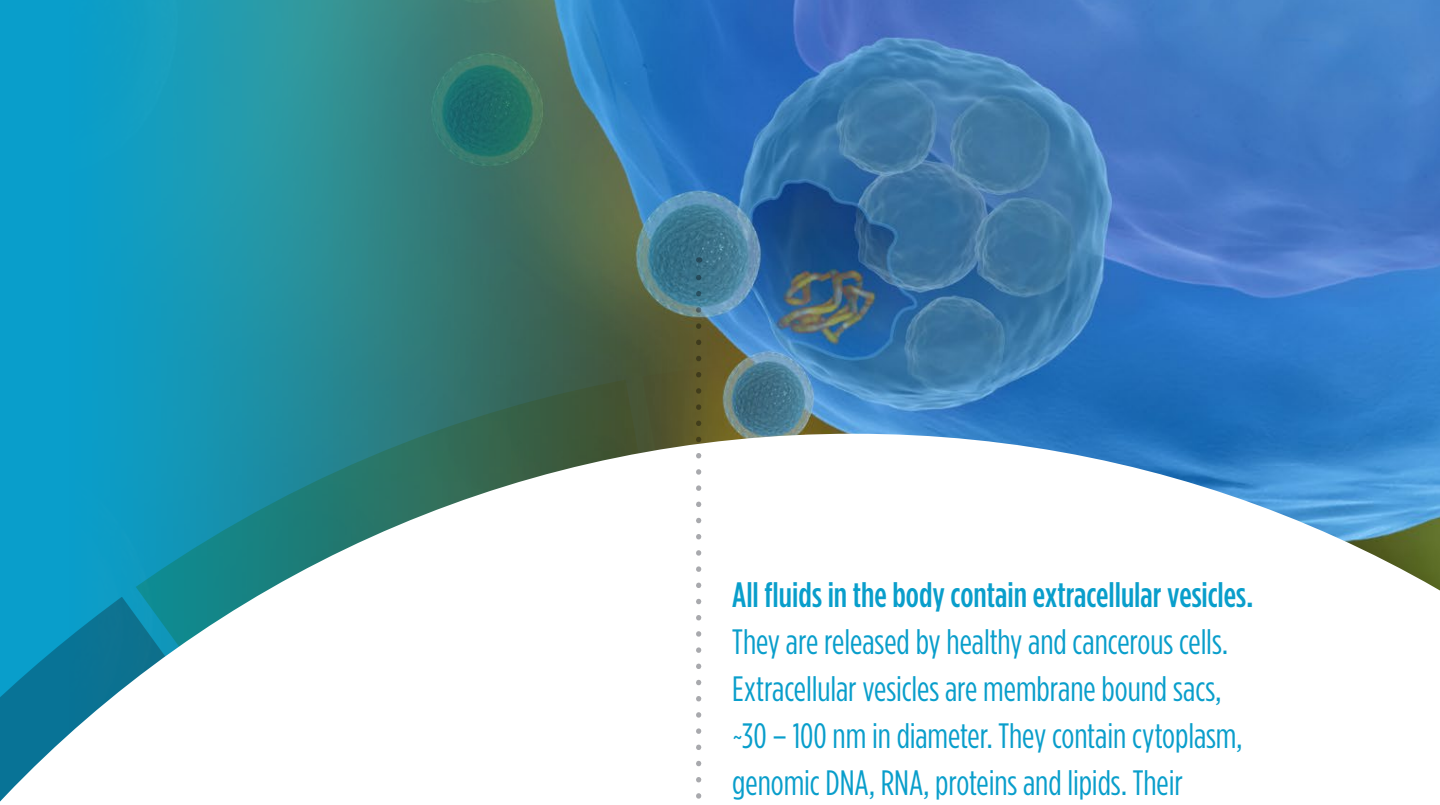
Trends in Extracellular Vesicle Research

BECKMAN COULTER
Life Sciences

Research into extracellular vesicles (EVs) has **increased over 180%** in the period from 2014 through 2017 as assessed by the number of peer-reviewed publications.

Indeed, the number of investigators self-identifying on the EVpedia website, a community portal for extracellular vesicle research, **nearly doubled** in the same timeframe.



All fluids in the body contain extracellular vesicles. They are released by healthy and cancerous cells. Extracellular vesicles are membrane bound sacs, ~30 – 100 nm in diameter. They contain cytoplasm, genomic DNA, RNA, proteins and lipids. Their biogenesis is metabolically regulated, indicating an evolutionary important process. Although previously observed, the were thought to be cellular garbage. However, it is becoming clear that they are THE mechanism for intercellular communication.

Harnessing this newly discovered cell communication process for therapeutic applications

The characteristics of EVs from diseased cells may vary significantly from healthy cells. This creates the opportunity to diagnose deeply embedded tumors using liquid biopsy (a blood or urine sample). Additionally, with further research we could learn to harness the potential to target specific messages to various cells in the body by injecting extracellular vesicles that have a cargo containing anti-cancer signals, such as oncogene or small-interfering RNAs.

Beckman Coulter surveyed investigators studying extracellular vesicles to understand key trends in the types of analysis and samples being used in these studies. Respondents from academia to industry totaling 238 investigators participated in the survey. This report shares some key insights from the summary data.

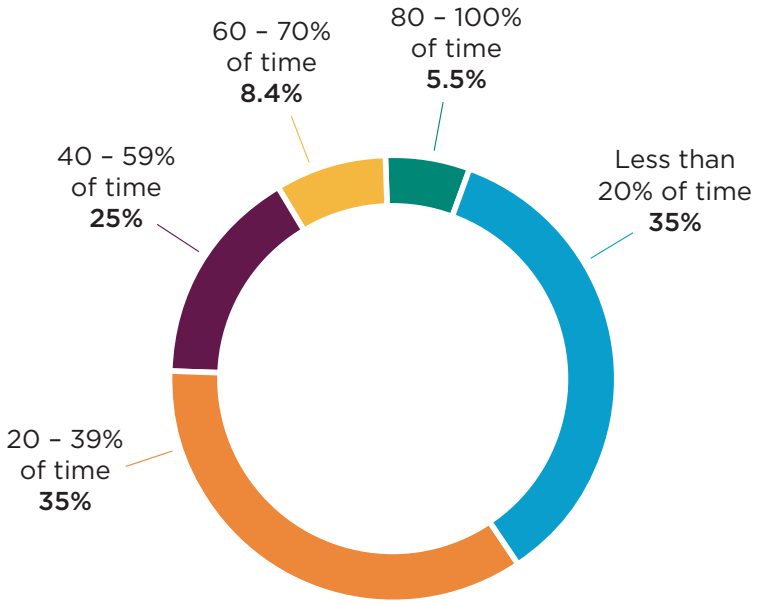
Mainstream Research

Investigators responded to the question, how much of your lab's time is allocated to the study of extracellular vesicles?

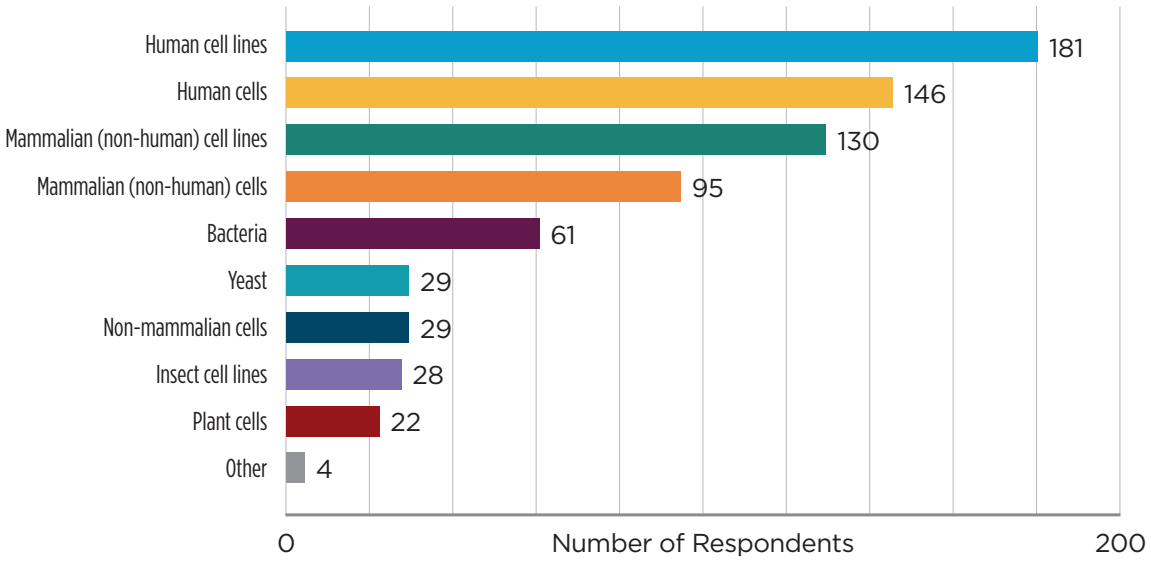
69% of respondents indicated that less than half of their time is spent on EVs. Less than 6% of respondents indicated that 80-100% of their time is spent on EVs. Together these indicate that the field has advanced beyond a niche area intensively explored by a few highly specialized investigators.Human and mammalian cell types are the most prevalent sources of extracellular vesicles but also included are bacteria, yeast, and even plants. Prominent sample types include cell culture, but also primary sources such as plasma, serum, and even whole blood.

Q

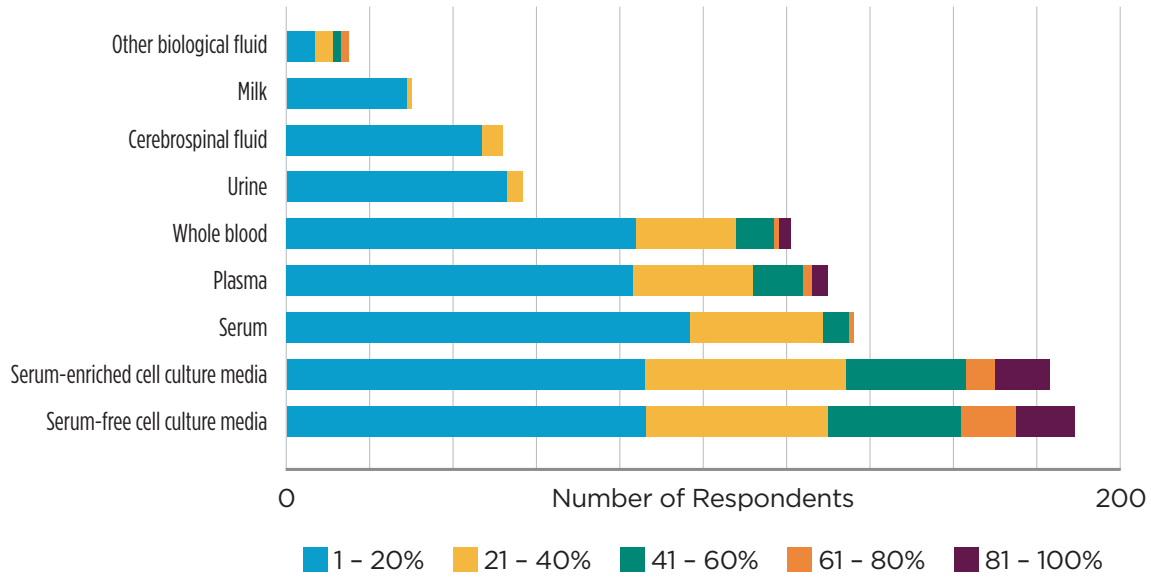
How much of your lab's time is allocated to the study of extracellular vesicles?



Q Which of the following cell types do you obtain extracellular vesicles from?



Q What percentage of your extracellular vesicle research does each sample type account for?



"Exosomes have received tremendous attention in recent years due to the fact that the biological fingerprints of exosomes practically mirror those of the parental cells.

Although the exact biological functions of exosomes remain to be fully deciphered, increasing evidence has indicated that exosomes play a vital role in many cellular processes like cell-cell communication, coagulation, antigen presentation, waste management, as well as transfer of proteins and nucleic acids. Even though exosomes were discovered more than three decades ago, researchers are just starting to unravel the mystery of these extremely small extracellular vesicles. Originally considered as experimental artefacts, waste, or remains of diseased cells, exosomes are now believed to be a central part of a new form of cell-cell communication."

– Staff Scientist in a Biopharmaceutical Company

Techniques & Collaboration

The workflow for extracellular investigations includes three main phases: isolation, characterization, and downstream analysis.

The survey asked respondents to identify the methods used at each phase. A variety of techniques are used, with ultracentrifugation, Western blot, and *In vitro* functional analysis being the most prevalent for each of the three phases—isolation, characterization, and downstream analysis, respectively. Sorting is an attractive technology for isolating defined populations of extracellular vesicles.

We asked the respondents to share their thoughts about the direction of the field. A theme of increased standardization and tools to increase the confidence in the isolation steps emerged from the responses.

Q What improvements could advance the field of extracellular vesicle research?

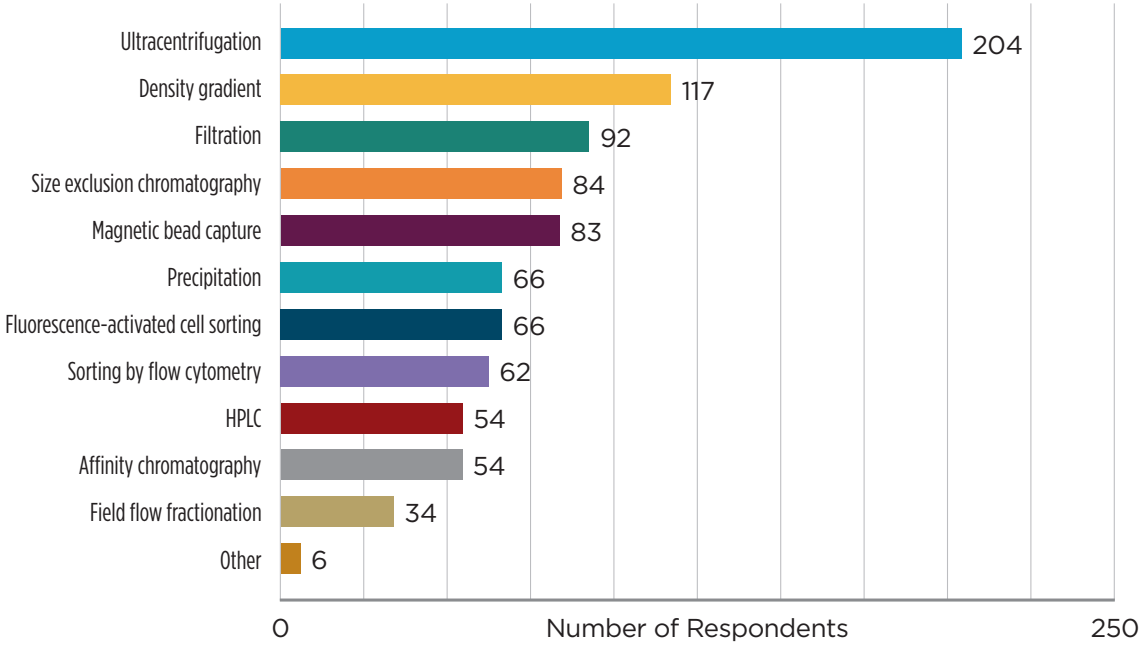
A: "Standardized reference material for instrument calibration, higher sensitivity flow cytometers, cell sorter that can sort exosomes, better precipitation kits."

– Principle Investigator at a University

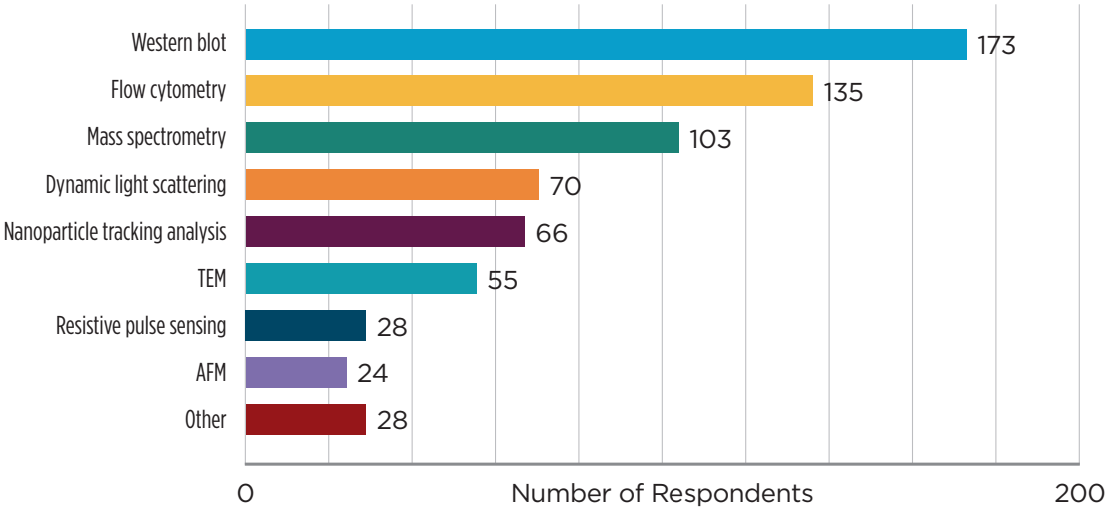
A: "The main problem remains the purity of extracellular vesicle. Most findings need to be reevaluated due to the lack of careful isolation. Even myself, I am not very satisfied with my own extraction and purification procedures. One key improvement would be to class, sort or extract one class of extracellular vesicle among a population of various microparticles produced by cells."

– Lab Manager at a University

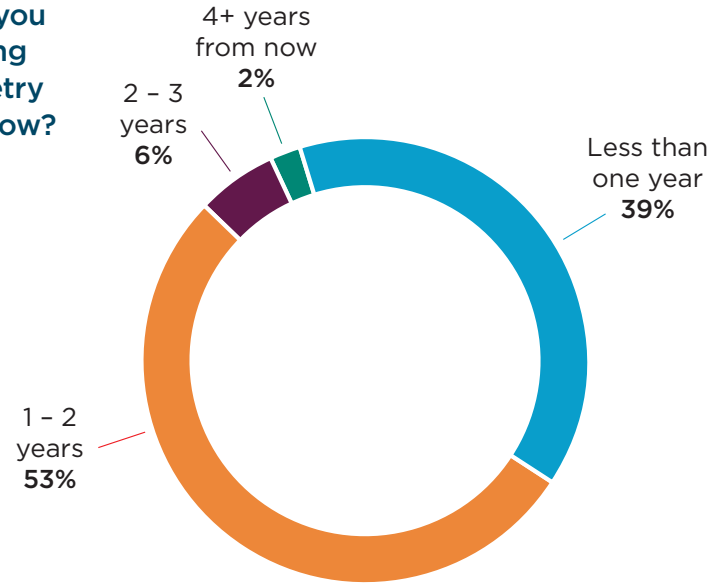
Q Which of the following techniques do you use to extract/isolate extracellular vesicles from cells?



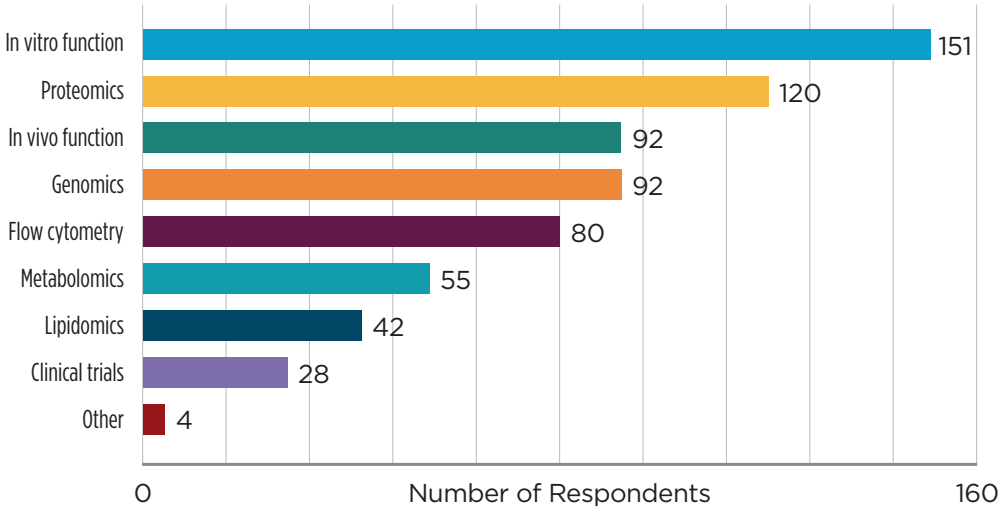
Q Which of the following techniques do you use to characterize extracellular vesicles?

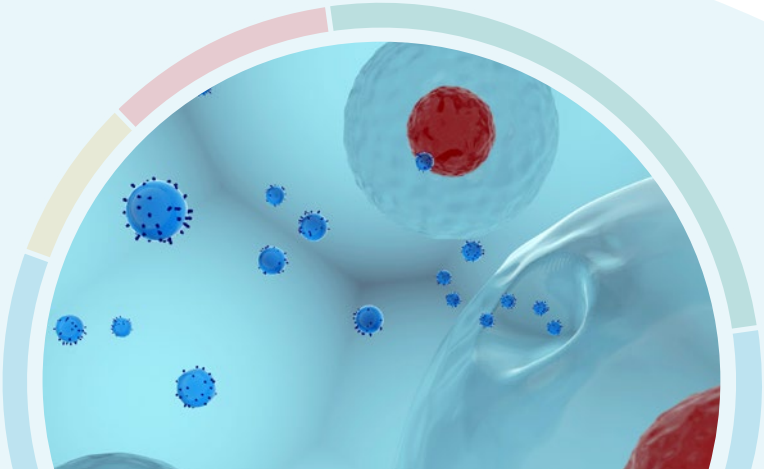


Q How interested would you be in adding or adopting sorting by flow cytometry in your isolation workflow?



Q What downstream analysis are isolated extracellular vesicles used for?

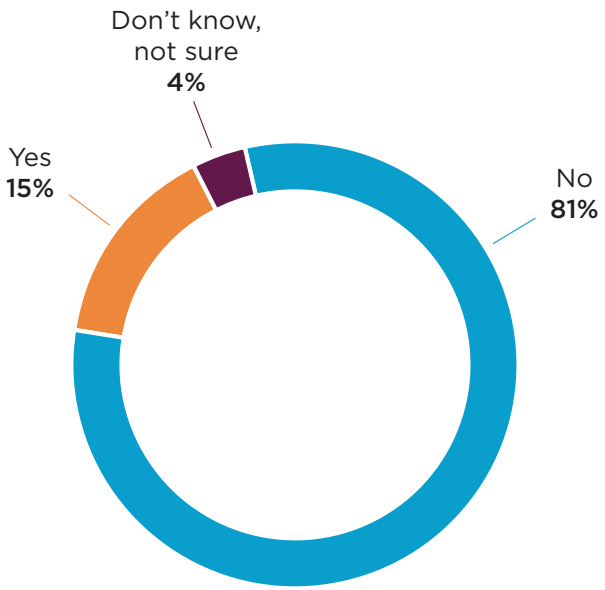




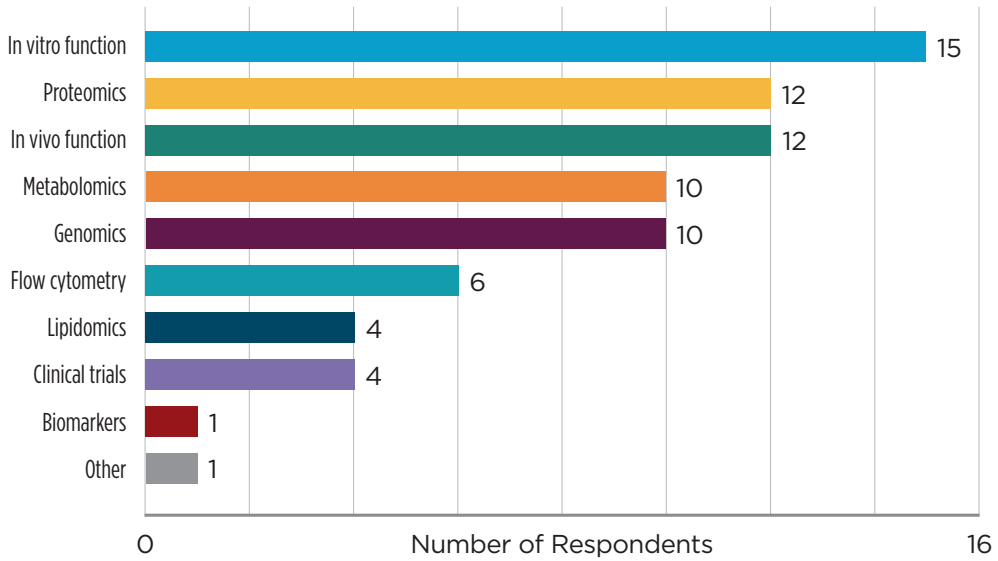
Collaborations with Industry

Approximately 30% of the respondents were from industry. We asked these respondents about their interest in entering into collaborations or contract research with academia to provide the expertise needed for extracellular vesicle investigations. A majority of these respondents 58.4% indicated that these types of collaborations are of interest. A follow up question explored the particular expertise needed for their projects.

Q **Do you anticipate beginning or entering into any collaborations with academic researchers on extracellular vesicles?**



Q **What application areas will your collaboration with academic researchers on extracellular vesicles cover?**



"Extracellular vesicles are not our core competency. I guess the variability of results is quite larger if one does only occasional excursions into this field.

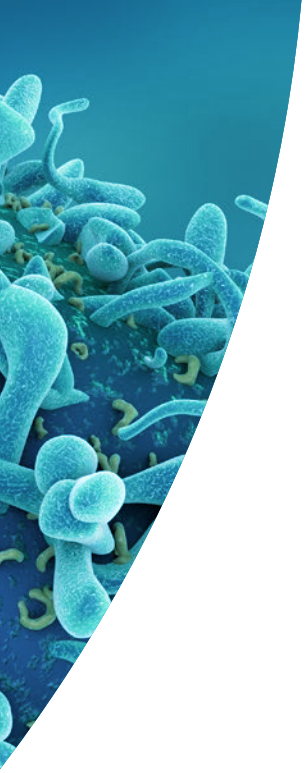
We have been thinking of teaming up with the extracellular vesicles expert at our university.

The field is relatively new and everybody seems to do things differently. Standardization would maybe help..."

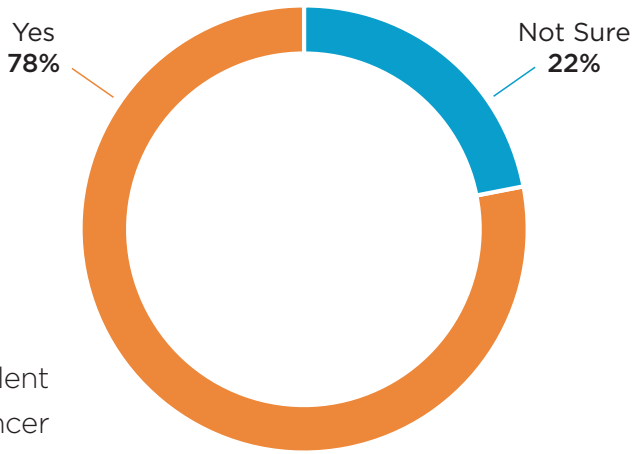
– Principle Investigator at a University

Translating to a Clinical Setting

Given the interest and excitement for the therapeutic applications for extracellular vesicles, we explored insights from investigators on how quickly and in what areas EVs could translate to a clinical setting.

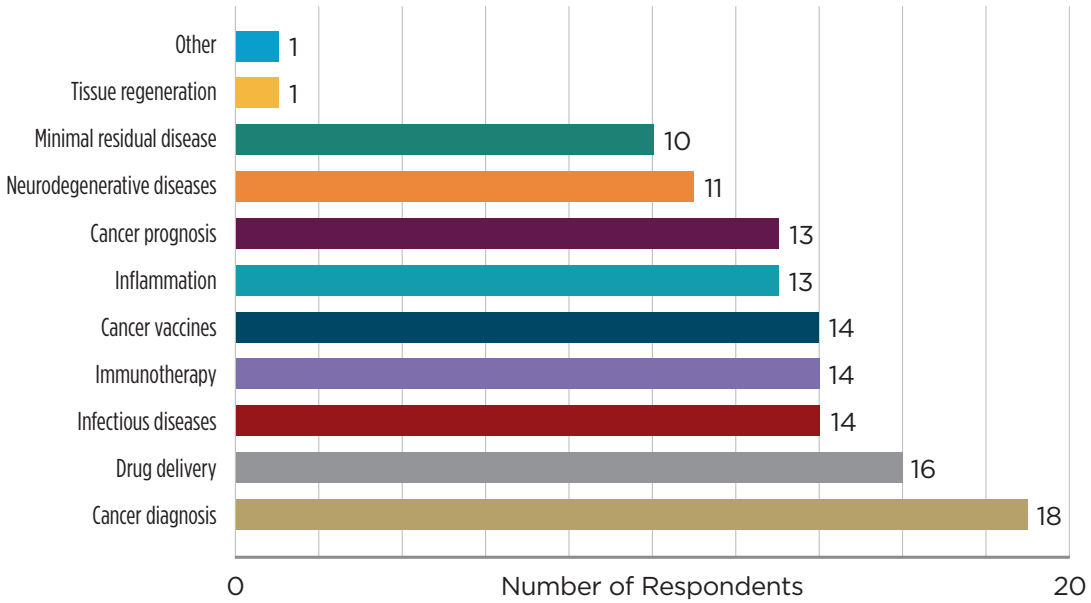


Q **Do you believe that funding for extracellular vesicle research will shift from basic research to clinical trials and clinical diagnostics?**



Over 70% of respondents indicate that funding will shift from basic research to clinical trials and diagnostics. The timeframe for the shift varied widely. The most prevalent area for clinical application was cancer diagnostics, however a wide range of therapeutic applications were also selected.

Q **Which area(s) of extracellular vesicle research do anticipate transitioning from basic research to clinical trials and clinical diagnostics?**



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