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Long noncoding RNA LOXL1-AS1 regulates prostate cancer cell proliferation and cell cycle progression through miR-541-3p and CCND1

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ABSTRACT

Prostate cancer is one of the most frequent malignancies affecting men. Long non-coding RNAs (lncRNAs) are involved in the pathogenesis of prostate cancer. LncRNA LOXL1-AS1 participates in the pathogenesis of the exfoliation syndrome. However, the role of LOXL1-AS1 in cancer remains largely unknown. Here, we found that LOXL1-AS1 down-regulation inhibited prostate cancer cell proliferation and cell cycle progression. RNA sequencing analysis revealed that it regulates the expression of cell cycle-related genes. LOXL1-AS1 is predominantly distributed in the cytoplasm, where it interacts with miR-541-3p. In addition, miR-541-3p targets the cell cycle regulator CCND1 in prostate cancer cells. LOXL1-AS1 down-regulation inhibits the expression of CCND1 and cell cycle progression, whereas these effects are abolished upon miR-541-3p suppression. In summary, our study revealed that LOXL1-AS1 regulates prostate cancer cell proliferation and cell cycle progression through miR-541-3p and CCND1. Modulation of their levels may be used to treat prostate cancer.

1. Introduction

Prostate cancer is one of the most common malignancies affecting men and is a tremendous health threat [1]. Elucidation of the molecular mechanism leading to the occurrence of prostate cancer is of great importance for the treatment of this cancer. Although much progress has been made, the pathogenesis of prostate cancer still needs to be clarified.

Long non-coding RNAs (lncRNAs) are a class of non-coding RNAs that are more than 200 nucleotides in length and lack coding capabilities [2,3]. LncRNAs participate in the regulation of various cellular processes, including apoptosis, differentiation, and proliferation [4–7]. The expression of lncRNA is precisely regulated under physiological conditions and its dysregulation leads to the pathogenesis of various diseases [8,9]. Aberrant expression of lncRNA correlates with the pathogenesis of different types of cancers, in which they participate in cell signaling [2,7,10]. Moreover, studies have found that lncRNAs play an important role in the pathogenesis and progression of prostate cancer [11]. However, limited lncRNAs related to prostate cancer have been characterized, which warrants further investigation.

LOXL1-AS1 is a long non-coding RNA that is encoded on the opposite strand of the lysyl oxidase-like 1 (*LOXL1*) gene. It plays a functional role in cellular stress response and correlates with the development of the exfoliation syndrome [12]. LOXL1-AS1 is highly expressed in the mesenchymal subtype (MES) of glioblastoma and promotes the expression of MES signature via the NF-κB pathway [13]. Another study found that LOXL1-AS1 regulates the proliferation and metastasis of medulloblastoma by activating the PI3K/AKT pathway [14]. However, the role of LOXL1-AS1 in cancer remains largely unknown and whether LOXL1-AS1 plays an important role in prostate cancer needs to be elaborated.

In this study, we found that LOXL1-AS1 is required for proliferation and cell cycle progression in prostate cancer cells. The results demonstrate that LOXL1-AS1 is predominantly located in the cytoplasm and functions as miRNA sponge to regulate the expression of miR-541-3p. In addition, we found that LOXL1-AS1 regulates prostate cancer cell proliferation and cell cycle progression through CCND1, which is the target of miR-541-3p. In summary, our study

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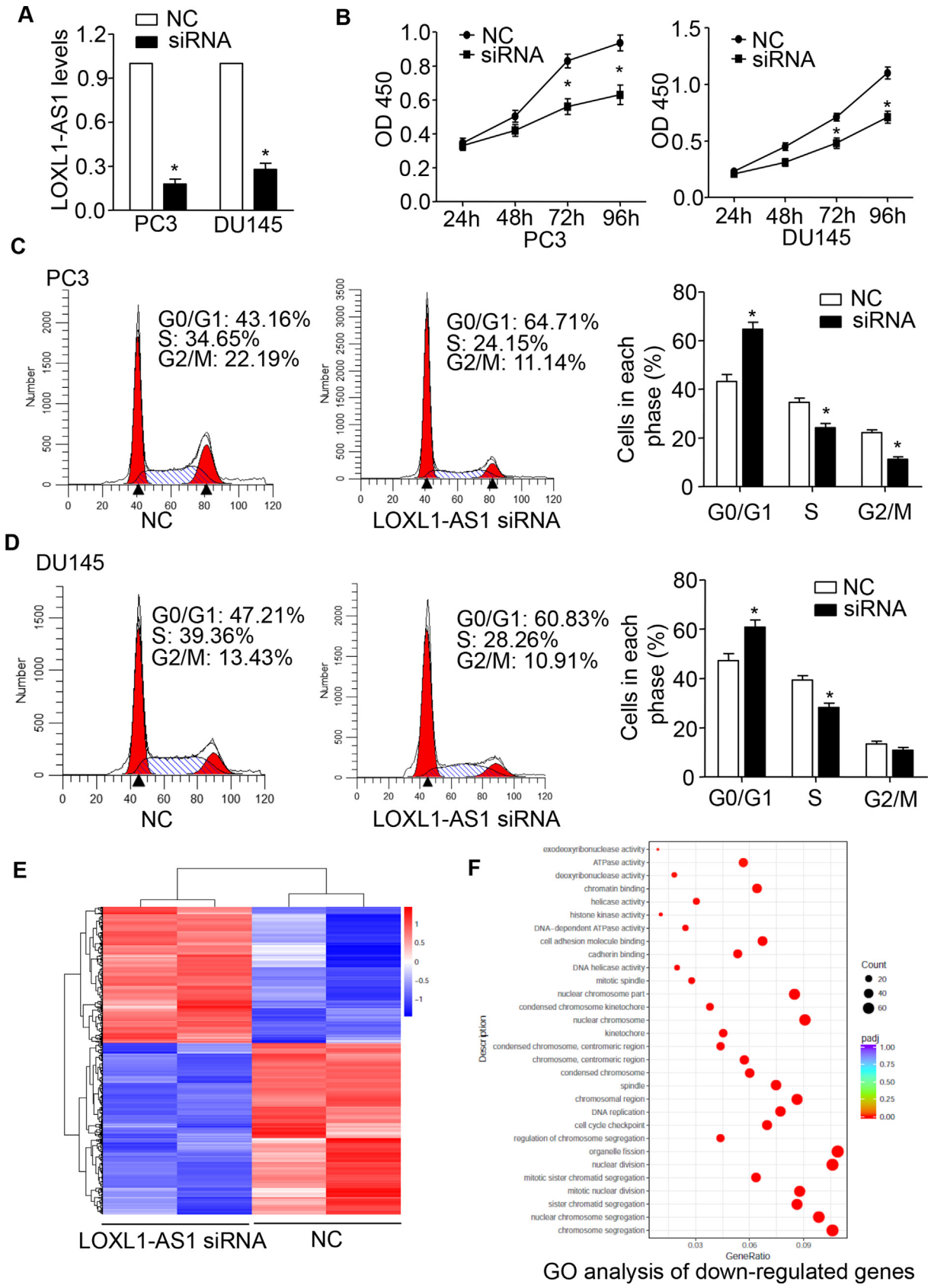

Fig. 1. Long non-coding RNA (lncRNA) LOXL1-AS1 regulates prostate cancer cell proliferation and cell cycle progression.
(A) The expression of LOXL1-AS1 is significantly knocked down by LOXL1-AS1 siRNA. PC3 or DU145 prostate cancer cells were transfected with 50 nM negative control (NC) or siRNA targeting LOXL1-AS1 (siRNA), and the expression of LOXL1-AS1 was analyzed by qRT-PCR. $^{*}P < 0.05$ versus NC group. (B) Knockdown of LOXL1-AS1 significantly inhibits the proliferation of prostate cancer cells. PC3 or DU145 cells were transfected with NC or LOXL1-AS1 siRNA (siRNA) and the cell proliferation was analyzed by CCK-8 assay at the

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