proteomics

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From Physics to Proteins

Armed with a PhD in physics and a desire to apply his technology savvy, Alexey Nesvizhskii is shaping a career around seeking out the more interesting questions in science. This drive led him to bring his expertise to proteomics, specifically in the development of computational tools to parse out the seemingly endless stream of data generated by mass spectrometry-based technologies.

"This is a really active field," he says, "and when you have an active field [in which] people are developing new technologies, new chemistries, new ways of generating data — they end up with data and no really good way to analyze it. That's where I come in."

Title: ***Assistant Professor of Pathology, University of Michigan***

Education: ***PhD, Physics, University of Washington, 2001***

Recommended by: ***Phil Andrews, Steven Carr***

Nesvizhskii dove into this proteomic imbroglio first as a postdoc and later as a research scientist in Ruedi Aebersold's lab at the Institute of Systems Biology. There, he worked to develop algorithms and computational tools for processing and validating proteomic data, as well as for mining and integrating information derived from proteomics, genomics, and metabolomics. He's continued to extend these approaches at his current post in the University of Michigan's pathology department. "Probably most applications are going to be disease-related," he says, "but the methods can be applied in general to proteomic data generated from model or human systems."

In his current work, Nesvizhskii says that identifying post-translational modifications from mass spec-based data is an increasingly salient problem, especially considering his new clinical post and the relevance of phosphorylation and glycosylation to cancer. His aim instead is "to go beyond this typical proteomics-based approach, where you collect data and compare it by searching across databases to identify peptides and proteins."

Looking ahead

Nesvizhskii sees the field moving toward more targeted analyses, by which researchers may evaluate data they've accumulated to seek out interesting trends that will dictate strategies taken at the experimental level. He notes that earlier researchers were more interested in exploring the proteome and seeing what could be identified using mass spec. "In the last five years, we've realized that there are a lot of challenges in terms of the dynamic range," and that getting down to the level of biologically or disease-relevant proteins is the current challenge.

Publications of note

Nesvizhskii, along with co-investigators at ISB, pioneered a method designed to increase the amount of information that can be extracted from MS/MS datasets. The method picks up spectra where conventional sequence database searching falls short, with the result that iterative searches can pave the way to new insights drawn from existing datasets. The paper, entitled "Dynamic spectrum assessment and iterative computational analysis of shotgun proteomic data," published in *Cellular Proteomics* earlier this year.

Last year, Nesvizhskii co-authored a paper with Ruedi Aebersold reviewing the difficulties of interpreting shotgun proteomic data. This kind of data is "peptide-centric," the authors wrote in *Molecular and Cellular Proteomics*, leading to problems in determining the true nature of proteins in a sample. Aebersold and Nesvizhskii also touched on the state of protein sequence databases, and the need for a common computational infrastructure to integrate proteomic and transcriptional data.

How to succeed in science

"If you're a computational scientist like me, the key is to be really interdisciplinary, to know as much as you can about biology so you can speak the same language [as biologists], and, at the same time, to know as much as you can about technology so that you can suggest ways to design experiments," Nesvizhskii says. *— JC*