Do Brain Cells Run Out of Gas?

Within each cell reside hundreds of tiny gas stations known as mitochondria. These essential organelles generate a large share of the fuel, a molecule called ATP, that cells use to power their biological machinery.

There's a suspicion, admittedly controversial, that problems with these energy-supplying mitochondria contribute to the progression of age-related neurodegenerative illnesses such as Alzheimer's, Parkinson's, and Huntington's diseases, says Douglas C. Wallace of Emory University School of Medicine in Atlanta. Wallace discussed the latest research linking mitochondria to these debilitating brain disorders at last week's Short Course on Mammalian Genetics at Jackson Laboratory in Bar Harbor, Maine.

In 1993, Wallace and his colleagues reported on comparisons of the mitochondrial DNA of Alzheimer's patients and that of people without Alzheimer's, who served as controls. This genetic material, which contains all the instructions necessary for mitochondria to function and replicate, is independent of the DNA found in a cell's nucleus.

Wallace's group discovered that a particular mutation in mitochondrial DNA showed up in more than 5 percent of Alzheimer's patients but in less than 1 percent of a random group of people without the disease. An independent research team, in a study that carefully matches the age of Alzheimer's patients with that of controls, now strengthens the finding, says Wallace.

That support comes in the July 18 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, where Gino Cortopassi and Timothy Hutchin of the University of Southern California in Los Angeles report that 8.3 percent of the Alzheimer's patients they studied had the mitochondrial DNA mutation that Wallace investigated, while only 0.34 percent of age-matched controls did.

In other recent work, Wallace and his colleagues documented how often a specific portion of mitochondrial DNA was missing in various regions of the brain. The brains of Alzheimer's and Huntington's patients had strikingly different patterns of this mutation than did those of controls, says M. Flint Beal of Massachusetts General Hospital in Boston.

Overall, this collection of mitochondrial data suggests to Beal, Wallace, and a few others that mitochondrial defects may predispose people to neurodegenerative diseases late in life.

One possible explanation, says Wallace, centers on the idea that every tissue requires a minimum amount of energy to function, the brain being the most energy-demanding tissue of all. As people age, mitochondrial energy production naturally declines, the result of accumulated DNA mutations within mitochondria. Normally, production starts out so high that this decline rarely pushes cellular energy levels below the brain's threshold during a normal life span. But a person who starts life "low on gas," perhaps because of an inherited mitochondrial DNA mutation or other genetic flaw that alters the cell's energy balance, may cross that threshold at a younger age. Brain cells starved of energy would then die, says Wallace.

Another possibility, put forth by Cortopassi and Hutchin, is that mitochondrial defects produce abnormal buildups of free radicals, highly reactive molecules that may be toxic to cells. When mitochondria create ATP, they generate a small number of free radicals. Defects in the organelles could increase free radical production and gradually create dangerous amounts of the molecules.

Studies on animals support the importance of mitochondria in brain disorders. When investigators destroy mitochondria or inhibit the activity of enzymes crucial to mitochondrial function in rats or mice, the rodents develop behavioral or physical attributes of Alzheimer's, Huntington's, and Parkinson's diseases. "I think the evidence that mitochondria play a role in neurodegenerative disease is stronger than ever," says W. Davis Parker Jr. of the University of Virginia School of Medicine in Charlottesville.

Other investigators find the evidence less conclusive.

"It's far from clear what's going on with mitochondria," say Alison Goate of Washington University School of Medicine in St. Louis. For example, she told SCIENCE NEWS, a study she just led, similar in design to that of Cortopassi and Hutchin, found no disparity in the number of controls and Alzheimer's patients with the mutation Wallace and his colleagues studied.

And when the USC duo extended their analysis to another group of brains, they didn't find as large a distinction between the control and Alzheimer's groups, admits Cortopassi. To resolve the issue, he says, "it's going to be important to follow this up in other human populations."

— J. Travis

Plants recruit oil-detoxifying microbes

The 1991 Gulf War brought oily devastation to much of the Persian Gulf region (SN: 11/16/91, p.316). But testifying to this environment's resiliency, signs of a natural recovery are emerging—even around the perimeter of former oil lakes created by war-ravaged pipelines and wells. From this defiled desert landscape, wildflowers reemerged unexpectedly last year.

Biologists analyzing the spring-blooming plants' tentative comeback now believe they may have unearthed—literally—the roots of a natural, low-tech, and relatively low-cost strategy for cleansing oiled soil: plant cultivation.

"These plants should not have grown at all, because oil contains aromatic compounds, which are toxic," observes Samir Radwan, who led the probe. But when he and his colleagues at the University of Kuwait in Safat dug into the crude-soaked desert, they found the wildflowers' roots not only healthy but free of oil (see photo).

The only logical explanation, Radwan says, was that the roots recruited ubiquitous oil-degrading microbes to clean up. So his team cultured bacteria and fungi residing in the oily sand. And in the July 27 NATURE, they report that the root zone was indeed a rich reservoir of well-known oil-eating microbes.

Radwan *et al.*/NATURE

Flower removed from the edge of a former oil lake in Kuwait's desert. While shoot wears a black, oily collar, soil microbes kept the roots free of oil.

Immediately adjacent to the roots, one family of bacteria (*Arthrobacter*) accounted for fully 95 percent of the resident microbes. "But go out just 1 centimeter from the root and you find a completely different microflora [community of fungi and bacteria]," Radwan observes. These organisms, too, degraded oil, the microbiologist reports.

The annuals that his team studied in the desert belong to the same family as sunflowers (*Compositae*). To find out what other plants might survive, the Safat team tainted the sand in greenhouse pots to match the petroleum concentrations in which the wildflowers had been growing—10 percent crude oil by weight. Most of the corn, barley, wheat, termis (a legume), and tomatoes planted in this oiled sand not only germinated but grew into healthy-looking plants, albeit 25 to 40 percent smaller than those raised in clean sand. Naturally occurring microbes also kept roots growing in the tainted sand free of oil.

Oil alone entices many petroleum-noshing bugs to immigrate to polluted areas. However, the rich nutrients exuded by plant roots—such as sugars, amino acids, oxygen, and vitamins—make that environment even more welcoming, Radwan observes. For this reason, his team recommends "densely cultivating suitable plants in polluted Kuwaiti desert areas as a promising approach for their bioremediation."

In fact, this "solar-powered system may find very wide application in many different parts of the world and with many different contaminants," argues toxicologist Barbara T. Walton of Oak Ridge (Tenn.) National Laboratory.

Other groups, her own included, have reported evidence that root-zone microbes have the potential to degrade a number of noxious contaminants, from organic solvents and TNT to persistent pesticides. Critics, however, have questioned the prospects for such "phytoremediation" under the extreme conditions that can plague polluted sites. Now, Walton says, Radwan's team "offers in-your-face evidence that this [phytoremediation] can clean up a contaminant of widespread concern—oil—under extreme conditions."

What's more, phytoremediation could cost far less than conventional cleanup technologies, notes Burt Ensley of Phytotech in Monmouth Junction, N.J.

Because soil-cleaning plants may absorb some of the toxic materials around them, Walton believes that the trick will be to identify plants for cultivation that won't tempt growers or wildlife to dine on them. *—J. Raloff*

Circuitry simulates genetic networks

Thinking of organisms as chemical machines has become commonplace among biologists. But following through on that metaphor by mapping out all the molecular mechanisms, feedback loops, and signaling pathways of even one microorganism has proved to be an extraordinarily difficult task.

So many mechanisms signal each other at once that researchers liken a cell's information-processing network to a telephone system.

For Harley H. McAdams, a physicist formerly with Bell Laboratories in Murray Hill, N.J., and Lucy Shapiro, a molecular biologist at Stanford University School of Medicine, that comparison turned out to be more than just an analogy. Together, they have devised a circuit diagram to describe the major signaling pathways of a common bacteriophage.

Those signaling pathways, they explain in the Aug. 4 SCIENCE, depend on clusters of genes that operate in concert to yield fully functional biological mechanisms. Such genetic networks, comprising several hundred genes, "are difficult to analyze with currently available techniques," they state.

Capitalizing on the parallel functions of genetic "circuits" and electric circuits, they have adopted a "hybrid modeling approach" that integrates biochemistry into ordinary circuit diagrams. In this way, they can account for the choice of replicative strategies the bacteriophage lambda makes after infecting *Escherichia coli*.

"In some sense, this is the next step for the genome project," says Shapiro. "Scientists are sequencing lots of genes, then trying to figure out how they relate to each other in a given cell.

"But unless we can analyze logically how these genes work together, we'll never understand how organisms work," she adds. "This method provides a systematic way of thinking about complex networks of genes."

McAdams admits that a great disparity exists in time scales between genetic switching circuits and electric switching circuits, but he observes that the two have much in common.

In electric circuits, the flow of electrons defines connection pathways. Similarly, chemical signals carried by proteins constitute a pathway. Moreover, because many biochemical paths flow at the same time, microorganisms, despite their tiny volumes, are cabable of processing a tremendous amount of information.

This feature permits enormous amounts of "genetic computation within any living organism," McAdams and Shapiro state.

"This model is a beautiful piece of work," says William F. Loomis, a biologist at the University of California, San Diego, who wrote a commentary accompanying the report, "because it works. The output fits the measured data," he adds. "All of the parameters are reasonable. It's robust. That constitutes a tremendous success."

By describing one genetic network, Loomis points out, McAdams and Shapiro have effectively challenged others to describe similar networks "controlling such things as cancer, growth, or aging.

"In biology, a single gene rarely works alone," he continues. "Genes work in networks. So genetic networks are the real unit of evolutionary selection."

"This is a new viewpoint that I think will greatly impact how we look at genetic data," Loomis concludes. "I think that's pretty important." *—R. Lipkin*

Faulty seals delay shuttle

It wasn't just a routine delay that prevented the space shuttle Endeavour from taking off as planned on Aug. 5. NASA announced late last month that it has postponed the flight until at least mid-August, while the agency struggles with a problem it discovered in rocket boosters after the last two shuttles returned to Earth. Tiny leaks from burning fuel had slightly scorched O-ring seals between metal joints at the nozzle of the boosters, which are reused on other flights.

NASA scientists emphasize that the leaks differ in several ways from those that led to the fatal explosion of the Challenger shuttle in 1986. The redesigned O-rings seal a different joint in the booster. And in contrast to the rings used in 1986, which failed to maintain a good seal after being subjected to freezing temperatures on the launch pad, neither the current rings nor the surrounding joints appear to have a design flaw.

Instead, engineers believe that the scorch marks, which resemble pinpricks no more than a few thousandths of an inch deep, stem from the way technicians apply a rubberlike compound that serves as one of several thermal barriers between the hot gas and the O-rings. Tiny holes somehow created in the compound appear to channel the fuel to the O-rings. In 11 previous instances, investigators had found such channels, but they had not found burn marks in those cases.

At a press briefing at NASA's Johnson Space Center in Houston last week, NASA shuttle operations director Brewster Shaw said he was hopeful that engineers could correct the problem in a few weeks, perhaps at the launch pad. Further delays could postpone an October linkup between the Atlantis shuttle and Mir, the Russian space station (SN: 5/20/95, p.312). *—R. Cowen*