Therapeutic monoclonal antibody okayed

The Food and Drug Administration (FDA) has approved a monoclonal antibody for use in acute rejection episodes following kidney transplants. Though monoclonal antibodies are already used on blood and tissue for diagnostic purposes, last week's announcement marked the first time such an antibody has been okayed for use in humans. In making the announcement, FDA Commissioner Frank E. Young said he expects more monoclonal antibodies will be approved following controlled clinical trials.

The tricky thing about kidney transplants these days is not the operation itself but the recipient's attempt to reject the organ, even when a close relative is the donor. Rejection comes in three phases – the hyperacute stage immediately following the transplant, the acute stage days or weeks later, and the chronic stage, which lasts as long as the transplanted organ. All are presently prevented or controlled with drugs, which are not always effective.

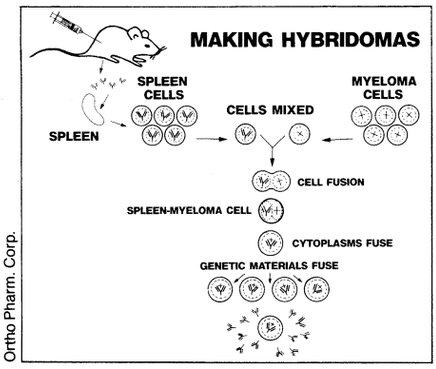
The newly approved monoclonal antibody, called OKT3, attacks T cells, a subset of which can cause acute rejection of the kidney. In a previously reported human trial, OKT3 reversed acute rejections in 58 of 62 transplant recipients, or 94 percent. Conventional drug treatment with steroids or cyclosporine was able to reverse rejection in only 45 of 60, or 75 percent, with failure commonly resulting in the loss of the kidney.

OKT3 is given as a one-shot injection when an acute rejection occurs; within hours, the T cells burst and the episode halts. While the kidney is protected, there can be some side effects, including fevers, chills, tremors, shortness of breath, chest pain and nausea.

The FDA approval applies to use of the antibody in an initial acute rejection. Whether it will prove valuable for subsequent attacks, or whether the body's immune system will disable the foreign antibody, remains to be seen.

Monoclonal antibodies are made by hybridomas, which are hybrids of antibody-producing cells and long-lived tumor cells. To make a hybridoma, researchers immunize an animal, in this case a mouse, with a specific substance, in this case human T cells. The mouse's antibody-producing spleen cells are collected and fused to tumor cells. Each resulting hybrid is cloned, and the clonal line that produces the desired antibody is selected and put into a production line.

Hybridomas are already used for producing uniform antibodies needed in diagnostic testing kits. And several human trials are under way to test the ability of monoclonal antibodies to combat cancer and immune system diseases.



Ortho Pharm. Corp.

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About 7,000 kidney transplants are done each year in the United States, and about 60 percent of them result in acute rejection. But the OKT3 work is expected to have implications beyond this group. "The theory of using a [mouse] monoclonal antibody in man is now established," says Thomas Zuck of the FDA. "The safety issues are behind us."

– J. Silberner

Biotech rules released

After a five-month delay, the President's Office of Science and Technology Policy has released its framework for the regulation of biotechnology. Signed by President Reagan June 18, the package of guidelines and rules uses what it calls "a mosaic of existing federal law," dividing responsibility among the agencies already regulating the young industry on a *de facto* basis (SN: 6/7/86, p. 366). It took effect upon signing.

The policy has drawn fire from several directions. Some scientists are displeased that certain organisms from which a gene has been deleted are being exempted from rigorous review. Jeremy Rifkin of the Foundation on Economic Trends says he will challenge the new policy in court. The U.S. Congress continues work on its own biotechnology legislation. □

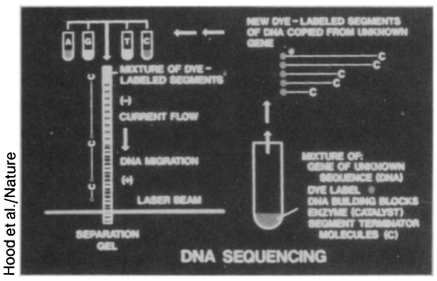
Speed-reading the genetic code

Three billion units long, the complete set of human genes has posed an unapproachable barrier to scientists craving access to the information it contains. The barrier still stands, but technology has taken great leaps toward it in the last decade. One of the most promising is the first automatic DNA sequencer, recently announced by researchers at Caltech in Pasadena. The machine, although still a "model T" version, sharply reduces the chances of error in reading DNA while speeding the process and cutting the costs, Leroy Hood told SCIENCE NEWS. Hood worked with a team of colleagues to develop the new sequencer.

The gene sequencing technique that has been in use is a laborious, multistage process; and at a cost of $1 to $5 to sequence each nucleotide base (the "beads" on the "add-a-pearl" string of DNA), it is also prohibitively expensive for a large-scale project. The automatic sequencer will bring the cost down to pennies per base, Hood says, and eventually may be able to do as much in a day as a researcher now can do in a year. While the new technique is no more accurate in its ability to distinguish among bases, it all but eliminates the possibility of mistakes in the transcription of data.

The automatic sequencer – which was reported in the June 12 NATURE – allows researchers to begin projects that were beyond imagination a few years ago, according to Hood. "The problems of sequencing the human genome are problems of technology," he says. "In a sense, it's like going to the moon. We know we can do it now; it's just a matter of inventing machines."

– L. Davis



Hood et al./Nature

The new sequencing technique, like the old one, starts by generating fragments of the DNA sequence under analysis, using analogs of the bases – cytosine (C), guanosine (G), adenosine (A) and thymidine (T) – as segment terminator molecules (DNA synthesis terminates wherever the base-analog is incorporated). By varying the concentration of the terminator molecules, a researcher can generate fragments of different lengths, each fragment representing successive occurrences of a given base. The fragments are put on an electrically charged gel column, where they migrate downward, the smallest fragments moving fastest. Because the new technique uses dye labels to distinguish each of the four terminator molecules, all the fragment subsets can be put on the column at once. Using the old method, a researcher had to examine four gel columns to determine the relative lengths of DNA fragments, and manually transfer the collated information to a computer; here, a computer automatically notes the order of the fluorescing dyes as fragments pass a laser at the bottom of the column.