probe, which then channels them to a detector. "The probe can take two electrons if the [island] contains one extra electron pair, but zero electrons if the [island] doesn't have the electron pair," says Nakamura. "That's why we can distinguish the two electron states."

Still, Nakamura acknowledges that this simple demonstration remains far from a useful quantum computer. The main problem is that the paired electrons oscillate back and forth for only about 2 nanoseconds before they are torn apart and siphoned off by the probe electrode. "That's not enough to do any computation," says Nakamura. To be useful, researchers would like their qubits to be stable indefinitely. Efforts around the globe are now likely to focus on that goal, as well as on stringing a number of electronic qubits together to construct the first electrically controlled quantum computer.

–ROBERT F. SERVICE

CANCER RESEARCH

New Model for Hereditary Breast Cancer

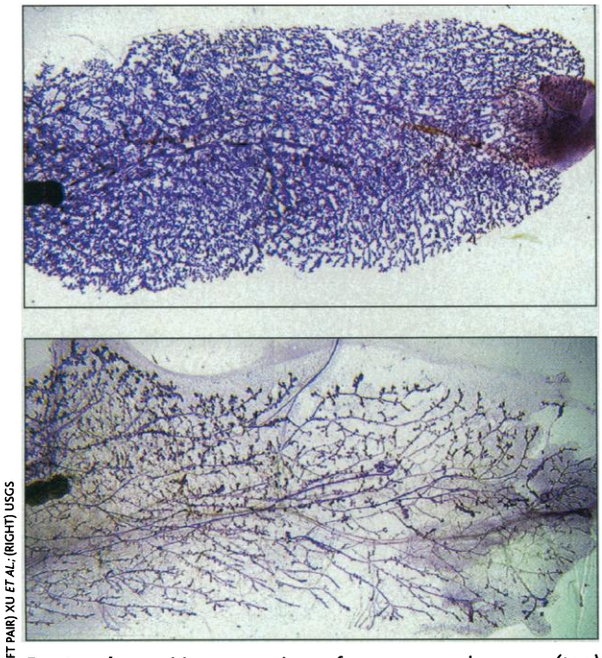
Breast cancer strikes about one out of nine Western women in their lifetime and is second only to lung cancer as a cause of cancer deaths in women. For women who have mutations in *BRCA1*, one of two genes linked to the 5% or so of the cases that are hereditary, the disease is even more fearsome. They have a 70% chance of getting it. Now, researchers have an important new clue about how breast cancer develops, at least in these women.

The clue, in the form of an animal model for the disease, comes from the joint effort of two teams led by Chu-Xia Deng and Lothar Hennighausen at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In a paper in the May issue of *Nature Genetics*, the researchers report that they have inactivated, or knocked out, the *BRCA1* gene in mice exclusively in the cells where breast cancer normally originates—the epithelial cells lining the milk ducts.

Previous efforts in which genetic tinkers knocked out one or both copies of the gene in all mouse tissues produced disappointing results. Women with *BRCA1* mutations are born with one inactive copy, while the other becomes inactivated later. But the animals with one inactivated copy did not get tumors at all, and those with two inactivated copies from the beginning died before birth. In contrast, the NIDDK team found that their animals do develop breast cancers, starting when they are about 10 months old. "This is quite exciting. Such an animal model is invaluable for understanding the role of *BRCA1* in familial breast cancer," says Andrew Futreal of Duke University Medical Center in Durham, North Carolina, a *BRCA1* co-discoverer.

In keeping with previous work indicating that *BRCA1* is involved in repairing defective genes, Deng, Hennighausen, and their colleagues have found that breast cells lacking an active *BRCA1* gene are prone to accumulating additional defects—most prominently the loss of the *p53* tumor suppressor gene—that might be crucial contributors to cancer development. What's more, Futreal says, the new animals could prove useful in evaluating new treatments or chemopreventive drugs that might delay or even block the onset of breast tumors.

To knock out the gene specifically in breast tissue, Deng and Hennighausen engineered a so-called conditional mutant mouse strain. They first created mice with a genetic tag, called a loxP sequence, at two different spots within the *BRCA1* gene. Then the team crossed the loxP mice with another transgenic strain carrying the gene for a molecular scissors, an enzyme called Cre recombinase. To make sure that the *Cre* gene is active only in the mammary epithelial cells, the researchers combined it with the regulatory DNA elements of a milk protein produced only in this tissue. The Cre recombinase recognizes the

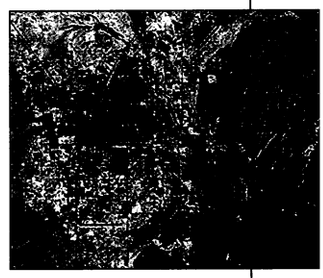


CREDITS: (LEFT PAIR) XU *ET AL.*; (RIGHT) USGS

Duct reducer. Mammary tissue from a normal mouse *(top)* shows a dense network of ducts, whereas tissue from a *BRCA1* conditional knockout *(bottom)* has far fewer ducts.

ScienceScope

Earth to NASA Researchers continue to have concerns about NASA's blueprint for a new generation of Earth-observing missions. Echoing earlier reviews, a National Research Council (NRC) panel last week said that although the space agency is on the right track with plans to launch a new group of smaller, cheaper, and more sophisticated probes starting in 2003, NASA still needs a science strategy to make sure it gets the most out of its orbiting fleet, which will monitor everything from land uses (right) to ocean temperatures.



The NRC group, led by atmospheric scientist Marvin Geller of the State University of New York, Stony Brook, also warned the agency against relying on a proposed polar orbiting satellite system to collect long-term climate data after an array of current instruments expire early next decade. "There is skepticism about putting all the eggs in that basket," says one academic. NASA earth science chief Ghassem Asrar was unavailable for comment, but one colleague predicts he "will be able to live with these recommendations."

New Blood Infusion Europe's top fusion research center is getting a change in leadership. After 18 years at the helm, Klaus Pinkau will step down on 1 May as scientific director of the Max Planck Institute for Plasma Physics in Garching and Greifswald, Germany. The new boss will be Alexander Bradshaw, director of the Fritz Haber Institute in Berlin and president of the German Physical Society.

Bradshaw, a chemist who switched to synchrotron studies of matter, inherits one of the continent's most active fusion programs. It is the European headquarters for the International Thermonuclear Experimental Reactor (ITER) project and is building Wendelstein 7-X, an experimental reactor, in Greifswald.

Pinkau—who will stay on as an ITER adviser through the end of the year—will be a hard act to follow, says Martin Keilhacker, director of the Joint European Torus in Abingdon, Britain. But he says Bradshaw is "a very good scientist and administrator."

Contributors: Eliot Marshall, David Malakoff, Alexander Hellemans

loxP sites and chops out the intervening part of the *BRCA1* gene, inactivating it. Sure enough, some of the resulting mice developed breast cancer in at least one of their 10 mammary glands between 10 to 13 months of age.

Deng concedes that there are slight differences between his mice and women with *BRCA1* mutations. Mice at 10 to 13 months of age are analogous to women in their 50s, while *BRCA1*-related breast cancers usually occur before menopause. Also, only 22% of the animals get the cancer, although Deng expects that more will as they age. Still, cancer biologist Bert Vogelstein of The Johns Hopkins University School of Medicine says that the animals provide the first "experimental system to figure out the way the *BRCA1* gene works."

The NIDDK researchers began getting their first hints of how *BRCA1* loss might lead to breast cancer when they looked at the milk ducts in mutant animals that were pregnant or lactating. "The mammary glands were smaller [in the mutants], and there is very sparse and sometimes abnormal branching" of the ducts, Deng says. At the same time the team observed extensive programmed cell death, or apoptosis, in the mammary tissue of mutant mice. "At first glance that looked quite inconsistent" with a gene abnormality that supposedly predisposes to the excessive cell proliferation of cancer, Deng says.

A peek at the chromosomes of tumor cells helped explain this apparent paradox, however. In cells lacking *BRCA1*, the entire genome seemed intrinsically unstable: There were extra copies of individual chromosomes, and some had large deletions or were fused to bits and pieces from other chromosomes. That makes sense, because previous studies had found a connection between *BRCA1*, as well as the other hereditary breast cancer gene, *BRCA2*, and the repair machinery for the chromosome breaks that lead to such instability.

Deng speculates that in the absence of *BRCA1*, cells accumulate enough DNA damage to trigger safeguards that cause them to stop dividing or even undergo apoptosis. That would explain the high cell-death rates seen in the mutant animals. However, the genetic instability also increases the mutation rates of crucial tumor-suppressor genes or cancer-promoting oncogenes—which may eventually overcome the growth controls and spur the development of tumors.

The Deng-Hennighausen team already has evidence connecting the *BRCA1* defect to the loss of *p53*, the well-known tumor suppressor gene that is itself mutated in about 50% of all familial breast cancers. They found that the mouse *p53* gene is either totally silent or severely scrambled in two-thirds of the tumors in their *BRCA1* knockouts. The researchers also found that inactivating one copy of the *p53* gene in the *BRCA1* mutants accelerated tumor formation in the animals and drastically increased the cancer incidence to some 75%.

Hennighausen says he plans a variety of follow-up experiments with the mutant mice. For example, he wants to know whether the tumors spread as frequently as they do in human breast cancer patients and whether their growth is stimulated by the female hormone estrogen, as also happens in some human patients. If so, the animals would be good models for testing therapies.

Other researchers are also eager to get their hands on the long-awaited mice. Says Hennighausen, "We received several phone calls from people requesting the animals."

–MICHAEL HAGMANN

ITALY

University Funding to Be Tied to Performance

MILAN—Italy's reformist minister for universities and research, Ortensio Zecchino, is taking on the country's inefficient university system. A new bill, now awaiting the attention of the relevant parliamentary committee, would force universities to conduct annual assessments of the quality of their teaching and research and tie their level of government funding to the outcome. It would also give professors monetary incentives to get their students to complete their degrees and pass their exams on time. "This bill is a further step on the way to developing a more effective verification of results in the Italian academic world," says Zecchino, who has already pushed through an overhaul of the National Research Council masterminded by his predecessor, Luigi Berlinguer (*Science*, 30 October 1998, p. 855).

> "Any law improving the system of evaluation is certainly welcome."
>
> —Luciano Modica

Previous Italian governments have tried with little success to impose assessments on the country's universities, which are almost exclusively government-funded. In 1993, universities were required to set up internal evaluation panels to assess teaching and research, but the system never worked well. Seven out of the 54 panels across the country never met and about half the panels never presented a report, while many of those that were completed turned out to be of little use. In 1996, a "national observatory" for the assessment of the university system was created, but it also has had little impact.

If Zecchino's bill passes, the observatory would be replaced by a new national committee. "It will not be just a change of name," assures Zecchino; "the national committee will have a much more incisive power." The committee will have seven members, some of whom will come from abroad, and it will set general criteria for the universities to carry out their evaluations. Every university will have to set up a new internal evaluation panel with no more than nine members, one-third of whom must come from outside the university. The methods the panels will use to evaluate research and teaching have not yet been spelled out, but in their evaluation of teaching the panels must take into account student assessments of their teachers' performance—a new departure in Italy. According to the bill, assessments will not affect the careers of individual professors; they are for funding purposes only.

The panels will be required to submit their reports to the national committee each year. And from 2000 onward, a portion of the government's funding for universities will be distributed by the committee according to the strength of these evaluations. Those universities that fail to submit an evaluation will receive none of this funding.

The bill also aims to tackle the chronic problem of students not completing their degree courses. Only 13% of Italian students take their exams on time, and only about 30% of those who enroll eventually graduate. Zecchino is proposing to put up $150 million over the next 3 years in incentives for professors to get students through their courses successfully. Universities would bid for this money by proposing projects to improve degree success rates. Zecchino's ministry will provide one-third of a project's funding at the outset and the remainder when it begins to show results.

Luciano Modica, rector of the University of Pisa and president of the Italian Conference of Rectors, says "any law improving the system of evaluation is certainly welcome, but it is not true that in the Italian academic world assessment of quality is completely nonexistent."

Giuseppe Palumbo, deputy of the main opposition party and vice president of the parliamentary committee that will scrutinize the bill, approves of Zecchino's plans in principle. But he believes that they are very ambitious and probably too idealistic. For example, he notes that there are so many students in some Italian university