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News in brief

Targets and mechanisms

Genetic link to prostate cancer

The inactivation of two genes that are frequently mutated in human prostate tumours causes 100% incidence of prostate cancer in mice, a recent study has shown. Researchers at Memorial Sloan-Kettering Cancer Center (MSKCC; New York, NY, USA) have found that mutation of one copy of the *Pten* gene and both copies of the *p27* gene results in prostate tumours in mice that share the same features as those that arise in humans[1].

Researchers can now use these mice as a model that will lead to improved methods for testing potential therapies for the disease. Further, this model will aid future investigation into the genetic mechanisms behind various forms of prostate cancer, and could enable physicians to diagnose prostate cancer more rapidly and refine their treatment of different tumour types. However, further studies and clinical trials will be required to establish whether the effect of these mutations is similar in humans to that observed in mice.

1 Cristofano, A.D. *et al.* (2001) Pten and p27KIP1 cooperate in prostate cancer tumor suppression in the mouse. *Nat. Genet.* 27, 222–224

SPAN-X – a diagnostic aid?

A team of researchers at the University of Virginia Health System (Richmond, VA, USA) has identified a novel gene, *SPAN-X*, which might ultimately lead to improved diagnosis and treatment for some cancers. In the body, this gene only occurs in the normal testis; however, recently the team found that it is also present in various tumours, including skin, breast, prostate and ovary[2].

It has been shown previously that some proteins are testis-specific; they are established in puberty, and are hidden from the immune system to protect them from being rejected. By contrast, in cancer cells, these proteins are not protected, and therefore might be good targets for anti-tumour therapy.

'Based on our findings, it seems possible that as some tumours become cancerous and develop irregularly, they may begin to mimic the way genes are expressed during sperm formation,' says John Herr, Director of the Center for Research in Reproductive Health (University of Virginia Department of Cell Biology).

The team is currently examining stored tissue samples to evaluate how frequently *SPAN-X* occurs in different cancers. If there is a link between specific levels of *SPAN-X* and a particular type of cancer, this might ultimately lead to the development of a test for earlier diagnosis of cancer.

2 Westbrook, V.A. *et al.* (2001) Differential nuclear localization of the cancer/testis-associated protein, SPAN-X/CTp11, in transfected cells and in 50% of human spermatozoa. *Biol. Reprod.* 64, 345–358

Genetically predisposed to comfort eating?

A recent study suggests that dopamine deficiency in the brain might clarify why certain individuals pathologically overeat, resulting in severe obesity[3]. The neurotransmitter, dopamine, helps control feelings of pleasure and regulates the rewarding properties of food. The researchers indicated that individuals deficient in dopamine receptors might have to eat more food than those without this deficiency, to induce feelings of satisfaction and gratification.

The study compared ten severely obese individuals (275–390 lb) with ten control individuals (121–198 lb). The body mass index (BMI) was calculated for each individual: the average BMI was ~51.2 in the obese group and 24.7 in the control. Positron-emission tomography scans and other tests were used to measure dopamine receptors in the brain. Dopamine receptor availability was significantly lower in the obese group than the control, and BMI correlated negatively with measures of dopamine receptors.

'Currently, the most appropriate practical application of this finding is to urge overweight individuals to exercise. In laboratory animals, exercise has been shown to increase dopamine release and to increase the number of dopamine receptors, which could help quell the urge to pathologically overeat,' says Gene-Jack Wang, head of the research team (Brookhaven National Laboratory, Upton, NY, USA).

3 Wang, G-J. (2001) Brain dopamine and obesity. *Lancet* 357, 354

Markets

Generic drug manufacturing impacts patented drug's revenue

The introduction of generic drug manufacturing in Brazil following new sector legislation is having a detrimental impact on the revenue gained from the original patented drug, claims the *Gazeta Mercantil* in Brazil (courtesy of John P. Stewart). For example, the antibiotic Keflex, which was originally produced by Eli Lilly, has seen a 30% drop in its revenue (from R$6 million per month) while the generic brand, Cefalexina, has produced a revenue of R$2.1 million in its first eight months of production. To reduce the impact of this alternative market, Novartis has decided to open a manufacturing plant in Brazil and to separate the sales division of generic medicines from patented therapies.

Slow start to 2001 for Biotech stocks

Almost all of the Burrill Biotech Indices fell in price for the month of January 2001, reported Burrill & Company (San Francisco, CA, USA) recently. The fall (of 2–10%) compares with increases in the Dow Jones index (0.9%), Russell 2000 index (5%) and the Nasdaq (12%) for the same period, and follows growth of 5–12% in December 2000. Burrill & Company Chief Executive Officer G. Steven Burrill said that there was still demand for biotech stocks but that 17 biotech lock-ups had expired in January, creating a surplus in the market. He thought that positive fourth quarter and year-end results, together with a few IPOs, would trigger an increase in stock values.

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Interleukin proteins provoke antiviral response in asthma

The interleukin-12 (IL-12) p40 protein is overactive in asthma sufferers and during viral bronchitis, a recent study has shown[4]. Researchers at Washington University School of Medicine (St Louis, MO, USA) have shown that bronchial epithelial cells, which are known to host viruses, have a pivotal role in asthma. It is proposed that the normal antiviral response hosted by the epithelial cells can be perturbed by viral infection, possibly during infancy, thus changing the inflammatory response to future viruses and causing asthma.

The protein responsible for this reaction is thought to be IL-12 p40, which has been shown to be selectively active in the bronchial epithelium. The localization of IL-12 p40 to epithelial cells correlates with the fact that these cells produce a known antiviral agent on stimulation by a virus. Moreover, a variant of IL-12 protein, p80, has been identified and is thought to recruit a specific subset of macrophages. Further investigation of the mechanisms of the antiviral response in bronchial epithelial cells and elucidating how viral infection disrupts this response could ultimately aid the design of potential asthma therapies.

4 Walter, M.J. *et al*. (2001) Interleukin 12 p40 production by barrier epithelial cells during airway inflammation. *J. Exp. Med*. 193, 339–352

Marijuana as potential anti-emetic for cancer patients

Marijuana could prove useful as an anti-emetic drug for people undergoing cancer chemotherapy, according to a recent report. Researchers at The Kirksville College of Osteopathic Medicine (KCOM) have recently found a link between a cannabinoid (marijuana) receptor and vomiting (emesis)[5] using the established model of emesis, the least shrew (*Cryptotis parva*).

Because cannabinoid agonists prevent emesis, it was postulated that by blocking either cannabinoid receptor 1 or 2 (CB_1 and CB_2, respectively), vomiting would be induced. Therefore, the potential of either a CB_1 or CB_2-receptor antagonist to cause emesis was studied. Interestingly, both the proportion of animals and frequency of vomiting was significantly increased in animals administered with the CB_1-receptor antagonist, but not in animals given the CB_2-receptor antagonist. In a further experiment, the researchers induced vomiting in the shrew models by administering the CB_1-receptor antagonist, SR141716A, and measured the frequency of emesis before administering several CB_1-receptor agonists. They determined the order of potency based on reduction of vomiting frequency for each of the agonists and found that Δ^9-tetrahydro-cannabinol and other synthetic analogues were capable of reversing the effects of the emetic CB_1-receptor antagonist. This research has identified CB_1 as a molecular switch in the mechanism of emesis and could, therefore, be useful in the development of anti-emetic therapies.

5 Darmai, N.A. (2001) Δ^9-Tetrahydrocannabinol and synthetic cannabinoids prevent emesis produced by the cannabinoid CB_1 receptor antagonist/inverse agonist SR141716A. *Neuropsychopharmacology* 24, 198–203

Artificial primosome for DNA labelling and sequencing

An artificial primosome has been developed for DNA diagnostics as an alternative to the traditional primer-extension assays commonly used for DNA labelling and sequencing[6]. The major limitation of current assays is that only purified single-stranded DNA can be primed. This is time-consuming and can result in mispriming at sites elsewhere in the DNA sequence, particularly with large target molecules.

Researchers at the Center for Advanced Biotechnology, Boston University (Boston, MA, USA) have designed an artificial primosome that consists of a pair of peptide nucleic acid (PNA) 'openers' and an oligonucleotide primer. This nanostructure is reported to have the capacity to direct a primer-extension reaction in a sequence-specific manner within double-stranded DNA, hence eliminating the need to denature and/or purify the target DNA sample. Non-denaturing DNA sequencing avoids complications caused by folded structures ('difficult-to-read' sites) that can form in long denatured or single-stranded templates. Further, because only the short priming site is exposed by PNA openers, the remainder of the DNA retains its duplex structure, which eliminates the risk of mispriming.

Another advantage of this system is the possibility of incorporating numerous labels into designated DNA regions, in contrast to the non-specific labelling by

Clinical trials

First AIDS vaccine enters clinical trials in Africa

The first preventive AIDS vaccine designed specifically for use in Africa has entered clinical trials in Nairobi. These trials have been endorsed by the Kenyan government after approval was granted by Kenya's National Council on Science and Technology and Kenyatta National Hospital's Ethics and Research Committee. The vaccine candidate is a result of the International AIDS Vaccine Initiative-funded research by the Medical Research Council Human Immunology Unit (MRCHIU) at Oxford University (Oxford, UK) and Nairobi University (Nairobi, Kenya). Existing and future patents covering the vaccine will be owned jointly by these institutions, which have agreed that the patents will be used to ensure global access to the vaccine.

The vaccine is based on subtype A of HIV, which is the most prevalent form in East Africa. In women repeatedly exposed to HIV, a minority has resisted infection, and it is hoped that the vaccine will stimulate a response comparable with that seen in this group. Andrew McMichael (MRCHIU) commented that: 'Our research indicates that this vaccine has a very good chance of stimulating cellular immune responses to HIV… [and] that white blood cells activated by the vaccine can destroy virus-infected cells.' He adds that 'for HIV, this approach may be more effective than the traditional vaccine approach of stimulating antibodies.'

Several of the 18 volunteers have already been screened for the trial, which has been through rigorous safety and ethical protocols. Although more than 25 potential HIV vaccines have been tested in humans, this is the first example of a vaccine candidate that is designed specifically for Africa, which has suffered the worst of the HIV epidemic.

methods such as nick-translation. The researchers speculate that this technology could also be used in single-nucleotide polymorphism (SNP) analysis and for intracellularly manipulating gene expression.

6 Demidov, V.V. *et al.* (2001) An artificial primosome: design, function, and applications. *ChemBioChem* 2, 133–139

Miscellaneous

GSK develops new R&D organizational strategy

At GlaxoSmithKline's (GSK) recent *Inaugural Media Meeting*, Jean-Pierre Garnier (CEO of GSK) oulined their new R&D organizational strategy for the recently merged company. He said that the R&D process could be broken up into three sections. The initial search for new drug targets from, for example, the human genome, which requires the use of expensive technologies, needs the involvement of the full company. However, after selection of a target, for a product to be found that works and that can be moved into the clinic, he said that 'the company needs to be nimble.' He said 'this is why biotechnology companies are so good at research and therefore we have created a structure in GSK that allows for this.'

Garnier has created six autonomous 'companies' within GSK. The objectives for these companies are to take the targets and discover new drugs, and then prove they work in the clinic. He said the final stage of preparing the dossier for the regulatory authorities is then best performed by the full 'mother' company. The six sub-companies will cover:

- Anti-infective drugs
- Cardiovascular, oncology and genito-urinary drugs
- Respiratory and anti-inflammatory drugs
- Metabolism, bone and antiviral drugs
- Psychiatry
- Neurology.

He said the plan was to have one financial resource across all the sub-companies and then offer incentives to the teams to work more quickly in their fields. Those that find novel drugs will be rewarded, even if their findings are actually more suitable for a disease in one of the other sub-company's areas.

Garnier was highly confident that this new strategy would work. He said: 'No-one has ever done this before but we are pretty much certain it will work. We have already conducted a trial of this strategy at SmithKline Beecham, where we isolated one area (antibiotics and antivirals), and we found that this group were able to work much faster than before.'

Large budget for Taiwanese herbal medicines development

The Chinese government has set aside NT$3.5 billion over five years for the development of Chinese herbal medicines in Taiwan according to *The China Post* (courtesy of John P. Stewart). Recently, some Chinese herbal medicines have been shown to be effective in the treatment of lung and liver cancer and the aim is to turn the island into an international centre for herbal medicines. However, only NT$200 million of the NT$500 million allocated for this year has actually been distributed because few people are actually aware of this program.

Aradigm and Genentech agree to discontinue development of rhDNase

Aradigm Corporation (Hayward, CA, USA) have mutually agreed with Genentech (San Francisco, CA, USA) to discontinue the development of rhDNase using Aradigm's proprietary AERx® pulmonary drug delivery system. rhDNase is the active ingredient in Genentech's currently marketed product Pulmozyme® (dornase alfa) inhalation solution. The decision was blamed on commercial considerations and the two companies will now be investigating the feasibility of using AERx in relation to other Genentech compounds. As part of this new agreement, Genentech will not require Aradigm to repay the loan of funds required to conduct development to date.

RNA Cancer Research Center established in Berlin

It was recently announced that a National Foundation for Cancer Research (NFCR) Center is to be established in Berlin (Germany). The Center, funded by the NFCR, will draw on the expertise of scientists from the Freie Universität of Berlin (Germany) and the RNA Network, a body formed to administer and coordinate RNA-based projects in the Berlin area, and will focus on cancer-related RNA-derived research.

The new Center will be headed up by Volker Erdmann, a pioneer in RNA research and Chairman of the RiNA. The NFCR is one of an international network of centres and will offer opportunities for collaboration will other centres around the world through a flexible funding mechanism. The Center will also enable Volker Erdmann and his team to carry out some bold and blue-sky research in the hope of finding new breakthroughs in the treatment of cancer.

Website for information on Singapore biomedical research

The Economic Development Board and the National Science and Technology Board of Singapore have launched a website, which aims to provide information on biomedical sciences-related activities and initiatives in Singapore, according to the *Straits Times Weekly*, Singapore (courtesy of John P. Stewart). Bio-Singapore.com is intended to include information on new technologies being developed that have commercial potential as well as provide information to entrepreneurs on how to start up new biomedical companies.

Unique global anti-cancer alliance re-declares aims

The World Summit Against Cancer (WSAC) initiative re-declared its aim to defeat cancer within our lifetimes. The initiative, under the auspices of the United Nations Educational, Scientific and Cultural Organization (UNESCO) and supported by Bristol-Myers Squibb and Ortho Biotech, brings together politicians, economists, cancer researchers, healthcare professionals, patient advocates, celebrities and industry from around the world in an attempt to coordinate available resources most effectively.

Since the first year's Summit, held in February 2000, more than 50 agencies, such as the Australian Cancer Society, the Cancer Research Campaign (UK) and The Susan G. Komen Breast Cancer Research Campaign (USA) have joined the initiative. This year's Summit will focus on tobacco and cancer, research, education and training, and patient advocacy.

Institutions join forces to find cause and cure for arthritis

Top researchers from the University of Maryland School of Medicine (Baltimore, MD, USA), The Johns Hopkins School of Medicine (Baltimore, MD, USA) and the National Institutes of Health (Bethesda, MD, USA) will be brought under the same roof for the first time in the new Maryland Arthritis Research Center (MARRC; Baltimore, MD, USA), launched by the Arthritis Foundation (Maryland Chapter, MD, USA).

The MARRC will focus on looking into how abnormalities in the immune system cause arthritis and related disorders such as rheumatoid arthritis, systemic lupus, erythematosus, scleroderma and polymyositis and, ultimately, find a cure. This initiative is being initially funded by the Arthritis Foundation, but will also receive a US$3 million start-up grant to ensure its financial viability for its first three years. Arthritis is the top cause of disability in the US and affects one in every six Americans.

First Virtual Research Institute established

A Virtual Research Institute has been set up by Boehringer Ingelheim (Ingelheim, Germany), which they say is the first of its kind. The Institute will focus on aging and is designed to create a virtual network of scientists in the Pan-Pacific area.

Haruo Sugano, the Honorary Director of the Cancer Institute in Japan will be heading the Institute, which is hoped to increase the knowledge base of biology and to obtain access to innovative research programmes.

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People

Four new Directors for Exelixis

Four senior scientists join the drug discovery team at Exelixis (San Francisco, CA, USA). Peter Lamb joins as Senior Director of Molecular Pharmacology and Structural Biology, Kirk McMillan joins as Director of New Lead Discovery, John Nuss joins as Senior Director of Chemistry and Yifan Zhai joins as Director of Pharmacology. George Scangos, President and CEO of Exelixis, hopes that these appointments will help accelerate the pace of the company's drug discovery pipeline.

Lamb comes to the position from being Director of Transcription Research at Ligand Pharmaceuticals. He also has a background in cell-based assays for lead discovery and characterization, as well as in signal transduction and oncology. McMillian joins the company from Pharmacopeia, where he was Assistant Director of Drug Discovery. His research background specifically covers human nitric oxide synthase, as well as the general fields of biochemistry and combinatorial chemistry. Nuss leaves the job of Director of Organic and Medicinal Chemistry at Chiron Corporation to provide Exelixis with expertise in small-molecule drug discovery and combinatorial chemistry. He also has a background in oncology and diabetes. Zhai comes from the position of Senior Research Scientist in the Department of Cancer Research at Bayer where he worked as part of the Bayer–Millennium Pharmaceutical Joint Cancer Team.

Long joins KuDOS Board

Ronald Long, Deputy Chairman of Amersham Pharmacia Biotech (APBiotech) and Vice-Chairman of Nycomed Amersham, has joined the Board of Directors of KuDOS Pharmaceuticals Ltd (Cambridge, UK) as Chairman. Previous positions held by Long include CEO of APBiotech since the merger of Amersham International's Life Science with Pharmacia Biotech, before which he was Commercial Director and then Managing Director of the Life Science business.

US Director for Singapore genomics program

Edison Liu, Director of the Division of Clinical Sciences of the National Cancer Institute (Bethesda, MD, USA) has been appointed as Executive Director of the Genomics Program for the Republic of Singapore. This appointment comes at a time when the republic plans to spend ~US$4 billion on their biomedical research infrastructure over the next 4–5 years. On the appointment, Liu said: 'The dream of genomic research requires significant partnerships between academia, industry and government. The Government of Singapore is unified, organized and strategic and, together with the academic establishment, pro-industry. Singapore is a country that understands and is committed to scientific development.'

Other advantages of Singapore cited by Liu were the highest educational standards in mathematics and science in the world and English as the spoken language. He also suggested that there could be specific significant advantages for genetic research in Singapore, saying that, 'The relevant resources for human genomics research are the ethnic diversity and the well-kept clinical databases. Such untapped resources might help speed up genetic research.' The main goal of the program is the creation of a database of Asian genomic information.

New CEO for EPIcyte

Christopher Clement, recently Senior Vice-President and Chief Marketing Officer of Ares-Serono Group, has just been appointed to the post of CEO of EPIcyte Pharmaceuticals (San Diego, CA, USA). Clement is hoped to bring significant expertise in operation and product development in the pharmaceutical and biotechnology industries. Clement has previously also been responsible for the US women's health business in the Ares-Serono Group, together with a variety of management positions at Searle Pharmaceuticals, Ciba-Geigy and Merck and Co.

Mich Hein, President of EPIcyte said: 'Chris has a proven track record in the planning and introduction of pharmaceutical and biotechnology products. This will be key as EPIcyte further develops its internal pipeline in the initial areas of infectious disease and sexual health and in broader corporate licensing arrangements of the Plantibody™ technology.'

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