Abstract

Hindbrain Dorsal Interneurons - Molecular Regulators That Govern Their Circuit Formation

Ayelet Kohl[1], Avihu Klar[2] and Dalit Sela-Donenfeld[1]

1.Koret School of Veterinary Medicine, Developmental Neurobiology, Rehovot, 76100, Israel
2.The Hebrew University of Jerusalem, Medical Neurobiology, Jerusalem, 91120, Israel

Hindbrain dorsal interneurons (HdIs) constitute a main communication route between sensory modalities and motor outputs in the peripheral nervous system, brain and spinal cord. Yet, only little is known regarding circuit formation of HdIs. In this research, we have characterized two populations of hindbrain dorsal interneurons, dA1 and dB1, that differ in their transcriptional codes, axonal projection patterns and target selection.

Novel genetic tools were utilized to label dA1 and dB1 neurons at early and late stages of avian embryonic development. Using dA1/dB1-specific enhancers, combined with Cre/Lox conditional expression system, the distinct axonal projection patterns of dA1 and dB1 neurons were identified. The axons of dA1 neurons projected mainly contralaterally, and turned longitudinally at the lateral and dorsal funiculus. In contrast, the axons of dB1 neurons extended at the ventral funiculus at the ipsi- and the contra-lateral sides of the floor plate. The targets of dA1 and dB1 axons were followed at late developmental stages using the PiggyBac-mediated DNA transposition method. dB1 axons were found to extend and form synapses in the Purkinje layer of the cerebellum whereas dA1 axons targeted the EGL, IGL and Purkinje layers of the cerebellum, as well as the medulla cochlear nuclei.

Studying of the mechanism that regulates the specific patterns of dA1/dB1 axonal projections revealed a fundamental role of the Lim-homeodomain proteins. Alternating the code of dA1 Lim proteins (Lhx2/9) into dB1-Lim code (Lhx1/5), and vice versa, modified dA1/dB1 axonal patterns to project along the routes of the reciprocal subgroup, without affecting cell-fate acquisition. Together, this research provides new knowledge to the assembly of trajectories, targets and connectivity of hindbrain dorsal interneurons as well as to molecular mechanisms that control these patterns.