

map, the researchers treated the DNA sequentially with two enzymes, each of which cuts it at different, specific sites, leaving the DNA fragments lined up in the right order.

After each enzyme treatment, the researchers measured the fragments. They put DNA pieces of known lengths on the slide for reference and used fluorescence microscopy to digitally image the DNA fragments. Finally, a sophisticated computer program developed by NYU's Bud Mishra and Thomas Anantharaman compiled the map showing the cut sites. "It's a brilliant [approach]," says Welles.

The payoff will come as an international team completes the actual sequence of the parasite's genome, and later, as new genes are found with the help of the genetic map. In genome sequencing, researchers first generate lots of tiny, overlapping bits of DNA, then they assemble them in the right order along the chromosomes to get the full genome sequence. Now, they can use the locations of the cuts and of the microsatellite markers to figure out where newly sequenced DNA belongs along the *P. falciparum* genome. "They provide a scaffolding of sequence that we can use as a reference," says Leda Cummings, a molecular biologist who is sequencing the parasite's DNA at The Institute for Genomic Research in Rockville, Maryland.

Indeed, with the help of these and other maps, the sequencers expect to finish the malarial genome by the end of 2001. Welles predicts that with this sequence and the many other experimental resources that are becoming available (see p. 1251), the parasite's secrets "are going to unroll very rapidly." As for the chloroquine-resistance gene that sparked the map work? It's been found, says Welles, and its identity will soon be published.

—ELIZABETH PENNISI

NEUROBIOLOGY

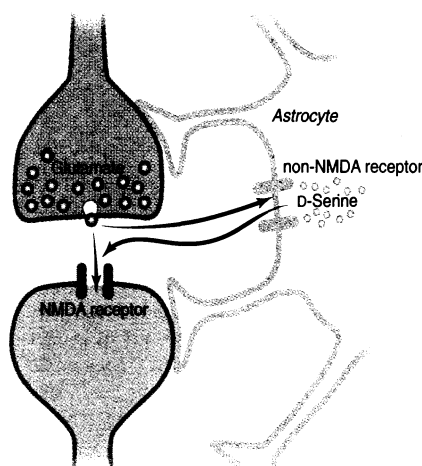
Key Brain Receptor Gets An Unusual Regulator

A team of researchers at The Johns Hopkins University School of Medicine has unearthed a strange new regulator of nerve cells—a looking-glass molecule not previously known to be made by higher mammals. In the 9 November *Proceedings of the National Academy of Sciences*, neuroscientist Solomon Snyder and his colleagues report that they have cloned a brain enzyme that makes the amino acid D-serine, rounding out their case that this unusual molecule plays a central role in learning and memory.

Snyder's team had previously implicated the amino acid as an activator of the so-called NMDA receptor—a molecule with

pivotal roles in learning, brain growth, and brain cell death. But as Snyder himself concedes, the idea that D-serine acts on the NMDA receptor was so radical that people "paid no attention" to it. For one, the NMDA receptor was supposed to be activated by the neurotransmitter glutamate in partnership with another amino acid, glycine. For another, D-serine would be an extraordinary glutamate partner indeed as "D," or right-handed, forms of amino acids were not supposed to be made by mammals.

But cloning the enzyme that makes D-serine proves that the amino acid is made in the brain. Snyder's team went on to trace the enzyme to the same cell type, astrocytes, and the same brain areas where D-serine is found. And to nail their case, they showed that destroying D-serine in the brain greatly reduces NMDA receptor activity. "It's a significant advance," says neuroscientist



Cross-talk. Under glutamate's influence, astrocytes release D-serine into the synapse between two neurons (left).

Joseph Coyle of Harvard Medical School in Boston. "They've now characterized at a molecular level a key new participant in NMDA receptor function."

Medicine should also benefit, as the newly cloned enzyme, called serine racemase, provides a novel target for drugs to treat a range of neurological conditions in which NMDA receptors play a role. Drugs that block or quiet the enzyme, for example, might be used to quell anxiety and epilepsy and prevent damage from strokes, which can be caused by excessive activity at NMDA receptors. On the other hand, stimulating serine racemase might improve schizophrenia symptoms, which are partly caused by depressed NMDA receptor function.

Snyder became intrigued with D-serine in the early 1990s, after stumbling across an obscure paper by scientists at the National Institute of Neuroscience in Tokyo, who had detected the amino acid in rat

ScienceScope

Biomed Headhunting As government contracts go, it's small—but possibly very important for the future of biomedical research. The Department of Health and Human Services (HHS) is paying the National Academy of Sciences \$25,000 to help find a successor to National Institutes of Health director Harold Varmus, who plans to depart at year's end. Academy president Bruce Alberts, with the assistance of Institute of Medicine president Kenneth Shine, has promised to deliver a list of "six to 12" suitable candidates to HHS secretary Donna Shalala later this month. She will forward the recommendations to President Clinton, who gets the final say.

Slam Dunk A high-stakes donor wants to help the next generation pump up Israeli science. U.S. industrialist William Davidson last week made the largest individual gift ever to the Weizmann Institute of Science in Rehovot: \$20 million intended to enliven classroom science.

The Weizmann, a \$180-million-a-year operation, already is the largest producer of science teaching tools for Israel's secondary schools. But the new Davidson Institute of Science Education aims to add new curricula and programs such as Perach, in which 25,000 undergrads tutor disadvantaged students in exchange for scholarships. The gift is an "investment in the future," says Davidson, CEO of Michigan's Guardian Industries and a partner in the Detroit Pistons basketball franchise.

Weizmann officials have their work cut out for them. According to Rami Rahimi-moff, a former Hebrew University-Hadassah Medical School dean, studies show outstanding Israeli students shunning science and "looking to get rich quick" in other fields.

Case Dismissed Suing a professor for stealing one's ideas may become more difficult in New York state, thanks to a recent court decision. Judge Emily Jane Goodman of the state Supreme Court for New York City last month dismissed a suit brought by Sheng-Ming Ma, a former Columbia University Ph.D. candidate in mathematics, who claimed his thesis adviser misappropriated his work (*Science*, 23 April, p. 562). After summarizing the complex issues at stake—including the question of whether a new math proof was valid—Judge Goodman concluded: "This court cannot fathom how I or a jury could decide which theorem is correct." The decision may put a chill on such cases in New York, including a suit by nutritionist Antonia Demas claiming that her adviser at Cornell University took her ideas.

of Caltech. Astrophysicists who saw BOOMERANG's temperature map believe that the data will pinpoint the first and second acoustic peaks and perhaps even outline the third. Their locations could make the flatness of space unmistakable, and they could also reveal how the makeup of the universe is divided between matter and a mysterious "vacuum energy" called the cosmological constant.

Other missions will provide a check on any conclusions. A balloon mission that flew over Texas in June, called MAXIMA, may also map the first and second acoustic peaks, says cosmologist George Smoot of Lawrence Berkeley National Laboratory in Berkeley, California, who led the original COBE analysis. And next fall, NASA will launch the long-awaited Microwave Anisotropy Probe to chart the background temperature fluctuations from orbit, with unprecedented precision.

For now, says astrophysicist Rocky Kolb of the Fermi National Accelerator Laboratory in Batavia, Illinois, BOOMERANG "certainly seems to show that we live in a flat universe." But he adds, "I'm a little worried about that, because it's the expected result. It's always easier to see what you expect."

—ROBERT IRION

IMMUNOLOGY

Memory T Cells Don't Need Practice

Once learned, some abilities, such as swimming or riding a bike, are never forgotten even after years without practice. Others, say running a marathon, need a regular brushing up. Immunologists have long debated which category our immunological memory falls into. Once immune cells learn to recognize a particular antigen, such as a viral protein, do

of Emory University in Atlanta and Susan Swain of the Trudeau Institute in Saranac Lake, New York, shows that memory T cells don't need to repeat this experience: They persist and maintain their ability to recognize their specific antigens, even when put into mice that have been genetically altered to eliminate the MHC proteins, which makes antigen presentation impossible.

For many immunologists, the findings cast a final verdict on the long-standing controversy. "These two papers nail it down pretty firmly that you don't need antigen or some orthodox signaling by classical MHC molecules" to maintain T cell memory, says Peter Beverley of the Edward Jenner Institute for Vaccine Research in Compton, U.K.

Not everyone is convinced, however. Benedita Rocha of the Necker Institute in Paris, whose own work suggests a need for constant "tickling" of memory T cells by MHC molecules, says the experiments on which the findings are based are very complicated and pose many pitfalls. At best, she maintains, "the results are not conclusive yet."

Ahmed and his colleagues worked with so-called killer T cells, which, when activated, attack and destroy certain abnormal cells, such as those infected by viruses. The team began by immunizing normal mice with the lymphocytic choriomeningitis virus (LCMV), a well-known mouse pathogen. After waiting several months until the antiviral T cell memory was established, the researchers purified the animals' killer T cells, including any anti-LCMV memory cells, and then transferred the cells into two mouse strains that had no T cells of their own. The strains were genetically identical, with a single exception. One also lacked the gene for a protein called β_2 -microglobulin (β_2 M), which helps transport the class I MHC proteins needed for antigen presentation to killer T cells to the cell surface.

As a result, T cells transplanted to these mice should get little or no stimulation by antigen-presenting cells. Yet when the researchers recovered virus-specific T cells from the recipient mice 10 months later, they

found the same number of memory T cells regardless of whether β_2 M was present.

Rocha sees a flaw in this experiment: She suggests that the MHC class I-positive T cells might have stimulated each other. Ahmed and his colleagues tried to guard against the possibility by testing memory T cells that themselves lacked β_2 M, but Rocha maintains that "even these so-called MHC class I-negative T cells are not completely devoid of MHC." Immunologist Peter Doherty of St. Jude Children's Research Hos-

they need constant reminders to stay on top of things, or are their memories permanent? Two reports in this week's issue of *Science* (pp. 1377 and 1381) now bolster the notion that immune cells never forget.

The immune cells in question are T cells, which spring into action to kill infected cells or orchestrate other immune responses when other cells "present" them with an appropriate antigen, together with a so-called MHC protein. The new work, which comes from two independent groups, led by Rafi Ahmed

ScienceScope

Early Birds The White House has moved with record speed in nominating two scientists to serve on the 24-member National Science Board, which oversees the National Science Foundation (NSF). Historically, the Administration has been slow to pick members for the panel, leaving it so short-handed at times that it was barely able to convene a quorum. But NSF officials credit Neal Lane, the president's science adviser and former NSF director, with shepherding the new nominees—crystallographer Michael G. Rossmann of Purdue University in West Lafayette, Indiana, and ecologist Daniel Simberloff of the University of Tennessee, Knoxville—through the bureaucracy for an announcement on 1 November, giving the Senate plenty of time to confirm them before their 6-year terms begin in May 2000. NSF hopes for similarly rapid action on replacing the remaining eight panelists whose terms end next spring.

A Wrinkle in Space-Time In 1916, Albert Einstein predicted that violent cosmic motions should send gravitational waves rippling through the fabric of space. This week, researchers inaugurated an unusual observatory designed to catch those elusive waves. The \$292 million Laser Interferometer Gravitational-Wave Observatory (LIGO)—which has facilities in Livingston, Louisiana, and Hanford, Washington—will use laser beams to continually measure the positions of mirrors suspended in vacuum tubes 4 kilometers apart. Researchers hope the delicate detectors can discern relative wiggles as small as 1/10,000th the diameter of a proton.

"I can't imagine a more exciting new window to open on the universe," says Caltech physicist Gary Sanders, LIGO's deputy director. But LIGO probably won't sense any shimmers in space-time until both facilities are fine-tuned and ready to start eyeing the gravitational universe in early 2002.

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