Abstract citation ID: bvac150.936

Genetics & Development

ODP281

JDP2 Interacts with MDM2 and Decreases MDM2-Mediated p53 Repression

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JDP2 and ATF3 belong to the family of AP-1 protein. JDP2, a transcription factor, can bind to AP-1 site as well as cAMP responsive element (CRE) site in numerous cis-elements of the target genes. JDP2 has been shown to be involved in cancer development and cell-cycle regulation. Previously, we had shown that JDP2 activates Mc2r transcriptional activity. Since ATF3 and JDP2 share high similarity in C-terminal domains with identities of 65% and ATF3 can bind to p53 and regulate p53 transcriptional activity and stability, we hypothesized that JDP2 may have ability to regulate p53 and MDM2 (the main regulator of p53). Herein, we demonstrate for the first time the relationship between JDP2 and MDM2. First, we found that JDP2 can directly bind to MDM2. Secondly, though ATF3 dose-dependently increases MDM2 level, JDP2 dose-dependently decreases MDM2 level. Moreover, the C-terminus of JDP2 is required for regulation of MDM2 level. Finally, using p53RE-Luc (14X) for p53 transactivation study, while MDM2 decreases p53 transactivation, JDP2 dose-dependently abolishes MDM2-mediated p53 repression. Taken together, our results demonstrate that JDP2 directly binds to MDM2 and reduces MDM2-mediated p53 repression, suggesting that JDP2 is a novel regulator of MDM2. Since p53-MDM2 pathway is an important regulator in endocrinology and reproduction, our finding provides a new layer of regulatory mechanism for fertility, tumor suppression, and longevity.

Presentation: No date and time listed