tors in underground laboratories around the world (see *Science*, 21 March 1997, p. 1736). Now, a collaboration working at the Gran Sasso laboratory in Italy's Apennine Mountains has picked up the strongest hint so far of passing WIMPs: a particle count that appears to vary with the seasons, as the Earth's orbit carries it into a galactic wind of WIMPs and then away again. The Gran Sasso result "is in favor of this modulation" with about a 99% level of statistical confidence, said Pierluigi Belli, a University of Rome physicist who is a member of the collaboration, called DAMA (for DArk MAtter).

The claim, which Belli announced here on 16 December at a gathering called—despite the location—the Texas Symposium on Relativistic Astrophysics and Cosmology, faces plenty of skepticism. But if WIMPs are real, they might settle a long-standing problem. The Milky Way and other galaxies spin so quickly that the gravity of their ordinary, luminous matter is not enough to keep them from flying apart. Perhaps 90% of the galaxies' mass has to consist of some unseen matter to add the extra gravitational glue. Theories of how elements were forged in the big bang, however, limit the universe's complement of baryonic matter—the ordinary stuff of which planets, stars, and people are made—to less than is required to make up the deficit.

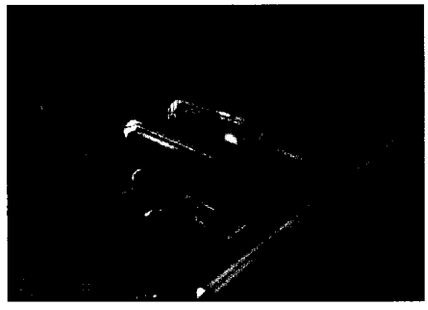
WIMPs have become a favorite candidate for fleshing out galaxies to the required mass, in part because they are natural consequences of some speculative theories of particle physics. In a theory called super-symmetry, which many theorists hope will extend the current picture of particles and forces, each known particle has a still-undiscovered massive partner. A WIMP of about the mass suggested by the DAMA results could be the lightest of these super-symmetric partners, a particle called the neutralino.

Detecting a WIMP is a matter of setting a trap and waiting. DAMA consists of nine 9.7-kilogram crystals of doped sodium iodide—a material that scintillates, or generates a flash of light, when one of its nuclei or electrons recoils after interacting with another particle. Photodetectors gather the light and the results are stored on computers for analysis.

Because of natural radioactivity in the rock and other materials surrounding the detectors, "there is a huge mountain of background signals," said Bernard Sadoulet of the Center for Particle Astrophysics at the University of California, Berkeley. To sort any WIMP signal from this noise, the DAMA researchers looked for a subtle seasonal variation in the scintillation counts. When the galaxy formed from a collapsing cloud of gas, the cloud's stately rotation was amplified, like that of a ballerina drawing in her limbs, so that the visible matter of the galaxy now spins rapidly, carrying the sun around the galactic center at some 220 kilometers per second. But the WIMPs would not have collapsed because they can't radiate photons to shed energy. Like the primordial gas cloud, they should hardly rotate at all. As a result, the sun should encounter the WIMPs as a kind of wind, said Sadoulet. Because Earth's orbital motion adds to the sun's velocity in the summer and subtracts in the winter, the WIMP signal should show a slight annual modulation.

In 1997, the DAMA group presented weak hints of a modulation. And now, based on 180 days of data collected from November 1996 to July 1997, they are more confident in claiming that they have seen "an effect satisfying all the distinctive requirements for a WIMP-induced process," as Rita Bernabei of the University of Rome, the DAMA group leader, puts it.

An unambiguous WIMP detection would delight theorists. But in sharp exchanges after Belli's talk, experimenters took aim at everything from the DAMA group's statistical analysis techniques to the fact that data presented so far cover mainly the rising part of the modulation. "You have not shown us that the signal is going up and down," said Sadoulet, "which would be much more convincing to the community."



Heart of a mountain. The Gran Sasso underground laboratory, which adjoins a highway tunnel.

"Yes, of course," Belli shot back. "This is a work in progress." Bernabei says that the collaboration is analyzing additional data "to verify the reproducibility of the effect—with proper features—over several cycles." Other evidence for the reality of WIMPs could also come from efforts to create supersymmetric particles in an accelerator at CERN, the European laboratory for particle physics in Geneva, and from other dark matter detectors such as those at Sadoulet's laboratory. Said Antonio Masiero, a theorist from the International School of Advanced Studies in Trieste, Italy, "Other WIMP experiments are close, so it is starting to be exciting."

–JAMES GLANZ

NEUROBIOLOGY

Filling in the Blanks of The $GABA_B$ Receptor

Valium and its copycat drugs soothe jangled nerves by augmenting the actions of the brain's own sedative, a neurotransmitter known as γ-aminobutyric acid (GABA). They do this by binding to one of the cell-surface molecules through which GABA exerts its effects, the $GABA_A$ receptor. But neurons have other GABA receptors that could also serve as drug targets for treating disorders ranging from epilepsy to pain. Now, four research teams have discovered a feature of this second class of $GABA_B$ receptors that could open the way to more effective and subtle manipulations of the brain's GABA system.

The groups—one reporting its results in this issue of *Science*—have found that the $GABA_B$ receptor is not a single molecule but instead consists of two different proteins, neither of which is effective on its own. This marriage of two disparate proteins to produce a functional receptor offers greater opportunities for drug design, as researchers can now target each protein separately as well as the receptor as a whole. And it has researchers speculating that the same kind of marriage, called a heterodimer, might also turn up in other members of the receptor class to which $GABA_B$ belongs. These are known as G protein-coupled receptors for the kind of protein that relays their signal into the cell, and they number some 1000 in all.

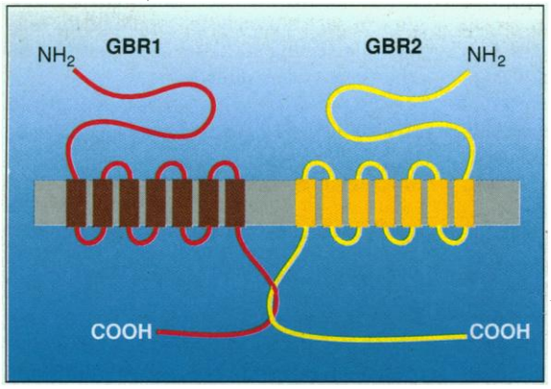
"This is pretty wild," says neurobiologist Roger Nicoll of the University of California, San Francisco. "No one had ever shown that these [G protein-coupled] receptors can form heterodimers." Kenneth Jones at Synaptic Pharmaceutical Corp. in Paramus, New Jersey, whose group reported its findings in *Nature*, says the research "has major implications" both for understanding the workings of this large class of molecules, which also includes receptors for the neurotransmitter serotonin and for opiates, and for developing novel drugs to block or stimulate them.

The discovery solves a mystery that arose early in 1997 when molecular biologist Bernhard Bettler at the drug giant Novartis in Basel, Switzerland, and his colleagues cloned the first gene for a $GABA_B$ component, a protein called GBR1. When inserted into cells, however, GBR1 could not perform a key function of natural $GABA_B$ receptors: opening membrane channels that allow potassium ions to flow out of the cell. Now, Bettler's team and three others have found out why.

Aware that something seemed to be missing from the receptor cloned by the

CREDIT: LABORATORIO NAZIONALE DEL GRAN SASSO

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

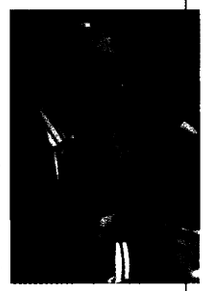
A TIME FOR FORWARD THINKING

"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.

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