Proteomics and networks

Different perspectives

General aspects of the Congress

The 19th IUBMB Congress was held in conjunction with the 2nd Annual Human Proteome Organisation (HUPO) Congress in Montreal, Canada, 8-11 October 2003. The original venue for the IUBMB Congress was to be Toronto, Canada, 20-24 July 2003, but that Congress was cancelled due to the SARS outbreak in that city in the first half of 2003.

The resultant HUPO-IUBMB 2003 Congress was an almost seamless merging of the two scientific programs. Credit is due to the committees of both international organisations, and the local Canadian Society of Biochemistry, Molecular & Cellular Biology, for the success of the meeting. Despite the circumstances of the short time to organise the revised program in Montreal, there was an appropriate mix between those topics focussing on proteomics and the broader themes of contemporary biochemistry and molecular biology. Given the natural overlap between these areas, it was certainly timely to have a strong focus on genomics and proteomics in the general biological and medical areas that are of interest to biochemists and biomolecular biologists.

The overall attendance was about 2000, somewhat less than anticipated. In addition to the disruptive effects of having the IUBMB Congress rescheduled, two factors were suggested to have reduced the number of registrants. First were the dates 8-11 October coinciding with the first teaching week of semester in North America. Second were the restrictions, in the light of the current increased security situation in the USA, on multiple re-entry to the USA by students and postdoctoral trainees on exchange visitor visas, who would normally have been expected to make up a substantial percentage of registrants at an IUBMB Congress.

Different perspectives

From the viewpoint of a protein chemist, the rescheduling of the IUBMB Congress was a fortuitous event, bringing it into conjunction with the HUPO Congress. From the perspective of a molecular or cellular biologist, the joint meeting enabled a close-up view of the developing technologies in proteomics that can potentially enrich our understanding of many biological issues. The IUBMB program had a more molecular flavour than our ComBio meeting in Melbourne, although there were still numerous examples in the former of applications in the cell biology area. Despite the absence of some speakers who could not make the transplanted meeting, the Congress was full of high-level science and spirited discussions. This was exemplified in the session on biological energy transduction - the three excellent speakers, concluding with Les Dutton’s simple knockout studies and elementary work on pH dependence of electron shifts, engaged in animated repartee that sparkled well after the session ended.

Proteomics and networks

The proteomics presentations integrated productively with the biochemistry and molecular biology, and this synergy permeated from the plenary talks through the symposia to the poster sessions. It is ambitious to single out individuals for excellence, but the session on global analyses of Annotation, Structure and Function brought together the themes of the meeting admirably; Michael Snyder’s synthesis of genome analysis, high-throughput cloning and expression, and functional (binding, enzyme activity) screening encapsulated the quality of this joint meeting.

The most crowded (non-plenary) session was on Proteomics: Past, Present and Future, presented by Samir Hanash, Chair of the Human Proteome Initiative Committee. This was followed by Denis Hochstrasser’s sweeping discourse on five dimensions of disease in which he showed the increasing importance of proteomics in clinical medicine.

There were numerous presentations devoted to development and applications of the latest technologies in protein analysis, from mass spectrometric identification of targets to high-throughput structural analysis. Application of proteomics in drug discovery and sorting of lead compounds, or as a routine tool for clinical diagnostics – even by mass spectrometry – were only two of the many exciting indicators of where proteomics can go, other than just attempting to describe all the proteins in a given biological sample. Several lunchtime workshops were organised by the commercial exhibitors and were well attended. A number of interacting committees presented their strategies and progress on efforts to standardise nomenclature, methods and databases in the rapidly expanding field of proteomics – an admirable initiative in these early years of the field’s development. A handy piece of reading matter to go with all these presentations was the Nature Insight supplement to Nature Biotechnology (13 March 2003) that contains a series of reviews on technical aspects of proteomics and its applications. All of these reviews were authored either by presenters at the HUPO-IUBMB Congress, or by scientists who have recently been to Australia and spoken at ComBio meetings.

Of course genomics plays a strong role alongside proteomics, and this was featured at the Congress in many presentations and the
ensuing discussion. Likewise, attempts are being made to describe cells fully in terms of genomics, proteomics and metabolomics. Increasingly, the language of "small world networks" is facilitating our understanding of the organisation of the plethora of individual elements in the highly complex collections of data generated by genomics and proteomics. One very useful component of the mass of free promotional material in the Congress satchels was the recent issue of Science (26 September, 2003), which contained a special section on Networks in Biology. This included review and commentary articles on topics as varied as molecular networks, neuronal networks, bacterial cell cycle as a regulatory network in time and space, and social insect networks. The prevailing and integrating theme is that we have to "think" networks in order to be able to assimilate the mass of data from clusters of genes that are co-regulated, or complex protein-protein interaction networks in one cell, not even to mention metabolic pathways and their regulation, if we are to have any hope at understanding and modelling the cell in both detailed and global terms.

Plenary speakers

The quality of presentations by plenary speakers in many respects sets the tone for the other features of a conference, especially where there are subsequent multiple parallel sessions. This was certainly the case with the Montreal Congress, where the plenary speakers maintained the superlative standards that one expects to find at an International Congress of Biochemistry and Molecular Biology. Of the nine Plenary lectures, five were IUBMB Named Lectures and two were lectures given by Canadian recipients of prestigious CSBMCB prizes; HUPO organised two Plenary lectures. Individual presentations are detailed below:

**Tony Pawson** (Canada; Hayaishi Lecture) gave an elegant easy-listening lecture from the discoverer of SH2 domains. He highlighted the modularity of proteins and how linking of various binding domains with each other forms the basis of networks, and went on to describe recent transfection studies with "synthetic" modules that impart novel phenotypes to cells.

**Shuh Naruyima** (Japan; Yagi Lecture) spoke about Rho and Rho effectors in the organisation of the actin cytoskeleton and the regulatory networks that control this activity. He showed the importance of these proteins in cell division and cytokinesis, particularly in the recruitment of microtubules to the kinetochore. Alberto Kornblihtt (Argentina; PABMB Lecture) emphasised the significance of alternate splicing in providing diversity of gene expression of mammalian genomes. He showed how the rate of transcriptional elongation by RNA polymerase II can determine the frequency with which alternative splice sites are used (in terms of access to the spliceosome apparatus of donor and acceptor splice junctions in the nascent transcript).

**Jean-Marc Egly** (France; Ochoa Lecture) gave an impassioned lecture, often laced with humour, on the TFIIH mammalian transcriptional complex. He described how a detailed analysis of the relationship of the various subunits of this complex, as well as mutations in different domains of individual helicase subunits, leads to significant insights into human diseases such as Xeroderma pigmentosum, tricho-tyriodystrophy and Cockayne syndrome. These diseases involve not only DNA repair defects but also a slowed basal transcription rate overall, as well as derangement of regulated transcription of other genes via the phosphorylation functions of TFIIH.

**Suzanne Pfeffer** (USA; Slater Lecture) described her work on regulation of receptor trafficking by Rab GTPases. She first placed her studies in the broad context of these proteins as master regulators of a wide range of membrane traffic events, defects in which lead to various human diseases. She went on to focus on her studies on the Rab9 GTPase that is essential for transport of mannose-6-phosphate receptors between late endosomes and the Golgi complex.

**Charles Boone** (University of Toronto) gave the CSBMCB Merck-Frosst Lecture (the equivalent of ASBMB’s Roche Lecture for younger high-achievers). He described his elegant automated studies of ordered arrays of yeast mutants to undertake systematic analysis of genetic interactions, and so generate a network of genes clustered in closely related functions. The map he produced has properties of a ”small world network”, where the genetic networks reflect biochemical or functional pathways already known. These can be used to identify targets (e.g. for cancer therapy) based on integration of genetic networks with data sets from chemical/genetics and protein interactions.

**Victor Ling** (University of British Columbia) gave the CSBMCB Roche Diagnostics Award Lecture (this is the equivalent of ASBMB’s Lemberg Lecture but is only awarded every second year; in the alternating years CSBMCB awards the Jeanne Manery Fisher Memorial Lectureship to a Canadian female scientist [in the field of biochemistry, molecular biology or cell biology] resulting from her outstanding contributions to research, teaching or community service). Ling’s remarkable exploration of cancer genomics focussed on a systematic study of the gene expression profile of human tissue samples prepared by laser capture microdissection, at various stages of malignancy. In this protocol, a few nanograms of tissue yielded within 2 minutes sufficient RNA to make a good cDNA preparation by RT-PCR. He also showed how a microarray based on human BAC clones (the whole genome on two slides!) can be used to screen DNA from such tissue samples for genetic damage, such as segmental deletions or amplifications. Finally data from SAGE analysis of transcription, linked to genomic and protein databases, enables new approaches to understanding the organisation of human genes in networks of associated functions, in both normal and pathological states.

The two HUPO plenary lectures were given by two of the 2002 Nobel Laureates in Chemistry who made pioneering discoveries in mass spectroscopy applied to biological molecules. **John Fenn** (Virginia Commonwealth University, Richmond, Virginia, USA) spoke on the topic ‘Electrospray wings for molecular elephants’. **Koichi Tanaka** (Shimadzu Corporation, Kyoto, Japan) gave his lecture on ‘Structural characteristics of protein: post-translational modifications using a MALDI QIT TOF mass spectrometer.’