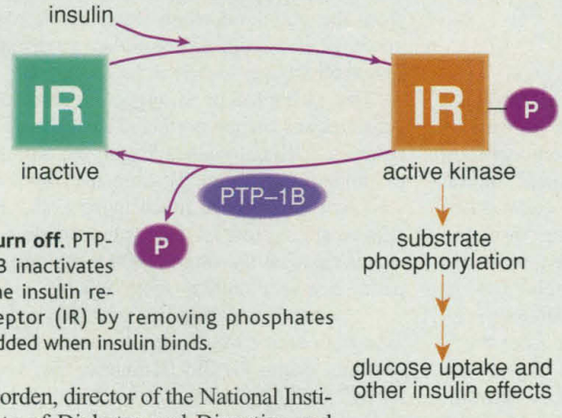
Tremblay of McGill University in Montreal, came to that conclusion by creating a line of mice lacking an enzyme called protein tyrosine phosphatase–1B (PTP-1B). Those animals, the researchers found, are more much sensitive to insulin's blood sugar–lowering effects than control animals. Because type 2 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.

CREDIT: (TOP) ARGONNE NATIONAL LABORATORY; SOURCE: (BOTTOM) CHIDAMBARAM RAMACHANDRAN

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.

dence into a consistent picture of Japanese origins, which is presumed to rest on two distinct waves of migrants, "could set an example for [work on] other regions" with more complex migratory patterns.

–DENNIS NORMILE

SCIENTIFIC MISCONDUCT

Chinese Journals Pledge Crackdown

BEIJING—Chinese journals and scientific societies have embraced a new code of conduct designed to reduce the incidence of plagiarism, fabrication, and other acts of misconduct. The policies, adopted last month at a national meeting here, are meant to alert editors and authors to a problem that Chinese authorities see as a threat to their rising investment in research.

The campaign, organized by the China Association for Science and Technology (CAST), is the most visible to date on this sensitive topic (*Science*, 18 October 1996, p. 337). Two 1997 cases, involving duplicate publication of research from its magazines, prompted the association's Committee of Morality and Rights of Science and Technology Researchers to convene a meeting of representatives from several hundred scientific societies and journals. On 1 February the group endorsed a seven-part "Moral Convention."

The one-page statement asks journal editors to refrain from publishing poor-quality, "from-a-buddy" articles, to reject articles of questionable authorship, and to weed out multiple submissions. It suggests that authors found to have committed plagiarism, fabrication, or falsification of data be warned in writing, followed by a boycott of future articles, notification of their home institution, and public disclosure of their misdeeds. CAST is also thinking about asking all journals signing the convention to reject any articles for up to 10 years from authors found guilty of misconduct, and to make their names public.

In addition to recommending ways to stamp out misconduct, the convention also affirms the role of authors and seeks to promote better communications between journals and the scientific community. It asks journals to notify authors of the status of their submissions within a reasonable period of time and to respect their "rights and interests."

Chinese journals and science officials have long been concerned about scientific misconduct, especially plagiarism, but the two 1997 incidents brought the issue to a head. In one case, an associate professor at the Higher Education Research Center of Nanjing Teachers' University copied an entire article on pay disparities in the labor market from *Science and Technology Guide*, a monthly CAST publication that is widely circulated, and published it in another, less prominent journal. The plagiarism was discovered after the two journals merged their editorial offices and CAST became publisher of both journals. The second incident involved a faculty member at the Institute of Higher Education of Tongji University in Shanghai, who copied an article in the *Guide* about chaos theory. The plagiarism was spotted by a reader.

Both plagiarists were identified in a May 1997 article in the *Guide*, which has decided not to accept any more submissions from the authors. "There must be no compromise over dishonesty and no cover-up. Taking pity will harm the cause of science," says Cai Decheng, former standing vice president of the *Guide*.

Chinese scientists and journal editors see the convention as a useful tool and a necessary step in combating misconduct. "These cases of misconduct have ruined scientific values and damaged academic standards," says Zhang Yutai, first secretary of the CAST Secretariat. But some scientists worry that it will not be sufficient to root out the problem. "The burden of proof is mainly on the journals themselves," notes one director of CAST who requested anonymity. "But it is difficult for editors to raise copyright or other legal issues with the wrongdoer." Journals that decide to conduct investigations often get little help from the home institutions, notes one editor: "Some institutions and universities cover up the wrongdoing to protect their own reputation."

> **"There must be no compromise over dishonesty. Taking pity will harm the cause of science."**
>
> **—Cai Decheng**

The process needs to go a step further, agrees Tsou Chen-lu, a professor of biophysics and former head of the National Laboratory of Biomacromolecules in Beijing. "What we need is a convention on morality and behavior of Chinese science researchers that builds upon this convention," says Tsou. Without a broad national policy, he and other scientists fear that self-interest may stifle efforts to root out misconduct.

–JUSTIN WANG

Justin Wang writes for *China Features* in Beijing.

CREDIT: SAM KITTNER

ScienceScope

The Devil Is in the Data Rita Colwell (below), director of the National Science Foundation, has taken the unusual step of opposing new data access regulations being proposed by her own Administration. The law, written last year by Senator Richard Shelby (R–AL), is designed to force taxpayer-funded scientists to turn over their raw data to anyone who files a Freedom of Information Act request. The White House Office of Management and Budget (OMB), however, has attempted to limit the law's reach by interpreting it narrowly (*Science*, 12 February, p. 914). Under rules the OMB hopes to finalize by 30 September, researchers would have to disclose only published data used to develop policy or rules.

But that compromise doesn't sit well with Colwell. "No matter how narrowly drawn," the rule "will likely harm the process of research in all fields," she wrote in a 22 February letter to OMB Director Jacob Lew. Instead, she urges the White House to get behind a bill sponsored by Representative George Brown (D–CA) that would repeal the law.

Australia's Food Court A special "citizens court" will put genetically modified (GM) foods on trial in Australia next week. Sponsors of the unusual courtroom drama, including the Australian Museum and private groups, hope it will help forge a consensus on how the government should regulate the controversial products.

On 10 March, 14 lay jurors will gather at the Old Parliament House in Canberra to begin questioning a range of experts on eight hotly debated questions, including whether Australia should support international regulation. The jury's verdicts—to be rendered after 3 days of testimony—could help shape government regulations, such as GM food labeling requirements due in May. Observers hope the trial, modeled after a public-input process developed in the Netherlands, will help steer officials to wise decisions. Jurors "can be pretty damned insightful and see through the guff to the heart of the matter," says biologist Richard Jefferson of Cambia, a Canberra-based agricultural research institute.

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