

# Gene Therapy NEWS



The **Human Genetics Advisory Commission** (HGAC; London, UK) set up to consider the "broad, social, ethical and/or economic consequences of developments in human genetics" met for the first time on February 28. One of the first subjects discussed was the announcement on February 19 that the **Association of British Insurers** (ABI; London, UK) - an organisation with 440 member companies representing virtually the whole of the British insurance company market - will require people seeking life insurance to disclose the results of any genetic tests they have taken.

This will apply for the next two years as a way of predicting the effects of genetic tests on the insurance company, according to **Tony Baker**, deputy director general of the ABI. He says that the ABI is "unlikely to change that stance after two years as the statistics gathered over two years are unlikely to indicate the degree of vulnerability of the industry." At the moment, the results of a test will not affect applicants if the life insurance policy is linked to home purchase up to £100,000. So an applicant with family history of Huntington's disease, for instance, would have a higher premium compared with an applicant with no family history. If, however, the applicant took a test which was negative, he or she would be able to get a normal premium, according to Baker. If the applicant took the test and was positive, the premium would still be assessed on the basis of family history. A positive test for Huntington's would mean that an applicant would find it very difficult to get life insurance, but applicants with family history of Huntington's are equally unlikely to get life insurance. Baker stressed that no-one would be required to take a genetic test before applying for insurance.

The next stage for the ABI is to establish a genetics committee to draw up a list of genetic tests, the results of which would

have to be disclosed. Many of these tests are still in the very early stages of development. The committee would also establish a code of practice to regulate the confidentiality, handling and use of the information. The committee's aim, says Baker, "is to ensure that the information is correctly used by the companies."

The HGAC decided to set up a group to explore the issues raised by the ABI announcement. The group will report on the effects of the new developments in human genetics on insurance, patents and employment at the next meeting which will be held on May 15. The HGAC will also receive and consider a report of the genetic services provided by the National Health Service at the next meeting in order to discuss the ways this information could be used for treating inherited disorders and cancer. The members of the HGAC are Colin Campbell (chair), Cairns Aitken, Michaela Aldred, Martin Bobrow, Doris Littlejohn, Norman Nevin (chair of the UK Gene Therapy Advisory Committee), Onora O'Neill, John Polkinghorne (UK Advisory Committee on Genetic Testing), George Poste (chairman of research and development at Smithkline Beecham) and Moira Stuart (a British TV news presenter).

**Introgen Therapeutics** (Austin, TX, USA) has received a \$5 million milestone payment from **Rhone Poulenc Rorer** (RPR; Paris, France) as part of the two companies' \$50 million collaboration on *p53* and K-ras gene therapy which started in 1994. Introgen's ongoing Phase I clinical trials have confirmed that delivering a normal *p53* tumour suppressor gene using an adenovirus has a therapeutic effect in tumours caused by *p53* mutations. Phase II/III trials on the *p53* therapy are expected to begin later in 1997 in the US for head and neck cancer. Phase I trials in head and neck cancer, and in hepatocellular cancer are scheduled to begin in 1997 in Europe while an Investigational New Drug application has been filed in Japan for a Phase I clinical

trial on non-small cell lung cancer.

**ARIAD Pharmaceuticals** (Cambridge, MA, USA) and **Genovo** (Philadelphia, PA, USA) have formed a collaboration to develop gene therapy products, combining ARIAD's gene expression regulation technology with Genovo's gene transfer technologies. The aim is to develop constructs for injection into muscle or skin, the expression of which would be initiated by oral administration of a small molecule drug in a dose-dependent manner. This could be achieved using Genovo's viral and non-viral vectors to deliver ARIAD's two part transcription factor constructs. ARIAD's constructs initiate expression of a therapeutic gene such as growth hormone on binding in a tripartite interaction with the drug rapamycin (see *Gene Therapy News* 3: 842). A product may be ready for clinical trials in 1998.

**Genzyme** (Cambridge, MA, USA) has agreed to acquire the genomics company **PharmaGenics** (Allendale, NJ, USA) in exchange for 4 million shares of Genzyme stock. PharmaGenics' serial analysis gene expression (SAGE) technology will be incorporated into the new Genzyme

## News in Gene Therapy

Gene Therapy's News section covers scientific and commercial news. The News section is produced by the London editors of *Nature Biotechnology* magazine and includes company news, news of clinical progress and research news. Gene Therapy News also welcomes correspondence (scientific and otherwise) and information on forthcoming meetings, personnel changes and research funding. Items for consideration should be sent by electronic mail, or by fax or mail to:

Gene Therapy  
Attention: Dr Emma Johnson  
Macmillan Magazines  
Porters South  
4-6 Crinan Street  
London N1 9XW, UK  
Tel: +44-171-843-4991  
Fax: +44-171-843-4998/4996  
Email: e.johnson@biotechnology.com

Molecular Oncology (GMO) division which will concentrate on four key areas: genomics, gene therapy, gene diagnostics and small molecule combinatorial chemistry for drug discovery. The GMO division will market and licence SAGE to other biotechnology companies, creating funding for its initial research commitments. These are two gene therapy programmes for melanoma and various projects in the immunotherapy, tumour suppressor and cytotoxic gene fields.

**AASTROM Biosciences** (AASTROM; Ann Arbor, MI, USA) has announced an initial public offering of 3 million shares of common stock at \$7 per share. AASTROM's leading product is the AASTROM<sup>TM</sup> Cell Production System of disposable cassettes and reagents for clinical cell culture for stem cell therapies.

**GeneMedicine** (The Woodlands, TX, USA) has received clearance from the US Food and Drug Administration (FDA; Rockville, MD, USA) to start a Phase I clinical trial using its proprietary non-viral delivery system to deliver IL-2 for the treatment of head and neck cancer. The IL-2 construct will be administered via direct injection into the tumour thus avoiding some of the toxic side effects of systemic IL-2 administration. The announcement triggered a \$500,000 milestone payment from **Boehringer Mannheim** (Boehringer; Mannheim, Germany) as part of the agreement signed in July 1995, under which Boehringer has already made payments to GeneMedicine of \$11 million in research funding and \$8 million in equity investments. Additionally, Boehringer's parent company, Corange Ltd. (Bermuda), bought \$4 million worth of GeneMedicine common stock at \$7.5 per share, raising its shareholding in GeneMedicine to 10%.

**Oxford BioMedica** (Oxford, UK) has acquired exclusive licensing rights to **Isis Innovation's** (Oxford, UK) hypoxia response element technology which is a gene switch for selective destruction of solid tumours. Oxford Biomedica hope to use the switch in combination with its retroviral delivery system in cancer therapies. **Peter Nolan**, former head of the biotechnology unit at the **UK Department of Trade and Industry** (London, UK), has been appointed director of operations and **Chris Bebbington** will be head of research, joining from **Celltech** (Slough, UK) where he was head of the gene therapy programme.

**Targeted Genetics** (Seattle, WA, USA) has begun a Phase II clinical trial of its AAV-CFTR treatment to prevent sinusitis in cystic fibrosis patients. The Phase I clinical trials demonstrated that the vector, tgAAV-CFTR, causes no damaging side effects, and provides efficient gene transfer resulting in gene persistence for up to 70 days. The 50 patients in the Phase II will receive tgAAV-CFTR in one sinus and a placebo in the other. **Phyllis Gardner**, associate professor of molecular pharmacology and medicine at Stanford, is the principle investigator in the double blind trial at the **Stanford Medical Center** (Stanford, CT, USA).

**Onyx Pharmaceuticals** (Richmond, CA, USA) has expanded its Phase I clinical trial using the ONYX-015 adenovirus that targets p53-deficient tumour cells to include pancreatic cancers as well as head and neck cancers. In normal cells, the adenoviral protein E1B 55k protein binds to p53 so that the virus can take control of the infected cell, replicating many times before killing the cell and infecting neighbouring cells. This protein is deleted in ONYX-015 viruses so they cannot

replicate in normal cells, only in p53-deficient tumour cells which produces selective elimination. The extended trial on pancreatic cancer patients will be carried out at the **University of California, San Francisco Medical Center** (San Francisco, CA, USA) under **Sean Mulvihill**, principal investigator, **Alan Venook** and **Robert Warren**.

Preliminary results from **Cell Genesys's** (Foster City, CA, USA) Phase II clinical trials on an AIDS gene therapy have prompted the company to plan expansion in the form of a new manufacturing process and pilot trials for enhanced detection of the antiviral effects of replication-inhibiting drugs in patients. Results from the trial show that killer T cells from a healthy identical twin, that are engineered to selectively destroy HIV-infected cells and infused into an HIV-infected twin, persist for at least six months. The cells were administered in conjunction with antiviral drugs including protease inhibitors but Cell Genesys hope that elimination of the HIV-infected cells will reduce this continuous requirement.

**Cantab** (Cambridge, UK) and **Marie Curie Cancer Care** (MCCC; London, UK) have formed a new company, **Phogen**, to develop the VP22 herpesvirus technology developed by **Peter O'Hare** at the **Marie Curie Cancer Research Institute** (Oxted, UK) as a transport system for therapeutic molecules such as drugs, genes or proteins. MCCC will licence VP22 to Phogen and Cantab will fund research for the first two years. Both companies will have equal share in Phogen equity. VP22 is exported from the cell into the nuclei of surrounding cells so drugs or genes linked to the protein will be targeted to cell nuclei. *Nature* **385**: 721-725

## RESEARCH

Using an adenovirus vector carrying a GDNF gene, researchers at the **University of Rochester** (New York, NY, USA) have protected rat brains against the Parkinson's-like symptoms of dopaminergic (DA) neuron deterioration, induced by the neurotoxin, 6-hydroxydopamine (6-OHDA). Forty-two days after OHDA injection, only 21% of the DA neurons had deteriorated in rats that had received the GDNF vector

compared with 69% of rats who received a mutant GDNF gene, a vector carrying a marker gene or no vector. *Science* **275**: 838-841

Challenge with the purine, adenosine, produces marked airway obstruction in asthma sufferers. Using an antisense oligodeoxynucleotide (ODN) targeted to the human adenosine A<sub>1</sub> receptor mRNA, which also inhibits binding in the allergic rabbit model, **Jonathan Nyce** at **EpiGenesis Pharmaceuticals** (Greenville, NC, USA) and James

**Metzger** at the School of Medicine at **East Carolina University** (Greenville, NC, USA) desensitised rabbits to both adenosine and the dust-mite allergen. Rabbits which received adenosine in combination with the ODN exhibited a 75% decrease in A<sub>1</sub> receptor density compared with control rabbits and this effect was dose-dependent. ODN-treated rabbits also had a 61% reduction in bronchial hyperresponsiveness in response to histamine challenge. *Nature* **385**: 721-725