

Frequently Asked Questions

1. What is "proteomics"?

The term "proteome" was first used in 1994 to refer to all the proteins in a cell, tissue, or organism. Proteomics refers to the study of the proteome. Because proteins are involved in almost all biological activities, including disease, the proteome is a critical target for understanding how disease arises and how to prevent it.

2. How does the proteome compare to the genome?

The total number of proteins in human cells is estimated to be between 250 thousand to one million, of which only a small percentage has been sequenced or identified. The complete proteome has not been characterized for any organism. In contrast, the genome (the entire set of genes) for several organisms has been sequenced, including humans. The human genome is estimated to contain about 21,000 protein-encoding genes.

Besides the disparity in numbers of proteins and genes, another important difference between the genome and proteome is that the genome is static and relatively unchanged from day to day. Cellular proteins, on the other hand, are continually moving and undergoing changes such as binding to a cell membrane, partnering with other proteins, gaining or losing chemical groups, or breaking into two or more pieces.

Several other properties of proteins add to the complexity: proteins can vary among individuals, between cell types, and even within the same cell under different conditions. One gene can encode more than one protein (even up to 1,000), and one protein can be modified in multiple ways, which may change its behavior. The quantity of different proteins can also vary greatly. For example, in human blood, the concentration of the protein albumin is more than a billion times greater than interleukin-6. This makes it difficult to measure such low abundance proteins, many of which may have direct relation to cancer or other diseases.

3. What is the promise of proteomics for the early detection and treatment of cancer?

The greatest promise for the early detection of cancer lies in the ability to find valid molecular indicators, or biomarkers, of the disease. While genes are the "recipes" of the cell, containing all of the instructions for assembly, proteins are the products of these recipes and function as the cellular "engines," the molecules that do much of the actual work to keep the cell and the body functioning. The finding that tumors "leak" proteins into blood, urine, and other accessible bodily fluids has led to the possibility of diagnosing cancer at an early stage simply by collecting such fluids and testing them for the presence of cancer-related proteins, or biomarkers. Such biomarkers might also be valuable for monitoring the response to cancer during treatment or detecting the recurrence of tumors after treatment.

4. What is the proteomics “problem?”

While there are well over 1000 cancer protein biomarker candidates described in the literature, very few are clinically validated or have made it into a molecular diagnostic product. This discrepancy indicates that there is a biomarker pipeline problem somewhere between discovery and the clinic.

Biological samples, particularly at the protein level, are immensely complex and variable. However, an even greater level of variability is introduced by the different proteomic tools and methods used to analyze those samples because laboratories across the country collect, store, and study proteins in different ways. This lack of standardization makes it very difficult to separate the true biological complexity from the variables introduced by the laboratory work itself – and is also why many biomarker candidates fail to be clinically validated because a greater number of artifacts than clinically relevant biomarkers are “discovered.”

5. Why is it important to remove experimental variability?

Proteomics holds great promise in many fields, including cancer, but this will only be realized when experimental variability is eliminated (or reduced as much as possible) so that biology can be discovered. Only then will a greater number of protein biomarkers be advanced into molecular diagnostic tests for the early detection and treatment of cancer, ensuring that patients reap the rewards of the molecular revolution faster and more effectively.

6. What is the National Cancer Institute (NCI) Clinical Proteomic Technologies for Cancer (CPTC) initiative?

The CPTC is a five-year, \$104 million initiative aimed at addressing and reducing the layers of variability that prevent progress in applying proteomic insight to clinical practice. This program is bringing together the best minds in proteomics to fix the protein biomarker pipeline with a set of standards, protocols, reagents, etc. – a kind of “proteomics toolkit” for the field – so that proteomic biomarker discoveries can be translated to clinical utility.

The CPTC is composed of three major, integrated programs: the Clinical Proteomic Technology Assessment for Cancer (CPTAC) program, the Advanced Platforms and Computational Sciences program, and the Proteomic Reagents and Resources Core.

7. Why is the CPTC initiative government funded?

The NCI recognizes not only the promise of clinical proteomics for cancer, but also the challenges that this research community must overcome. Understanding that fixing the proteomics “issues” are too great an endeavor for a single institution – it will take an entire community – the NCI launched the CPTC initiative.

8. Who did NCI consult with in the development of this program?

The CPTC initiative was created in collaboration with the international proteomic community. The NCI initiated a series of meetings that brought together leading cancer and proteomic experts, including scientists, clinicians, and engineers, to define the challenges facing clinical cancer proteomics and outline potential solutions. Working together with NCI scientists and program directors, these experts identified the most effective strategies that the NCI should take to help the

field realize its potential for diagnosing, treating, and preventing cancer. As a direct result of their work the NCI launched the CPTC initiative in 2006.

9. What communities are involved in the CPTC initiative?

The CPTC has created a protein research infrastructure by working in partnership with scientists from nearly 50 federal, academic, and private sector organizations. The members of this network have joined together to use the science of cancer proteomics to develop life-saving biomarker tests and other resources that will benefit patients.

In addition to the external scientific community, the CPTC is working in partnership with existing NCI programs:

*NCI-designated Cancer Centers are assisting the CPTC in discovering biomarkers for specific cancer sites

(e.g., breast, lung, prostate, and colon).

*The NCI Early Detection Research Network (EDRN) and Specialized Programs of Research Excellence

(SPOREs) are helping to take basic research findings from the laboratory to create clinical applications for patients.

*The cancer Biomedical Informatics Grid (caBIG®) is building an information system (also called an informatics grid) that will help scientists share information about proteins related to cancer.

10. What is CPTC going to provide to the community?

CPTC is providing the standards and tools needed to ensure that proteomic data are reproducible in any laboratory through the creation of a “proteomics toolkit,” which will contain optimized tools, protocols, and reagents. Developed in collaboration with six leading institutions and by the National Institute of Standards and Technology (NIST), these resources will be provided to the scientific community at little to no cost.

Using these resources, investigators will have the assurance that protein measurement results are due to changes in the biological sample and not to variability in the instrument, assay performance, reagents, operator, or site. This will dramatically improve the quality of biomarker candidates that enter the clinic for validation – and will lay the foundation for the next generation of molecular diagnostics.

11. Where can I find more information about NCI’s CPTC initiative?

Additional information about the NCI CPTC initiative can be found at

<http://proteomics.cancer.gov/>.

For more information about cancer, please visit the NCI Web site at

<http://www.cancer.gov> or call NCI’s Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).