

MDM2 regulates TP53 stability and EGFR controls BRCA1 expression

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Abstract

We investigated the regulatory relationship between TP53 and MDM2 in human cells. TP53 is a tumor suppressor that activates downstream targets including CDKN1A. Here we show that MDM2 negatively regulates TP53 protein stability, and that EGFR signaling modulates BRCA1 expression in breast carcinoma cells.

Methods

HeLa and MCF7 cells were cultured under standard conditions. We performed CRISPR knockout of MDM2 and measured TP53 levels by western blot. EGFR was inhibited with gefitinib and BRCA1 transcript abundance was quantified by RT-qPCR. RNA sequencing was used to profile transcriptomic changes.

Results

Knockout of MDM2 increased TP53 protein levels approximately threefold, confirming that MDM2 regulates TP53. Loss of TP53 reduced CDKN1A induction. EGFR inhibition decreased BRCA1 expression, indicating that EGFR regulates BRCA1 in this context. VEGFA was upregulated following TP53 loss.

Discussion

Our findings establish that the MDM2-TP53 axis controls CDKN1A activation and that EGFR signaling is an upstream regulator of BRCA1. These perturbation experiments support a model in which TP53 is a master regulator of the cell-cycle response.