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.