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“Our brains are composed of neuronal circuits with an estimated 100 trillion connections. My lab is interested in unmasking the strategies that nature has devised to generate this immense diversity of cells and complexity of connections by focusing on the way that the spinal cord is assembled during fetal development. We expect this information to provide novel insight into how we can harness ‘embryonic pathways’ to repair or augment the central nervous system to treat birth defects, injuries, diseases, and aging.”

The neuromuscular circuitry that controls bodily movements relies on constant sensory feedback to fine-tune its commands to hundreds of muscles. Muscle fibers are each controlled by one motor neuron in the spinal cord that relays signals from the brain; sensory receptors send information from the periphery back to the central nervous system. These nerves are not unlike a roadway, with orderly traffic moving in both directions.

The traditional view has been that during embryonic development, sensory and motor neurons are able to incorporate into tightly coordinated pathways without getting mixed up because growth cones—structures that guide growing axons to their destination—are studded with Eph proteins that constantly search their environments for molecules called ephrins, which nudge them in the right direction. (Axons are long projections that conduct electrical impulses away from the nerve cell body.) Researchers in Pfaff’s laboratory, however, found that neurons not only carry both types of proteins, but that the role of Ephs and ephrins can change, raising the question of what happens when adjacent neurons bump into one another.

To find the answer, Pfaff’s team studied sensory and motor neurons, which extend their axons along the same pathway to the periphery. They found that with ephrin/Eph signaling intact, the axons sorted into separate fascicles containing either sensory or motor axons, but never both. When they deleted EphA3 and EphA4 in motor neurons, however, sorting between the fascicles of the motor and sensory axons broke down; instead of reaching for muscles, some motor neurons made a U-turn, joined the sensory lane, and headed back toward the spinal cord.

Ephrin and Eph both appear to control where the axons grow and to maintain the normal arrangement between the motor and sensory pathway. They also play a major role in preventing spinal cord neurons from regenerating after injuries. As scientists in the spinal cord field work to overcome the block preventing axonal growth within the central nervous system, Pfaff’s findings demonstrate that this research needs to be approached cautiously, lest it promote indiscriminate motor axon growth and cause severe problems.

For more information, please visit
salk.edu/faculty/pfaff.html

Left to right:

Front row: Grainne Whitman, Ariel Levine, Becky Hensley, Todd Macfarlan, Annie Onanong Chivatakarn, Laura Franco, Sam Pfaff, Christopher Hinckley, Benjamin Gallarda, Shane Andrews, Karen Lettieri, William Alaynick

Back row: Wesley Gifford, Marito Hayashhi, Tiffany Poon, Dario Bonanomni, Matthew Pankratz, Joseph Tsai, Ge Bai, Matthew Sternfeld, Shawn Driscoll

