News in brief

Targets and mechanisms

Early biomarker for Alzheimer's disease and Down's Syndrome?

Two recent studies have shown a dramatic increase in isoprostane levels in the urine of people suffering from Alzheimer's disease (AD) and Down's Syndrome[1,2]. Researchers at the University of Pennsylvania Medical Center (Philadelphia, PA, USA) hope these findings could provide an early diagnosis tool for these two diseases.

In AD, they showed that levels of isoprostane, produced from fat and lipids by free radicals, correlate directly with tau protein and amyloid levels. This provides the possibility for a much simpler diagnosis than using tau protein, as this is only found in the CSF and therefore requires lumbar puncture for the measurement of this marker. The study involved comparing isoprostane levels in the CSF, blood and urine in 35 clinically diagnosed AD patients with 25 healthy volunteers.

Free radical damage in the brain is also a key part of Down's Syndrome, and sufferers often exhibit AD-like brain lesions in early adulthood. A comparison of isoprostane levels in those with Down's Syndrome compared with matched controls also showed a correlation with the duration of the disease.

The researchers now plan to look at levels of isoprostane in mild cognitive impairment (MCI), which leads to a clinical diagnosis of AD in up to 45% of cases.

1 Pratico, D. *et al.* (2000) Increased 8,12-iso-iPF2α-VI in Alzheimer's disease: correlation of a noninvasive index of lipid peroxidation with disease severity. *Ann. Neurol.* 48, 809–812

2 Pratico, D. *et al.* (2000) Down's syndrome is associated with increased 8,12-iso-iPF2α-VI levels: evidence for enhanced lipid peroxidation *in vivo*. *Ann. Neurol.* 48, 795–798

Oestrogen replacement therapy for treatment of Parkinson's disease

Oestrogen has been shown to maintain the integrity of dopamine neurones, and thus might be a potential therapy for Parkinson's disease. In a recent study by researchers at Yale University (New Haven, CT, USA), female monkeys were ovariectomized, and the effect of oestrogen replacement therapy monitored. The density of nigrostriatal dopamine neurones was calculated after 10 or 30 days of oestrogen deprivation. These neurones form the part of the brain that produces dopamine, the destruction of which is associated with the development of Parkinson's disease and dementia. Interestingly, the density of dopamine neurones is greater in females than in males, which could explain why men and post-menopausal women are more likely to develop Parkinson's disease. It was found that oestrogen deprivation results in a significant loss of nigra dopamine cells and that oestrogen replacement therapy can restore the density of these cells if administered within 10 days[3]. After 30 days, these cells appear to be permanently destroyed.

The proportion of cells lost after oestrogen deprivation is significant enough to mean the difference between the development of severe Parkinson's disease and having little or no symptoms. Researchers are now investigating whether larger doses or prolonged administration of oestrogen or other hormones could affect neurone integrity, with a view to using this as a treatment strategy for Parkinson's disease and other memory-impairing disorders.

3 Leranth, C. *et al.* (2000) Estrogen is essential for maintaining nigrostriatal dopamine neurons in primates: implications for Parkinson's disease and memory. *J. Neurosci.* 20, 8604–8609

Sea squirts provide hope for infertility treatment

Sea squirts could prove to be invaluable models for research into infertility, according to a recent report. A team of scientists at Newcastle University (Newcastle, UK) have found that these tiny slug-like creatures, which inhabit the North-East coast of England in their millions, have a similar embryo to humans. Although the sea squirt is a basic animal, its early stages of life are thought to be almost identical to those of a human.

The aim of current research is to study the protein in sea squirt sperm that triggers fertilization, which is known as the activating factor. This factor is thought to cause chemical changes in the egg, and it is speculated that the protein might be missing or non-functional in infertile men. It is hoped therefore, that by studying this protein in sea squirts, researchers will learn more about the activating factor, while eliminating the need to experiment on human eggs and embryos. This information might then be applied to human infertility research, with a view to developing a functional human equivalent of the protein.

Tonga under the spotlight

An Australian biotechnology company, Autogen (Melbourne, Australia), has paid an un-named sum for the exclusive rights to study the gene pool of the South Pacific island of Tonga. The island's isolated gene pool and rigid family-based society make it an attractive prospect for research into the genetic causes of diabetes and obesity, two diseases that are prevalent on the island. The company has promised that a proportion of any royalties that derive from the study will be given to the Polynesian kingdom.

Low-level manganese exposure is a risk for Parkinson's disease

Low levels of manganese are reported to affect the brain in a way that exacerbates Parkinson's disease. In a paper soon to be published in *Neurotoxicology and Teratology*, researchers from the University of California (Santa Cruz, CA, USA) have confirmed earlier suggestions from epidemiological studies that elevated exposure to manganese is a risk for Parkinson's disease. Using rat models of Parkinson's disease, they studied the effects

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of low levels of manganese on the acceleration of the disease. It was found that manganese toxicity and Parkinson's disease affect different pathways involved in muscle control. However, it is thought that if two areas of the brain are weakened, an additive effect is observed, therefore increasing risk of disease.

The toxic effects of manganese are well known from studies of miners and can cause a disease called manganism, which has similar symptoms to Parkinson's disease. The results of this study further suggest that manganese presents a potential risk to human health because of its ubiquity in the environment and its increasing use in industry.

Role for *Spirulina* in immunity

Spirulina can boost the immune system by stimulating the secretion of cytokines according to a recent report[4]. The blue-green algae, which has been used as a food supplement for 20 years, is naturally found in extremely alkaline lakes, but is now grown commercially in large-scale ponds. *Spirulina* is rich in antioxidants, vitamins and minerals and has been previously implicated in the modulation of the immune system: it suppresses the release of histamine in rats[5]; increases antibody responses and the activity of natural killer cells in chickens[6]; and activates macrophages and enhances phagocytosis in cats[7]. *Spirulina* also has therapeutic effects on hyperlipidaemia and obesity: studies have shown that *Spirulina* decreases total serum cholesterol and low-density lipoprotein[8] and, in obese patients, dietary intake of *Spirulina* resulted in significant weight loss[9].

In this latest report, researchers at the University of California at Davis (CA, USA) studied the effect of *Spirulina* on the secretion of cytokines in peripheral blood monocytes. They found that *Spirulina* significantly enhanced the secretion of interleukin-1β (IL-1β), IL-4 and interferon-γ (IFN-γ). Induction of IFN-γ secretion was comparable with that caused by phytohaemagglutinin (PHA) stimulation, and was greater than the induction of IL-1β and IL-4, which suggests that *Spirulina* is more effective at generating a Th1-type immune response.

4 Mao, T.K. *et al*. (2000) Effect of *Spirulina* in the secretion of cytokines from peripheral blood mononuclear cells. *J. Med. Food* 3, 135–140

5 Kim, H.M. *et al*. (1998) Inhibitory effect of mast-cell mediated immediate type allergic reactions in rats by spirulina. *Biochem. Pharmacol*. 55, 1071–1076

6 Qureshi, M.A. *et al*. (1996) Dietary *Spirulina platensis* enhances humoral and cell-mediated immune function in chickens. *Immunopharmacol. Immunotoxicol*. 80, 225–235

7 Qureshi, M.A. and Ali, R.A. (1996) *Spirulina platensis* exposure enhances macrophage function in cats. *Immunopharmacol. Immunotoxicol*. 18, 465–476

8 Nakaya, N. *et al.* (1988) Cholesterol lowering effect of *Spirulina*. *Nutr. Rep. Int*. 37, 1329–1337

9 Becker, E.W. *et al.* (1986) Clinical and biochemical evaluations of the alga *Spirulina* with regard to its application in the treatment of obesity: a double-blind cross-over study. *Nutr. Rep. Int.* 33, 565–574

Markets

HIV treatment donation for developing countries

Boehringer Ingleheim (Ingleheim-am-Rhein, Germany) has joined the effort to try to help supply drugs for the treatment of HIV for the developing countries. Viramune (nevirapine) has been made available free-of-charge to women in hospitals in the Republic of Congo for the prevention of mother-to-child transmission (MTCT) of HIV-1 for the next 5 years. According to the Congolese government, 100,000 adults and children were estimated to have HIV/AIDS in the Congo by the end of 1999. The supply of the drug in the Congo will be supported by HIV prevention campaigns, counselling for pregnant women and the establishment of new HIV test centres.

This initiative by the company is part of the collaborative effort together with Bristol-Myers Squibb, F. Hoffman-La-Roche, GlaxoWellcome and Merck & Co. and several United Nations agencies (WHO, UNICEF, UNFPA and UNAIDS) to explore practical ways to make HIV/AIDS therapies available and affordable to those in developing countries.

Sales of drugs to manage arrhythmias will increase modestly over the next ten years

Major market (US, France, Germany, Italy, Spain, UK and Japan) sales of drugs to manage arrhythmias are forecasted to increase from nearly $1.8 billion in 1999 to $2.6 billion in 2009, according to a recent Decision Resources (Waltham, MA, USA) report entitled *Arrhythmias*. Arrhythmias encompass a wide range of conduction anomalies including benign (extra beats), chronic (atrial fibrillation) and fatal (ventricular tachycardia and ventricular fibrillation) forms. Because they affect a large patient population that will require a high level of drug treatment, and because of the need for therapies that prevent the recurrence of atrial fibrillation and for non-pharmacological and safer alternatives, this area is of great current interest to the pharmaceutical industry. Exciting areas of development in the field include the novel anticoagulants, which might offer an alternative to warfarin (DuPont Pharmaceuticals' Coumadin), and the take-over of the Class I drug market share by novel Class III drugs.

Biotechnology sector on the up

The biotechnology sector has had its best year ever on both sides of the Atlantic, according to the International Biotechnology Trust. During the first three quarters of 2000, 70 new biotechnology companies were listed on the stock exchanges in the US and Europe. There has also been a significant increase in the amounts of capital being raised at IPO from £15–25 million up to an average of £60 million (BioWorld). Of the US$28.85 billion raised for the biotechnology industry in the first 9 months of 2000, US$2.98 billion was in venture capital fund-raising, US$6.55 billion was in IPOs, US$5.66 billion was in follow-on investments and US$13.66 billion was in all other financings (BioCentury). Although the European biotechnology market continued to expand and mature, Germany has seen the most rapid growth in its fledgling industry while investors have remained cautious in the UK, favouring a select group of biotechnology companies.

Ebola virus vaccine breakthroughs

Protein sequence identified for Ebola virus vaccine development

A protein sequence has been identified that might prove useful in the development of a vaccine against the deadly Ebola virus. Researchers at the University of Pennsylvania (Philadelphia, PA, USA) have discovered a proline-rich (PY) motif within the VP40 protein, which is thought to mediate self-exocytosis (budding) of the protein from the host-cell membrane[10]. Harty and coworkers also demonstrated that this motif allows VP40 to interact with several other cellular proteins. Moreover, mutation of the VP40 protein substantially impaired the virus' ability to bud from mammalian cells.

It is speculated that VP40 is functionally similar to the Gag and M proteins of retroviruses and rhabdoviruses, respectively, and that these viruses might share the same mechanisms of budding. Ebola virus is fatal in almost 90% of patients, and this discovery could be crucial in the development of antiviral agents to combat the disease.

10 Harty, R.N. *et al.* (2000) A PpxY motif within the VP40 protein of Ebola virus interacts physically and functionally with a ubiquitin ligase: implications for filovirus budding. *Proc. Natl. Acad. Sci. U. S. A.* 97, 13871–13876

Vaccine protects against Ebola virus in monkeys

Animals can successfully mount an immune response to an Ebola virus vaccine, a recent report has revealed[11]. Researchers at the Vaccine Research Center (US National Institutes of Health, Bethesda, MD, USA) and the Center for Disease Control and Prevention (Atlanta, GA, USA) administered a DNA vaccine that encoded glycoproteins found on the surface of the virus. This vaccine was found to induce an immune response without concurrent illness. This was boosted by exposing the monkeys to a cold virus that had been modified to express Ebola nucleoprotein and three types of Ebola glycoprotein, which further increased the production of antibodies and the activation of T cells. Of all the monkeys exposed to Ebola virus, only those that had received the vaccines survived, and six months after exposure, all surviving monkeys were symptom-free and had no evidence of Ebola virus in their blood. Future research will focus on the efficacy of such vaccines against different Ebola strains, and studying the type of immune response that is induced.

11 Sullivan, N.J. *et al.* (2000) Development of a preventative vaccine for Ebola virus infection in primates. *Nature* 408, 605–609

Miscellaneous

Pharmaceutical firms buy goods online but drag feet over e-based R&D

Pharmaceutical companies are second only to the retail sector in using the Internet for purchasing goods, announced a recent report by e-Net Software (Bath, UK). The figure (45%, compared with 70% for retail) refers to office supplies, computer hardware and software and reflects the advantages conferred to large companies when bulk buying/ordering. However, the interest in new technology does not stretch to 'direct' services, with less than 10% using the web to buy laboratory equipment, tools or components. Echoing this feeling, a recent survey (*PharmaDevelopment* 2000, Cambridge, UK) of professionals in the pharmaceutical industry found that 27% preferred paper to Internet-based systems for conducting clinical trials and regulatory processes. Although preparing online processes can require extensive planning, savings from e-development are predicted to be in the region of 30–50% (PriceWaterhouseCoopers, London, UK).

Governments

New Government website for IP

The Department of Trade and Industry (London, UK) has launched a new Intellectual Property (IP) website to help both people with little knowledge of IP and more experienced users. The website (http://www.intellectual-property.gov.uk) provides a comprehensive database of copyrights, trademarks, patents and designs, as well as the latest news and links to other IP-related websites.

Mergers and acquisions

Merger to unify microplate instrumentation brands

Dynex Technologies Corporation (Chantilly, VA, USA) and Labsystems Oy (Helsinki, Finland) have announced that they are merging to form a company called Thermo Labsystems.

With immediate effect, they are replacing all previous brands from both companies with Thermo Labsystems for microplate instrumentation and Thermo Microtiter for microplates.

This merger follows a new corporate strategy by the parent company of Dynex Technologies (Thermo Electron Corporation) to establish a strong affiliation between its more than 80 brands and to promote itself as a single unified company.

Access to large wound healing market

Modex Therapeutics (Lausanne, Switzerland) has purchased the wound healing company, BioCare Biotechnologie für die Therapie (Leipzig, Germany), to provide Modex with direct access to the German market for their EpiDex product.

BioCare was purchased for DM2.3 million, a maximum DM1.1 million being paid upfront in Modex's treasury shares, and a maximum of DM1.2 million being payable in cash before 31 December 2003 depending on BioCare achieving certain milestone objectives. Modex will also pay some time-limited royalties to the sellers on future sales of EpiDex in Germany.

BioCare currently manufactures and sells ThromboKinin, an autologous growth factor product for skin ulcers, and Epigraft, an autologous hair-to-skin product.

Christian Toloczyki, who established BioCare, will become General Manager of BioCare in the merged company and will lead the launch of EpiDex in Germany.

British approve of genetic research but have little confidence in state regulation of data

Most people in Britain agree that human genetic research will lead to cures for disease and healthier babies, according to a survey commissioned by the Human Genetics Commission (HGC), a national advisory body in the UK. The survey of 788 members of the Government-organized 'People's Panel' also revealed that the Panel members had little or no confidence that regulation of scientific developments would be able to keep pace with current progress in the field.

With regard to the healthcare and workplace implications of genetic profiling, three quarters of those questioned said genetic tests should not be incorporated in the setting of insurance premiums, but a third felt it appropriate that health and life insurers see test results before they agree to provide cover. In the workplace, 72% of people were opposed to employers using genetic information to determine whether their staff was likely to become ill or take early retirement. However, 70% were happy for an employer to have access to the information if it was used to determine whether people might be sensitive to substances such as chemicals.

The public consultation will continue until March 2001 with final recommendations due to go before ministers in the third quarter of 2001.

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People

Young Scientist Prize winner: explanation for two-level immune system?

The 2000 Young Scientist Prize, awarded annually since 1995 by *Science* and Amersham Pharmacia Biotech, was given to Alka Agrawal (Stamford, CT, USA). Applicants for the $25,000 prize are required to have recently earned their PhD and to submit a 1000-word essay based on their dissertation. The essays are judged on the quality of the research and the applicants' ability to articulate how their work contributes to the field of molecular biology.

Alka Agrawal did her PhD at Yale University (New Haven, CT, USA) under the supervision of David G. Schatz and Quinn M. Eastman, where she showed that the *RAG1* and *RAG2* genes can carry out transposition reactions in the test-tube which, if they occur *in vivo*, could be involved in DNA translocations associated with certain cancers. Agrawal further proposed that millions of years ago, a RAG transposon produced our current two-level immune system, including immunoglobulin and T-cell receptor gene segments, by splitting sequences that are then duplicated. On her discoveries, Agrawal said: 'We observed an unexpected product in our tests and, oddly enough, it turned out to be really important. It was one of those serendipitous moments in scientific investigation when a big puzzle suddenly falls into place.'

Four regional winners for each of the four geographical regions of North America, Europe, Japan and all other countries were also awarded. These $5000 awards went to:

- Yuki Yamaguchi (University of Tokyo, Japan) for providing insights into how HIV proliferates as viral genetic sequences elongate during transcription;
- Rafal Ciosk (University of Vienna, Austria) for inventing an assay to study cohesion proteins linking sister chromatids in a budding yeast model;
- Douglas M. Heithoff (University of California–Santa Barbara, CA, USA) for identifying the 'switch' that makes bacteria pathogenic; and
- Avraham Yaron (Hebrew University, Jerusalem, Israel) for helping to explain a crucial molecular mechanism involved in chronic inflammatory diseases and tumour cell resistance to chemotherapy.

Four professors for Biotica Technology Scientific Advisory Board

Biotica Technology (Cambridge, UK) has just appointed four professors to their Scientific Advisory Board: Eric Cundliffe, Iain Hunter, Craig Townsend and John Vederas. The company focuses on the discovery of novel biopharmaceuticals through the targeted alteration of biosynthetic pathways producing natural products.

Cundliffe is currently Professor of Biochemistry at the University of Leicester (UK) and has worked primarily on the biochemistry and genetics of *Streptomyces* and on antibiotic resistance. His previous positions have included Director of the Leicester Biocentre until 1990. Hunter is currently Professor of Molecular Microbiology (Department of Pharmaceutical Sciences, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, UK) where he is researching the genetics of industrially important microorganisms, particularly *Streptomyces*.

Townsend is Alsoph H. Corwin Professor of Chemistry in the Departments of Biology and Biophysics at the John Hopkins University (Baltimore, MA, USA). His areas of expertise include natural product biosynthesis, the enzymology and molecular biology of secondary metabolism, small-molecule–DNA interactions and rational drug design. Finally, Vederas is Professor of Organic Chemistry at the University of Alberta (Edmonton, Alberta, Canada) and is mostly interested in the formation of important biological molecules such as antimicrobial peptides, amino acid metabolites and polyketides through the use of a variety of techniques including organic synthesis, NMR and MS, isotopic techniques and natural product isolation.

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