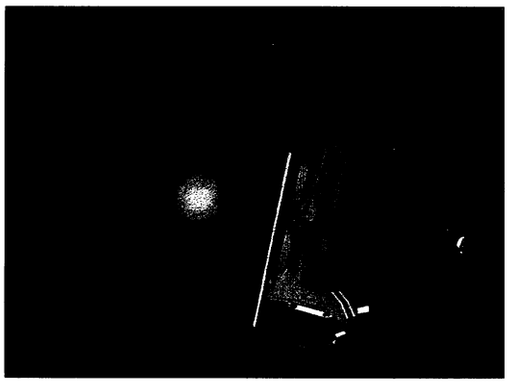
Space Infrared Telescope Facility (SIRTF), scheduled for launch in 2001. In the same bill, the subcommittee proposed a $25 million cut (a reduction of 0.7%) in the budget of the National Science Foundation (NSF), with an $8.5 million (0.3%) increase for research.

A few days later, though, the full House appropriations committee repaired some of the damage. It added back $400 million to NASA's budget, rescuing SIRTF and the Mars missions, yet leaving NASA's total appropriation about 7% below the current level. No one mended the hole in NSF's budget, and researchers were left wondering where this turbulent process will leave them in the fall.

The cuts were necessary to stay within spending caps Congress adopted in 1997, which neither Congress nor the White House is willing at this stage to lift. "The allocation [for the fiscal year 2000 budget] was significantly lower than last year's budget, so we needed to find money," a subcommittee staffer told *Science*. Because the subcommittee didn't want to cut housing programs and intended to boost spending for veterans' medical care—both in the subcommittee's jurisdiction—"we only had limited choices, and NASA was our first choice," he adds.

Space scientists are still reeling. Carl Pilcher, science director for Solar Systems Exploration at NASA, says many felt the subcommittee's message was: "You're done; finish what's on your plate, close the shop, turn off the lights, and go home." Pilcher calls the vote "the most severe cut in NASA's 40-year history." Planetary scientist Steven Squyres of Cornell University in Ithaca, New York, the chair of NASA's Space Science Advisory Committee, agrees. The initial proposal "was a going-out-of-business budget for space science. Except for missions that are well on their way to the launch pad, it would have effectively zeroed out all future missions," he says.



Threatened. NASA's infrared space telescope SIRTF was cut by one House panel and rescued by another.

To repair the initial cuts in NASA's budget, the full appropriations committee shifted $400 million from the Corporation for National and Community Service (Americorps) to NASA. "I'm absolutely delighted about the $400 million, especially since it all goes into space science," says Squyres. But others fear that killing the national service corps will invite a presidential veto.

And although SIRTF survived, other space projects are still endangered. The "faster, cheaper, better" Explorer astronomy missions and the Discovery planetary missions, for instance, would be reduced by $60 million each. In addition, CONTOUR, a $50 million comet mission, would be canceled altogether. And the Research and Technology account would lose $100 million. Louis Friedman, executive director of the Planetary Society, warned in a statement that "the remaining cuts are still draconian and will throw NASA into turmoil."

NSF came through the ordeal clinging to a survival budget, but with future plans in tatters. Its strategy of bundling much of its requested $218 million increase into the Administration's multiagency $366 million information technology initiative was shot down by both the subcommittee and the full committee. The legislators gave NSF only $35 million of its $146 million request in that area and nothing for a requested $35 million terascale computer. Members were put off by the initiative's size, and they feared that any competition for the new machine would favor NSF's two existing supercomputer centers at the University of California, San Diego, and the University of Illinois, Urbana-Champaign. "Even if they had the money, they'd have wanted to phase it in," explains a House aide. "They also didn't want to let the haves get even further ahead."

Next, the VA-HUD bill moves to the floor of the House, where a vote could occur before Congress begins a recess this weekend. Although space science supporters may try to seek changes, "appropriations bills are hard to overturn," a Capitol Hill source says. "Right now the odds are with the bill passing" in the House. Then the process will begin all over again in the Senate, giving science lobbyists another chance. Says Squyres, "I don't think I've made my last visit [to Washington, D.C.] this summer."

–MICHAEL HAGMANN

With reporting by Jeffrey Mervis.

CELL BIOLOGY

Gene Linked to Faulty Cholesterol Transport

From a secluded island off the coast of Virginia in the Chesapeake Bay comes a genetic treasure that lay buried for centuries in the inhabitants and their descendants. This population carries a rare hereditary disorder, called Tangier disease—after the name of the island—characterized by a defect in cholesterol management that leaves the patients with yellow tonsils, oversized spleens, and scant amounts of the heart-protective high density lipoprotein (HDL) cholesterol in their bloodstreams. In the August issue of *Nature Genetics*, three groups now report that they have nabbed the gene at fault in Tangier disease—a discovery that not only sheds light on this condition, but may also lead to a better understanding of a much more common genetic deficiency that carries a high risk of heart attack.

The gene identified by the three groups, which were led by Michael Hayden of the University of British Columbia in Vancouver, Gerd Schmitz of the University of Regensburg in Germany, and Gerd Assmann of the Westlischen Wilhelms University in Münster, Germany, encodes a member of a large family of proteins that shuttle molecules into and out of cells. Although this particular family member, known as ABC1 (for ATP-cassette binding protein 1), had been unearthed before, researchers had not yet pinned down its exact function.

The new work suggests that ABC1 transports cholesterol from inside cells to the cholesterol-enveloping proteins waiting outside to carry it as HDL cholesterol particles to the liver for recycling back to cells in the body. Christopher Fielding of the Cardiovascular Research Institute at the University of California, San Francisco, who co-authored a *Nature Genetics* "News and Views" item on the three papers, notes that it's been 25 years since researchers learned how cholesterol gets into cells via the LDL receptor. But, he says, "this is the first time we know anything about how it comes out."

Even more promising is the finding by Hayden's team that defects in the *ABC1* gene also pop up in patients with familial HDL deficiency syndrome (FHA), a disorder characterized by low blood levels of HDL cholesterol and a high risk of coronary disease. That result could be "a bonanza," says cardiologist Dennis Sprecher of the Cleveland Clinic in Ohio. "There are piles of low HDL syndromes," he notes, and the new discovery raises the possibility of developing drugs that protect against heart attack by targeting ABC1 and thus increasing HDL cholesterol levels in the blood.

CREDIT: JPL/NASA

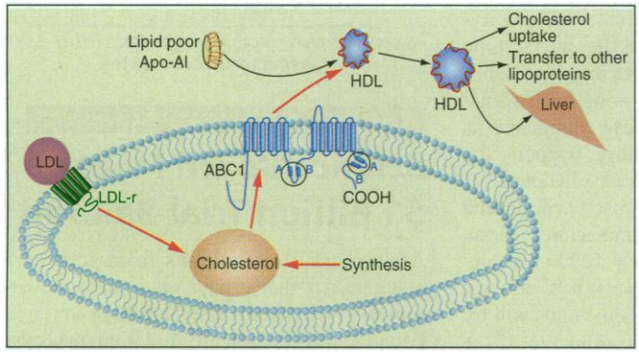
The search for the Tangier culprit was a sprint to the finish after a very long marathon. Donald Frederickson, then at the National Institutes of Health in Bethesda, Maryland, discovered the disease in 1961. Not until 1998, however, did longtime Tangier researcher Assmann—formerly a postdoc in Frederickson's lab—and his colleagues finger a region of chromosome 9 as the location of the Tangier disease gene. But that still left the major job of finding the gene itself.

Enter Hayden's group in Vancouver. The researchers pinned down the approximate location of the gene by looking to see which chromosome 9 "markers" were consistently found in Tangier patients, but not in unaffected family members—an indication that the gene and marker are close to one another. Once they found such a link, the researchers had help from nature in pinpointing the exact gene: One patient was the child of two first cousins, and thus, Hayden's team reasoned, he likely had the same mutation in both copies of the gene. That conjecture, together with their analysis of FHA families, led the team to the *ABC1* gene, which had been cloned in 1994 by Giovanna Chimini's group at the French research agency INSERM-CNRS in Marseille Luminy, but whose function was then still unknown. "Basically, we squeezed as much juice as we could from the genetic data we had," Hayden says.

Meanwhile, Schmitz's group in Regensburg was using a more biochemical approach to pinpoint the gene. They looked for genes that were expressed differently in the cholesterol-laden cells of Tangier patients than in normal cells. This search also fingered the *ABC1* gene as the most likely candidate—an identification that was confirmed when the gene turned up mutated in all five Tangier patients that the Schmitz team studied. In addition, Chimini's group had already inactivated the gene in mice, and when Schmitz and his colleagues examined those animals, they found that they had developed symptoms similar to those of Tangier disease. Finally, Assmann's group found *ABC1* through a combination of the techniques used by the other groups.

Evidence from Hayden's and Schmitz's groups indicates that ABC1 normally transports cholesterol out of the cell. For example, Schmitz found that cells engineered to make extremely high amounts of the protein were so depleted of cholesterol that they died, while cells in which ABC1 synthesis was inhibited accumulated more, much as cells from Tangier patients do.

So far, however, the research has not resolved a conundrum about Tangier disease: Even though all the patients have low HDL cholesterol concentrations in their blood—a condition thought to predispose to the artery-plugging lesions of atherosclerosis—some seem to escape coronary disease. That puzzle is heightened by the Hayden group's results linking *ABC1* mutations to FHA, an HDL cholesterol problem in which patients do show an increased risk of heart attack. The Vancouver group has so far screened 20 FHA families for *ABC1* mutations and found them in eight.



The way out. ABC1 normally carries cholesterol out of the cell for uptake into HDL particles. But if *ABC1* mutations prevent that, cholesterol may build up in cells while blood HDL levels go down.

CREDIT: S. CLEE, G. LIU, AND M. HAYDEN

One possible explanation for the apparent paradox, Schmitz says, is that the transporter has a dual role—both ferrying cholesterol out of the cell and directing cells such as macrophages, a type of immune cell, to specific locations in the body. His hypothesis is that a mutation in one spot may send cholesterol-laden macrophages off to the spleen, lymph nodes, or tonsils for processing—hence the oversized tissues characteristic of Tangier disease—whereas a different *ABC1* mutation may cause the macrophages to stick to the vessel wall, in that case leading to atherosclerosis and heart disease.

Further work will be needed to test those ideas, as well as to see how common *ABC1* mutations are in FHA. But the new findings raise the possibility of developing drugs that protect against heart disease by raising blood HDL levels—a feat no one has yet accomplished. Even if ABC1 doesn't pan out as a target for such drugs, researchers may yet find other potential targets. "This should open the doors to a general research effort into what regulates cholesterol coming out of cells," Fielding says. "There may be other mechanisms, but this is the first one, and it is a good place to start." **–TRISHA GURA**

Trisha Gura is a free-lance writer in Cleveland, Ohio.

ScienceScope

Pet Projects The Japanese government is preparing to give science a hefty 9% raise in next year's budget. But researchers aren't quite ready to celebrate: Much of the increase appears slated for projects that will be hand-picked by Prime Minister Keizo Obuchi's office.

Agency spending guidelines, adopted by the Cabinet last week, include a new $2.17 billion account for R&D in information, life, and environmental sciences deemed to have potential for a high economic payoff. Science spending in usual accounts for the fiscal year starting in April 2000 will be nearly flat, says Nobuhiro Muroya, deputy director of planning for the Science and Technology Agency. The majority of the increase will go to the new category; to vie for funds, each ministry must propose projects to the prime minister's office, which will assess the projects—likely ones already on the drawing board—according to yet-to-be-defined criteria.

"This came up so suddenly, I don't think anyone in the science community knows anything about it," says one senior scientist. But they will soon: It should become clear by the end of this month which projects are on the funding fast track.

Beyond the Numbers A new report offers stern advice for academic mathematicians: Pay more attention to the world around you, or at least to the other departments in your university.

To learn how math departments view themselves—and how they're viewed on campus—a task force of the American Mathematical Society (AMS) spent 7 years interviewing the chairs of half the nation's Ph.D.-granting math departments and 30 of their deans. They found a dramatic dichotomy in perceptions. "There wasn't a dean who didn't say math was the leading cause of complaints" at his university, says AMS executive director John Ewing. And whereas most mathematicians saw their discipline as central to the sciences, says Ewing, most deans viewed mathematics as one of the most "insular" departments on campus.

The report recommends that department chairs reward faculty members who focus on instruction, forge collaborations with other departments, and devote more resources to outreach and to remedial education. The payoff may well be more money for research, says Ewing: "Their life as a research department depends on ... their teaching."

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