

Gene related to aging plays role in stem cell differentiation

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A gene shown to play a role in the aging process appears to play a role in the regulation of the differentiation of embryonic stem cells, according to researchers from the Center for Stem Cell Biology and Regenerative Medicine and the Department of Medicine at Thomas Jefferson University.

In the study, published online in the journal *Aging Cell*, the researchers identified a protein interaction that controls the silencing of Oct4, a key transcription factor that is critical to ensuring that [embryonic stem cells](#) remain pluripotent. The protein, WRNp, is the product of a gene associated with Werner syndrome, an autosomal recessive disorder hallmarked by premature aging. The [gene expression](#) in Werner syndrome closely resembles that of normal aging, and as a result, Werner syndrome is an accepted model of aging.

They first found that WRNp accumulates at the Oct4 [promoter](#) in differentiating stem cells. They then found that WRNp interacts with another protein called Dnmt3b to control [DNA methylation](#) at the Oct4 promoter, according to researchers led by René Daniel, M.D., Ph.D., associate professor of Medicine.

Previously, Dnmt3b was identified to be a key player in the DNA methylation of the Oct4 promoter. DNA methylation of the Oct4 promoter inactivates the Oct4 gene. The inactivation, or silencing, of this gene is necessary for stem cell differentiation.

"We showed that the depletion of WRNp blocked the recruitment of Dnmt3b to the Oct4 promoter, and resulted in reduced methylation," Dr. Daniel said. "The reduced DNA methylation was associated with continued Oct4 expression, which resulted in attenuated differentiation."

Until now, the focus of studies on the role of WRNp in aging has been on telomeres. These studies have shown that telomeres undergo accelerated shortening and loss in Werner syndrome cells. But it remains to be shown if this is the major role that WRNp plays in the [aging process](#).

"These results reveal a novel function of WRNp, and demonstrate that WRNp controls a key step in pluripotent stem cell differentiation," Dr. Daniel said. "Our data support the emerging hypothesis that attenuated stem cell differentiation is involved in aging. This lack of differentiated cells may contribute to failure to maintain organ or tissue function in the later stages of life."

Provided by Thomas Jefferson University

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