Jaeglé's group also reached saturation in their device, which is pumped by a large infrared laser. "It was a surprising discovery that with a mirror that reflects only over a few centimeters we could multiply by a factor of 100 the intensity of the radiation," he says.

The feat takes Rocca's tabletop laser closer to practical application. For the first time, he and his colleagues announced, they could measure "a substantial energy output from such a tabletop device." The result has excited a community of potential users, he says. "We have been approached by a very large group of people who either are starting up experiments or are planning to start experiments."

Although Rocca's laser looks a lot like the tabletop device researchers dream of, its soft x-rays have wavelengths a little too long for some tastes. "If he would get down to [10 or 20 nanometers], his x-ray laser would catch on much faster," says Dennis Matthews of LLNL, who developed the first x-ray laser with substantial amplification in the early 1980s. "Then you would be doing things people travel to synchrotrons for." Synchrotrons, massive electron-storage rings, are currently researchers' only source of nearly coherent x-rays. Rocca is also trying to boost his machine's repetition rate, now at one shot a minute. If he could achieve his goal of one shot per second, says Matthews, his laser "would put out as much energy per second as you normally get on a beam line on a large synchrotron."

There are plenty of other obstacles standing in the way of a practical x-ray laser. Current x-ray mirrors—complex structures typically consisting of 800 to 1200 molybdenum carbide and silicon layers half a wavelength thick—don't stand up well to the harsh conditions of the hot plasma and the intense radiation, and most of them last just one shot. But a group led by Troy Barbee Jr. of LLNL reported at the meeting that by building multilayer mirrors from new materials—using silicon carbide in place of silicon, for instance—they improved the structures' heat resistance enough to withstand a few shots. These new mirrors should not only improve the lasers themselves but also make it easier to harness the x-rays they produce. "We can do interferometry and various kinds of imaging, a whole variety of things that you couldn't possibly do 2 years ago," says Barbee.

X-ray laser researchers believe that their devices are now in the stage that optical lasers reached in the early 1960s, when they ceased being laboratory curiosities and began opening up a huge variety of applications. Says Jaeglé, "We have reached a turning point: The x-ray laser leaves the area of the study of plasmas to become a laboratory source."

–Alexander Hellemans

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IMMUNOLOGY

Muscling Transplants Into Mice

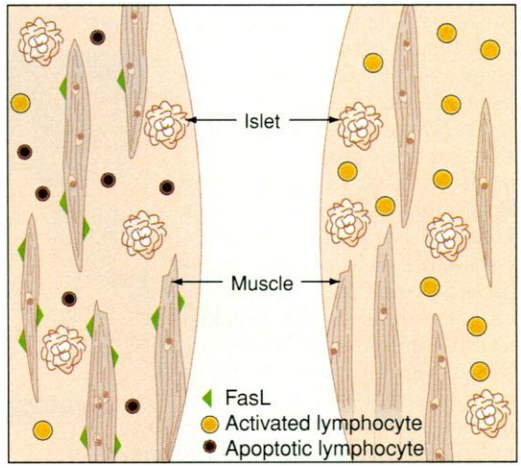
Rejection threatens all tissue transplants, as the immune system seeks out and destroys foreign cells. Yet this threat does not exist everywhere in the body. Like safe havens for refugees, the body harbors protective pockets, in the eye and testis, for example, where transplants are safe from immunologic patrol. Creating similar "immune-privileged" pockets to protect a new heart, liver, or kidney graft has long been a transplant biologist's dream. Now researchers at Children's Hospital of Philadelphia have devised a way to do that by genetically engineering muscle cells to produce a key ingredient of immune privilege: a protein known as the Fas ligand, or FasL, that can induce immune cells to kill themselves.

On page 109, transplant surgeon Henry Lau, molecular biologist Christian Stoeckert, and two colleagues report using their muscle-cell bodyguards to protect transplants of islet cells, the insulin-producing cells of the pancreas, in diabetic mice. "It's a stunning advance," says Douglas Green of the La Jolla Institute for Allergy and Immunology in California. "It's almost the Holy Grail of immunosuppression to restrict the suppression to the environment of the graft."

Richard Duke of the University of Colorado Health Sciences Center in Denver, whose team was the first to find a role for FasL in immune privilege, calls the work "a home run." The finding, Duke says, not only opens the door to a possible treatment for the 700,000 people in the United States with insulin-dependent diabetes, but also holds promise for people receiving other types of tissue and organ transplants who now must take immunosuppressive drugs, which often lead to infections and cancer.

In conceiving their islet-grafting strategy the Children's Hospital team took its cue from a great deal of work showing that FasL and its partner, a protein called Fas found on immune-cell surfaces, help shut down immune responses. They do this by inducing immune cells to kill themselves in a process called apoptosis. FasL sends the death signal by binding to its receptor, Fas, which transmits it to the cell interior. This interaction is also the basis for immune privilege, as Colorado's Duke and his colleague Donald Bellgrau showed last year for the testis (*Nature*, 19 October 1995, p. 630), while Thomas Ferguson's team at Washington University Medical School in St. Louis produced similar findings for the eye (*Science*, 17 November 1995, p. 1189).

Several researchers quickly began trying to express FasL in a variety of tissues in hopes of using the molecule as a transplant tool, but Lau's is the first group to claim a victory. After showing that muscle cells genetically engineered to make FasL kill tumor cells expressing Fas in lab culture, they began the transplant studies. For these, the team transplanted islet tissue wrapped with the engineered muscle cells under the kidney capsules in 31 diabetic mice. They compared these to 16 control mice, including some who received only islets and others who received islets cloaked in unaltered muscle. Not only did the engineered muscle cells prolong survival of the islet-cell grafts compared to the controls, presumably by killing T cells before they got to the islet cells, they did so in a dose-dependent way: Transplanting 10,000 muscle cells lengthened average survival from 10 to 26 days, while transplanting 2 million muscle cells upped survival to more than 84 days.



SOURCE: LAU *ET AL.* ILLUSTRATION: K. SUTLIFF

Muscular bodyguards. Muscle cells expressing FasL (*left*) protect islets by inducing immune-cell suicide.

The downside is that more than half the mice receiving the top dose lost their grafts within 80 days, in part because the muscle cells stopped expressing FasL. Thus, before any studies begin in humans, biologists must find a way to ensure long-term FasL expression. What's more, the experiment was done in mice with chemically induced diabetes, so the finding must be confirmed in mice with naturally occurring autoimmune diabetes. Still, researchers are confident that, as La Jolla's Green puts it, this FasL work represents "the beginning of a new era in transplantation."

–Ingrid Wickelgren

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