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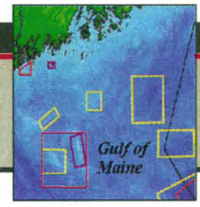
How sunspots might change climate



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Sanctuaries on the sea floor

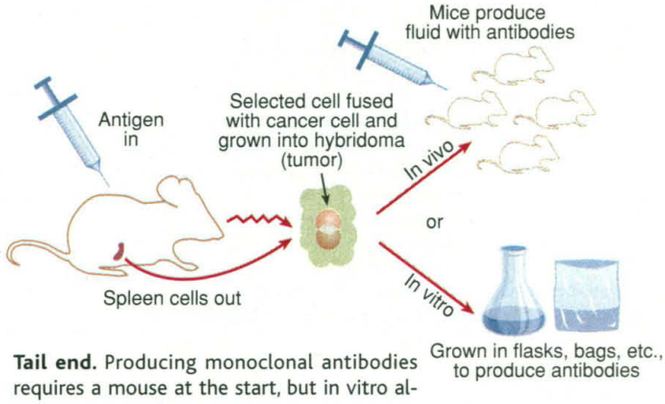
IMMUNOLOGY

Alternatives to Animals Urged For Producing Antibodies

A National Academy of Sciences (NAS) panel has concluded that biomedical researchers should produce most types of monoclonal antibodies using methods that don't require killing mice. But it argues that the use of mice is essential in some cases and should not be banned. Observers say that the committee's report,* released this week, could help prevent a long-running feud from escalating into a high-stakes legal fight.

Two animal rights groups—the American Anti-Vivisection Society (AAVS) of Jenkintown, Pennsylvania, and its research arm, the Alternatives Research and Development Foundation (ARDF) of Eden Prairie, Minnesota—have threatened to sue the National Institutes of Health (NIH) to prevent researchers from using a technique, known as the mouse ascites method, to manufacture monoclonal antibodies. Researchers using the method inject an antigen, or disease-causing agent, into a mouse so that its spleen cells begin producing antibodies—immune system proteins that react to the antigen. Then, spleen cells producing the desired antigen are removed and fused with fast-growing cancer cells to produce a hybridoma, or tumor, that manufactures one kind of antibody. To increase production, researchers inject the hybridoma into the abdominal cavity of a mouse, where the cells grow and secrete the antibody. Technicians harvest the antibodies from the swelling abdomen using a syringe. Typically, scientists can "tap" a mouse only a few times before it dies or must be killed.

Many monoclonal antibodies can be grown by culturing the hybridoma in plastic flasks or bioreactors, then isolating the antibodies. But U.S. researchers still tap an estimated 1 million mice per year to produce monoclonals used for everything from analyzing tissue samples to attacking cancer.



Tail end. Producing monoclonal antibodies requires a mouse at the start, but in vitro alternatives exist for extraction.

In an April 1997 petition, the AAVS charged that NIH was ignoring its own animal care guidelines by not doing enough to promote alternatives to the ascites method. It demanded that the agency prohibit researchers it funds from using the method unless they could show it was essential. Such rules, the group noted, would bring the United States in line with four European nations—the United Kingdom, Germany, the Netherlands, and Switzerland—that ban routine use of the ascites method, with some exceptions. But NIH concluded that a ban was "not appropriate" and that, although many alternatives appear promising, some antibodies cannot be grown outside mice or are too expensive to culture.

Unwilling to take no for an answer, however, AAVS revised its petition in March 1998 and threatened to sue if the agency again rejected its request. Seeking an outside opinion, NIH asked the National Research Council, the NAS's contracting arm, to convene a blue-ribbon panel to assess the alternatives.

The report, by an 11-member panel led by pathologist Peter Ward of the University of Michigan Medical School in Ann Arbor, estimates that alternatives to mice are available about 90% of the time. And it concludes that "tissue culture methods for the production of monoclonal antibodies should be adopted as the routine method unless there is a clear reason they cannot be used." The panel opposed a European-style ban, however, noting that some antibodies—such as one widely used to prevent transplant patients from rejecting their new organs—resist being raised in a flask, for reasons that are still not understood. And it said that culturing might be too expensive for researchers who need only small quantities. "This is not the time to abandon the ascites method," says Ward.

Although neither NIH nor animal rights advocates had seen the report as *Science* went to press, one activist was cautiously optimistic that his group's concerns had been heard and that a courtroom showdown could be avoided. "We recognize some researchers are going to have to use mice," says the ARDF's John McArdle, a former animal researcher. "But they should be obligated to consider alternatives before just doing what they've always done."

–DAVID MALAKOFF

*Monoclonal Antibody Production, a report of the Institute for Laboratory Animal Research, National Research Council.

HUMAN EVOLUTION

Forming the Robust Australopithecine Face

Some 2 million years ago, three species of hominids roamed the savannas of Africa, showing the world a most peculiar face. With their massive molars, tall jaws, and bony skull crests, these three robust australopithecines are generally regarded as a side branch to human evolution. But there the agreement ends. Older analyses suggested that, like fashion designers who converge on a similar style, these hominids were distantly related creatures who evolved their heavy-jawed, Darth Vader look independently. But on the basis of their many facial similarities, recent analyses have concluded that the three form their own small hominid family. Now on page 301 of this issue, a researcher offers a new explanation for why robust australopithecines look the way they do—and suggests that they may not be so closely related after all.

Researchers have identified 50 or more skull characteristics shared by all the robust australopithecines, but anatomist Melanie McCollum of Case Western Reserve Uni-

SOURCE: ADAPTED FROM "MONOCLONAL ANTIBODY PRODUCTION," NATIONAL RESEARCH COUNCIL