

Clues to Down's syndrome origins

Scientists at the University of Cambridge (Cambridge, UK), University College London (London, UK) and the University of Wisconsin-Madison (WI, USA) have discovered some of the key cellular and molecular processes that give rise to Down's syndrome. The study, published in a recent issue of the *Lancet* [9], was the first of its kind to use human cells.

According to Clive N. Svendsen, a UW-Madison Professor of Anatomy and Neurology and director of the stem-cell research programme at the UW-Madison Waisman Center (a leading centre for the study of human development and neurodegenerative diseases), 'These findings point to a serious deficit in specific genes known to be important for neuronal development.'

The research determined that a neuron-specific growth-associated protein (SCG10), which is regulated by the neuron-restrictive silencer factor (REST), was almost undetectable in samples of Down's syndrome. This suggests a link between dysregulation of REST and some of the neurological deficits that characterize Down's syndrome.

Although these are preliminary results, identification of faults in the behaviour of key genes that cause Down's syndrome could lead to better treatments and even possible novel drug or gene therapies. 'Until now, we have only had mouse models..., which have not been so faithful in reproducing all aspects of Down's syndrome,' explains Svendsen. He added, 'now we have a complementary source of human stem cells with extra chromosome 21, and which can be grown indefinitely and used by a large number of scientists.' He continues to explain that this makes a

'nice model for drug...intervention to try and get (the developing brain) back to normal neuronal production from the stem cells. If we can understand the loss of neurons in Down's syndrome, I think it may lead to some novel treatments in the future.'

- 9 Bahn, S. *et al.* (2002) Neuronal target genes of the neuron-restrictive silencer factor in neurospheres derived from fetuses with Down's syndrome: a gene expression study. *Lancet* 359, 310–315

Miscellaneous

Three-way collaborations for breast cancer

The University of Cambridge (Cambridge, UK) is to collaborate with NextGen (Huntingdon, UK) and Cytomyx (Cambridge, UK) in a three-year research programme to develop a series of protein biochips for the analysis of breast cancer. The project, part-funded by the Department of Trade and Industry's (DTI; London, UK) LINK Programme in Applied Genetics, the Biological and Biotechnology Sciences Research Council (BBSRC; Swindon, UK) and the Medical Research Council (MRC; London, UK), will provide the University with new proteomics technologies. In turn, NextGen will develop a range of breast cancer protein biochips and a high-throughput automated protein expression Protein Library Management System (PLMS). Cytomyx will build a repository of clones for use in genomics and proteomics-based drug discovery.

'This initiative...allows us to access new technology in protein expression analysis and to combine this with the genomics

and transcriptomics information we are already gathering,' said Carlos Caldas, University of Cambridge and Cancer Research Campaign researcher. 'Our aim is to make the database and bioinformatics tools we develop freely available to the research community,' he said.

A separate collaboration between Oxford GlycoSciences (OGS; Oxford, UK), Medarex (Princeton, NJ, USA) and Genmab (Copenhagen, Denmark), will lead to the creation of an array of novel medical products for breast cancer. The development effort is designed to lead to a broader panel of complementary breast cancer treatments, including new antibody and vaccine therapies, and biomarkers, that have been discovered through OGS' proteomics platform with Medarex and Genmab's combined strengths in creating and developing immunological products. The first product, a fully human therapeutic antibody that targets heparanase 1, an enzyme involved in the growth and spread of many cancers, is expected to enter clinical trials in approximately one year.

Initially seven disease targets that appear to be expressed in tumours of >85% of women with breast cancer have been chosen for further development. Medarex will then aim to create human antibody therapeutics and/or tumour vaccines based on these disease targets. The program will also aim to produce well-tolerated therapeutic intervention at multiple stages of the disease.

News in Brief was written by
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People

New President and COO for Emisphere Technologies

Emisphere Technologies (Hawthorne, NY, USA) has appointed Alan William Dunton to the new position of President and Chief Operating Officer. Dunton joins the

company from The Janssen Research Foundation (JRF), which is a Johnson & Johnson company, where he was most recently President of JRF and Managing Director of Janssen Pharmaceutica. Prior to working at Janssen, Dunton was Group Vice-President of Development at the R.W.

Johnson Pharmaceutical Research Institute, which is also a Johnson & Johnson company.

On the appointment, Michael M. Goldberg, Chairman and CEO of Emisphere Technologies commented that: 'Dr Dunton brings to Emisphere significant experience in pharmaceutical industry management, along with hands-on clinical development expertise...we are pleased we will be able to draw upon Alan's prior success with advancing research programs to successful commercial products.'

Management and Scientific Advisory Board changes at Microbia

John J. Talley, the inventor of Celebrex, will join Microbia (Cambridge, MA, USA) as Vice-President, Drug Discovery, while the Nobel Laureate, Elias James Corey, will join the company's Scientific Advisory Board.

Talley joins the company from 15 years' working at G.D. Searle & Co (Pharmacia Corporation), most recently as Senior Research Fellow, and has been the lead inventor of a number of drugs including Celebrex, Bextra, Dynastat (all designed as cyclooxygenase COX-2 inhibitors) and several HIV protease inhibitors.

Professor Corey has been a Professor of Chemistry at Harvard University since 1959 and is currently Sheldon Emery Research Professor of Chemistry. In 1990, he was awarded the Nobel Prize in Chemistry for the development of retrosynthetic analysis. He has also provided significant contributions in the areas of using computers to design synthetic routes to create organic molecules, the development of fundamental logic of chemical syntheses, as well as the design of numerous synthetic methods and the establishment of the structure of many chemical compounds. He has also received more than 50 international awards and honorary degrees, including the National Medal of Science in 1990, is a member of the National Academy of Sciences, and is the author of more than 900 publications in peer-reviewed scientific journals.

Leroy Hood joins Paradigm Genetics board

Leroy Hood, President and Director of the Institute of Systems Biology (ISB), has joined the Board of Directors of Paradigm Genetics (Research Triangle Park, NC, USA). In addition to his current position at the ISB, Hood is also a professor at large for the Keck Graduate Institute of Applied Life Sciences and an Affiliate Professor of the University of Washington's Bioengineering, Computer Science and Immunology Departments. Hood is a member of the National Academy of Sciences, the American Philosophical Society and the American Association of Arts and Sciences. He is also a member of the American Association of Immunologists, the Association of American Physicians and the Society for Integrative and Comparative Biology.

Hood commented that: 'Paradigm Genetics is a pioneer in the emerging science of metabolomics...[and] I believe metabolomics will prove to be a very valuable complement to traditional genomic technologies. It holds great promise in the field of systems biology, with the potential to accelerate and improve the analyses of drug targets, lead compounds and predictive medicine.'

Peter Barrett leaves Celera for Atlas Venture

Peter Barrett, a co-founder of Celera Genomics, has moved to Atlas Venture (<http://www.atlasventure.com/>) and will lead the company's investments in US life science companies. Barrett co-founded Celera in 1998 with J. Craig Venter and held the position of Executive Vice-President and Chief Business Officer at the company. Prior to this, Barrett was Vice-President of the Life Science Division at Perkin-Elmer and was responsible for the company's acquisition of Applied Biosystems in 1993.

Jean-Francois Formela, Senior Principal of Atlas Venture said: 'Peter has been associated with some of the most outstanding developments in the industry, including the formation of Celera. ...[Peter's] strong track record will be a tremendous asset to us in further growing companies in our investment portfolio and identifying new investments with the best potential.'

New Genomics Business Manager for TAP

The Automation Partnership (TAP; Royston, Hertfordshire, UK) has announced the appointment of Rod Westrop as its Genomics Business Manager. Westrop was previously Managing Director of Jarvis Porter Healthcare, and has also held the positions of European Director of Sales and Business Development at Lark Technologies and Account Manager for Amersham Pharmacia. Richard Archer, the Chief Executive of TAP commented that: 'As the genomics industry continues to develop, the need for high-throughput screening of drug candidates and gene and protein expression will become a serious bottleneck. Rod's successful experience in leading companies will be a key part to further building TAP's genomics business.'

New Chief Business Officer for GeneFormatics

GeneFormatics (San Diego, CA, USA) has appointed Vincent P. Gotz as Chief Business Officer. Prior to joining GeneFormatics, Gotz was Vice-President, Business Development at Epicyte Pharmaceutical. He has also previously held several management positions at Dura Pharmaceuticals (including Senior Director, Technology, Licensing and Partnering) and various R&D and strategic development positions at Marion Merrell Dow. John Chiplin, President and CEO of GeneFormatics said: 'Vincent's broad-based understanding of pharmaceutical development and a proven record of success in technology assessment, deal structuring, and international negotiations will be invaluable as we continue to pursue collaborations with biotechnology, genomic and pharmaceutical companies.'

Brian R. MacDonald joins 3-Dimensional Pharmaceuticals

Brian R. MacDonald has been appointed to the position of Vice-President, Development at 3-Dimensional Pharmaceuticals (Yardley, PA, USA). MacDonald was most recently Group Director, Emerging Therapeutic Areas, North America Medical Affairs at GlaxoSmithKline. He previously held several senior R&D positions with SmithKline Beecham and a variety of teaching positions with the University of Pennsylvania and the University of Bath (UK). 'Brian's experience in drug development and his great ability to link clinical development and discovery research will be of great importance as we advance our discovery programs into the clinic,' commented David U'Pritchard, CEO of 3-Dimensional Pharmaceuticals.

The company has also appointed William Claypool, CEO of Phoenix Data Systems, to its Board of Directors. Claypool has also previously held several key management positions in SmithKline Beecham, including the position of Senior Vice-President and Worldwide Medical Director, Clinical Research and Development.

People was written by
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