Researchers to develop probes to study cellular GPS

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An international group of researchers from Carnegie Mellon University, Goettingen Medical School in Germany and the University of Cambridge in the United Kingdom have received a Human Frontiers Science Program (HFSP) grant to develop molecular probes that will help researchers better understand the "cellular GPS" system that guides neurons to create a properly wired nervous system.

In the course of the development and repair of the nervous system, nerve cells, also called neurons, seek to find other specific nerve cells with which they connect to form a synapse. At the synapse, information is passed from cell to cell via electric impulses, underlying the nervous system's essential processes like perception and thought.

"A human has 100 billion neurons, and each of those neurons makes between 1,000 and 30,000 very specific connections. If those billions of neurons were randomly connecting, it wouldn't work — the number of connections would get too big and the nervous system would be horribly mis-wired," said Marcel Bruchez, associate research professor of chemistry and program manager of Carnegie Mellon's Molecular Biosensor and Imaging Center. "Neurons have a very well-defined map to follow for finding the right connections, but we don't understand how they read this map."

Leading the nerve cells to their specific targets are growth cones, specialized structures within the tip of the neuron's axon. Within each growth cone is a tiny molecular navigational system that guides the nerve

cell down a winding path while sensing the cellular terrain, allowing the cell to find its synaptic target.

"Everything a growth cone needs to find its neuron's connection exists inside the growth cone. It doesn't need to communicate with the nucleus, which is what we always think of as the cell's brain," Bruchez said. "The growth cone is autonomous, like a robot or GPS system that reads the map and decides the direction in which the neuron should go."

Bruchez and colleagues, which include Fred Wouters from the Goettingen Medical School and Christine Holt from the University of Cambridge, believe that the growth cone makes decisions through a combination of integrated molecular cues. However, since the growth cone is so small and only contains a small fraction of the nerve cell's content, it has been difficult to study the molecular processes at play in neuronal navigation. Traditionally to see such processes, researchers would load the growth cone with dyes that would make the cellular actions visible under a microscope, but introducing large amounts of dye to this limited cellular environment would disturb cellular function.

Through the HFSP-supported project Bruchez and colleagues will attempt to develop a sensitive set of probes that will report on the molecular activities at the growth cone including protein synthesis, protein degradation and protein folding. If successful, the probes could yield vital information about how the nervous system develops and repairs.

Source: Carnegie Mellon University (news : web)