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Researchers identify how to switch off cancer cell genes

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A new study led by researchers at the University of Southern California (USC) identifies how genes are silenced in cancer cells through distinct changes in the density of nucleosomes within the cells.

The findings, published in the Nov. 13 issue of the journal *Cancer Cell*, will enable researchers to explore new therapies to switch the genes back on and may lead to novel treatments for human cancers, says study lead author Peter A. Jones, Ph.D., D.Sc., director of the USC/Norris Comprehensive Cancer Center and Distinguished Professor at the Keck School of Medicine of USC.

"The study shows for the first time exactly how genes get shut down in cancer cells," Jones says. "It identifies what the target looks like so that new therapies can be designed to turn them back on."

The study showed that silencing of transcription start sites in some cancer cells involves distinct changes in nucleosomal occupancy'or the density of nucleosomes'in the cell. Researchers found that three nucleosomes, almost completely absent from the start site in normal cells, are present in the methylated and silenced promoter, suggesting that epigenetic silencing may be accomplished by the stable placement of nucleosomes into previously vacant positions.

DNA cytosine methylation'the addition of a group of specific chemicals to a stretch of DNA that can lock or silence a gene'may ultimately lead to silencing by enabling the stable presence of nucleosomes at the start

sites of cancer-related genes, the study suggests.

"We believe these findings will contribute to the development of cancer therapies," Jones says. "We were surprised to find how rigid the inactive structure is, and how rapidly it can be dissolved by drug treatment."

Source: University of Southern California