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The Proteomics of Networks and Pathways: A Movie Is Worth A Thousand Pictures

Douglas M. Sheeley*

This special issue of *Molecular and Cellular Proteomics* highlights some of the science that has come out of the National Technology Centers for Networks and Pathways (TCNP)[1] program, supported by the National Institutes of Health Common Fund. That program, which has drawn to a close after a planned 10-year run, was a response to the perceived need for greater emphasis on developing and using proteomics to understand the spatial and temporal dynamics of protein interactions. Proteomics was not adding as much as it could to our understanding of how systems change.

Proteomics technologies have been limited in their ability to reliably, let alone quantitatively, capture changing protein interactions in time and space. Contextualizing proteomic data by integrating it with information from real-time imaging, biosensors, and so on is also a real challenge. The limitations of proteomics technologies have often forced investigators to treat dynamic systems artificially as if they were static. As with early photography, our approaches to proteomics often impose long exposure times on the "subjects" (the systems being studied). The "images" captured are vague and broadly defined, such as "normal *versus* diseased," "the yeast interactome," or "the nuclear pore complex." Inadequate tools can make us blind to the dynamics of biological systems, at least from a proteomics perspective. The result is that transient interactions or rapid changes in protein activity, location, or post-translational modification are just a blur—like a bird flying through the frame of a carefully composed long-exposure photograph.

TCNP tried to address this challenge by creating technologies to reveal the ever-changing nature of protein interactions, modifications, translocation, expression, and activity, and to do so at very high temporal, spatial, and quantitative resolution. Complementary strategies—sometimes building on, sometimes independent of those used in conventional proteomics—help improve our ability to focus on dynamic processes, allowing researchers to break out of that artificially static view of complex systems.

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[1] The abbreviation used is: TCNP, the National Technology Centers for Networks and Pathways.

The TCNP Program—The TCNP program was a trans-NIH initiative developed and administered by a team of program officers from several NIH institutes and centers. In phase I of the program (fiscal years 2004–2008), five TCNP locations were supported with awards of $12 million to $17 million over 5 years. After a midcourse review of the program in 2008, an open competition was held in 2009 to support three centers for an additional 5 years (phase II, fiscal years 2009–2013). The phase II centers awarded were all among the original five from phase I.

The program funded multidisciplinary research centers that worked together as a consortium with the common goal of creating new technologies to study the proteomics of dynamic systems at the highest possible level of quantitative, spatial, and temporal resolution. When they were started, these centers were very unusual among NIH-supported proteomics programs because they focused on both protein interaction and quantitation, and they had a multidisciplinary focus that included imaging, probe development, molecular biology, and modeling but deemphasized mass spectrometry. An important factor allowing the program to do that was the substantial investment that other NIH programs continued to make in advancing mass spectrometric methods for proteomics.

The articles that follow showcase a few of the most recent accomplishments of the scientists whose work has been enabled by the TCNP program. One thing that should be obvious from these accounts is the complementary relationship between technological advances and the biomedical research they enable. Throughout the decade-long program, the centers collaborated with biomedical researchers who understood that their work would benefit from early access to emerging technologies. In turn, the centers benefited from access to projects that could serve as a proving ground. Those iterative interactions between technological development and biomedical applications served the program well. There is still a great deal of work to be done in this area, but we are in a far better position today than we were 10 years ago.

A Legacy of Resources—Although TCNP funds principally supported technological innovation, the centers have also been a resource for the community, committing substantial resources to collaboration with and training of biomedical researchers. The centers developed a broad range of re-

agents, vectors, cell lines, methods, and technologies that are now freely available (see below).

Scientists in the TCNP program have shared tools and expertise with hundreds of researchers, providing courses, online resources, and hands-on training for non-specialist biomedical researchers. In many respects, the center investigators continue this work today and continue to assist researchers who need access to the tools and expertise they have to offer. These tools will continue to be available as support for this work transitions to other NIH programs, providing important insights into the networks and pathways that are important in human health and disease.

For more information on the TCNP program and the available resources developed in the program, go to http://commonfund.nih.gov/bbpn/index.

* To whom correspondence should be addressed: Douglas M. Sheeley, Sc.D., Division of Biomedical Technology, Bioinformatics, and Computational Biology, National Institute of General Medical Sciences, National Institutes of Health, 45 Center Drive, Bethesda, MD 20892. Tel.: 301-451-6446; E-mail: dms@nih.gov.