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Regulation of p73 and its role in suppressing metastasis

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p73 is a member of the p53 tumor suppressor family, which transactivates p53-responsive genes and mediates DNA damage response. Similar to p53, p73 is also maintained at a very low level in non-stressed cells but it rapidly gets induced and activated upon genotoxic insults. The objective of our study was to find out novel interactors of p73 which distinctively regulates its stability and activity in normal state and upon DNA damage. We performed a sequential immunoprecipitation screen to identify p73-associated proteins which specifically interact with p73 under unstressed and genotoxic stress conditions. Our differential proteomics screening lead us to identification of many p73-associated proteins. Our results demonstrated that, TRIM28, a RING-type E3 ubiquitin ligase interacts with p73 under unstressed conditions but not after etoposide treatment. TRIM28 ubiquitylates and targets p73 for proteasome-mediated degradation in normal conditions; however, upon genotoxic stress, phosphorylation of p73 at tyrosine 99 position by c-Abl kinase leads to abrogation of its interaction with TRIM28 thereby promoting p73 stabilization. On the contrary end another protein, MED15, only interacts with tyrosine 99 phosphorylated p73 and it serves as a co-activator of p73. Abrogation of MED15 expression leads to decline in p73-mediated transactivation and disrupts p73 tumor suppressor and anti-metastatic functions. Furthermore, p73 is emerging as an important player in suppression of metastasis. In this direction, we performed a customized quantitative RT-PCR array analysis. We identified several novel downstream targets of p73 which have anti-metastatic functions. Thus our work provides extensive insights regarding anti-metastatic role of p73.

Biography

Yatendra Kumar Satija has completed his PhD from National Institute of Immunology. He is currently working as DST-INSPIRE Faculty at Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi. He has published four papers in reputed journals (publications in *Oncogene*, *Molecular Cell*, *International Journal of Cancer and Transcription*). He has been serving as an Editorial Board Member and Reviewer Board Member of several national and international journals. He has received many awards including DST International Travel Support Award, CSIR foreign travel grant, Best Award on National Science Day Competition at NII, CSIR-JRF etc.

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