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*Br J Ophthalmol* 1999 83: 389  
doi: 10.1136/bjo.83.4.389

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## Newsdesk

### Prospects for gene therapy

Three research groups have reported their success with a novel approach to gene therapy in which inactive therapeutic genes are introduced into the body and then precisely controlled by administration of a pill which activates them for a predetermined time. This represents a new form of drug delivery according to the researchers and opens the door to many treatments not previously thought possible. The group led by James H Wilson, director of the Institute for Human Gene Therapy at the University of Pennsylvania used a patented technology from the biotechnology company ARIAD Pharmaceuticals Ltd, known as ARGENT gene activity, to introduce the new genes into the organism via a muscle-directed approach. Using an engineered version of the adeno-associated virus (AAV) vector, which achieves long term protein secretion without inducing an immune response, the researchers have introduced the gene for erythropoietin under control of the antibiotic rapamycin.

### Radical proposals for clinical governance by the RCP

Radical and comprehensive proposals have been put together by the Royal College of Physicians of England to set standards of practice for physicians in the UK as part of the profession's response to the government's drive towards clinical governance. These include annual job review and performance appraisal by a clinical or medical director; a personal development plan for all doctors, which would include analysis of the doctor's clinical performance in such activities as ward rounds and outpatient clinics, for instance, teaching, and research; a requirement to participate in all local and national audits and to put into effect the recommendations from such procedures; the setting up of a standards committee that would oversee the management of the programme; and peer assessment using multidisciplinary teams. In addition, the RCP is producing guidelines on "Good medical practice for physicians". There is little doubt that such proposals are welcomed, and other colleges are likely to follow suit as evidenced by the publications emanating from the College of Ophthalmologists to name but one, but it is probably too late in view of the government's determination to introduce separate procedures for clinical governance. The nature of medical practice in the UK is clearly undergoing a continued process of change and overhaul.

### Angiogenesis inhibitor preserves function in spinal cord injury

Researchers at Vanderbilt University in Tennessee have shown (*Proceedings of the National Academy of Sciences of the USA* 1998;95:13188-93) in a mouse model of spinal crush injury that intravenous injection of an inhibitor of angiogenesis, which they

termed CM101, allowed full recovery of function in over 90% of the tested animals compared with none in the placebo treated controls. This remarkable result was attributed to the belief that much of the failure of neural tissue to recover is due to the fact that it usually meets competition from the faster growing non-neural scar tissue, which rapidly repairs the tissue defect. The role of cells involved in wound healing modulating the overall recovery of injured nerve tissue was further underlined by a report showing that macrophages when exposed *ex vivo* to nervous tissue could promote the reconstitution of transected nerves (*Nature Medicine* July 1998). These results have implications for a wide variety of cases in which the wound healing response deleteriously affects nerve function and may be important for ocular conditions—for example, proliferative vitreoretinopathy, proliferative diabetic retinopathy, and the sequelae of glaucoma surgery.

### Gene therapy for retinitis pigmentosa?

A recent study of the rat model for retinitis pigmentosa (*Nature Medicine* 1998;4:967-71), which used ribozymes to repair a defect in codon 23 of the rhodopsin molecule, in which the amino acid histidine is substituted for proline, has shown that photoreceptor rescue is possible, at least in the short term. *In vivo* expression of either a hammerhead or hairpin ribozyme in this rat model apparently slowed the rate of photoreceptor degeneration for at least three months. Ribozymes, which are RNA molecules that can also act as enzymes by cutting a complementary mRNA sequence, would thus appear to have potential as a form of treatment for this dominantly inherited disease.

### Telomerase-expressing RPE cells for treatment of ARMD

Transplantation of RPE cells has been proposed as a potential treatment for certain forms of age related macular degeneration as well as retinitis pigmentosa. For instance, the "dry" form of macular degeneration, which is by far the commoner form of ARMD, is characterised by patchy RPE and choroidal atrophy, presumably owing predominantly to primary senescence of the RPE cells. However, a problem with the use of cells that have been cultured *ex vivo* before transplantation is that they apparently undergo accelerated aging when they are reintroduced into the organisms. Immortalisation of such cells by procedures involving oncogene manipulation is hazardous because of the possibility of initiating malignant changes in the cells. Now a team from Geron Corporation in collaboration with scientists at the University of Texas have found that inducing the expression of telomerase, an enzyme system involved in cell cycle regulation, can allow the indefinite proliferation of RPE cells as well as other cells

such as fibroblasts without apparently leading to dysregulated cell proliferation and tumour formation. In effect, it extends the lifespan of the cells by about three times the normal level, which is of particular value in RPE cells that might be used for transplantation. The company therefore believes that the regulated expression of telomerase can be used to postpone or even reverse senescence and age related pathologies, including ARMD, skin atrophy, and atherosclerosis.

### FDA approves vaccine for Lyme disease

Lyme disease, the infection caused by the organism *Borrelia burgdorferi*, affects the joints, skin, and eyes. Nearly 100 000 cases have been reported in the USA alone since 1982, causing a major health economic burden, but the disease may soon be under control if the vaccine LYMERix recently approved by the FDA in the USA proves to be effective. LYMERix is a genetically engineered product containing lipoprotein OspA, an outer surface protein from borrelia. The vaccine is marketed by SmithKline Beecham and is recommended for use by people in areas of risk.

### Human monoclonal antibody treatment for rheumatoid arthritis

Cambridge Antibody Technology (CAT; Melbourn, Cambridgeshire), producer of fully human monoclonal antibodies using phage technology, has reported encouraging results from a phase Ib/IIa trial of an anti-TNF $\alpha$  monoclonal antibody for the treatment of rheumatoid arthritis. The antibody, when administered either intravenously or by self injection subcutaneously, reduced the severity of the arthritis for periods of up to six months and allowed repeated injections of the antibody without the development of immunological reactions. Phage technology is a radically different procedure from conventional monoclonal antibody manufacture and CAT currently holds a phage library containing in the region of 100 billion human antibodies. Using high throughput techniques, CAT can produce information on 1000 target peptide antigens each month and with a further proprietary technique, CAT then has methods to determine whether the targeted antigen is relevant to initiation or progression of the disease or is merely participating in the disease process as an "epiphenomenon". In this way the importance of any particular gene product can be determined at an early stage. CAT plans to initiate three to four clinical programmes every year from the year 2000. In recognition of its contribution, and specifically for its development of a monoclonal antibody treatment for use as an anti-scarring agent in ophthalmology, CAT was awarded the coveted 1998 Prix Galien Award by the Rt Honourable Frank Dobson MP in January 1999 for which there are continuing phase I/IIa trials.