Transgenic songbirds provide new tool to understand the brain

September 29 2009

A new genetic tool will enable scientists to study vocal learning and neurogenesis at the molecular level in songbirds.

You can learn a lot from an animal. By manipulating the DNA of mice, flies, frogs and worms, scientists have discovered a great deal about the genes and molecules behind many of life's essential processes. These basic functions often work about the same in people as they do in "model" animals. But if you want to study more sophisticated cognitive processes such as humans' ability to learn language from one another, you need a more sophisticated organism. For the first time, researchers have devised a way to alter the genes of the zebra finch, one of a handful of social animals that learn to "speak" by imitating their fellows.

After decades of studying the behavior and anatomy of vocal learning, scientists will be able to use the technique to explore vocal learning at the molecular level. The new tool, reported online in the September 28 issue of *PNAS Early Edition*, may also reveal secrets about exactly how, when and why some neurons are replaced in the adult brain.

"The roadblock had been that you couldn't manipulate the genes," says Fernando Nottebohm, Dorothea L. Leonhardt Professor and head of the Laboratory of Animal Behavior at The Rockefeller University, where the research was conducted. "Ultimately, you have to understand how things are working at the most basic molecular level, and this will take our research there."

Nottebohm, Research Associate Robert Agate and colleagues adapted a method used to alter quail genes for use in the finch. The researchers used an HIV-based lentivirus that is able to insert attached genes into the genome of the hosts it infects. To prove the method works, the scientists inserted genes that produce green fluorescent protein in cells throughout the body. They found that they had to inject at least 10 times as much of the viral vector into finch embryos than in quail for the genes to take root. But after refining the method, they produced several birds that had incorporated the genes into their germline cells, meaning they could pass them along to their offspring.

These "founder" transgenic songbirds did not suffer any obvious side effects from the genetic experiment: They developed normally, learned to sing, and mated. But because of the fluorescent protein produced throughout their bodies, they glow green when exposed to a specific wavelength of blue light. The green can be best seen before the hatchlings' feathers grow in, but can still be glimpsed in the eyes, legs and around the beaks of the older, feathered birds.

The transgenic songbirds will enable Nottebohm, who discovered neuronal replacement in the adult vertebrate brain and described the neural circuitry by which songbirds learn to sing, to investigate the genes that control these processes. "With transgenic songbirds, we hope to have a splendid tool to get into the molecular biology of vocal learning and neuronal replacement in an adult vertebrate brain," Nottebohm says.

Source: Rockefeller University (news : web)