Lab sheds light on molecular machinery required for translation of histone crosstalk

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The Stowers Institute's Shilatifard Lab has published findings that shed light on the molecular machinery required for the translation of histone crosstalk, or communication between histones.

Published in today's issue of *Cell*, "Histone Crosstalk between H2B Monoubiquitination and H3 Methylation Mediated COMPASS" examines the yeast homologue of the mammalian MLL complex, a histone methylase involved in the development of childhood Acute Myeloid Leukemia.

Histones are important components of chromatin, the packing material surrounding chromosomal DNA. Also, histones play an important role in the regulation of gene expression. Histone H3 can be modified by methylation and this modification is an essential part of gene expression.

Several years ago, the Shilatifard Lab identified the first histone H3 lysine 4 (H3K4) methyltransferase, known as COMPASS, in yeast. Soon thereafter, it was established that the MLL protein in humans also existed in a COMPASS-like complex capable of methylating H3K4. In 2002, the Shilatifard Lab reported the existence of the first histone crosstalk between histone H2B monoubiquitination for the regulation of histone methylation by COMPASS.

"We now know that this mode of histone crosstalk is highly conserved from yeast to humans, but until now, its molecular mechanism of action was poorly understood. Jung-Shin Lee, a Postdoctoral Research Associate in my laboratory, was able to demonstrate the molecular machinery required for the translation of this histone crosstalk," said Ali Shilatifard, Ph.D., Investigator and senior author on the paper.

This work demonstrated that the Cps35 subunit of COMPASS is required to translate the crosstalk between H2B monoubiquitination and H3 methylation by COMPASS.

"Given the importance of histone methylation by the MLL complex and leukemia pathogenesis, defining the molecular machinery involved in this process could be highly useful," said Dr. Shilatifard.

Source: Stowers Institute for Medical Research