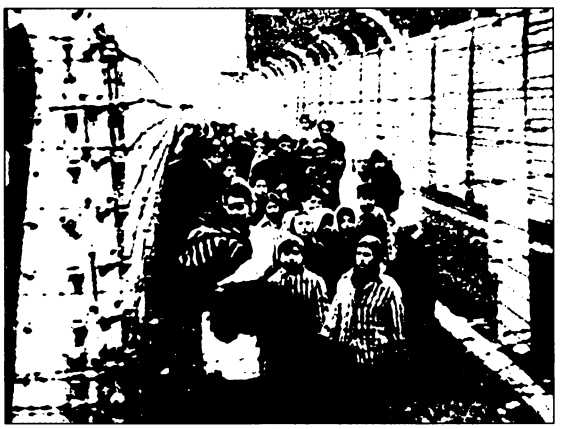
about what Mengele did to her. Benoit Massin—a French historian on the Max Planck team who is trying to document more links between Mengele and KWG researchers—said he was eager for any details that she could give because "we know very little so far about the Mengele experiments involving spinal injections." Massin recently uncovered new evidence that Mengele's experiments on children's eyes at Auschwitz had been done on behalf of a scientist at Verschuer's institute. Such links are difficult to prove, because few records survived the war, and Mengele himself escaped to South America, where he died in secrecy in 1979.



Liberated from Auschwitz. Twins experiment subjects Eva (closest to nurse, front) and Miriam Mozes.

The commission is continuing to sift through whatever evidence it can turn up. Carola Sachse, a historian who heads the commission's six-researcher team, said the group is trying, for example, to gain access to more Soviet records related to the KWG and to concentration camps but has encountered obstacles. Although many documents of Nazi crimes are irretrievably lost, some survivors say that as full an accounting as possible of the misdeeds will ease their minds and, perhaps, help prevent similar atrocities in the future. "Human beings made Auschwitz," says Laks. "It was here, amongst us. And there is no guarantee that it will not return—anywhere." **–ROBERT KOENIG**

DNA SEQUENCING

Genome Teams Adjust To Shotgun Marriage

CHEVY CHASE, MARYLAND—Half a dozen reporters showed up at a meeting near Washington, D.C., on 6 June expecting to see a shootout between rival experts on genome assembly. But no one fired a shot. Instead, the scientists quietly discussed flaws in both versions of the human genome sequence—one assembled by a publicly funded consortium of 16 labs and the other by the biotech company Celera Genomics of Rockville, Maryland. The participants batted around new ideas for deciphering very large genomes, possibly by combining the best methods from both teams. The goal, said Chad Nusbaum, assistant director of sequencing at the Whitehead Institute Center for Genome Research at the Massachusetts Institute of Technology, should be to find the cheapest strategy that can also "pass the platypus test"—that is, make sense of a complex genome that's never been explored.

One reason the discussions, which were held at the Howard Hughes Medical Institute in Chevy Chase, Maryland, were calm is that the chief combatants were absent. Eric Lander, a leader of the publicly funded team and director of the Whitehead genome sequencing center, stayed away, as did Celera president J. Craig Venter. Gerald Rubin, Hughes's chief scientific officer, who hosted the meeting, said it would have been "a distraction to the press" to have them present.

For months, Lander and Venter have been trading barbs over the quality of the other team's methods of assembling the human genome sequence from raw DNA data. Lander doesn't think Celera's whole-genome shotgun assembly—an approach that relies heavily on computer power—can work without the supporting maps and other data from the public consortium. Venter, who claims his team recently reassembled the human genome sequence without using any public data, says that Celera's method works even better on its own. The public databases are riddled with vector-contaminated DNA sequence and other problems, Venter asserts.

Celera bioinformaticist Granger Sutton presented data that bolster the company's claims that its assembly method not only worked on the human genome but is improving and may be able to resolve platypus-like genomes. Sutton reported a dramatic improvement in the consolidation of human DNA sequence into "scaffolds"—Celera's term for DNA sequence that has been placed in order in large pieces but still has gaps. Celera's first draft of the genome sequence had 119,000 scaffolds; now, Sutton said, without using any public data, the company has assembled the genome sequence into just 6500 scaffolds. The "gap" area also dropped roughly in half, to 134 million base pairs. He made equally impressive claims for Celera's assembly of mouse DNA. Other speakers didn't challenge the numbers but noted that the data are not freely available and cannot be validated without a subscription.

Several others, including James Mullikin of the Sanger Centre in Hinxton, U.K., argued for a hybrid approach for deciphering genomes. Mullikin outlined a plan that would begin by quickly churning out whole-genome shotgun data, partly to give information to biologists. The early data might also help determine the prevalence of problematic repeat sequences in a species, Mullikin said: The more repeats, the more tedious clone-by-clone analysis may be required to assemble the genome sequence and identify genes. In parallel, Mullikin said, researchers should collect physical markers and build maps to help locate data along the chromosomes. "You should always build a map," because the relative cost is small, he said.

Some researchers were interested in trying to assemble genome sequences on the cheap, using a hybrid method and just a threefold depth of sequencing data. But others warned that this might not produce big enough scaffolds. Even Gene Myers, Celera's informatics chief, said, "If some projects go to 3× and stop, I'm a little worried that you won't be able to get order and orientation." Instead, he said, "you should just go to 5× and take the extra hit" in costs.

The participants seemed to agree on at least two points. First, more research is needed on "repeats," blocks of almost identical DNA sequence that appear to be 10 times more common in the human genome than in those of the fruit fly or nematode. Existing assembly programs can't handle them well and often delete them. But, argued molecular geneticist Evan Eichler of Case Western Reserve University in Cleveland, Ohio, these repeats may contain unique elements of the human genome and should not be slighted. Second, everyone wants better software for assembling genome sequences. Already, publicly funded teams at a half-dozen labs

Model organism? New methods should be able to solve the genome sequence of a genetically unmapped animal, such as the platypus.

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are testing new programs with names like JAZZ, Arachne, and Euler. U.S. Human Genome Project leader Francis Collins predicts that by "late summer" everyone will have access to such souped-up computer tools. If so, by September, genome assembly could be a whole new ball game.

–ELIOT MARSHALL

NEURODEGENERATIVE DISEASE

Using the Fruit Fly to Model Tau Malfunction

In the slow-motion train wreck that is Alzheimer's disease, different types of debris pile up inside and outside dying brain neurons. But despite decades of research, researchers still don't know exactly what kills the cells.

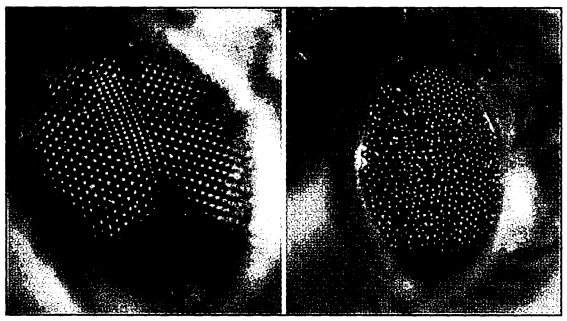
Most attention has focused on defects in a protein called β amyloid, which clumps up into plaques outside neurons and seems to throw the switch that first steers the cells off course. But inside neurons, another protein called tau may act as an accomplice. In Alzheimer's brains, tau forms part of abnormal intracellular structures called tangles, although it's not clear whether tangle formation is the cause or result of the neuronal degeneration. It is clear, however, that other human dementias can be caused by tau defects even in the absence of plaques, indicating that here at least the tau defect is primary. Now a new fruit fly model may help reveal just how defective tau sends healthy brain cells veering off track.

In work published online by *Science* on 14 June (www.sciencexpress.org), Mel Feany of Harvard Medical School in Boston and her colleagues show that fruit flies producing human tau undergo brain neuron degeneration, although, in a surprising finding, the dying fly neurons do not contain tangles. It's "very elegant, nicely done work," says Zaven Khachaturian, senior scientific adviser to the Alzheimer's Association. "It could change the focus of research for developing treatments [for dementias]."

No mutations in the *tau* gene have been linked to Alzheimer's, but in 1998, researchers discovered that *tau* mutations do cause a group of dementias with the unwieldy name hereditary frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17). To find out how tau damages neurons, Feany's team introduced either the normal human *tau* gene or a mutant version that causes FTDP-17 into fruit flies. Flies with either gene died younger than controls, but the effect was most pronounced in those with the mutant gene, the researchers report. The results suggest that the normal and mutant tau had each taken its toll.

The researchers then watched what happened to the nervous systems of both types of transgenic flies as they aged. Brain cells in day-old flies were fine, but neurons in doddering 30-day-old flies had disintegrating cell nuclei and other organelles. "We saw them falling apart," Feany says. The human tau proteins especially damaged neurons that communicate using the neurotransmitter acetylcholine—a group of cells that are also hit heavily in Alzheimer's disease.

Together, the results suggest that the fruit flies with human tau mimic the tau-induced damage seen in Alzheimer's disease, FTDP-17, and other dementias in which tau goes awry, Feany says. But the absence of tangles in the transgenic flies was puzzling. Because the brains of FTDP-17 patients contain copious tangles, some researchers speculate that the cells are killed by tangles that gum up their internal works, although others suggest that soluble forms of defective tau proteins can kill without forming tangles. The flies with the mutant tau protein support the latter view, Feany says: Even though no tangles formed in their neurons, the cells died anyway.



Rough and ready. Because fruit flies expressing mutant tau have smaller, rougher eyes (right) than is normal (left), they should help researchers identify new dementia-related genes.

CREDIT: MEL FEANY/HARVARD MEDICAL SCHOOL

Some experts caution, however, that the lack of tangles might mean that flies aren't a good model of human dementias. "The worry is that cells are dying by a different mechanism than neurons do when they make tangles in Alzheimer's disease," says neuroscientist John Hardy of the Mayo Clinic in Jacksonville, Florida.

Others don't see a problem. "I'm not bothered one bit that [they] didn't find tangles," says neuropathologist John Trojanowski of the University of Pennsylvania School of Medicine in Philadelphia, one of the researchers who linked *tau* mutations to FTDP-17. Because the protein normally stabilizes microtubules, which help ferry life-sustaining molecules to nerve endings, he suggests that defective but soluble tau might kill neurons by crippling their transport system. Others say

ScienceScope

Cracking the Code A team of cryptographers is suing the Recording Industry Association of America (RIAA) over the right to present a paper at a conference. In a federal court suit filed last week, Princeton University computer scientist Ed Felten and colleagues claim that a provision of the 1998 Digital Millennium Copyright Act (DMCA) unconstitutionally limits researchers from sharing information.

Last year, Felten's team claimed to have cracked a digital "watermarking" scheme for music. But earlier this year the researchers dropped plans to describe their feat at a conference after feeling threatened by the RIAA, which could have sued under the DMCA (*Science*, 4 May, p. 826). The suit seeks to clarify their right to present the work in public.

The lawsuit is "inexplicable," says RIAA general counsel Cary Sherman, because the group doesn't intend to sue the team. But Gino Scarselli, a lawyer for the cryptographers, says that the court needs to "look at the long-term effects of the [DMCA]. ... At its very core, it is a constraint on publication."

Partnership Perils A new report outlining best practices for university-industry partnerships is ruffling some feathers. The Business–Higher Education Forum last week released "Working Together, Creating Knowledge: The University-Industry Research Collaboration Initiative," which uses case studies to highlight the promise and peril of linking scholars and corporate dollars.

The report—produced by a panel led by Pfizer CEO Hank McKinnell and Nils Hasselmo, president of the Association of American Universities—highlights what McKinnell calls "the best of times and the worst of times." In particular, he says that Monsanto's collaboration with Washington University in St. Louis is a good model, whereas Novartis's arrangement with the University of California, Berkeley, raises some red flags.

McKinnell's comments weren't welcome at Berkeley. "It is understandable why the CEO of a large pharmaceutical company would strongly prefer the Washington University–Monsanto agreement," says Berkeley economist Gordon Rausser. "Under this agreement, Monsanto controls the research agenda. ... Such terms would not be acceptable [at Berkeley]." The Berkeley deal, he noted, conforms to the report's recommendations.

Contributors: Eliot Marshall, Robert Koenig, Charles Seife, David Malakoff