

SUMO protein guides chromatin remodeler to suppress genes

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In an in vitro study, led by Grace Gill, PhD, Tufts University School of Medicine, researchers discovered how a protein called SUMO (Small Ubiquitin-related Modifier) guides an enzyme complex that alters the structure of chromatin to regulate expression of genes. Chromatin is a compacted mass of DNA and protein that make up chromosomes. The interaction between SUMO and the enzyme complex is of interest in the study of cancer and neurodegenerative diseases such as Alzheimer's, where aberrant gene expression and altered SUMO function are thought to be indicative of disease.

The [protein](#) called SUMO is known to chemically modify other proteins, called transcription factors, which in turn enables the meticulous regulation of genes. Gene regulation is a fundamental biological process that allows necessary genes to be turned on or off in specific cell types.

The researchers found that SUMO interacts with an enzyme complex (LSD1/CoREST/HDAC) that alters [chromatin](#) structure to regulate genes within cells. The researchers found that the interaction between SUMO and this enzyme complex is responsible for preventing aberrant expression. Aberrant [gene expression](#) is a common feature of cancer and other disorders and altered SUMO processes might contribute to neurodegeneration.

"We've only known for about 10 years that SUMO chemically modifies proteins. We have a good understanding of how SUMO modifies other proteins, but the actual mechanism of how this modification alters cell

function is not well known. Our study uncovers a fundamental aspect of how SUMO works, which has implications for many diseases. Until now, SUMO and LSD1/CoREST/HDAC have not been studied together; we've found out how they work together to turn off certain [genes](#)," says Gill.

The Gill Lab is continuing to investigate SUMO-dependent cell activity to delineate the complex genetic mechanisms that support gene regulation.

First author Jian Ouyang, PhD, is a postdoctoral associate in Gill's lab, formerly in the department of pathology at Harvard Medical School.

Senior author Grace Gill, PhD, is an associate professor at Tufts University School of Medicine and a member of the genetics and cell, molecular and developmental biology program faculties at the Sackler School of Graduate Biomedical Sciences at Tufts, formerly in the department of pathology at Harvard Medical School.

More information: Ouyang J, Shi Y, Valin A, Xuan Y, and Gill G. Molecular Cell. 2009 (April 24); 34(2): 145-154. "Direct Binding of CoREST1 to SUMO-2/3 Contributes to Gene-Specific Repression by the LSD1/CoREST1/HDAC Complex." Published online April 23, 2009, doi: 10.1016/j.molcel.2009.03.013

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