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H3K9 methyltransferase G9a negatively regulates UHRF1 transcription during leukemia cell differentiation

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Histone H3K9 methyltransferase (HMTase) G9a-mediated transcriptional repression is a major epigenetic silencing mechanism. UHRF1 (ubiquitin-like with PHD and ring finger domains 1) binds to hemimethylated DNA and plays an essential role in the maintenance of DNA methylation. Here, we provide evidence that UHRF1 is transcriptionally downregulated by H3K9 HMTase G9a. We found that increased expression of G9a along with transcription factor YY1 specifically represses UHRF1 transcription during TPA-mediated leukemia cell differentiation. Using ChIP analysis, we found that *UHRF1* was among the transcriptionally silenced genes during leukemia cell differentiation. Using a DNA methylation profiling array, we discovered that the *UHRF1* promoter was hypomethylated in samples from leukemia patients, further supporting its overexpression and oncogenic activity. Finally, we showed that G9a regulates UHRF1-mediated H3K23 ubiquitination and proper DNA replication maintenance. Therefore, we propose that H3K9 HMTase G9a is a specific epigenetic regulator of UHRF1.

Biography

Sang-Beom Seo has completed his PhD from State University of New York/Binghamton and Post-doctoral studies from Pennsylvania University School of Medicine. He is the Chairperson of Department of Life Science, Chung-Ang University in Seoul, Korea. He has published more than 65 papers in reputed journals.

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