OTUD1 chemosensitizes triple-negative breast cancer to doxorubicin by modulating P16 expression

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**Objective**

Chemotherapy remains a critical component of triple-negative breast cancer (TNBC) treatment; however, patients often develop resistance to chemotherapeutic agents. In this study, we aimed to analyze the expression level of OTUD1 in triple-negative breast cancer and explore its role and molecular regulatory mechanism in chemotherapy resistance of triple-negative breast cancer.

**Methods**

The expression of OTUD1 in breast cancer and its prognosis were analyzed by bioinformatics and the CCK-8 cell proliferation assay and colony formation assay were used to detect whether OTUD1 was involved in the regulation of TNBC cell proliferation. Moreover, the potential interaction proteins of OTUD1 were analyzed by immunoprecipitation and mass spectrometry, and the interaction between OTUD1 and 16 was further clarified by protein co-immunoprecipitation, the expression levels of OTUD1 and P16 in triple negative breast cancer tissues were analyzed by immunohistochemistry and Western blot. In addition, the tumor-bearing nude mouse model was established to further evaluate the role of OTUD1 in regulating the sensitivity of TNBC to doxorubicin in vivo.

**Results**

Our results indicated that upregulation of OTUD1 expression inhibits TNBC cell proliferation and enhances its sensitivity to doxorubicin. Additionally, rescue experiments confirmed that the chemosensitizing effect of OTUD1 overexpression could be reversed by the inhibition of P16.Moreover, Animal experiments showed that OTUD1 enhanced the chemosensitivity of TNBC cells to DOX in vivo.

**Conclusions**

Therefore, our findings reveal that OTUD1 sensitizes TNBC cells to DOX by upregulating P16 expression, suggesting a potential new diagnostic biomarker and therapeutic target for the future treatment of TNBC.