

Lab characterizes gene essential for prenatal development of nervous system

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The Stowers Institute's Trainor Lab has demonstrated the role of a gene important to the embryonic development of the nervous system, a process that requires coordination of differentiation of immature neural cells with the cycle of cell division that increases their numbers. Until now, the mechanisms regulating these distinct cellular activities have been poorly understood. The findings will be published in the Feb. 15 issue of *Development*.

In this work, the team used gain- and loss-of-function mutations in mice to isolate novel roles for the mouse Cux2 gene in regulating neurogenesis. They established that Cux2 directs neuroblast development, neuronal differentiation, and cell-fate determination in the spinal cord by coupling progression through the cycle of cell division with differentiation of neural cells by direct activation of two key neurogenic determinants, Neurod and p27Kipl.

"We were excited to uncover, for the first time, multiple functional roles for a Cux-like homeodomain transcription factor in regulating key aspects of spinal cord neurogenesis," said Angelo Iulianella, Ph.D., Senior Research Associate and first author on the publication. "The demonstration that Cux2 integrates cell-cycle progression with neural progenitor differentiation and cell-fate determination provides a much clearer picture of the complex process of neurogenesis."

"The impact of cell cycle length on the formation of interneurons versus motoneurons was a surprising finding," said Paul Trainor, Ph.D.,



Associate Investigator, and senior author on the publication. "Ongoing work involves global proteomic analyses aimed at identifying the complete set of Cux2-interacting partners. We believe these efforts will be essential to understanding how Cux2 elicits its multiple functions during neurogenesis."

Further analysis of Cux2 will make it possible to extend these findings not only to spinal cord development, but also to the mammalian cortex, where Cux genes demarcate specific upper layers of cortical neurons and may have played a role in the expansion and increased complexity of the cortex during evolution.

Source: Stowers Institute for Medical Research

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