



2003/2004 MSPPSA SERIES

# PROTEIN EXPRESSION SYSTEMS

AN ANALYSIS OF  
MARKET SIZE & GROWTH  
MARKET SHARE  
PURCHASE PLANS &  
SUPPLIER ASSESSMENT FOR  
THE U.S. LIFE SCIENCE RESEARCH MARKET

*A Multi-Client Report*

by  
PhorTech International  
San Carlos, California

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# I. BACKGROUND



## A. SURVEY OBJECTIVES

The purpose of this survey was to provide our clients with an analysis of the current U.S. market for protein expression products including a detailed examination of six different cell systems. This will focus on the attitudes and expectations of researchers who are currently using protein expression in their work.

The survey was Web-based, at a location on our Web site made known to respondents through an email invitation. The surveying was blind, with no reference made to any of our clients for the survey. To encourage respondents to express themselves freely, the survey was anonymous, and made frequent use of open-ended questions.

Several demographic screens were used to characterize respondents. These include the type of organization and scientific discipline.

Early on in the survey, respondents were asked whether they are currently using recombinant protein expression in their work. Respondents not working in this area were directed to back out of the survey, as they were not qualified to continue.

Researchers answering this question affirmatively were directed to indicate which of six cell systems are currently being used in the laboratory for protein expression. Possible responses include mammalian, baculovirus/in-sect, yeast, prokaryotic, cell-free, plant, or alternately, an optional 'other' category in which respondents could provide a brief description of the unlisted system being expressed. They were then asked to estimate the average expenditure per year on all expression products and to indicate what percent change in use is anticipated over the coming 12 months.

These researchers were then directed to provide further details about current spending, identifying the cell system, major suppliers and the percent of the total expression budget which each represents. Respondents were also queried as to the reason behind purchasing these brands of protein expression products and to indicate if there were any suppliers from which they refuse to purchase. Those answering affirmatively were then asked to identify the brand and explain the reason behind their responses. Suggestions for improvements to specific protein expression products were solicited next.

The five parts making up the final question in this introductory section asks respondents to provide the highest ranked protein expression system manufacturer from a list of 9 companies and an optional 'other' category for each of the following criteria: best value for money, most consistent quality, fastest delivery, widest product range, and most committed to protein expression.





The next series of questions, addressing respondents' protein expression and subsequent purification, begins with several multiple choice questions regarding the origin of proteins used for expression, the types of proteins being expressed and the methods used for purification. More specifically, researchers are also asked to provide the number of chromatographic steps it typically takes to purify the protein of interest satisfactorily. The number of constructs cloned or expressed on a monthly basis is also measured.

Going into greater detail, the next query is a modified audit in which respondents indicate the expression system, the expression rate typically obtained and the amount of expressed protein typically required for each expression system used for up to a total of 3 different systems. Respondents are then asked to indicate whether they use an automated protein purification system, and if so, to provide the brand, model and year of acquisition.

The characteristics of the expressed proteins, that is whether it needs to be a soluble protein, functional protein or have 'other' characteristics is queried next. Researchers using protein expression are also asked what post-translation modifications the expressed proteins need to have from a list of five options or, alternately, an 'other' unlisted modification accompanied by a short description. The last query in this section asks respondents to describe downstream applications using unaided recall.

The remainder of the survey is broken into sections, each covering a different cell system. The first of these sections is addressed to those researchers working with mammalian expression systems. Respondents working with these protein systems were first asked to indicate the number of mammalian preps their laboratory performs on a monthly basis, and whether they use a specific expression system for production of proteins in these cells. The next 3 multiple-choice questions ask respondents to first identify which of 7 expression systems (plus an optional 'other' system) are used most often. Then, researchers are asked to select the types of vectors used most often from a list of 8 options or a ninth 'other' category, followed by the final query examining the most frequently used epitope tags for detection and analysis of recombinant proteins in mammalian cells (from a list of 10 options and an 'other' category).

Respondents currently working with insect expression systems are then asked to indicate how many insect expression preps are performed in their lab on a monthly basis, and to provide a yes/no response regarding whether they use baculovirus to produce recombinant proteins in insect cells. Those answering affirmatively were then asked to describe what types of baculovirus DNA is used to generate a recombinant virus. The next series of 4 multiple choice questions asks respondents to identify which baculovirus transfer vectors used most often, what insect cell lines currently used to produce recombinant proteins in these cells, and what fusion tags are used to purify these





recombinant proteins. In addition, researchers currently performing insect expression are asked to indicate which of two (plus the optional 'other') nonlytic stable systems are used to express recombinant proteins in insect cells.

The next three questions are addressed to respondents working with protein expression systems. After an initial query requesting the total number of yeast expression preps performed per month in the laboratory, respondents are also asked to indicate the strains of yeast used to produce recombinant proteins and the fusion tags currently used to purify these expressed proteins.

Respondents using prokaryotic expression systems are queried next, first providing the total number of prokaryotic expression preps typically performed on a monthly basis in the laboratory. Four additional multiple choice questions ask these researchers to indicate the prokaryotic expression systems in use, the promoter used most often, the fusion tags used for purification, and the most common protease cleavage enzymes.

The next two questions look at respondents' use of the final type of system, based on cell-free or in-vitro expression. Researchers using this system are also asked to indicate the total number of preps performed in the laboratory on a monthly basis using this system followed by a single open-ended query regarding the reasons for choosing cell-free or in-vitro expression systems in their work.

Major objectives of this survey were to determine the present market size and share of expenditure for major suppliers of protein expression products in general, and for each cell system. Customer satisfaction with these suppliers will also be measured, as will anticipated near future usage of this technique. Finally, specific characteristics of respondent's current usage of each cell system is examined.

The audits should permit the evaluation of our clients' present market positions, identify marketing strengths and weaknesses, and suggest strategies to develop or improve sustainable competitive advantage.

This report is the fourth 2003/2004 study in a growing series of market research analyses that began in 1993. We plan to continue the series, adding titles and alternating between U.S. and international markets, depending upon our clients' suggestions and support.

Reports already published in this 2003/2004 series covers the following U.S. topics:

Molecular Biology Reagent Systems, Vol. 2  
Proteomics Research, Volume 1  
Proteomics Research, Volume 2.





Reports released in the 2002/2003 series include the following U.S. topics:

DNA Amplification Instrumentation  
DNA Amplification Reagents & Methodology  
Microplate Reader & Equipment Market

Topics in the U.S. series published in 2001/2002 include:

Electrophoretic Instrumentation & Reagents  
Molecular Biology Reagent Systems, Vol. 2

This series also includes the following reports covering international markets:

Densitometers & Image Analysis in Europe  
DNA Sequencing in the Far East.

The 2000/2001 series covered the following three reports:

U.S. DNA Amplification  
U.S. Molecular Biology Reagent Systems, Vol. 1  
Molecular Biology Reagent Systems, Vol. 1 in the Far East.

In the 1999/2000 series, we have released three reports examining the following markets. These are:

Microplate Equipment in Europe  
DNA Sequencing in the U.S.  
Monoclonal Antibodies in the U.S.

The following nine titles have been released in the series for 1998/1999:

Cell & Tissue Culture in the U.S.  
Cytokines & Growth Factors in the U.S.  
DNA Amplification in the Far East  
DNA Sequencing in Europe  
Electrophoretic Gel Media in Europe  
HPLC in the Life Sciences in the U.S.  
Molecular Biology Reagent Systems, Vol. 1  
Molecular Biology Reagent Systems, Vol. 2 in the Far East  
Protein Expression Systems in the U.S.

The following titles have been released in the U.S. series for 1997/8:

DNA Sequencing  
Molecular Biology Reagent Systems, Vol. 1  
Molecular Biology Reagent Systems, Vol. 2  
Molecular Diagnostics.





Clients are reminded that additional copies of any of these reports that have been purchased in the past are available at a modest cost. Please contact us for further details. Those wishing to know publication dates for any of these reports, or wanting to read summaries of the 72+ reports in this series are invited to visit our Web site at: [www.phortechn.com](http://www.phortechn.com).





## B. SURVEY METHODOLOGY

E-mail invitations to take part in the survey were sent to 4,325 life science researchers from a single source, the PhorTech panel consisting of a cross-section 5,000 US life science researchers. These were assigned validation codes containing a prefix A through F. The first 934 invitations, coded with the letters C or D, were sent on June 25<sup>th</sup>. These were followed by a further 947 invitations on June 30<sup>th</sup> with validation codes beginning with an E or an F. These were supplemented with an additional 985 invitations (coded with an A) on July 8<sup>th</sup>. The final 988 emails were sent on July 10<sup>th</sup>. Respondents to this final list have validation codes starting with a B.

There were a combined total of 488 email messages returned as undeliverable. This corresponds to an undeliverable rate of 11.3%. By deducting this (488) from the 4,325 outbound invitations, we calculate that a total of 3,837 U.S. and Canadian life science researchers received invitations to participate in the survey.

The questionnaires were anonymous, using a combination of tabular entry, check-offs, and open-ended probes. However, almost all respondents did identify themselves by filling in the prize entry form. This makes it possible for us to double-check the responses to any questions by telephoning respondents, improving the overall confidence in the data. We did not observe any survey fatigue in this questionnaire, and felt that respondents spent considerable time explaining their positions on the open-ended questions.

The survey was closed on July 22<sup>nd</sup>, by which time we had received a total of 370 valid responses from the 3,837 invitations for an overall response rate of 9.6%. This met our expectations. The overall statistical results that will be presented in the final report will be accurate to within  $\pm 5.1$  percentage points at the 95% confidence level.

In our experience, 95% confidence levels are appropriate primarily for scientific experiments. Most business people making decisions are content to be right more often than they are wrong. In this case, a 65% confidence level, (in which you would be right twice as often as you would be wrong) is more appropriate. Conveniently, 65% confidence levels are nearly exactly one half the size of the 95% level, thus our 65% levels would be  $\pm 2.5\%$  for all respondents.

According to the binomial distribution theory, these values are valid when the measured event has about a 50% probability. When the measured event is considerably more rare than this, the corresponding confidence intervals get smaller. On the other hand, these confidence intervals are valid for answers based upon the complete pool of respondents. When analyzing data for a





group that includes only a small segment of respondents, the answers are less certain and confidence intervals are correspondingly larger.

In this report, we will calculate more exact individual confidence intervals when appropriate. In our comments, we will note whether given differences are significant at either the 65% or 95% level. To aid our client in determining the appropriate confidence interval for various combinations of sample size and measurements, we have created the following table. Just read the closest percentage on the left and find the closest sample size column. The intersection will show the confidence interval for that combination. For example, a measured 35% value with a sample size of 200 has a 95% confidence interval of  $\pm 6.6\%$ .

95% Confidence Intervals for Various Percentages & Sample Sizes

Percent	n=10	n=20	n=50	n=100	n=200	n=500	n=1000
5%	$\pm 13.5\%$	$\pm 9.6\%$	$\pm 6.0\%$	$\pm 4.3\%$	$\pm 3.0\%$	$\pm 1.9\%$	$\pm 1.4\%$
10%	$\pm 18.6\%$	$\pm 13.1\%$	$\pm 8.3\%$	$\pm 5.9\%$	$\pm 4.2\%$	$\pm 2.6\%$	$\pm 1.9\%$
20%	$\pm 24.8\%$	$\pm 17.5\%$	$\pm 11.1\%$	$\pm 7.8\%$	$\pm 5.5\%$	$\pm 3.5\%$	$\pm 2.5\%$
35%	$\pm 29.6\%$	$\pm 20.9\%$	$\pm 13.2\%$	$\pm 9.3\%$	$\pm 6.6\%$	$\pm 4.2\%$	$\pm 3.0\%$
50%	$\pm 31.0\%$	$\pm 21.9\%$	$\pm 13.9\%$	$\pm 9.8\%$	$\pm 6.9\%$	$\pm 4.4\%$	$\pm 3.1\%$
65%	$\pm 29.6\%$	$\pm 20.9\%$	$\pm 13.2\%$	$\pm 9.3\%$	$\pm 6.6\%$	$\pm 4.2\%$	$\pm 3.0\%$
80%	$\pm 24.8\%$	$\pm 17.5\%$	$\pm 11.1\%$	$\pm 7.8\%$	$\pm 5.5\%$	$\pm 3.5\%$	$\pm 2.5\%$
90%	$\pm 18.6\%$	$\pm 13.1\%$	$\pm 8.3\%$	$\pm 5.9\%$	$\pm 4.2\%$	$\pm 2.6\%$	$\pm 1.9\%$
95%	$\pm 13.5\%$	$\pm 9.6\%$	$\pm 6.0\%$	$\pm 4.3\%$	$\pm 3.0\%$	$\pm 1.9\%$	$\pm 1.4\%$





# II. DEMOGRAPHIC SEGMENTATION





## QUESTION 1.

### **Question:**

Do You currently use any recombinant use any protein expression systems in your work?: Yes (*Please continue*): No (*Sorry, but current experience necessary. Please stop now.*)

### **Rationale:**

This question is a primary screening question, which identifies whether a researcher is currently working in this area. Respondents answering this question negatively are directed to back out of the survey, as they are not qualified to continue.

### **Results:**

Since only researchers who are currently working with protein expression systems were included in this analysis, all of the respondents included here answered this question affirmatively.





## QUESTION 43.

### Question:

How would you best describe your organization? (*Select one*): Academia, Biotech/pharma industry, Hospital/medical school, Other Industry, Private research foundation, or Government agency.

### Rationale:

With the responses to this question, we examine the distribution of these researchers across the six organization classifications. This will identify where our respondents are located and primary sources of funding for work involving protein expression. These groupings will also be used in conjunction with the responses to other questions to enable identification of similarities and differences between the usage of this technique amongst researchers from various organizational segments.

### Results:

Before analyzing, the data required some editing in order for responses to be consistent. In order to reflect the source of funding, those working in either a hospital, medical school or health science center have all been categorized as a hospital or medical school. Researchers working in private research foundations, many of which have an email ending in .org, and those receiving private funding from organizations such as HHMI, have been classified as private research foundations. NIH, VA Medical Centers and military organizations are considered to be government agencies.

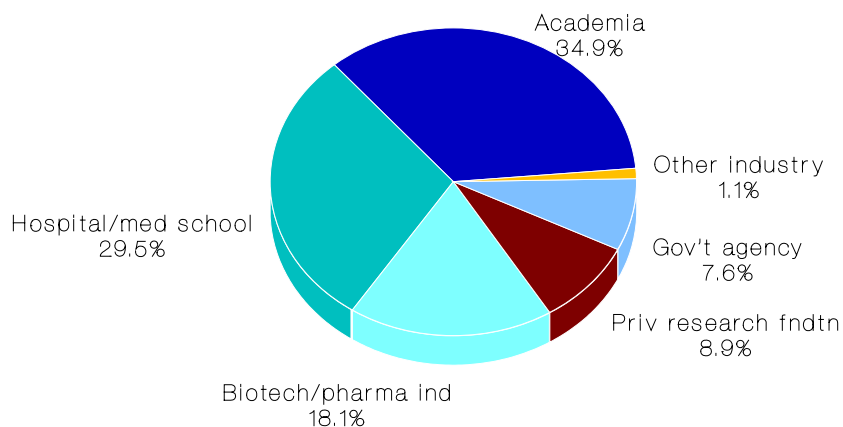
The distribution of all 370 respondents to this survey are depicted in the pie chart at the top of the next page.

Academia has the largest presence, including nearly 35% of our protein expression system users followed closely by the 30% working in a hospital or medical school laboratory. An additional 18% are located in either the biotechnology or pharmaceutical industry. Government agencies and private research foundations are each represented by just under 10% while the remaining 1% are associated with other industries.





### Distribution by Type of Organization All Respondents 2003 U.S. Protein Expression Survey



030723 - PhorTech International 03pex43

#### Analysis:

On the following pages, we present a list of the organizations represented by the respondents to this survey. These are first sorted according to the type of organization and then presented in alphabetical order. We begin with the locations of U.S. respondents who are currently using in vitro assays beginning with the largest sector, academia.

#### Location of Researchers Using Protein Expression Systems, by Type of Organization

##### Academia

- AML
- Boston University
- Brandeis University
- California Institute of Technology
- Cancer Institute of NJ
- Colorado State University
- Columbia University
- Cornell University
- Dartmouth College
- Denver University
- DePauw University
- Framingham State College
- Franklin & Marshall College
- Harvard University
- Indiana University
- Institute of Biosciences and Technology, TAMUSHSC, Houston
- Institute of Biotechnology, UTHSCSA, San Antonio
- Louisiana State University





Michigan State University  
Midwestern University  
Montana State University  
North Carolina State University  
Ohio State University  
Oklahoma State University College of Veterinary Medicine  
Oregon Health & Science University  
Pennsylvania State University  
Purdue University  
Rensselaer Polytechnic Institute  
Rockefeller University  
Rutgers University, New Brunswick  
Rutgers University, Piscataway  
Southwest Texas State University  
Stanford University  
SUNY at Buffalo  
Texas A&M University  
Tulane University  
University of Alabama, Birmingham  
University of Alabama, Tuscaloosa  
University of Alberta  
University of Arizona  
University of California, Berkeley  
University of California, Irvine  
University of California, San Diego  
University of California, Santa Barbara  
University of Central Arkansas  
University of Cincinnati  
University of Connecticut  
University of Delaware  
University of Florida College of Pharmacy  
University of Florida, Gainesville  
University of Florida, Lake Alfred  
University of Guelph  
University of Hawaii, Manoa  
University of Illinois, Chicago  
University of Illinois, Urbana  
University of Louisville  
University of Maine  
University of Manitoba  
University of Maryland School of Pharmacy, Baltimore  
University of Maryland, College Park  
University of Minnesota  
University of Missouri  
University of Nebraska, Lincoln  
University of North Carolina, Chapel Hill  
University of North Dakota  
University of Pittsburgh  
University of Rochester  
University of South Florida





University of Texas, Austin  
University of Texas, Dallas  
University of Toronto, Mississauga  
University of Virginia  
University of Washington  
University of Wisconsin, Madison  
University of Wisconsin, Parkside  
Vanderbilt University  
Western Illinois University  
Winston-Salem State University  
Yale University

#### Hospital/Medical School

Baylor College of Medicine  
Beth Israel Deaconess Medical Center  
Boston University Medical School  
Case Western Reserve University  
Center for Engineering in Medicine (CEM)  
Children's Hospital of Michigan  
Columbia University  
Creighton University School of Medicine  
Dana Farber Cancer Institute  
Dartmouth Medical School  
Drexel University, College of Medicine  
Duke University, Medical Center  
East Carolina University School of Medicine  
Emory University  
Harvard Medical School, Boston  
Harvard Medical School/Massachusetts General Hospital  
Hillman Cancer Center  
Johns Hopkins School/Public Health  
Johns Hopkins University  
Loyola University Medical Center  
Louisiana State University Neurosciences Center, New Orleans  
Louisiana State University Health Sciences Center, Shreveport  
Marshall University School of Medicine  
Massachusetts General Hospital  
Medical College of Wisconsin (MCW)  
Medical College of Georgia  
Medical University of South Carolina  
Massachusetts Eye and Ear Infirmary, Harvard Medical School  
Mt Sinai School of Medicine  
Northwestern University, Chicago  
Northwestern University, Evanston  
Pennsylvania State Hershey Medical Center  
Pennsylvania State School of Medicine  
Rhode Island Hospital  
Stanford University School of Medicine  
SUNY Upstate Medical University  
Thomas Jefferson University





Tufts University School of Medicine  
University of Maryland, School of Medicine  
University of Alabama, Birmingham  
University of California, Davis  
University of California, Davis School of Medicine  
University of California, Irvine  
University of California, Los Angeles Medical School  
UCONN-Health Center  
University of California, San Diego  
University of California, San Francisco  
University of North Carolina, Chapel Hill  
University of North Dakota School of Medicine  
University of Arkansas for Medical Sciences  
University of Cincinnati Medical Center  
University of Iowa  
University of Kansas Medical Center  
University of Kentucky College of Medicine  
University of Louisville Health Sciences Center  
University of Miami  
University of Michigan  
University of Minnesota  
University of Missouri-Columbia  
University of Nebraska, Medical Center  
University of New Mexico  
University of Pennsylvania  
University of Pittsburgh  
University of Rochester, Medical School  
University of Tennessee, HSC  
University of Utah  
University of Vermont  
University of Virginia  
University of Washington  
University of Wisconsin  
University of North Texas Health Sciences Center  
University of Texas Southwestern Medical Center  
University of Texas Health Sciences Center, Medical School  
Virginia Commonwealth University  
Washington University School of Medicine  
Wayne State University  
Wake Forest University School of Medicine

**Biotechnology/Pharmaceutical Industry**

Abbott Labs  
Alexion Pharma, Inc  
Ambergen  
Applied Biosystems  
Array Biopharma  
Astrazeneca R&D, Boston  
AutoGenomics Inc  
BD Biosciences





Celgene  
Cell Signaling Technology  
Cellomics, Inc  
Cellular Genomics, Inc  
Clongen Labs  
Concurrent Pharmaceutical  
Digital Gene Technologies  
Dow Chemical  
Eli Lilly & Co  
ENZO Life Sciences  
Eppendorf 5' Prime  
FDAH, Inc  
Genencor International Inc  
Genentech, Inc  
Genomic Institute of the Novartis Research Foundation (GNF)  
Human Genome Sciences  
ImmvaRx  
Intervet, Inc  
J&J PRD LLC  
La Jolla Pharmaceutical  
Merck Research Labs  
Millennium  
Monsanto Calgene Campus  
Monsanto-AA2G  
Myriad Proteomics  
Novation Pharmaceutical, Inc  
Novel Avenue Technologies  
Novozymes Biotech, Inc  
Oxford Biomedical Research  
Pfizer, Groten  
Pfizer, Chesterfield  
Pfizer Global R&D, Ann Arbor  
Pierce Biotechnology, Inc  
Planet Biotechnology, Inc  
Promega Corporation  
Protometrix  
Regeneron Pharmaceutical  
Ribonomics, Inc  
Roche Palo Alto LLC  
Schering-Plough Research Institute  
Stine Biotechnology  
Sunol Molecular Corporation  
TEI Biosciences, Inc  
Unigene Labs, Inc  
VaxInnate Corporation  
Vicuron Pharmaceutical  
Wyeth Pharmaceuticals, Cambridge  
Wyeth Research, Women's Health Research Institute  
Wyeth Vaccines, W Henrietta





#### **Private Research Foundation**

A I Dupont Nemours  
Boston Medical Center  
Cedars Sinai Medical Center  
Cincinnati Children's Hospital  
Cleveland Clinic  
Fred Hutchinson Cancer Research Center  
Geisinger Health System  
H Lee Moffitt Cancer Research Institute  
HHMI/Columbia University  
HHMI/University of California, San Diego  
HHMI/UT Southwestern Medical Center  
IICC  
John Wayne Cancer Institute  
Joslin Diabetes Center  
Lankenau Institute for Medical Research  
Mayo Clinic, Rochester  
Mayo Clinic, Scottsdale  
Roswell Park Cancer Center  
RTI International  
Southern Research Institute  
St Jude Children's Research Hospital  
Southwest Foundation for Biomedical Research  
Scripps Research Institute  
Stowers Institute for Medical Research  
Wistar Institute  
Palmetto Health South Carolina Cancer Center  
UT MD Anderson Cancer Center  
Wood Hudson Cancer Research Lab  
Barbara Ann Karmanos Cancer Institute

#### **Government Agency**

Argonne National Lab  
Biotechnology Research Institute, Canadian National Research Council (BRI-CNRC)  
ENRM Veterans Hospital  
Minnesota Department of Natural Resources (MN DNR)  
New York State Dept of Health  
NIH /Nat'l Institute of Dental and Craniofacial Research (NIDCR)  
NIH/Nat'l Cancer Institute (NCI), Frederick  
NIH/Nat'l Cancer Institute (NCI), Laboratory of Experimental & Computational Biology (LECB)  
NIH/Nat'l Cancer Institute (NCI), Rockville  
NIH/Nat'l Heart, Lung and Blood Institute (NHLBI)  
NIH/Nat'l Institute of Diabetes and Digestive and Kidney Diseases(NIDDK)  
NIH/Nat'l Institute of Environmental Health Sciences (NIEHS)  
Oregon National Primate Research Center  
Pacific Northwest National Lab  
US Army  
US Army Medical Research Institute of Infectious Diseases (USAMRIID)  
US Army Research Institute of Environmental Medicine





USDA- Agricultural Research Service (ARS), Columbia  
USDA- Agricultural Research Service (ARS), Kerrville  
VA Medical Center, Detroit  
Walter Reed Army Institute of Research (WRAIR)

**Other Industry**

Charles River Labs  
ConAgra  
Heska Corporation  
Labs at Bonfils





## QUESTION 42.

### Question:

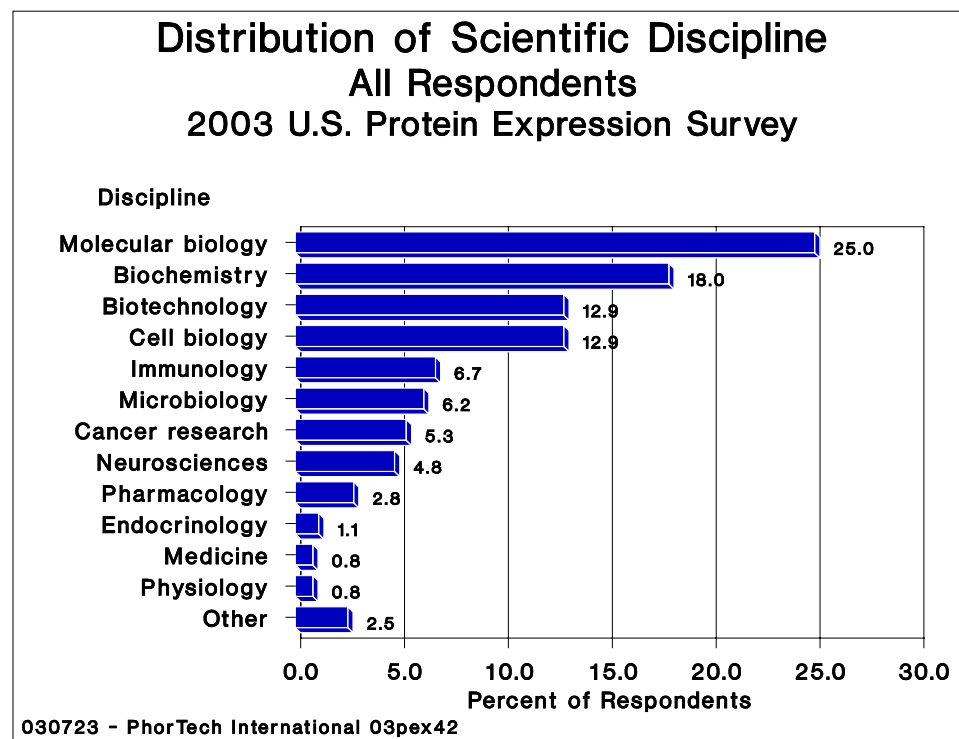
Please select the closest scientific discipline to the one in which you are involved (*Select one*): Biochemistry, Biotechnology, Cancer research, Cell biology, Endocrinology, Immunology, Medicine, Microbiology, Molecular biology, Neurosciences, Pharmacology, Physiology or Other discipline.

### Rationale:

With the responses to this question, we will examine the primary scientific discipline of respondents who are currently working with protein expression systems.

### Results:

The results for the 356 respondents who answered this question are presented in the following horizontal bar chart.



### Analysis:

Molecular biology is the most common scientific discipline, including 25% of the respondents to this survey. A further 18% indicate their primary discipline as biochemistry with an equal number of respondents, 46, responding with biotechnology and cell biology. Combined, these four areas include 68.8% of the respondents answering this question.





The remaining 111 protein expression users, not working in one of these four scientific disciplines, are spread over the remaining 9 areas listed on the survey with immunology microbiology and cancer research each accounting for more than 5% of respondents followed closely by the 4.5% in the neurosciences. Amongst the least frequently mentioned disciplines are endocrinology, medicine and physiology, each cited by 4 respondents or less, while pharmacology and those working in an 'other' unlisted discipline include 10 and 9 respondents, respectively.

