



CLINICAL PROTEOMIC
TECHNOLOGIES FOR CANCER

Advancing Protein Science for Personalized Medicine



eProtein

Letter from the Director



Dear Colleagues,

We are extremely pleased with the amount of interest the Clinical Proteomic Technologies for Cancer (CPTC) initiative has received at various national forums over the past few months. At US HUPO this past February, for example, our Clinical Proteomic Technology Assessment for Cancer (CPTAC) centers presented their latest research findings to a packed, standing-room only audience. In addition, at the American Association of Cancer Research (AACR) 2009 Annual Meeting, CPTAC successfully hosted a special Methods Workshop Session titled "CPTC Proteomics Technology Platforms for the Cancer Biomarker Pipeline." It has become increasingly apparent that the scientific community supports our efforts to build more refined, efficient, and reliable biomarker discovery and verification pipelines. These pipelines are anticipated to produce better credentialed candidate leads, ultimately accelerating the discovery of new cancer biomarkers. As more of our findings go into the public domain, we look forward to enhancing our interactions with the greater scientific and clinical communities. ■

A Clinical Proteomic Technologies for Cancer initiative publication that builds connections throughout the proteomics community

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NCI and FDA Engaged in Active Dialogue on the Analytical Validation of Clinical Proteomic Technologies

The National Cancer Institute (NCI)-U.S. Food and Drug Administration (FDA) Interagency Oncology Task Force (IOTF) Molecular Diagnostics subcommittee held a workshop in Cambridge, Mass. on October 30, 2008, bringing together almost 60 participants representing the

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A Physician's Perspective Protein Markers of Risk and Prognosis: A Role for Proteomics

While breast cancer remains the most common cancer of North American women, population-based statistics indicate that for the first time in history, incidence and mortality rates have been falling over the past 10 years. Reduced mortality rates are likely the consequence of earlier diagnosis and more effective treatment modalities developed over the past few decades. One is tempted to speculate that even earlier diagnosis will result in even

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NCI and FDA Engaged in Active Dialogue on the Analytical Validation of Clinical Proteomic Technologies

(continued from cover)

National Institutes of Health (NIH), FDA, industry, academia, and standards organizations. These key stakeholders in the proteomics community gathered to explore the regulatory requirements that will be needed to validate protein-based marker panels and any new technologies (hardware) for their intended use.

According to Mansfield, holding the workshop in conjunction with the CPTC annual meeting was a perfect opportunity to involve CPTC scientists who are currently working through the issues that the FDA will need to address when reviewing 510(k) submissions for proteomic technologies such as mass spectrometry and affinity arrays.

participants will develop a workshop summary for publication that will discuss the analytical validation issues that specific proteomic technologies should address when seeking FDA approval. Second, the group will create mock 510(k) regulatory submissions for two technologies—mass spectrometry and affinity platforms—drawing on information gathered during the workshop and extending the dynamic conversations held throughout the day.

Together, these documents will help orient the FDA to proteomic technologies in novel diagnostics and serve as a springboard for guidance to the proteomics community. ■

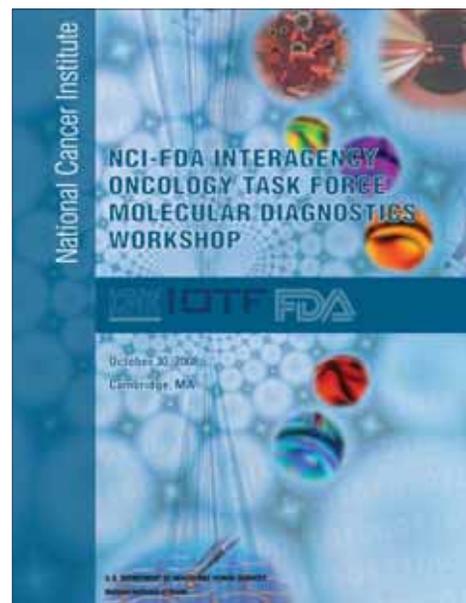
“There’s really no guidance for multiplex proteomic assays. We’ve seen some mass spectrometry assays come through here, but none of them have been for proteomics ...and there are unique issues when you start to do a multiple test in a single tube or platform.”

The IOTF was formed in 2003 to enhance and accelerate the overall process of developing new cancer diagnostics and therapeutics. “The molecular diagnostics group was formed a couple of years ago, and Henry [Rodriguez] and I were named as the subcommittee co-chairs. Together, we decided we would focus on an area of unmet need, which is proteomics,” explains Elizabeth Mansfield, Ph.D., a Senior Policy Analyst in the Office of In Vitro Diagnostic Devices at the FDA.

“There’s really no guidance for multiplex proteomic assays. We’ve seen some mass spectrometry assays come through here, but none of them have been for proteomics; they have all been metabolites, so we’re kind of naïve on that [the protein] side,” says Mansfield. “In terms of multiplex immuno-affinity assays, we actually don’t see very many of those either, and there are unique issues when you start to do a multiplex test in a single tube or platform.”

There were six case studies given by representatives from the FDA and other members of the proteomics community that addressed issues expected to be faced in the 510(k) submission process when the technologies are ready, including how to qualify a proteomic technology, specimen and population issues, statistical issues, and understanding the regulatory pathway to commercialization. The result was a highly engaging workshop with both groups—the FDA and the proteomics community—posing relevant questions to each other with the goal of understanding the challenges and needs of each side.

“We laid the groundwork for a good understanding of each other,” says Mansfield. However, the interaction will not end there. Invited participants are in the process of developing two sets of documents that will keep the conversation—and the momentum—going. First, the group of invited



Information on the NCI-FDA IOTF Molecular Diagnostics Workshop deliverables will be posted at <http://proteomics.cancer.gov> as it becomes available.

A Physician's Perspective

Protein Markers of Risk and Prognosis: A Role for Proteomics (continued from cover)



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better outcomes, hence the enthusiasm with which high-throughput methods for genomics, proteomics, and metabolomics have been greeted.

Gene expression profiles have been explored over the past decade, and their clinical application revealed moderately accurate prognostic value and for some available assays, the ability to predict response or benefit from specific systemic therapies. However, gene expression profiles are obtained from tumor material, so they do not lend themselves for prediction of risk (except for carriers of known adverse mutations, e.g., BRCA1/2 carriers), or for early diagnosis. Furthermore, while gene profiling provides an overview of the genome, it does not always reveal how genomic changes can lead to disease.

It was for this reason that experiments to identify specific protein profiles that can be identified in the bloodstream have been pursued with vigor in recent years. The

underlying hypothesis was that tumor cells, exhibiting a number of molecular genetic anomalies, would produce abnormal types or quantities of proteins, that these proteins could be identified in biological fluids *in vivo*, and that they would lead to the identification of subjects at risk and could also be used to effect diagnosis of breast cancer at an earlier time than currently available diagnostics would permit. Furthermore, such markers might enhance the diagnostic accuracy of mammography and sonography and might serve to enrich populations of healthy subjects who would most benefit from systematic screening. When this hypothesis first surfaced, the available technology was inadequate to test it.

Despite improvements in technology over the past few years, there remains a general lack of understanding of the reproducibility and sensitivity of various discovery proteomics platforms for the detection of real differences between samples. Lack of knowledge has fueled skepticism in the scientific and medical communities about the capabilities of proteomics to be able to deliver. Clearly, there are a multitude of analytical and preanalytical variables that pose significant challenges

to the translation of proteomic discoveries into clinical applications. The best way forward to developing this knowledge is through highly collaborative and integrated consortia of expert proteomic groups such as those formed through the NCI's CPTAC program. Properly designed inter-laboratory studies applied to relevant, carefully annotated biological samples, with the results analyzed with appropriate informatics and biostatistics will be essential to forming a clear understanding of the capabilities and limitations of proteomic technologies.

We must combine the necessary knowledge, expertise, and technology to develop these novel markers; however, the challenges involved in this process are daunting. In addition to conceptual and technological progress, our methodology must be flawless to identify and validate markers and to determine in prospective trials their clinical value and contribution to the management of diagnosis, treatment, and prevention of breast cancer. Addressing and reducing all layers of variability at every step of the biomarker pipeline through multidisciplinary approaches will be vital to realizing the promise of proteomics. ■

Honors

Dr. Hortobagyi's research includes combination chemotherapy regimens, presurgical chemotherapy, and targeted therapies for all stages of breast cancer. He has contributed more than 800 articles to scientific journals, authored and co-authored 13 books, and contributed over 130 chapters to textbooks. For his efforts in breast cancer research, Dr. Hortobagyi has received worldwide honors. In 2001, President Jacques Chirac named him Chevalier of the Order of la Legion d'Honneur de France. In 2003, Dr. Hortobagyi received the Glen Robbins Award in Breast Cancer Research from the New York Cancer Society and the Metropolitan Breast Cancer Group, and the Bristol-Myers Squibb 2003 Horizon Scientific Award. The Mexican Society of Oncology named him the 2005 World Leader in Oncology. Dr. Hortobagyi was elected President of the American Society of Clinical Oncology (ASCO) for the 2006–2007 term.

Lack of Metrics and Standards in Proteomic Discovery Technologies Hinders Innovative Research for Rare Diseases



Jeffrey Kaufman

The personal experiences of Marnie Kaufman and her husband Jeff with adenoid cystic carcinoma (ACC) gave rise to the Adenoid Cystic Carcinoma Research Foundation (ACCRF). Mrs. Kaufman is a survivor of ACC—a rare, slow-growing cancer of the head and neck that typically originates in the salivary glands. Although the removal of her parotid gland and a course of radiation treatment sent her cancer into remission, the slow and persistent growth of ACC necessitates regular screenings for metastasis.

Dismayed by a lack of ongoing research in ACC, the Kaufmans decided to battle the disease on another front. In December 2005, they founded the ACCRF. Mr. Kaufman would eventually leave his role as a senior portfolio manager with Putnam Investors to take on the full-time job of Executive Director of the ACCRF.

The mission of the ACCRF moves away from a traditional advocacy focus on patient support and education; the Foundation concentrates instead on coordinating ongoing research efforts to accelerate improvements in cancer treatment and the discovery of a cure. The approach of the ACCRF is simple:

“CPTC is providing a valuable service in addressing the challenge of validating the output of proteomics research.”

advance discovery by identifying scientists and institutions working on the best research platforms and approach them with proposals for research partnerships. In doing so, the ACCRF seeks to establish a virtual network of ACC-focused researchers and clinicians to share resources and research findings.

During its short history, the ACCRF has developed a broad portfolio of research investments based on a wide array of platforms. Partnerships with the Sanger Institute, Göteborg University in Sweden, Harvard Medical School, and Johns Hopkins University have researchers developing a central biobank of ACC specimens, exploring gene mutations associated with ACC, and identifying gene targets through RNA interference techniques.

Despite the innovative and cutting-edge nature of the research funded by the ACCRF, its scientific advisory board has expressed hesitance in supporting proteomics-based research. “Due to concerns about the ability to replicate data collected through proteomics research, our organization has elected to focus our research investments in other areas,” says Mr. Kaufman.

The ACCRF is not alone in recognizing a lack of standards in proteomics research methods. The NCI attributes the vast discrepancy between the number of cancer protein biomarkers that have been

described in scientific literature to date—over 1,200—and the surprisingly few that have transitioned into clinical applications to a lack of standardized procedures.

While ACCRF has not formally partnered with CPTC thus far, they are very encouraged by the work that the CPTC researchers are doing. “CPTC is providing a valuable service in addressing the challenge of validating the output of proteomics research,” Mr. Kaufman states. “I am confident that the work of CPTC will have an important impact on the future of proteomics research initiatives of the ACCRF.” ■

“Due to concerns about the ability to replicate data collected through proteomics research, our organization has elected to focus our research investments in other areas.”

The Patient as Stakeholder: CPTC Engagement with Patient Advocates



Elizabeth Neilson

The ultimate goal of the CPTC initiative is to advance protein biomarkers 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. While optimizing clinical proteomic technologies is crucial to this goal, CPTC recognizes that their work cannot be completed without considering another perspective—the patients eagerly awaiting these clinical breakthroughs.

To gain insight into the patient perspective, CPTC established a connection with NCI's Consumer Advocates in Research and Related Activities (CARRA) organization. Since 2007, CARRA advocates have played an increasingly vital role in developing and executing the CPTC mission and objectives.

CARRA advocates offer a rich perspective on the experience of a cancer patient. Volunteers with the organization have backgrounds as cancer survivors, caregivers, or they have at least two years of involvement in cancer-related activities. Additionally, they must also volunteer with a cancer advocacy or support organization. "The volunteers' personal connections with cancer, combined with exposure to others' experiences with the disease through their volunteer activities, ensures that CARRA members are well

"By responding to the feedback provided during our consumer testing, CPTC was able to produce an end product that clearly communicates the potential of proteomics research to patients."

equipped to represent the needs of the broader cancer community," says Elizabeth Neilson, an Advocacy Relations Manager in NCI's Office of Advocacy Relations.

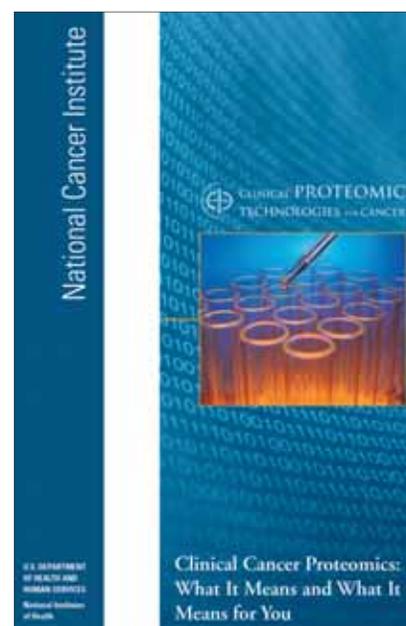
The brochure, *Clinical Cancer Proteomics: What It Means and What It Means for You*, provides a tangible example of the two-way information link between CPTC and CARRA. The five-page brochure is a means to communicate the complexities of proteomics research to the general public. While CPTC was responsible for the development of the brochure content, CARRA provided valuable feedback from advocates that impacted the final product.

By "testing" the brochure with cancer survivors and caregivers with a wide range of backgrounds—from attorneys, to business owners, to college professors—CARRA discovered that an initial draft of the brochure was too technical for the general public. "By responding to the feedback provided during our consumer testing, CPTC was able to produce an end product that clearly communicates the potential of proteomics research to patients," Ms. Neilson comments. "The brochure also provides a much-needed resource for the [CPTC] leadership and researchers to explain their research to the general public."

CPTC and CARRA continue to facilitate communication between the research and the patient. A webinar designed to educate patient advocates about proteomics research was conducted on March 19, (see *Industry News*, page 8) and a targeted research effort with advocates involved

with NCI-funded Specialized Program of Research Excellence (SPORE) programs and Cooperative Groups is in the pipeline to identify gaps in the understanding of proteomics research.

The partnership between CPTC and CARRA is a truly symbiotic relationship. Patients and advocates are informed about research in proteomics-based technologies with the potential to improve detection and treatment of cancer, and this newly informed group ultimately helps accelerate the adoption of these technologies as they become clinically available. Meanwhile, researchers and clinicians have a constant reminder of the patients that their work will impact. As this information sharing continues, the collaboration between CPTC and CARRA strengthens, and a better outcome for patients comes within reach. ■



Researcher Spotlight: Daniel Liebler, Ph.D.

Analyzing the Subtleties of Cancer-Relevant “Proteotypes”



Daniel Liebler, Ph.D.

Proteins are involved in almost all biological activities, including disease, and researchers are trying to identify proteins that can be used as biomarkers to better detect and treat cancer. The proteome—the collection of proteins in a cell or tissue—provides a rich source of biological information for these challenging studies.

Daniel Liebler, Ph.D., of Vanderbilt University, and current Chair of the CPTAC Program Coordinating Committee, is trying to compare proteomes between cancer-relevant tissues to identify biomarkers. “The term we are using to represent the proteomic differences [between tissues] is proteotypes, which is analogous to the term genotype,” explains Liebler, who introduced this concept during a presentation at the NIH on February 6, 2009 as part of the Protein Interest Group seminar series.

“Shotgun proteomics” is the most powerful platform that researchers use for analyzing complex proteomes. Analogous to the shotgun genome sequencing strategy that was used to sequence the human genome, proteins are “cut up” into little pieces called peptides, data is collected on the peptides using analytical

platforms, and then computers put the pieces back together to deduce what proteins are present.

Although powerful, variable performance of this approach can prevent detection of very subtle differences between proteomes. To overcome this barrier, Liebler and colleagues developed and implemented a new analytical platform for shotgun proteomics that they are currently applying to colon cancer samples.

“A 2mg piece of tissues gives us approximately 4,000 protein identifications. If we compare [the proteotypes] of a normal colon tissue and a large adenoma, the difference between these data sets is in the neighborhood of 150 proteins,” explains Liebler, who pointed out that cancer and normal tissue contain two very different proteotypes.

Can we compare proteotypes that contain much more subtle differences? For example, how many proteins will differ between two stage 2 colon cancers, one of which is likely to recur as a more aggressive disease in a few years after surgery and the other, which is likely to never recur? “What is the difference between these much more subtle phenotypes? They’re both cancers. They both look the same to the pathologist, and in fact, there aren’t any good markers that allow us to predict which tumor’s going to be the aggressive recurring disease,” explains Liebler.

To determine if their platform is sensitive enough to detect such subtle differences, Liebler conducted proof of concept studies on cell lines because they are very well characterized. They analyzed the proteomes from a collection of colon cancer cell lines that differ only

in expression of DNA mismatch repair genes. They found that although the proteomes are essentially identical, the DNA mismatch repair-deficient cell lines differ in the expression of a number of proteins whose genes are known to be affected by this pathway. Thus, these proteotypes reflect known biology.

Following the success of these proof of concept studies, Liebler and colleagues are now using their shotgun proteomics platform to analyze tissues retrospectively from patients with stage 2 colon cancers, with goal of characterizing distinct proteotypes for colon cancer recurrence. If successful, their work could help pave the way for the next generation of cancer diagnostic testing—proteotyping.

In December 2008, Dr. Liebler was elected as a fellow of the American Association for the Advancement of Science (AAAS). ■

“The term we are using to represent the proteomic differences [between tissues] is proteotypes, which is analogous to the term genotype.”

Researcher Spotlight: Richard Smith, Ph.D.

Pushing the Limits of Protein Biomarker Candidate Detection



Richard Smith, Ph.D.

A biomarker is a molecule, such as a protein, that is present in the body's tissues or fluids and can alert doctors to disease. Finding valid biomarkers is of high interest, for example, for the early detection and more effective treatment of cancer. It is anticipated that cancer cells "leak" proteins into bodily fluids, suggesting that clinicians can potentially detect protein biomarkers with a simple blood or urine test. However, discovering these biomarkers is not so simple.

Proteins exist in a wide range of concentrations in human plasma, spanning several orders of magnitude, and the proteins of interest—the ones most likely to be the telltale signs of cancer—are expected to be present in extremely tiny quantities. Identifying and measuring these dilute proteins has proven to be a significant challenge using current technologies.

To address this problem, Richard Smith, Ph.D., Director of the NIH Research Resource for Integrative Proteomics at the Pacific Northwest National Laboratory, is developing a significantly more sensitive and robust cancer biomarker assessment platform for the analysis of human blood plasma. This platform,

which is being developed through CPTC's Advanced Proteomic Platforms and Computational Sciences program, aims to make biomarker discovery and the subsequent follow up (verification studies) much more effective.

"We've developed a new platform that's based on a combination of ion mobility separations that follow fast liquid chromatography separations and ultra-fast mass spectrometry," says Smith. In the past year alone, Smith and his team have shown that this platform has the capability to expand the dynamic range of measurements significantly so that low abundance proteins—at least one order of magnitude lower in abundance than can be detected in plasma using current technologies—can be detected. And do so faster.

"This new technology opens up a large number of potential biomarkers that have previously been beyond the range of what we can do," says Smith. There is also good indication that they can potentially add another order of magnitude onto their current detection levels, which would significantly increase sensitivity. Three patents have been received for parts of this new platform's technology.

Efforts in biomarker discovery generally involve identifying many proteins in a very limited number of samples followed by verification studies in a much larger number of samples, using more targeted and sensitive measurements as a means to whittle down what is often a large set of candidates prior to clinical validation. This platform will allow researchers to take many more protein measurements during the initial discovery phase, and it has the potential to help find which candidates can be useful biomarkers for cancer detection. By effectively collapsing

the discovery and verification phases due to its higher measurement throughput and sensitivity, this technology may eliminate the need for, or greatly shorten, that second step.

"With the success of the platform and its utilization in biomarker discovery, the biomarker discovery process will be faster and much more effective," explains Smith. "What we're trying to do is make a considerable leap in the performance of measurement technology so as to make biomarker discovery both faster and more effective." ■

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Industry News

Molecular & Cellular Proteomics Introduces New Guidelines for Clinical Proteomics Manuscripts

In keeping with the tradition that it established when instituting standards for articles reporting protein identifications,¹ *Molecular & Cellular Proteomics (MCP)*, published by the American Society for Biochemistry and Molecular Biology, has now developed guidelines for manuscripts that report clinically relevant proteomic studies.² The guidelines were initially drafted at a meeting that was held in Copenhagen in April of 2008 with the participation of about two dozen stakeholders covering various areas of expertise, such as pathology, biobanking, medical law and ethics, statistics, various proteomic technologies, as well as different clinical areas. Following a period of public consultation, the guidelines were duly edited and adopted in January of this year. The guidelines describe information that is required before *MCP* will consider any germane submission further as well as discretionary information that, if available, will be helpful to reviewers and will add to the value of the reported data. The editors and staff of *MCP* view these guidelines as an essential step in the process of ensuring that the rapidly developing area of clinical proteomics advances in a productive and effective fashion. The Guidelines may be viewed at www.mcponline.org.

¹ R. A. Bradshaw, A. L. Burlingame, S. Carr, and R. Aebersold (2006) Reporting Protein Identification Data: The Next Generation of Guidelines. *Mol. Cell. Proteomics*, 5: 787 - 788.

² J. E. Celis, S. A. Carr, and R. A. Bradshaw (2008) New Guidelines for Clinical Proteomics Manuscripts. *Mol. Cell. Proteomics*.

hPDQ: A Near-Term Practical Step towards a Large-Scale Human Proteome Project

A Human Proteome Project (HPP), a natural successor to the Human Genome Project, will one day bring enormous benefit to patients in the form of personalized medicine. Although scientific objectives and technical merits to such an endeavor remain unclear, a group of researchers involving academia and industry have proposed an alternative, tactical approach for providing a more basic map of the human proteome. Instead of mapping every human protein, the Human Proteome Detection and Quantitation (hPDQ) initiative takes a targeted approach that would enable researchers to measure defined collections of human proteins in biological samples with high sensitivity and absolute specificity. A two-year pilot would seek to target 2,000 human proteins that have biomarker potential.¹ This would be followed by an additional 18,500 proteins over a five year period. This initiative, which can be thought of as an incremental first step towards a massive, large-scale effort, could be just what HPP will need to get off the ground and running.

¹ N. L. Anderson, N. G. Anderson, T.W. Pearson, C. H. Borchers, A. G. Paulovich, S. D. Patterson, M. Gillette, R. Aebersold, and S. A. Carr (2009) A Human Proteome Detection and Quantitation Project: hPDQ. *Mol. Cell. Proteomics*, Jan 7 [Epub ahead of print]

Promise and Reality of Proteomics Webinar

The NCI Office of Advocacy Relations hosted a webinar on March 19, 2009 on the role of protein science in the early detection of cancer as part of the Understanding NCI: Toll-Free Teleconference Series. Dr. Rodriguez and other speakers discussed the challenges facing clinical proteomics and the innovative ways that NCI's CPTC initiative aims to develop new, more refined, efficient, and reliable biomarker discovery and verification pipelines. This webinar can be found at: <http://proteomics.cancer.gov/library/webinars.asp>

Speakers include:

- Henry Rodriguez, Ph.D., M.B.A., Director, Clinical Proteomic Technologies for Cancer, NCI Center of Strategic Scientific Initiatives
- Amanda G. Paulovich, M.D., Ph.D., Oncologist and Cancer Geneticist, Director, Early Detection Initiative, Fred Hutchinson Cancer Research Center
- Elda Railey, Co-Founder of Research Advocacy Network

Podcast Series

"The Promise of Proteomics for Personalized Medicine" is the first of a three part podcast series, made available on March 20, 2009, developed to provide listeners with information about research advances being made in proteomics. This podcast can be found at: <http://proteomics.cancer.gov/library/podcasts.asp>.



CLINICAL PROTEOMIC
TECHNOLOGIES FOR CANCER

Advancing Protein Science for Personalized Medicine

Upcoming Events

May 12-13, 2009

Data Release Workshop

Organized by: Genome Canada

Ottawa, Canada

October 5-7, 2009

Clinical Proteomic Technologies for Cancer

3rd Annual Meeting Hyatt Regency Bethesda

Bethesda, MD

For a full list of upcoming events, visit

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

We are deeply saddened to hear about the passing of our colleague, Dr. Katheryn Resing, from the University of Colorado at Boulder. We extend our heartfelt condolences to her family, friends, and colleagues during this difficult time.

Contact Information

For more information about the CTPC, please visit

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The NCI Clinical Proteomic Technologies for Cancer initiative seeks to foster the building of an integrated foundation of proteomic technologies, data, reagents and reference materials, and analysis systems to systematically advance the application of protein science to accelerate discovery and clinical research in cancer.



Reagents Data Portal

<http://antibodies.cancer.gov>

<http://dshb.biology.uiowa.edu>

Newly Released Antigens and Antibodies

| Antigen | Antibody |
|--|---|
| Aldo keto reductase Family 1 Member B1 | CPTC-AKR1B1-1 CPTC-AKR1B1-2 CPTC-AKR1B1-3 |
| Annexin A1 | CPTC-ANXA1-1 CPTC-ANXA1-2 CPTC-ANXA1-3 |
| Chromogranin A | CPTC-CHGA-1 CPTC-CHGA-2 CPTC-CHGA-3 |
| Crystallin Alpha B | CPTC-CRYAB-1 CPTC-CRYAB-2 CPTC-CRYAB-3 |
| Ezrin (p 81) | CPTC-Ezrin-1 |
| Gelsolin | CPTC-Gelsolin-1 |
| Glutamate Cysteine Ligase Regulatory Subunit | CPTC-GCLM-1 CPTC-GCLM-2 CPTC-GCLM-3 |
| Glutathione S Transferase M1 | CPTC-M1-1 CPTC-M1-2 CPTC-M1-3 CPTC-M1-4 |
| Glutathione S Transferase M2 | CPTC-M2-1 CPTC-M2-2 CPTC-M2-3 |
| Interleukin 18 | CPTC-IL18-1 CPTC-IL18-3 |
| Lactoglutathione Lyase | CPTC-GLO-1 CPTC-GLO-2 CPTC-GLO-3 |
| Ornithine Decarboxylase 1 | CPTC-ODC1-1 CPTC-ODC1-2 CPTC-ODC1-3 |
| Peroxiredoxin 4 | CPTC-PRDX4-1 CPTC-PRDX4-2 CPTC-PRDX4-3 |
| Squamous Cell Carcinoma Antigen 1 | CPTC-SERPINB3-1 CPTC-SERPINB3-2 CPTC-SERPINB3-3 |