CLINTON TRANSITION

Healy Stays, Fetal Tissue Ban Goes

The science news that grabbed headlines during President Clinton's first week in office was the change he made by lifting the ban on federally funded fetal tissue research. But for most scientists, what Clinton didn't change could matter more: After a week of uncertainty (*Science*, 22 January 1992, p. 447) he retained—for the time being, at least—virtually all the outgoing administration's presidentially appointed science officials.

Among the science policy heavyweights given temporary reprieves were: Bernadine Healy, director of the National Institutes of Health (NIH); Food and Drug Administration (FDA) commissioner David Kessler; National Aeronautics and Space Administration (NASA) administrator Daniel Goldin; William Happer, the energy research director at the Department of Energy; and John Knauss, head of the National Oceanic and Atmospheric Administration. (Walter Massey, the National Science Foundation director, was never in danger of losing his job, thanks to a 6-year appointment.)

When Clinton turns his attention to the top science posts later on, some of these folks are likely to be replaced. But for the next few months this familiar cast of characters will be around. That's a sharp turnaround from 2 weeks ago, when the outgoing Bush Administration said it would accept the resignations of all top political appointees, and it looked as though NIH, FDA, and NASA would be without top administrators in the early days of the Clinton Administration. But Clinton's aides convinced the Bush White House to leave the top science appointees in place, and continuity has been maintained.

If Clinton badly wanted to maintain the status quo atop the science agencies, he wanted equally badly to change the status quo on fetal tissue research. The timing of the measure, on his second day in office, was intended not just to coincide with the 20th anniversary of *Roe* v. *Wade* but also to allow researchers to make a 1 February deadline for submission of grant proposals to NIH. At least four groups have proposals for research on the use of fetal tissue transplants to treat Parkinson's disease ready for submission before the deadline, according to Richard Fuller of the American Federation for Clinical Research (AFCR).

Research groups welcomed the lifting of the ban, which Andrew Hoffman, the AFCR president, described as "a very dark chapter in American science." But AFCR's Fuller worries that Clinton missed the point by packaging the fetal tissue order with several abortion-related measures, including lifting the "gag rule" that prevented abortion counseling at federally funded health clinics. "We had hoped that he would separate [fetal tissue] from the abortion issue—it's a science issue," said Fuller. AFCR and other research groups have spent much of the past 2 years lobbying Congress to treat the issue as one of research freedom that is independent of the abortion debate.

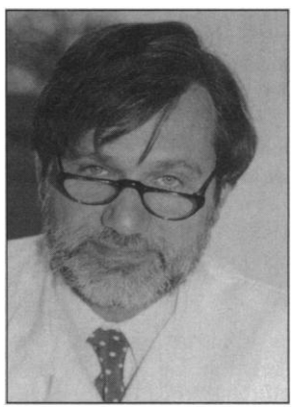
One research issue that remains up in the air after Clinton's order is the fate of the fetal tissue bank George Bush created last year after he vetoed legislation that would have lifted the ban. The bank was intended to collect tissue from ectopic pregnancies and spontaneous abortions, thereby sidestepping the politics of the abortion issue. Those sources have been widely criticized by researchers as insufficient in quantity and quality for the job. Now that the ban has been lifted, researchers can use tissue from induced abortions, of which there are much greater supplies and local sources. That could make the fetal tissue bank unnecessary, according to Duane Alexander, who directs the preparations for the bank at NIH. But it wouldn't be hard to put a stop to the program; no tissue has actually been collected, and the bank itself wasn't expected to come into existence until late spring.

–Christopher Anderson

NEUROGENETICS

Disease Gene Search Goes Big Science

There is good evidence that inherited susceptibilities underlie the development of psychiatric diseases such as manic depression and schizophrenia. Yet finding the genes responsible is proving to be one of the most frustrating pursuits in all of science. Only a few years ago it looked as though researchers were on the verge of identifying a manic depression gene as well as one that influences the development of schizophrenia. But those hopes were dashed when subsequent work failed to confirm the initial sightings.



ESF project coordinator. Jacques Mallet.

Far from giving up, however, psychiatric geneticists are now pinning their hopes on "big science"—consortia of researchers banding together to identify many families with multiple cases of schizophrenia or manic depression and using the tools of the Human Genome Project to pin down the genes passed along in those families. Two separate projects based on this model—one in Europe and one in the United States—are now undertaking just that task.

For the European consortium of 20 collaborating groups organized by the European Science Foundation (ESF), the moment has arrived when the search begins in earnest. Earlier this month, the consortium secured the services of Généthon, the industrial-style French genome center that's at the forefront of gene-mapping technology (*Science*, 24 April 1992, p. 463), to screen the members of their families for genetic markers that could lead them to the disease genes. The researchers involved are confident that the 2-year, $500,000 effort will at last yield results that can stand up to scrutiny. "If genes of major effect exist," says psychiatric geneticist Peter McGuffin, from the University of Wales College of Medicine and a member of the project's steering committee, "we should find them." The U.S effort won't be ready to begin similar systematic genotyping of manic depression and schizophrenia family members for a year or so, but it will also be a large-scale effort, involving seven groups coordinated by the National Institute of Mental Health (NIMH). (The NIMH effort will also look for Alzheimer's disease genes, involving three additional groups.)

Both the U.S. and European projects are designed to map chromosomal locations of disease genes as a first step toward isolating them. What distinguishes the ESF and NIMH efforts from other searches for mental disease genes is that both consortia have compiled unprecedentedly large collections of families having several affected members. The European effort, for example, will type 2000 subjects from more than 100 families for 300 genetic markers spread through the genome. And U.S. project leaders eventually hope to genotype more than 2800 individuals from some 400 families for an as yet undecided number of markers.

The ESF and NIMH consortia wanted so many families, says Darrell Kirch, scientific coordinator for the NIMH-led project, because that's the only way to obtain statistically significant results for these genetically complex disorders. Gene mappers work by looking within families that have several members with a particular genetic disorder for previously mapped marker genes that are inherited along with the disease—and so must be near neighbors of the gene at fault. But the current best guess is that up to five important genes contribute to each of the susceptibilities to manic depression and schizophrenia,

says ESF consortium chairman Jacques Mallet, of the Centre National de la Recherche Scientifique's molecular neurobiology lab at Gif-sur-Yvette, near Paris. Since two or more disease-causing genes could be present in any one afflicted family, it's difficult to determine whether a particular marker is inherited along with the disease by looking at just a few families.

The search for the genes underlying mental illness is also confounded by the difficulty of diagnosing the conditions, and with small numbers of people in a study, a change in the diagnosis of only one or two can wipe out a seemingly positive linkage finding. Indeed, that's what seems to have happened to the linkage reported in 1987 by a team led by Janice Egeland of the University of Miami School of Medicine between manic depression and a gene on chromosome 11, based on a study of a single extended Amish family (*Science*, 17 November 1989, p. 886).

The ESF researchers believe their sample will be large enough to avoid similar problems, and the new deal with Généthon has further added to their confidence—removing lingering worries about the logistics of such a huge genotyping program. The original idea was for the participating groups to do the genetic screening themselves. But those plans began to change last fall, after a Généthon team led by Jean Weissenbach published in the 29 October 1992 issue of *Nature* a high-density linkage map containing hundreds of evenly spaced markers covering some 90% of the human genome. The map was ideal for the planned ESF gene search, Mallet says. And although Weissenbach's genetic probes are available to anyone, Généthon can do the job much more efficiently than a scattered collection of small genetics labs. "It would have been possible" without Généthon, says Mallet, "but with great difficulty."

Given past disappointments, some researchers aren't yet willing to bet that the ESF-Généthon collaboration will yield the promised harvest of positive linkage results. But if not, don't expect the psychiatric genetics community to revert to its old "small science" approach. If the first 2-year search is unsuccessful, Mallet is already contemplating a second trawl through the genome using a different set of markers. And, even if the ESF and NIMH-led projects individually give inconclusive results, it should be possible to combine their schizophrenia- and manic depression-affected families to create an even larger sample, as the respective project leaders have taken care to harmonize their methods. They plan to use many of the same markers, for example. With that prospect on the horizon, the world's psychiatric geneticists may soon find themselves amply compensated for the frustration they've endured.

–Peter Aldhous

SCIENTIFIC MISCONDUCT

MSU Officials Criticized for Mishandling Data Dispute

A stunning rebuke has just been delivered to top research administrators at Michigan State University (MSU) for their handling of a messy custody fight between a professor and his former graduate student over rights to data and research materials.

MSU officials initially sided with the graduate student, who removed materials from the lab of the principal investigator (her ex-professor) and used them to prepare a paper on which she was listed as the sole author. But late in 1991, after the professor filed misconduct charges against the student and three MSU faculty scientists who helped her publish the paper, university officials agreed to take a closer look. They called on Washington, D.C., lawyer and scientific misconduct expert Barbara Mishkin to put together an independent panel of inquiry. After a review costing MSU close to $300,000, the panel has now reached a verdict: MSU officials not only took the wrong side, they made an ugly dispute worse. Indeed, the panel concluded, MSU's actions "undermined important academic values such as respect for scholarly excellence, collegiality, and professional courtesy."

MICHIGAN STATE UNIVERSITY

More than he bargained for. Percy Pierre launched inquiry.

A 100-page summary of the panel's findings* and several appendices were delivered to MSU president Gordon Guyer on 14 December and the summary has been made available to *Science*. MSU officials have declined to comment, and the researchers who were criticized in the report have been unwilling to defend themselves in public, pending action that could be taken by the university, and perhaps by overseers at the Department of Health and Human Services (HHS). But even as this tortuous process grinds on, one outcome is clear: University officials—especially vice president for research Percy Pierre—have been put in a tight spot. Just how tight is illustrated by the fact that Pierre, who inherited this dispute when he was made vice president in late 1990, is among the officials criticized by the report, yet he may be responsible for acting on its recommendations.

Whatever happens on MSU's campus, the repercussions of this case could extend into the wider scientific community. It raises the question of whether universities are capable of handling misconduct allegations fairly—an issue that critics such as Representative John Dingell (D–MI) have examined repeatedly in the past. Will Dingell focus congressional attention on this imbroglio in his backyard? That remains to be seen.

The roots of the dispute reach back to an incident in May 1989, when an MSU microbiologist, Jeffrey Williams, dismissed Ph.D. student Maie ElKassaby from his lab for what he described as "insubordinate behavior." The student had been working on an international project, funded by the National Institutes of Health (NIH), that focused on the uptake by human tissue of an antiparasite drug called ivermectin (see box). The project, headed by Williams, involved researchers at the Upjohn Company and physicians in Mexico and Sudan. After dismissing Elkassaby, Williams became furious when she kept tissue data she had worked on, refusing to return them to Williams or his collaborators.

If Williams thought the university would back him up, he was sorely disappointed. MSU officials, citing the student's right to free speech and the right of researchers to publish data they had worked on, advised associate dean of the school of osteopathic medicine Justin McCormick—a microbiologist—and two faculty pathologists to help her prepare a paper on the sequestered data. Williams objected and refused to have anything to do with the paper. The Upjohn collaborators on the Sudan project also informed MSU officials that they wouldn't participate in the publication because they had been denied access to the data. McCormick, however, helped ElKassaby revise the paper and persuaded the editor of *Tropical Medicine and Parasitology* in Germany to accept it. (It eventually appeared in the June 1991 issue.) Williams was not cited as a contributor, nor, the Mishkin report says, was he allowed to see the text before publication.

MSU's official support of ElKassaby prompted Williams to file charges of scien-

*"Report of the Investigative Committee to Michigan State University on Allegations of Scientific Misconduct Relating to Research Supported by NIH Grant No. AI-16312 (Sudan Grant)," December 4, 1992.