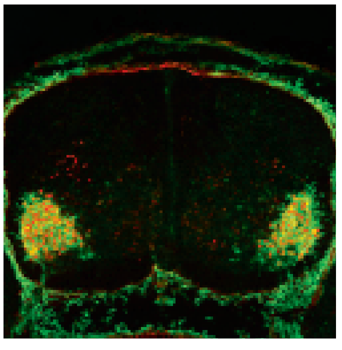
# Guiding Motor Neurons

RESEARCHERS ARE UNTANGLING HOW A PROTEIN HELPS POINT MOTOR NEURONS TOWARD THEIR CORRECT DESTINATIONS.

Every movement, from picking up a pencil to doing a backflip, requires the precise wiring of specific neurons in the body. If a motor neuron destined for the leg instead wound its way along an arm during development, chaos would ensue.

"Mammalian limbs possess over 50 muscle groups and each is innervated by its own, dedicated, set of motor neurons," says HHMI investigator Thomas M. Jessell, whose lab at Columbia University has studied a key gene for controlling that specificity.



A cross section of an embryonic spinal cord, with clusters of FoxP1 labeled in red.

The Jessell lab had already found that the *Hox* family of genes plays a role in determining which neurons go where. But there are 21 *Hox* genes involved in mice neuron development, and so probing their function further by gene inactivation would be a laborious task. Jessell and his colleagues searched for factors that might be required for *Hox* activity and discovered that the transcription factor FoxP1 is needed for the activity of all 21 Hox proteins, permitting a way of inactivating all Hox proteins involved in spinal motor neuron differentiation. "FoxP1 gives us access to the entire Hox program at one fell swoop," says Jessell.

The team looked in mice with mutated FoxP1 to see whether motor neurons would simply stall at the base of a limb. Instead, they observed the axons of motor neurons projecting along random paths in the limb.

"It's as if you're blindfolded in a garden maze and told to keep moving," Jessell says. "You'll take any of the paths that are available to you, but you'll just be wandering aimlessly."

This randomness is a disaster for motor control, he says. In effect, the mice with the mutation have a spinal motor system that resembles those found in more primitive vertebrates. The results are published in the July 25, 2008, issue of *Cell*.

Mice with a complete loss of FoxP1 activity die before they're born, so Jessell and his colleagues are now developing ways to eliminate the protein solely from motor neurons. They hope to elucidate the biochemical and functional connection between FoxP1 and the Hox proteins. ■ —SARAH C.P. WILLIAMS

## IN BRIEF

Since the drugs could be used by athletes who want an edge, Evans also developed a test that can detect whether the drug is present in serum, plasma, or urine. The World Anti-Doping Agency has placed both drugs on its list of prohibited substances for 2009 and is working to implement the analysis to retroactively test athletes who competed in the 2008 Olympics.

### UNDERSTANDING BACTERIA'S GROUP DYNAMICS

By itself, one bacterium can't do much damage. It's their ability to band together that allows some bacteria to cause such deadly infections.

New details on how bacteria detect each other to initiate these group behaviors—such as inducing virulence or expressing a useful gene simultaneously—could help scientists develop strategies to fend off bacterial attacks. Bonnie L. Bassler, an HHMI investigator at Princeton University, has made just such progress.

Bassler and her colleagues study quorum sensing: the capacity of bacteria to communicate, sense each other, and coordinate activities. "You need a lot of bacteria working together to make some tasks successful," says Bassler. The researchers most recently took advantage of a marine bioluminescent bacterium with a useful property: *Vibrio harveyi* lights up only when sufficient numbers of the organism come together.

The team screened 30,000 bacteria lines with mutations in LuxN—the receptor that detects signaling molecules from neighbors. They found mutants that light up before the quorum is reached, and ones that never light up, no matter how crowded they become. They also screened 35,000 chemicals in search of compounds that can inhibit bioluminescence and found 15 that specifically disrupt quorum-sensing mediated communication.

By combining data from the two hunts, published in *Cell* on August 8, 2008, scientists are gaining a better picture of how bacteria initiate group behaviors, and what it takes to artificially interfere with these processes. They learned that LuxN's position in the bacteria is what allows it to detect signaling molecules from neighbors, but not those produced within the same cell.

### NEW DISEASE-SPECIFIC STEM CELL LINES

New stem cell lines, created from patients with 10 different genetic disorders, will allow researchers to study the diseases at a depth never before possible. The researchers, led by HHMI investigator George Q. Daley of Children's Hospital Boston, used a set of genetic reprogramming factors to turn diseased adult cells into stem cells, which can be coaxed to develop into many different tissue types.

"This enables us to model thousands of conditions using classical cell culture techniques," says Daley.

In the past, researchers wanting to study diseased cells from patients were limited by the short life spans of human cells grown in laboratory dishes. They often relied on cells modified to live forever, but these changes cast doubt on whether the cell's physiology remained the same.

Now, the researchers can use the stem cell lines—which model diseases such as Duchenne muscular dystrophy, Becker muscular dystrophy, type 1 diabetes, Parkinson's disease, Huntington's disease, and Down syndrome—to observe how the diseases develop in different tissue types. The cells will also offer a proving ground for screening drugs to treat the diseases. The details of the stem cells were published online in *Cell* on August 7, 2008.

The Harvard Stem Cell Institute will make the lines available to other researchers as quickly as possible, says Daley. The scientists are working on generating lines for other diseases as well.

Jeremy Dasen / Jessell lab