There is little question that the human brain is a black box: we have a reasonable understanding of what it does, and we have even come to understand which of its regions are involved in performing which functions, but we have little comprehension of how it does what it does.

That is why the Harvard Stem Cell Institute Nervous System Diseases Program is aimed at expanding our understanding of, and developing treatments for, discrete diseases whose symptoms are seen on the periphery of the system, and whose causes might be said to be found at the input junctions of the black box, in addition to deep within its circuitry.

As Jeffrey Macklis, MD, leader of the Nervous System Diseases Program explains, “the nervous system is so immensely complex, with so many different types of neurons and glia, that every disease of the nervous system is unique.” But there are some common components: many neurodegenerative diseases, whether they affect speech and language, movement, hearing, or vision, affect one or two specific, but very different, types of nerve cells.
Neuron Specialization

Macklis notes that in the eye, there are specific neurons that send impulses from the retina into the brain; in the ear, another form of neuron translates vibrations in the inner ear into signals to the brain stem, which are then sent deep into the brain; in Parkinson’s disease, nerve cells that make a brain chemical called dopamine which helps to control muscle movements are slowly destroyed; and, in motor neuron diseases, such as ALS (Lou Gehrig’s disease) or spinal muscular atrophy (SMA), still different types of neurons connecting from the cerebral cortex of the brain to the spinal cord, and from the spinal cord to muscles of the body, are affected.

Understanding Neuron Development

The HSCI Nervous System Diseases program has brought together researchers studying the development of each of these different neuronal systems, and other scientists and physicians studying their deterioration and the diseases caused by that deterioration. “Understanding how those cells develop is essential to being able to re-create them. And ultimately what we’d like to do is rebuild them. Or we’d like to build billions and billions of them in dishes to study the disorders and discover drugs to treat them,” Macklis explains. “Thus we have working groups in inner-ear, retina, and motor systems, where several laboratories are approaching the problem at different levels of analysis. One or two might look at basic development; others may be looking at how we use those molecules to activate stem cells or progenitors that are already there. And other laboratories are working on taking those molecular recipes and using them to create appropriate neurons from ES [embryonic stem] and iPS [induced pluripotent stem] cells for studying new therapies.”

International Think Tank

Not content with being dependent on local expertise, one of the most powerful aspects of the HSCI Nervous System Diseases Program is that its focus is local but its scope and reach is international. Every year for the last five years, the program has sponsored a multi-day “think tank,” bringing the world’s leading researchers in a particular disease area or cell type to Harvard. The purpose of the meeting is to share the latest scientific findings, share those more broadly through white papers, and identify areas for joint research projects and collaborations. In short, our goal is to harness the world’s best thinking to drive the entire field forward to develop answers to one of the most challenging areas of science and address the growing burden of disease.