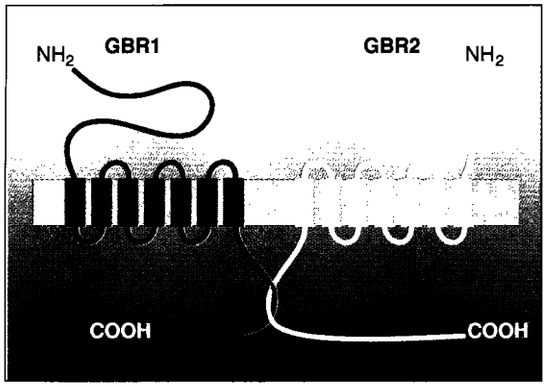
Bettler team, groups led by Hans-Christian Kornau of the biotech firm BASF-LYNX Bioscience AG in Heidelberg, Germany, and by Fiona Marshall at Glaxo Wellcome's Molecular Pharmacology unit in Stevenage, England, coaxed yeast cells to express the tail of GBR1. The tail was to serve as a bait for picking up any proteins that interact with it and might be needed for $GABA_B$ function. Both teams turned up the same protein, which Kornau dubbed GBR2. Like GBR1, GBR2 turned out to contain seven hydrophobic regions that could thread through the lipid-rich cell membrane and two ends that could project inside and outside the cell. This structure suggested that GBR2 is also a receptor, and thus that two receptor molecules may operate as a duet in cells.



Together. Functional $GABA_B$ receptors require an interaction between the GBR1 and GBR2 proteins.

Meanwhile, the Novartis, Synaptic, and Glaxo teams were searching the GenBank human gene database for proteins resembling GBR1 in hopes of finding one that would do a better job of reproducing the $GABA_B$ receptor's functions. Remarkably, they all picked out the same protein that had popped up in the yeast. But when the researchers coaxed cultured cells to express GBR2, along with the requisite potassium channels, this receptor also failed to produce robust potassium currents in response to GABA treatment.

Thinking they had missed the active part of the $GABA_B$ receptor, the Synaptic team was about ready to give up when they looked at the expression patterns of both GBR1 and GBR2 in sections of rat brain, and noticed a striking overlap. This overlap, which the other scientific teams also saw, suggested that the two proteins may work together in individual neurons.

And that's what all the groups have now shown. When they expressed both GBR1 and GBR2 in cultured frog or human cells, the cells produced potassium currents. "It worked beautifully," says Jones. The Novartis group went one step further: Aided by specific antibodies, they demonstrated that the two proteins are closely associated on individual brain neurons. In addition, the Kornau group has mapped the site where the two proteins interact.

The BASF-LYNX group reports its findings on page 74; the other three papers appeared in the 17 December 1998 *Nature*. Together, the four papers suggest that GBR1 and GBR2 cooperate in at least two ways. First, the proteins are likely to help each other transmit GABA's signal within a neuron, allowing the neurotransmitter to activate the potassium channels. In addition, GBR2 may help shuttle GBR1 to its final location on the cell membrane, since the Glaxo team showed that GBR1 does not get to the membrane unless GBR2 is present.

Whatever the nature of the partnership, by providing a fully functional receptor, the discovery of GBR2 should help researchers design new drugs that work through $GABA_B$. Drugs that target $GABA_B$ might, for example, provide a new range of therapies that help depress the excessive neuronal firing characteristic of epilepsy, pain, and anxiety, or perhaps help relieve neuronal inhibition to bolster memory or ameliorate depression. As yet, however, nobody can predict how successful such drug development efforts will be. "We're still far from a direct clinical application," says Kornau, "but knowing this receptor's structure is a significant step forward."

–INGRID WICKELGREN

CREDITS: (LEFT) HANS-CHRISTIAN KORNAU; (RIGHT) RICK KOZAK

Moon-Forming Crash Is Likely in New Model

The greatest accident in Earth's history was probably no accident at all, according to new computer simulations of the early solar system. Planetary scientists believe that sometime in the first 100 million years after the solar system took shape from gas and dust, a Mars-sized planet smashed into Earth. The impact liquefied Earth's surface and ejected a huge blob of material that coalesced into the moon. Far from being a chance encounter that defied all the odds, the new simulations suggest, an impact like this is expected to occur in the solar system's first 100 million years.

"The lesson is that giant impacts are common," says Robin Canup of the Southwest Research Institute (SWRI) in Boulder, Colorado, who developed one of the models. "They're not the wild, ad hoc event that they were once believed to be." Her simulations,

ScienceScope

A TIME FOR FORWARD THINKING

"I never think of the future—it comes soon enough," Albert Einstein once declared. But for those who don't share the great physicist's ambivalence about where time's arrow is taking us, we preview what may be some of 1999's science headlines:

Disposable Income? Expect to hear less grumbling among postdocs. Thanks in part to a $2 billion budget boost, the National Institutes of Health (NIH) will increase stipends for its postdoctoral fellows by up to 25% this year. A newly minted Ph.D. can expect an annual salary of $26,256, up from about $21,000 last year. Veterans with 7 or more years in the trenches will get $41,268.

You'll Know It When You See It A 2-year struggle to define scientific misconduct should end when a U.S. government panel releases guidelines this spring.

Gene Machine DNA sequencing virtuoso J. Craig Venter should know by autumn if his scheme for speed-reading the human genome will fly—or fizzle (*Science*, 15 May 1998, p. 994). Venter's corporate partner, Perkin-Elmer Corp., expects to begin delivering the project's key technology—several hundred speedy sequencers—to his Maryland headquarters in late spring. Test runs on fruit fly DNA should tell Venter if he's off to a soaring start—or grounded by technical snags.

Lucky 22 Meanwhile, other genome sequencers hope to have the first human chromosome—number 22—finished sometime before June. Keep up with the project's progress at www.sanger.ac.uk/HGP/Chr22

Take Me to Your Leader 1999 will be a soul-searching time for several pillars of the U.S. scientific establishment. The Howard Hughes Medical Institute is looking to name a new leader to guide the nation's largest private biomedical grants program. Also in play are the top slots at the Memorial Sloan-Kettering Cancer Center and *Science* magazine. Listen for whispers about Harold Varmus possibly giving up his director's chair at NIH.

CONTINUED ON PAGE 17

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

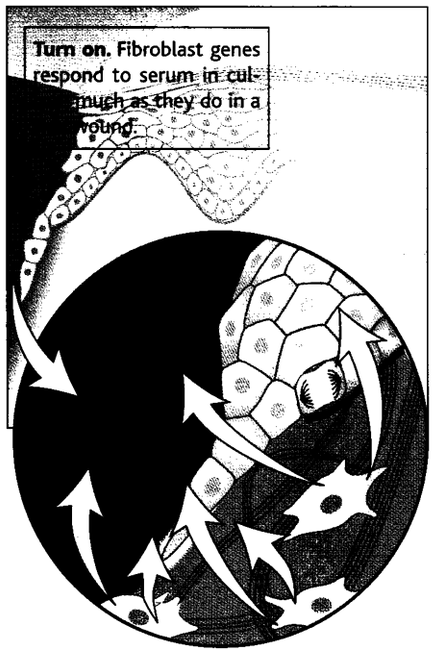
Michael Baker writes from Seoul.

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 cul- much as they do in a 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.