

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 Wellems.

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. Wellems 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 Wellems, and its identity will soon be published.

—ELIZABETH PENNISI

NEUROBIOLOGY

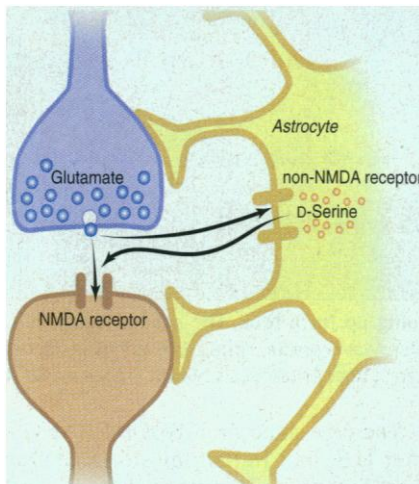
Key Brain Receptor Gets An Unusual Regulator

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.

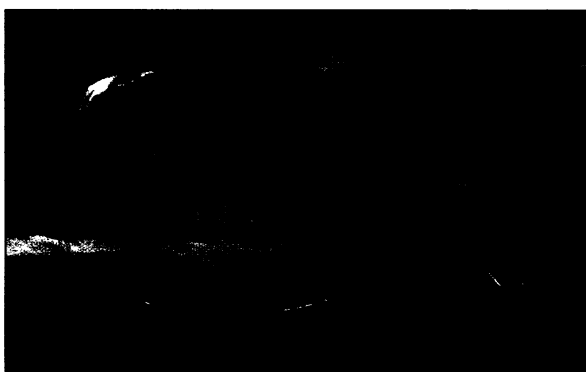
Weizmann officials have their work cut out for them. According to Rami Rahimi-moff, a former Hebrew University-Hadassah Medical School dean, studies show outstanding Israeli students shunning science and "looking to get rich quick" in other fields.

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.

COSMOLOGY

Balloon Flight Brings Cosmic Glow Into Focus

Seven years ago, the Cosmic Background Explorer (COBE) satellite thrilled cosmologists by revealing subtle temperature ripples in the faint microwave glow that pervades the universe. The ripples were the first glimpse of imprints left on the young universe during its birth in the big bang. But COBE could only view great chunks of the sky at once, so the fine details of the ripples remained elusive. Now, a telescope carried aloft by a balloon has scrutinized the microwave glow much more closely—giving cosmologists who have seen the early results another thrill.



Going up for a look. The balloon-borne BOOMERANG cosmic microwave probe, riding the gondola at right, is readied for launch near Antarctica's Mount Erebus on 29 December 1998.

The data come from BOOMERANG, a joint U.S. and Italian mission that flew over Antarctica for more than 10 days in December 1998 and January 1999. BOOMERANG's 1.3-meter telescope—soaring 36 kilometers high, above the atmosphere's moisture—zeroed in on fluctuations some 35 times smaller than COBE did. A preliminary display of the resulting temperature map sent ripples through an audience of astrophysicists at a recent meeting.* “It was a moment like seeing the COBE data for the first time,” says astrophysicist Craig Hogan of the University of Washington, Seattle. “It’s the most beautiful map of the sky I’ve ever seen.”

BOOMERANG researchers are closely guarding their analysis until it is complete, which could take many months. But cosmologist Andrew Lange of the California Institute of Technology (Caltech) in Pasadena, the U.S. team leader, says the final results will expose the intricacies of the sky’s temperature variations as never before. “We have moved into a new epoch,” Lange says. “These are the first maps in which you can actually look and

point in great detail at which parts of the sky are hot and which parts are cold.” Lange and cosmologist Paolo de Bernardis of the University of Rome, La Sapienza, who leads the Italian component of the team, think the tiny temperature bumps will help cosmologists pin down the proportions of matter and energy in the newborn universe.

The radiation measured by BOOMERANG and a myriad of other current and planned cosmic microwave probes is a cosmic fossil, dating from when temperatures in the young universe were so high that light and matter seethed together in an interacting soup. Small gravitational disturbances inside this plasma tried to draw the matter into clumps, but radiation pressure from the energetic photons fought back. The tug-of-war drove a series of acoustic oscillations within the fluid, much as drawing a bow across a violin’s strings causes the instrument’s wood to resonate at many different frequencies. Then, when the cosmos reached an age of about 300,000 years and cooled enough for energy to stream through the matter unimpeded, the photons escaped. They form the faint microwave background we see today, imprinted with the remnants of those primordial oscillations.

Cosmologists typically graph the oscillations as a function of power (differences in temperature) and angular scale (their apparent sizes on the sky). The resulting “power spectrum” resembles a roller coaster, with a high initial peak followed by ever-diminishing peaks, which mark the higher frequency overtones of the first oscillation peak. As it turns out, the details of those peaks—such as their relative heights and their precise angular scales—encode critical information about the nature of the cosmos.

For example, the first peak should fall at a scale of about 1 angular degree in a universe containing just the right density of matter and energy to make space geometrically flat, so that parallel light rays remain parallel forever. A flat universe is expected in a popular scenario of cosmic origins called inflation, which posits an extraordinarily fast expansion of space within a fraction of a second after the big bang. Other probes of the microwave background have suggested that the first peak meets this test, with varying degrees of confidence (*Science*, 17 September, p. 1831).

But “in order to really believe these results, we need to be able to see the higher peaks as well,” says theorist Marc Kamionkowski

brains. Although the rats might have acquired it from their food, Snyder thought its presence might be more than accidental. He noted that the Tokyo team had found D-serine in brain areas rich in NMDA receptors, and that other workers had shown that the amino acid stimulates the receptor in slices of brain tissue.

To follow up on his hunch, Snyder put his then-graduate student, Michael Schell, to work making antibodies to D-serine to use for mapping its brain distribution more precisely. Applied to brain slices, the antibodies homed in on the D-serine, showing that it is indeed closely juxtaposed to NMDA receptors. The researchers also discovered, to their surprise, that the cells housing D-serine are not neurons but “supporting” cells called astrocytes, and that glutamate could spur D-serine’s release from those astrocytes. From those findings, reported in 1995, the researchers surmised that when a neuron dumps glutamate into a synapse, the transmitter not only sticks to the NMDA receptor but simultaneously triggers the release of its coactivator, D-serine, from an adjacent astrocyte.

The evidence for this offbeat theory was still circumstantial, however, so Snyder set out to find proof. To nail D-serine’s origin to the brain, Snyder’s postdoc, Herman Wolosker, went after the enzyme that makes it, serine racemase. He first purified the enzyme from rat brain, a tour de force completed earlier this year. And now, Wolosker, Snyder, and Seth Blackshaw have cloned the gene for serine racemase and shown that it is active in the same astrocytes that harbor D-serine, making D-serine’s role in the brain hard to dispute. “The paper is extremely tight,” says neuroscientist Gavril Pasternak of the Memorial Sloan-Kettering Cancer Center in New York City. “It all fits together nicely.”

In as yet unpublished work, Snyder and his colleagues, Jean-Pierre Mothet and the University of Chicago’s Angele Parent, added a final buttress to the case by showing that the brain’s D-serine really does act on the NMDA receptor. They applied D-amino acid oxidase, an enzyme that degrades D-serine, to rat brain slices and cell cultures. As predicted, the enzyme drastically reduced NMDA receptor transmission.

Still to be determined, however, is exactly what role D-serine plays in the brain. For example, neuroscientists will want to know whether it will totally supplant glycine as glutamate’s coactivator of the NMDA receptor, and if not, how the two share the job. But by uncovering this surprising new neuronal regulator, Snyder’s team has pointed scientists toward original ways of tinkering with and exploring the mind.

—INGRID WICKELGREN

* Cosmic Genesis and Fundamental Physics, Sonoma State University, Rohnert Park, California, 28 to 30 October.