reaction." This view is supported by jury member Miguel Virasoro, director of the International Center for Theoretical Physics in Trieste, Italy, who comments in his personal capacity that "everyone, absolutely everyone was agreed that Amit was ideal."

The jury then forwarded its choice to the SFP for ratification. At the same time, Abou-Chacra was informed of the result by another jury member, ENS physicist Franck Laloë. Just over a week later, letters protesting the decision began pouring into Balian's office from Lebanon, signed by political leaders, the Islamic Association, the League of Professors, and leaders of the CNRSL. In addition, a flurry of articles appeared in the Lebanese press—including at least one by Abou-Chacra himself—demanding that the vote be overturned.

At this point, the French embassy in Beirut appears to have taken notice of events. Leduc says she received "two or three" telephone calls from the embassy's attaché for scientific and cultural cooperation, Henri Genaud. "He was annoyed at the reaction in Lebanon, and he wanted it to stop," Leduc told *Science*. "He was in favor of suspending the medal to calm things down." In an e-mail to Balian, dated 10 November 1998, Leduc describes her conversations with Genaud more explicitly: "The embassy is very clear: They think that the harmful effect of this award to Amit will be significant for the political, scientific, and university relationships between the two countries."

Genaud says he became involved in the affair in a "personal capacity" and not as an official representative of the embassy. But a more intimate involvement by French foreign affairs officials is implied by a 25 January 1999 e-mail from Genaud to Balian. Shortly before, SFP officials had finally decided that Amit would not get the prize, and Balian had asked Genaud to look over a draft communiqué announcing this decision. In the message, Genaud states that he had contacted "the services of the French foreign affairs ministry, the Lebanese CNRS, the Lebanese ministry of higher education ... and the Lebanese Prime Minister Sélim Hoss to obtain, on the one hand, a green light on the text of the communiqué and, on the other hand, assurances as to its publication and the reactions that it would possibly draw."

Genaud suggested to Balian a number of changes to the communiqué, including cutting out a reference to Amit's refusal to serve in the Israeli army of occupation in Lebanon. In the end, however, the SFP opted for a shorter version of the communiqué, which said that the prize would not be given in 1998 due to the "serious and multiple difficulties" which had arisen, and did not mention Amit.

Balian insists that political pressure had no effect on the SFP's decision which, he says, was based solely on the irregularities in jury membership. "The French government cannot interfere in this affair, it is private." But Leduc says the embassy's attitude was indeed part of the reason she and some other jury members urged the SFP not to approve the choice of Amit. "There were pressures from the embassy, from the CNRSL, and from other organizations," she says. "We would have been able to resist political pressures if the jury had functioned normally." On the other hand, Leduc adds, if the jury had "functioned normally" she is certain "the vote would have been different."

"I have no shadow of a doubt that they are all acting with constructive, ethical concerns in mind."

—Daniel Amit

But ENS physicist Antoine Georges, a jury member who strongly supported Amit, says "it seems very shocking to me that the SFP could decide to not give a medal on the basis of the nationality of the candidate." And Toulouse says, "The Lebanese never had the chance to know who Daniel Amit was. They said we must wait until the political situation is better, but that is completely contrary to the scientific spirit, which is to be in advance." Virasoro agrees: "One cannot renounce principles because there could be reactions or, even worse, because there is pressure."

Balian counters that awarding the medal to Amit would have "created hostility between Lebanese and Israelis, which contradicts the aim of the medal. ... We cannot give this medal to an Israeli without a lot of psychological preparation." And this sad affair has now called into question the future of the prize: The SFP is studying whether to continue its sponsorship of the Rammal Medal.

Such a decision would not sit well with Rammal's family, some of whom live in southern Lebanon. Ali Rammal, the Lebanese physicist's younger brother—an information technologist who lives in Paris—recently wrote to the SFP's current president, Jean-Paul Hurault, expressing the family's "profound surprise" at the recent turn of events and asking Hurault to "clarify your position concerning the future of the medal." Ali Rammal told *Science* that although the family has "no opinion either for or against" the choice of Amit, "we want the spirit of the medal to be respected." Moreover, he adds, "The guardian of the spirit of the medal today is Gérard Toulouse."

As for Amit, he is philosophical about not receiving the prize. "All actors involved are lifelong, dear friends of mine," he told *Science*. "I have no shadow of a doubt that they are all acting with constructive, ethical concerns in mind. Unfortunately, as human beings, we must learn to live with morally unresolvable situations." —MICHAEL BALTER

CELL BIOLOGY

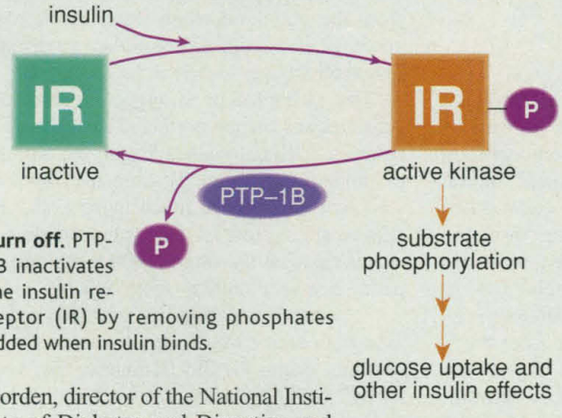
New Clues Found to Diabetes and Obesity

For the 15.7 million Americans with type 2 diabetes, good health means daily vigilance. To head off the eye, kidney, and heart damage the disease can cause, sufferers must follow strict diet and exercise regimes to prevent their blood sugar levels from soaring. Because those measures don't work for everyone, however, some people also need drugs to keep their blood sugars in check. And with nearly 200,000 people dying of diabetes complications each year, better drugs are still sorely needed. On page 1544, a research team based in Canada reports that it has identified a major new target for such a drug—and possibly for anti-obesity drugs as well.

The team, led by molecular biologist Brian Kennedy of the Merck Frosst Center for Therapeutic Research in Pointe Claire-Dorval, Quebec, and biochemist Michel

Tremblay of McGill University in Montreal, came to that conclusion by creating a line of mice lacking an enzyme called protein tyrosine phosphatase–1B (PTP-1B). Those animals, the researchers found, are more much sensitive to insulin's blood sugar–lowering effects than control animals. Because type 2 diabetes is thought to result from an inability to respond to insulin, rather than to an inability to make the hormone as is the case for the type 1 form of the disease, the findings raise the possibility of treating type 2 diabetes with drugs that block PTP-1B activity.

The mutant mice also turned out to undergo a more surprising change: Unlike normal mice, they could eat a high-fat diet without gaining much weight. The researchers do not yet understand this connection, but the result suggests that PTP-1B–blocking drugs might be useful for treating obesity, too. Phillip Gorden, director of the National Institute of Diabetes and Digestive and Kidney Diseases, calls the findings "very interesting and very important."



Turn off. PTP-1B inactivates the insulin receptor (IR) by removing phosphates added when insulin binds.

In the current work, Kennedy, Tremblay, and their colleagues were following up on test tube studies by their group and others showing that PTP-1B removes certain phosphates from the receptor that transmits insulin signals to the cell interior. The addition of those phosphates, which occurs when insulin binds the receptor, touches off a cascade of enzyme reactions inside muscle and liver cells. This tells the cells to take up glucose and sock it away as the storage carbohydrate glycogen, thus lowering blood sugar concentrations. Removal of the phosphates by PTP-1B should therefore turn off the signal cascade, and that's what researchers found in the test tube studies. To see whether the enzyme does the same in the body, the McGill team inactivated the PTP-1B gene in live mice. That "was the way to show whether the enzyme was important or not," Tremblay says.

And important it was. Mice lacking the gene maintained normal blood glucose levels after a meal, even though they had half as much insulin in their blood as normal mice. In addition, a shot of insulin caused some of the PTP-1B–deficient mice to move so much glucose into their cells that they passed out from low blood sugar—something that never happened to the wild-type mice that received the same dose, Kennedy says. Together, those results showed that the knockout mice were more sensitive to the hormone than their wild-type cousins.

The group also showed that these effects are due to increased insulin receptor activity in the knockout animals. The receptor is a tyrosine kinase, an enzyme that when activated, in this case by insulin, adds phosphates to residues of the amino acid tyrosine in its target proteins. The researchers found that in the absence of PTP-1B, the receptor attached 2.5 times as many phosphate groups to the next protein in the insulin signaling cascade than it normally does.

So far, all the results had been in healthy mice, rather than diabetic ones. Obesity predisposes to type 2 diabetes in ways researchers do not fully understand. So to see if knocking out PTP-1B helps diabetic mice become more insulin-sensitive, the researchers tried to induce the condition by fattening both normal and mutant animals on rodent chow with 10 times the normal amount of fat. Only the normal mice became obese and showed signs of diabetes. "We expected both [strains] to become fat," Kennedy says, "but right off the bat it became obvious that the knockout mice didn't gain as much weight."

Equally important, the mice without PTP-1B appear healthy. Because tyrosine phosphatases may help check cell growth, "you might have had a beneficial effect on insulin signaling, but you also might have had tumors," says endocrinologist Jeffrey Flier of Harvard Medical School. But the PTP-1B knockout mice have now passed the advanced age of 2 years and show no signs of cancer.

Still unclear is how enhanced signaling through the insulin pathway protects against obesity, although the researchers speculate that it might boost energy consumption by liver and muscle cells. Also unknown is whether PTP-1B overactivity plays a role in excess weight gain in normal animals—or in people. But even if it doesn't, that might not matter for developing an anti-obesity drug, says diabetologist Barry Goldstein of Thomas Jefferson University in Philadelphia: "The fact that the results are so clean, that there are apparently no other phenotypic changes, makes [PTP-1B] a very exciting drug target."

–DAN FERBER

Dan Ferber is a writer in Urbana, Illinois.

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ScienceScope

The Source Is With Him The U.S. Department of Energy (DOE) has tapped David Moncton (below)—head of the Advanced Photon Source (APS) at Argonne National Laboratory in Illinois—to lead construction of the agency's new science flagship, the Spallation Neutron Source (SNS). The change comes after a January advisory panel report criticized Oak Ridge National Laboratory in Tennessee, where DOE plans to build the SNS, for lacking the skills necessary to manage the $1.3 billion project.

Work on the SNS, which will create neutron pulses for studying the atomic structure and physics of materials, is scheduled to begin this year and finish in 2005. But reviewers worried that Oak Ridge's Bill Appleton, the project's original midwife, lacked experience with building monumental science facilities. Moncton, on the other hand, shepherded the $812 million APS—where he will retain a quarter-time position—to completion. That, together with his training as a neutron scientist, makes him "the right man for the job," says Brian Kincaid, former director of the Advanced Light Source at Lawrence Berkeley National Laboratory in California.

Stem Cell Take-Home Test Every institute chief at the National Institutes of Health (NIH) has a homework assignment this spring. The taskmaster is Senator Arlen Specter (R–PA), chair of the appropriations subcommittee that approves the NIH budget. The topic, assigned by Specter during a 23 February hearing on NIH's budget: Explain why human embryonic stem cell research is important to your scientists.

Specter wants the essays because he's worried that NIH's plan to fund human stem cell research is becoming "a real battleground." Legal experts at the Department of Health and Human Services (HHS) ruled in January that a congressional ban on funding of human embryo research doesn't apply to stem cells derived from embryos (*Science*, 22 January, p. 465). But 70 conservative House members and 7 senators strongly disagree. They wrote to HHS Secretary Donna Shalala asking her to halt NIH's plan to forge ahead with stem cell research. But Shalala and NIH Director Harold Varmus say they won't retreat—even if they are getting poor grades from some lawmakers.