'Roadmap' tracks trajectories of embryo development

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Scientists have mapped out the key molecular changes that orchestrate how embryonic mouse cells differentiate into the diverse cell types that will ultimately form all the different tissues and organs of the adult animal.

This "roadmap" of mouse embryogenesis will help researchers understand the molecular programs that control how different specialized cell types emerge from less differentiated cells as an embryo grows and develops not only for mice, but also for humans, said Jay Shendure, professor of genome sciences at the University of Washington School of Medicine, scientific director of the Brotman Baty Institute for Precision Medicine and a Howard Hughes Medical Institute Investigator.

"We begin life as a one-cell zygote and that cell, in just a few weeks or months, divides and differentiates into hundreds of cell types," Shendure noted. "So, the question is: How does that happen? What paths do cells take? What are the genes that shape those decisions?"

The researchers reported their findings today in the journal *Nature Genetics.* Chengxiang Qiu, a computational biologist and doctoral student in the Shendure lab, was lead author of the paper,

To map out this process, Shendure and his colleagues drew on publicly available data collected from mouse studies that used a technique called single-cell RNA sequencing (scRNA-seq).

This technique allows scientists to identify and quantify the levels of different messenger RNA molecules within individual cells. Because these mRNA are copied from activated genes, their presence in a cell

indicates which genes are active at a given point in time.

To supplement these data, the researchers also used scRNA-seq data they had generated from about 150,000 embryonic mouse cell nuclei sampled every two hours over a critical 24-hour period beginning on the eighth day of mouse embryonic development.

Qiu combined these data, and after adjusting them to account for differences in the techniques used by different researchers, identified the states of the embryonic cells at 19 stages spanning from day 3.5 in the mouse embryonic development to day 13.5, when most of the key embryonic structures have appeared. In mice, gestation, from a single-cell zygote to a live-born pup, takes only 21 days.

The resulting map traces out the changes in gene activity as the cells develop and differentiate into different cell types. Of particular interest is the activity of genes for key regulatory proteins, called transcription factors, that orchestrate cell growth, development and function, said Qiu.

"As embryogenesis proceeds, the cells branch off into different cell types like branches of a tree," said Qiu. "Transcription factors that are active at these branch points tend to be specific for a new cell type." On the other hand, some transcription factors appear active in many different cell types, Qiu noted, suggesting they play a more general role in regulating cell growth and function.

Going forward the researchers hope to obtain scRNA-seq data from more and more points in embryonic development to capture changes in gene expression in more detail. The team hopes the new map, called TOME (Trajectories Of Mammalian Embryogenesis), will serve as a resource for researchers working on many aspects of embryonic development.

More information: Chengxiang Qiu, Systematic reconstruction of cellular trajectories across mouse embryogenesis, *Nature Genetics* (2022). DOI: 10.1038/s41588-022-01018-x

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