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FOXO1 degradation by G9a-mediated methylation promotes cell proliferation in colon cancer

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Post-translational modifications of Forkhead family transcription factor (*FOXO1*) have been known as important regulatory modes for its diverse activities. Several modifications of *FOXO1* including acetylation, phosphorylation and ubiquitination were reported. However, lysine methylation of *FOXO1* has not been identified yet. Here, we report that *FOXO1* is methylated by G9a at K273 residue in vitro and in vivo. Methylation of *FOXO1* by G9a increased interaction between *FOXO1* and a specific E3 ligase skp2 and decreases *FOXO1* protein stability. In addition, G9a expression was increased by insulin and resulted in insulin-mediated *FOXO1* degradation by K273 methylation. Tissue array analysis indicates that G9a was overexpressed and *FOXO1* was decreased in human colon cancer. Cell proliferation assays revealed that cell proliferation is increased by G9a-mediated *FOXO1* methylation. In addition, fluorescence-activated cell sorting (FACS) analysis indicated that apoptosis is more increased in presence of *FOXO1* compare with *FOXO1* knock out cells. Therefore, G9a specific inhibitor, BIX-012494 can regulate cell proliferation and apoptosis via inhibition of *FOXO1* methylation.

Biography

Sang-Beom Seo has completed his PhD from The State University of New York at Binghamton, USA. He is currently working as a Professor in Chung-Ang University, Seoul, South Korea.

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