genomic databases to answer biological questions. Unlike the current approaches, these databases will allow a systematic information-based approach to studying the biology of thousands of genes at a time. High-density microarray technology developed by Affymetrix is being used to put every gene on a chip. These chips can be probed to determine when a gene is turned on or off in a variety of cells or tissues of choice and the effect of drug treatment on the expression of the gene. For example, all 20,000 genes expressed in activated T cells can be put on a chip and probed for effects by various immunosuppressive agents or ligands. Comparative genomics is also being performed at Incyte. Relational databases using information from the microarrays are being developed for building future bioinformatic capabilities at Incyte.

Dr Robert Jackson (Chiroscience, Cambridge, UK) was the plenary speaker at the 'Bioinformatics' session. Biological systems are complex but can be modelled using multiple parameters. Bioinformatics has been driven by the genomics effort as well as by HTS. The database will allow prediction of drug metabolism and toxicity, as well as the response duration from pharmacological information. At Agouron, these databases were used for the development of their HIV protease inhibitor. Information relative to the life cycle of the virus, the pharmacokinetic parameters of the protease inhibitor and the activity of the compound against the virus were taken into consideration when building the database.

Dr Kevin Oldenburg (Dupont Merck, Wilmington, DE, USA) spoke about his work in miniaturization of HTS to increase screen throughput. He presented a 9,600-well format for soluble enzyme, microbial-based screens, a 2,400-well format (0.2 µl per well) for enzyme and cell-based format (0.5 µl per well) and 960 wells for SPA receptor assays (20 µl per well). The liquid is dispensed 'on the fly' by careful timing for 10 nl delivery. The wells were designed with slanted sides to be able to receive compounds on beads. Evaporation results in a 28% loss of volume within 15 min, and humidity control is necessary. Microbial assays used the green-fluorescent-protein reporter. A matrix metalloproteinase assay for MMP-3 was described using fluorogenic reporters that had sufficient sensitivity for reading in the 9,600-well format. The equipment was produced in collaboration with BioDot in Canada.

In addition to the sessions mentioned above, there were 70 poster presentations. The adaptation of new technology, such as time-resolved FP to screening, and SPA to develop homogeneous screens, was described in these posters. Also, 72 companies exhibited their technologies to the registrants of the SBS.

All in all, this Annual Meeting was very successful; new information was exchanged between friends, and new friends were made.

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Electrical genes

Japanese chemists have developed an electrochemical sensing system for genes. The technology offers the possibility of replacing expensive, short-lived and troublesome radioisotopes used in medical labelling with an inexpensive and safer approach and could speed up drug research into genetic diseases.

Toshihiro Ihara and his colleagues in the Dept of Chemical Science and Technology at Kyushu University, Japan describe in a recent issue of *Chem. Commun.* (1997, 1609–1610) how they have modified an electrode sensor to respond to the presence of specific genes without the need for a radioisotopic label. They constructed their gene-sensing system using an active iron molecule, a so-called ferrocene, and a modified DNA probe with a nucleotide strand anchored to a gold electrode. The ferrocene undergoes reduction–oxidation reactions, depending on its chemical surroundings, and produces an electrical signal as it does so. The nucleotide strands – short lengths of DNA, chosen to target a known gene – produce a response in the presence of the target only.

'The detection procedure is very simple,' explains Ihara. The electrode sensor is placed in a sample solution containing the DNA of interest, such as a body fluid sample from a patient suspected of having a genetic disease. If there is a match between the nucleotide strand and a gene in the sample then an electrical signal will flow in the electrode and be easily detected.

By carefully choosing the nucleotide strand to match disease-inducing genes, the investigators can effectively detect the presence of such a gene in a patient without exposing the patient to radioisotopes. 'The strategy of the sensor is universal,' says Ihara. 'In principle, all genes responsible for certain diseases can be the target of the sensor by choosing an appropriate sequence of the redox active probe (ferrocene-modified DNA probe).'

'Radioisotopes are widely used as labels because of their high sensitivity,' explains Ihara. 'However, because of their hazardous nature and short shelf-life, the development of an alternative detection system is eagerly hoped for.' His team's system could be just such a convenient and practical alternative.

The researchers concede that they have not yet optimized the measurement conditions of the device, but they are working on it. 'We have now confirmed that the sensor responds to at least attomole concentrations (10^{-18}); this is of course sufficient for practical use,' adds Ihara. Industrial collaborators will hopefully commercialize the system. 'Our interest is in the performance of the system for detecting disease-inducing genes. Commercial development is beyond our scope, although of course we hope for it,' Ihara remarks.

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