Growing nerve fibers get some guidance

In the developing human embryo, a mere wisp of tissue called the neural plate gives rise to a nervous system consisting of billions of interconnected nerve cells. To establish the trillions of connections among them, these neurons extend long fibers, or axons, that snake their way through the embryo.

Scientists seeking to understand the chemical cues that guide these fibers are now focusing on a protein called Slit. In both invertebrates and vertebrates, Slit or its relatives repel the growth of certain axons. Yet the molecules have a friendly side, too. They can encourage axons to sprout secondary branches, another feat crucial to the development of the nervous system.

In four papers in the March 19 CELL and one in the April NEURON, scientists describe the proteins' contrasting roles. In fruit flies, for example, certain axons that try to cross the midline, which divides the insect's developing nervous system from top to bottom, come to a dead halt and retract. It's like hitting an "electric fence," says David L. Van Vactor of Harvard Medical School in Boston.

The shocking element in that fence turns out to be Slit. "Slit is expressed right down the midline. It's really potent at setting a boundary between the two sides of the nervous system," says Corey S. Goodman of the Howard Hughes Medical Institute (HHMI) at the University of California, Berkeley, who is a coauthor of three of the papers.

The story of Slit extends into higher organisms. Marc Tessier-Lavigne, an HHMI investigator at the University of California, San Francisco, and his colleagues report that mammals have at least three versions of Slit, all of which can repel axons at the midline or elsewhere.

For example, groups led by Yi Rao of Washington University School of Medicine in St. Louis and Alain Chédotal of Salpêtrière Hospital in Paris show that in chicks and rodents, some of these Slit proteins repel growing axons that came from brain regions such as the hippocampus and olfactory bulb.

Goodman and his colleagues also have evidence that the protein can repel migrating muscle-precursor cells from certain areas of the fruit fly embryo. These areas have cells that secrete Slit into their surroundings, where it sticks to other proteins or slowly diffuses to extend the repellent zone.

The role of Slit proteins in axon branching may be as important as their ability to repel those fibers. Most nerve cells ultimately connect with multiple targets, in the brain or elsewhere, that are separated by considerable distances. An axon may grow steadily toward one main target, but secondary axons, or collaterals, can shoot off from the axon's main trunk. Some collateral axons don't appear until a day after a parent axon has passed by a secondary target.

"They just pop out of the axon," notes Dennis O'Leary of the Salk Institute for Biological Studies in La Jolla, Calif.

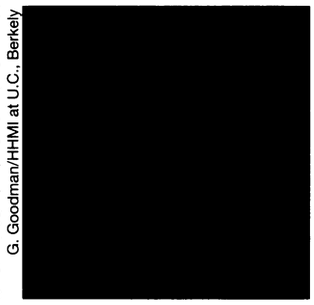
O'Leary and his colleagues have for years studied how vertebrate axons from the brain's cortex travel down to the spinal cord, forming branches all along the way. They've shown that the targets of collateral axons secrete soluble factors that penetrate the parent axon and induce it to branch at that site.

Slit proteins emerged as candidates for such a factor when Kuan Hong Wang, one of Tessier-Lavigne's colleagues, purified a molecule that seemed to provoke collateral branching in test tube studies. After determining the protein's amino acid sequence, he realized it was a fragment of one of the molecules that his laboratory mates had identified as axon repellents.

"There was absolutely no reason to believe there was any relationship between the two [projects]. We were totally surprised," says Tessier-Lavigne.

He and O'Leary stress that the mechanism behind the Slit fragment's ability to enhance collateral branching remains unclear. It may stimulate the budding of collateral axons, notes Tessier-Lavigne, or may merely stabilize fledgling axons induced to branch by other, unknown factors.

A fuller understanding of Slit proteins, he adds, might one day allow physicians to employ them in repairing the nervous system, such as in cases of spinal cord injuries. —*J. Travis*



G. Goodman/HHMI at U.C., Berkely

A protein called Slit (red) prevents growing nerve fibers (green) from crossing the center of a fly's developing nervous system.

China's air pollution chokes crop growth

With China's economy and population expanding at breakneck speed, its infamous air-pollution problems have started to claim new victims. Data collected at rural Chinese sites indicate that ozone pollution has already reached the point where it's harming agriculture—raising questions about whether the world's fastest developing country will be able to feed itself in the next century.

"There has been a lot of discussion of whether China can meet its future food demands, but there has been very little discussion of how regional environmental degradation is affecting agriculture there," says William L. Chameides of the Georgia Institute of Technology in Atlanta, who led the study.

When ozone, a highly reactive gas, builds up in the lowest layer of the atmosphere, it harms plants and animals. The pollutant forms when hydrocarbons and nitrogen oxides mingle in the air and get cooked by sunlight. Both these ingredients come from the incomplete combustion of fossil fuels. Hydrocarbons also are released by vegetation.

In a collaboration with Chinese researchers, Chameides and his U.S. team analyzed ozone measurements made at four rural sites in China during 1994 and 1995. These are the first systematic ozone readings taken outside cities in China, according to the researchers.

They found the highest pollutant concentrations at two places: an agricultural town called Linan, near the coastal city of Hangzhou, and a part of Hong Kong Island upwind of the city. At both spots, ozone often exceeded 60 parts per billion, an approximate threshold for harmful effects. Experiments in the United States and elsewhere have shown that the range of ozone exposure at these two Chinese sites is enough to reduce crop yields by 10 percent or more, the scientists report in the April 1 GEOPHYSICAL RESEARCH LETTERS.

The scientists were surprised to find the highest ozone readings in fall, winter, and spring—the reverse of the U.S. pattern. In China, they say, summer storms are strong enough to clear out polluted air from the coastal sites where the measurements were made.

The highest ozone readings in the study occurred in Linan, which sits in the Yangtze River Delta, one of China's most important agricultural regions. The timing of the air-pollution problems threatens the delta's winter wheat crop, which supplies 20 percent of China's total wheat harvest, say the researchers.

Chameides' team used a computer model to see how far the ozone problem might extend beyond the four measured spots. In the simulation, harmful concentrations of ozone blanketed much of eastern China.

The Chinese pollution measured is "what you'd see at a rural U.S. site in summer, maybe a little bit dirtier," says Jennifer A. Logan, an atmospheric chemist at Harvard University.

Agricultural studies in the United States suggest that ozone pollution reduces U.S. crop yields by $5 billion to $10 billion annually, says Ellis B. Cowling of North Carolina State University in Raleigh. —*R. Monastersky*