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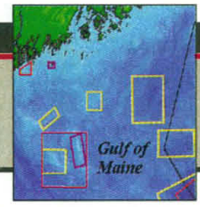
How sunspots might change climate



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Sanctuaries on the sea floor

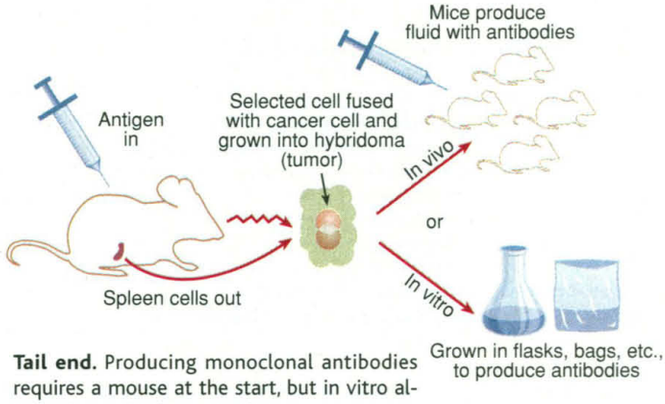
IMMUNOLOGY

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.

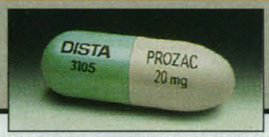
HUMAN EVOLUTION

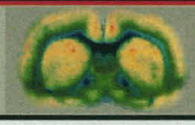
Forming the Robust Australopithecine Face

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-

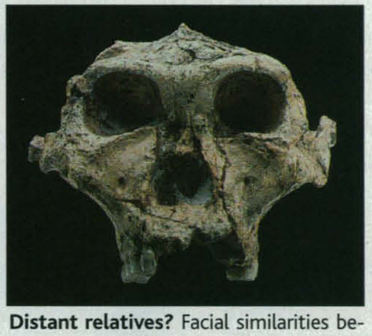
SOURCE: ADAPTED FROM "MONOCLONAL ANTIBODY PRODUCTION," NATIONAL RESEARCH COUNCIL





versity in Cleveland, Ohio, says that the facial traits are the developmental consequences of a single character—a unique combination of cow-sized molars and small front teeth. "There are not 50 or 70 traits in the [hominid] skull that evolve independently," and studies that assume so are deeply flawed, says McCollum. Instead, she argues that the robust australopithecines look alike because their unusual teeth force the hominid face to take on its distinctive robust shape. Even if the robust australopithecine species evolved separately on opposite sides of Africa, "as long as they have big molars and small front teeth, their faces will look alike," she says.

Although some researchers note that previous analyses have raised similar cautions, many say that the paper is a needed tonic for the field. "It's high time this kind of thing was said," says Tim White, a paleoanthropologist at the University of California, Berkeley. The anatomical features used for phylogenetic analysis "have become too atomized," he says. Adds Daniel Lieberman, a paleoanthropologist at George Washington University in Washington, D.C., "She's created a challenge for us to better define what a good trait is biologically."



Distant relatives? Facial similarities between two different robust australopithecines—*A. boisei* (*top*) and *A. robustus* (*above*)—may have evolved independently.

To analyze the way australopithecine faces grew, McCollum studied how the differently shaped skulls and faces of living hominoids—humans, chimpanzees, gorillas, and orangutans—grow during postnatal development. The comparison showed that teeth drive the shape of much of the rest of the face. For example, the australopithecines' massive molars require a tall back jaw, along with big jaw muscles and the skull-crowning crests that serve to anchor them. And their small front teeth change the configuration of the floor of the nose. In order to balance the competing demands of the growing mouth and nose, including the tall back jaw, the palate, the boundary between all these areas, thickens, forming a massive bone in the center of the face. The rest of the face then has to adjust to this bone, with the net result being a face so tall that it almost rises above the brain.

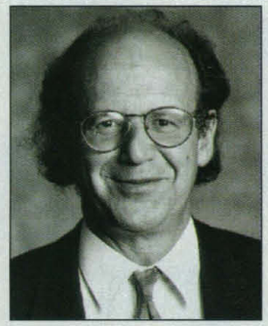
The analysis "shows that if you have similarities in dental pattern, then you're going to get similarities in facial features," says McCollum. Selection—perhaps for crunching tough nuts and tubers—shaped the teeth, and the striking facial shape just came along for the ride. Thus it doesn't make sense to count up facial changes when deciding who's most closely related to whom, says McCollum. "We've been chasing a red herring." To sort out the robust lineage, researchers should instead "look for traits in the shape of [australopithecine] teeth," she says. And although she doesn't do the analysis, she points out that variations in tooth shape suggest the robust australopithecines may not be closely related. If she's right, then paleoanthropologists will be heading back to the bench with only their dental calipers in hand.

Bernard Wood, a paleoanthropologist at George Washington University, notes that others have argued before that teeth are the best features to use in phylogenetic analyses of human ancestors. But others welcome the work's larger implication: that any traits used in phylogenetic studies should be scrutinized from a developmental perspective. "I'm thrilled," says developmental biologist Rudy Raff of Indiana University, Bloomington, who has long argued for explicit consideration of development in evolutionary studies. "She's looked at the growth consequences—what big teeth do to the shape of the skull during development. That adds a dimension that's not usually thought about." –VIRGINIA MORELL

CREDITS: (TOP TO BOTTOM) JEAN MIELE/LDEO PHOTO FILE; NATIONAL MUSEUM OF TANZANIA, DAR ES SALAAM/DAVID L. BRILL; TRANSVAAL MUSEUM, PRETORIA/DAVID L. BRILL

COLUMBIA UNIVERSITY

Earth Institute Director Bows Out



Stepping down. Eisenberger.

An ambitious attempt to bring scientists from diverse disciplines together to study global problems is about to get fresh leadership. Peter Eisenberger, the controversial director of Columbia University's Earth Institute, resigned on 24 March, citing differences over the institute's direction as well as his health. Columbia has named executive provost Michael Crow, a key force behind the creation of the Earth Institute, as its interim leader until a replacement is found.

Columbia lured Eisenberger from Princeton University, where he had founded the Materials Institute, to head the new Earth Institute in 1995. Eisenberger's mandate was to bring members of a vaunted physical sciences team at Columbia's 50-year-old Lamont-Doherty Earth Observatory (LDEO)—renowned for their research on topics like plate tectonics—together with experts on the main campus, in research cultures ranging from biology to social science, to work on climate change and other pressing societal issues. Not surprisingly, the wrenching changes drew resistance, with many scientists complaining that Eisenberger was slighting traditional areas like petrology and rushing headlong into squishy realms such as the economics of global climate change (*Science*, 22 May 1998, p. 1182).

The culture clash and Eisenberger's management style may have precipitated his resignation, observers say. LDEO geochemist Wallace Broecker, who doesn't hide his distaste for Eisenberger's leadership, says he's "not a good manager," and he "does not know that much about the Earth." Broecker says he's "delighted" he'll be getting a new boss. He's not the only Columbia scientist who Eisenberger rubbed the wrong way. Oceanographer Taro Takahashi, associate director of LDEO, says the hard-driving Eisenberger "didn't listen to people very well," al-