the Kyunghee results, says he has "lots of questions" for the researchers, including whether the introduced genes were actually in charge of cell division.

An expert at one of Seoul's biggest in vitro fertilization clinic, who asked not to be identified, says the Kyunghee doctors "are not experts" on cloning and have few published papers. He sees the experiment as a response to heavy competition among what he calls "test tube baby centers" (there are up to 30 in Seoul, and 80 nationwide), noting that such publicity might be expected to drum up more business.

The announcement nevertheless produced a strong public outcry, with newspaper editorials evoking the specter of "large numbers of Adolf Hitlers." In a brief telephone interview, Lee professed "surprise" at the strong reaction. Ethical oversight of research is sparse in Korea, and many university programs have no ethics committees to judge experiments. The Korean Fertility Society visits fertilization centers, but offers no certification or regulation.

Responding quickly to the outcry, several legislators say that they want to ban all human cloning experiments except those that relate to disease research. One proposal already before the National Assembly would give the job of reviewing such experiments to a committee of representatives from government, religious groups, research, and industry. Seo says he hopes any legislation would still permit in vitro research with embryos up to 14 days old, but that it may be difficult to find support for such an approach. "Before [the experiment], congressmen were cooperative," he says. "But now they are really anxious."

–MICHAEL BAKER

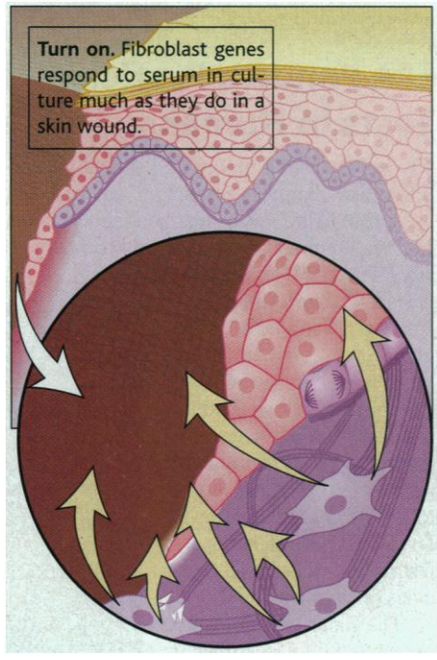
Michael Baker writes from Seoul.

MOLECULAR BIOLOGY

DNA Chips Give New View of Classic Test

It's a simple experiment, one that cell biologists have been doing for at least a quarter-century. Take a culture of connective tissue cells called fibroblasts, deprive them of nourishing serum for 2 days, then add back the serum and watch the genes that turn on as the fibroblasts grow. By now, you might think that biologists would have the cells' responses pretty well figured out. You'd be mistaken.

The standard view has been the serum's growth factors and other nutrients switch on the fibroblasts' cell proliferation program, stimulating them to divide. But on page 83, molecular biologists Patrick Brown and Vishwanath Iyer of Stanford University and their colleagues report a very different picture. Using a DNA chip that allowed them to monitor more than 8600 genes at once, the Stanford team found that the serum not only stimulates cell division, it also turns on genes needed for wound healing.



Turn on. Fibroblast genes respond to serum in culture much as they do in a skin wound.

CREDIT: K. SUTLIFF

The work demonstrates the power of DNA chips for looking at how entire batteries of genes coordinate their activity. It also shows that even isolated cells can react as if they were still in intact tissue, initiating gene changes that would bring about the cell-to-cell interactions needed for wound healing. With this new approach, says Jennifer Lippincott-Schwartz, a cell biologist at the National Institute of Child Health and Human Development in Bethesda, Maryland, "Pat Brown is offering us a whole new way of looking at cellular connections."

Brown and his colleagues have been perfecting the DNA microarrays that were crucial to this experiment for the past several years. With a customized machine, they cover glass slides with microscopic dots of immobilized DNAs, each representing a different gene. Exposed to fluorescently labeled DNA copied from the mRNA made by the corresponding gene, a spot will light up—a sign that that gene is active. To date, the researchers have shown they can use these arrays to monitor gene expression in a variety of organisms, including yeast and the plant *Arabidopsis* (*Science*, 23 October 1998, p. 699). When they were ready to try it using human DNA, they turned to the serum response system because the genes involved had supposedly been so well characterized. "It was a way to check out the [microarray] system and to learn new things," Brown says.

After the team made an array representing about 8600 human genes, Iyer withdrew the serum supply that nourished his cultures

ScienceScope

Downsized Will Japan's Science and Technology Agency lose its Cabinet seat on 1 April, when the government plans to demote two VIPs from the 20-member body? The agency is vulnerable to an April Fool's Day massacre because it is supposed to merge in 2001 with the larger Ministry of Education, Science, Sports, and Culture, which will likely retain its Cabinet status.

Immune to Criticism? A White House advisory panel slammed President Bill Clinton a few weeks ago for not aggressively following up on the goal he announced in May 1997 to develop an AIDS vaccine within 10 years. But Clinton assured the panel that NIH is about to address one criticism by finally naming a director for a new NIH vaccine institute. Insiders say the leading contender is University of Michigan, Ann Arbor, molecular biologist Gary Nabel, who won't comment. His selection could rub some researchers the wrong way: Though he is a respected authority on HIV gene therapy, Nabel has published little, if any, AIDS vaccine research.

Burial Rights? Will Kennewick Man, the 9000-year-old skeleton found on the banks of Washington's Columbia River in 1996, go under the microscope—or back underground? A federal judge may answer that question this year. Scientists want to analyze the bones to learn more about early Americans, but a Native American tribe wants the remains reinterred.

Tale From the Crypt In March, code breakers at a Rome conference will help the National Institute of Standards and Technology pick five finalists for a new Advanced Encryption Algorithm—the mathematical tool used to keep electronic financial transactions secure. Cryptologists recently broke the current code, which has lasted more than a decade. The eventual winner, to be chosen next year, should instantly become the world's most popular security algorithm.

Techno-Tension Tamer Technology-transfer folks are keeping an eye out for long-awaited guidelines and standard contracts for governing the exchange of new technologies, due out in draft form next month from NIH. Rising tensions over how to share and protect potential money-making inventions prompted a committee to urge NIH to come up with the new rules. Their report can be found at www.nih.gov/news/researchtools/index.htm

Contributors: the *Science* news staff.

of human fibroblasts to get the cells to shut down most of their genetic activity. Two days later, he added back a 10% serum solution. To see which genes were affected by the serum addition, Iyer purified mRNAs from subsets of the cells at various intervals during the next 24 hours, labeled the cDNAs made from those mRNAs with fluorescent dyes, and exposed each batch to the array. By monitoring which DNAs in the array bound the cDNAs, he and his colleagues were able to tell which genes were active at what times. With the aid of a computer program that examined the 500 most active genes, the researchers grouped those with similar activity patterns.

The computer program showed a coordinated response to serum by 28 genes known to be involved in controlling cell proliferation. The fastest to respond—some turning on within a few minutes after the serum exposure—were genes that make proteins that regulate the expression of other genes. These prodded the cells to copy their DNA and divide. Some of the active genes turned off within an hour; others remained active for several hours. A different subset of genes quieted down in response to serum, including those that keep the cell in a nondividing state.

But other sets of genes not involved in cell division also responded to the serum. Serum addition activated eight genes whose proteins elicit immune responses, 19 genes known to be involved in rebuilding damaged tissue, and a dozen whose proteins stimulate the growth of new blood vessels. The fibroblasts essentially reacted to exposure to serum in culture much as they would in the body if blood had seeped into a fresh skin wound. "If you look at the papers and the review articles [about the serum response model], everything is interpreted in terms of how [the results] fit into cell proliferation," Brown points out. "But that's not what the model was about."

Given that fibroblasts are known to help with healing, these findings are perhaps not surprising. Researchers "will be slapping their foreheads" for not having recognized it sooner, admits Stanford's Gerald Crabtree, and will see their work in a new light.

The work is also a taste of what is to come as researchers use microarrays to analyze gene expression in other mammalian systems. As Harold Varmus, director of the National Institutes of Health, pointed out last month in San Francisco at a meeting of the American Society for Cell Biology, "we will [eventually] be looking at the totality of gene behavior in individual cells, even [in] whole organisms" with microarrays. And that, he predicts, "is going to change our view of how life works." **–ELIZABETH PENNISI**

TOXICOLOGY

EPA Ponders Pesticide Tests in Humans

The volunteers drank corn oil spiked with a poisonous chemical as doctors watched for symptoms like sweating, headaches, and nausea. Inhuman torture or scientific necessity? That 1997 experiment was in fact performed legally on paid subjects in England by a commercial lab, but it is among several such experiments that spurred the Environmental Protection Agency (EPA) to convene an expert panel last month to lay the groundwork for its first-ever set of rules for testing the toxicity of pesticides on people.

How safe? Pesticides may be tested in humans as well as applied by them.

The panelists, who met on 10 and 11 December in Arlington, Virginia, wrestled mightily with the issue without pinning it to the mat. Some argued that pesticide experiments on humans might be permissible in the absence of alternatives such as studies of farm workers exposed to a pesticide on the job, although they insisted on a stringent ethical review of the experimental protocols. But others urged EPA to reject human data, especially from studies done merely to market a product. "I heard a lot of ethical and scientific concerns about those data," says Lynn Goldman, who stepped down on 31 December as head of EPA's Office of Prevention, Pesticides, and Toxic Substances, which hopes to issue draft regulations by this spring.

The current debate is an outgrowth of efforts to beef up protection against pesticide toxicity, which have spawned a backlash that could increase the number of tests done on humans. The agency now sets safe levels at one-hundredth the pesticide concentration found to have no effects on animals, partly on the assumption that humans might be more sensitive to the chemicals than lab rats. A 1996 law aimed at protecting children could lead to another 10-fold reduction in acceptable levels of toxicity. That further tightening has so concerned pesticide companies that some have proposed dumping animal-only tests in favor of direct tests in adult humans.

> **Human pesticide testing "makes me morally queasy, but not to the point where I'd say, 'ban it.'"**
>
> **—Arthur Caplan**

The EPA was already concerned about this possibility when the Environmental Working Group, a Washington, D.C.–based activist group, reported last July on the use of human volunteers in recent pesticide tests mostly in the United Kingdom. The publicity prompted EPA to check its own files, which contained the results of eight human no-effects studies—some recent, others decades old. In most cases, it was unclear whether the studies had been approved by an ethical panel called an Institutional Review Board, as required by a government-wide standard called the Common Rule. "We were terribly concerned ... because to observe no adverse effect levels, somebody's going to have to have an adverse effect," Goldman says.

Last month's panel, with experts on topics ranging from bioethics to toxicology, examined both the science and the ethics behind such testing. Several observers noted that many of the tests submitted to EPA included only a handful of subjects—too few to yield statistically significant results. If human tests are done, they "should be scientifically valid," said computational biologist Chris Portier of the National Institute for Environmental Health Sciences in Research Triangle Park, North Carolina.

At the same time, University of Rochester toxicologist Bernard Weiss pointed out that human data can offer valuable insights on topics such as toxicity mechanisms or individual sensitivity differences. Others noted that the tests, however unsettling at first glance, are similar to a Phase I clinical trial, where healthy volunteers are often used to test a candidate drug for side effects. University of Pennsylvania bioethicist Arthur Caplan says that human pesticide testing "makes me morally queasy, but not to the point where I'd say, 'ban it.' " Like other committee members, however, he emphasized that EPA should require companies to comply with the Common Rule, which is now applied only to agency-funded research.

To some panelists, however, the value to society of a new pesticide pales in compari-

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