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Long non-coding RNA MNX1-AS1 promotes hepatocellular carcinoma proliferation and invasion through targeting miR-218-5p/COMMD8 axis

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ABSTRACT

Long noncoding RNAs (lncRNAs) are involved in tumorigenesis. Previously, lncRNA MNX1-AS1 was reported to increase the malignancy of ovarian cancer, cervical cancer and lung cancer. However, the potential function of MNX1-AS1 in hepatocellular carcinoma (HCC) remains unclear. In this study, we found that MNX1-AS1 was remarkably upregulated in HCC tissues and cell lines. Furthermore, MNX1-AS1 overexpression was related to advanced stage and metastasis, and predicted poor prognosis. Loss-of-function assays showed that MNX1-AS1 knockdown suppressed the proliferation, migration and invasion of HCC cells *in vitro*. Further investigation indicated that MNX1-AS1 silencing delayed HCC growth *in vivo*. Mechanistically, we identified that MNX1-AS1 was a competing endogenous RNA (ceRNA) for miR-218-5p. We demonstrated that MNX1-AS1 promoted COMMD8 expression through sponging miR-218-5p, and then contributed to HCC progression. Restoration of COMMD8 significantly reversed the effects of MNX1-AS1 knockdown. Taken together, our findings demonstrated that MNX1-AS1 promoted the malignant properties of HCC through targeting miR-218-5p/COMMD8 pathway.

1. Introduction

Hepatocellular carcinoma (HCC) is a very common cancer worldwide and one of the leading causes of cancer-related death [1]. Because of high incidences of recurrence and invasiveness, the outcomes of HCC patients remain poor [2]. The five-year survival rate of HCC patients is quite low [3]. Although great efforts have been made, still there is no effective therapeutic strategy against HCC. Thus, it is urgently required to explore the molecular mechanism of HCC progression and develop novel therapeutic targets.

Long noncoding RNAs (lncRNAs) are a group of noncoding RNAs with over 200 nucleotides in length and little protein-coding potential [4]. LncRNAs exert important roles on human cancers [5]. Growing evidence has indicated that many lncRNAs are aberrantly expressed in tumor tissues, such as lymphoma [6], breast cancer [7], colorectal cancer [8] and HCC [9]. Besides, emerging studies reported that lncRNAs may be potential biomarkers for diagnosis and prognosis [10,11]. Moreover, accumulating researches show that lncRNAs could regulate several biological processes of tumor cells, including growth, survival, differentiation and metastasis [12]. For instance, lncRNA AFAP1-AS1 sponges miR-423-5p to promote metastasis of nasopharyngeal carcinoma [13]. LncRNA DGCR5 inhibits growth and invasion of HCC via regulating miR-346/KLF14 axis [14]. LncRNA SOX2OT contributes to metastasis of non-small-cell lung cancer by sponging miR-132 [15].

As a recently identified lncRNA, MNX1-AS1 has been reported to promote ovarian cancer cell proliferation and migration [16]. Recently, MNX1-AS1 was also found to promote progression of colon cancer and lung cancer [17,18]. However, the influence of MNX1-AS1 on HCC remains unclear. Here, we found that MNX1-AS1 expression was upregulated in HCC tissues and its upregulation predicted poor prognosis. We revealed that MNX1-AS1 knockdown suppressed the proliferation, migration and invasion of HCC cells through targeting miR-218-5p/COMMD8 pathway. Hence, our study identified a novel signaling of MNX1-AS1/miR-218-5p/COMMD8 axis involved HCC progression.

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