Collapse of Embryonic Identities and Emergence of Functional Diversity during Motor Neuron Maturation

March 10

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:

Tulsi Patel, Ph.D.

Assistant Professor

Department of Neuroscience and Cell Biology

Rutgers Robert Wood Johnson Medical School

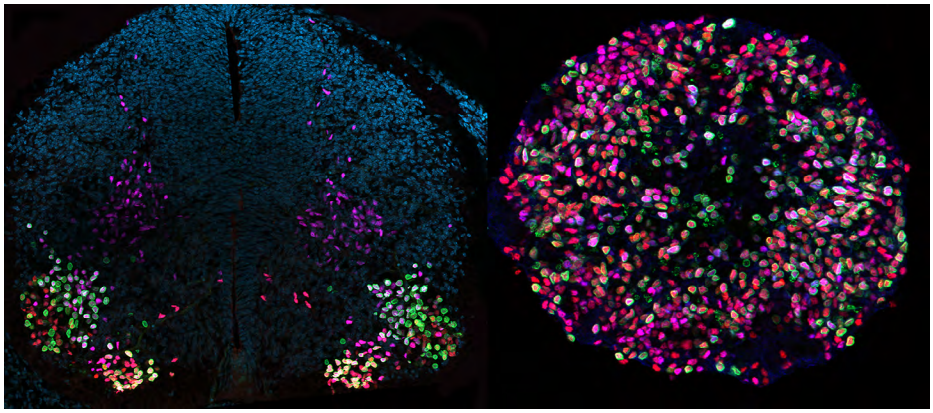
Rutgers University

Host: Edmund Au, Ph.D.

For more information contact
Darlene White
daw9085@med.cornell.edu

Abstract

Neurons born in the embryo undergo an extended maturation process in which they form circuits, refine synapses, and acquire subtype-specific functions. How individual neuron types orchestrate this progression remains unclear. Using single-nucleus multiome sequencing, we tracked the transition from specification to functional maturation in mouse skeletal motor neurons (SMNs). We find that SMN transcriptional diversity is highly dynamic. At embryonic day15.5, during target innervation, SMNs segregate into dozens of subclusters corresponding to known motor columns and pools defined by their target-specific gene programs. By postnatal day 3, many of these embryonic signatures collapse, and SMNs converge into a more molecularly homogeneous state. During the first two postnatal weeks, SMNs diversify again, acquiring the gene expression programs that define mature alpha, gamma, and type 3 motor neuron subtypes. Integrating chromatin and transcriptional data, we identified transcription factors that drive this second phase of diversification. Loss of these factors disrupts acquisition of mature functional subtypes. Our work reveals a unique developmental trajectory in which diversity within a neuron type fluctuates dynamically over time to meet evolving functional needs. Ongoing work aims to define the molecular mechanisms governing sequential subtype specification and to generate mature SMN subtypes from stem-cell–derived neurons.



Publications

1. Chen, Y., Chi, H.-M., Tian, A., Miller, A. & Patel, T. *From Wiring to Firing: Collapse of embryonic identities and emergence of functional diversity during motor neuron maturation.* bioRxiv, 2025.2008.2012.669897 (2025). https://doi.org/10.1101/2025.08.12.669897.

2. Lowry, E. R. et al. Embryonic motor neuron programming factors reactivate immature gene expression and suppress ALS pathologies in postnatal motor neurons. Nat Neurosci (2025). https://doi.org/10.1038/s41593-025-02033-x.

3. Patel, T. et al. *Transcriptional dynamics of murine motor neuron maturation in vivo and in vitro.* Nat Commun 13, 5427 (2022). https://doi.org/10.1038/s41467-022-33022-4.

Burke Neurological Institute
Academic Affiliate of Weill Cornell Medicine
785 Mamaroneck Avenue, White Plains, NY 10605
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