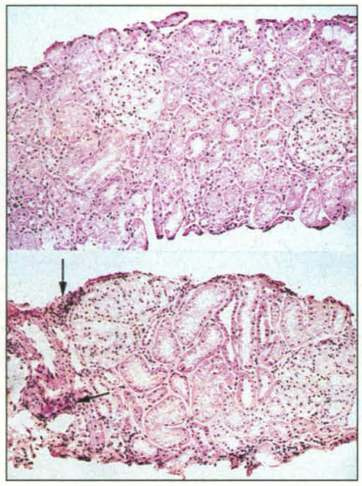
T cells encounter a foreign molecule such as those on transplanted tissue, they become activated and produce more CD154, which in turn binds to a receptor called CD40 on other immune cells. That sends a signal for an all-out, devastating assault on the transplanted organ. The antibody is designed to block the attack by binding to CD154 and preventing it from binding to its receptor.

The strategy has so far surpassed expectations. Building on initial animal trials, the team transplanted new kidneys into 25 juvenile monkeys. To increase the challenge, donors and recipients were mismatched for the major histocompatibility complex, the series of proteins on cells that help the immune system distinguish between native and foreign cells. The mismatch had lethal consequences: Control monkeys given either no treatment or standard immunosuppressive drugs rejected the organs and died in 9 days or less.

But animals given the drug fared much better. A group of nine monkeys received weekly doses of the antibody for 1 month and monthly doses for 5 months afterward. All treatment was then stopped. More than a year after treatment, eight of that group are still alive and well. The one death was due to complications during a routine blood draw, and an autopsy revealed that the monkey had normally functioning kidneys when it died. Another monkey from a different trial received a transplant in March 1997, was given a month of therapy, and has been living off a mismatched kidney ever since. "It just works every time," says Harlan of the drug. "I'm half expecting the balloon to pop at some point, but so far it hasn't."



No reject. Transplanted monkey kidney tissue *(bottom)* shows clusters of active immune cells (arrows), but looks like healthy tissue *(top)* and functions normally.

The technique, moreover, is not limited to kidney transplants. Kenyon's team has achieved similar success using the same antibody to block rejection of pancreas cell transplants in monkeys. In a paper in press at the *Proceedings of the National Academy of Sciences*, she reports that all six monkeys who received the CD154 antibody with their transplants have functioning islet cells as much as a year and a half later.

So far, Kirk and Harlan haven't been able to detect any side effects. Their monkeys have normal numbers of immune cells, did not develop wound infections, and responded normally to vaccines, indicating healthy immune function. Initial safety trials of the drug in humans, ongoing for more than a year, haven't produced any side effects, either. "I'm sure there are some downsides," says Kirk, "but we haven't found them yet."

One puzzling finding is that standard immunosuppressive drugs seem to interfere with the antibody's effect: Of the 11 animals that received a combination of standard immunosuppressors and the antibody, five died after acute rejection episodes. And no one is sure why the monkey's immune system accepts the foreign tissue long after the drug is stopped, although there are several theories.

Some scientists suspect that T cells activated by the foreign organ but lacking the CD154 signal simply die shortly after a transplant, although it's not clear why new generations of T cells wouldn't recognize and attack the tissue. Others suspect that the "stalled" T cells may somehow be protective. Biopsies of the transplanted kidneys reveal small clusters of activated T cells, which look like the ones seen in a few rare patients who, against doctors' orders, stop taking immunosuppressive drugs and surprisingly don't reject their transplants, says transplant immunologist Hans Sollinger of the University of Wisconsin, Madison. That may also help explain why the antibody performs poorly in combination with immunosuppressive drugs, which block T cells' initial activation.

That interference has made it difficult to design human trials for the new drug. Asking patients to forgo standard drugs to allow the experimental treatment to work is a "daunting" ethical challenge, says transplant immunologist Laurence Turka of the University of Pennsylvania. But the promising animal data prompted the National Institutes of Health last year to set aside a wing in its clinical center for trials of tolerance-inducing therapies, and researchers have enrolled a few patients for trials of a combination of the new drug and low doses of standard immunosuppression. If those prove as successful as the monkey trials, transplants may become an easier choice. **–GRETCHEN VOGEL**

CREDITS: (LEFT): KIRK *ET AL.*, *NATURE MEDICINE* 5, 6 (JUNE 1999); (TOP RIGHT) DFG; (BOTTOM RIGHT) RUPERT OBERHAUSER/BLACK STAR

GERMAN SCIENCE POLICY

Panel Calls for More Flexibility in Research

Germany's vaunted research system may be too rigid for its own good. Critics have accused it of being overly hierarchical and too slow to respond to hot research areas, and complained that it tends to hold back some young researchers by keeping them under the thumb of older professors. Last week, an international panel of prominent scientists echoed some of those gripes and went on to suggest a raft of reforms that aim to achieve more flexibility, greater cooperation between research institutes and universities, and give postdocs considerably more independence.

Reform school. Winnacker and Bulmahn back change.

The report was requested by the Federal-State Commission for Educational Planning and Research Promotion (BLK), which represents research and higher education ministries at the state and national level. In a summary issued last week, the 10-member panel—led by materials scientist Richard Brook, chief executive of Britain's Engineering and Physical Sciences Research Council—praised the overall quality of German research, which is based on three pillars: universities, the Max Planck Society, and the DFG basic research granting agency. "This is a strong, high-achieving research system," says Brook.

But the panel also highlights areas in

need of improvement. It recommends that the traditionally independent Max Planck Society forge closer ties to universities and develop research groups that can respond more quickly to rapid new developments in science. In addition, it suggests that universities replace the post–Ph.D. "habilitation" qualification for aspiring professors with something like the U.S.–style "assistant professor" system, and that the DFG restructure its peer-review system and its strategy for promoting new disciplines. Overall, panelists found, the research system tends to be driven by middle managers, such as Max Planck institute directors. "There are great merits in a strong middle, but we'd also like to see a bit more life at the upper and lower levels," says Brook, who directed a Max Planck institute in Stuttgart from 1988 to 1991.

After its yearlong inquiry, the panel concluded that closer cooperation between Max Planck institutes and university researchers might help improve what Brook calls the "mixed reputation" of German universities. Some scientists criticize Germany's university system for being too rigid, especially during the habilitation years. German federal research minister Edelgard Bulmahn, deputy chair of the BLK, has pointed out similar shortcomings. In a recent interview with *Science*, she said she wants to phase out the habilitation—a lengthy process during which postdocs do major projects under the strict supervision of professors—and bolster ties between university and nonuniversity research. Last week, Bulmahn called for "an intensive discussion" of the report's findings.

Brook says the panel found the DFG granting agency to have "a conservative nature" that could be revitalized by revamping aspects of its structure and programs, and perhaps by more actively steering researchers toward areas of research that it deems important. The report suggests a "strategically oriented program" for research grants, as well as a more active approach to funding progressive university programs, such as those supporting the early independence of young scientists. It also recommends opening up the DFG's peer-review system—for example, by including more women and younger researchers as reviewers.

Both the DFG and Max Planck responded swiftly to the report. The DFG's president, biochemist Ernst-Ludwig Winnacker, calls it "a thorough analysis" and says the DFG has already set up new funding programs for independent young scientists and is expanding its roster of peer reviewers. But Winnacker questions the suggestion that the DFG cherry-pick areas of new high-priority research: "The DFG cannot, must not, and should not compete with the federal and state governments, which are extensively involved in research funding that is guided by general political criteria."

In a statement, Max Planck said it was already "well prepared" to implement some of the commission's suggestions, in part because the society is in the midst of an internal reassessment, and also because it has already taken steps to strengthen its connections to universities and to bolster its programs for young researchers. The society plans to establish several "International Max Planck Research Schools" near universities, increasing the number of Ph.D. students who conduct research at its institutes.

Brook says he expects German research to continue to thrive, especially if reforms are embraced: "It's much more difficult to evaluate a high-quality research system, such as Germany's, than a low-quality one."

–ROBERT KOENIG

PHYSICS

Come Fly With Me, Goldin Tells Physicists

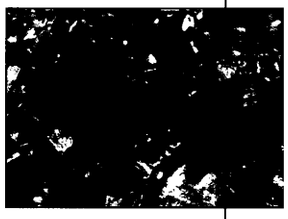
BATAVIA, ILLINOIS—Space is the final frontier for particle physics, NASA Administrator Daniel Goldin declared in a 28 May press conference here at the Fermi National Accelerator Laboratory (Fermilab). But Goldin's vision of joining forces with the Department of Energy (DOE) and other agencies in an all-out assault on the mysteries of gravity and high-energy physics failed to uplift some listeners when he labeled Earth-bound accelerators—the focus of DOE's high-energy physics program—a "smokestack approach" to research.

The message of the press conference, which also included representatives from DOE and the National Science Foundation

All aboard. Goldin wants high-energy physicists to propose space experiments.

ScienceScope

Experimental Shellfish Mussel Shoals—now known as Muscle Shoals—may once again live up to its name. The U.S. Fish and Wildlife Service (FWS) announced last week that it wants to reintroduce 16 species of endangered shellfish to the 20-kilometer stretch of Alabama's Tennessee River, once known for its dense populations of freshwater mussels.



In the 1930s, pollution and dam construction devastated the shelly shoals. But the river has bounced back, and biologists believe that they could soon begin to restore monkeyface, pigtoed (above), and other mussels. Before replanting can begin, however, the FWS has to reassure some local shellfish harvesters and governments that the protected species won't bring unwanted regulation. To jump that hurdle, the service has proposed calling the returnees "nonessential experimental" populations, a designation that "will avoid lawsuits," says one FWS official. Shellfish friends and foes have until 26 July to comment.

Making Amend(ment)s The battle over a law that requires federally funded scientists to hand over raw data to anyone who files a request has shifted back to Congress. This spring, the White House Office of Management and Budget (OMB) collected more than 8,000 comments on its proposal for implementing the 8-month-old measure, many from scientists worried that it would hinder research by threatening patient confidentiality and proprietary collaborations with companies. In response to that concern, House appropriations committee members James Walsh (R–NY) and David Price (D–NC) plan to offer an amendment to OMB's funding bill that would put a 1-year hold on the law pending a study on its effects.

Business groups are squaring off over the amendment. Supporting the delay are pharmaceutical, biotech, and other firms, including GM and IBM. They are opposed by a legion of oil companies, the U.S. Chamber of Commerce, and small business groups. No use handicapping this contest: "It could go either way," says a Walsh staffer.

If approved by the House and Senate, the amendment—which could be offered as early as next week—wouldn't go into effect until 1 October, after OMB is expected to have issued its final rule.

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