

## The call of the human proteome

A Human Proteome Project has been proposed. To ensure that such a project will have a transformative impact on biology, its scope should be determined by wide and open discussion.

The Human Genome Project demonstrated the power of data-driven, large-scale 'omics' projects and revolutionized the way biology research is performed. A systematic project to characterize the protein products of the human genome in some ways seems like a natural extension. As proteomics technologies have rapidly progressed, the idea of a complementary proteome project has gained traction. As an initiative under the umbrella of the Human Proteome Organization (HUPO), an international organization whose mission is to foster proteomics research to better understand human disease, a group of researchers have now proposed an internationally coordinated, systematic Human Proteome Project (HPP) (*Mol. Cell. Proteomics* 9, 427–429, 2010).

The ambition of the HPP working group is certainly to be commended, and nearly everyone involved in proteomics would concur that it is time for the field to get more attention. Researchers generally agree that the resources resulting from the HPP, such as well validated affinity reagents and a dedicated portal to information about human proteins, would be very valuable for the broader biology community. However, whether a human proteome project will transform biology in the way that the Human Genome Project did, what the scope of such a project should be and what the right time to begin the project is are questions that need to be carefully scrutinized by the field.

Unlike the finite genome, the dynamic human proteome is almost impossible to define. The complexity is enormous. Whether a systematic project makes sense and whether it will result in faster progress and yield biological insights are important issues to discuss. Many within the proteomics field have questioned whether a systematic project with a large enough scope could ever be devised to truly understand the human proteome. They argue that traditional hypothesis-driven research is the proven way to address questions of biological and clinical interest. Such differences of opinion should be taken into account when refining the current HPP proposal. If the project is to be a success, the proposal must have strong community support.

As a definable endpoint to the HPP, the working group has proposed a gene-centric approach whereby at least one main protein product of each of the 20,300 predicted protein-coding genes will be characterized in terms of abundance, interaction partners and expression localization, serving as the backbone of a

human proteome 'encyclopedia'. However, many in the proteomics field believe that this targeted approach misses an opportunity for biological discovery. Mass spectrometry, slated to play a major role in the HPP, is well suited to a discovery-based approach, they argue, and this is where it can add real value. Deciphering the function of protein post-translational modifications in particular is an area where proteomics can make a unique impact, and many do not feel that this will be adequately addressed using the gene-centric strategy that the HPP working group advocates.

Whether the HPP should begin now, using current technology, has also been questioned. Mass spectrometry technology has certainly had a rocky past; in particular, the reproducibility of the technology has come under fire. In a Commentary on page 681, six leaders in the proteomics field come to the defense of mass spectrometry's reputation and argue that it has advanced to a stage where it is now ready to address biological questions about the human proteome (editorial note: the authors are not all affiliated with the HPP working group). They make a compelling case for the reproducibility of the technology, with the caveat that it must be appropriately applied and the limitations must be understood.

While it is time for the debate about the reproducibility of mass spectrometry to end, the technology is still in the midst of rapid development that will likely yield faster, more sensitive and cheaper instruments, as well as methods for greater multiplex analysis. The proteomics community should come to a consensus about whether it is premature at this time to begin a comprehensive human proteome profiling effort or whether, akin to the Human Genome Project, a large-scale project is needed to catalyze further technology development that will drop costs and time.

Though many questions remain about whether the HPP should be pursued at this time, and in its currently proposed form, it has had a positive impact in forcing people to think about what is needed to advance the proteomics field. Proteomics researchers will have an opportunity to discuss the HPP later this month in a dedicated session at the HUPO 9<sup>th</sup> Annual World Congress in Sydney. We hope they will seize this opportunity to tackle these questions and articulate a community-supported plan for the human proteome that will drive proteomics research forward for the benefit of all.