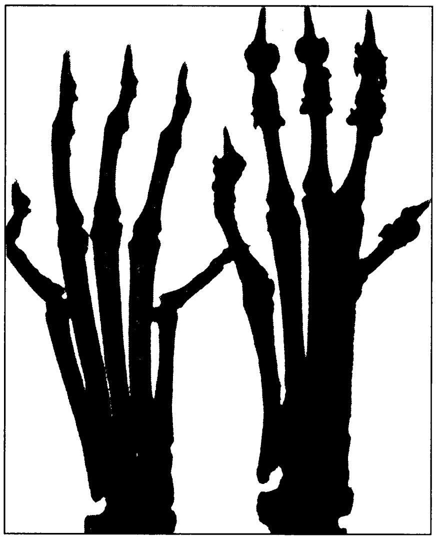


Foot fault. Mineral deposits and bone formation around toe joints of mouse with mutation in the *ank* gene (mutant foot shown on right, normal skeleton on left).

marks, including deposition of calcium phosphate crystals in the joints and degradation of cartilage, the smooth, gel-like cushions at the tips of the bones. "The *ank* mouse immediately attracted a lot of interest from arthritis specialists," says Kingsley. But the genetic defect remained elusive.

Other researchers had linked the *ank* mutation to mouse chromosome 15. To narrow the search further, Kingsley and his colleagues engaged in a brute-force breeding effort, crossing *ank* mice with another strain and then picking those with the *ank* mutation from more than 4000 offspring. They finally homed in on a 150,000–base pair stretch of DNA containing 11 candidate genes—"none of which had any obvious link to arthritis" at first, recalls Kingsley.

When the team compared the sequences of the 11 genes between normal and mutant mice, letter by letter, they found a single typo in one of the genes that led to a protein about 10% shorter than the normal version. The gene is highly conserved among vertebrates—the human counterpart is about 98% identical—but strikingly absent in invertebrates, which lack skeletons and, hence, bones, joints, and arthritis. Further strengthening the case, in mouse embryos the *ank* gene is most active in developing cartilage.

Kingsley's team had no idea what the normal gene does, but an intriguing clue came from Yusuke Nakamura and his colleagues at the University of Tokyo, who had recently identified the genetic defect behind a similar mouse disease—and determined that its protein product normally generates pyrophosphate on the outside of joint cells to keep the joints scale-free. When the Stanford team measured pyrophosphate levels in cultured cells derived from *ank* and normal mice, they found that the chemical accumulated in cells from the *ank* mice but decreased in the culture medium. Kingsley speculates that in its normal form, the ank protein may be "a pyrophosphate channel that allows pyrophosphate levels to remain high in cartilage throughout life" to prevent calcium phosphate crystal formation in the joint cleft. When that protein is defective, however, pyrophosphate is sequestered inside the cells and crystals can build up in the joint fluid, leading to inflammation and joint destruction.

Rheumatologist Michael Doherty of the City Hospital in Nottingham, United Kingdom, notes that the *ank* mouse "most closely resembles familial chondrocalcinosis," a genetic disease that leads to crystal deposition in numerous joints and shows a similarly imbalanced pyrophosphate distribution in the joints. In several afflicted families, moreover, the genetic defect has been mapped to the same chromosomal region that harbors the human *ank* gene. "It's a really hot candidate for [human] chondrocalcinosis," says Matthew Brown, a skeletal geneticist at the University of Oxford.

The role of pyrophosphate in osteoarthritis is unclear, however. Doherty points out that some osteoarthritis sufferers have too much instead of too little pyrophosphate in their knee fluid, suggesting a different disease mechanism. "I'd say the likelihood that this leads to some interventions [for osteoarthritis] in the near future is pretty low," he says. Nonetheless, "David's study is fascinating, because it sheds light on the molecular mechanism of what's happening in the *ank* mouse." —MICHAEL HAGMANN

U.K. FUNDING

New Program Supports Facilities, Stipends

CAMBRIDGE, U.K.—British scientists are celebrating a $1.7 billion windfall, announced last week by the U.K. government, to shore up deteriorating facilities and raise stipends for Ph.D. students. The 2-year spending boost is intended to keep the pool of British science well stocked, both by attracting more talented students into the field and stemming the flow of scientists out of the country. But the benefits are not spread evenly across the research spectrum.

The extra money, to begin in 2002, surpasses the wishes of the scientific community to extend the popular Joint Infrastructure Fund (JIF) beyond next year. Both are bankrolled by the government and The Wellcome Trust charity, but the new Science Research Investment Fund will spend at an annual rate almost double the 3-year, $1.2 billion JIF. The largesse amounts to a roughly 20% increase in the overall science budget, says Peter Cotgreave, director of the Save British Science Society. U.K. Chancellor Gordon Brown said that "the scale of this investment is unprecedented, ensuring world-class facilities for world-class science."

JIF has been doling out competitive grants of at least $1 million to universities for everything from purchasing pricey instruments to building world-class facilities. The latter include a tropical medicine research center at the University of Oxford and a human genetics institute at the University of Newcastle upon Tyne. Success rates have been running at about 20%, and the last call for grants is slated for October. Last week's announcement in essence extends JIF for 2 years (see table).

Government officials said they hope the new fund will ensure that the country's most productive institutions don't lose their edge. A cost-sharing provision aimed at making the money go farther also favors well-endowed universities by making mandatory a practice, begun under JIF, that institutions contribute 25% to a project's overall cost. Major universities such as Oxford and Cambridge "will find it relatively easy to unlock the money," Cotgreave predicts. On the other hand, he says, the country's dozens of former polytechnics are likely to flounder in the hunt for matching funds.

To bolster the quantity and quality of future scientists, the government will also boost annual science and engineering Ph.D. stipends from $10,000 to $14,000 by 2004. That hike, which analysts estimate will cost $80 million, follows a January plea from the U.K. Life Sciences Committee, an umbrella

A WINDFALL FOR BRITISH SCIENCE

Source	Purpose	Amount (in millions $)
Department of Trade and Industry; Higher Education Funding Council	New facilities and equipment; renovations; all fields	1080
Wellcome Trust	New facilities and renovation; limited to biomedical sciences	360
Office of Science and Technology	Modernize research council institutes; national projects	160
Research councils	Higher doctoral stipends	80

CREDITS: (TOP TO BOTTOM) D. KINGSLEY/STANFORD UNIVERSITY; U.K. TREASURY organization for 15 British societies, to stem a perceived brain drain to better paying Ph.D. programs outside the United Kingdom. It should also reduce the average debt of a science major entering graduate school, now roughly $8000, says Peter Campbell, a biochemist at University College London.

The move to beef up infrastructure and raise stipends "will go some way toward attracting and retaining good scientists in the U.K. science base," says Sir Aaron Klug, president of the Royal Society. However, Klug and others admit that it won't address another source of brain drain—U.K. postdocs headed to the United States for positions not available at home. **–RICHARD STONE**

PARTICLE PHYSICS

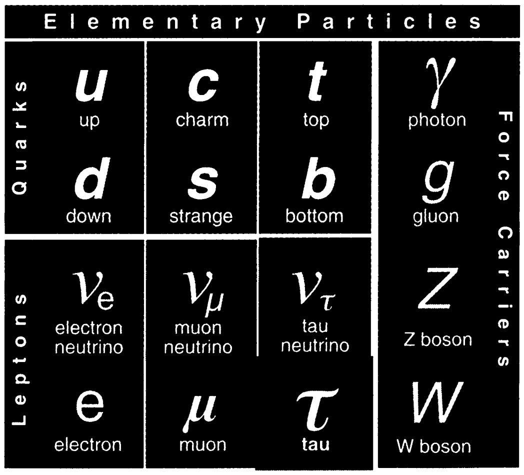
CERN Collider Glimpses Supersymmetry—Maybe

It's a notion worthy of *The X Files*: a shadowy world of doppelgangers, existing in eerie counterpoint to the one we know. Last week, particle physicists at the CERN laboratory in Switzerland announced that they may have caught the first glimpse of that world. By smashing together matter and antimatter in four experiments, they detected an unexpected effect in the sprays of particles that ensued. The anomaly is subtle, and physicists caution that it might still be a statistical fluke. If confirmed, however, it could mark the long-sought discovery of a whole zoo of new particles—and the end of a long-standing model of particle physics.

Other scientists are intrigued by the findings. "Often with an anomalous result, after a few hours' work, you say, 'This can't be right,' but here this is not the case," says Gordon Kane, a physicist at the University of Michigan, Ann Arbor. But they are also skeptical. "After having been bitten 15 times, I'm twice shy," jokes CERN physicist John Ellis. "I think it's probably going to turn out to be some background fluctuation, unfortunately."

The finding threatens the slightly creaky Standard Model of particle physics, which provides a mathematical framework that binds together all of the fundamental particles (quarks, neutrinos, electrons, taus, muons, gluons, and so forth). And it supports a newer, fancier model known as supersymmetry. By linking the particles that make up matter (fermions) with those that carry forces (bosons), supersymmetry unifies all the quantum forces at very high energies. In the process, it also doubles the roster of particles. Each fermion, such as a quark, neutrino, electron, or tau, has a bosonic twin: an s-quark, neutralino, s-electron, or s-tau. Likewise, every boson has a fermionic twin: The photon has the photino, and each gluon has a gluino.

The CERN scientists put the models to the test at the Large Electron-Positron Collider (LEP), a 27-kilometer magnetic ring near Geneva where physicists had long been smashing electrons and antielectrons together, creating showers of subatomic debris. They were particularly interested in showers containing pairs of tau particles. Like electrons, muons, and quarks, tau particles are thought to be fundamental particles—indivisible chunks of matter. The Standard Model allows several different chains of particle interactions, known as channels, by which a colliding electron and antielectron can produce a pair of tau particles. Supersymmetry allows not only all of those channels, but also others that involve the twin particles unknown in the Standard Model. Each theory



Half full? Swiss results hint that each "standard" particle (above) has a shadowy supersymmetric twin.

CREDIT: CERN

also predicts how many tau particles ought to result from collisions at different energies—but the answers aren't always the same.

Those differences were the test. At low energies, the number of tau particles LEP produced matched calculations based on the Standard Model. But in 1998, when engineers at CERN pushed the energies of the collisions above 189 billion electron volts, things began to change. "Over the last couple of years, there has been a slight excess," says CERN physicist Gerardo Ganis. Instead of observing about 170 tau pairs of a certain type, as the Standard Model predicts, physicists have seen 228—a figure consistent with supersymmetry.

Barring some unknown type of systematic error that affects each of the four experiments, each experiment has roughly a 5% probability of seeing the excess because of a chance statistical fluctuation, Ganis says. "But when put together, it's a fraction of a

ScienceScope

Life Count It's a Herculean bookkeeping exercise, but taxonomists the world over are completing the first phase of an international effort to compile an Internet-based directory of all known life-forms. Dubbed Species 2000, the collaborative research project begun in 1996 aims to link existing databases on everything from blue whales to microscopic bacteria. The result would be a boon for basic research as well as biodiversity and conservation efforts.

It's no easy task. "Our virtual catalog has to be created from an array of autonomous databases all around the world, which are on different platforms and quite variable in terms of quality and content," says project coordinator Frank Bisby of the University of Reading, U.K. The software to make the links, however, is now in place, and by the end of the year, taxonomists will connect as many as 20 databases, comprising about 300,000 species. To complete the final catalog encompassing all 106 global databases and nearly a million species, however, researchers will need a hefty cash injection. "It costs well over $100 per species to set up a global database," says Bisby.

Sowing Solutions Genetically modified (GM) crops are critical to feeding the world's booming population, but scientists and industry must find ways to enhance and share their benefits, according to a report issued by seven science academies around the world this week. The backlash in Europe and the United States against GM foods was one impetus for the report, says U.S. National Academy of Sciences president Bruce Alberts. Partly to counter what he calls the "hysteria," his institution worked with the Royal Society of London and the Brazilian, Chinese, Indian, Mexican, and Third World science academies. The resulting report calls for more research on GM crops useful in developing countries, such as nutrient-enchanced foods and salt-tolerant plants.

Perhaps the strongest message concerns patents and technologies that would prevent farmers from saving seeds. The academies urge companies and research institutions to "make arrangements to share GM technology," including "special exemptions" for poor farmers. Says Alberts: "There has to be a solution that would help everybody to come out better."

Contributors: Eliot Marshall, Dennis Normile, Michael Hagmann, Jocelyn Kaiser