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마우스 배아줄기세포에서 SIRT1의 etoposide에 의한 DNA damage response 조절효과

전북대학교 의과대학 내과학교실

응웬탕 퉁, 정유진, 노정미, 강경표, 이식, 박성광, 김원

SIRT1 Modulates Embryonic Stem Cell Programmed Death by Regulation of DNA Damage Response

Nguyen-Thanh Tung, Yujin Jung, Jeong Mi Noh, Kyung Pyo Kang
Sik Lee, Sung Kwang Park, Won Kim

Department of Internal Medicine, Chonbuk National University Medical School

An orchestrated signaling cascade termed the DNA damage response (DDR) leads to the cellular response to damage, including cell cycle arrest, DNA repair and induction of apoptosis. Etoposide is widely used in the treatment of cancer including leukemia. Pluripotent stem cells have a highly efficient DNA repair system that becomes less efficient during differentiation. SIRT1, also known as NAD-dependent deacetylase, involved in various different normal physiologic and disease processes. In this study, we evaluated whether SIRT1 had an effect on embryonic stem cell programmed death in response to DNA damage induced by etoposide. Phosphorylation of H2AX, Chk1, and P53 was more strongly activated in Sirt1+/+ mESC than in Sirt1-/- mESC at equivalent doses of etoposide. Acetylation of P53 was more increased in Sirt1-/- mESC than that of Sirt1+/+ mESC. Decreae of SIRT1 reduced accumulation etoposide-induced intracellular reactive oxygen species. Moreover, flow cytometric analysis of cell cycle progression demonstrated that SIRT1 extend the cell cycle arrest induce by etoposide. The protein levels of LC3-II was down-regulated in Sirt1-/- mESC. Taken together, these findings indicate that SIRT1 modulates embryonic stem cell programmed cell death in response to DNA damage

Key Words: 배아줄기세포, 에토포사이드, DNA손상반응, SIRT1
Embryonic stem cells, Etoposide, DNA damage response, SIRT1