New drug helps close macular holes

A drug that improves on the current approach to treating macular holes, a disorder that can result in severe loss of vision, shows increasing promise in patient trials.

The drug consists of TGF-beta$_2$, a growth factor protein that plays a key role in healing wounds. Originally derived from cow bones, the substance can now be made in the laboratory to better meet the increasing demand, says Ann Hanham, medical director of Celtrix Pharmaceuticals in Santa Clara, Calif., the company that developed it.

In the early 1990s, Bert M. Glaser and his colleagues at St. Joseph Hospital in Baltimore tested the growth factor for the first time in humans. Vision improved in 10 of the 11 patients who received the highest dose. They could see at least two additional lines on a standard eye chart, Glaser's group reported in the July 1992 OPHTHALMOLOGY. In a separate study, about half the patients undergoing traditional surgery for macular holes had improved vision, compared to over three-quarters of patients receiving the new treatment, says Hanham.

Within a month, researchers at three hospitals will finish enrolling patients for a final efficacy trial. In that study, surgeons will use either the new drug treatment or the standard procedure on 120 volunteers and will follow the patients for 12 months. This is the first trial to employ a recombinant form of the growth factor, rTGF-beta$_2$.

The study is taking place at the University of Miami School of Medicine, the Beaumont Hospital in Royal Oak, Mich., and St. Joseph Hospital.

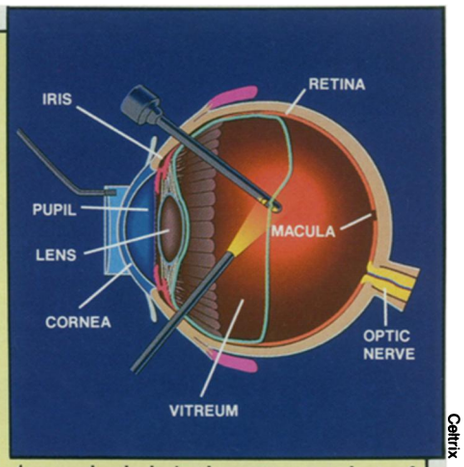
In response to the Food and Drug Administration's recommendation to meet patients' demands for the new treatment, Celtrix has applied to FDA to begin selling the drug this fall – after it sees the initial results from the current study, yet before FDA approves full-scale commercialization of the product, says Hanham. The company would provide the drug to about 500 additional patients at the three centers. Celtrix also hopes to distribute the growth factor to seven more centers by 1995.

So far, approximately 700 people have received the drug as part of various safety and efficacy studies, says Hanham, who addressed a conference on clinical trials organized by BIO/TECHNOLOGY magazine last week.

Glaser and his colleagues are also enrolling volunteers for a study investigating whether the growth factor can help treat the much more common age-related macular degeneration.

Macular holes occur in fewer than 10,000 people each year, primarily 50- to 70-year-olds, and usually are the result of aging. An eye injury, such as getting smacked with a baseball, can also create a hole.

The hole "results in a very distinct anatomic change" and leaves individuals unable to read or drive, Hanham explains. It normally occurs when the eye's vitreum shrinks and pulls away from the retina. Pockets form around the hole and under the retina, collecting fluid and creating "quite a severe loss of vision," she says.



Celtrix

A macular hole in the eye gets a dose of growth factor from a tool (above), while a light (below) illuminates the procedure.

Normally, surgeons simply remove the vitreum to prevent it from pulling on the retina and replace it with a gas bubble, which eventually fills with natural fluids.

The new approach involves these same procedures, but physicians drip growth factor on the hole to encourage healing. The protein forms fibrous tissue, heals the hole, and seals the edges of the retina, Hanham explains. However, surgery on the vitreum usually results in cataracts, which can be removed.

If the FDA approves the product for sale, "it's going to be expensive," Hanham acknowledges. – *T. Adler*

Some cigarette makers manipulate nicotine

In testimony before Congress 3 months ago, Food and Drug Administration Commissioner David A. Kessler laid out circumstantial evidence that tobacco manufacturers manipulate the amount of nicotine in U.S. cigarettes – presumably, he said, to foster addiction to their products (SN: 5/14/94, p.314).

Last week, Kessler again testified before the House Subcommittee on Health and the Environment. This time, he documented compellingly how one company controls the nicotine in its products.

The proof developed out of documents obtained from the Louisville, Ky.-based Brown & Williamson (B&W) Tobacco Corp. and interviews conducted with its officials. Sifting through the information, FDA learned that B&W had bred a tobacco known as Y-1. Its leaves contain more than 6 percent nicotine by weight – twice that in most comparable tobaccos.

Y-1 apparently traces to unsuccessful attempts at creating high-nicotine tobaccos during the 1970s by breeder James F. Chaplin, then with the U.S. Department of Agriculture. Chaplin shared seeds for several experimental lines – none yielding unusual nicotine levels – with B&W. Using a mix of conventional and advanced breeding techniques – such as anther culture, tissue culture, hybrid sorting, and protoplast fusion – B&W eventually produced Y-1.

The company then shipped seeds of the new breed to Rio Grande do Sul, Brazil, where they were planted. It imported harvested leaves back to the States. B&W, which has more than 3 million pounds of Y-1 in U.S. warehouses, included the tobacco last year in some of its Viceroy, Richland, and Raleigh cigarettes. Why? B&W told FDA it wanted to reduce the tar in its brands while maintaining traditional levels of nicotine.

Kessler also cited at least one unnamed U.S. cigarette maker that adds ammonia to chemically alter – or free up – nicotine in its tobacco. "It is our understanding," Kessler testified, "that an experimental cigarette made of reconstituted tobacco treated with ammonia has almost double the nicotine-transfer efficiency [bioavailability]" of untreated tobacco.

Additional evidence Kessler presented illustrates that B&W and other cigarette makers have known for decades not only that nicotine is addictive, but also that it possesses other pharmacological (tranquilizing) properties. Such data help establish the manufacturers' "intent" in controlling nicotine, Kessler testified. Intent is important because federal law defines a drug as anything "intended to affect the structure or function of the body."

Deliberately manipulating cigarette recipes to provide smokers with what manufacturers knew to be a pharmacologically active, addictive substance would amount to selling a drug, Kessler said. FDA would then be responsible for regulating this drug – unless Congress explicitly forbids it to do so. Kessler said FDA has been investigating cigarettes – and sharing its nicotine findings – in hopes of obtaining "guidance" from Congress on whether and how the agency should regulate cigarettes. – *J. Raloff*