of information technology in a variety of fields, from medicine to transportation. At MOST, he built up a loyal following among scientists. "He is a man of action and principle who [has] an easygoing style," says Sun Chenbei, a former MOST staffer who is now China representative for a Canadian consulting company.

Zhu, a polymer chemist, has been named vice chair of the Education, Science, Culture, and Health Committee in the national legislature. **–DING YIMIN**

Ding Yimin writes for *China Features* in Beijing.

BEHAVIORAL GENETICS

## Study Suggests Pitch Perception Is Inherited

Can't carry a tune? Chances are you can lay a lot of the blame for that on your genes, according to a report on page 1969. By studying twins' ability to perceive sour notes in familiar tunes, a U.S.–British team has concluded that the perception of relative pitch is highly heritable and is dependent on higher brain functions. And that, say geneticist Dennis Drayna of the National Institute on Deafness and Other Communication Disorders and colleagues, means that pitch perception may offer a window into brain processes that are also used in language.

The researchers administered a test, called the Distorted Tunes Test (DTT), to 284 pairs of female twins, about half of them identical and ranging in age from 18 to 74, from the St. Thomas' U.K. Adult Twin Registry. The DTT plays short snatches of 26 familiar melodies, from "Turkey in the Straw" to "Silent Night," most of them with one or more notes altered. Subjects indicate whether the tune sounds right. The distortions in the DTT are all obvious, with no pitch altered by less than a halftone. Some tunes are drastically altered (see sample from "America the Beautiful"). So anyone who gets more than three wrong is judged to be somewhat tune-deaf.

Because the identical twins' responses correlated far better than those of the fraternal twins—0.67 versus 0.44—Drayna's team believes that the trait is strongly influenced by genes. Indeed, the team estimated the heritability for tune deafness at 0.80. That's about as high as it ever gets for genetically complex traits, rivaling features such as height. "These results demonstrate for the first time the powerful influence of genes on the ability of humans to recognize correct pitch and melodies," says co-author Tim Spector, who heads the twin research unit at St. Thomas' Hospital in London.

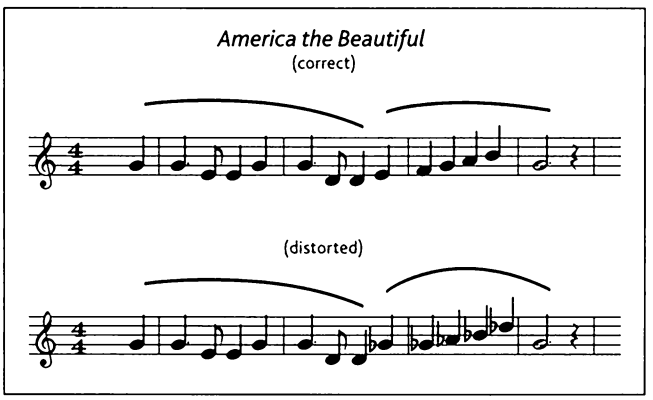
Brain researchers are fascinated by pitch perception, because it taps into cognitive functions, Drayna says. A person can do well on an audiological test and still flunk the DTT—and vice versa—showing that the "musical pitch perception is largely independent of peripheral hearing," the researchers conclude. And although absolute pitch (the ability to recognize an isolated note) is to some degree trainable, scores on tests of relative pitch perception "don't change appreciably over an individual's lifetime," says Drayna—a finding suggesting that, as with language, there's hard wiring involved.

Evan Balaban of The Neurosciences Institute in San Diego agrees that the study is an "important" one that "is looking at something very likely to be a central [brain] function." The study clearly demonstrates a biological basis for pitch discrimination, Balaban says. But he's reluctant to buy the heritability estimate, in part because twins are somewhat more prone than nontwins to developmental disabilities. As evidence, he points out that almost 40% of the twins showed some evidence of deficits in pitch recognition compared with 27% in the control population. The authors argue that their twins are no different from the general population, in which 5% have severe deficits in pitch recognition. They say cultural unfamiliarity with some of the tunes might have lowered the scores a bit.

Scientists hope the study of pitch will provide a lever for studying communication disorders. "The pitch contour of the voice communicates a lot of information about emotions, [so] to tell the difference between different pitch contours would use some of the same abilities" as are used in talking, notes Balaban. Severe defects in pitch perception therefore "could be a subtle indicator" of imperfections in wiring in language-related cortical areas. Drayna agrees, citing as "tantalizing evidence" anecdotal reports of severe tune deafness in people with certain speech and language disorders, such as a problem with processing spoken words known as "cluttering."

Other researchers are also in hot pursuit of brain clues offered by pitch perception. In a paper published in the January issue of *Developmental Psychology*, psychologist Jenny R. Saffran of the University of Wisconsin, Madison, reported that 8-month-old infants, "like many songbirds," may come equipped with absolute pitch—further evidence of the importance of pitch recognition for language learning, she says. Saffran speculates that this knack, which is rare in adults but can be enhanced by early training, is superseded by relative pitch perception as the brain develops. And that talent, which is both more useful and more cerebrally sophisticated, now appears to be primarily determined by the genes.

**–CONSTANCE HOLDEN**




**Tin ears.** About 5% of the population wouldn't have a clue which is the right version.

AIDS VACCINES

## Long-Lasting Immunity Conferred in Monkeys

Faced with the lack of a critical reagent, Harriet Robinson of Emory University in Atlanta was forced to redesign an AIDS vaccine experiment. From that minor setback has emerged an impressive finding about the lasting power of her vaccine approach.

In a paper published online today by *Science* (www.sciencexpress.org), Robinson, Emory colleague Rama Rao Amara, the paper's first author, and others describe a two-step AIDS vaccine strategy they developed in collaboration with Bernard Moss of the National Institute of Allergy and Infectious Diseases (NIAID). In a large monkey experiment, this vaccine appears to have stimulated long-lasting immunity. "It's among the most exciting concepts that we've seen in this [monkey] model," says Peggy Johnston, head of NIAID's AIDS vaccine program.

Robinson, Amara, Moss, and co-workers built their experiment around a laboratory-made, hybrid virus called SHIV, which is part HIV and part SIV, a simian AIDS virus. They first injected 24 monkeys with a vaccine that contained several SHIV genes stitched into a circular piece of bacterial DNA. Following vaccination with this relatively easy-to-make "naked DNA," the researchers gave the animals a booster shot consisting of a variety pack of SHIV genes carried by recombinant modified vaccinia Ankara (MVA), a version of the virus used as the smallpox vaccine. Rather than raising antibodies that can derail the AIDS virus before it causes an infection, both the naked DNA and MVA vaccines primarily stimulate the immune system to target and eliminate already infected cells.

Robinson and colleagues planned to test this approach by "challenging" the vaccinated monkeys with an inoculum of SHIV placed in the animals' rectums. This is a more real-world test than injecting the virus under the skin or into a muscle. To do the experiment, the researchers needed a "challenge stock," a batch of SHIV that had been tested on monkeys to determine the minimum amount of virus needed to establish an infection rectally. After she had started vaccinating monkeys, Robinson realized that she would have to make the challenge stock herself, which took three tries.

By the time they challenged the 24 vaccinated monkeys, 7 months had elapsed since the animals had received a booster shot. "Originally we had planned to challenge at 3 months," laughs Robinson. The vaccinated animals became infected with the SHIV, but 20 weeks later, 23 of 24 monkeys had controlled the infection and had suffered no immune damage, the researchers report. All four of the unvaccinated control animals, in contrast, had consistently high levels of SHIV in their blood, and their immune systems steadily declined; all the control monkeys subsequently died from AIDS. "This is the closest thing to a real-life challenge that we've seen yet," says James Bradac, who heads the NIAID division that oversees monkey trials of AIDS vaccines.

An HIV version of this DNA/MVA vaccine—which has no company behind it but is being manufactured under contract—is slated to begin human trials in the United States by early next year. **–JON COHEN**

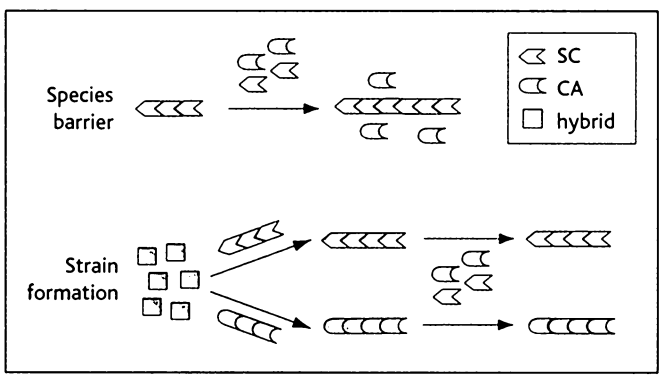
PRION RESEARCH

## Getting Yeast Prions to Bridge the Species Gap

The sheep disease scrapie has been around for centuries without infecting humans. But the strikingly similar "mad cow disease," a progressive and ultimately fatal neurodegenerative condition, has apparently slipped from infected cattle into the human population. Both scrapie and mad cow disease are almost certainly transmitted by an abnormally folded form of a protein, known as a prion. That has left researchers with the problem of trying to figure out what determines whether a particular prion disease can spread from one species to another. New results with yeast prions may now provide a clue.

Although yeast prions are not infective, their behavior resembles that of mammalian prions in some ways. Both form when a normal prion protein adopts an abnormal shape or conformation. This abnormally folded protein can then induce the same shape change in other normal copies of the same protein, causing them all to clump together in insoluble aggregates. In the case of mammalian prions, these may damage the brain, while the aggregated yeast prion proteins lose their normal activity.

Ordinarily, a yeast prion from one species of yeast cannot induce the shape change in the corresponding prion protein from another species. But work reported in the 8 March issue of *Nature* by Jonathan Weissman and Peter Chien of the University of California, San Francisco, indicates that this species barrier can be overcome if the prion protein can adopt multiple structures and can thus interact with prion proteins from more than one species. If something similar happens with the prion that causes mad cow disease, it might explain how it is able to cause disease in humans as well as cattle.




**A promiscuous prion.** *S. cerevisiae* (SC) and *C. albicans* (CA) prions won't mix (top), but both will coax a hybrid protein into prion fibers that remember the shape of the protein that seeded them (bottom).

Weissman and Chien performed their experiments on the yeast prion protein Sup35. Previous work had shown that the Sup35 proteins from the yeast species *Saccharomyces cerevisiae* and *Candida albicans* can't induce one another to change shape and form insoluble prion aggregates. To figure out the structural basis for this species barrier, the researchers replaced the normal *SUP35* gene of *S. cerevisiae* with a three-part hybrid gene consisting of the DNAs encoding 40 amino acids from the *Saccharomyces* protein, 100 amino acids from the *Candida* protein, and the portion of Sup35 responsible for its normal biological function, which is turning off protein synthesis at certain sequences. They also added to these cells a separate piece of DNA encoding the prion-forming part of either the *Candida* Sup35 or of the *Saccharomyces* Sup35. The researchers wanted to see if either of the proteins made by these DNAs could push the hybrid protein into a prion state.

The *Candida* protein and the *Saccharomyces* protein turned out to be equally effective in switching the hybrid protein into the prion form in cells. But the phenotype of those cells, a result of the biologically active domain of the hybrid being turned off, was more severe in the cells induced with the *Candida* protein.

To determine whether these differences, reminiscent of prion strains previously seen in both yeast and rodent models, were due to different conformations of the hybrid prion, Weissman and Chien turned to the test tube, where prion proteins form long, organized fibers. Consistent with their results in yeast cells, the researchers found that fragments of prion fibers, made up of either the *Saccharomyces* protein or the *Candida* protein, could accelerate the hybrid protein's incorporation into prion fibers.

The real surprise came when the researchers let these test tube polymerization reactions run until essentially no remnants of the original *Saccharomyces* or *Candida* fibers remained. Chimeric fibers that had been seeded by *Saccharomyces* fibers would in turn trigger prion formation only by the *Saccharomyces* protein. Likewise, chimeric fibers seeded by the *Candida* protein would seed soluble *Candida* protein but not soluble *Saccharomyces* protein. The chimeric fibers, apparently, could "remember" the shape of the protein that had originally seeded them even though that protein was gone.

How the hybrid protein is able to structurally adapt to prions from both species is unclear. "We have to start looking at this experimentally," Weissman says. He hopes to get structural information about the chimeric fibers by examining them using atomic force microscopy or cryo-electron microscopy.

Researchers are already intrigued, however, by what the results suggest about the source of the species barrier. "It's not just the differences in amino acid sequences, but also the differences in conformation that the prion takes" that may establish that barrier, says yeast prion researcher Susan Liebman of the University of Illinois, Chicago.

The big question now is whether something similar can explain why the mad cow disease prion, but not the one that causes scrapie, can cause disease in humans. "Yeast is a simple way to carve out one step, and that's conversion of normal protein into another, oligomeric [prion] form," says physical biochemist Peter Lansbury of Harvard Medical School in Boston. "Beyond that, people really need to think about the huge differences [between yeast and mammalian prions]." **–R. JOHN DAVENPORT**

ILLUSTRATION: ADAPTED FROM CHIEN *ET AL.*, *NATURE* 410 (8 MARCH 2001)