Researchers discover universal molecular 'flag' that highlights critical genes

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After probing more than 200 genetic data sets, researchers at the Stanford University School of Medicine have identified a molecular flag that labels genes critical to a cell's function.

The flag appears to exist universally—in cells ranging from worms to humans—and can be used to help decipher the function of unfamiliar cells, said Anne Brunet, PhD, associate professor of genetics and senior author of the study. For example, by examining a cell's collection of flagged genes, researchers can classify a cell as a muscle, skin or other type of cell.

"This is the new era of using available data to make really new hypotheses and new discoveries," Brunet said. "This paper exemplifies why it's nice to be at Stanford where we're embracing big data."

The study was published in the July 31 issue of *Cell*.

This identifying flag is a long molecule, abbreviated as H3K4me3, that attaches to the proteins associated with DNA called histones. Other researchers had spotted this flag, but no one had probed its prevalence or significance. It generally marks about 1,000 genes in each cell, but the genes flagged vary among types of cells, Brunet said.

The molecule does not cue the cells to make more of the proteins encoded by the genes it marks. Instead, Brunet said, she believes it regulates how frequently the DNA is transcribed, ensuring that the

critical proteins are produced methodically, like clockwork, rather than in spurts of rapid transcription followed by transcription-free gaps.

Uncharted territory

"I think the notion of transcriptional consistency is new, and it's very important," Brunet said. "This is completely uncharted territory."

Brunet and her team searched computerized data sets for the flag and genes associated with it in a variety of cell types and species and built a new database available for other researchers— bddb.stanford.edu —to examine the flag's association with genes in a variety of cells.

The researchers also mapped the flagged genes in mouse neural stem cells, the regenerative cells of the adult brain. The flag identified previously recognized genes that were critical, but it also marked several less well-understood genes, Brunet said. Researchers could also work backwards, using the flagged genes with known functions to figure out the cell type.

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The lead authors of the study are postdoctoral scholar Bérénice Benayoun, PhD; graduate student Elizabeth Pollina; and Duygu Ucar, PhD, a former postdoctoral scholar who is now an assistant professor at The Jackson Laboratory for Genomic Medicine in Connecticut.

In the future, Brunet said, her team plans to examine the molecular flag's role in maintaining a cell's identity when faced by environmental changes, as well as its role in aging.

Provided by Stanford University Medical Center