biocompare® Surveys & Reports

Flow Cytometry:

Current Trends and Future Outlook

Executive Summary

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Report Introduction

The 2006 Flow Cytometry Report is composed of a market overview and an introduction to the 2006 Flow Cytometry Survey, which contains questions about flow cytometry systems and the related applications that researchers are using. The report also includes a discussion of the survey results, conclusions and recommendations drawn from both the market analysis of flow cytometers and the survey data. The market overview describes the use of flow cytometers in the life science research arena to examine individual cells and their expression of both DNA and protein. Applications to pathology and immunology have driven the use of flow cytometry in various disciplines and expanded its functions to include cell-based assays, pharmacogenomics, and stem cell research.

While instrument costs are high, the flow cytometry market continues to grow and is not expected to plateau for several more years. In 2003, industry analysts valued the flow cytometry market at $650 million, and anticipate a 15% annual rise to reach $1.3 billion by 2008. Market leaders BD Biosciences and Beckman Coulter captured over 80% of this market in 2003, and BD currently holds over 50% market share, due to increasing revenues in benchtop analyzers, cell sorters, and other immunocytometry products. Dako (formerly DakoCytomation), Partec, Cytopeia, and Guava Technologies are also gaining strength in this area.

Preclinical and biomedical labs represent nearly two-thirds of the flow cytometry market, often requiring more access than a current core facility is often able to provide. Clinical diagnostics is an important facet of such labs but face budgetary constraints of healthcare payors and providers who require convincing demonstrations of the impact of such expensive technologies on patient care. A current, urgent need is for quantitation of CD4 markers in HIV-infected patients, particularly in third-world countries, where more affordable instrumentation is critically needed. Advances in the use of charge-coupled devices (CCD) may help drop the price of these instruments by substituting the 100-fold less expensive light-emitting diodes from the CCD for the flow cytometry lasers. These smaller, more robust, less expensive analyzers may serve a much-needed niche in a variety of clinical applications.

Market Overview

The goal of many life science researchers is to examine gene and protein expression profiles in specific sub-populations of cells. While the tools for doing this used to be the domain of immunologists interested in examining the cell surface marker profile of lymphocytes, now researchers from a wide range of disciplines are following suit. And the piece of instrumentation that these scientists have turned to is the flow cytometer. Using flow cytometers has allowed researchers to correlate the unique patterns of genetic and/or protein expression to the signature of diseases and the various underlying pathologies that lead to the same disease phenotype. With such emphasis on genomic and proteomic approaches, flow cytometers have found utility beyond its traditional role in immunology. Histologists, pathologists and hematologists are embracing flow cytometers to carry out an expanded menu of functions and a diverse selection of assays.

"Cell-based tools such as tissue microarrays and flow and image cytometry combine with techniques of immunohistochemistry and molecular in situ hybridization probes to create new approaches to cell and tissue observation, diagnostics and pharmacogenomics," according to Kalorama Information's report on cell-based diagnostics[1].

The first flow cytometers date back to World War II when the U.S. Army commissioned Northwestern University to develop a device for the rapid detection of biological warfare agents. After decades of evolution and technological advancement, the instruments are now becoming as common and as user-friendly as thermal cyclers. Whether benchtop or industrial-sized, most flow cytometers operate by focusing streams of cells past a laser light source. Fluorescent probes bound to the cells emit signals that are recorded and converted into data for later analysis. This mechanism enables analysis at rates topping 100,000 cells per second[2] and at sensitivities to detect fluorescent molecules at concentrations as low as 10 to 100 picomolar[3] . With a cell sorting feature, the instrument also segregates cells based upon the fluorescent probes detected.

Price tags range from about $50,000 up to $500,000. The high cost means that most academic researchers would require a grant to purchase a flow cytometer. Usually, this means appealing to federal agencies, such as the National Institutes of Health. Despite recent constraints with federal funding, the market for the devices continues to grow. In addition, "pharmaceutical companies seek tools that speed the process of bringing new drugs to market," according to Beckman Coulter's 2005 annual report[4].

Experts agree. "The market has been climbing with a pretty steep curve," said Howard M. Shapiro, M.D., a recognized flow cytometry expert and historian. "It's not near to hitting a plateau, not for another several years."

By Shapiro's rough estimate, preclinical and biomedical research labs represent about two-thirds of the market. Labs replacing outdated instruments are upgrading to newer units that can detect four or more fluorescent colors, which are much less essential for clinical labs. Another segment of researchers have outgrown their organization's core facility and need their own instruments for

Market Overview (continued)

greater access. Flow cytometers are crucial for stem cell research. More widespread is the device's employment for screening cells for green fluorescent protein, a popular marker of gene expression.

"Cell biologists and geneticists are now starting to use flow cytometers because they want to know which cells have green fluorescent protein," said Shapiro, author of "Practical Flow Cytometry, 4th edition" (Wiley 2003), the central text on the subject. "Close to 50% of all the cell sorting being done is for sorting cells" that are transfected with green fluorescent protein.

In the book, Shapiro attempts to paint a worldwide landscape of the types of flow cytometers in use. Most researchers are currently using benchtop models that use air-cooled argon ion lasers and can detect fluorescent colors in three or four spectral regions, such as green, yellow, red and/or orange. Whereas 12,000 to 20,000 of these models were in operation in 2003, more elaborate benchtop instruments, which contain a second laser and can detect about six fluorescent colors, numbered about 2,000[5]. About 3,000 to 5,000 flow cytometers that work through a confocal microscope were in operation in 2003[6].

These units represent the more than 90 companies[7] offering instruments, services, reagents, software and other accessories. According to Kalorama's report, Becton Dickinson and Company's BD Biosciences division (San Francisco, Calif.), Beckman-Coulter Inc. (Fullerton, Calif.) together had a grip on 81% of the flow cytometry market in 2003[8]. Other leading companies include DakoCytomation A/S (Glostrup, Denmark). Also leading the pack are Partec GmbH (Munster, Germany), Cytopeia Inc. (Seattle, Wash.) and Guava Technologies Inc. (Hayward, Calif.).

All tolled, the market was worth an estimated $650 million[9] in 2003, according to Kalorama's report. With a compound annual growth of 15%, revenues should reach $1.3 billion by 2008. Company reports point strong sales of both instruments and reagents, such as immunohistochemical and in situ stains and probes, as the primary drivers of growth.

"It is pretty much established that BD now has well over 50% of the market for both benchtop analyzers and cell sorters," said Shapiro, who serves as a flow cytometry consultant with his company The Center for Microbial Cytometry in West Newton, Mass. "Dako is likely to be second in sorters, with Beckman Coulter third while second in the benchtop analyzer market."

BD Biosciences has reported increasing revenues[10] for their immunocytometry products for the past several years. This is demonstrated with 2004 revenues of $397 million, representing a 20% increase over 2003 revenues of $332 million. The company points to strong sales of its newly introduced BD FACSCanto and BD FACSArray analyzers, in addition to continued popularity of the BD FACSAria cell sorter and the company's cell analysis reagents, for the growth. The immunocytometry division continued its climb with 2005 revenues of $452 million, representing a 14% increase over 2004.

Market Overview (continued)

Beckman Coulter's[11] cellular systems division reported a 2.1% revenue increase in 2005, pointing to the FC 500 and XL flow cytometer lines as primary contributors of growth, in addition to the company's high-throughput hematology systems. In 2004, overall revenues for biomedical research demonstrated a 5.5% growth over 2003. The company owes such progress to an 8.4% increase in sales of the Cytomics FC 500 series and related reagents, as a result of ongoing enthusiasm for proteomics research. Sales of consumable supplies, service and chemistry kits accounted for about 64% of 2003 revenues.

Newly developed techniques such as bead-based approaches and miniaturized tools should have little effect on such healthy revenues, Shapiro said. Lab-on-a-chip flow cytometry systems require repeated purchases of expensive chips. In addition to their lack of precision and sensitivity, the flow cytometry chips operate at about one-hundreth the speed of full-size instruments. Bead-based assays are divergent enough to grow alongside the burgeoning cell-based market, he said. Bead-based assays generated revenues of $5 million in 2003[12], according to Kalorama. With an estimated 43% annual growth, these revenues should reach $30 million by 2008.

However, charge-coupled devices (CCD), which are now used for most imaging systems, may very well threaten to slash the price of instruments. These "imaging ones can match the performance and dramatically drop the price" of the current flow cytometers, which "won't get dramatically cheaper," Shapiro said. The reason mostly lies in the price of lasers, which cost 100 times that of the light-emitting diodes of a CCD imaging instrument.

Markets that have yet to be penetrated mostly consist of poor countries that can't afford the tens of thousands of dollars for the least expensive instruments. Among the most urgent needs is CD4 counting in HIV-infected patients. BD Biosciences, Partec, Guava, Beckman Coulter and Point-Care Technologies Inc. (Marlborough, Mass.) are all "trying to compete in that area, which requires relatively small, rugged and inexpensive instruments," Shapiro said. And the newer CCD-based analyzers are those that can be made "smaller, more robust and less expensive than any flow cytometers with quoted prices well under $10,000. These instruments may also be used in place of and/or in addition to benchtop flow cytometers in many labs in more affluent countries."

The clinical diagnostic market looks promising as "increased knowledge about the cell processes that lead to disease and increased prevalence of the most pressing chronic diseases have spurred demand for more and more sophisticated cell-based analyses," according to Kalorama's report[13]. However, growth in this market faces the constraints of healthcare payors and providers, who are requiring stringent validation of the expensive tests to "prove a significant positive financial impact on patient care."

Market Overview (continued)

1. "Cell-based Diagnostics: Technology, Applications and Markets", Kalorama Information, January 1, 2005.
2. Shapiro HM, "The Evolution of Cytometers", Cytometry Part A, 58A:13-20, Wiley-Liss Inc. 2004.
3. Edwards BS et al, "Flow Cytometry for High-throughput, High-Content Screening", Current Opinion in Chemical Biology, 8:392-398, 2004.
4. Beckman Coulter Inc, Form 10-K for period ending December 31, 2005, Filed February 24, 2006.
5. Shapiro HM, "Practical Flow Cytometry, 4th edition", John Wiley & Sons, July 2003.
6. Ibid.
7. Bonetta L, "Flow Cytometry Smaller and Better", Nature Methods, 2:785-795, 2005.
8. "Cell-based Diagnostics: Technology, Applications and Markets", Kalorama Information, January 1, 2005.
9. Ibid.
10. Becton Dickinson and Company, Form 10-K, for period ending September 30, 2005, filed December 09, 2005.
11. Beckman Coulter Inc, Form 10-K for period ending December 31, 2005, Filed February 24, 2006.
12. "Cell-based Diagnostics: Technology, Applications and Markets", Kalorama Information, January 1, 2005.
13. Ibid.

Survey Introduction and Methodology

The 2006 Flow Cytometry Survey is designed to provide life science vendors of flow cytometry systems with a better understanding of how their products are used in the research environment and how their company specifically rates among the survey participants. Data were gathered from questions regarding: how often flow cytometry is used (and for which applications), if the researcher owns, shares, or uses a flow cytometer as part of a core facility, which reagents and equipment are used, the goals of the research, what brands of flow cytometer systems, kits, and reagents are used, how key features and system attributes are rated, which molecule types and cell types are analyzed, which fluorochromes or fluorescent dyes are used, how often flow cytometry is performed (and on how many samples), if sample number is expected to change, how flow cytometry compares with high content analysis (HCA), how many colors are used (and how many gates are typically created per experiment), which specific software types are used and the most important features of the software, how flow cytometry information is obtained, and suggestions for next-generation equipment, software, kits, and reagents.

The 2006 Flow Cytometry Survey consisted of 29 questions. Of these, 10 included "other" as an answer choice and 1 was open-ended. Five questions were used for demographic information. The survey was administered on-line from March 27th – April 5th, 2006, and the data gathered, tabulated, and presented here.

Appendix I: Questionnaire

1. **Please characterize how often you use flow cytometry in your research or work?**
   - Frequent use – daily
   - Regular Use –once or twice a week
   - Occasional Use –once or twice a month
   - I do not use flow cytometry – exited from survey

2. **Which best describes your current flow cytometry facility?**
   - My lab owns a flow cytometer
   - My lab shares a flow cytometer with a few other labs
   - My lab uses a flow cytometer core facility
   - Other (please specify)

3. **Which of the following do you use in your flow cytometry experiments?**
   - Flow cytometer system
   - Cell sorter
   - Flow cytometry kits
   - Positive control cells
   - Fluorochrome-labeled primary antibodies
   - Fluorochrome-labeled secondary antibodies
   - Fluorescent particles/microspheres for calibration
   - Fluorescent dyes for labeling antibodies/conjugates
   - Quantum dots
   - Flow cytometry data analysis software
   - None of the above

4. **What is the goal of your research?**
   - Basic research
   - Target validation
   - Assay development
   - Other (please specify)

5. **What brand of flow cytometer do you PRIMARILY use?**
   - BD Biosciences
   - Beckman Coulter
   - Guava Technologies
   - Dako (formerly DakoCytomation)
   - Partec (GCAT)
   - Cytopeia
   - Cytek
   - Amnis Corporation
   - I don't know
   - Other (please specify)

6. How satisfied are you with the following features of your [pipe brand] flow cytometer? (Rank from 1 to 8: 1= Not at all, 7= Very Satisfied, 8=N/A)

- Power (number of colors)
- Cell sorting capability
- Speed/Throughput
- Footprint (instrument size)
- Technical support
- Software performance

7. What brand(s) of flow cytometry kits and/or reagents do you use? (check all that apply)

- BD Biosciences
- Cell Signaling Technologies
- Invitrogen/Molecular Probes
- eBiosciences
- Guava Technologies
- R&D Systems
- Sigma-Aldrich
- Bender MedSystems
- Stratagene
- Other (please specify)
- Calbiochem
- Chemicon/Upstate
- Roche Applied Science
- Serotec
- Duke Scientific
- BioLegend
- Beckman Coulter
- Dako (formerly DakoCytomation)
- Promega

8. Which of the following flow cytometry applications do you perform? (check all that apply)

- Light Scatter
- Immunofluorescence
- Gene Expression and Transfection
- Cell sorting
- Fluorescence
- DNA Content Analysis/DNA Staining
- Metabolic Studies
- Other (please specify)

9. Which of the following molecule types do you analyze by flow cytometry?

- Cytokines
- Cytokine receptors
- Chemokine receptors
- Glycoproteins
- CD markers / cell surface markers
- Stem cell markers
- Chemokines
- Cell cycle proteins
- Apoptosis proteins
- Adhesion molecules
- Modified proteins (phosphorylated, etc)
- Other (please specify)

10. How long have you been performing flow cytometry?

- Less than 1 year
- 2 to 5 years
- 6 to 10 years
- 11 to 15 years
- More than 15 years

11. Which of the following cell types do you use in flow cytometry applications?

- Epithelial-like cells (HeLa, CaCo2)
- Endothelial-like cells (HUVEC, BAEC)
- Neuroblastoma (CLBPEC, SHEP)
- Melanoma
- Myotubes/myoblasts/muscle cells
- Primary cells
- Granulocytes
- Hematopoitiec stem cells
- Other (please specify)
- Fibroblast-like cells (HEK 293, Cos-7)
- Hepatocyte-like cells (HEPA-1, HepG-2)
- Leukemia cells/Lymphoblasts (Jurkat, K562)
- Monocytes/macrophages
- Keratinocytes
- Lymphocytes
- Embryonic stem cells
- Dendritic cells

12. What fluorochromes or fluorescent dyes do you use? (check all that apply)

- Pacific Blue
- Phycoerythrin (PE)
- Cy5.5
- Alexa 610
- Indo-1
- Monochlorobimane(MCB)
- Rhodamine
- Alexa 488
- PE/Cy7
- PerCP
- Cascade Yellow
- Texas Red
- Cy7
- Alexa 700
- Hoechst 33342
- Allophycocyanin (APC)
- GFP
- PE/Cy5
- APC/Cy7
- PE/Texas Red
- Fluorescein Isothiocyanate (FITC)
- Cy5
- Alexa 405
- Alexa 750
- Cascade Blue
- Propidium Iodide
- Alexa 647
- PE/Cy5.5
- APC/Cy5

13. How often does your research require cell sorting capabilities?

- Often
- Sometimes
- Rarely
- Never

14. How many samples do you measure with flow cytometry per week?

- Less than 1
- 1 – 10
- 11 – 20
- 21 – 30
- 31 – 50
- 51 – 100
- More than 100

15. How do you expect the total number samples measured by flow cytometry to change over the next 12 months?

- Increase by > 50%
- Increase by 25% - 50%
- Increase by 10 – 25%
- Increase by 1% - 10%
- No change
- Decrease by 1% - 10%
- Decrease by 10% - 25%
- Decrease by 25% - 50%
- Decrease by > 50%

16. Please rate the following flow cytometry system attributes? (Rank from 1 to 4: 1= Very Important, 4= Not Important)

- Software features
- Hardware features
- Applications supported
- Throughput
- Affordability/Price
- Services/support

17. How do you view flow cytometry compared to High Content Analysis (HCA)? (check all that apply). High Content Analysis (HCA) = multiparameter analysis using high-throughput sub-cellular imaging)

- I don't need HCA as flow cytometry gives me the throughput I need
- I don't need HCA as flow cytometry gives me the information/content I need
- I don't need HCA as flow cytometry gives results that HCA does not
- I currently use both flow cytometry and HCA
- I would like to start using both flow cytometry and HCA in the next 1 to 2 years
- I expect to start using both flow cytometry and HCA in the next 3 to 5 years
- I currently use HCA in preference to flow cytometry
- I expect to use HCA in preference to flow cytometry in the next 1 to 2 years
- I expect to use HCA in preference to flow cytometry in the next 3 to 5 years

18. How many colors do you typically use on your flow cytometer?

- 1	- 2	- 3
- 4	- 5	- 6
- 7	- 8	- More than 8

19. Which of the following flow cytometry software types do you primarily use to analyze data?

- Software package that came with the flow cytometer
- Third party flow cytometer software – purchased
- Third party flow cytometer software – freeware

20. What software do you use to analyze your flow cytometry data? (check all that apply)

- FCS Express from De Novo Software
- ModFit LT from Verity Software House
- WinList from Verity Software House
- CellQuest Pro from BD Biosciences
- BD Attractors from BD Biosciences
- Expo 32 from Beckman Coulter
- Guava Cytosoft from Guava Technologies
- Other (please specify)
- FlowJo from FlowJo LLC
- QuantCALC from Verity Software House
- WinList 3D from Verity Software House
- Paint-A-Gate Pro from BD Biosciences
- BD FACSDiva from BD Biosciences
- Summit from Dako (formerly DakoCytomation)
- FloMax from Partec

21. How many gates do you typically create when analyzing a single flow cytometry sample?
- 0
- 1 – 2
- 3 – 5
- 6 – 10
- 11 – 15
- 16 – 20
- More than 20

22. Please rate the importance of the following flow cytometry data analysis software features to your research? (1 = Not at all important, 5 = Very important)
- Online documentation
- Technical support
- Histogram plot
- Ability to create a variety of gate shapes
- Export data capability
- 2D Plots (dot, density, contour)

23. Do you have any suggestions you would like to provide to suppliers when designing next generation flow cytometry equipment, software, and kits and reagents? (open-ended)
Flow Cytometers:
Kits and reagents:
Software:

24. When looking for flow cytometry reagents, where do you typically search to find the reagent you need? (check all that apply)
- Supplier website
- Biocompare
- Google
- Yahoo
- Purdue Flow Cytometry Board
- Colleagues
- Other (please specify)

Demographic Questions

1. In which type of institution do you work?
- Academic
- Pharmaceutical
- Private Research
- Other (please specify)
- Biotechnology
- Government
- Clinical Diagnostic Testing

2. Which title best applies?

- Professor/Instructor
- Business Development Director/Manager
- Department Head
- Account Manager
- Staff Scientist
- President/CEO/Owner/VP
- Postdoctoral Fellow
- Consultant
- Process Engineer
- Research Director/VP of Research
- Technician/Research Assistant
- Graduate Student
- Principal Investigator
- Lab Director/Chief Scientist
- Procurement Manager
- Other

3. Which of the following are your key areas of research or work?

- Bioinformatics
- Genomics/Genetics
- Drug Discovery
- Marketing/Sales
- Bioengineering
- Purchasing
- Microbiology/Virology
- Cell Biology
- Administration
- Pharmacology/Toxicology
- Neuroscience
- None of the Above
- Immunology
- Diagnostics/Pathology
- Biochemistry
- Molecular Biology
- Proteomics
- Other (please specify)

4. Which best describes your purchasing authority?

- Authorize
- Recommend
- Evaluate
- No Purchase Role

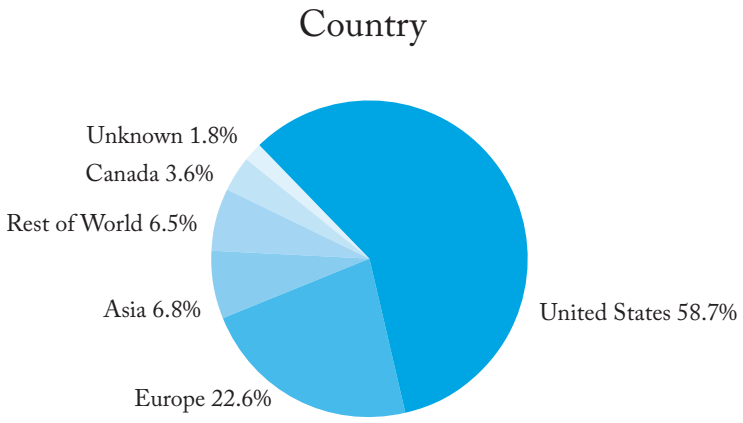
Appendix II:
Presentation of Survey Data

Demographic Survey Data

Country

62% of the survey participants are from the United States and Canada; 23% are from Europe; 7% are from Asia.
N=443

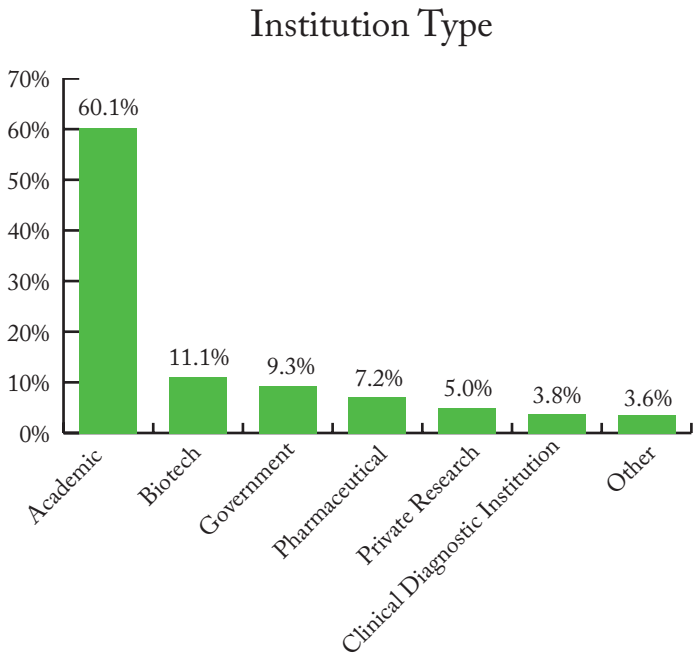
Country	Frequency	%
United States	260	58.7%
Europe	101	22.6%
Asia	30	6.8%
Rest of World	29	6.5%
Canada	16	3.6%
Unknown	7	1.8%



What is your Institution Type?

60% of survey participants are from academia while 18% are from biotech and pharmaceutical companies.
N=443

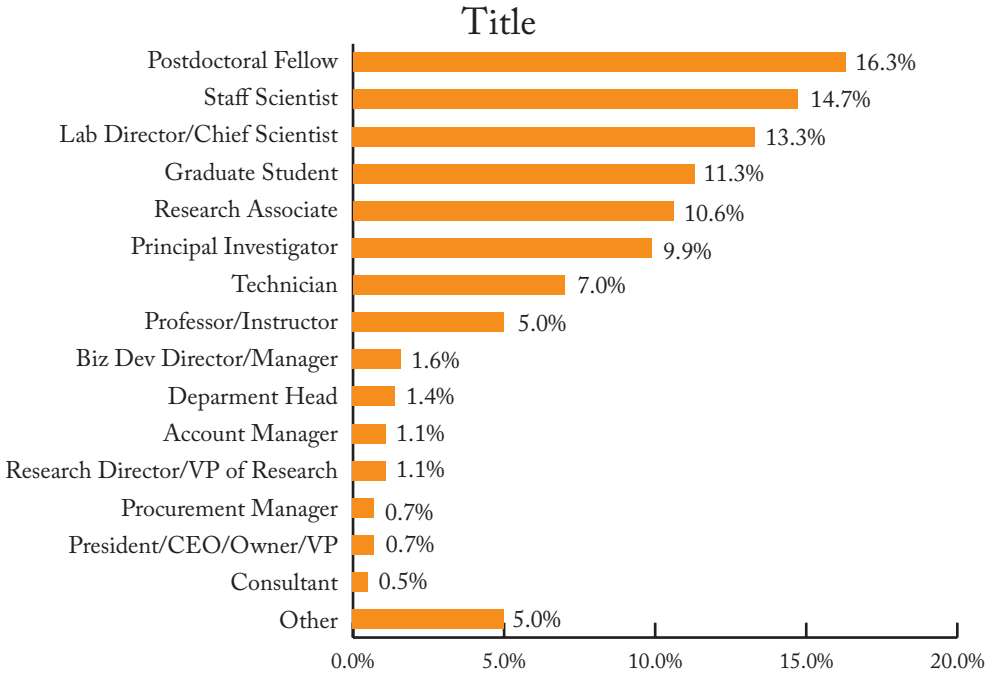
Institution Type	Frequency	%
Academic	266	60.1%
Biotech	49	11.1%
Government	41	9.3%
Pharmaceutical	32	7.2%
Private Research	22	5.0%
Clinical Diagnostic Institution	17	3.8%
Other	16	3.6%



Which title best applies?

70% of survey takers work at the bench*.
N=443

Institution Type	Frequency	%
Postdoctoral Fellow	72	16.3%
Staff Scientist	65	14.7%
Lab Director/Chief Scientist	59	13.3%
Graduate Student	50	11.3%
Research Associate	47	10.6%
Principal Investigator	44	9.9%
Technician	31	7.0%
Professor/Instructor	22	5.0%
Biz Dev Director/Manager	7	1.6%
Department Head	6	1.4%
Account Manager	5	1.1%
Research Director/VP of Research	5	1.1%
Procurement Manager	3	0.7%
President/CEO/Owner/VP	3	0.7%
Consultant	2	0.5%
Other	22	5.0%



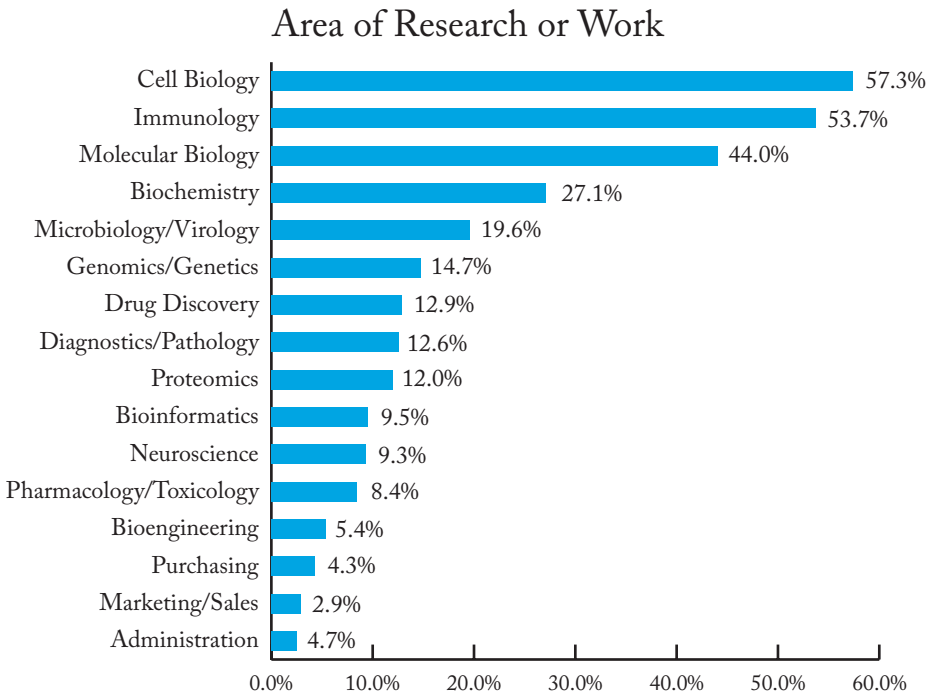
*Includes: Postdoctoral Fellow, Staff Scientist, Graduate Student, Research Associate, Principal Investigator, Technician.

Which of the following are your key areas of research or work? (check all that apply)

The majority of survey takers are cell biologists (57.3%) and immunologists (53.7%).
N=443

Research Area	Frequency	%
Cell Biology	254	57.3%
Immunology	238	53.7%
Molecular Biology	195	44.0%
Biochemistry	120	27.1%
Microbiology/Virology	87	19.6%
Genomics/Genetics	65	14.7%
Drug Discovery	57	12.9%
Diagnostics/Pathology	56	12.6%
Proteomics	53	12.0%
Bioinformatics	42	9.5%
Neuroscience	41	9.3%
Pharmacology/Toxicology	37	8.4%
Bioengineering	24	5.4%
Purchasing	19	4.3%
Marketing/Sales	13	2.9%
Administration	11	2.5%
Other	21	4.7%

Which of the following are your key areas of research or work? (check all that apply)



Which best describes your purchasing authority?

87% of survey participants either authorize or recommend purchases.
N=443

Purchasing Authority	Frequency	%
Authorize	170	38.4%
Recommend	214	48.3%
Evaluate	37	8.4%
No purchase role	22	5.0%