

## Mutant p53 gain-of-function induces epithelial-mesenchymal transition through modulation of the miR-130b-ZEB1 axis

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The tumor suppressor gene p53 has been implicated in the regulation of epithelial-mesenchymal transition (EMT) and tumor metastasis by regulating microRNA (miRNA) expression. Here, we report that mutant p53 exerts oncogenic functions and promotes EMT in endometrial cancer (EC) by directly binding to the promoter of miR-130b (a negative regulator of ZEB1) and inhibiting its transcription. We transduced p53 mutants into p53-null EC cells, profiled the miRNA expression by miRNA microarray, and identified miR-130b as a potential target of mutant p53. Ectopic expression of p53 mutants repressed the expression of miR-130b and triggered ZEB1-dependent EMT and cancer cell invasion. Loss of an endogenous p53 mutation increased the expression of miR-130b, which resulted in reduced ZEB1 expression and attenuation of the EMT phenotype. Furthermore, re-expression of miR-130b suppressed mutant p53-induced EMT and ZEB1 expression. Importantly, the expression of miR-130 was significantly reduced in EC tissues, and patients with higher expression levels of miR-130b survived longer. These data provide a novel understanding of the roles of p53 gain-of-function mutations in accelerating tumor progression and metastasis through modulation of the miR-130b-ZEB1 axis.

### Biography

Peixin Dong obtained his medical degree at the Harbin Medical University in 1997 and a PhD from the Department of Gynecology at Hokkaido University in 2008 with a thesis entitled 'p53 dominant-negative mutant R273H promotes invasion and migration of human endometrial cancer. He worked as a gynecologist in Harbin Medical University (1997-2002) and Fudan University (2008-2010). From 2002-2004, he worked in the Department of Obstetrics & Gynecology, Fukuoka University, Japan as a visiting scientist. Since 2010, he became an assistant professor in the Department of Gynecology, Hokkaido University, Japan. His research focuses on the molecular mechanisms of cancer metastasis, especially on the roles of mutant p53 Gain-of-Function in endometrial cancer progression and the regulatory effects of microRNAs on epithelial-mesenchymal transition.

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