Mapping the Human Proteome Using Antibodies

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A great need exists for the generation of protein-specific affinity reagents to explore the human proteome. With this background, the HUPO Antibody Initiative (HAI)\(^1\) was started in 2005 with the objective to promote the generation and use of well validated antibodies toward human proteins. The initiative is currently chaired by Mathias Uhlen with Michael Snyder (Yale University, New Haven, CT) and Peter Hudson (Commonwealth Scientific and Industrial Research Organisation (CSIRO), Parkville, Victoria, Australia) as co-chairs. Several workshops have since been held to coordinate efforts and funding in the area. At the end of 2005, the National Cancer Institute (NCI) of the National Institutes of Health organized a workshop in which the conclusion was that validated and well characterized affinity capture reagents (e.g. antibodies, aptamers, and affibodies) will play a key role in proteomics research platforms for the prevention, early detection, treatment, and monitoring of cancer (1). Recently (May 2007), the Protein Capture Tools proposal was selected by the National Institutes of Health Roadmap initiative for staged implementation (www.nihroadmap.nih.gov). Similarly a European Union-funded program, ProteomeBinder, started in 2006 with the aim to coordinate efforts in Europe involving more than 20 research groups from both the European Union and the United States (2).

The mission of HAI is to endorse the production of well characterized sets of renewable (preferably monoclonal) antibodies or other affinity reagents for various protein assays and to ultimately generate paired antibodies/affinity reagents for all human proteins produced as a sustainable resource. The paired antibodies should preferably be produced toward two separate and non-overlapping epitopes of the same protein target to facilitate the validation of specificity by allowing comparisons between the paired antibodies with regard to staining pattern across various analysis platforms. Paired antibodies also allow for coupled assays with high signal-to-noise ratios such as capture/detection (sandwich) assays and other assays with requirement for dual binding to increase specificity and sensitivity.

The presence of a multitude of protein isoforms, such as splice variants, combinatorial variants, post-translational modifications, specific proteolysis, and genetic variability (alleles), makes the human proteome space huge, and the initial ambition of a genome–wide antibody-based proteomics effort has therefore been suggested to be directed to the non-redundant proteome defined as a representative protein from every gene locus (3). The current estimate of the size of the non-redundant proteome is \(\sim 23,000\) proteins (Ensembl, www.ensembl.org), and at present more than 16,000 of those have been manually annotated by the Swiss-Prot/UniProt effort (www.uniprot.org).

The HUPO Antibody Initiative consists of two separate activities: 1) the development of a virtual antibody resource of validated antibodies and 2) a protein atlas for the expression and localization of human proteins in normal and disease tissues. The Antibody Resource database is aimed to produce a comprehensive catalogue of validated antibodies through a community-based effort. The objective is to create a format for submission of data on affinity reagents along with application-specific validation. The primary data from the quality assurance should preferably be submitted and made available through the database. This initiative depends on input from a large number of academic groups and commercial companies. A pilot version of the resource database will be presented at the fourth annual HAI workshop to be held in Seoul, Korea on Sunday October 7, 2007. The workshop will focus on the progress and time plans for the antibody portal.

The Human Protein Atlas program (www.proteinatlas.org) is aimed to provide a comprehensive and annotated database of high resolution images showing tissue profiles in normal and cancer tissues (4). Version 2.0 of this publicly available database was released at the 6th annual HUPO conference in Long Beach in 2006 doubling the number of proteins to more than 1300 human proteins with \(\sim 1.2\) million immunohistochemistry images. A new version (3.0) will be released October 8, 2007 at the 7th annual HUPO conference in Seoul, Korea, and the plan is to again double the content of the database and to release at least 2 million images representing more than 2500 human proteins. The short term objective of this effort is to generate data for \(\sim 8000\) proteins by the end of 2009, and the mission is to generate a draft version of the complete proteome by 2015, 10 years after the public release of the first version of the Protein Atlas portal.

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‡ The abbreviation used is: HAI, HUPO Antibody Initiative.

REFERENCES


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