

Government and Society

HUPO's Human Proteome Project: the next big thing?

In what is being described as the human genome project for proteomics, HUPO has officially launched an ambitious global initiative called the Human Proteome Project. John Bergeron, who is at McGill University (Canada) and is a past president of HUPO, coordinated discussions on the project at this year's Fourth International Barbados Proteomics Conference, held January 4–11. Instead of soaking up rays, conference participants hammered out a preliminary plan of action to characterize one protein for every gene in the human genome.

“What we guarantee at the end of this is that you will know the representative proteins of all 21,000 genes, where the proteins are located, which cells are expressing them, and how frequently they're seen around the world,” says Bergeron. The proposed gene-centric initiative involves subprojects centered around three major proteomics methods: MS, antibodies, and protein–protein interactions (PPIs). Two posttranslational modifications (glycosylation and phosphorylation) also will be studied.

In the pilot phase, researchers will analyze the proteins expressed by genes on chromosome 21, which is the smallest chromosome in humans. Bergeron explains that, interestingly, genomics scientists still do not agree on the number of protein-coding genes that exist on this chromosome, so the Human Proteome Project plans to settle the debate. After work is completed on chromosome 21, the group will expand its efforts to the rest of the human proteome.

To tie together the results from the various subprojects, participants plan to develop an integrative bioinformatics platform. Currently, separate databases house information on MS results, antibodies, and PPIs, but to answer biological or clinical questions, investigators must search each resource, says Lennart Martens at the European Bioinformatics Institute. With an integrated bioinformatics solution, “the user can do this kind of query, and a software layer will actually go to the individual resources, request the relevant information, and then combine the data across all of these to come up with a reasonable answer,” he explains.

But is the technology really ready for such a large-scale project? “Proteomics is ready for prime time,” answers Bill Hancock, who is at Northeastern University and is president of U.S. HUPO. “Not everything has to be perfect, but if you're pooling 4 million spectra, then the ones in which there was a bad instrument setting or whatever are just going to drop out.” To demonstrate the readiness of the technology, Bergeron points to the HUPO protein standards developed by Invitrogen that were tested in 24 labs last year. Initially, only 6 of the labs identified the correct 20 proteins in the standard. However, when members of Bergeron's team interviewed the researchers who came up with the wrong answers, they realized that simple errors, such as digestion problems and the use of the wrong database,

were to blame for the incorrect identifications. After correcting for the mistakes, all labs identified the proteins in the mixture. “You basically had no excuse for not getting 100% correct,” he says.

Similarly, Bergeron says that a re-examination of raw data from the HUPO Plasma Proteome Project (PPP) revealed that many scientists made simple mistakes that could be accounted for. “When you see the HUPO test-sample results and these results, you’re convinced that proteomics technology works,” he explains. In addition, Martens says that the technology already exists for the integration of bioinformatics resources; a coordinated effort and perhaps a little tweaking are all that is needed to provide the integrative base layer.

The Human Proteome Project is intended to complement, not compete with, the other, more focused HUPO initiatives, such as PPP. Bergeron says that members of those initiatives are welcome to join the new project.

The idea for a single HUPO project actually came from representatives of the European Commission (EC) during meetings in 2006 about the protein standards. The concept was mentioned at subsequent HUPO meetings, but it really gelled at this year’s Barbados gathering, which was organized with input from the EC. “The discussions were vibrant,” recalls Peipei Ping, who is at the David Geffen School of Medicine at the University of California Los Angeles. “People were trying to see how we could move this thing from just a dream into reality.” Since the Barbados meeting, Bergeron and Hancock have approached the U.S. National Institutes of Health (NIH) with details about the project. Hancock says that NIH representatives were interested in the endeavor, especially as a way to foster collaborations across the agency’s institutes and centers.

Bergeron has prepared a report for HUPO members to review. After they reach a consensus, HUPO representatives probably will hit the road again and have additional discussions with NIH to figure out how this global HUPO initiative will contribute to the health-based mandates of the agency, says Hancock. Also, Bergeron envisions that funding from many diverse sources, including the EC and NIH, will be necessary. The project is not restricted to HUPO members; anyone who is interested is welcome to join, he says.

—Katie Cottingham