you cannot put a stop-codon in – a lot of the standard ways to try to verify that you are dealing with the right locus are just not available, so you have to invent new techniques.'

Hüttenhofer adds that it will be tricky to find a phenotype: 'Mutations in snmRNAs usually do not have the same dramatic effect as in proteins, since the nucleotide sequence is not translated into an amino acid sequence.' And, he continues, with behavioural diseases, it is a problem to find valid mouse models in the first place.

Damage to the control architecture

Despite all these hurdles, John Mattick, a geneticist at the University of Queensland (Brisbane, Australia; http://www.imb.uq.edu.au), believes that McInnes is heading in the right direction. Mattick has argued for years that RNAs have a crucial role in regulating gene expression. In fact, he thinks they might be more important than most people realize even today: 'While the genomes of the higher organisms have increased their protein-coding capacity substantially, the major increase has been a massive expansion of non-coding RNA sequences. I think that the shift from simple organisms to complex organisms required a radical change in the genetic operating system, so that gene expression could be co-ordinated and networked far more densely.'

Mattick claims that the regions in our genome that had been thought to be largely junk are in fact a sophisticated control architecture for eukaryotic systems (see Fig. 1, [2]). He is therefore convinced that snmRNAs have a crucial role in the development of disease. 'I think we have got past the phase now of identifying mutations that affect proteins and give you component damage (even though we have not identified all of them, by any means). Now, we are in the much more difficult phase of trying to identify mutations in this much larger amount of control architecture, which affect growth, development and physiology in much more subtle ways. But my bias is to think that the majority of the genetic components of common diseases lie in this architecture, rather than in changes or damage to the components.'

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Encapsulated cell technology could prevent blindness

Clyde M. Burnham, freelance writer

Inevitable blindness caused by retinitis pigmentosa could be a thing of the past. A team of researchers led by Weng Tao of Neurotech USA (http://www.neurotech.fr) have demonstrated a therapeutic technique in dogs – encapsulated cell technology – which holds promise for preventing the retinal degeneration of human retinitis pigmentosa [1].

Retinitis pigmentosa is a group of hereditary retinal diseases characterized by degeneration of the photoreceptor cells. Beginning in childhood, night blindness occurs first, then a loss of the peripheral visual fields and finally loss of the central visual fields. Over the course of several decades, the usual endpoint is total blindness. Seven of the 20+ mutations that cause the disease have been identified and characterized [2] with most of the described mutations affecting the phototransduction mechanism in the photoreceptor cells.

Preserving function

Several growth factors, neurotropic factors and cytokines have been shown to preserve photoreceptor cell function in animals [3]. Unfortunately, in most of these early studies the therapeutic agent was introduced into the eyeball by repeated injections. This is not, of course, a desirable technique for treating a long-term human condition.

Based on earlier work by her group at Neurotech USA, and by others, Tao engineered cells to produce human ciliary neurotrophic factor (CNTF), a factor that is protective of photoreceptor cells. Tao's group encapsulated the cells in a proprietary

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capsule of semi-permeable membrane. The pore size of the membrane is large enough to allow entry and exit of nutrients, waste products and the target therapeutic protein CNTF. The pore size, however, is too small to admit either antibodies or immune system cells. The implanted cells, and the factors they manufacture, are thus free of immune system attack in any host into which they are placed.

Animal models

Tao and colleagues implanted these capsules into one eye of dogs with the rcd1 model of canine retinitis pigmentosa. The capsules were in place for seven weeks, early in the life cycle of the dog, in which time almost 50% of the photoreceptor cell degeneration takes place. After seven weeks, the eyes with the implants showed an increased survival of photoreceptor cells, compared with the untreated eyes. There was a threshold effect, with CNTF levels below the threshold producing no protection for the photoreceptor cells. There was also a dose-related effect with higher levels of CNTF production providing increased survival of the photoreceptor cells. Perhaps of equal importance to the photoreceptor cell protection was that the eyes with implants showed no adverse effects. Tao, who trained in pediatrics and biophysics, is Vice President for Research and Development of Neurotech USA. She says that based on this and her earlier studies in animals, 'we would like to bring this technology to human clinical trials.'

Cell encapsulation

The technology of encapsulating live cells has been a central interest of Dwaine Emerich for a decade. Emerich, Vice President for Research of Sertoli Technologies (http://www.sertoli.com), says that safety and longevity are important as this work is carried forward in humans. Emerich's work has shown that fouling of the pores of the semi-permeable membrane could be the determining factor for longevity of the implant. His group, as well as Tao's, has shown useful function of encapsulated cells for time periods as long as a year [4]. He says, 'an implant lifetime of several years is entirely possible,' and adds that clinical trials in humans will show if there are unintended results caused by the implants. CNTF, although of human origin, could, when used alone, cause unexpected results as CNTF might require as yet unknown co-factors to be beneficial in the human eye. An equally possible alternative is that substances secreted along with CNTF by the encapsulated cell implant could be harmful to the human eye with long-term exposure.

Paul Sieving, a researcher at the National Eye Institute (NEI; http://www.nei.nih.gov) expects to collaborate with Tao's group in human clinical trials based on this research. He points out that his group at the NEI is increasingly conducting work that is guided by molecular biology and genetics. He welcomes the opportunity to help bring work such as this to clinical fruition, which could keep this type of hereditary blindness under control.

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Asia bioinformatics: a new import–export industry

J.C. Louis, freelance writer

The buzzword in bioinformatics in Asia at the end of 2002 is more 'jump-start' than 'start-up'. Ambitious government programs are providing the impetus for new ventures in Singapore and Japan. The two countries diverge, mirroring nearly opposite approaches: Japan finds off-shore start-ups to partner with its domestic giants, while Singapore spawns start-ups, and imports skilled labor or international partners to match its immense domestic investments.

Three of Japan's big-name computer firms – Fujitsu (http://www.fujitsu.com), Hitachi (http://www.hitachi.com) and Itochu (http://www.itochu.co.jp) – are actively involved in the bioinformatics arena. In July, Fujitsu announced bioinformatics software for high-speed genome analysis, which predicts the function of unknown genes by

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