CLINICAL APPROACHES

EXOSOMES AS BIOMARKERS:

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

EXOSOMES AS BIOMARKERS TO:

- Confirm Modification
- Indicate Response to 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

IMPLANTATION OF DONOR CELL OR DONOR EXOSOMES

Donor Cell

IMPLANTATION OF GENETICALLY MODIFIED DONOR CELL OR EXOSOMES

Genetically Modified Donor Cell

### 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 (lncRNA, miRNA, and more), proteins, & DNA

**Stable**

- 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

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

