

ProteomeBinders consortium makes big plans

The organizers of the ProteomeBinders consortium have their work cut out for them. According to Mike Taussig, who is at the Babraham Institute (BI) (U.K.) and is the coordinator of the project, participants plan to develop a resource infrastructure of binding reagents and tools for the study of the entire human proteome. He says that such a resource “would give us the opportunity to discover the functions of proteins which, at the moment, are unstudied” because of a lack of reagents.

Currently, the project is funded by the EU 6th Framework Programme as a 4-year Infrastructure Coordination Action to lay the groundwork and formulate a sound plan of attack. Funds for the hands-on bench work will be requested at the next EU call for proposals.

The consortium has its roots in discussions that began 5 years ago among scientists who were brought together by the European Science Foundation (ESF) program for functional genomics. Their mission was to predict which areas of genomics would be important in the future. Taussig credits Ulf Landegren, who is at the University of Uppsala (Sweden) and is now a member of ProteomeBinders, with recognizing the need for a comprehensive binder collection. Spurred on by these discussions, Taussig started making calls and found that a few small-scale European efforts were generating these reagents, but they weren't coordinated with one another. So he organized two ESF workshops on the topic and enlisted the participants to become members of a pan-European effort that eventually became known as the ProteomeBinders consortium. The project was officially launched in March 2006 as a consortium of 26 European labs and 2 U.S. labs. (U.S. investigators can attend meetings and help plan the group's activities, but they are not eligible to receive EU funds.)

One of the consortium's main goals is to organize efforts to produce a collection of reagents, such as antibodies, that can bind to proteins that comprise

the human proteome. Although many antibodies have been generated by academic and commercial laboratories over the years, most are directed against relatively few popular targets. Another wrinkle is that some antibodies may be useful for only certain types of applications. For example, an antibody may recognize the denatured form of a protein on a western blot but not the folded form present in a living cell. “I think tailoring the binder to the job will be a very important part of the

reagent base,” she says. Binders will be tested for performance and specificity.

In addition to producing the resource, the group will develop new binder-based tools for proteomics. Participants plan to create various assays, including high-throughput arrays. These techniques will be used in applications, such as biomarker detection. This activity, therefore, could lead to the development of new clinical diagnostics.

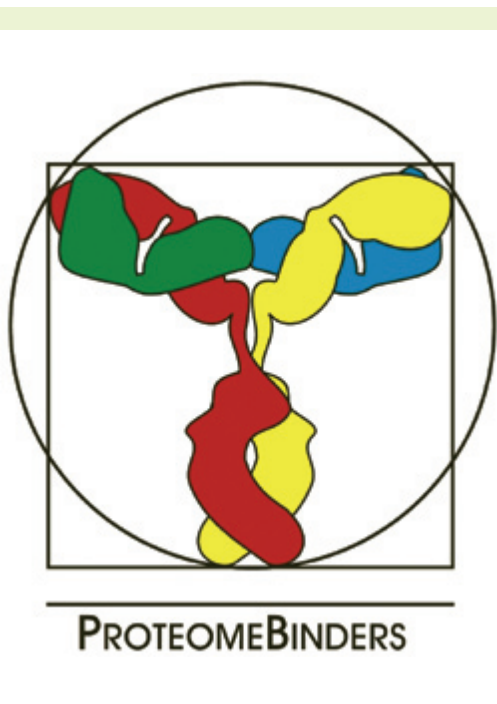
All of the reagents will be made available to researchers at cost, and data resulting from the project, including quality-control information, will be freely accessible in large databases that are being developed by the bioinformaticians in the group. These participants also have been working closely with the HUPO Proteomics Standards Initiative to create a binder ontology.

The creation of a proteome-wide binder resource itself will be a challenge, but before that can begin, ProteomeBinders members still have a lot to consider during the coordination stage. Plenty of details are still up for debate. For example, now that the researchers have decided to generate these binders, which protein targets will be first in line? The researchers haven't agreed on a strategy yet, but Taussig says two prominent views are being considered. “One view is that we should focus on defined protein families of interest, such as transcription factors and cell-signaling proteins, and systematically produce consistent

and complete sets of reagents for those. The other is to focus on those proteins for which there are no reagents, to make sure everything is covered,” he explains. Regardless of how the researchers eventually tackle the problem, Taussig says that up to 100,000 new reagents must be generated to cover the proteome, including splice variants and posttranslationally modified forms.

ProteomeBinders members are undaunted by this huge task, says Taussig. Participants are taking it one step at a time and are in it for the long haul. The project “will be a very long-term effort,” says Stoevesandt.

—Katie Cottingham



Bound to the proteome. Members of the ProteomeBinders consortium plan to assemble a collection of molecules that bind to the human proteome.

work,” says Taussig. But antibodies are only the beginning. The consortium also plans to investigate the production of other reagents, such as protein scaffolds, nucleic-acid-based aptamers, and small molecules. “The idea is to have a specific reagent, no matter what its nature is, for every target,” says Taussig.

Validation is an important part of the project, says Oda Stoevesandt, who is at BI and is the administrator for ProteomeBinders. She points out that such information is not always available for the binding reagents that are currently used by scientists. “We will define a set of quality-control methods that are consistently applied across the whole