Altered Antibody Boosts Transplants

The immune system takes a dim view of transplants. Any tissue or blood that doesn't come from an identical twin counts as foreign matter to be destroyed. Treatment with immune-suppressing drugs can counteract such rejection, but it leaves the individual vulnerable to cancer or other ills. Even with drug treatment, many patients reject transplants.

At the core of this reaction is a molecule called CD154. It signals T cells—the immune system's shock troops—to spring into action against transplants. Two studies in rhesus monkeys now show that a drug called hu5C8 can waylay this attack without shutting down the rest of the immune system. The antibody binds to CD154, blocking the chain reaction that would have led to overzealous manufacture of T cells.

In a study described in the June NATURE MEDICINE, scientists gave nine rhesus monkeys kidney transplants from unrelated donors and also intravenous doses of hu5C8, which is made by Biogen in Cambridge, Mass. Previous studies showed that this genetically engineered version of a human antibody might block T cell activation (SN: 8/9/97, p. 84).

One of the nine treated monkeys died of unrelated causes, but the other eight are thriving with their transplanted kidneys. Five of these animals completed their 5-month regime of antibody treatment about a year ago, says study coauthor Allan D. Kirk, a transplant surgeon at the Naval Medical Research Center in Bethesda, Md.

Four other monkeys, which received a transplant but not the antibody, rejected the transplanted kidneys within 8 days. Eleven monkeys getting a combination of the antibody and standard immune-suppressing drugs showed mixed results—some rejected the organs, others didn't.

In a separate study, researchers removed the pancreases of six rhesus monkeys and then gave them hu5C8 along with new pancreatic islet cells from unrelated donors. The transplanted cells, placed in the monkeys' livers, weren't rejected, says study coauthor Norma S. Kenyon, a transplant immunologist at the University of Miami School of Medicine. Two monkeys that didn't receive the antibody rejected islet cells.

This study, to be published this summer in the PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, raises hopes for diabetes patients. Islet cells normally make the hormone insulin, and the transplanted cells started producing it immediately. The experiment suggests a means to reverse type 1, or juvenile-onset, diabetes, a condition in which islet cells are destroyed. "I don't want to raise false hopes, but I think this is a very big step forward," Kenyon says.

In a study of baboons to be published soon in DIABETES, Kenyon and her colleagues show that hu5C8 also reversed rejection in four baboons that had earlier received islet-cell transplants.

"This is an exciting drug," says Mitchell L. Henry, a surgeon at Ohio State University in Columbus. He's impressed that two types of organ transplants succeeded.

In all these experiments, the antibody's precise role remains a mystery.

"Our immune system didn't evolve [just] to keep us from getting transplants. It is aimed at infectious pathogens," says endocrinologist David M. Harlan of the Naval Medical Research Center in Bethesda, Md., who participated in all three studies, as did Kirk. Transplant rejection may simply be a case of mistaken identity, and CD154 may somehow remedy the problem.

Evolution may have provided compounds that act as shutoff switches each time T cells are produced to mount an attack, Harlan suggests. The antibody hu5C8 may somehow tap into that mechanism, he says.

This model could explain why suppression drugs hampered hu5C8's effectiveness in the kidney-transplant experiment. The drugs could be keeping T cells from processing a shutoff signal, Kirk says.

"The lesson is that we must choose our signals carefully, not simply block them all," says Polly Matzinger of the National Institute of Allergy and Infectious Diseases in Bethesda, Md., writing in NATURE MEDICINE. *—N. Seppa*

New elements pop in, cousins may linger

Two new elements, numbers 116 and 118, have winked briefly into existence during high-energy impacts inside a particle accelerator, scientists announced this week. The not-yet-confirmed findings may spark even more element discoveries this year, several researchers say, that may spill from the heavy end of the periodic table of elements like fruit from a cornucopia.

Out of that horn of plenty, experimenters later may pluck long-predicted, extraordinarily stable, superheavy isotopes, the findings suggest. Isotopes are versions of an element that differ only in their numbers of neutrons.

The discoveries are "really very exciting news," comments Sigurd Hofmann of GSI, the German center for heavy-ion research in Darmstadt. Experiments have begun there this week to attempt to duplicate and improve upon the results, he says.

Victor Ninov of Lawrence Berkeley (Calif.) National Laboratory led a team of government and university scientists in the recent experiments. By pummeling a lead target for more than 10 days with roughly a million trillion krypton ions, the team made three atoms of 118, which quickly decayed into 116, 114, and other elements.

Prevailing wisdom held that the approach wouldn't work because it involved hurling unusually heavy particles against the target. The team tried anyway, encouraged by the calculations of Robert Smolańczuk, a Fulbright scholar from the Soltan Institute for Nuclear Studies in Warsaw, Poland, who is working at the Berkeley lab.

"By golly, the miracle did happen. It's really exciting," says the lab's Albert Ghiorso.

Given the surprising success of the approach, Ken Gregorich, also of the Berkeley lab, expects researchers there, at GSI, or in Russia soon to fire krypton at bismuth to make element 119. Because 119 would decay into the yet-undiscovered 117, 115, and 113, science could gain four new elements in one fell swoop. "It will happen somewhere before the end of the year," Gregorich predicts.

In the Berkeley experiments, the isotopes of 116 and 118 lasted only about 1.2 milliseconds and 200 microseconds, respectively. Nonetheless, their lifetimes were long enough to indicate that current investigations are converging on a cluster of exceptionally stable superheavy isotopes. Such isotopes may survive many years.

Heavy-element researchers say that this cluster inhabits an island of stability in a sea of short-lived isotopes.

The new discoveries follow closely upon the first sighting of element 114 by a Russian-American group (SN: 2/6/99, p. 85). That experiment was hailed as the first to reach the stability island.

"It's exciting, of course, because [the isotopes of 116 and 118 are] also on the edge of this superheavy element island," says Ron Lougheed of Lawrence Livermore (Calif.) National Laboratory, who was a member of the Russian-American team. The island may harbor "a whole new chemistry" that can be explored if its isotopes last long enough, he says. *—P. Weiss*