

Cell cycle arrest by jun dimerization protein 2 (JDP2) involves indown-regulation of cyclin A2

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Progression of the cell cycle in mammalian cells is regulated by cyclin-dependentkinases (CDKs) and cdkinhibitors. Cyclin A is a rate-limiting component required for both the initiation of DNA synthesis and entry into mitosis. Jun dimerization protein 2 (JDP2), a member of the AP-1 family, is able to form homodimers, and, also, heterodimers with other members of the AP-1 family, such as c-Jun, JunB, JunD and ATF2, and with a member of the C/EBP family, C/EBP γ . JDP2 most likely participates in the repression of transcription via multiple mechanisms, which include DNA-binding competition and inactivation of formation of heterodimer with other members of the AP-1, recruitment of HDAC 3, inhibition of histone acetylation (H4K16Ac, H4K8Ac, H3Ac) and the direct regulation of chromatin assembly (1). However, the details of the physiological role of JDP2 in cell fate remain unknown. We previously reported that “knock-out” of Jdp2 affects adipocyte differentiation (2) and resistance to replicative senescence (3) and these regulations were proceeded through inhibition of histone acetylation (1, 2) and methylation (3).

We report here a novel role for JDP2 as a regulator of the progression of normal cells through the cell cycle. Fibroblasts derived from embryos of Jdp2KO mice proliferated more rapidly and formed more colonies than wild-type fibroblasts. JDP2 was recruited to the promoter of the gene for cyclin A2 (*ccna2*) at AP-1 site. Cells lacking Jdp2 had elevated levels of cyclin A2 mRNA. Moreover, reintroduction of JDP2 resulted in repression of transcription of *ccna2* and of cell cycle progression. Thus, transcription of the gene for cyclin A2 appears to be a direct target of JDP2 in the suppression of cell proliferation (4)(5).

Biography

Kazunari K. Yokoyama completed his Ph.D. at University of Tokyo, Department of Science, Division of Biophysics and Biochemistry. He has published more than 230 papers included Nature, Science, Nature Genetics, Molecular Cell, Genes & Development, Nature Structural Biological Chemistry, EMBO J and Proc Natl Acad Sci USA and serving as peer reviewer of Japanese International Awards of Sciences, Japan Awards and member of American Association for Cancer Research, American Society for Microbiology and International Stem Cell Research.

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