Clinical trials

In the next 12 months, Linda Pilarski and Andrew Belch, from the University of Alberta's Department of Oncology, plan to conduct a clinical trial of the toxin in six multiple myeloma patients undergoing stem cell transplants. Stem cells will be harvested for all patients, but only some of them will be treated with the toxin. PCR will be used to check that the tumour has been successfully eradicated in the sample, and the final outcomes will be compared between those treated with toxin and those that are not. 'Myeloma patients have the worst prognosis of the three cancer groups that we have been studying for this procedure, which makes them the most suited group of patients to provide the proof-of-concept of this technique', says Gariépy.

The technology has been patented by Gariépy and the Ontario Cancer Institute. Select Therapeutics (Cambridge, MA, USA) has entered into a commercial partnership with the team and is preparing the toxin for the trial.

REFERENCES

1 O'Brien, A.D. *et al.* (1992) Shiga toxin: Biochemistry, genetics, mode of action, and role in pathogenesis. *Curr. Top. Micro. Immunol.* 180, 65

2 LaCasse, E.C. *et al.* (1999) Shiga-like toxin 1 receptor on human breast cancer, lymphoma and myeloma and absence from $CD34^+$ hematopoietic stem cells: Implications for *ex vivo* tumor purging and autologous stem cell transplantation. *Blood* 94, 2901–2910

3 LaCasse, E.C. *et al.* (1996) Shiga-like toxin purges human lymphoma from bone marrow of SCID mice. *Blood* 88, 1561–1567

Janet Fricker

A Boston T party – The highlights

With the first of many key drug discovery meetings in the year 2000 rapidly approaching, now might be a good time to reflect on one of the major meetings of 1999, IBC's *Drug Discovery Technologies '99*, which was hosted by the historic city of Boston, MA, USA (16–19 August 1999)[1]. The meeting was aggressively focused on new technologies and strategies to expedite the drug discovery process. Topics such as toxicity prediction, strategic alliances and collaborations, target discovery and validation through genomics and miniaturization, and biochip technologies were all the subject of review and discussion.

Delegate numbers exceeded 2000, and included 62 speakers and 152 exhibitors who showcased the products of more than 150 equipment, instrumentation and software suppliers. While there was a reasonable delegate attendance from other countries, those from the US dominated the event, making up 81% of the attendees. Europe provided 13% of the delegates, while Canada and the Far East totalled just 6%. The meeting was orientated towards the industrial sector of drug discovery as reflected by the fact that 93% of the delegates were from industry.

Keynote speakers

The keynote speakers succeeded in rousing the audience with their presentations. Leroy Hood (University of Washington, Seattle, WA, USA) gave a futuristic presentation, based on ideas that are already being developed, highlighting the convergence of the information technology and biotechnology disciplines, the concept of systems biology, and the need for cross-disciplinary technology development. He discussed the next generation of DNA sequencers, which will be microchannel-based and could be capable of sequencing single molecules, and highlighted the potential for making chips containing double-stranded promoter regions to capture all the active transcription factors present in a cell. Other aspects discussed included optical-fibre single nucleotide polymorphism (SNP) genotyping, and two-colour proteomic analysis using different hydrogen isotopes and gene expression analysis in single prostate cancer cells. This analysis technique uses yeasts, flies and worms to model human cancer pathways by removing the equivalent of the human tumour suppressor gene, replacing it with the normal or mutated human gene and observing the alteration of gene expression in the model organism. The University of Washington is currently setting up the Institute for Quantitative Systems Biology and is creating novel academic–industrial partnerships.

Michael Pavia (Millennium Pharmaceuticals, Cambridge, MA, USA) gave a thought-provoking presentation in which it was stressed that the pharmaceutical industry will not be sustainable unless the time from discovery to market is reduced. Pavia advocated integrating the technology and making it more comprehensive and industrialized, noting that only those who harness information appropriately will remain in the pharmaceutical race. Pavia strongly suggested that drug discovery should

1359-6446/00/$ – see front matter PII: S1359-6446(99)01465-8

Leroy Hood, University of Washington, WA, USA.

Michael Pavia, Millennium Pharmaceuticals, Cambridge, MA, USA.

Stuart Schreiber, Harvard Institute of Chemistry and Cell Biology, Cambridge, MA, USA.

be industrialized using other industries as a model. George Poste (SmithKline Beecham, Harlow, UK) also noted that information management was the single most important challenge of the future, and suggested that target validation (the correlation of genes to disease states) is an important bottleneck that should be addressed.

An excellent session on strategic alliances and collaborations in drug discovery attracted a significant attendance from professionals in pharmaceutical and biotechnological business development, strategical planning, licensing and technological acquisition. The discussion between delegates in this session highlighted the importance of bringing together the research and business development aspects of drug discovery. Presentations focused on overcoming the bottlenecks in drug discovery and new technologies to expedite the discovery process. A key theme this year was the concept of effective management of the immense quantity of information being generated in R&D.

Toxicity prediction in drug discovery was also a major topic covered. One of the more intriguing presentations was given by Bonnie Gould Rothberg (CuraGen Corporation, New Haven, CT, USA). Rothberg's presentation focused on pharmacogenomics programs designed to provide gene-based information on the mechanisms of action and toxicity of compounds in development. Data was presented that demonstrated the effectiveness of pharmacogenomic analysis in elucidating previously uncharacterized molecular basis of toxicity, mechanisms of action, suitable clinical surrogate markers of drug activity and locations of human polymorphism that could predict human responses to drug candidates. Other sessions addressed the crucial issues of overcoming key bottlenecks, target discovery and validation, and miniaturization and biochip technologies.

Upcoming meetings

It might be appropriate to complete this brief report with a short update of some of the key drug discovery meetings coming up this year. Particularly essential for Europe is the IBC *Drug Discovery Technologies 2000* meeting which will be held in Basel, Switzerland (10–12 April 2000). This conference promises to merge an interdisciplinary forum highlighting the innovative technologies being implemented by the Biopharmaceutical sectors with a strategic forum evaluating the crucial driving forces affecting drug discovery programs.

Keynote presentations will be provided by Peter Ringrose (President, Bristol-Myers Squibb Pharmaceutical Research Institute, USA), Rolf Krebs (CEO, Pharmaceuticals, Boehringer Ingelheim, Germany), Timothy Wells (Director of Institute, Serono Pharmaceutical Research Institute, Switzerland) and Michael Pavia. Sessions will cover proteomics and its therapeutic applications, novel assay development, advanced informatics and computational approaches, early high-throughput ADME (adsorption, distribution, metabolism and excretion) and toxicology studies, the impact of pharmacogenomics and pharmacogenetics, and miniaturization and biochip technologies.

For dates and contact details of other major discovery meetings such as ISLAR (Boston, MA, USA), the Society of Biomolecular Screening (Monterey, CA, USA) and Drug Discovery Technologies 2000 (Boston, MA, USA), see the diary section.

REFERENCE

1 Rink, T.J. (1999) A Boston T Party. *Drug Discovery Today* 4, 249–250

Drug Discovery Today