NEUROSCIENCE

A Mitochondrial Alzheimer's Gene?

Researchers have known for years that energy metabolism is abnormally low in the brains of patients with Alzheimer's disease (AD). Now, a team led by Robert Davis, at the San Diego biotech company MitoKor, and neurologist W. Davis Parker, of the University of Virginia School of Medicine in Charlottesville, offers a possible genetic explanation: Most AD patients seem to have inherited high levels of a mutant form of cytochrome oxidase (CO), a mitochondrial enzyme that is a key part of the cell's energy-producing machinery.

The finding, which is reported in the 29 April issue of the *Proceedings of the National Academy of Sciences*, could lead to a diagnostic test for the disease. Beyond that, it supports earlier suspicions that poor energy metabolism may contribute to the neurodegeneration that occurs in AD. Indeed, Alzheimer's researcher Bruce Yankner of Harvard Medical School calls the result "by far the strongest evidence" yet that a CO defect is involved in triggering the disease.

The current work is an outgrowth of Parker's 1990 discovery that CO activity is low in the blood platelets of AD patients. Subsequent studies also found low CO activity in Alzheimer's brains. The enzyme is there, but it doesn't work correctly, which suggests that it might be mutated, says Parker.

Three of the 13 proteins that make up the CO molecule are encoded not in the nucleus, but in the mitochondrial DNA. The team looked at those genes, as studies have shown that children of mothers with AD are more likely to get the disease than are children of affected fathers. That suggests a mitochondrial gene could be causing a predisposition to AD, as virtually all of the thousands of mitochondrial genomes we inherit come from our mothers.

The team found a relatively common variant of the mitochondrial genome in which two of the CO genes are consistently mutated. The variant turned up both in AD patients and normal controls, but it made up a higher percentage of the mitochondrial genomes in the patients: In 60% of the 506 AD patients examined, more than 20% of their mitochondrial genomes had the mutant form, while only 20% of the 95 controls (normal subjects and people with other neurological diseases) had mutation levels that high. One-fifth of the AD patients had mutation levels of 32% or more, higher than any controls. MitoKor is creating a diagnostic test based on the mutation assay.

The team showed that these CO gene mutations have physiological effects by transferring mitochondria from AD patients into cultured cells that lack mitochondrial DNA. The resulting cells had impaired energy production, reflected by their high production of oxygen free radicals, the damaging molecules produced when energy-generating processes don't run to completion.

The findings could provide several links with other areas of AD research. Free radicals, which damage cell membranes, have been implicated in the destruction of neurons in Alzheimer's. And 4 years ago Yankner and his colleague Dana Gabuzda linked CO activity to another possible cause of AD: They poisoned CO in cultured cells and found an increase in a direct precursor of β amyloid, the protein that forms the core of the senile plaques found in the brains of AD patients.

The new work falls short of proving that CO mutations help cause AD, but the idea deserves to be explored, says Yankner: "It is not an area that has attracted a great deal of attention in Alzheimer's research, but it might now."

–Marcia Barinaga

EVOLUTIONARY BIOLOGY

Catching Lizards in the Act of Adapting

When evolutionary biologists transplanted small populations of *Anolis sagrei* lizards from Staniel Cay in the Bahamas to several nearby islands 20 years ago, they thought that the reptiles would go extinct. Indeed, that was the outcome the researchers planned to study. But instead of expiring, the small brown lizards, like Oklahoma land-rush settlers, flourished—even though their new homes differed dramatically from their original island. And the "extinction" study turned into a demonstration of evolution in action.

In the current issue of *Nature*, Jonathan Losos of Washington University in St. Louis and his colleagues report that the transplanted lizards appear to be in the first stages of an adaptive radiation, undergoing the kind of body changes needed to inhabit a new environment. Such changes could in time turn each island's population into a separate species—the same process that led to the great diversity of finches that Darwin spotted on the Galápagos Islands, and to the galaxy of *Anolis* lizards themselves (150 species in the Caribbean alone). In particular, the researchers saw the lizards' hindlimbs grow shorter, an apparent adaptation to the bushy vegetation that dominates their new islands.

The change was rapid, but others have also demonstrated the speed with which organisms can adapt in the wild (*Science*, 28 March, pp. 1880 and 1934). More important, by drawing on previous studies of anole adaptations, the Losos team was able to predict precisely how the lizards' bodies would change in response to their new homes. The leg-length change they observed might not be genetic, some researchers note; it could be environmental—the equivalent of a bodybuilder's muscles. But if it is rooted in the genes, then the study is strong evidence that isolated populations diverge by natural selection, not genetic drift, as some theorists have argued. "It's the first attempt to make a prediction about how the theory of evolution will work—and then show that it does happen as predicted," says University of California, San Diego, evolutionary biologist Trevor Price.

PATTI MURRAY/ANIMALS, ANIMALS

Reptile moves. New home leads to shorter legs in *Anolis* lizards.

Once Losos and his colleagues realized that their transplanted lizards were surviving instead of becoming extinct, they decided to study how they were adapting. They focused on how the habitat change affected the length of the animals' hindlegs because Losos had previously demonstrated that the trait correlates with the lizards' preferred perch. For instance, species living on tree trunks have longer legs than do those living on twigs, apparently because they can trade the agility that comes with shorter legs—crucial on bushy vegetation—for the increase in speed that longer limbs provide. Because Staniel Cay, the home of the founding population, is covered with scrubby-to-tall forest, the anoles there are long-legged.

But the 14 lizard-free islands that the researchers seeded with the Staniel Cay pioneers have only a few trees; most of their vegetation is bushy and narrow-leafed. "From the kind of vegetation on the new islands, we predicted that the lizards would develop shorter hindlimbs," says Losos. And although they are not as ground hugging as a Chevy low-rider, statistical analysis shows that, after 10 to 14 years on the new islands, these anoles do indeed grow shorter rear legs than do their ancestors.

For this change to be the first step toward the formation of new species, though, the change in limb length would have to be a genetic trait that would be passed on to the animals' progeny. But some researchers doubt that such rapid morphological change, coming in a few generations, could have a genetic basis. "They have seen a lot of evolution in a very short time," notes evolutionary biologist David Wake of the University of California, Berkeley. Losos concedes that there is as yet no evidence that the shorter hindlimb length is strongly heritable. Without that, he notes, he can't exclude the possibility that the lizards' legs develop differently on the bushy vegetation than on trees because the different vegetation types exert different stresses on the leg bones.

This kind of "developmental plasticity" would depend only on the type of environment and might not be transmitted to the offspring. "They don't have the evidentiary data to support either hypothesis," says Wake. Indeed, he even questions whether the Losos team has in fact demonstrated that the legs get shorter. He points out that the researchers did not take leg measurements from the founding populations on the new islands—not realizing that they were going to thrive. Instead, they measured lizards living today on Staniel Cay and used their legs to compare to these transplanted populations.

To help resolve these issues, Losos is now raising anoles in a variety of laboratory environments to see if the lizards consistently change morphologically from the stresses of living on different surfaces. If they do, this would favor the developmental plasticity idea.

He's also trying to take his natural radiation experiment one step further by introducing two closely related species of lizards on lizard-free islands. "That's the next step," he says. "If they compete and alter their habitat use in the presence of this other species, will that lead to a [further] morphological change?" It's that kind of competition, between populations that had started to diverge and were then reunited, that researchers say led to the rich diversity of Galápagos finches.

But whether the lizards continue to evolve depends largely on the winds of fate, says Losos. These islets are periodically swept by hurricanes that could whisk away every trace of anolian evolution—the outcome he originally pictured for them.

–Virginia Morell

BIODIVERSITY

Dams Drain the Life Out of Riverbanks

A team of researchers studying biodiversity on riverbanks in central and northern Sweden has some bad news for managers of water resources: Plant communities along the banks of rivers dammed for hydroelectric power contain significantly fewer species than those alongside neighboring free-flowing rivers. These findings, reported on page 798, are likely to fuel debates in Sweden and elsewhere on licenses for new dams and other water-regulation schemes. "The results of this study are likely to be applicable to regulated rivers in many other regions," says ecologist Stuart Pimm at the University of Tennessee, Knoxville.

Riverbanks provide a variety of environments for plant life. The inflow of nutrients and sediments; changing water levels over the seasons, which can create specialist niches; and waterborne dispersal of seeds all contribute to a rich diversity of species. It has long been known that the construction of dams and changing water levels can have a disastrous impact on original bank communities, but there is considerable debate among ecologists about how well plant populations recover and reestablish themselves alongside new, regulated water courses. "There have been many studies on the physical changes in regulated water courses and how plants adapt to these changes, but no one until now has looked systematically at the effects of regulation on plant biodiversity," says river ecologist Jack Stanford at the University of Montana's Flathead Lake Biological Station in Polson.

Ecologist Christer Nilsson and colleagues Roland Jansson and Ursula Zinko of the University of Umeå in Sweden set out to answer this question by studying the vegetation at almost 90 sites alongside hydroelectric power "schemes"—each of which can incorporate a number of dams and reservoirs. Some dams in the region date back to the 1920s, and "the regulation patterns of these systems have not changed since the schemes were first built," says Nilsson. The team also studied several undisturbed rivers in the same region as controls—something that is becoming difficult in many other areas of the world.

The team compared both the simple number of species and an index of "species richness," which compensates for differences of riverside areas. Half the samples were at main storage reservoirs, where water levels can vary substantially, and half were alongside smaller dammed reservoirs, or "impoundments," downriver, which directly feed the turbines and show much less variation in water level.

The team found about one-third fewer species around storage reservoirs than at comparable undisturbed sites; the index of species richness was only about one half for these sites. At impoundment sites, the richness index was comparable with that at control sites, but 15% fewer species were crammed into the much narrower band of habitat than in natural rivers.

By studying the vegetation alongside regulation schemes built between 1 and 70 years ago, the team also found that the number of species growing along the water's edge appears to increase slowly after the construction of a dam. They found that the number appeared to increase for an average of 34 years alongside storage reservoirs, and for 13 to 18 years alongside impoundments. Once plant communities reach these ages, however, their development

CHRISTER NILSSON/UMEÅ UNIVERSITY

Draining away. Plant life never fully recovers on the banks of dammed reservoirs.

appears to halt. "No further increase in species numbers has occurred, and the community looks permanently different," says Nilsson. "And evidence from the oldest dam schemes suggests that these communities are now declining in species number."

Some ecologists suggest that this impoverishment in riverside plant life might have a significant impact on the aquatic ecosystems. "We're just beginning to get some glimmers of the effects on biodiversity of changes in these habitats," says Pimm. "These changes are likely to lead to higher local extinction rates for some species."

The Swedish results are likely to fuel current debate on the relicensing of schemes to regulate water. "Many Swedish hydroelectric schemes were built about 30 years ago and must now undergo assessment for relicensing under Swedish requirements," says Nilsson. Concerns about their environmental impact have already led to proposals for a 5% increase in flow through the schemes. But, Nilsson says, "Our results suggest that for the same reduction in generating capacity, it would make more sense to close down one in 20 schemes and restore their original river courses." Stanford agrees: "It's becoming increasingly clear that we have to restore some of the natural attributes of river systems."

–Nigel Williams