National Cancer Institute

OFFICE OF CANCER CLINICAL PROTEOMICS RESEARCH

Clinical Proteomic Tumor Analysis Consortium

Interrogating Cancer Biology to Address Clinically Relevant Questions

Mission

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) represents a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows.

NCI Clinical Proteomic Tumor Analysis Consortium

The National Cancer Institute's (NCI) Clinical Proteomic Tumor Analysis Consortium (CPTAC) represents a network of Proteome Characterization Centers, which coordinate and conduct research and data sharing activities to comprehensively examine genomically characterized cancer biospecimens. Importantly, CPTAC data with accompanying assays and protocols are made publicly available. This multidisciplinary (proteomics, genomics, bioinformatics, experimental design, statistics, cancer biology and oncology) and integrated consortium identifies proteins that result from changes in cancer genomes and their related biological processes.

Understanding these functional changes at the protein level is the next step in better defining the molecular mechanisms of cancer, such as the dysregulated signaling pathways responsible for tumorigenesis and metastasis. Therefore, CPTAC will analyze changes in protein expression, their post-translational modifications and variations, as well as those in protein-protein interaction and signaling networks responsible for the pathological state of cancer.

Scientific Approaches

The primary approach of CPTAC involves an initial discovery stage where analysis of genomically characterized starting material (tumors) will be performed to broadly interrogate the protein inventory, some of which will be prioritized as potential candidates with protein changes between case and control, followed by a verification stage where biologically and/or clinically important proteins are targeted with quantitative assays.

During the discovery stage, there are two related approaches to integrate genomics and proteomics information from a common biospecimen.

The **"targeting genome to proteome"** approach is where a genomic dataset defines the proteins (candidates) to be targeted in proteomic measurements. In this approach, proteomic labs seek to detect and quantify protein products that correspond to splice variants, mutations, insertions, deletions, and other genomic changes.

In a **"mapping proteome to genome"** approach, the integration of the genomic and proteomic datasets is delayed until after the completion of both types of measurements. This approach allows a broader inventory of detectable proteins in a tumor, including identification of post-translational modifications that may be critical to cell signaling pathways and networks. In addition, the mapping approach can be used to improve the quality of genome annotations (proteo-genomic mapping), as it provides confirmation of protein-coding genes. The combination of these two approaches is anticipated to produce a more comprehensive inventory of detectable proteins in a tumor and advance our understanding of cancer biology. The protein candidates identified during the discovery stage will then be selected and configured into multiplexed verification assays to test in relevant cohorts of biospecimens in the verification stage.

NCI Program Integration

CPTAC adds to NCI's ongoing initiatives in molecular-based programs, such as **The Cancer Genome Atlas** (TCGA). A joint effort of the NCI and the National Human Genome Research Institute, TCGA is a comprehensive and coordinated effort to accelerate our understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing. A unique feature of CPTAC is the use of genomically characterized biospecimens from TCGA as one of the sample sources for the discovery stage. These biospecimens have undergone extensive genomic characterization and will provide a wealth of genomic data that can be used to refine protein targets and develop a clear biological hypothesis in furthering our understanding of cancer biology. CPTAC will be able to leverage its state-of-the-art, standardized proteomic technologies to comprehensively translate cancer genomes to cancer proteomes.

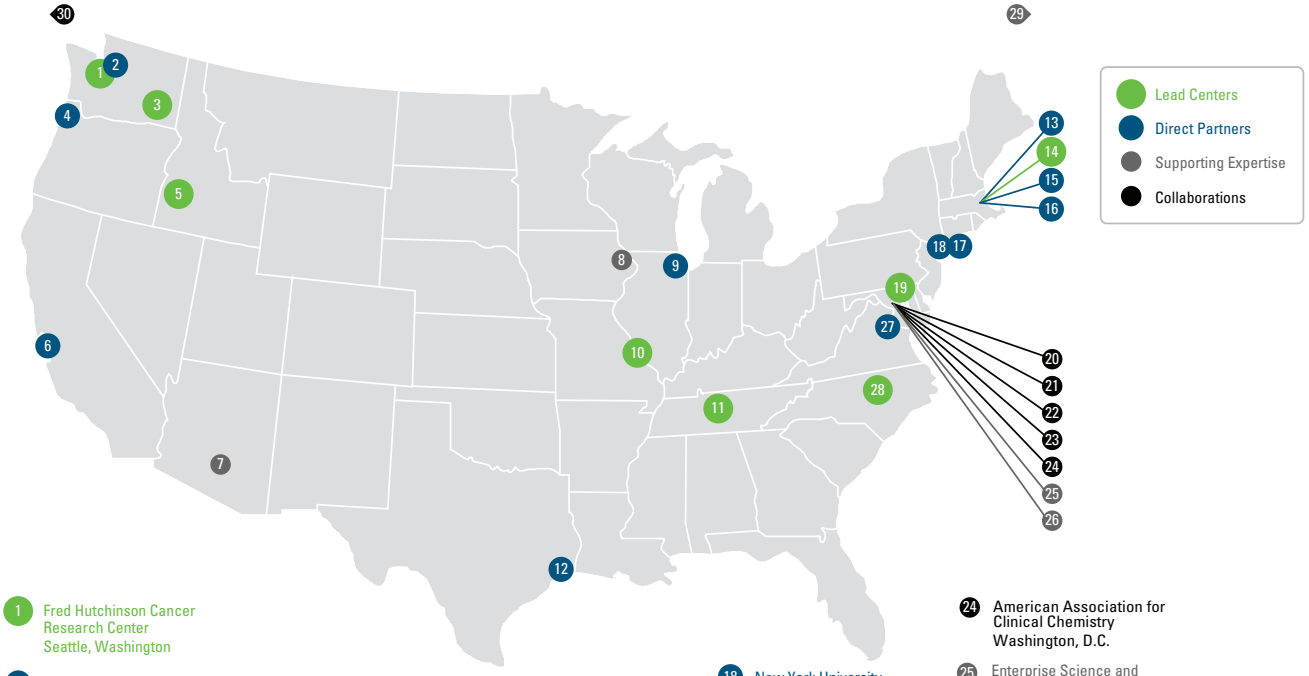
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Components of CPTAC

CPTAC is composed of a network of Proteome Characterization Center teams, a Data Coordinating Center, and a Resource Center. As shown in the map below, CPTAC incorporates the expertise of investigators from throughout the country. In addition to the primary lead Proteome Characterization Centers (green), there are direct partners with several other institutions (blue) to improve the reach and breadth of work. In addition to the PCCs as part of CPTAC, the Data Coordinating Center coordinates the data produced from the CPTAC investigators and ensures that this data is made publicly available. The Resource Center serves as a collection and distribution hub for common biospecimens for the PCC Network and houses the Antibody Portal (antibodies.cancer.gov), which addresses the research community's need for well-characterized reagents by implementing a rigorous system for evaluating antibodies through a well-defined characterization pipeline. Through a series of interagency agreements and contracts, with institutions and groups (gray), the Office of Cancer Clinical Proteomics Research has established an antibody production program that provides materials for both CPTAC and the entire scientific community. To further advance the mission of CPTAC and to advance the field of proteomics, the office collaborates actively with other governmental and nongovernmental agencies (black), including the National Heart, Lung, and Blood Institute, the National Institutes of Standards and Technology, the US Food and Drug Administration, the Korean Institute of Science and Technology, and the American Association for Clinical Chemistry.

Clinical Proteomic Tumor Analysis Consortium



1 Fred Hutchinson Cancer Research Center, Seattle, Washington
2 University of Washington, Seattle, Washington
3 Pacific Northwest National Laboratory, Richland, Washington
4 Oregon Health Sciences University, Portland, Oregon
5 Boise State University, Boise, Idaho
6 Stanford University, Stanford, California
7 Arizona State University, Tempe, Arizona
8 Developmental Studies Hybridoma Bank, Iowa City, Iowa
9 University of Chicago, Chicago, Illinois
10 Washington University of St. Louis, St. Louis, Missouri
11 Vanderbilt University School of Medicine, Nashville, Tennessee
12 The University of Texas M.D. Anderson Cancer Center, Houston, Texas
13 Massachusetts Institute of Technology, Cambridge, Massachusetts
14 The Broad Institute of MIT and Harvard, Cambridge, Massachusetts
15 Massachusetts General Hospital, Boston, Massachusetts
16 Harvard Affiliated Hospitals, Boston, Massachusetts
17 Memorial Sloan Kettering, New York, New York
18 New York University, New York, New York
19 Johns Hopkins University, Baltimore, Maryland
20 Food and Drug Administration, Silver Spring, Maryland
21 National Cancer Institute, Bethesda, Maryland, Frederick, Maryland
22 National Heart, Lung, and Blood Institute, Bethesda, Maryland
23 National Institute of Standards and Technology, Gaithersburg, Maryland
24 American Association for Clinical Chemistry, Washington, D.C.
25 Enterprise Science and Computing, Inc., Rockville, Maryland
26 Georgetown University, Washington, D.C.
27 Virginia Tech, Falls Church, Virginia
28 University of North Carolina, Chapel Hill, North Carolina
29 KTH Royal Institute of Technology, Stockholm, Sweden
30 Korea Institute of Science and Technology, Seoul, Republic of Korea

FOR MORE INFORMATION:

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health
National Cancer Institute
Office of Cancer Clinical Proteomics Research
31 Center Drive, MSC 2580
Bethesda, MD 20892-2580

Phone: (301) 451-8883
E-mail: cancer.proteomics@mail.nih.gov
Web site: http://proteomics.cancer.gov

NIH Publication No. 12-7843
12-2011