Cancer Gene May Be Relatively Common

A year and a half ago, two separate groups of researchers found defects in a particular gene among several families with a rare, inherited syndrome of breast cancer and malignancies of bone and soft tissues. "Breast Cancer Gene Found," trumpeted some of the headlines of news stories on the development, "Screening Test Available Soon." But at the time, scientists could only speculate that the same gene underlies cases of breast cancer in families without a history of the unusual disease, called Li-Fraumeni syndrome (SN: 12/1/90, p.342).

Now, two other research teams — one including some members from an earlier group — have verified that hypothesis. In back-to-back papers in the May 14 NEW ENGLAND JOURNAL OF MEDICINE, they report that heritable defects in a gene named p53 can show up in cancer patients with no previous family history of the disease.

Although the finding still does not confirm p53's role as *the* breast cancer gene, experts agree that it has important implications for the prevention and treatment of many types of cancer. They say it suggests that physicians could use tests for defective p53 genes to identify patients at high risk of developing cancer, particularly if those patients have a close relative with cancer. They add that it might also help doctors single out and follow more closely those cancer patients likely to get a second, different type of cancer later in life.

The normal protein encoded by an intact p53 gene is known to be involved in telling a cell when to stop dividing. Researchers have found defective p53 genes in most types of malignant tumors. They believe the p53 gene mutates in some people only after the process of cancer has begun, whereas in others — including those with Li-Fraumeni syndrome — the p53 mutations are present from birth in every cell in the body.

In the first study that contributed to the new finding, a team led by cancer researcher David W. Yandell of the Massachusetts Eye and Ear Infirmary in Boston analyzed DNA taken from the blood cells of 196 people with various types of sarcoma, or cancer of the bone or soft tissues. Fifteen of the patients had either a family history of cancer or more than one type of cancer in their lifetimes. For controls, the researchers analyzed DNA from 175 healthy volunteers and from 25 people with noncancerous bone or soft-tissue tumors.

They found that eight of the 196 sarcoma patients (4 percent) had mutations in the p53 gene, while none of the 200 controls had such mutations. Moreover, three of the eight sarcoma patients had no family history of cancer, suggesting that their mutations originated in their mother's egg or father's sperm. Two of these patients had had two different types of cancer during their lives; the third died from his first cancer. One of the surviving patients went on to have a daughter with an identical mutation who developed cancer during childhood.

Yandell concludes that p53 mutations "look much more extensive than just Li-Fraumeni syndrome." Although researchers must perform further studies to determine the proportion of cancers caused by the defective gene, "it looks like there are probably lots of patients out there who have multiple primary cancers in their lifetime that can be traced to p53," he asserts.

In the other study, investigators led by pediatric oncologist Stephen H. Friend of Massachusetts General Hospital Cancer Center in Charlestown examined whether p53 might underlie the cancer risk of children and young adults with multiple cancers. Friend also led one of the earlier groups that studied Li-Fraumeni syndrome. The new study turned up p53 mutations in four of 59 patients (7 percent). Although none of the four had a family history of cancer, close relatives of three of these patients had the same p53 mutation and were diagnosed with cancer during the study period.

Friend says his group's study "gives us a clue that [p53] . . . might be useful in screening people who had no reason to believe they were at an increased genetic risk for cancer." But he cautions that p53 is probably responsible for only a fraction of all cancers: An unpublished study by his group indicates that only 1 percent of women with breast cancer have a defective p53 gene. Friend's team is now studying all new cases of childhood bone sarcoma in the United States to determine whether p53 accounts for a greater fraction of these cancers.

Alfred G. Knudson of the Fox Chase Cancer Center in Philadelphia calls the new studies "exciting. . . . I think it's going to make people scurry around to see why some families show more [cancers due to] the gene than others."

"I'm sure we'll learn that there are other, modifier genes involved," he adds.

— C. Ezzell

New approach makes silicon's red glow blue

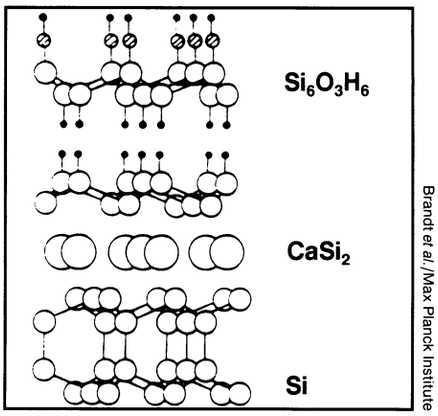
Research done more than a century ago sheds new light on the recent discovery of luminescence in silicon, a semiconductor previously thought to lack the ability to emit a strong glow. Just two years ago, British scientists obtained luminescence at room temperature from silicon samples made porous by etching in acid. That announcement and subsequent reports that light or electricity will make porous silicon emit light prompted a flurry of research because of the possibility of making silicon-based optoelectronic devices (SN: 2/15/92 p.103).

But silicon in those applications may not require acid etching at all, says Martin S. Brandt of the Max Planck Institute for Solid-State Science in Stuttgart, Germany. In combing the German scientific literature, he and his colleagues discovered reports from 1863 and the 1920s discussing the conversion of a silicon-calcium compound to a strongly luminescing silicon material called siloxene.

Following up on that research, the Stuttgart team has now demonstrated the potential for incorporating siloxene thin films onto silicon computer chips. "It would be, in principle, compatible with existing silicon technology," Brandt says.

He and his colleagues first grow the calcium-silicon compound on silicon and then create a thin film of siloxene by replacing the calcium with hydroxyl groups. With this technique, they have made a 400-nanometer-thick siloxene film that "has the same properties as porous silicon," Brandt reported this month at the Materials Research Society's spring meeting, held in San Francisco.

"That's an exciting possibility," comments Ulrich M. Gösele, a solid-state physicist at Duke University in Durham, N.C. Siloxene presents a better surface for attaching metal contacts than does the



Brandt *et al.*/Max Planck Institute

Diagram shows formation of siloxene ($Si_6O_3H_6$) from calcium-silicon compound ($CaSi_2$) deposited on silicon (Si).

fragile, much-pitted porous silicon. But to really be useful, siloxene also needs to luminesce when subjected to electrical current, he says. Moreover, researchers have not demonstrated that siloxene can be doped and fashioned into practical devices, says Reuben T. Collins of IBM's Thomas J. Watson Research Center in Yorktown Heights, N.Y.

Using a charge-coupled device, the Stuttgart group showed that siloxene materials can emit a rainbow of colors, including porous silicon's red and blue, a color not yet reported from porous silicon and one crucial for creating color displays or signs, Brandt says.

A siloxene molecule groups six silicon atoms as a hexagonal ring with three oxygen and six hydrogen atoms attached. These rings link up, using an oxygen atom to bridge two rings, and arrange in flat layers, Brandt explains. He adjusts the color of the luminescence by replacing the other attached atoms with different chemical side groups.

Siloxene that forms on surfaces of porous silicon during acid etching could cause that material's luminescence, says Brandt, noting similarities in the optical properties of the two types of silicon materials.

Leigh T. Canham of the Defense Research Agency in Malvern, England, who first described luminescing porous silicon, proposes a different mechanism. He suggests that luminescence occurs because etching creates silicon crystals so thin that an effect called quantum confinement occurs. After light or electrical current excites electrons in these 1- to 5-nanometer-thick "quantum wires," these "confined" electrons can calm down again only by emitting light.

But for both these explanations, "the arguments are a bit indirect," says Collins. Other researchers have proposed different mechanisms for luminescence, and while many have some evidence to back up their ideas, no single model seems to explain all the observations. Indeed, a combination of mechanisms may lead to silicon's bright glow.

"It could be quantum confinement *and* siloxene," Gösele suggests. — *E. Pennisi*

Picking out the Lymes from the lemons

Ever since Lyme disease became well known back in the '70s, Lyme-transmitting ticks have aroused a public worry much like that caused by frothy-mouthed dogs. And with 1,282 cases of Lyme disease reported across the United States so far this year, no one denies that the disease poses a real health threat. But some researchers are beginning to wonder whether Lyme may produce a previously undocumented symptom: paranoia.

Researchers at the University of Connecticut Health Center in Farmington and the Yale-New Haven Hospital examined 70 children diagnosed with Lyme disease and found that only 53 percent of them actually harbored the Lyme-causing bacterium, *Borrelia burgdorferi*. The remaining 47 percent, they discovered, had been misdiagnosed. To confirm these findings, the researchers telephoned parents of the misdiagnosed children one to three years later and found that advanced symptoms of the disease never materialized.

"The problem of Lyme disease is real, but I think a lot of people have become hysterical about it, including some doctors," says study coauthor Henry M. Feder Jr., a pediatrician at the University of Connecticut Health Center. Feder reported his group's findings at the American Pediatric Society meeting in Baltimore last week.

In its early stages, Lyme disease produces symptoms — such as fever and muscular aches — similar to those of many other illnesses. This makes diagnosis difficult. "If a doctor sees a patient and wants to make the symptoms fit Lyme disease, he can do it. That's the tricky part of it," Feder says.

Furthermore, blood tests widely used to screen for Lyme disease often yield ambiguous results. These tests look for antibodies in the bloodstream. But since the body mounts a very weak immune response to *B. burgdorferi*, the antibodies sometimes elude detection, making diagnosis a judgment call. Moreover, commercially available test kits vary widely in their reliability. Feder's group carefully prepared their own blood test rather than use a commercial kit.

Faced with inconclusive evidence, physicians often prescribe antibiotics just in case. But this approach has risks too. For example, freely distributed antibiotics could allow other infectious organisms to build up a tolerance, notes Andrew Spielman of the Harvard School of Public Health in Boston.

In recent years, scientists have developed more accurate tests that look for *B. burgdorferi* DNA rather than for human antibodies (SN: 12/9/89, p.374), but these genetic tests haven't become widely available. Until they do, diagnosing Lyme disease will continue to involve an element of guesswork. At the same time, Feder advises clinicians to weigh the evidence and the odds more carefully: "If someone gets a tick bite in a Lyme-endemic area, the risk is one in 100 of getting [the disease]. So saying, 'Uh-oh, a tick bite, you're in big trouble' — that, in my mind, is just not right." — *M. Stroh*

Flash-in-the-plasma generation of X-rays

The firing of extremely brief, intense pulses of laser light into solid targets has an extraordinary effect on ordinary matter. Electrons in the material rapidly absorb energy, and these hot electrons in turn force the ejection of other electrons from atoms to produce a high-temperature spark of plasma at the solid's surface, from which X-rays emerge.

The use of a novel laser capable of firing powerful pulses of infrared light lasting only 120 femtoseconds (quadrillionths of a second) has now enabled researchers at Stanford University to generate bursts of "hard" X-rays having energies greater than 1 million electron-volts. In previous, similar experiments, other research groups had reported X-ray energies less than one-tenth as high.

"We detected surprisingly large amounts of very hard X-rays," says Jeffrey D. Kmetec, now at Lightwave Electronics in Mountain View, Calif. "No one had looked for them before." He reported the new findings at the Quantum Electronics and Laser Science Conference, held this week in Anaheim, Calif.

The Stanford group used a custom-built, titanium-doped sapphire laser to generate five pulses per second of light at a wavelength of 807 nanometers. Tightly focused onto a tantalum target about 1 millimeter thick, each laser pulse delivered energy to a tiny spot on the metal target's surface at a rate greater than 10^{18} watts per square centimeter.

The researchers estimate that the hot flash accompanying each brief pulse yielded about 1 million X-ray photons having energies greater than 1 million electron-volts. That output suggests an unexpectedly efficient source of hard X-rays.

Kmetec and his co-workers suspect that this high-energy radiation arises from the passage of highly energetic electrons through the solid target. However, because no one has investigated in any detail the conditions that exist within a laser-bombarded material during the very short time intervals involved in these intense interactions, it isn't clear yet exactly what physical mechanism creates the hard X-rays.

"It's not a regime that we've accessed before," says Mordecai D. Rosen of the Lawrence Livermore (Calif.) National Laboratory. "It's an area that I'd like to study. It's critically important to the field to know just what hot electrons are made and why."

Fast, compact X-ray sources capable of delivering short but extremely bright pulses of radiation may prove valuable in the study of materials undergoing rapid changes and as a means of supplying energy to an X-ray laser. — *I. Peterson*