**Abstract form**

Targeting the USP7-CDK1 axis suppresses estrogen receptor-positive breast cancer progression

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**Purpose**

Treatment for estrogen receptor-positive breast cancer (ERPBC) in the metastatic setting comprises endocrine therapy with targeted cyclin-dependent kinase (CDK) 4/6 inhibitors, which are effective for a median of approximately 2 years. Recently, new treatments have been explored to improve outcomes for patients with advanced or metastatic ERPBC, including novel anti- ERPBC genes and combination therapies that target multiple pathways involved in the growth and survival of ERPBC. This study investigated the additional characteristics of ubiquitin-specific-processing protease 7 (USP7) in ERPBC by exploring the relationship between the expression of USP7 and CDK1. We investigated the expression and effects of USP7 in ERPBC and demonstrated that CDK1 levels are regulated by USP7, which promotes tumor progression in ERPBC.

**Materials and Methods**

In-vitro and in-vivo xenograft studies were carried out to assess the regulatory role of USP7 in ERPBC.

**Results**

Inhibition of USP7 activity repressed proliferation, induced apoptosis, suppressed migration and invasive activities, and reversed the epithelial-mesenchymal transition of ERPBC. Mass spectrometry analysis indicated that USP7 regulates CDK1 expression, which is highly expressed and correlates with a poor overall survival rate in ERPBC. USP7 directly interacts with CDK1 and regulates its stability. Furthermore, targeting USP7-CDK1 axis exhibits significant therapeutic activity in a xenograft mouse model and primary cell models of ERPBC.

**Conclusion**

The current study investigated the function and molecular pathways of USP7 in ERPBC and demonstrated that USP7 plays a critical role by targeting CDK1. This study also demonstrated that targeting USP7-CDK1 axis could serve as a therapeutic strategy for overcoming the endocrine resistance of ERPBC.