

Controlling embryonic fate by association

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Association determines fate in embryonic stem cells, said Baylor College of Medicine researchers in a report that appears in the current issue of the journal *Nature Cell Biology*.

“These findings provide models of how the embryonic stem cell is maintained in its flexible state,” said Dr. Zhou Songyang, professor of biochemistry and molecular biology at BCM and senior author of the report. “It provides another hint as to how gene transcription is controlled in embryonic stem cells.”

One aim of embryonic stem cell research is to understand how the cells determine whether they will keep dividing and maintain a pool of embryonic cells, or start the process of cellular differentiation that results in different cell types.

Songyang and his colleagues found that two critical embryonic cell proteins – Nanog and Oct4 – associate with specific components that are parts of transcription repression complexes. These complexes affect the way that genes are expressed and carry out their tasks in the cell.

A special complex called NODE (Nanog and Oct4-associated Deacetylase) contains a critical component called Mta1 along with histone deacetylases. NODE associates with Nanog and Oct4 to control the fate of embryonic stem cells, said Songyang.

Histones are critical parts of genomic DNA structures or chromatins, acting as “spools” around which the genetic material winds in the

nucleus. The DNA wraps more tightly when deacetylase removes the acetyl tails from the histones. The tight wrapping makes it hard for genes to be transcribed into the message that allows them to carry out their roles in the cell.

“Think of it as the parts of a car,” said Songyang. “If you think of Nanog as the engine that drives it, you realize that the car still needs accessories like wheels, the tailpipe, etc. We are interested in the big machinery of which proteins (like Nanog) are the drivers. We want to understand the enzymatic activities of the complexes. Then we need to identify the individual parts and ask the big question: ‘How do different parts work together and why do you need special parts’”

“We noticed that there are many histone deacetylases,” he said. “Nanog uses these proteins to control gene expression and maybe also the chromatin state. When there is deacetylation, the gene is in a passive state.”

“The embryonic stem cell is always at the stage of deciding whether to divide (and make more embryonic stem cells) or to differentiate,” Songyang said. “All the extrinsic and intrinsic signals make the life of the embryonic stem cell transient. In other words, it has to be ready to go down either road.”

“It becomes an interesting question,” said Songyang. “Such a demanding state of readiness may mean that the embryonic stem cell requires a different complex at the chromatin than the somatic (or differentiated cell).”

Source: Baylor College of Medicine

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