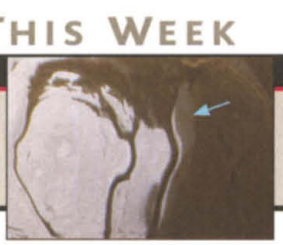

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Water ice on Mars

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Restrictions on tissue banks

MEDICAL RESEARCH

Inquiry Turns Into OK Corral for U.K. Primate Research

CAMBRIDGE, U.K.—University of Cambridge officials were hoping last week for a staid review of their controversial plan to build a $36 million neuroscience center on the outskirts of town. Instead, a hearing meant to be limited to zoning issues devolved into a circuslike referendum on primate research. The inquiry was a key step in a drawn-out process that is expected to culminate in a decision on the center's fate early next year.

The proposed facility would bring all of the university's primate research under one roof and expand work on potential treatments for everything from substance abuse and schizophrenia to Parkinson's and Alzheimer's diseases. A failure to win approval for the center—which has already landed $12 million in grants and could hire up to 60 scientists—"would have a big negative impact on neuroscience in the U.K. and Europe," warns John Capitanio, a psychologist at the California National Primate Research Center in Davis. Prominent U.K. voices agree. Primate research would "eventually be conducted elsewhere, possibly in countries with less rigorous legislation and lower standards of animal welfare," asserts Nancy Rothwell, president of the British Neuroscience Association.

Such arguments appear to have convinced Prime Minister Tony Blair, who warned in a speech last May that "we cannot have vital work stifled simply because it is controversial" and has said that the center's work would be in the national interest. But the university has had a hard time convincing local authorities that it would be in the city's interests as well. The inquiry is the university's third attempt to win approval from the South Cambridgeshire District Council, which had rejected previous proposals mainly on the grounds that anticipated protests against the center would further snarl Cambridge's notorious rush-hour traffic and perhaps pose a public safety risk. After the university appealed, the central government appointed a "planning inspector" to adjudicate the matter. The inspector will send a recommendation to the U.K.'s deputy prime minister, who will have the final say.

In September, the inspector, Stuart Nixon, ruled that he would not "hear evidence on public health, animal welfare, or moral arguments," setting the stage for what university officials had expected would be a straightforward hearing on how their revised proposal accounts for protests. Those hopes were dashed on the inquiry's first day, 26 November, when Nixon reversed himself and allowed animal-rights groups to present their case. First up was Richard Wald, a lawyer representing six such organizations, who denounced the center as "scientifically flawed and unreliable" and "neither of national importance [nor] necessity." The university had left itself in an awkward position to rebut such charges: It had barred its own scientists engaged in primate research from testifying, out of fear for their safety. That left the university's chief academic witness, Keith Peters, head of its Clinical School, virtually alone on the firing line. Peters assured the inspector that as few animals as possible would be used in experiments and that a state-of-the-art facility would be "more likely to provide better [conditions] for animal welfare." But Peters also stated, vaguely, that a national need for primate research is "self-evident" and had gone through "particularly stringent" peer review.

Wald pounced. He charged that Peters was "unable to say scientifically whether the underlying science can be applied to humans," and he asserted that experimentation that "may or may not lead to a cure … basically amounts to scientific dabbling." Peters shot back, "If you knew what the answer was, there would be no point in doing the research." But it was evident that the animal-rights campaigners had drawn first blood.

It was the opponents' turn to stumble when they attempted to support provocative claims that new drugs are not necessarily safer if they are tested in primates. Claiming that primate research has not yielded any insights into diseases such as atherosclerosis, cancer, and stroke, Ray Greek, medical director of a group called Europeans for Medical Advancement, concluded that "the abandonment of animal models is absolutely vital for medicine to advance." As evidence that primate research is unnecessary, Wald referred to an Alzheimer's vaccine that had moved directly from mouse experiments into clinical trials last year. Apparently, he was unaware that in January, the clinical trials were halted after 15 patients developed severe brain inflammation. Peters knew this, however, and noted, "You will find you have shot yourself in the foot, Mr. Wald."

Lost amid the spectacle of such repartee was testimony on the more substantive zoning issues, primarily traffic and safety. Representatives from the local council expressed support for the center in principle but demanded that the university choose a new site farther from the city center. The current site, a police officer said, risked increased "crime and disorder." The university held firm, however, arguing

Showdown. Protesters (*above*) gather outside a hearing (*right*) last week on the University of Cambridge's controversial proposal to build a primate research center; a decision is expected early next year.

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that the site's proximity to an imaging center and other labs would foster collaboration and better experiments. But the university was on less-sure footing when one official claimed that because center opponents are drawn from the "less radical end of the animal-rights movement," their demonstrations are likely to be "less frequent, smaller, and less aggressive." University officials did not explain how that jibed with their decision to bar researchers from testifying on safety grounds.

The inquiry was set to wrap up on 6 December, after which Nixon will compile a report for Deputy Prime Minister John Prescott. Although his boss has embraced the center, Prescott—who is expected to make a ruling early in 2003—has not expressed an opinion publicly. His decision will be final and binding on the university and the council.

–KERI PAGE

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GENOMICS

Sequence Tells Mouse, Human Genome Secrets

Sequencing a genome is a little like opening a present. Researchers have been tantalized for 3 years as they've unwrapped mouse DNA. Now, they're examining the contents and finding them even more exciting. This week, researchers from around the world describe what they have found so far: discoveries about the mouse genome that are providing insights into our own genetic code and making mice an even better biomedical research tool. "The data are turning out to be as valuable as we hoped," notes Karen Artzt, a geneticist at the University of Texas, Austin.

The mouse genome is only the second mammalian one sequenced to date. The ability to compare it to the closely related human genome "makes the [work] most meaningful," says Maja Bucan, a geneticist at the University of Pennsylvania in Philadelphia. An analysis of the sequence, published in the 5 December issue of *Nature*, is accompanied by five papers delving into the mouse's genetic characteristics and comparing them to those of humans. Some genes and other bits of sequence are similar across the board; elsewhere, there are intriguing differences.

Humans and mice have about 30,000 genes each—about 80% of which match up, reports a team led by geneticists Robert Waterston of the Washington University Genome Sequencing Center in St. Louis, Missouri, and Kerstin Lindblad-Toh of the Whitehead Institute/MIT Center for Genome Research in Cambridge, Massachusetts. But the human genome is longer—with about 3 billion bases, compared to the mouse's 2.5 billion. And the types of genes vary: The mouse has many more genes involved in reproduction, immunity, and olfaction, for example, and the genes in the first two categories have evolved much faster in mice than in humans.

Researchers have taken advantage of the similarities between human and mouse DNA to study where in the body genes are active.

Rodent roundup. The newly analyzed mouse genome and newly assembled rat sequence are helping researchers make sense of humans' genetic code.

"Knowing when and where a gene is expressed facilitates enormously further functional analysis," explains Marie-Laure Yaspo of the Max Planck Institute for Molecular Genetics in Berlin. A team led by Andrea Ballabio of the Telethon Institute of Genetics and Medicine in Naples, Italy, matched mouse sequence against the known genes along human chromosome 21. The researchers tracked the expression of each of these mouse genes—about 160 in all—at several stages of development, viewing expression in three dimensions in whole embryos. They also monitored which of these genes were active in 11 types of adult tissue, such as brain, muscle, and heart. In this way, they identified genes of interest, including one called *Adarb1* that's involved in heart development and might play a role in Down syndrome.

Yaspo and her colleagues took a similar tack in studying genes from chromosome 21, the shortest human chromosome, but they concentrated on brain development shortly after birth. They found that about half the mouse genes were active throughout the brain and half were expressed in specific regions.

Such studies can help researchers determine the functions of normal genes. But the data can also be used to home in on genes that cause disease, says Bucan. Once they find a few candidates, knowing where each candidate is active "will make getting the [right] gene easier," she points out.

Another study took a broad view of human chromosome 21, comparing its DNA and that of the mouse genome. Stylianos Antonarakis and Emmanouil Dermitzakis of the University of Geneva, Switzerland, and their colleagues report that only about half of the more than 3000 conserved sequences turned out to be genes. That other stretches of DNA are maintained through evolution means they must be important, possibly as regulators of gene activity, and could also play a role in human disorders, says Antonarakis. Indeed, notes Lindblad-Toh, "one of the highlights [of this week's reports] is that such a large fraction of the genome is conserved."

Other mouse-centered DNA studies should make the rodent even better suited for genetic studies, says Joseph Nadeau of Case Western Reserve University in Cleveland, Ohio. In one, Claire Wade of the Whitehead genome center compared the draft sequence, which comes from the B6 strain, with DNA from another mouse strain, cataloging the differences between individual bases. She and her colleagues found 80,000 of these single-nucleotide polymorphisms (SNPs), many of them clumped together in SNP-rich regions. These landmarks and their distribution should help researchers locate disease genes, Nadeau notes.

Adding to the genetic wealth, a team from Japan's Institute of Physical and Chemical Research (RIKEN) has released almost 61,000 sequences, called full-length cDNAs, derived from mouse RNA. Many of these sequences represent proteins made by the mouse genome. Surprisingly, the total number of cDNAs proved to be larger than the number of genes, indicating that some genes

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