

Proteomics' framework for success?

As Europe is rolling out its seventh Framework Program for funding research with some emphasis on post-genomics, initiatives are burgeoning in the community to establish a comprehensive resource of protein-affinity reagents. Will funding priorities and community-based efforts meet?

Researchers need good antibodies, or more generally, good protein-affinity reagents. The unreliable quality of commercially available antibodies has long plagued research across many disciplines. In proteomics, the problem is even more acute because efficiently probing the proteome would require a comprehensive set of such reagents that is now sorely lacking. So, logically, it is the proteomics field that has spawned several initiatives aimed at systematically generating affinity reagents against portions of the human proteome. The most ambitious of these projects so far is ProteomeBinders, a new European consortium presented on page 13.

Hitherto ProteomeBinders has been funded, under the sixth European Framework Program, at a very small level, which purposely limits its activities to strategic project planning. But in January the European Union kicks off its seventh Framework Program, the principal instrument that Brussels will use to fund scientific research for the next seven years—and the most ambitious funding program yet for research in Europe. Within that context, the European Union has a unique opportunity to positively impact research in many fields, in a concrete and substantial way, by providing generous and sustained support to ProteomeBinders.

Turning this project into a full-blown, large-scale reagent-generation program can drive the field and incite additional efforts in and outside Europe, but there will be many challenges. The venture of generating reagents to probe the proteome is often compared, in scale and nature, to the sequencing of the human genome, but in fact, it is substantially more complex. The main organizational issues it will have to face, though similar to those of the Human Genome Project, will be more complicated to solve. In particular, one can expect difficulties in balancing competition and collaboration, as well as in integrating the private and public sectors in the same effort.

Collaboration versus competition

The seventh Framework Program has put an extraordinary emphasis on 'Cooperation', one of the four pillars of the program that alone will receive more than 60% of the funds. This funding structure is meant to promote collaboration at the trans-national level. In this context, the multicenter core of ProteomeBinders is an ideal setup.

But in reality, the task of generating reagents against the proteome involves many choices—between types of reagents, selection and production technologies as well as possible ways of prioritizing the task. These diverse avenues will make collaboration difficult from the onset, even within a consortium. One can expect a fair amount of competition as well as some duplication of efforts within ProteomeBinders, and between its activities and those of other ongoing programs such as, for example, the US National Cancer Institute (NCI) Clinical Proteomics Initiative.

This said, the human genome venture has proven the motivating power of competition between the public and private sector, but also among academic centers. As for duplication, it may be beneficial to some extent because different types of reagents will serve different applications, and multiple reagents against the same protein will validate each other.

However, it was a particularly efficient characteristic of the Human Genome Project that once the goal was in sight, the public sector participants transitioned relatively naturally from a competing to a complementing scheme, allowing for well-organized sharing of the workload. Such transition may not be as natural for a more complex project, and efforts could become so scattered that they would not be easily coordinated or perhaps not in time to retain the interest of funding bodies.

What is needed is an overarching coordination structure to evaluate progress in each area and nudge the transition to widespread collaboration in a timely way. The Human Proteome Organization (HUPO), via its Human Antibody Initiative, has already been acting as a loose coordinator of activities that are burgeoning at the national level in Europe and in the United States. It has done so mainly by bringing together, during workshops, initiatives such as ProteomeBinders, the NCI Clinical Proteomics Initiative, the Human Protein Atlas under way in Sweden as well as projects at the UK Sanger center, and the US Argonne and Los Alamos National Laboratories.

This coordinating role should become increasingly important as the project advances. HUPO is well positioned to provide a forum for regular progress review against available funding. But scientists involved in these discussions will have to make increasingly

difficult choices and endorse the initiatives most likely to succeed. It will be crucial that individual scientists and funding bodies alike recognize these HUPO endorsements and adapt their priorities accordingly.

Integrating the public and private sectors

For all publicly funded initiatives that generate reagents or information, the public availability of the resulting resource is an important matter. But the head-to-head competition between private and public sector that has characterized the race for the human genome sequence is unlikely to be a viable scenario for the generation of proteome affinity reagents. The pre-existing model here is that antibodies are, in large part, commercial reagents. The commercial sector possesses the sort of production capabilities that will ultimately be needed, and given the potential market, it is likely that private players will also become increasingly involved in reagent development.

The position of ProteomeBinders on this issue is still poorly defined. The consortium has proposed an 'open-access' resource modeled on the American Tissue Culture Collection, which would provide reagents to users at cost and without restriction. But it does not seem realistic, or particularly cost-efficient, to build from scratch such a body that would be able to produce and sustain demand for thousands of reagents. The feasibility of outsourcing the reagents' production while still providing them to users at cost seems equally doubtful and somewhat in contradiction with the consortium's intention to honor intellectual property rights for new reagents and technology developers.

The view of funding agencies is similarly unclear. The seventh Framework Program will operate with public funds and as such

would likely promote open-access resources. But at the same time, the program puts a lot of emphasis on cooperation between public sector and industry, and on involving small and medium-sized enterprises in collaborative research and development projects. In doing so, the program is aligning itself with the so-called Lisbon strategy, a political statement in which the European Union pledged to use research and innovation to boost the economy, notably by promoting application of research in the private sector. Thus it appears unlikely that major European funding would go to a project excluding the private sector.

The real problem with commercially available antibodies is not as much their cost as their unreliable quality. What is really needed to remedy this problem is the implementation of quality standards. HUPO, during Human Antibody Initiative workshops, and ProteomeBinders (p. 13) have advocated the creation of reagent quality standards and certification programs. After reagent development, appropriate quality certification programs that could be applied to reagents regardless of where they are produced seems a better investment for public funds than production facilities. Here too, HUPO should have an important role in helping establish, endorse and implement quality standards.

Working out a satisfactory relationship between commercial and public sector may require some creativity but a scheme in which the resource is made available via commercial providers is not impossible if one can ensure reasonable pricing and high quality. Making trusted certification programs available upon users' request could drive a competition for quality in the private sector. Whatever agreement is reached, quality-control issues should be central to all publicly funded reagent initiatives.