Meeting report

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A report on the annual Association of Biomolecular Resource Facilities (ABRF) meeting, Austin, Texas, 9-12 March 2002.

This year's Association of Biomolecular Resource Facilities (ABRF) meeting, entitled "Biomolecular Technologies: Tools for Discovery in Proteomics and Genomics", emphasized the protein and DNA technologies that inspired the formation of the ABRF. Meeting abstracts and some presentation slides or posters are available through the ABRF website [http://www.abrf.org]. Some presentations are also submitted for publication in the ABRF journal, *Journal of Biomolecular Techniques*.

The plenary sessions emphasized the importance of technology development on scientific discovery, which is especially true for genomics and proteomics. Richard Wilson (Washington University School of Medicine, St. Louis, USA) summarized the development of techniques for physical mapping of the genome and discussed the importance of automating procedures for generating genome sequence information. He commented that the human genome sequence will be finished to coincide with the 50th anniversary of the discovery of the structure of DNA by Watson and Crick, in April 2003. He described his lab's collaboration with the lab of Eric Green (National Human Genome Research Institute, National Institutes of Health, Bethesda, USA) to analyze human chromosome 7, focusing on the *Pendrin* gene and the effect of its mutation on ear development. The gene is associated with 5-10% of cases of human hereditary deafness and also with enlargement of the thyroid (goiter) and encodes an anion transporter that, when mutated, is believed to damage (rupture) delicate ear structures. Pendrin knockout mice are deaf and a large portion of the progeny have an unusual phenotype of running in circles. Wilson also described his work on some large, highly repetitive (and therefore challenging) sequences on the human Y chromosome that may have biological significance for male fertility and sperm production.

Raymond Deshaies (Howard Hughes Medical Institute and California Institute of Technology, Pasadena, USA) described the use of mass spectrometry for dissecting the composition and function of protein networks. Focusing on how yeast chromosome replication complexes are regulated and integrated into various other processes, his laboratory has isolated complexes containing at least one tagged component and used multidimensional protein identification technology ('MUDPIT') to identify the proteins associated with the isolated complex. This technology applies a systematic approach to identifying interacting proteins: various purification steps are used to produce a plot of thousands of peptide peaks, each of which derives from a particular protein and can be partially sequenced by mass spectrometry. Once a protein is identified, its peptides can be 'ignored' in the plot, so that less abundant proteins are highlighted; the dynamic range of the experiment is thereby increased. MUDPIT technology has already successfully sampled proteins associated with the 26S proteasome and Deshaies has now applied it to the SKP1 protein complex that is involved in proteolysis, a more demanding application because the SKP1 complex is not as abundant and interacts with many proteins, each of which may be present in a different amount. This analysis identified proteins known to be in the complex, their possible partners, obvious contaminants and some possibly misidentified peptides. Deshaies stated that this successful 'proof of principle' experiment bodes well for continued employment opportunities for mass spectrometrists.

One unique aspect of the ABRF that is highlighted at the annual meeting is the work of the ABRF Research Groups. These groups conduct studies to assess the capabilities of core facilities and to provide materials to help member laboratories evaluate themselves. Information about each research group's study will be available at the ABRF website.

The Molecular Interactions Research Group was represented by David Myszka (University of Utah, Salt Lake City, USA), who described the group's study of a well-characterized enzyme-inhibitor interaction in terms of their assembly state (whether they form monomers, dimers, or higher-order complexes) thermodynamics and kinetics. Specifically, participants examined the interaction between carbonic anhydrase II and its substrate 4-carboxybenzene sulfonamide using analytical ultracentrifugation, isothermal titration calorimetry, and surface plasmon resonance, techniques that all examine non-covalent interactions between molecules. Essentially similar measurements were obtained using the three types of instrumentation. It was noted that immobilization of the enzyme on a biosensor surface did not alter its substrate-binding activity.

The Fragment Analysis Research Group compared laboratory protocols for multiplexing markers in a DNA fragment analysis application. Participants were given five fluorescently labeled primer pairs and two DNA template samples and were asked either to amplify all five markers in a single PCR reaction (multiplex PCR) or to assemble five separate reactions and pool them before loading into a single well of an electrophoresis gel. By performing a multiplex reaction, users save time and money**.** Doug Bintzler (University of Cincinnati, USA) presented the results gathered from 57 data submissions. The majority of the respondents chose to analyze the five samples by pre-PCR multiplexing, but a few used the individual reaction approach. The type of platform used to analyze the reactions contributed most to a respondent's success: capillary electrophoresis systems obtained the correct differences in length between alleles more frequently than slab gel systems.

Scott Buckel (Amgen, Thousand Oaks, USA) presented the Edman Sequence Research Group's study that challenged 72 participants to find the sequence of a protein with a heterogeneous amino terminus bound to a polyvinylidene fluoride (PVDF) membrane. Of the 31 participants who returned data for analysis, 9 correctly identified the 'difficult, but do-able' frayed protein as a flagellar assembly protein from *Salmonella typhimurium*.

David Arnott (Genetech, Inc., South San Francisco, USA) presented the results from the Proteomics Research Group's study, in which the group challenged participants to apply their favorite technique to identify proteins present in a 'simple' mixture. The samples were sent as tryptic digests to participating labs and contained proteins present in amounts ranging from 2 pM to 200 fM. Seven labs identified all proteins correctly; all of these used liquid chromatography and tandem mass spectrometry. The group reported that almost all respondents correctly identified the major protein (present at 2 pM); in contrast, in an earlier study, the majority of respondents incorrectly identified a protein species present at this same amount.

Finally, John Hawes (Indiana University School of Medicine, Indianapolis, USA) discussed the results of the DNA Sequencing Research Group's general survey of current DNA sequencing facilities. The group conducts this survey every other year to provide information about staffing, funding, chemistry or instrumentation in core DNA-sequencing facilities. Additionally, group member Tim Hunter (Vermont Cancer Center, Burlington, USA) discussed the preliminary results of their single-nucleotide polymorphism (SNP) study. Several DNA samples were mixed in a variety of ratios and sent to labs to determine the ratio(s) at which SNPs were detected. Study participation has been lower than expected, perhaps because participation required a significant financial and time investment. The group is continuing the study, and asks that more ABRF members participate to ensure that meaningful conclusions can be drawn from the data trends.

Overall, the meeting gave a useful overview of new and established techniques in biomolecular analysis. A highlight of the meeting was the ABRF Award presentation to John Bennett Fenn (Yale University, New Haven, USA) for his outstanding contributions to the field of electrospray ionization technology. Mark your calendars: ABRF 2003, "High Throughput Biology: Proteomics and Functional Genomics" will be held in Denver, Colorado, 10-13 February 2003.