

Mapping cells in the 'immortal' regenerating hydra

July 25 2019



Just a few millimeters long, the hydra has the ability to completely regenerate damaged body parts including its nervous system, making it practically immortal. UC Davis researchers are discovering how hydra achieves this and what the implications might be for human medicine. (Photo by Stefan Siebert). Credit: Stefan Siebert, UC Davis

The tiny hydra, a freshwater invertebrate related to jellyfish and corals, has an amazing ability to renew its cells and regenerate damaged tissue. Cut a hydra in half, and it will regenerate its body and nervous system in a couple of days. Researchers at the University of California, Davis have now traced the fate of hydra's cells, revealing how three lines of stem cells become nerves, muscles or other tissues.

Celina Juliano, assistant professor in the UC Davis Department of Molecular and Cellular Biology, project scientist Stefan Siebert and colleagues including Jeff Farrell, a postdoctoral researcher at Harvard University, sequenced the RNA transcripts of 25,000 single [hydra](#) cells to follow the genetic trajectory of nearly all differentiated cell types.

"The beauty of single-cell sequencing and why this is such a big deal for developmental biologists is that we can actually capture the genes that are expressed as cells differentiate from stem cells into their different cell types," Juliano said.

The study gives developmental biologists a high-resolution map of the three stem cell developmental lineages in hydra. The data set will help researchers understand regulatory gene networks in place early in evolution that are shared among many animals, including humans, Siebert said. Understanding how the hydra regenerates its entire [nervous system](#), for example, could help us better understand neurodegenerative diseases in humans.

Regenerates from three lines of stem cells

Hydra continuously renew their cells from three different stem cell populations. The researchers analyzed sets of messenger RNA molecules, called transcriptomes, from individual hydra cells and grouped the cells based on their expressed genes. They could then build a decision tree showing how each lineage of [stem cells](#) gives rise to

different [cell types](#) and tissues. For example, the interstitial stem cell lineage produces nerve cells, gland cells and the stinging cells in the animal's tentacles.

"By building a decision tree for the interstitial lineage, we unexpectedly found evidence that the neuron and gland cell differentiation pathway share a common cell state," said Juliano. "Thus, interstitial stem [cells](#) appear to pass through a cell state that has both gland and neuron potential before making a final decision."

The single cell molecular map also allowed Juliano and colleagues to identify genes that may control these decision-making processes, which will be the focus of future studies.

Researchers are especially interested in hydra's ability to regenerate its nervous system, which could give insights into treating trauma or degenerative disease in humans.

"All organisms share the same injury response pathway but in some organisms like hydra, it leads to regeneration," said coauthor and graduate student Abby Primack. "In other organisms, like humans, once our brain is injured, we have difficulty recovering because the brain lacks the kind of regenerative abilities we see in hydra."

More information: "Stem cell differentiation trajectories in Hydra resolved at single-cell resolution," *Science* (2019)
[science.sciencemag.org/cgi/doi ... 1126/science.aav9314](https://science.sciencemag.org/cgi/doi/10.1126/science.aav9314)

Provided by UC Davis

Citation: Mapping cells in the 'immortal' regenerating hydra (2019, July 25) retrieved 7 May

2024 from <https://medicalxpress.com/news/2019-07-cells-immortal-regenerating-hydra.html>

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