CORNELL CHRONICLE

Proteins unspool DNA so cells can take on unique properties

By Krishna Ramanujan | January 20, 2021

Biologists have long wondered how complex organisms contain a variety of dramatically different types of cells with specialized functions, even though all of those cells are genetically identical.

New research reveals how proteins, called "pioneer transcription factors," help turn on key genes that give cell types their unique properties and functions.

These pioneer factors, it turns out, help unspool tightly wound coils of DNA so that genetic blueprints in genes can be read and proteins that play roles in biological processes can be made.

The study in fruit flies, "**Pioneer-like Factor GAF Cooperates with PBAP (SWI/SNF) and NURF (ISWI) to Regulate Transcription** (http://genesdev.cshlp.org/content/35/1-2/147)," was published Dec. 10 in the journal Genes & Development.

"We know pretty well what pioneer factors are and what they do, but what we don't know is how they work exactly," said first author Julius Judd, a graduate student in the lab of senior author **John Lis** (https://mbg.cornell.edu/people/john-lis/), professor of molecular biology and genetics in the College of Agriculture and Life Sciences.

In a cell's nucleus, DNA is bound around a collection of histone proteins called nucleosomes. "DNA is wrapped around it and so the backside of the DNA is inaccessible to recognition because it's up against these proteins," Lis said.

As a result, the transcription factors and machinery required to read DNA sequences for making proteins can't access these genetic codes. Genes therefore exist in a default "off" state until the DNA can be accessed and the codes can be read.

In the study, the researchers focused on a suspected pioneer transcription factor found in fruit flies called GAGA-factor (GAF). Previous work in Lis' lab has shown that GAF binds to target genes and removes nucleosomes; that exposes DNA sequences that mark where transcription of a gene begins, called a promoter sequence.

Research in other labs also suggested that GAF plays a role in embryonic development. And the researchers had evidence that GAF interacts with two different complexes called remodelers, which catalyze the process of removing the nucleosomes from DNA. All of this evidence led Lis, Judd and colleagues to believe that GAF was indeed a pioneer factor.

To test their hypothesis, Judd ran a number of different genome-wide assays to monitor transcription; how accessible the chromatin (spooled DNA) is for transcription; where GAF binds; and the cellular levels of RNA that are translated into protein. They applied these assays both to untreated Drosophila cells and cells where GAF was depleted.

The studies revealed that when GAF binds to a target gene, it recruits a remodeler called PBAP, which

removes these nucleosomes and creates an accessible tract of DNA for transcription. Furthermore, at some genes nucleosomes immediately downstream of the promoter also need to be moved. In those cases, GAF relies on a different remodeler, called NURF, to push the first nucleosome along the gene out of the way to make it easier for the transcription machinery to transcribe the DNA.

“We found one pioneer factor that can interact with both remodelers and act at different steps in the process of transcription. That is what is particularly novel,” Lis said.

Prior evidence has identified remodeling complexes almost identical to PBAP and NURF in yeast, and there are suggestions that this process occurs in mice and possibly mammals. “We think the way these remodelers are working is a deeply conserved and the conclusions are broadly applicable,” Judd said.

Fabiana Duarte, Ph.D. ’16, a postdoctoral researcher at Harvard, is a co-author of the study.

The study was funded by the National Institutes of Health.

MEDIA CONTACT

Gillian Smith
gillian.smith@cornell.edu
(mailto:gillian.smith@cornell.edu)
607-254-6235 (tel:607-254-6235)

YOU MIGHT ALSO LIKE

Genetic transcription ‘pause’ is focus of NASA grant (/stories/2018/04/genetic-transcription-pause-focus-nasa-grant)

Engineered bacteria churn out cancer biomarkers (/stories/2020/09/engineered-bacteria-churn-out-cancer-biomarkers)