and their university counterparts, who earned up to 10% more. The differential was causing a "brain drain of CSIC scientists" to the universities, Tarrach says. He found himself under increasing pressure from the ranks: In a 4 December letter, 10 directors and scientists of CSIC institutes urged him to deal with a series of concerns about his management of the agency.

Tarrach's woes intensified after the oil spill. In a 24 January letter to *Science* (p. 511), 422 scientists accused the government of failing to adequately take into account the views of the scientific community. Although no government official was singled out in the letter, some researchers pin at least part of the blame on Tarrach. He has shown an "incapacity of leadership," charges Juan Eugenio Iglesias of the Institute of Materials Science in Madrid. Tarrach, he says, has demonstrated that "he serves the government rather than the scientists."

If that's the case, the government has found an odd way to express its appreciation. On 24 January, the conservative newspaper *ABC* announced Tarrach's resignation. Tarrach himself says he learned of his resignation from the news article; he blames his fall on the *Science* letter, which generated widespread press coverage in Spain that day.

In a written statement, the science ministry explained that Tarrach resigned because he "wished to return to the academic life." A spokesperson declined to comment on suggestions that the *Science* letter precipitated Tarrach's departure. Ironically, the CSIC official most responsible for dealing with the oil spill—Emilio Lora-Tamayo, CSIC vice president and head of the agency's scientific commission on the spill—is being tapped as Tarrach's successor. **–XAVIER BOSCH**

Xavier Bosch is a writer in Barcelona.

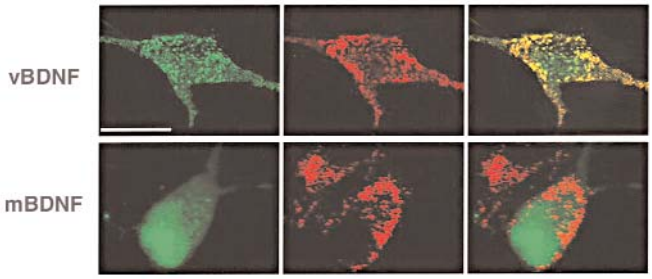
NEUROSCIENCE

Minor Variation in Growth-Factor Gene Impairs Human Memory

Buried deep within the brain, the sickle-shaped hippocampus helps determine what a person learns and remembers. Now, researchers have identified a tiny genetic variation that may influence just how effectively the hippocampus functions. The genetic twist may also affect a person's susceptibility to brain diseases such as Alzheimer's.

People carrying a particular variation in the gene for a protein called brain-derived neurotrophic factor (BDNF) didn't perform as well on a memory test as people with the standard version of the gene did, according to a report in the 24 January issue of *Cell* by Michael Egan, Bai Lu, Daniel Weinberger, and colleagues at the National Institutes of Health (NIH) in Bethesda, Maryland. Brain-imaging and other studies point to abnormal functioning of hippocampal neurons in those with the variation, which changes just one amino acid in BDNF, replacing valine with methionine at position 66 of the protein. Neurobiologist Susan Patterson of Columbia University in New York City says that the work "provides a very nice demonstration that BDNF plays a role in some forms of human memory."

The NIH team had ample reason to suspect that BDNF might be involved in memory and learning. Although it was originally discovered as a general facilitator of neuron growth and maintenance, over the past few years, numerous groups, including Lu's, have linked it to the neuronal remodeling that underlies learning and memory. In particular, they have found that it enhances a phenomenon called long-term potentiation (LTP), in which synapses, the connections between neurons, are strengthened when their neurons are stimulated simultaneously.



Delivery error. The red stain identifies the secretory vesicles, and the green stain identifies either the valine (*top*) or methionine (*bottom*) variant of BDNF in these hippocampal neurons. Merging the green- and red-stained images (*top and bottom right*) shows that only the valine variant ends up in BDNF's normal location in the vesicles.

In the first phase of their work, Weinberger and his colleagues searched gene databases for variations in BDNF that might influence the protein's function. They also wanted to see if any variations could be linked to schizophrenia, which is associated with derangements in hippocampal function.

The valine-to-methionine switch at ▶

CREDITS: (TOP TO BOTTOM) WORLD HEALTH ORGANIZATION; SOURCE: M. F. EGAN *ET AL.*, *CELL* 112, 257 (2003)

ScienceScope

Insider to Lead World Health Organization

A relatively unknown insider, Jong Wook Lee (right), has been tapped as the next director-general of the World Health Organization (WHO). The South Korean tuberculosis expert has worked at WHO for nearly 20 years, most recently as head of WHO's Stop TB antituberculosis program.

The 28 January vote by the organization's Executive Board at WHO's Geneva, Switzerland, headquarters was close: Lee received 17 votes to 15 for runner-up Peter Piot, head of UNAIDS. Three other finalists—Pascoal Manuel Mocumbi, prime minister of Mozambique; Ismail Sallam, Egypt's former health minister; and Mexico's health minister Julio Frenk—were eliminated in a first round of voting.

Lee has said he will work to decentralize WHO and strengthen its country and regional offices. Lee's current boss, David Heymann, executive director of WHO's division of communicable diseases, praised the board's choice. Lee "has shown great skills in working with partners in the private sector," he said, which will be important for the organization in coming years. The WHO General Assembly is expected to approve Lee's nomination at its meeting in May. He will take over from current Director-General Gro Harlem Brundtland at the end of June.

–GRETCHEN VOGEL

Indian Animal Activists Dropped From Oversight Panel

NEW DELHI—In a move likely to please the Indian biomedical community, ardent animal activists have been pushed off a committee that supervises animal experimentation.

Under animal-welfare activist and former union minister Maneka Gandhi, the Committee for the Purpose of Control and Supervision of Experiments on Animals conducted a series of inspections that found deficiencies at several well-known science institutes. But Gandhi lost her Cabinet post in July after a squabble with the former health minister, and her committee post last month. Now the panel has shed 10 of 28 members and been recast into a body of scientists and government officials.

Immunologist Satyajit Rath of the National Institute of Immunology in New Delhi welcomes the changes as a move toward more balanced oversight. But Gandhi sees it as "the end of the road for surprise inspections and rigorous oversight."

–PALLAVA BAGLA

site 66 looked promising, Weinberger says. It's a fairly common variant: Of 600 people the researchers examined, 32% had at least one copy of the oddball gene. And the variation is located in the so-called ZIP code of BDNF, a sequence that directs the protein to its correct destination in the cell. Thus, the amino acid change wouldn't alter BDNF function directly, but it could do so indirectly by causing the protein to end up at the wrong place.

Subsequent testing revealed no link between the methionine variant and schizophrenia risk. But the researchers did find that both schizophrenic and healthy subjects who carried the variant fared worse on a test that measures episodic memory—the ability to remember past experiences—than did people who had two copies of the valine version. Results on the test, in which subjects are asked to recall the elements of a short story that they have read, have been linked to activity in the hippocampus.

Brain-imaging studies confirmed that hippocampal function was abnormal in people with the methionine variant. In a different memory test, in which the hippocampus is normally deactivated, functional magnetic resonance imaging showed that activity in this brain region was actually turned up in people with the variant.

In addition, Weinberger's group used another imaging method to look at levels of a chemical called N-acetyl aspartate (NAA), an indirect measure of the richness of synaptic connections among neurons. Hippocampal NAA levels were lower in people with the methionine variant. All in all, Weinberger concludes, "the form of the gene you have influences how well your hippocampus works."

Further studies by the NIH team point to a possible reason for the impaired hippocampal function in people who make the variant BDNF. Normally, neurons secrete BDNF when they are stimulated. This is thought to help strengthen synapses, as in LTP. But studies of cultured hippocampal neurons showed that the methionine variant wasn't transported to the nerve endings as it should be. As a result, BDNF wasn't secreted when the neurons were stimulated.

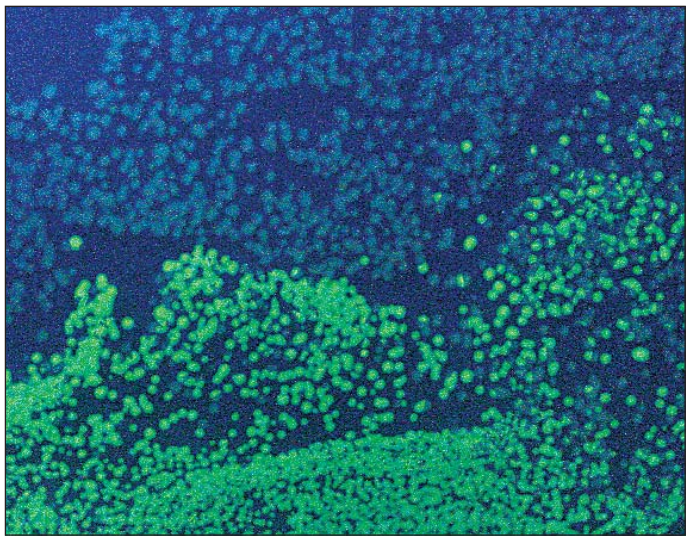
Neuroscientist Mu-ming Poo of the University of California, Berkeley, describes these findings as "very intriguing … a very bold link of a molecular defect with a defect in cognitive function."

Even so, Egan and others note that the variant's effect on memory is small, and it has no apparent effect on one's IQ. But the findings raise the possibility that people with the variant may be more vulnerable to memory loss that may come with advanced age or brain injury. "Everybody may not have the same genetic toolbox to deal with additional insult," as Weinberger puts it. **–JEAN MARX**

METABOLIC ENGINEERING

Researchers Create First Autonomous Synthetic Life Form

Peter Schultz is dissatisfied with the number 20. That's the number of amino acids that virtually all organisms use to construct proteins, the molecules that carry out the lion's share of chemistry within cells. Two years ago, a team led by Schultz, a chemist at the Scripps Research Institute in La Jolla, California, engineered the genes of a live organism—an *Escherichia coli* bacterium—to incorporate a 21st amino acid into its proteins. That made the bug the first synthetic life form with a chemistry unlike anything found in nature. To make proteins with unnatural amino acids, however, the researchers had to put that new amino acid into the bacterium's growth medium.



Extra edge? Tests should show whether bacteria engineered with a 21st amino acid (green) outcompete those with 20 (light blue).

Now, in a paper scheduled to appear in this week's issue of the *Journal of the American Chemical Society*, Schultz's team reports going one step further by engineering an *E. coli* that not only incorporates a 21st amino acid into its makeup but also manufactures the compound by itself.

"These results are very exciting," in part because they provide researchers with a new way to explore evolution, says David Liu, a chemist and specialist in molecular evolution at Harvard University in Cambridge, Massachusetts. "It's tantalizing to ask how can this organism evolve, now that it is equipped with a method for not only using a nonnatural building block but also for creating that building block," says Liu.

Getting an organism to expand its standard amino acid repertoire took some doing. Schultz's team has had to reengineer the basic machinery that cells use to make proteins. That machinery starts with trios of nucleotide bases, called codons, that make up DNA. Each codon directs a particular amino acid to be added to a protein chain. To create its first synthetic bug, Schultz's team co-opted a little-used codon—known as the amber stop codon—and reengineered the cellular enzymes to add a new amino acid, *O*-methyl-L-tyrosine, whenever it saw that codon.

In the latest work, Schultz—with students and colleagues at Scripps, the University of California, Berkeley, and the Genomics Institute of the Novartis Research Foundation in La Jolla—followed that same strategy with a new amino acid, *p*-aminophenylalanine. To enable the microbes to make the new amino acid on their own, they also spliced a trio of enzyme-producing genes from a strain of *Streptomyces* bacteria into the *E. coli*. Together with another enzyme already present in *E. coli*, these enzymes enabled the bugs to turn a common compound in *E. coli* called chorismate into *p*-aminophenylalanine, which protein-building enzymes then picked up and inserted into growing proteins.

What difference does the altered chemistry make? To find out, Schultz says, his team is randomly inserting amber stop codon mutations into the *E. coli* genome. Next, they plan to put these *E. coli* and the 20-amino-acid variety under selective pressure by changing their food supply and other factors, to see whether the bacteria with a 21st amino acid fare better than natural ones do. If so, he says, it would suggest that although biology has made do with 20 amino acids for billions of years, evolution could make use of plenty more. **–ROBERT F. SERVICE**

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