Exosomes Market Snapshot: circa September 2013

> Enal Razvi, Ph.D.

Biotechnology Analyst, Managing Director
SELECTBIO US
enal@selectbio.us
The focus of this GEN Market & Tech Analysis Report is to present some qualitative and quantitative market trends from our continuing tracking of the exosomes and microvesicles marketplace which is expanding and evolving rapidly. For this reason, this GEN Report is termed “circa September 2013” to reflect the dynamic nature of this space.

Primarily, the quantitative data presented herein have been derived from bottom-up market analyses on researchers working on exosomes and microvesicles and therefore represent research and adoption trends.

Given the fact that researchers in exosomes and microvesicles space generally refer to a “continuum of vesicles”, throughout this report we’ll refer to them collectively here as “Extracellular Vesicles (EVs)”
On August 13, 2013, the US NIH announced that it was funding US$17 Million for 24 research projects focusing on extracellular RNA (exRNA) communication in two areas:

- Focus is on clinical utility of exRNA as a potential biomarker
- Focus is on clinical utility of exRNA as a therapeutic

There are 10 research awards focusing on exRNA as a biomarker 8 awards focusing on exRNA for therapeutic purposes

- The NIH’s interest in this space is described clearly in the language for the RFA which states that the interest is in “extracellular RNA (exRNA)-based biomarkers derived from human body fluids, such as blood, saliva, urine, breast milk, amniotic fluid, cerebrospinal fluid, ascites and pleural effusions, in order to diagnose and monitor disease progression and response to therapy” The role of EVs is clear as the majority of the research efforts in this space are focusing on isolating/capturing EVs and then interrogating the cargo contained therein
- The second area focused upon is in “novel therapies based on exRNA signaling” and it represents the interest of the NIH in the development of agents that modulate signaling that is again believed to involve exosomes and other classes of EVs
And this Trend Continues...

- On **September 20, 2013** the US NIH announced that it would fund “up to US$3.8 million per-year for up to five years” to fund a consortium of researchers who will conduct a system analysis of extracellular RNA, total commitment of **US$19 Million**

- This funding commitment suggests that the role of exRNA molecules found in various classes of EVs is a subject of interest across the community with translational potential both diagnostics and therapeutics

- Indeed, the major driver of this push towards capturing and interrogating EVs comes from the potential of these vesicles as carriers of biomarker cargo that can be captured in a minimally-invasive manner and constitute “liquid biopsies” whereby disease progression and treatment effectiveness can be assessed via a simple blood draw, urine test or spinal tap rather than invasive, painful, and costly procedures to harvest tissues from internal organs in order to monitor the patient

**Major Driver of Translational Interest in Exosomes and Other Vesicle Classes:** Potential for Liquid Biopsy Development
EV Analysis Workflow and Methodologies Deployed

Front-end Isolation Methodologies:
- Ultracentrifugation
- Immuno-capture on beads
- Precipitation
- Filtration

Downstream Analysis of Cargo:
- Protein
- microRNA
- ncRNAs
- mRNAs

Methodologies Deployed Currently for Downstream Analysis of EV Cargo
- Size and Morphology Analysis using Electron Microscopy and Dynamic Light Scattering
- Cell Surface Market Analysis using Flow Cytometry
- Protein Analysis using Western Blots, ELISAs
- Proteomic Analysis using Mass Spectrometry
- RNA Analysis using qPCR and Next-Generation Sequencing (NGS)
Breakout of the Marketplace vis-à-vis Front-end Isolation Methodologies for EVs

More than Half of the Market is Utilizing Ultracentrifugation to Purify EVs which Remains the Gold Standard in this Space
Quantitative Penetrance of Activities into the Downstream Spaces

Majority of Efforts in this Field are Still in the Research Phase without Significant Translational Migration
Breakout of the Marketplace Based Upon Downstream Experiments/Applications Performed Currently on Exosomes Post-Isolation → Provides a Flavor of the Activities Being Performed Industry-Wide

- Western Blotting or other Methods for Protein Characterization: 36%
- qPCR (quantitative PCR)-based microRNA Expression Profiling: 29%
- Microarray-based microRNA Expression Profiling: 9%
- qPCR-based mRNA Mutation Detection: 2%
- Next Generation Sequencing (NGS) for mRNA Study: 9%
- Microarray-based Mutation Detection: 2%
- Next Generation Sequencing (NGS) for microRNA/small RNA Study: 13%
# Challenges and Opportunities in the Circulating Biomarkers Space

<table>
<thead>
<tr>
<th>Classes of Circulating Biomarkers</th>
<th>Challenges</th>
<th>Opportunities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulating Free DNA (cfDNA)</td>
<td>Identification of potential biomarkers relevant to disease</td>
<td>Minimally-invasive diagnostics and prognostics development</td>
</tr>
<tr>
<td>Circulating microRNAs [freely circulating or enveloped within exosomes]</td>
<td>Appropriate samples</td>
<td>Longitudinal analyses of patient response to therapies [such as cancer therapeutics] without the need for costly, invasive procedures</td>
</tr>
<tr>
<td>Circulating mRNAs [enveloped within exosomes]</td>
<td>Robust assays to characterize the biomarkers</td>
<td>Acceleration of adoption of personalized medicine</td>
</tr>
<tr>
<td>Circulating Oncoproteins</td>
<td>Statistical analyses</td>
<td>Tissue Specificity of Origin</td>
</tr>
<tr>
<td><strong>Circulating Exosomes, Microvesicles</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circulating Tumor Cells (CTCs)</td>
<td>Identifying those that are the most relevant with prognostic and/or predictive value</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Demonstration of clinical relevance for prognosis in the absence of large, multi-year prospective clinical trials of patient survival</td>
<td></td>
</tr>
</tbody>
</table>
Various Sources of Circulating Biomarkers: These are the Sources of Analytes for Liquid Biopsies

- Circulating tumor cells (CTCs)
- Placental, fetal cells
- Activated lymphocytes and other nucleated cells
- Necrosis
- Apoptosis
- Lysis

Source: Pamela Pinzani, Università degli Studi di Firenze.
In Summary

- The Broader EV Space Composed of Exosomes, Microvesicles [collectively “EV”] continues to Expand and Evolve
- We are Following the Qualitative and Quantitative Trends Closely as this is a Fast-Moving Marketplace
- There is Currently a Collision Taking Place Between the Various Classes of Biomarkers [tissue-based and circulating] and their Potential for Longitudinal Disease Monitoring/Treatment Effectiveness
- The Success of NIPT Provides a raison d'etre for Believing in the Potential Clinical Utility of Circulating Biomarkers in Oncology and Other Disease Classes
All the Stakeholders in Circulating Biomarkers Come Together in Boston in March 2014

- SELECTBIO Conference Brings Together all the Stakeholders in this Broad Space Composed of Exosomes, CTCs, microRNA, Epigenetic, and Circulating DNA: Circulating Biomarkers Summit 2014, March 24-25, Boston
- GEN Presents a Tutorial of Industry Trends from Various Perspectives
- For More Information, please e-mail: enal@selectbio.us