

BIOETHICS

Panel Proposes Tighter Rules for Tissue Studies

Clinical researchers have received a bioethics package for Christmas, and some may be afraid to open it. It appeared on 3 December in the form of a draft report from the president's National Bioethics Advisory Commission (NBAC) (posted on the Web at www.bioethics.gov) arguing for tighter controls over research on stored samples of human blood and tissue to protect the donors' privacy.

The "tissue issue," as Yale bioethicist Robert Levine calls it, has become a hot topic. Stored tissue can contain a gold mine of information for researchers tracking the spread of disease, hunting disease genes, and studying human genetic variation. And it's a huge resource: NBAC calculates that U.S. institutions hold more than 282 million samples of archived human tissue today. Although those who donated the material



Potential gold mine. Tissue bank at the Armed Forces Institute of Pathology.

probably gave broad consent for its use in research, ethicists believe that more specific consent may be needed for certain studies that could identify and stigmatize donors.

NBAC—a 17-member group of lawyers, ethicists, and medical professionals chaired by Princeton University President Harold Shapiro—began picking its way through this dense thicket 2 years ago. A draft report in late 1997 was withdrawn after it drew flak from clinicians and NBAC members. The new version, completely rewritten, is still likely to be controversial. Even before he had seen the details, pathologist John Trojanowski, an Alzheimer's disease specialist at the University of Pennsylvania, objected that its proposed new reviews and consent requirements would be so burdensome that they "would bring research to a standstill." But others were more accepting.

Judith Greenberg, who oversees the operation of a large human tissue collection for the National Institute of General Medical Sci-

ScienceScope

NIH TO REVIEW CONFLICT POLICIES

The National Institutes of Health (NIH) will take a closer look at the outside consulting fees earned by its scientists. This week, in response to a congressional query about an NIH scientist who received thousands of dollars in drug company fees, NIH director Harold Varmus requested a review of his agency's conflict-of-interest policies.

On 7 December, the *Los Angeles Times* reported that Richard Eastman, chief of the diabetes division at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), had received speaking fees for several years from the Warner-Lambert Co. of Morris Plains, New Jersey. Eastman told the *Times* that he did not take part in decisions affecting company products while he was a consultant, but he was in charge of a clinical trial that included a Warner-Lambert diabetes prevention drug called troglitazone. Last summer, after a patient taking the drug died, the NIDDK dropped the drug from the trial.

The story prompted Representative Henry Waxman (D-CA, above) to send Varmus a two-page list of questions about the case on 7 December. A "concerned" Varmus responded by asking the inspector-general of the Department of Health and Human Services to examine whether NIH staff involved in the case complied with federal conflict-of-interest guidelines. His staff is also reviewing how NIH's two dozen institutes and centers apply the rules, with an eye toward clarifying them.



ACADEMIC INBREEDING ATTACKED

South Korea wants to imbue its universities with a little fresh blood. The National Assembly is expected to pass a bill this session that would prohibit universities from filling more than half of new faculty openings with their own alumni.

Inbreeding has been a hallmark of top Korean schools. At the prestigious Seoul National University (SNU), for instance, 95.6% of the faculty are alums. Now, government officials want to reduce the in-house promotions in an effort to spread around the scholarly talent.

But some SNU administrators oppose any quota, arguing that SNU's star students are also the most-qualified professors. "The best candidates happen to be our alumni," says Lee Jung Jae, an SNU education professor. Electrical engineer Park Young Joon, however, favors the change. The current system, he says, makes it too hard to bring in new talent.

sleep and rise with waking. When the team boosted the norepinephrine level in anesthetized birds, the RA responses dropped. Margoliash notes that other as yet untested signaling molecules, such as dopamine, may contribute to the effect as well.

To Margoliash, the wide-open communication between HVC and RA during sleep suggests that that's when the birds learn to refine their songs. He speculates that even though a sleeping bird doesn't normally hear its own song, as the birds did in the experiment, its HVC neurons might spontaneously fire in the same pattern that is induced by the song while the bird is awake. That information would pass freely to RA neurons, which could use it to fine-tune the commands they give to the singing muscles the next time the bird sings. His team, he says, is now studying HVC firing patterns during sleep to see whether they do mimic the song response in awake birds.

Without such evidence, Mooney argues, the wide-open circuitry during sleep may be a "red herring," the result of the fact that the brain has little else to attend to. What makes the new work "profoundly important" in his view are the results obtained with birds that are awake, in which, he points out, RA's response to the HVC activity elicited by the song recordings is "throttled down," but "not shut down entirely." That "in-between state," he says, makes the circuits sensitive to modulating influences such as attention, which could regulate the information channels to control when song learning can occur.

Mooney finds the results tantalizing for another reason as well. They may provide a clue to a well-known human phenomenon: the loss of ability to learn new languages fluently at puberty. At puberty, bird songs become less responsive to auditory feedback. Mooney notes that sex hormones affect the turnover rates of norepinephrine in ways that could locally increase its levels, and he speculates that increases of sex hormones at puberty could reduce the bird's ability to self-correct its song. If so, he adds, it would "not be a big leap" to consider that a similar mechanism may be responsible for the problems humans have learning to speak a language like a native after puberty.

Those ideas remain to be tested, but to Nottebohm, that's another benefit of the new results. "What opportunities for future work," he enthuses. Indeed, just as the tenor and the zebra finch use feedback to fine-tune their songs, song researchers will likely be tweaking their hypotheses in response to these results and the new experiments they are bound to inspire.

—MARCIA BARINAGA

ences, says the new report “seems to have achieved a pretty reasonable balance.” And pathologist Jonathan Tait of the University of Washington, Seattle, after a quick reading, said he identified some vague spots, but thinks the report “doesn’t have severe problems.”

Today, an investigator often makes biological samples anonymous by stripping off names and other identifiers and replacing them with a code. Because these coded samples are considered to be exempt from normal consent requirements, researchers often share them with colleagues as though they were anonymous, without obtaining new consent from donors. Nor do researchers necessarily seek approval from local panels that monitor the use of human subjects—known as institutional review boards (IRBs)—to conduct research on such samples. But this could change.

To protect against loss of privacy, NBAC is proposing that unidentified samples be coded not by the investigator but by a third party, such as “an encryption service.” This would make it almost impossible for any researcher to identify the source. But if a researcher cannot or doesn’t want to make tissues truly anonymous in this way, NBAC says, the research should be approved by an IRB, which might also ask the researcher to obtain specific consent from the donors.

If a study might pose more than a minimal risk of harm to the donors, NBAC says, IRBs should take care to see that the risks are clearly described to donors before consent is sought. This is particularly important for “sensitive” projects such as research on behavioral genetics or for “studies differentiating traits among ethnic or racial groups, or research on stigmatizing characteristics such as addictive behavior.” If the IRB determines that donors of stored tissue samples were not adequately informed in the past, researchers might be required to go back to the donors seek a new consent. In addition, donors at this point would be given a chance to ask that their tissues not be used in this or any future research project.

Even if the IRB finds no need for this kind of renewed consent procedure in a particular study, NBAC recommends that tissue donors should be given a chance to opt out of any research they “might find objectionable on moral or other grounds.” NBAC doesn’t explain how: It just says that institutions “should consider the option of making a good faith effort to contact subjects to allow them to ‘opt out. ...’”

Some of these tough requirements were included in earlier drafts. But NBAC is taking a softer line on some issues. For example, it is not including a recommendation that researchers obtain “community consent” for genetic studies that might embarrass a particular ethnic group. Instead, the

new draft says researchers should “be mindful” that their research might harm a genetically linked group of people, and minimize the risk. NBAC also suggests—to reduce paperwork—that the requirement for consent be waived when research on identifiable tissues poses a minimal risk of harm.

Many critics of NBAC’s earlier draft are likely to agree with pathologist Jeffrey Cossman of Georgetown University, who says, “I think there’s been a major advance” in the report’s quality, “but this document isn’t ready for prime time.” It needs more polishing and another round of editing, he says. But time is running short. NBAC has set a deadline for all public comment of 17 January, and the panel could vote on a final report early next year. —ELIOT MARSHALL

LASER PHYSICS

Powerful Pulses Color Thomson Scattering

Not long after identifying the electron in 1897, British physicist J. J. Thomson watched it dance. He showed in 1906 that powerful pulses of light could make electrons oscillate up and down and reemit light at the same frequency in all directions, a phenomenon later dubbed Thomson scattering. Now, almost 100 years later, researchers have applied much stronger light to electrons and coaxed them into performing a more complex dance step, tracing out figure-8 shapes and reemitting the light in rainbow colors.

Researchers predicted the effect, called relativistic Thomson scattering, as early as the 1930s, but the intensity of light required to observe it was impractically high. Now, with the help of laser pulses compressed into split-second bursts of staggering power, a team of physicists at the University of Michigan in Ann Arbor has seen the phenomenon’s colorful signature. “We now have enough power to study nonlinear relativistic Thomson scattering,” says team leader Donald Umstadter, whose group reports the result in this week’s *Nature*.

Light can get an electron to dance because it is accompanied by an electric field vibrating across the direction of the beam. If the light is bright enough, the oscillating field grabs the charged electron and shakes it up and down. An oscillating electron naturally emits more electromagnetic radiation,

and because these electrons are moving at the same frequency as the incoming light, the emitted light has the same frequency. But light also has an oscillating magnetic field, perpendicular to both the beam and the electric field. A magnetic field also exerts a force on a moving electron, known as the Lorentz force, which is so weak that its effect is not normally observable. The Lorentz force is, however, related to the speed of the electron, so if the incoming light is very strong and it oscillates the electron very fast, the Lorentz force should kick in, broadening the electron’s normally linear motion into a figure 8.

To bathe the electrons in sufficiently bright light, team member Anatoly Maksimchuk built a tabletop neodymium-glass laser and squeezed its billionth-of-a-second pulses by a factor of about 1000, boosting their power to 4 trillion watts. Although more powerful lasers exist, Maksimchuk says it’s beam quality that counts. “Essential for this experiment is a high quality of the beam, very short pulse duration, and good focusability,” he says.

Aimed at a jet of helium gas in a vacuum, these pulses ionized the gas and simultane-

ously caused the freed electrons to oscillate. A charge-coupled device camera recorded the light emitted by the electrons from all angles around the apparatus. Just as predicted by theory, Umstadter and his colleagues saw light at the laser frequency as well as at multiples of that frequency, known as harmonics, each one emitted in a different direction. Umstadter notes that this is a definite signature of an electron moving in a figure-8 path and emitting light.

“It is the first time that we have been able to

directly observe the instantaneous motion of electrons in the combined field [electric and magnetic] of the laser,” says Umstadter. Doing so was no mean feat, says Antoine Rousse of the Applied Optics Laboratory at the Ecole Polytechnique in Palaiseau, France. “It is very difficult ... to extract the signal from background noise,” he says. “You need ingenuity to eliminate all the extraneous sources.”

“It really opens up a new subfield of physics—the study of the behavior of electrons at these extreme light intensities will give rise to many new interesting theoretical questions,” says Nicolaas Bloembergen, a pioneer of laser science at Harvard Universi-



Pulse power. The University of Michigan laser used to demonstrate relativistic Thomson scattering.

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