

## Newsdesk

### Drug discovery programmes and the human genome project

As the human genome project (HGP) reaches full identification of the 100 000 or so human genes, drug discovery programmes have been made much more effective and efficient. In addition, identification of proteins within the HGP has allowed their evaluation as drugs themselves. Some companies, such as Human Genome Sciences, Inc, capitalised on this approach even to the point where they have described the HGP as the pixelisation of the human (each new gene discovered being likened to a pixel on a computer image). Human Genome Sciences initially interacted with the Institute for Genomic Research, founded by J Craig Venter, and has patents that describe nearly 3000 full length, fully sequenced human genes. In fact, between 1993 and 1995, Human Genome Sciences isolated and sequenced more than 95% of all human genes, from 80% of which they have the potential to develop proteins. By using a process of rapid screening Human Genome Sciences can identify proteins with potential uses which have minimal or no side effects. Three of these are currently in some form of clinical trial—myeloid progenitor inhibitory protein 1 (MIP-1) which may be useful in protection of bone marrow progenitor cells during cancer therapy; keratinocyte growth factor 2 (KGF-2) which may also have uses in treatment of patients with skin and bowel cancer in promoting epithelial cell repair after radiation damage; and vascular endothelial cell growth factor 2 (VEGF-2) which is being assessed in treatment of ischaemic syndrome—for instance, in patients with peripheral vascular disease and diabetes. These new approaches to drug discovery and potential new therapies should also be of great value in ophthalmic diseases as we discover further genes regulating retinal cell function and control of intraocular pressure. However, since many ophthalmic diseases, especially those with a genetic component, tend to be rare disorders legislation akin to the US Orphan Drugs Act requires to be enacted in Europe. The first reading, therefore, of the Orphan Medicinal Products Act in March 1999 is welcomed by many in the pharmaceutical industry and should pave the way for considerably greater activity in this area by European biotech companies. Since the cost of bringing a new drug to the market could now be up to £400 million, according to the Office of Health Economics, new approaches to cutting these costs appear to be essential (Report: Updating the cost of a new chemical entity: Hannah E Ketler, Office of Health Economics, 12 Whitehall, London SWA 2DT).

### Corneal transparency

A recent study has addressed the question of the contribution that keratocytes might play in corneal transparency. In addition to the minimising effects on light scatter induced by the orthogonal arrangement of the fibres in the corneal stroma (destructive interference) and the periodic fluctuations produced in the refractive index by the regular arrangement of the components of the extracellular matrix,

keratocytes are now shown to contain abundant concentrations of enzyme systems which have similarities to lens crystallins (*J Cell Sci* 1999;112:613–22). Two water soluble proteins, the transketolase (TKT) and aldehyde dehydrogenase 1 (ALDH-1) are found only in keratocytes from transparent corneas and not from scleral fibroblasts or in cells from opaque corneas. The experiments were performed in rabbit keratocytes in vivo and in vitro and were initiated in an attempt to understand the corneal haze observed after excimer laser surgery in which backscatter appeared to derive from corneal keratocytes. The rabbit experiments revealed that this was because the “keratocytes” in the cornea after excimer laser were, in fact, myofibroblasts, which had migrated into the superficial cornea as part of the wound healing response, and that these cells did not contain the same concentration of crystallin-like molecules.

### Anticipating motion

The potential time difference between perception of motion and the actual event occasioned by the delay in transmission of the information from the retina to the visual cortex has for some time exercised visual psychophysicists, in finding the site at which compensation for this delay must occur. It is assumed that there must be some mechanism in place which will anticipate motion and currently this is thought to occur in the motion detection region of the visual cortex (see Newsdesk, *BJO* 1998;82:599). However, a recent paper in *Nature* (1999;398:334–8) suggests that motion anticipation is initiated in the retina itself where the first stages of visual processing occur—that is, the retinal ganglion cells (RGC). To do this, RGC apparently pool their information over large areas of the visual field encompassing many individual receptive fields. The mechanism is based on retinal cells using a biphasic firing response with inhibition of firing after a certain time delay which allows the peak firing rate to be shifted in time. At the same time the sensitivity of the cell to the stimulus is finely tuned to differences in intensity (contrast gain) similar to other cell responses adapting to light. Although the experiments were conducted in rabbits and salamanders, there is apparently sufficient experimental information and interpretation to indicate that similar mechanisms must also occur in primates, including humans. Intuitively, it would appear that this is likely in view of the very rapid responses which we make to anticipate moving targets—for example, in situations like driving motor vehicles. The dependence on contrast in such situations, compared with other types of motion detection, may be of considerable importance.

### UKTSSA

The United Kingdom Transplant Support Service Authority (UKTSSA) has published its preliminary report on overall activity of the service for the year 1998. The data highlight the shortfall in donors for corneal transplant (see Newsdesk, *BJO* 1998;82:8). There was a

10% fall in the number of donor corneas during this period but only a 2% fall in cornea transplant rates. While some regions such as Yorkshire, Wessex, Oxford, and the Republic of Ireland showed an increase in donor provision, many other regions such as Wales, Scotland, North and South Thames, and the Trent region showed significant drops in rates of donor supply. Areas with the greatest increase in corneal transplant activity were Trent, East Anglia, and Northern Ireland.

### Drug delivery systems for intraocular use

Phase II clinical trials of a new drug delivery system which involves direct intracameral instillation of dexamethasone in a polymer base have shown encouraging results in control of postoperative inflammation compared with conventional treatment with four times a day drop therapy, according to Oculex Pharmaceuticals (Sunnyvale, CA, USA). The drug polymer, Surodex, slowly degrades within the anterior chamber to deliver the drug and “eliminates concerns about toxicity”, according to company spokesmen, since no drug related adverse effects were reported during the course of the trials. Intraocular delivery systems appear to be under intensive development by several companies and would have significant advantages not only for eliminating toxicity but for delivering drugs directly to the site of action. Other conditions under active study are uveitis, age related macular degeneration, diabetic retinopathy, and cytomegalovirus retinitis.

### Save British Science

The organisation Save British Science (SBS) which, during the recent years and more than two governments, has been lobbying for improvements in the science base recently held a symposium in the wake of the British government's latest injection of financial and administrative reforms of British science. While SBS welcomed the change in attitude to science adopted by New Labour, the general view was that there was still considerable room for improvement. In particular, it was felt that British scientists are not sufficiently effective in converting basic research into commercial advantage because the gap between the bench and the factory is too wide. The £20 million fillip provided by the government in the University Challenge scheme to ease this problem was seen as too little: the scheme needs to be rerun in future years and to be expanded, according to SBS. The contrast with the American approach in which billions of dollars are poured into such schemes was highlighted. Value for money was also discussed but, in view of the risk element, expectations of success for all projects should not be unrealistic.

### Global theme issue

The 1999 global theme issue will be “Impact of new technologies in medicine”. Prospective authors please consider submission for this issue.



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