Messenger RNA with FLASH

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A study from the University of North Carolina at Chapel Hill has identified a key player in a molecular process essential for DNA replication within cells.

The new findings highlight a protein called FLASH, already shown to play a role in initiating apoptosis, or programmed cell death. Apoptosis is a normal biochemical response that occurs when a cell is damaged beyond repair after viral infection or accumulation of mutations that could lead to uncontrolled cellular proliferation, or cancer. Apoptosis is also crucial to the developing embryo through selective cell death, which allows proper differentiation of physical structures, such as fingers and toes.

According to senior study author Zbigniew Dominski, Ph.D., associate professor of biochemistry and biophysics at UNC, the new study demonstrates that FLASH is also required for the proper synthesis of histone messenger RNA, which gives rise to histone proteins.

Histones are the chief protein components of chromatin and act as a scaffold allowing packaging of DNA into a condensed form that fits inside the nucleus of a cell. As the DNA interacts with histones and with metabolic signals from within the cell, these proteins help regulate gene expression.

"Our study suggests for the first time that a potential link exists between the processes of histone messenger RNA formation and apoptosis," Dominski said. "FLASH is crucial for the production of histone

messenger RNA, without which the cell can't make the histone proteins around which DNA is packaged."

The research is described in the October 23rd issue of the journal *Molecular Cell*.

For the study, Dominski adapted a laboratory system that reproduces in the test tube what normally occurs in the cell when FLASH participates in the biochemical cleavage event that results in mature histone messenger RNA. This enabled his team to explore what might occur when FLASH was added or removed.

"We could then figure out exactly what portion of FLASH would restore the protein's function in generating histone mRNAs and remarkably, only the first 100 or so amino acids are required. The remaining 2,000 amino acids of this large protein likely control other processes in the cell, including apoptosis and DNA replication" he explained.

Source: University of North Carolina School of Medicine (news : web)

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