Histone H2B Ubiquitylation Slows DNA Replication and Promotes Genome Stability under Stress

A research team led by Dr. Cheng-Fu Kao, an Assistant Research Fellow at the Institute of Cellular and Organismic Biology together with researchers from several international institutions recently discovered that a histone modification, H2B ubiquitylation (H2Bub), plays a role in regulating DNA replication. They found that under replication stress, H2Bub ensures the stability and progression of DNA replication. The findings were published in the academic journal *PLoS Genetics*, on October 2, 2014.

DNA replication is the key process for transmission of genetic information; however, a variety of endogenous or exogenous stresses can halt or alter replication, which may result in genomic instability. Aberrant DNA replication results in mutations and chromosome rearrangements that may be associated with human disorders. The DNA of multi-celled organisms is wrapped in histones to form nucleosomes, and these nucleosomes constitute chromatin fiber. DNA replication occurs within the context of the complex chromatin structure. The research team demonstrated that when DNA replication is disturbed, histone H2B ubiquitylation promotes chromatin structure stability, and as such, histone H2B ubiquitylation acts akin to the brakes on a train to slow the rate of DNA replication, thereby preventing errors, DNA breaks, and other adverse consequences.

This study used yeast as a model to investigate how chromatin structure affects DNA replication. However, the molecular mechanisms of human cells are very similar to those in the simple single-cellular organism.

Dr. Kao said the results of the study prove that histone H2B ubiquitylation is directly involved in regulating activation of the DNA repair checkpoint (DNA Damage Checkpoint), and the results provide an opportunity to learn more about how cells maintain genome stability.

The co-first authors of the study are Dr. Chia-Yeh Lin and Research Assistant Miss Meng-Ying Wu.

The complete article entitled: "H2B Mono-ubiquitylation Facilitates Fork Stalling and Recovery during Replication Stress by Coordinating Rad53 Activation and Chromatin Assembly".

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Two of the research teams that collaborated on this study in Taiwan (led by Dr. Kao) and France (led by Dr. Didier Devys) also recently reported a novel role of H2B ubiquitylation in transcription regulation in another paper. The paper was published on September 15, 2014 in the journal Genes & Development.

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The full-length articles can be found at the websites of PLoS Genetics and Genes & Development at:
http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1004667
http://genesdev.cshlp.org/content/28/18/1999.long