Molecules that guide or nourish nerves

In every developing organism, nerve cells must thread their way through a jumble of other cells to particular targets, be they muscles, sense organs, or other nerve cells. Two reports now shed light on molecules that may guide or promote the survival of these connections.

In one experiment, geneticists determined that a particular docking site for nerve growth factors plays a role in the success of some nerve cell connections. In the other experiment, neurobiologists learned that nerve cells grow toward a chemical messenger called acetylcholine.

As a nerve cell develops, it sprouts axons and dendrites, appendages that eventually link it with other nerve cells. A specialized nerve growth cone makes up each appendage's leading edge. There, cellular fingers continually extend and retract, explains James Q. Zheng of Columbia University. Like insect antennae, these fingers sense the chemicals around them, some of which may define a pathway for the nerve.

Zheng and his colleagues used a very fine needle to squirt acetylcholine into one side of a dish containing a sprouting nerve cell taken from a frog. As the acetylcholine diffused away from the needle's tip, it created a concentration gradient that was strongest near the tip.

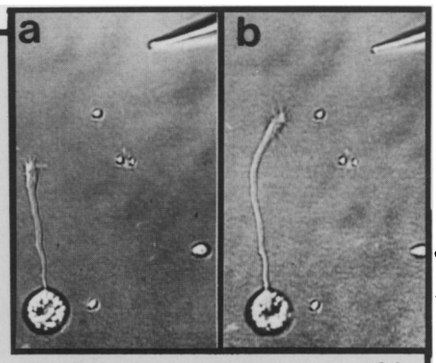
Two hours later, the nerve cell's axon had turned and grown about 25 micrometers toward the tip, Zheng and his colleagues report in the March 10 NATURE.

The researchers suspected that calcium was involved somehow. They observed that in a calciumfree solution the axons grew but did not turn. The same thing happened when they blocked acetylcholine's access to its docking sites, Zheng says. The arrival of acetylcholine seems to lead to a rapid influx of calcium into the cell, the appearance of many cellular fingers on the side of the growth cone facing the needle, and, finally, turning.

The researchers have yet to demonstrate that such gradients actually exist, however.

The experiments by Kuo-Fen Lee and Rudolf Jaenisch of the Whitehead Institute for Biomedical Research in Cambridge, Mass., and their colleagues involve genetically engineered mice. As these mutant animals develop, the researchers study why some nerve connections survive and others do not.

Mice that lack a particular docking site, the p75 receptor, fail to retain certain nerve connections from the brain to the pineal glands and the sweat glands in the lateral foot pads, they report in the March 11 SCIENCE.



Zheng et al./NATURE

After 2 hours, a nerve growth cone (a) turns and grows toward the source of acetylcholine (b).

Normally, p75 exists on nerves and on other types of cells along the path between the brain and the target glands. This receptor may help nerve cells make better use of the limited amount of growth factors available. Or it may create oases en route in which nonnerve cells gather nerve growth factors and then release them to help sustain nerves passing by, Jaenisch suggests. No one really knows for sure.

"We're seeing a very complex picture that we're just starting to unravel," he told SCIENCE NEWS. —*E. Pennisi*

How cooked meat may inflame the heart

Among the chronic diseases that characterize aging is inflammation and deterioration of heart tissue. This cardiomyopathy begins gradually as a symptomless death of muscle. If the damage becomes extensive, heart failure or degeneration of the arteries carrying blood from the heart can occur.

While viral and other diseases can trigger some cardiomyopathy, the primary cause of the condition remains unknown. However, a new study suggests that a share of this chronic disease may trace to consumption of heterocyclic amines (HCAs) — carcinogens that form in cooked meat (SN: 1/8/94, p.22).

Nutritionist Cindy D. Davis of the National Cancer Institute (NCI) in Bethesda, Md., and her coworkers decided to investigate this link after collaborators at NCI observed heart damage in monkeys with HCA-induced liver cancer. To determine whether the muscle degeneration was just a by-product of the cancer, the researchers administered high doses of two mutagenic HCAs — IQ and PhIP — to cultured cells for 2 hours and to adult male rats for 2 weeks.

Both brief experiments triggered a loss of mitochondria in heart muscle cells. Mitochondria provide cells with energy and are essential to their survival. As a result, "we observed cell death — a lot in the cell-culture studies, much less in the animals," Davis says.

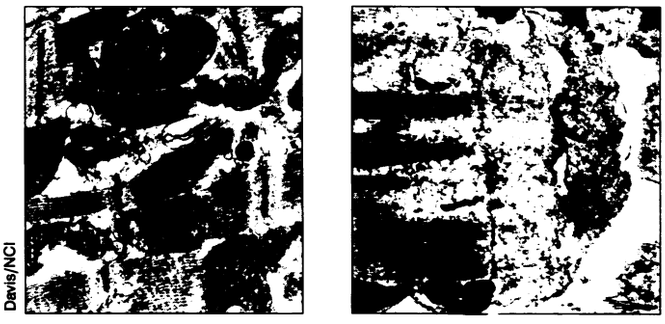
"We're not seeing cardiomyopathy per se," she points out, but adverse changes that "are suggestive of what might develop into cardiomyopathy." Moreover, Davis adds, these changes appear unrelated to liver cancer.

As in cancer studies, HCAs are not toxic to heart tissue unless transformed by liver enzymes. But once activated by those enzymes, HCAs circulate through the body and bind chemically — as adducts — to DNA in the heart, Davis and her coauthors report in the February TOXICOLOGY AND APPLIED PHARMACOLOGY.

Davis says that, although important, the heart adducts don't appear to account fully for the damage seen. For instance, she notes, "While there are higher levels of DNA adducts in heart cells exposed to PhIP than in those exposed to IQ, IQ is more toxic to heart cells."

An alternative mechanism to explain the new findings might involve the generation of free radicals — biologically damaging molecular fragments — as a consequence of exposure to HCAs, speculates NCI's Elizabeth G. Snyderwine, a coauthor of the new paper.

Because any loss of cardiac mitochondria will foster myopathy, the study's mitochondrial finding "certainly warrants scientific follow-up," observes Neal D. Epstein of the National Heart, Lung, and Blood Institute's cardiology branch in Bethesda. However, he adds, owing to the "exorbitant doses" of HCAs used here, it's too early to extrapolate these findings to humans. —*J. Raloff*



Davis/NCI

Left: Micrograph of heart tissue from healthy rat. Striated bands of muscle fibers are interspersed with well-defined mitochondria. Right: Similar tissue from HCA-treated rat exhibits massive structural degeneration.