both stimulate and inhibit cancer cell growth [3] additional pancreatic cancer cell lines should be studied before any general approach to pancreatic cancer can be formulated. Abbruzzese points out that many pancreatic cancers also overexpress epidermal growth factor (EGF), which is usually stimulatory and which the Korc group has shown also leads to poor prognosis. 'We have recently reported a Phase II trial in which we used a monoclonal antibody directed against EGF in patients with EGF positive pancreatic cancer. When the C225 monoclonal was given with standard chemotherapy, patients did fare better than those given standard therapy alone [4]. Using a soluble EGF receptor may also achieve a similar result,' says Abbruzzese.

Currently, Korc and colleagues are testing other forms of the soluble receptor and the protein itself for potential therapeutic activity but Korc stresses that all of this work is preliminary. 'Ideally, we would like to move forward to clinical trials within three years but there is so much more to do before considering trying this approach in humans, it is difficult to set a more precise timescale,' he concludes.

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Computer chip that could restore sight

Martina Habeck, Freelance writer

An artificial retina could one day offer useful vision to people who suffer blindness caused by diseases such as retinitis pigmentosa or age-related macular degeneration (AMD). Researchers are developing computer chips that are designed to imitate basic photoreceptor cell function; the microchip is to be implanted on the retina, where it would substitute for damaged cells, stimulating healthy neurons in the visual pathway. Scientists at the University of Southern California (USC; Los Angeles, CA, USA) have now gained FDA approval to test their implantable computer chip system in clinical trials. They hope to bring a product on the market within 3–5 years.

Vision loss from retinal degeneration

The retina consists of several cell layers that line the back of the eye. The photoreceptor cells, which are classified as rods and cones, are responsible for converting light into electrical impulses. These are relayed to ganglion cells, which transfer the signal via the optic nerve to the brain. However, when the photoreceptor cells are damaged by diseases, such as retinitis pigmentosa or AMD, the retina cannot process the light and the brain never receives impulses to form a complete image.

Blindness caused by retinal degeneration is a big problem. In 1997, the World Health Organization estimated that approximately 8 million worldwide are blind or severely visually disabled because of AMD (http://www.who.int/inf-fs/en/fact144.html), a disease caused by the degeneration of photoreceptors in the macula, the central portion of the retina responsible for perceiving fine visual detail. AMD is the most common cause of vision loss in older people and, because the global population is ageing, numbers are expected to increase further.

The number of people affected by retinitis pigmentosa is much smaller, but symptoms, such as loss of peripheral vision or night blindness, are already recognized in adolescents and young adults. The name retinitis pigmentosa refers to a group of inherited diseases that cause the degeneration of photoreceptors; the condition deteriorates throughout life.

Current treatment options for people with retinal degeneration are poor. Peter Dudley at the National Eye Institute (Bethesda, MD, USA) says, 'There is a real need to fix the problem.' The most popular approach to finding a cure is to look for a genetic culprit. 'But that has been difficult,' says Dudley, 'simply because it is like many complex diseases, such as diabetes, where you are likely to have many factors involved in the disease.'

An artificial retina

In an alternative approach, groups in the USA, Germany and Japan are working on strategies to bypass the damaged retina with an implantable computer chip. One

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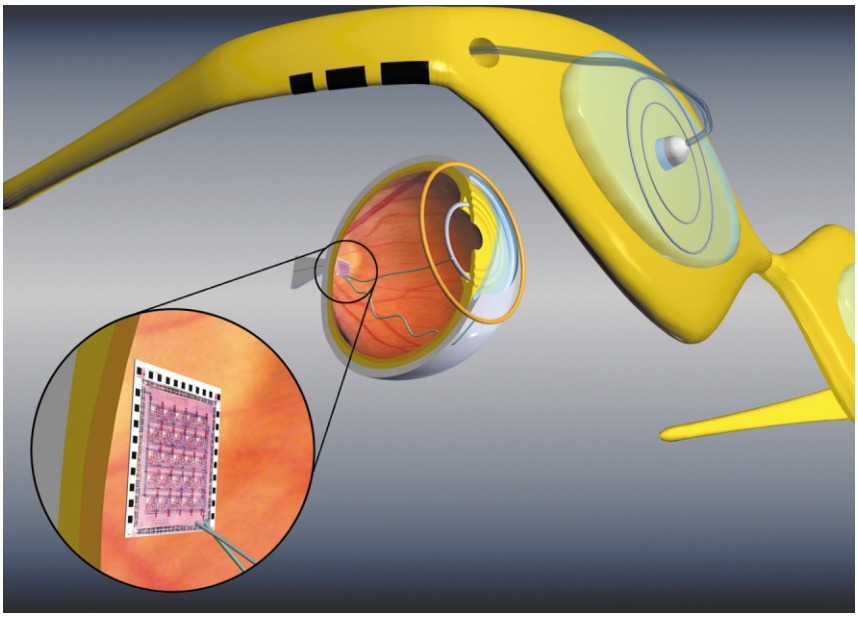

Figure 1. The retinal chip system. An external camera, mounted on a pair of glasses, captures a video image and transmits the image data by means of radio waves to the retinal chip. The yellow and blue rings are antennae implanted in the front part of the eye; they help to transfer power and data from the eye glasses to the chip. The magnified inset shows the computer chip implanted on the retinal surface. The entire device is powered by a battery pack (not shown) that can be worn in a front shirt pocket or on the belt. Kindly provided by Mark Humayun and the Intraocular Prosthesis Group at the Doheny Retina Institute at the University of Southern California (USC; Los Angeles, CA, USA).

of these teams is led by Mark Humayun at the USC. Fifteen years ago, inspired by the cochlear implant work, Humayun began to design a retinal equivalent. Humayun says, 'The chip was developed through close collaborations between physicians and engineers on our team.' Wentai Liu at the Department of Electrical and Computer Engineering at the University of North Carolina (Raleigh, NC, USA) helped them design and fabricate the first chip.

Since then, the chip has already undergone five different reiterations. Humayun explains that the latest device works as follows: a small camera (<1 cm in size), which is mounted on a pair of glasses, captures the image, digitizes it and then sends it wirelessly to a tissue-thin receiver chip, which is implanted directly on the retina near the ganglion cell layer (Fig. 1). The silicon chip receives the information, decodes it and then passes minute pulses along tiny platinum electrodes to excite healthy retinal neurons. 'When this information is transmitted to the brain via the optic nerve, the patient begins to see,' Humayun adds.

Early experiments in humans confirmed that the concept works [1]. Humayun and colleagues temporarily placed stimulating electrodes on the retina of blind volunteers. The electrodes were connected to an external computer chip, which emitted impulses representing various patterns. The patients were able to see spots of light and even recognize simple shapes.

Future work

Many issues still need to be investigated. For example, the team needs to show that the computer chip will remain in place and that the retina will tolerate the foreign device for several years. In experiments with dogs, the investigators implanted an electronically inactive electrode array onto the retinal surface. There was no significant damage to the underlying retina and the platinum and silicone arrays, as well as tiny metal tacks to keep them in position, were biocompatible and remained in place for 11 months [2]. To protect the computer chip from the vitreous fluid of the eye, the scientists have devised a hermetic seal made of ceramic and titanium.

Work has also begun to determine the electric charge necessary to stimulate the neurons. Other challenges include finding the proper frequency and kind of current to use, and finding the right size for the electrodes. Getting these parameters right will help to avoid the system's electromagnetic fields generating so much heat that the retina is burnt.

Based on the results so far, the USC group has won FDA approval for clinical trials, which it is planning to start within the next six months. From there, it will still be a long way before vision for the blind becomes reality, but the prospects are promising. Dudley concludes: 'It is not going to be a very good image, but if you are blind from a disease, any kind of indication of whether it is night or day, or where the doorway is, will be of tremendous benefit.'

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