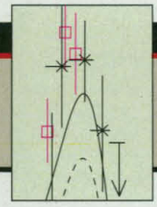
PAGE 1829
Europe's new research chief



1831
Clue to cosmic makeup

BIOMEDICINE

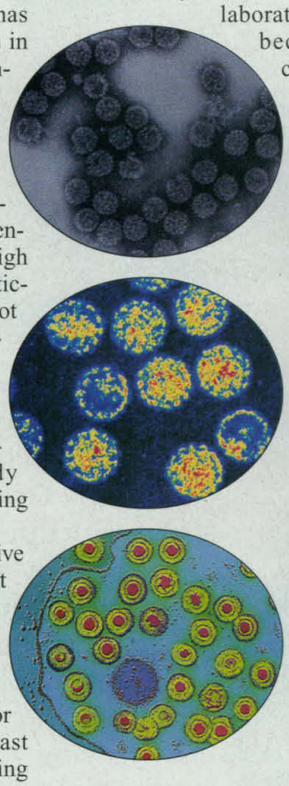
FDA Weighs Using Tumor Cell Lines for Vaccine Development

A technique for making vaccines that has been off limits in the United States for 40 years is now getting a second look from the U.S. Food and Drug Administration (FDA). Experts in cell biology, retrovirology, cancer, and vaccinology gathered in Rockville, Maryland, on 7 to 10 September to advise the FDA and other health agencies on the risks of using "immortal" and tumor-derived cells to generate viral particles for vaccines.

Since 1954, the U.S. government has ruled out the use of immortal cell lines in live vaccine production for fear that cancer genes or other hazardous factors might be transferred to people receiving vaccines. This risk has never been substantiated or quantified; some say it is entirely hypothetical. But many vaccine researchers now believe that the benefits of using immortal cell lines outweigh the risks. For example, one meeting participant said future AIDS vaccines may not be commercially viable unless manufacturers are allowed to use efficient tumor cell lines to generate reagents. According to William Egan of FDA's Center for Biologics Evaluation and Research, several groups have already applied to FDA to make products relying on immortal cell lines.

But FDA officials are not ready to give the green light—at least, not without more scientific support. It was clear at last week's meeting that FDA is particularly concerned about how consumers would view such a change. Already, public trust in vaccines is a bit shaky. For example, according to press reports last week, some parents in Wales are holding "measles parties" to infect their children with the disease rather than vaccinate them. To get concerns about a shift to immortal cell lines "out on the table," Egan says, FDA, the U.S. Centers for Disease Control and Prevention, the World Health Organization, the U.S. National Institutes of Health, and the International Association of Biologicals invited scientists to come to last week's 4-day brainstorming session.

Manufacturers have good reasons for wanting to use immortal cell lines. Viruses can't grow on their own, so companies that produce viral vaccines grow the target virus in living cells, for example, in chick embryos or monkey kidney cells. However, most normal cells have a limited lifetime in culture. It can be more efficient to use cells that have been modified to survive indefinitely. And some scientists argue that it is safer to rely on such well-characterized laboratory strains. But to become immortal, a cell must override the normal braking mechanism that controls growth. That change can arise in several ways, including by spontaneous mutations or infection with a cancer-causing virus. Regulators have feared that continuous cell lines might transmit their cancer-causing genes to vaccine recipients. They also worry that, because such cell lines are genetically unstable, they might cause disease directly by encouraging the growth of previously latent viruses or create a new infectious agent by recombining their DNA with the target virus.



Safe? Polio virus *(above,* infecting a cell*)* is grown in continuous cell lines for live vaccines used in Europe but not the United States. Experts are reviewing this policy difference and studying risks from viruses such as (*left,* from top) SV40, papilloma, and herpes.

These theoretical concerns are not new. In 1954, fearing that adenovirus vaccine made in tumor cells might cause cancer in recipients, the U.S. Armed Forces Epidemiology Board recommended that manufacturers use only normal cells to make the virus. But even normal cells carried risks. Most famously, some monkey kidney cells used to make polio vaccine carried SV40, a monkey virus that can cause tumors in hamsters and has been found in a few rare human cancers (*Science*, 7 February 1997, p. 748).

Even though continuous cell lines could be more thoroughly screened for hidden viruses, they still might pose unknown risks. The production of live vaccines requires a relatively gentle purification process, which might leave pieces of DNA from the host cell intact, posing a risk to vaccine recipients. Although the potential risk from a vaccine contaminated with a live cell or DNA fragments is probably slight, it is simply unknown, says molecular virologist John Coffin of Tufts University: "It's still a hypothetical risk, largely because there hasn't been any experimentation done."

There is a precedent for using continuous cell lines for live vaccines. Several European governments have approved the use of vero cells, an immortalized cell line developed from normal monkey kidneys, for the production of live attenuated polio vaccine. Although it is not approved for use in the United States, tens of millions of children around the world have received the vaccine since 1988, with no obvious ill effects. However, "very little postmarketing follow-up has been done," Coffin notes. And subtle effects might have so far gone undetected.

Quantifying such unknown risks is nearly impossible without more data, says Stephen Hughes of the National Cancer Institute. Hughes told the meeting attendees,

CREDITS: (CLOCKWISE FROM TOP RIGHT) CUSTOM MEDICAL STOCK; CHRIS BJORNBERG/PHOTO RESEARCHERS; CUSTOM MEDICAL STOCK; CDC

"I am not concerned" about the safety of continuous cell lines. "But the data we have are not sufficient to satisfy me as a scientist." To learn more, says Egan, the FDA plans to join European regulatory agencies in supporting experiments, such as testing the cancer-causing potential of DNA fragments, that will help quantify the risks. It is all right to "make mistakes in calculations," the FDA's Andrew Lewis said at the meeting. "But if we make mistakes in terms of delivering products that are unsafe, the costs will be incalculable."

–GRETCHEN VOGEL

CLIMATE CHANGE

New Center Gives Japan an Arctic Toehold

FAIRBANKS, ALASKA—Japan and the United States have launched a $32 million research center to plumb the consequences of climate change in the Far North. Late last month, researchers from the two countries gathered here on the campus of the University of Alaska, Fairbanks (UAF), to dedicate the International Arctic Research Center (IARC). Guided by representatives from several Japanese and U.S. organizations, the center plans to do "big picture, big science," says Gunter Weller, director of the Cooperative Institute for Arctic Research, an IARC partner based at UAF.

By compiling satellite data on everything from sea ice to vegetation patterns in the Arctic, where the effects of global warming are being felt first, IARC hopes to do some informed crystal-ball gazing. Most of the center's funding is expected to come from Japanese and U.S. agencies and universities. Besides supporting outside scientists, the center hopes to expand its 50-person research staff to 150 by 2005. The upshot, says Syun-Ichi Akasofu, IARC's U.S. director, will be clearer forecasts of global climate and of the ways perturbations in the Arctic might influence northern countries. "The ultimate purpose of IARC is to make it possible to predict global change," adds Taro Matsuno, director-general of Japan's Frontier Research Program, a key player at IARC.

Cold eye on climate. Arctic data can sharpen models, IARC's Akasofu says.

CREDITS: B. WUETHRICH

Climate models suggest that the Arctic is a good place for predicting climate changes, because global warming, stoked by rising levels of carbon dioxide and other greenhouse gases, should be amplified there. Higher temperatures melt permafrost—possibly liberating trapped CO_2 and methane, two greenhouse gases—and drive the boundary of permanent snow cover northward, eating away at a layer of white that reflects sunshine back into space. Both effects could feed back to spur global warming. Indeed, temperatures in many parts of the Arctic are already climbing faster than in regions to the south. Average annual temperatures in Alaska have increased 1 degree Celsius in each of the last 2 decades, whereas Earth's average annual temperature has increased less than 1 degree over the last century.

"People are seeing earlier breakup and later freeze-up of sea ice and warming of permafrost, and native people are talking about changes in wildlife," says John Calder, director of Arctic research at the National Oceanic and Atmospheric Administration, an IARC funder.

Changes in the Arctic may also be having effects at lower latitudes, a link that IARC researchers will probe. For instance, 6 years ago a quarter of Japan's summer crop of rice was wiped out during a frigid year that resulted from shifts in the Arctic atmosphere. Japanese researchers also worry that changes in Arctic Ocean circulation will further affect fisheries in the North Pacific and the Bering Sea, where disturbing shifts are already taking place.

Although both U.S. and Japanese officials say their governments are committed to the Arctic endeavor, which is an outgrowth of the "U.S.–Japan Common Agenda" signed by President Bill Clinton and former Japanese Prime Minister Ryutoro Hashimoto in May 1997, neither side has fully clarified how that commitment translates into cold cash. But the center's backers don't expect to have a tough time attracting funding or researchers: After all, IARC is a sleek new facility where the climate action is. "If you build it," Calder says, "they will come."

Land of opportunity. New center hopes to woo scientists to study the tundra and other global warming hotbeds.

–BERNICE WUETHRICH

Bernice Wuethrich is an exhibit writer at the Smithsonian's National Museum of Natural History.

NSF AND NASA BUDGETS

Rhetoric Meets Reality On the House Floor

A full-court press by Administration officials and scientific groups to fend off attacks on science funding was no match for congressional budget realities last week. The House of Representatives passed a spending bill that imposes deep cuts in NASA's budget and erases a proposed increase for the National Science Foundation (NSF). The Senate has yet to act on the bill—a $92 billion measure that funds housing, veterans' care, and dozens of independent agencies—and its fate is uncertain as Congress and the White House remain deadlocked over whether to lift tight caps on domestic spending or break their