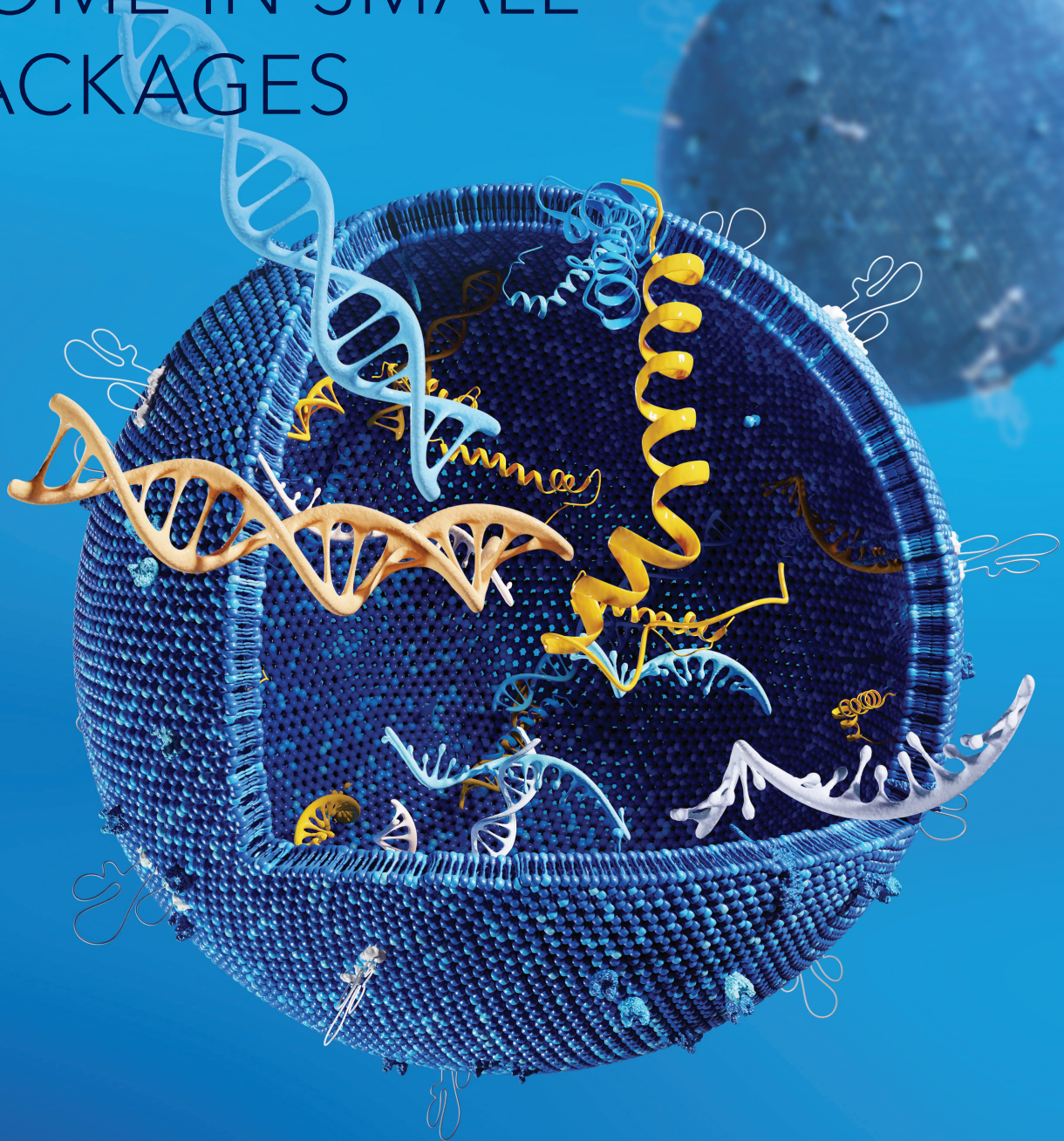


# EXOSOMES

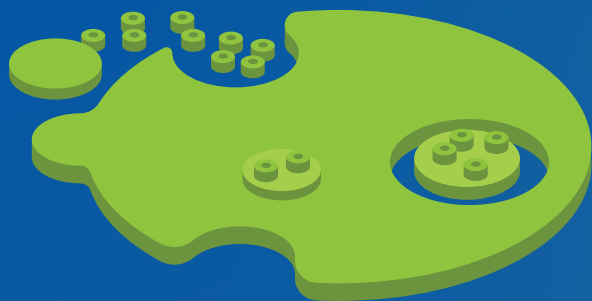
## GREAT THINGS COME IN SMALL PACKAGES



# MAKE EXOSOMES THE PLATFORM OF CHOICE TO LOOK AT CANCER AND BEYOND

## WHY EXOSOMES?

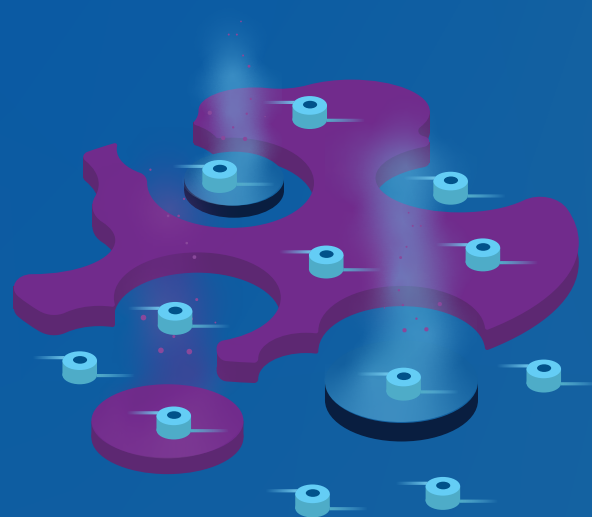
- Exosomes are secreted by all living cells into all biofluids and provides a snapshot of a living process
- Testing with a stable sample, amenable to frozen storage from CSF, plasma or other biofluids
- Combine gene expression biomarkers (RNA), DNA variant (e.g., mutations, fusions) and proteins
- Exosome approaches are non-invasive favoring biofluids to provide dynamic readouts rather than delayed information and an often inconvenient tissue biopsy method



LIVING CELL

## EXOSOMES

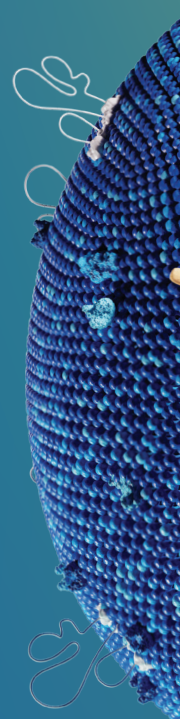
- 👍 Released from all cells and found in all biofluids.
- 👍 Rich source of information from the cell enabling complete transcriptome and proteome profiling.
- 👍 Amenable to frozen storage.
- 👍 More abundant than cfDNA or CTCs.
- 👍 Provides snapshot of living process.



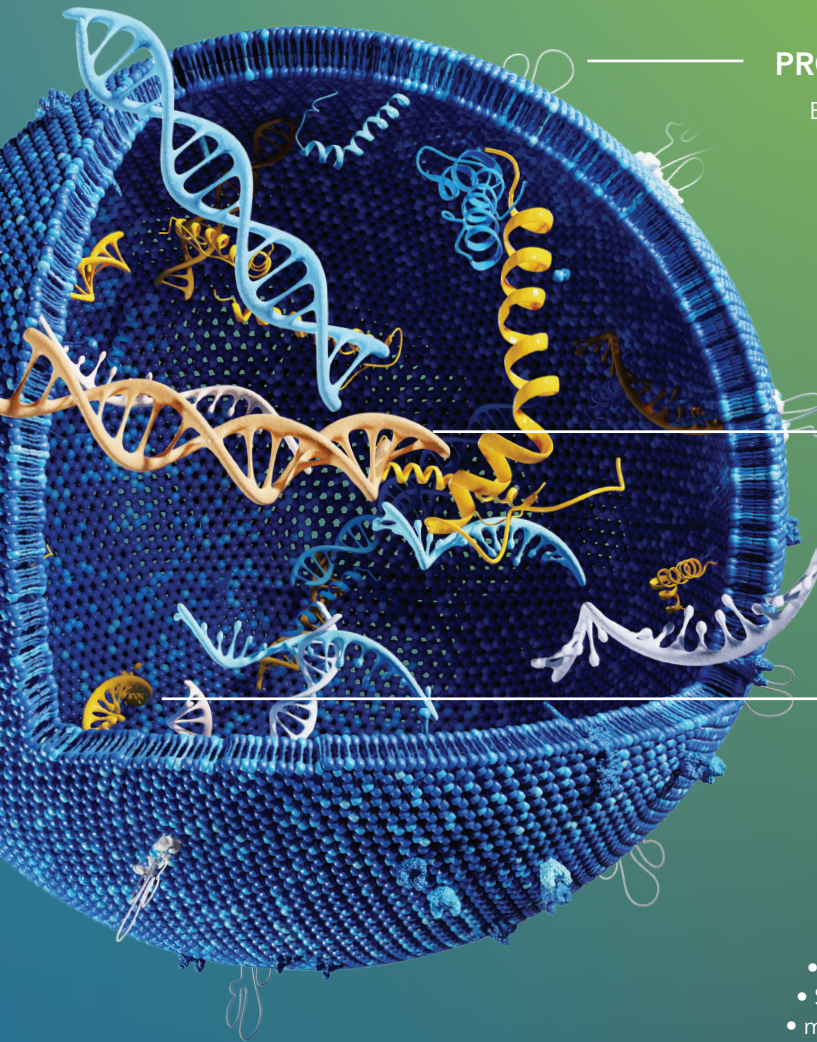
APOPTOTIC/  
NECROTIC CELL

## CIRCULATING CELL-FREE DNA (CFDNA)

- 👎 Released by dying tumor and normal tissues by apoptosis/necrosis.
- 👍 Amenable to frozen storage.
- 👎 Often highly limited concentration.
- 👎 Provides snapshot of dying process.



# WHAT IS AN EXOSOME?



## 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

## DNA

Exosomes contain DNA that remains an area of focus for research to understand more. It is largely considered a form of cell-free DNA (cfDNA).

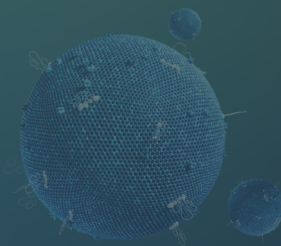
## RNA

Exosomes contain various types of RNA reflective of the cell of origin. Including tRNA, rRNA, ScaRNA, snRNA mRNA, miRNA etc. Profile the entire transcriptome including:

- mRNA:
  - Targeted mRNA analysis that
  - Profile entire transcriptome
- Long non-coding RNA
- Small non-coding RNA
- miRNA

## CIRCULATING TUMOR CELLS (CTCs)

- 🚫 Limited to tumor markers.
- 🚫 Often requires complicated processing.
- 🚫 Extremely low frequency when present even with high sample volumes.
- 👍 Often provides snapshot of living process.



# A SINGLE PARTNER FROM DISCOVERY TO KITTED PRODUCTS

Discovery

Preclinical Development

Discovery



Discover more about how Exosome Diagnostics can harness the power of exosomes



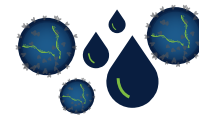
Exosomes are released from from the brain, kidneys, lungs, the prostate & more as an active process from living cells.

EXOSOME RELEASE



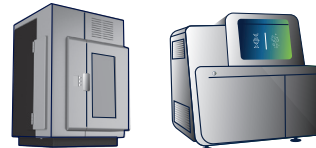
Exosomes are collected from various biofluids: Saliva, Plasma/Serum, CSF and Urine.

EXOSOME INTERPRETATION



Exosomes are stable pockets of enriched information that can be isolated from biofluids via patented approaches.

ANALYTE ANALYSIS

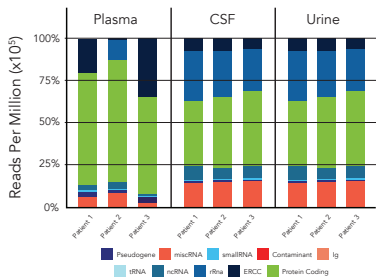


Exosomes are analyzed by various downstream methods including RNAseq whole transcriptome sequencing.

DATA INTERPRETATION



CLINICAL INTERPRETATION



Exosome RNA analysis enables real-time longitudinal monitoring of cellular process. Data supports biomarker discovery, patient stratification and longitudinal monitoring.



Exosome Diagnostics is one part of the larger Bio-Techne complete solutions offering in partnership. Bio-Techne can offer solutions across the drug development cycle by bridging companies under its umbrella.

Clinical Phase 1

Clinical Phase 2

Clinical Phase 3

Approval & Launch

### Discovery



#### Exosome-based Research

We are pioneers in exosome technology and for the past 12 years we've excelled in the field of liquid biopsies focused on exosome-based RNA, protein and cell free DNA (cfDNA) analysis.

- Exosome experts
- Most extensive intellectual property related to exosomes
- Experienced throughout the process of biomarker discovery, validation and commercialization; as evidenced with the ExoDx Prostate Test
- ISO/CLIA compliant IVD development with cGMP clinical grade capabilities.



#### Validation in Tissue

##### Tissue Biopsy & Spatial Analysis

Professional Assay Services (PAS) provides GCLP-compliant RNAscope, BaseScope™, and miRNAscope™ in situ hybridization (ISH) assay services to support clinical and pre-clinical studies for our academic and biopharma partners. We provide end-to-end solutions from sample procurement to ISH staining to image analysis and reporting.

### Single Site LDT



#### Asuragen

CLIA Lab in Austin, TX



CLIA Lab in Waltham, MA



#### Diagnostic Reagents

Bio-Techne produces high quality custom antibodies, proteins, and ELISA assays - leading to our customer's experimental breakthroughs. Our vast portfolio of sample testing services and product development means we can offer a variety of ways for you to streamline and improve your experimental processes. Partner up with our expert scientists to make your own customized reagents, catered to your unique specification.

- Design Control process compliant with 21CFR820 and ISO 13485/ MDSAP.

Asuragen supports a number of commercial reagents and controls and has design control process

### IVD Kitted Product



#### Asuragen

Reagent Kits for Genetics and Oncology research

Asuragen's unique and proprietary chemistries have the ability to detect and analyze targets with unprecedented ease, providing simple, streamlined, and easily deployable testing solutions to bring the routine analysis of these targets within the reach of laboratories everywhere.

- Bioinformatics expertise.
- Technology platform agnostic, pick best for needs.
- In-depth experience of FDA, CE-IVD, CFDA, MFDS, Health Canada & TGA IVD registrations.

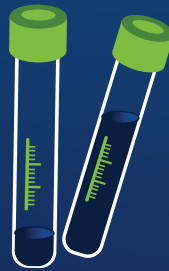
**The Bio-Techne family of companies gives life-science and clinical-diagnostic companies the solutions they need for success.** Collectively, the group provides a unique and all-encompassing portfolio of innovative products/tools and end-to-end custom services, including a large selection of small-molecule, protein and high-performance antibody manufacturing, high-quality diagnostic reagents and assay development, innovative tissue biopsy and testing, and comprehensive bioinformatics support.

# LET EXOSOMEDX SET YOU ON A PATH TO SUCCESS WITH OUR FLEXIBLE EXOSOME-BASED PLATFORM

## 1 COLLECT BIOFLUID



## 2 EXOSOME SELECTION



## 3 ANALYTE EXTRACTION



### CHOOSE THE BIOFLUID

Interrogate Multiple Biofluids

- CSF
- Plasma/Serum
- Tissue
- Urine
- Saliva

### CHOOSE ALL EXOSOMES OR TISSUE SPECIFIC

Minimal sample volumes required

- Total
- Enriched
- Depleted

### PATENTED EXOSOMAL ISOLATION PROTOCOLS: RNA, PROTEIN, OR DNA

Detect the same RNA diversity as tissue

- ExoLution Plus
- ExoLution RNA
- ExoProtein
- UPrep

## 4 ANALYSIS PLATFORM



### GLOBAL PROFILING OR SELECT ANALYTE ANALYSIS

Highly Sensitive with a wide dynamic range

- ELISA/Western blot
- RNASeq
- RT-qPCR
- NGS Panels
- Aka for More Options That Are Available

## 5 BIOINFORMATICS ANALYSIS



### CHARACTERIZE PATIENT SAMPLES & CELL TYPES

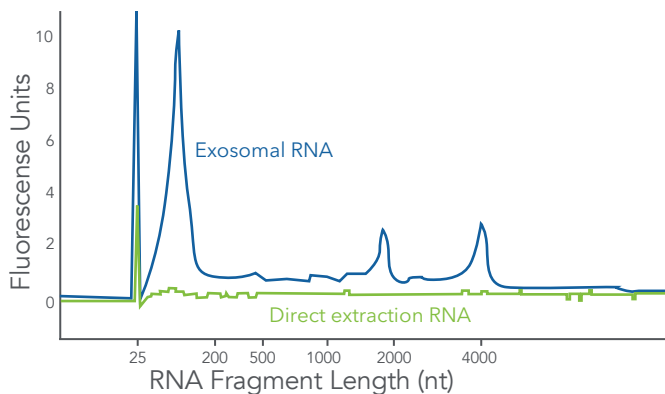
- Biomarker Discovery
- RNA or Protein Biomarker Expression
- Mutation or Copy Number Detection
- RNA-based Variant Detection

**PATENTED TECHNOLOGIES** FOR EXOSOME ISOLATION ALLOW THE STUDY OF RNA, CFDNA, PROTEIN AND EVEN POST-TRANSLATIONAL MODIFICATIONS

# WE ARE EXPERTS IN CUSTOM PROJECTS AND CUSTOM OFTEN COMES WITH SEVERAL QUESTIONS!

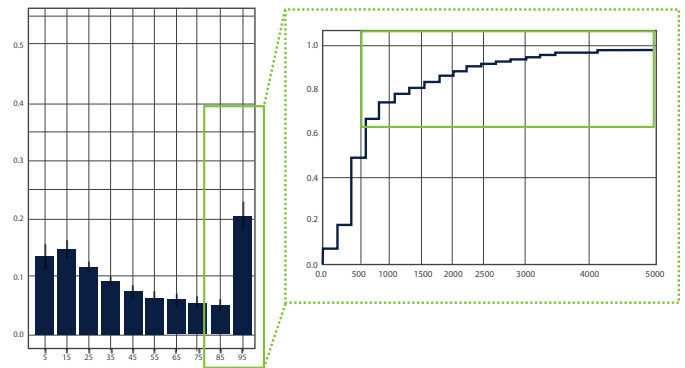
## WHAT IS THE QUALITY OF THE RNA EXTRACTED?

Exosome extraction and analysis will produce higher quality RNA than direct extraction.



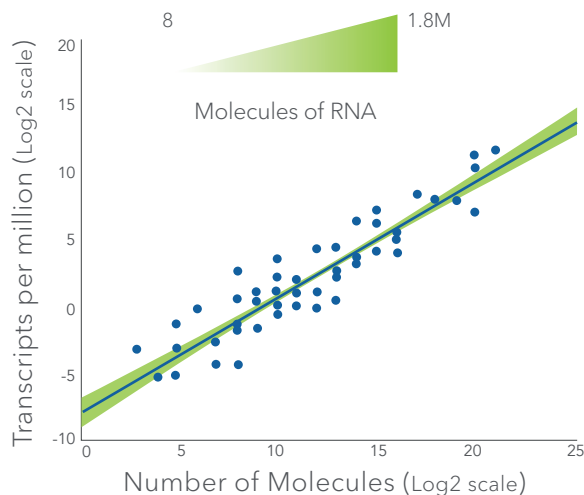
## IS THERE ADEQUATE RNA COVERAGE?

A significant portion of the transcripts are covered  $\geq 80\%$  of which a large fraction is  $\geq 1\text{kb}$  in length



Successfully detects the 82.0 kb transcript (*Titin*) with  $> 80\%$  coverage

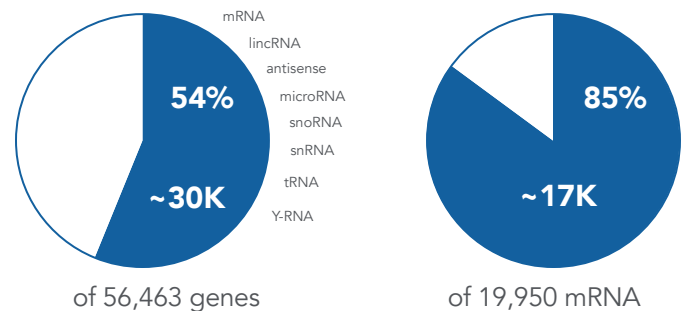
## HOW ARE ASSAYS CONTROLLED?



Each assay is uniquely quality controlled, as an example of RNA quality control we show here an Ambion® ERCC spiked RNA control assay where each sample is spiked with a known quantity and sequenced. You can see from this assay an approximate dynamic range of the RNA assay.

## HOW LIKELY IS A PARTICULAR GENE OF INTEREST ABLE TO BE STUDIED?

Observed is blue and not observed is in white, as you can see there is adequate coverage of both total RNA and mRNA

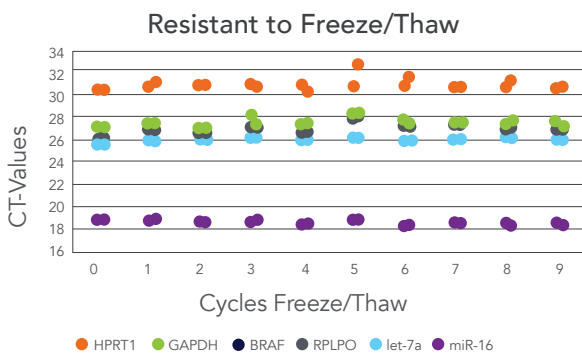
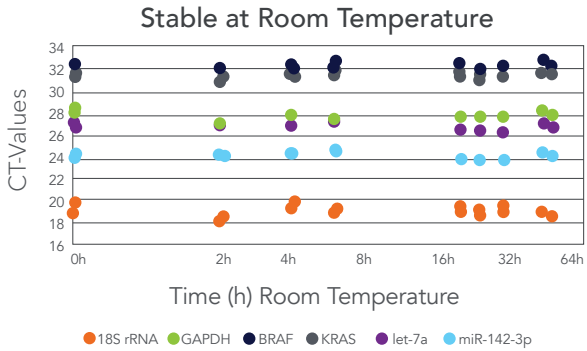


## HOW DOES LIQUID BIOPSY COMPARE TO TISSUE ANALYSIS?

Diversity/detection in liquid biopsy is the same as tissue. Observed is blue and not observed is in white. Comparable diversity and detection was determined.

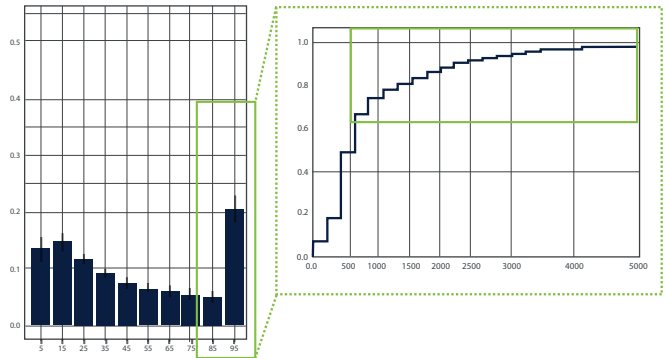


## ARE SAMPLES STABLE?



## HOW LONG ARE SAMPLES STABLE FOR?

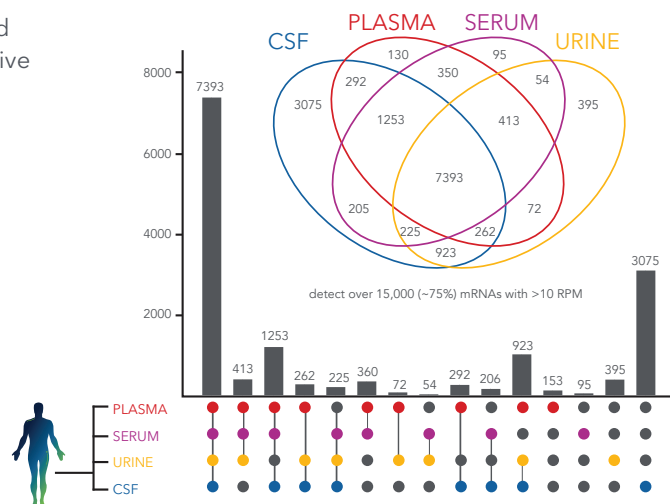
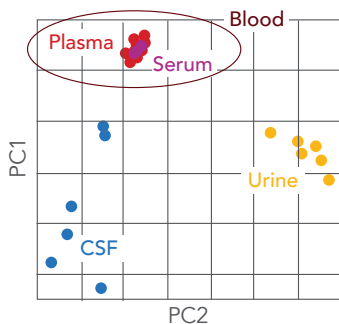
Exosomes are highly stable for >10 years at -80 °C



Successfully detects the 82.0 kb transcript (*Titin*) with > 80% coverage

## WHICH BIOFLUID IS RIGHT FOR YOUR PROJECT?

A large percentage of the observed transcripts are shared across one or more biofluids but each biofluid has exclusive components and their own individual signatures.



## HOW LONG DOES A PROJECT TAKE?

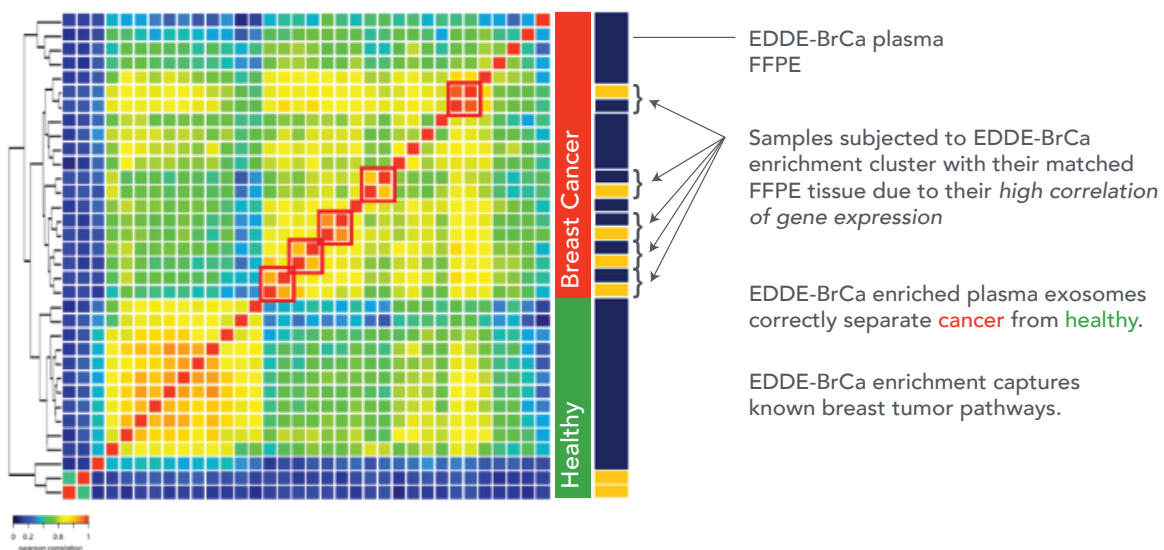
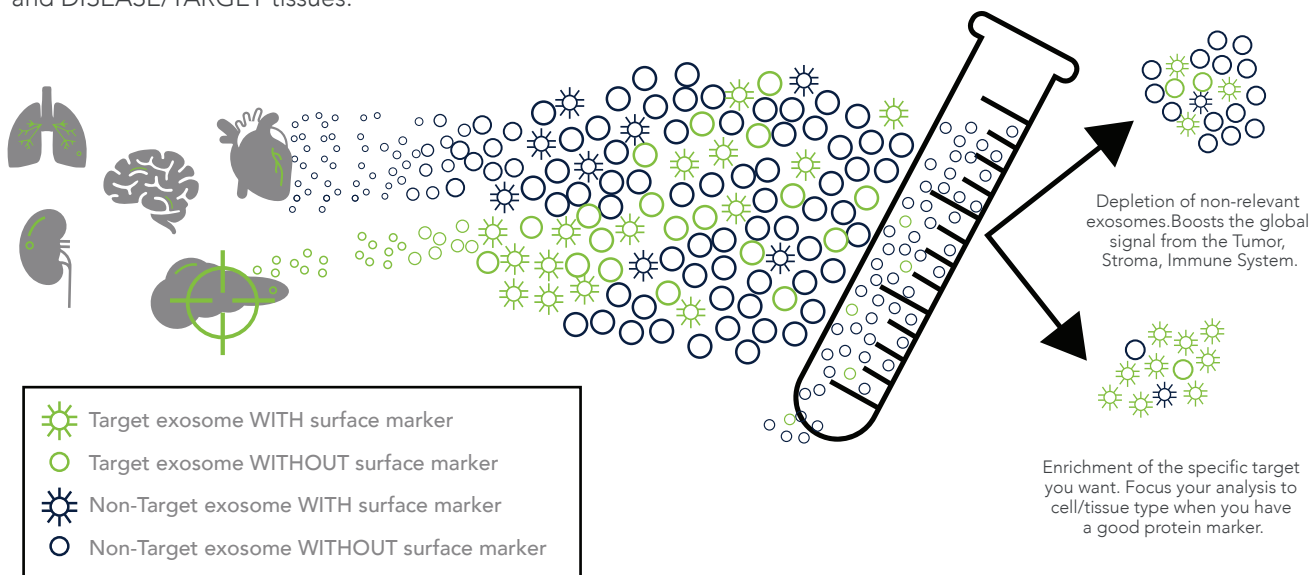
We work quickly and efficiently to deliver you high quality results. Timing is project dependent.

# WHAT IF I ONLY WANT TO LOOK AT CERTAIN CELL TYPES?

ExosomeDx Depletion for Enrichment (EDDE), is a novel and proprietary protocol for specifically enriching or depleting populations for exosomes. EDDE can be tailored for either RNA-or protein-based downstream analyses.

Billions of exosomes are shed into the blood by cells within both HEALTHY and DISEASE/TARGET tissues.

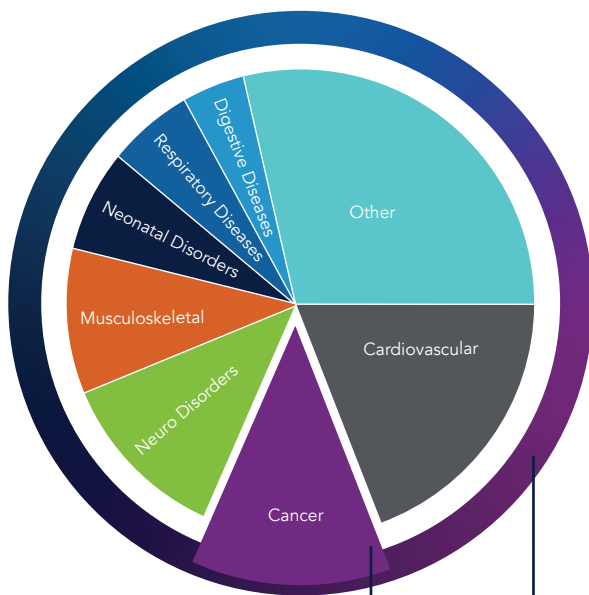
Only a fraction of which will be derived from your TARGET tissue/cell type.



# ADVANTAGES WITH EXOSOMES

Exosomes are the path to non-invasively longitudinally monitor patients and samples. Analyze rare mutations, fusions, splice variants and whole transcriptome sequencing with exosomes. Exosome diagnostics has worked historically in many disease areas including Immuno-Oncology, Neurology, Cancer and many more.

## POTENTIAL ADVANTAGES OF EXOSOMES



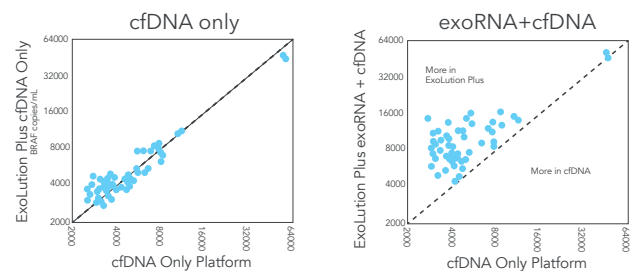
ctDNA and CTCs so far limited to late-stage oncology.

Exosome RNA profiling enables oncology and non-oncology applications.

## ADVANTAGES OF EXOSOMES IN CANCER RESEARCH

Leverage the advantages of exosomes in cancer research.

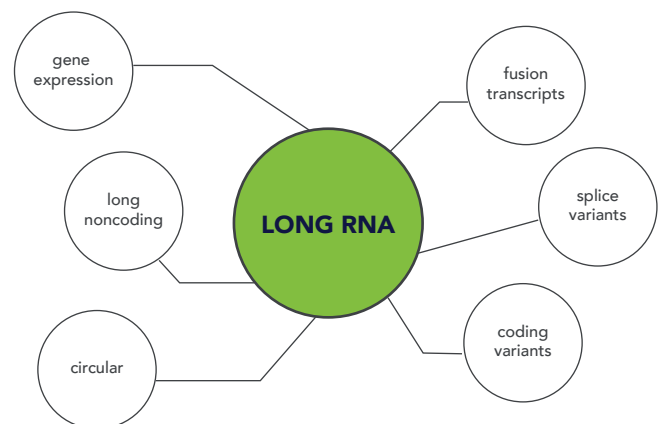
- Exosomes are more abundant than cfDNA or CTCs
- 1 tumor cell can release more than 10,000 exosomes per day
- ExoRNA + cfDNA Panels are superior to cfDNA alone



(Left) ExoLution Plus extracts amounts of cfDNA as the gold standard cfDNA kit. (Right) 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.

## ACCESS THE COMMERCIAL EXOSOME RNA-SEQ SERVICE

The future of therapeutics may lie in long RNA though the majority of clinically actionable RNA biomarkers are currently mRNA. Research in literature and increased financial support in R&D efforts are shifting the tide to various forms of RNA.



# GENOMIC SOLUTIONS

We leverage our expertise in molecular biology and diagnostics, other brands, and our CLIA certified laboratories to bring you science of the highest quality.

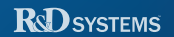


# ASSAYS

Our immunoassay and *in situ* hybridization RNA kits are built with our proteins & antibodies.

# INSTRUMENTS

Manual & automated protein analysis solutions that improve the efficiency of process work streams and quantitation of proteins.



# CONTROLS AND CALIBRATORS

We build controls & calibrators using our IVD proteins, antibodies, and nucleic acids and IVD packaging & logistics.



# PROTEINS

# ANTIBODIES

# SMALL MOLECULES

Large catalog of research reagents plus custom development capabilities.



Exosome Diagnostics, Inc. | 266 Second Ave., Suite 200, Waltham, MA 02451 | 1-(844) 396-7663 | [exosomedx.info@bio-technie.com](mailto:exosomedx.info@bio-technie.com)  
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