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Dennis O’Leary, together with his research group, studies critical genetic and molecular mechanisms that regulate brain development, using the mouse as a primary model system. His work focuses on two important questions: how the brain assembles itself during development, including its wiring, and how different parts of the cerebral cortex, the largest and most complex part of the brain, become uniquely specialized to perceive vision and touch, as well as generate movements. O’Leary’s goal is to understand the mechanisms used by the brain to accomplish these crucial tasks, providing the knowledge required to prevent genetic disorders and disease or to repair defects.

O’Leary’s previous work demonstrated that specific wiring between parts of the brain or from the eye to the brain arises from initially exuberant connections between neurons, followed by a selective pruning, occurring by the degeneration of many of the early connections to retain only the correct ones. These connections are formed by axons, the outgoing “wires” on each cell that convey electrochemical impulses between neurons. Among O’Leary’s current work, he is studying the molecular mechanisms that decide which axons die or live, and once this selection is made, how those axons fated for death are actually eliminated. This work has important implications for the mechanisms that underlie most, if not all, neurodegenerative diseases, including Alzheimer’s and Parkinson’s.

In a distinct set of projects, O’Leary has recently identified specific transcription factors (proteins that regulate large sets of genes to specify the properties of cells and tissues) that specify progenitors, or natural stem cells, in the developing brain to make parts of the cerebral cortex that are specialized to process vision or touch. By manipulating these genes in mice, he can, for example, make the visual or touch processing parts of the cerebral cortex larger or smaller, which initiates a cascade of changes in other parts of the brain outside the cerebral cortex and has a significant influence on behavior. This work has implications for many neurological disorders, including autism and other genetic-based brain disorders that have prominent behavioral components.

A common link among the studies performed by O’Leary and his research team is the identification of genes that control important developmental functions and the molecular mechanisms by which they operate, thereby providing a framework for potential treatments in the future.

For more information, please visit www.salk.edu/faculty/o’leary

From left to right: Kyucheol Cho, Yoo-Shick Lim, Daichi Kawaguchi, Adam Stocker, Carlos G. Perez-Garcia, Dennis O’Leary, Todd McLaughlin, Andreas Zembrzycki, Berta Higgins, Haydee Gutierrez, Brenda Beckett