

long, 10 times the length of the average gene—researchers may turn up scores of mutations, and the task of cataloging the impact of all of them could take several years.

Despite such hurdles, diagnostic tests for some *BRCA1* defects could be available in 6 months to 2 years, predicts Donna Shattuck-Eidens, who led the *BRCA1* effort at Myriad. Myriad has applied for a patent on the gene and has licensed its use for the development of drugs and diagnostic kits to Eli Lilly, which, besides contributing people power to the winning effort, also funded Myriad to the tune of \$1.8 million.

Not everyone is thrilled by the prospect of an imminent *BRCA1* test, however. In a written statement, Fran Visco, president of

the National Breast Cancer Coalition, an activist organization of breast cancer patients headquartered in Washington, D.C., expressed concerns that “we may soon have a test that will tell a woman [that] she may have as much as an 85% chance of getting the disease, for which there is no known cure and which she cannot prevent.” The test may actually do harm, argues Visco, because women who test positive risk losing their health and life insurance (*Science*, 22 July, p. 464).

And for some, the gap between understanding the genetic basis of cancer and learning how to treat the actual disease needs the most concerted research effort. “We’re going to have many examples of people clon-

ing cancer-susceptibility genes, without any idea of how we are going to treat these people differently,” says Stephen Friend of Massachusetts General Hospital in Boston. National Cancer Institute director Samuel Broder agrees: At the NIH press conference, he pointed to one finding that has drawn little attention: A small minority of women can carry a mutant version of *BRCA1* and remain cancer-free into their eighties. That suggests that some as-yet-unidentified genetic, environmental, or dietary factors can ameliorate the impact of a rogue copy of *BRCA1*, allowing a woman to dodge her genetic destiny. Discovering those factors, says Broder, should be a “high research priority.”

—Rachel Nowak

CANCER TREATMENT

Boron Therapy Gets Early Test

Last week, for the first time in 33 years, U.S. researchers pumped a boron compound into the blood of a patient with incurable brain cancer, wheeled her up to a nuclear reactor, and irradiated her brain with neutrons. In theory, the boron compound will serve to concentrate the deadly effects of the radiation in the tumor, while sparing healthy tissue. But the patient, her family, and the researchers—a team at Brookhaven National Laboratory—can only hope that the theory will prove correct. The last time boron neutron capture therapy (BNCT) was tried in the United States, it failed to kill the tumors and even hastened the deaths of some patients. The researchers think they’ve now laid the groundwork for BNCT to work. But they never expected to be trying it this soon.

As this article went to press, the patient remained in good condition, according to her doctor, but complications from the therapy could arise anytime within the first several weeks. And while the patient copes with her medical uncertainties, BNCT researchers are facing uncertainties of their own, brought on by their decision to bow to political pressures and treat the woman months before they had planned to begin clinical trials of BNCT.

Just last summer the researchers were publicly voicing fears that premature trials could lead to a spectacular failure and kill research in the whole field (*Science*, 22 July, p. 468). But now, although Darrel Joel, chair of Brookhaven’s medical department, admits that he and his colleagues changed their plan under pressure from the patient, her family, and the Department of Energy, he maintains that the treatment was ready for clinical use. “We did not have all the information we might have had prior to treatment, but we were reasonably well prepared,” he says.

For BNCT to work, the boron compound has to concentrate selectively in the tumor.

There, the boron nuclei are meant to capture neutrons and fission into energetic fragments that kill the cancer cells. In the first trials, boron lingering in the brain capillaries spread the radiation damage beyond the tumor and killed four subjects. But since then researchers have developed better boron compounds and tested their promise by “curing” rats with implanted tumors, says Joel. And preliminary human studies, in which researchers infused the boron into brain cancer patients and tracked its distribution, convinced Joel and his colleagues that the disaster of 30 years ago won’t happen again.

They expected to treat their first few patients starting next year. But among the patients who took part in the distribution studies was a Long Island resident named Joann Magnus. Magnus, who has discussed her case freely with reporters, had surgery to remove the bulk of her cancer, an aggressive tumor called glioblastoma, last spring. When it recurred, however, she had a second surgery and decided to seek the full treatment.

When Brookhaven told her that its reactor was not going to be ready to deliver neutrons to experimental patients until 1995, she appealed to energy secretary Hazel O’Leary, whose agency funds Brookhaven. Her letter landed on the desk of Martha Krebs, a physicist who heads energy research and has said publicly that the Department of Energy has gotten a “slow start” in developing BNCT. Krebs says she then leaned on Brookhaven to speed up preparations to treat Magnus and other patients. Collaborating doctors at Beth Israel Hospital applied to the FDA for a special, one-time permit for testing the treatment, known as a single-patient IND (investigational new drug) protocol. The permit was granted, but the agency will

Ller Undergoes Novel Therapy
A Treatment Moving Moment Before Its Time
But doctors still wary of procedure
Ller fights lab for experimental therapy

not discuss its rationale for the decision.

The result was that Joel and his colleagues were unable to complete the series of distribution studies they had originally planned, and they’ve had to work faster than intended to ready the neutron beam. But Magnus’s doctor, Richard Bergland of Beth Israel Hospital, says Magnus was a good first patient. The site of her tumor made it easy to target with the neutron beam, Bergland says, and the distribution studies showed that the boron had concentrated in her tumor significantly better than it had in five other patients. “She was the perfect patient for this beam,” says Bergland.

Medical ethicist Arthur Caplan of the University of Pennsylvania thinks the decision to treat Magnus raises questions, however. A terminal condition doesn’t necessarily justify subjecting a patient to a potentially harmful medical experiment. “[Harm] could mean dying sooner, or dying more painfully,” Brookhaven’s Jeffrey Coderre responds that he and his colleagues were careful to calibrate the dose of boron and neutrons to safe levels.

Then again, if Magnus recovers, it may be difficult to hold back the floodgates of desperate patients. Joel says the treatment won’t be available to other patients until the researchers have watched Magnus’s progress for 2 or 3 months. But Brookhaven sources say that the publicity surrounding her case has already prompted a flurry of inquiries. And the pressure may jeopardize careful study of the treatment, says Caplan. “Compassion [can] make it impossible for us to learn what works and what doesn’t work.”

—Faye Flam

SOURCE: NEWSDAY