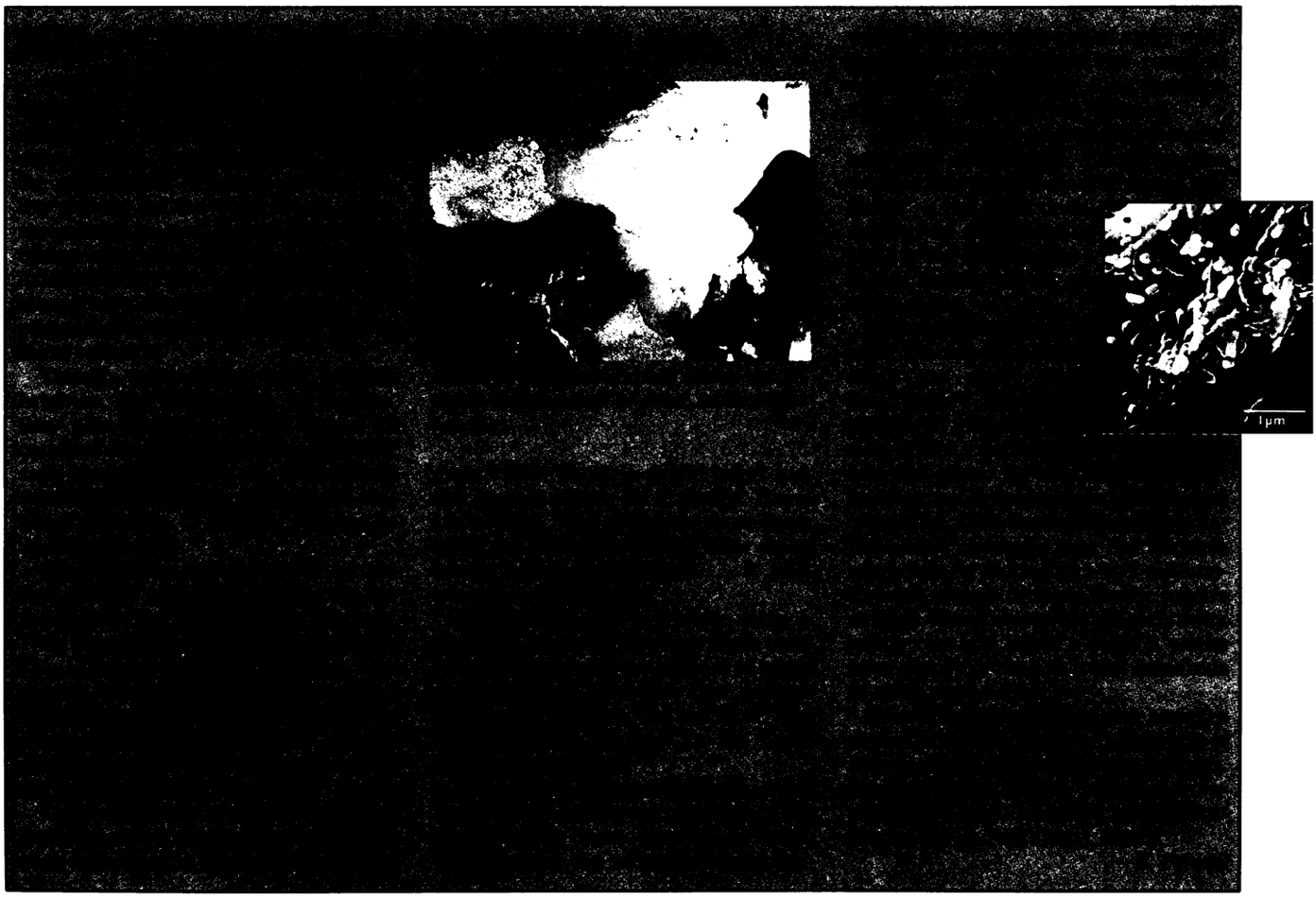
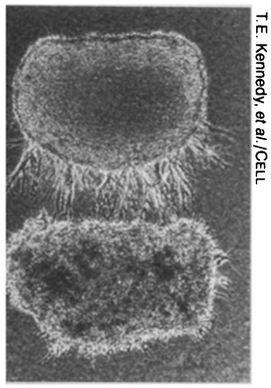


Axon acts: The unbearable likeness of being

The epithet "you worm" might gain new meaning if researchers are right that two proteins recently found in the brains and spinal cords of chicks are shared by at least one and perhaps many other species. Two papers in the Aug. 12 CELL describe the proteins, netrin-1 and netrin-2, and their close similarity to the protein unc-6, known to be a key factor in the neural development of the nematode, or common roundworm.

Neurons have three parts: a cell body; the winding axon that transmits a nerve signal to the next cell; and dendrites that branch out from the cell body and receive input from axons of other neurons. Axons, then, provide the main communication link for nerve cells. "Netrins are signals that diffuse through the cellular environment and which attract the axons to their targets," explains Marc Tessier-Lavigne, a Howard Hughes Medical Institute researcher at the University of California, San Francisco, and a coauthor of both papers.


T.E. Kennedy, *et al.*/CELL

Cells engineered to secrete recombinant netrin-1 protein (bottom) attract growing axons from a piece of embryonic rat spinal cord (top).

In 1988, Tessier-Lavigne, Marysia Placzek, Jane Dodd, and Thomas M. Jessell, then all at Columbia University in New York City, were the first to describe chemotropism at work in the spinal cord. Though they couldn't identify the protein responsible for this phenomenon of chemical attraction, they knew that neural axons responded to a signal from cells in the lower spinal cord of embryonic rats.

One hundred years ago, the Spanish neuroscientist Santiago Ramón y Cajal postulated that diffusible chemical attractants weave neural networks by sending signals to the developing brain. The discovery of the netrins reinforced Ramón y Cajal's early theory by isolating two of the postulated chemical attractants that direct movement and growth of axons in the spine.

"This work provides the first convincing demonstration of an endogenous chemoattractantlike molecule within the developing vertebrate nervous system," says Jessell, a Howard Hughes Medical Institute researcher at Columbia University.

The team purified the two netrin proteins from 25,000 embryonic chick brains and obtained a partial amino acid sequence of the proteins. They then cloned the genes encoding the proteins and engineered cell lines to secrete netrins. Finally, they added the netrins to petri dishes containing pieces of rat spinal cord.

Viewed microscopically, the axon tips — called growth cones — reached toward the netrin-secreting engineered cells. "The novelty of our research is that the netrins are the first diffusible chemoattractants to be isolated," says Tessier-Lavigne. "Previously, people had identified other types of molecules that can guide axons, such as diffusible inhibitors of axon growth."

Just as axons in the brain can be summoned to the lower spine, they can be turned away. Tessier-Lavigne explains that repellent molecules, such as a group known as collapsins or semaphorins, send a chemical message to axons, saying, "Don't come this way." Neurobiologist Corey S. Goodman, a Howard Hughes Medical Institute researcher at the University of California, Berkeley, believes that these attractant and repellent molecules may work simultaneously in embryonic development. — *G. Marino*