

TRANSCRIPTOMICS

## Hydra springs eternal: a new resource maps cell differentiation at single-cell resolution

Siebert, S. et al *Science* **365**, eaav9314 (2019)

The mythical Hydra was a beast quite adept at re-growing its heads...at least until it met Heracles. The much smaller and much more real lab animal doesn't have heads *per se*, but it shares its namesake's ability to regenerate and replace tissue. Even in the absence of injury (heroic or otherwise), every cell in the animals' body is replaced about every 20 days. Those cells differentiate from one of three lineages: endodermal epithelial, ectodermal endothelial, and interstitial. But how does a particular cell type, say a neuron or a stinging nematocyst, differentiate from its stem cell progenitor?

It's a beastly question that motivates research in many different animals, but one that a new resource from Celina Juliano's lab at the University of California, Davis, might help those in the *Hydra* community slay. Juliano and her colleagues recently took on the labor of mapping cell differentiation trajectories for *Hydra* at single-cell resolution.

They used a microfluidics-based single-cell sequencing technique called Drop-seq. The process is fairly straightforward, says Juliano: *Hydra* are dissociated into single cells—a mix of stem cells, differentiated cells, and those in transition—and an oil is used to create nanoliter-sized liquid droplets containing one cell and one barcoded 'bead.' A lysis buffer breaks open the cell to release the transcripts inside for sequencing; the barcoded beads meanwhile allow the researchers to keep track of the cellular origins of all that RNA.

The first step of the analysis involved creating a digital expression matrix, with *Hydra*'s genes on one side and all the sequenced cell data on the other. From there, cells were grouped into clusters using the *Seurat* R package to construct a molecular map of cell states; another R package called *URD*, originally built by co-author Jeffrey Farrell at Harvard for zebrafish, was then

used to build the different differentiation trajectories.

Perhaps surprisingly, the team didn't find any major surprises once they completed their initial map. "*Hydra* works as we think it works," Juliano says. The resource however should provide a valuable starting point for now figuring out the molecular details that enable *Hydra* to maintain its homeostatic state. "We have this map of gene expression, and not just of stable cell types but expression as cells are starting to differentiate," she says. "Now we can start to understand cell differentiation starting from a much more informed place."

Work with *Hydra* labors on.

Ellen P. Neff

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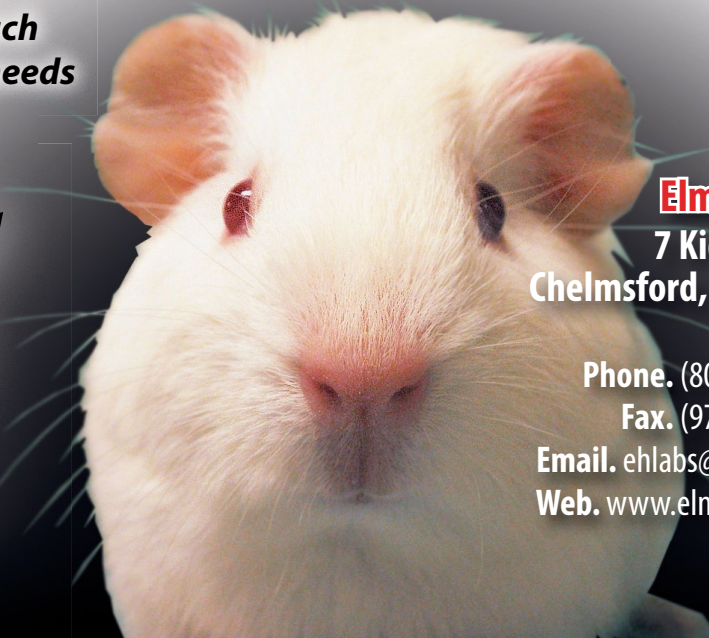
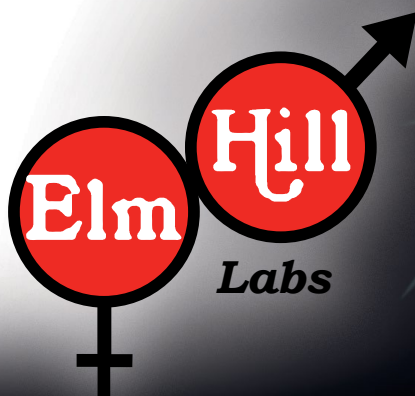
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