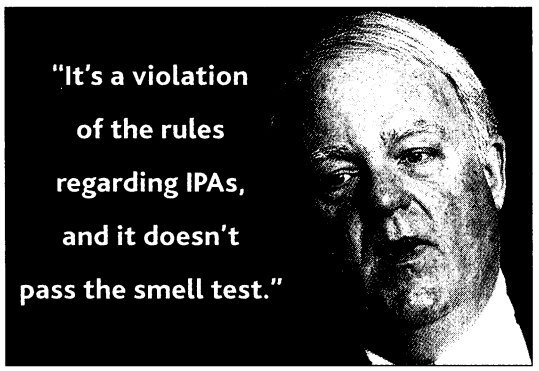
Colwell, who needs both men as allies in the annual fight for federal dollars.

On 17 May Sensenbrenner proposed cutting the director's travel budget, staff levels, and her ability to temporarily transfer employees to outside organizations as part of legislation, H.R. 4485, to authorize NSF's programs for the next 4 years. He says it's a response to the "fiasco" stemming from NSF's reaction to rule-breaking by Luther Williams, former head of the education directorate. Williams was fined $24,900 in June 1998 for improperly accepting outside honoraria (*Science*, 26 June 1998, p. 2053). "They completely mishandled the case," Sensenbrenner says about NSF's decision to reprimand Williams but allow him to keep his job for more than a year. Then, last summer, the agency reassigned him under the Intergovernmental Personnel Act (IPA) to a new program run by Louisiana's Tulane University (*Science*, 13 August 1999, p. 997).



In particular, Sensenbrenner says he's incensed because Williams was allowed to retire 5 months after the reassignment, rather than return to NSF, and because the Tulane program's founder, president emeritus Eamon Kelley, also heads the National Science Board. "[The first] is a violation of the rules regarding IPAs," he says, "and [the second] doesn't pass the smell test." An NSF spokesperson said that Colwell did not wish to comment on the matter.

The reauthorization bill, which sets funding levels for individual programs, would prohibit NSF from detailing staff to any outside organization as an IPA, mandate ethics training for all NSF staff, and require Colwell to update Congress twice a year on the training and related matters. "It's an attempt to make sure that this stuff never happens again," says Sensenbrenner. He calls the language "a preemptive strike" to protect NSF against legislators who might use the controversy as an excuse to trim the agency's budget. The bill matches the president's 17% requested increase for NSF in the fiscal year that begins on 1 October and includes much more modest annual increases—from 2.5% to 3.3%—for the next 3 years. "I'm a fan of NSF, but sometimes basic research is a hard sell," he explains.

Two days after Sensenbrenner introduced his bill, Smith introduced his own version, H.R. 4500. It hews closely to Sensenbrenner's on most counts—but omits the prohibition on IPA transfers as well as the travel cuts and the ethics program. Legislative aides say it is highly unusual for a subcommittee chair to introduce a bill that competes with one by his boss. In another bizarre turn, H.R. 4500 was actually Smith's second NSF authorization bill. The day before, he introduced H.R. 4491, which retains all of Sensenbrenner's punitive language and differs only in proposing two, rather than four, years of future budgets. Smith declined to comment on either of his bills, but Capitol Hill sources speculate that the earlier version had been filed in haste.

Sensenbrenner says that he hopes the full science committee can take up his bill sometime this month. Such a move would bypass Smith's basic science subcommittee, which oversees NSF, but Sensenbrenner says it is standard practice. The move would also make it harder for Smith to hold a hearing on his legislation.

Even if approved, however, Sensenbrenner's bill stands only an outside chance of being considered by the full House before Congress adjourns in the fall. It also lacks a counterpart in the Senate. The bill's demise certainly wouldn't upset NSF officials, who hope that the flap doesn't affect their long-term relationship with their closest congressional overseers. **–JEFFREY MERVIS**

CREDITS: (TOP TO BOTTOM) S. KITTNER; PXE INTERNATIONAL

BIOMEDICAL RESEARCH

Patients Help Track Down Disease Gene

In the Terry household, patient advocacy is a family affair. At age 11, Elizabeth Terry testified before Congress to promote biomedical research. Her mother travels around the country seeking out patients with pseudoxanthoma elasticum (PXE), the disease Elizabeth and her younger brother, Ian, were diagnosed with some 5 years ago. Their father makes regular trips to the local medical library to follow up leads.

Together, they established and run a patient advocacy group from their house, one that is promoting "a new breed of advocacy," says Francis Collins, director of the National Human Genome Research Institute in Bethesda, Maryland. Like the Hereditary Disease Foundation, which played a pivotal role in coordinating research and tracking down the gene for Huntington's disease, the Terrys' organization has become "aggressively involved in the science," says Collins, as well as in securing funding and working with PXE patients. In the past few weeks, their relentless work has paid off in a big way.

Their organization, PXE International, has helped three research teams pinpoint the identity of the gene for this rare inherited disorder. Two labs, led by Charles Boyd at the University of Hawaii, Honolulu, and Arthur Bergen at the Netherlands Ophthalmic Research Institute in Amsterdam, report their results in the June issue of *Nature Genetics*; the third group, led by Jouni Uitto at Thomas Jefferson University in Philadelphia, published its findings in the 23 May *Proceedings of the National Academy of Sciences.*

But PXE International isn't the only patient group to play a key role in unmasking the identity of the PXE gene. An older, albeit less media-savvy, organization called the National Association for PXE (NAPE) teamed up with the March of Dimes, a Texas dermatologist, and a Harvard genetics lab to help place the gene for this disorder on the genome map—literally—in 1997. Now, the collaboration, led by Klaus Lindpaintner, a physician-geneticist at Harvard's Brigham and Women's Hospital, has also identified the gene itself. It reported its results online in the 26 May *Journal of Molecular Medicine*.

All the researchers say that having a group of families willing to work with them was critical to their success. "If the patient community had not been involved, there would have been no studies," agrees Sherri Bale, a geneticist with GeneDX, a start-up in Rockville, Maryland, that makes genetic diagnostic tests.

Young advocate. Elizabeth Terry urges Congress to spend more money on biomedical research.

The four teams converged on a little-studied gene, called *ABCC6* or *MRP6*, on chromosome 16 as the culprit in PXE. Traditionally considered a skin disease, PXE causes calcium to accumulate in connective tissue of the eye, gut, heart, and skin, sometimes causing vision loss, gastrointestinal

bleeding, and heart as well as skin problems. The researchers do not yet know how mutations in the gene, which seems to be involved in transporting material in and out of cells, lead to the disease. One puzzle is that the gene is most active in the liver and kidneys, and the researchers have found very little evidence of the protein in the skin, as they would have expected. That leads Uitto to speculate that "it may well turn out that PXE is primarily a metabolic disorder, and the connective tissue manifestations are secondary phenomena." He adds, "Once we figure out what the normal gene does, we might be able to help these patients."

The hunt for this gene has been long and frustrating. Indeed, several groups put their efforts on hold in the late 1980s, and the search languished until around 1994. Then, after a chance meeting, Lindpaintner teamed up with Kenneth Neldner, a dermatologist at Texas Tech University Health Sciences Center in Lubbock. Neldner had been working with NAPE, an organization started in the late 1980s by Diane Clancy, a PXE patient in Albany, New York, out of her living room. The two researchers contacted NAPE members and got PXE patients and their families to donate the blood samples they needed to track down the gene. By 1997, Neldner and Lindpaintner had narrowed their search to the short arm of chromosome 16; Bergen had also found a connection between PXE and that part of chromosome 16.

Shortly before that connection was made, Sharon and Patrick Terry entered the picture. Concerned that too little work had been done to understand PXE, they turned to the Washington, D.C.–based Genetic Alliance, an umbrella group of patient organizations, for advice on setting up their own advocacy group. After consulting with geneticists, the Terrys established a blood bank, persuading PXE patients and families from all over the world to send in blood samples and to have their family histories documented. When she learned about Lindpaintner's and Bergen's success in localizing the gene, Sharon Terry helped organize a meeting of all the researchers on the trail of the PXE gene. At first it seemed the groups would collaborate. But tensions arose over sharing data and, eventually, NAPE and Lindpaintner went their own way.

Because the relevant section of chromosome 16 had been sequenced and studied by then, the various teams knew there were six genes in that region. None looked like an obvious candidate for causing the disease, so the researchers simply scanned for mutations, working painstakingly one gene at a time. Boyd recounts that his team found nothing interesting in the first five genes they examined. But "the moment we started looking at the ABCC6 gene, we ran into mutations," he says. Individuals with PXE had several distinctive changes in the gene, whereas DNA samples from 100 healthy individuals showed no mutations. The evidence, Lindpaintner agrees, "is very much cut and dried," leaving little doubt that this is the right gene.

Even before the gene's function is understood, it may prove useful in diagnostic tests. PXE symptoms and age of onset vary quite a bit. Now it should be easier to get definitive confirmation of the disease, says Boyd, and also to identify asymptomatic carriers. Both Boyd and Lindpaintner suspect that, depending on the mutation, apparently asymptomatic carriers may face unrecognized risks—such as a greater propensity toward heart disease or eye problems early in life that might be reduced by modifying the diet or monitoring eyesight carefully to detect early signs of vision loss.

Both the patient groups and the researchers are now planning their next steps. "We realize [the gene] is not the end of the road," says NAPE spokesperson Carol Daugherty. In the works are efforts to learn more about how the gene functions in cells and whether the variability in the disease's course is linked with particular mutations. Daugherty says she regrets that NAPE and PXE have been unable to join forces. Nevertheless, she adds, "each group takes its separate road to what I'm sure is a common goal—improving the lot of individuals with PXE."

–ELIZABETH PENNISI

OCEANS POLICY

Clinton to Expand Marine Reserve Areas

A wave of announcements last week lifted the spirits of marine conservationists and researchers. Standing on a sun-dappled Virginia beach, President Bill Clinton on 26 May ordered federal agencies to develop an expansive new network of marine reserves in U.S. waters. The move came a few days after The Pew Charitable Trusts established a high-profile oceans commission that supporters hope will energize efforts to study and protect the sea. Adding to the bounty, federal officials also announced that they will shift shipping lanes away from environmentally sensitive areas off California, while researchers began an ambitious effort to count all forms of marine life (see p. 1575).

In his appearance at the Assateague Island National Seashore, Clinton outlined a new executive order that seeks to protect a bigger portion of U.S. waters—which stretch for 320 kilometers offshore—from fishing, drilling, and other activities. Currently, less than 1% of the vast U.S. coastal territory is protected, demarcated by a dozen marine sanctuaries and other wildlife refuges or parks (*Science*, 25 July 1997, p. 489). To boost the total, Clinton ordered the Interior and Commerce departments to come up with a plan for designating and managing an integrated system of marine protected areas. To start, he wants improved safeguards for 12,000 square kilometers of coral reefs in the Northwest Hawaiian Islands, home to nearly 70% of U.S. reefs.

Sunken treasures. Executive order would strengthen safeguards on coral and other marine resources.

While it's not clear if such bureaucratic efforts will pay off, "I can't think of a better way to begin the first summer of the new century," said Elliott Norse, president of the Marine Conservation Biology Institute in Redmond, Washington. He and others are pushing to increase U.S. protected waters to 20% of the total by 2015.

The new Pew Commission on Oceans, to be led by New Jersey's Republican governor, Christine Todd Whitman, and packed with political and business heavyweights, hopes to repeat the impact of an earlier oceans panel. The 1969 Stratton Commission, chartered by Congress, sparked the creation of the National Oceanic and Atmospheric Administration and new coastal conservation legislation. But it also unintentionally encouraged overexploitation of the sea's once seemingly limitless resources, says Carl Safina of the National Audubon Society in New York City.

The new panel, Safina says, has a chance to take a "clear, cold look at what's needed and what is appropriate now—and that's long overdue." The commission will hold its first meeting in July, with a final report due in 2002.

–DAVID MALAKOFF

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