Genomics for business

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Three parallel sessions were held at the recent conference organized by eyeforpharma (London, UK; http://www.eyeforpharma.com) in Basel, Switzerland on 28–30 November 2000: *Genomics for Business*, *e-R&D Strategies for Pharma* and *e-Business for Pharma*. The conference opened with a special event comprising an audience with two of the greatest scientists of our times – Stephen Hawking (Lucasian Professor of Mathematics at the University of Cambridge, Cambridge, UK) and Francis Collins (Director of the National Human Genome Research Institute, Bethesda, MD, USA). Hawking discussed the future evolution of the human race and his belief that: 'We will never reach a final steady state, the end of development. Instead, we shall continue to change, at an ever-increasing rate.' He also suggested that the complexity of the human race as well as its DNA will increase without waiting for the slow process of evolution. Furthermore, he predicted that genetic engineering will probably be used in the future for improvement of the human race.

Collins followed the talk by reviewing the progress of the Human Genome Project and the data that is now available (http://www.ensembl.org/genome/central/). He discussed the impact of this information on healthcare in the future as well as the ethical and social issues surrounding genetic testing. He predicted that genetic testing and pharmacogenomics, together with integration of diagnosis and therapy, would be part of medical practice by the end of 2010 and genomic medicines would be fully established in the following decade.

Is pharma producing enough genome-based drugs?

At the combined keynote session on the first day, William Haseltine (Human Genome Sciences, Rockville, MD, USA), opened with a provocative lecture in which he lamented the fact that the pharmaceutical industry is not producing enough new drugs, certainly not those based on our knowledge of the genetics of many diseases. His company is developing four of the five genome-based protein drugs (the fifth is by Amgen) and he believes that 50% of the drugs of the future will be proteins or antibodies. He is critical of the pharmaceutical industry and its belief that 90% of the drugs are chemistry-based with only 10% being genome-based. In contrast to the several years required for conventional pharmaceuticals, the time from identification of a novel human protein as a target to the initiation of a clinical trial is 6–9 months. However, many of the delegates from pharmaceutical companies that carry out a considerable amount of genome-based drug development did not agree with Haseltine's statement.

Strategies for drug discovery

Other sessions were devoted to the discussion of drug discovery technologies and business strategies of various companies. Description of these is given in a more detailed report on this topic[1]. Although throughput has increased, technology has not delivered as yet and productivity has not gone up. Some of the problems in the industry are perceived to be escalating costs and lack of innovation.

Christine Debouck (SmithKline Beecham, Brentford, UK) described the impact of genomics on drug discovery in a large pharmaceutical company. The company is using several gene targets for drug discovery including ≈200 orphan G protein-coupled receptors (GPCRs), of which 10% (i.e. ≈20) have been matched to a ligand[2]. An example was given of the selective tissue gene product expression of cathepsin K, a novel osteoclast-specific cysteine protease. Research data have demonstrated that inhibition of cathepsin K results in a diminution of osteoclast-mediated bone resorption[3], and is therefore a new potential drug target for osteoporosis.

Claes Wahlestedt (Karolinska Institutet, Stockholm, Sweden) described the strategic prioritization of gene targets at Pharmacia (Peapack, NJ, USA) where he is the Director of Worldwide Genomics and R&D. From thousands of genes, only 3000–8000 have a potential implication for disease. Of these, the druggable targets are only about 1000–4000. The number of fully developed drugs from these is expected to be approximately 15. Technologies for target validation used at Pharmacia include antisense, ribozymes and RNAi (RNA interference), which are easy to use and efficient. RNA (through the use of mRNA Accessible Site Technology) is preferred as a drug target, as only 1–5% of antisense oligonucleotides are effective. A high-affinity DNA analogue, locked nucleic acid (LNA), confers several desired properties to antisense agents. LNA–DNA copolymers exhibited potent antisense activity on assay systems as varied as a GPCR in living rat brain to an *Escherichia coli* reporter gene[4]. Other technologies used are viral delivery, gene regulation (zinc fingers), antibodies and chemical knockdown.

Protein-based drug discovery

Some of the promising technologies in the post-genomic era are based on proteomics[5]. Tim Harris (Structural GenomiX, San Diego, CA, USA) described

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how the power of protein structure is being harnessed to alter the way drugs and compounds are discovered. Using a target-directed approach, the company is devoted to transforming sequence data from the Human Genome Project and similar commercial ventures into novel three-dimensional (3-D) protein structures. Information on the 3-D structure of a target protein, integrated with chemistry and biology using bioinformatics tools, increases the efficiency of drug discovery[6]. From target selection to cloning, expression and purification, to X-ray diffraction and structure determination, the entire operation is dedicated to quickly and responsively producing protein structures of interest to the industry.

Jan Vanoostrum (Novartis, Basel, Switzerland) described the application of proteomic technologies to drug discovery within the functional genomics platform of a major pharmaceutical company and suggested that proteomics fits well with genomic technologies. In this setting, proteomics encompasses scientific applications, informatics tools and robotics. Application of the Novartis/Affymetrix gene chip has enabled identification of protein families according to different tissues, each with a different expression pattern. A future challenge for proteomics is the expected exponential increase in the number of targets to a range of 5000–10,000, owing to a rapid evolution of high-throughput techniques. Research therefore needs to be geared towards speed prioritization.

Concluding remarks

The conference was extremely well-organized and well-attended with a roster of top authorities in genomics and drug discovery technologies. An open forum (such as that provided at this conference) helps in the exchange of useful information and promising strategies can be identified. The impressions left by attendance at the conference were that the major pharmaceutical companies for drug discovery use genomic technologies abundantly in-house as well as through collaborations with biotechnology companies. Post-genomic technologies, particularly proteomics, are considered to be promising for meeting the future challenges of drug discovery. e-R&D, the topic of the parallel sessions, is highly relevant to drug development, as it is transforming the way business is done. However, it is premature to try to measure the economic impact of these technologies in pharmaceutical industry and available information is still limited.

References

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