THE NATION'S NEWSPAPER

Special e-print Edition

USA TODAY

NO. 1 IN THE USA

As seen in USA TODAY Life

February 13, 2006

Maze of cystic fibrosis is getting a little clearer

'Exciting time' as disease is fought from all directions

By Liz Szabo
USA TODAY

When Chip Hawkins was born, the prognosis for patients with cystic fibrosis was bleak. Most died as children.

Hawkins, now 38, shows how far patients with the rare genetic disease have come, experts say, and how their quality of life may improve even more.

Hawkins is a scientist at Baltimore's Johns Hopkins University, where he creates "transgenic" mice, some of which have been modified to carry the cystic fibrosis gene. That allows doctors to study the disease and test new medications.

"This is an exciting time," says Pamela Davis, a professor at Case Western Reserve University who specializes in cystic fibrosis. "We're almost at the point of changing this from a fatal disease to a nuisance."

Doctors today are attacking the disease at every level, thanks partly to the Cystic Fibrosis Foundation's efforts to jumpstart research, says Robert Beall, president and chief executive officer of the foundation.

Drug companies usually are reluctant to invest in a relatively rare disease, Beall says. They are more attracted to larger markets — such as the 100 million Americans with high cholesterol — than "orphan" diseases such as cystic fibrosis. About 30,000 Americans have the disease.

That's why the foundation pays for its own studies, Beall says. Its network of researchers now leads many of the early studies to test unproven therapies. Once those drugs appear effective — and have a greater chance of getting to market — biotech companies are more likely to take over.

If the therapies work out, the foundation uses its share of proceeds to finance other research. In all, the foundation has paid for more than 30 clinical trials since 1998.

"We have worked to reduce their risk of getting involved in cystic fibrosis," Beall says.

Advocates for other orphan diseases have been inspired by the foundation's success. In a recent report about ways to develop more drugs for pediatric cancer, the Institute of Medicine, which advises Congress on health, suggested that children's advocates study the Cystic Fibrosis Foundation's example.

Beall says the foundation is pursuing a number of strategies.

▸ **Gene therapy.** The disease is caused by mutations in a single gene. These mutations disrupt the flow of salt through the cells lining the lungs and pancreas. That leads people with cystic fibrosis to produce sticky mucus that clogs the airways of the lungs. Patients develop chronic lung infections which, for many patients, eventually prove fatal.

Scientists identified the gene in 1989. At the time, many experts predicted that a cure was around the corner, says Preston Campbell, executive vice president of medical affairs at the foundation.

Getting the gene where it needs to go, deep inside the lungs, has proved challenging. Initially, doctors tried delivering genes through a sort of Trojan horse, Campbell says. They hid them inside the shell of a empty cold virus, hoping the virus would "infect" lungs cells with the healthy gene. But the viruses irritated the body, which attacked the cold bug and caused inflammation.

Researchers have not given up, however.

Scientists are experimenting with delivering genes inside nanoparticles, ones small enough to slip through the cracks of a cell wall, "like wind going through a log cabin," Campbell says.

Years of progress

Progress in fighting cystic fibrosis has accelerated in recent years:

1953: Researchers develop "sweat test" to diagnose cystic fibrosis.
1950s: Pancreatic enzymes help patients improve their nutrition and maintain weight.
1989: Scientists discover the gene that causes the disease.
1993: The Food and Drug Administration approves Pulmozyme, the first biotech drug designed for cystic fibrosis. This enzyme breaks down the thick mucus that clogs patients' lungs.
1997: The FDA approves TOBI, or inhaled tobramycin, an antibiotic that helps fight dangerous infections.
2002: Research shows that Zithromax, or azithromycin, can improve lung function and reduce hospitalizations by half.
2006: Doctors show that inhaling very salty water can help clear mucus and prevent complications.

Source: Cystic Fibrosis Foundation

The youngest patients might benefit most from gene therapy, Davis says.

Doctors might have an easier time getting drugs or genes into babies whose lungs have not yet become clogged, Davis says. If doctors could correct their genetic defect, these children might never get sick. Eighteen states and Washington, D.C., test newborns for the disease, which allows doctors to treat them earlier; 13 states plan to begin screening babies in the next year or so.

▸ **Drugs to combat the protein involved in cystic fibrosis.** Finding the

gene has helped scientists better understand the underlying cause of the disease, Beall says. In people who have the disease, an abnormal gene leads to the creation of a defective protein, which keeps salt from moving around properly. Doctors would like to find a drug compound that could fix the protein or at least help it do a better job, he says.

In the past, scientists could screen two or three compounds at a time. New technology allows doctors to test thousands of compounds a day, Beall says. Doctors hope to test a number of promising compounds in patients by the end of the year.

▸ **Drugs with new uses.** The foundation is also supporting the study of drugs originally created for dry eye and rheumatoid arthritis, Beall says.

Hawkins says he is willing to join future clinical trials if he can help combat his disease. He says he is relieved that his health has remained stable for eight years.

"I don't ever feel impatient," Hawkins says. "These are small steps, but every year or so there are some new drugs.

"Until a cure is found, and as long as there are steady improvements, that's the way to go."