

STEM CELL RESEARCH

U.K. Backs Use of Embryos, Sets Vote

with the rat genome in hand, "you can take the power of mouse genetics and the power of rat physiology and link them together," says Howard Jacob, a physiological geneticist at the Medical College of Wisconsin in Milwaukee.

NHLBI has supported rat genome work since 1995, although Jacob notes that "it's been a stealth project" that hasn't received wide notice. The project has generated sequencing tools, such as a physical map of the rat genome and a set of bacterial clones of rat DNA, but full-scale sequencing was on hold. In the past year, however, the big genome-sequencing centers have expanded their capacity so much that NHGRI director Francis Collins became convinced that they could tackle the rat genome as they were finishing the human genome and preparing the mouse draft. In May, the NHLBI advisory council agreed to put aside \$32 million in 2001 and another \$26 million in 2002 for the rat.

But NHGRI has advanced its troops even before the new year begins, shifting two groups, the Baylor College of Medicine in Houston and Genome Therapeutics Corp. (GTC) in Waltham, Massachusetts, into the rat effort. Baylor's Richard Gibbs will put the remaining \$14 million from his mouse grant toward the rat, and GTC's Doug Smith will divert about \$10 million from mouse and human sequencing for GTC's initial rat work. Together, they hope to sequence the entire rat genome once over within a year. The two centers are likely to be among those that receive the NHLBI contribution, which will be used to sequence the genome at least four times over to produce a rough draft.

If all goes well, the mouse and rat genomes will be available at the same time. Because the two rodents are separated by about 16 million years of evolution—while the human and mouse are separated by 80 million years—the rat and mouse genomes will share some DNA that is not obviously conserved between either rodent and the human genome. Thus, the rat genome should help to identify regulatory regions that might be missed in a mouse-human comparison.

NHGRI plans to push ahead on the mouse genome to produce a high-quality, complete version. So far, that's not in the cards for the rat. But that suits Jacob just fine, even though he works on the rat. He says: "I think it does not need to be finished at the current cost for finishing."

—ELIZABETH PENNISI

LONDON—The U.K. government leaped into an ethical minefield last week, endorsing a report it had commissioned that calls for an expansion of research on human embryos. The report advocates tapping embryos for their stem cells, unspecialized cells that may ultimately serve as seed material for growing tissues to treat diseases. It also opens the door to cloning human embryos for research—an activity that has triggered sharp debate. Legislation implementing the recommendations will go to Parliament for a vote this fall.

If passed, the new U.K. regulations would likely be more permissive than guidelines expected out shortly from the U.S. National Institutes of Health. With Canada, Germany, and Japan also hammering out guidelines, says stem cell researcher John Gearhart of The Johns Hopkins University School of Medicine, "you'll soon see other players in the field."

Current U.K. rules allow research on human embryos only for studies aimed at improving infertility treatment, devising better contraceptives, and screening for genetic abnormalities before implantation. Nearly all embryos used in such studies are leftovers from in vitro fertilization clinics, and research is limited to embryos less than 2 weeks old, before neural development occurs.

But recent advances in stem cell research prompted the U.K. Department of Health to ask its chief medical officer, Liam Donaldson, to appoint an independent panel to review the science and ethics of human

POSSIBLE USES OF TISSUE DERIVED FROM STEM CELLS TO TREAT DISEASE

Cell type	Target disease
Neural (nerve) cells	Stroke, Parkinson's disease, Alzheimer's disease, spinal cord injury, multiple sclerosis
Heart muscle cells	Heart attacks, congestive heart failure
Insulin-producing cells	Diabetes
Cartilage cells	Osteoarthritis
Blood cells	Cancer, immunodeficiencies, inherited blood diseases, leukemia
Liver cells	Hepatitis, cirrhosis
Skin cells	Burns, wound healing
Bone cells	Osteoporosis
Retinal (eye) cells	Macular degeneration
Skeletal muscle cells	Muscular dystrophy

ScienceScope

DNA Across the DMZ The tears were real last week when members of 200 families torn asunder 50 years ago by the division of the Korean Peninsula were reunited briefly in Seoul and in Pyongyang. But many of the estimated 10,000 South Koreans with offspring in both countries may not live to see their long-lost North Korean children. A new initiative, however, could keep genealogies intact—and perhaps resolve inheritance disputes between North-South siblings.

On 1 September I.D. Gene, a Seoul-based paternity testing firm, plans to start taking saliva samples from any of the 10,000 South Korean parents who are willing. The sampling is free, but I.D. Gene will charge its usual fee (about \$400) for typing the 10 nanograms or so of nuclear DNA in each sample. Efforts to get the government involved with the project have so far failed, says I.D. Gene CEO Yeon-Bo Chung, a Harvard-trained biologist. So a group of private benefactors, including the drug firm Korean Green Cross Inc., is bankrolling the estimated \$80,000 sampling and storage costs.

Typing DNA from siblings alone may not cement a family connection, as siblings often have fewer DNA sequences in common with each other than with each of their parents. That's why preserving the older generation's DNA is crucial, says Chung. "Unless somebody collects the samples right now, they will not be available when they are desperately needed in the future."

Doubling Double Hit The campaign to double the budget of the National Institutes of Health (NIH) has won a pair of high-profile endorsements. Democratic presidential candidate Al Gore last week promised to "double the federal investment in medical research" in his nomination acceptance speech to the Democratic National Convention in Los Angeles. Not to be outdone, Republican rival George W. Bush's campaign said their candidate also backs the doubling push, begun 4 years ago by biomedical research advocates.

Both Bush and Gore, however, have yet to endorse the more ambitious agenda of Gore's running mate, Senator Joe Lieberman (D-CT). Lieberman is a major backer of bipartisan legislation that recommends doubling the government's entire \$35 billion nondefense, nonbiomedical research portfolio by 2010. Many lobbyists say that NIH's rapid growth in the past 2 years has skewed the federal portfolio and that other agencies need to catch up.



embryo research. The panel delivered its report in May, and last week the Department of Health unveiled both the report and the government's response. The department is now discussing with the research councils, which dole out much of the government's science funding, how to fund more human embryo research.

Topping the panel's list of recommendations is a call for allowing researchers to extract embryonic stem cells, which can be coaxed to form various cell types. Culled from 5- to 6-day-old embryos, such cells might be grown in the test tube into tissues suitable for transplantation. The hope is that embryonic stem cells would serve as a stopgap until scientists learn to reprogram adult cells to serve as stem cells. "Winding the clock back on adult cells is very much the Holy Grail of stem cell research," says Donaldson. But scientists shouldn't count on adult cells, warns Peter Andrews of the University of Sheffield, who studies human embryonal tumor cells. "In the end," he says, "the therapeutic approach will be the one that's easiest to follow."

The report also advocates the limited use of nuclear transfer techniques as a source of stem cells. To ensure that tissue grown from stem cells is not rejected as foreign by a patient's immune system, a nucleus from one of the patient's own cells would be fused with an egg that had its nucleus removed, and the egg would then be prodded to divide. However, clinical research to test therapeutic cloning is a long way off and may require additional legal safeguards, says Donaldson: "We're talking about research at this stage, not treatment." Making babies from cloned human embryos—the reproductive cloning that the sheep Dolly made famous—would remain a crime under British law.

A third line of research backed by the report would explore the feasibility of preventing the 50 or so diseases caused by mutations in the genes carried by mitochondria, the powerhouses of the cell. Mitochondria are handed down only by the mother, and one approach might be to transplant the nucleus from an egg of an affected woman into an egg from a normal donor stripped of its nucleus, and then fertilize the hybrid egg.

Donaldson says the recommendations do not break new ethical ground but simply expand research already allowed under current law. Still, rather than risk defections, the ruling Labor Party plans to allow Parliament members to vote their conscience on the sensitive issue.

The battle lines are already drawn: Opposition Member of Parliament (MP) Liam Fox, a physician who serves as the Conservative Party's "shadow" health secretary, has come out against therapeutic cloning. He has an influential ally in Cardinal Thomas

Winning, head of the Roman Catholic Church in Scotland, who in the 20 August *Sunday Telegraph* equated therapeutic cloning with killing human beings and called on MPs to outlaw it.

Andrews, who has received heart-wrenching phone calls from people whose loved ones suffer from diseases that might be treated someday with stem cell-derived tissue, hopes the scientific argument will prevail: "If we don't start investigating, we aren't going to get the answers we need."

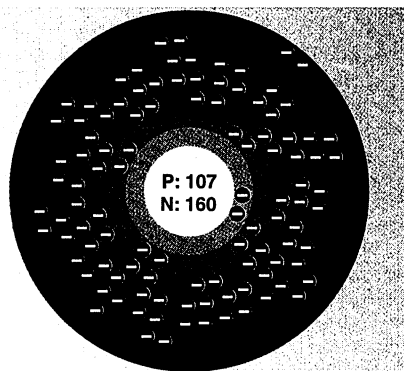
—RICHARD STONE

NUCLEAR CHEMISTRY

Element 107 Leaves The Table Upright

Hard as it is to make new elements, it's a lot easier than figuring out how they behave chemically. Consider element 107, bohrium. It was first glimpsed in 1976 by high-energy physicists at the Joint Institute for Nuclear Research in Dubna, Russia. Not until this week, however, did an international team of chemists report on the first successful analysis of its chemical properties. "This is exceptional work," says Walter Loveland, a nuclear chemist at Oregon State University in Corvallis, calling the Swiss-led effort "a unique event and a serious advance in chemistry."

The results, announced at a meeting of the American Chemical Society,* show that bohrium behaves almost exactly as theorists predicted it would. "Bohrium is boring," says team member Andreas Tuerler. But that



No threat. Despite its complex structure, bohrium upheld the chemical status quo.

straight-arrow comportment, he adds, is itself something of a surprise.

To predict the properties of unknown elements, chemists consult the periodic table, a chart that sorts elements into families according to the arrangement of electrons in their reactive outer shells. For the 115-odd known elements, the table works uncannily

well. But sooner or later, physicists believe, it is bound to become a victim of Einstein's theory of relativity.

The more massive an element is, they point out, the faster its electrons swarm the nucleus. Eventually, the electrons should start to show relativistic effects—changes of mass that will distort the shape of the swarms. Those distortions should give ultraheavy elements properties that could not be predicted by looking at their lighter kin. Elements 105 and 106 showed hints of unruly behavior, and scientists were eager to see if bohrium would be the straw that broke the camel's back.

Testing the chemistry of such elemental heavyweights, however, is exceedingly difficult, largely because the unstable nuclei at their cores fragment into smaller, more stable "daughter nuclei" almost the instant they come into being. A bohrium nucleus created in 1981 lasted only 9 milliseconds—far too short to run through chemical experiments. Fortunately, single elements can come in various flavors, or isotopes, each of which harbors a different number of neutrons. And some isotopes live longer than others.

So nuclear chemists Tuerler, Heinz Gaggeler, and their colleagues at the Paul Scherrer Institute in Villigen, Switzerland—along with team members from Germany and the United States—smashed a beam of neon atoms into a berkelium target, creating two new bohrium isotopes. One of those, ^{267}Bh , possessed a half-life of 17 seconds—long enough to make it an excellent candidate for testing its chemical reactivity.

From its electronic structure, nuclear chemists judged that ^{267}Bh should behave similarly to other elements in group 7 of the periodic table, such as technetium and rhenium. To test that hypothesis, Tuerler's team swept the atoms directly from their production facility into a 1000°C flow chamber, where they met up with hot oxygen and hydrochloric acid (HCl), gases that react readily with technetium and rhenium. What was left then passed through a chromatography column cooled to a comparatively chilly 70° to 180°C. Bohrium by itself can't make this journey in the cold, as it will quickly fall out of the gas and settle on the sides of the apparatus. But if it were anything like technetium and rhenium, it would continue to float freely if it combined with oxygen and HCl to make BhO_3Cl , barium oxychloride.

That's exactly what the researchers found. Running day and night for a month, the experiment produced only six atoms of the long-lived ^{267}Bh . But each atom flew through the full chemical separator, where its fingerprint-like decay pattern was picked up by detectors. Bohrium's chemistry was nailed, and the element certified as an obedient member of group 7. The results preserve the periodical table—for now.

—ROBERT F. SERVICE

* 220th ACS National Meeting, Washington, D.C., 20–24 August.