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FOXP4-AS1 participates in the development and progression of osteosarcoma by downregulating LATS1 via binding to LSD1 and EZH2

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ABSTRACT

Osteosarcoma (OS) is the most common malignant bone tumor in children and adolescents. LncRNA has been confirmed to participate in a variety of cancers. The purpose of this study was to explore the effect of FOXP4-AS1 on the development of osteosarcoma (OS) and its underlying mechanism. FOXP4-AS1 expressions in 60 OS tissues and paracancerous tissues were detected by qRT-PCR (quantitative real-time polymerase chain reaction). We confirmed that FOXP4-AS1 was overexpressed in OS tissues than that of paracancerous tissues. The disease-free survival and overall survival of OS patients were not correlated with age, gender and tumor location, but remarkably correlated with FOXP4-AS1 expression, tumor size and lung metastasis. For *in vitro* experiments, MG63 cells expressed a higher expression of FOXP4-AS1, whereas U2OS cells expressed a lower expression, which were selected for the following studies. Overexpressed FOXP4-AS1 led to enhanced proliferation, migration and invasion, shortened G0/G1 phase, as well as inhibited cell cycle. Knockdown of FOXP4-AS1 in MG63 cells obtained the opposite results. Furthermore, RIP assay indicated that FOXP4-AS1 could inhibit LATS1 expression by binding to LSD1 and EZH2, so as to participate in OS development. In conclusion, these results revealed that FOXP4-AS1 is overexpressed in OS, and is the independent risk factor in OS prognosis. Upregulated FOXP4-AS1 promotes the proliferation, migration and cell cycle, but inhibits apoptosis of OS cells. Furthermore, FOXP4-AS1 participates in the development and progression of OS by downregulating LATS1 via binding to LSD1 and EZH2.

1. Introduction

Osteosarcoma (OS) is a common malignant bone tumor in children and adolescents, which is characterized by high invasiveness and early systemic metastasis. Globally, the incidence of OS is about 1–3/1,000,000 per year [1]. Combination treatment of surgical resection and chemotherapy has become the standard treatment strategy for OS, which has remarkably improved the overall survival [2]. However, a great number of OS patients would experience resistance to chemotherapeutic drug, which is the severe obstacle in treating metastasis and recurrence of OS [3]. Although great advances have been made in searching for new treatment methods, the overall survival of OS patients is still unsatisfactory [4]. Biological characteristics of OS have been well studied, however, origination, metastasis and chemotherapy resistance of OS are rarely reported. Nowadays, lncRNAs have reported to exert crucial role in the development and progression of OS [5].

Only about 2% of the human genomic RNAs can encode proteins. Most of these transcribed RNAs are non-coding RNAs (ncRNAs), which are classified into small non-coding RNAs (small ncRNAs) and long non-coding RNAs (lncRNAs) based on their transcript length. LncRNA is a transcript that does not encode proteins [6]. LncRNA has been confirmed to participate in a variety of cancers [7], including osteosarcoma. It is reported that some certain lncRNAs could regulate OS pathogenesis such as cell growth,

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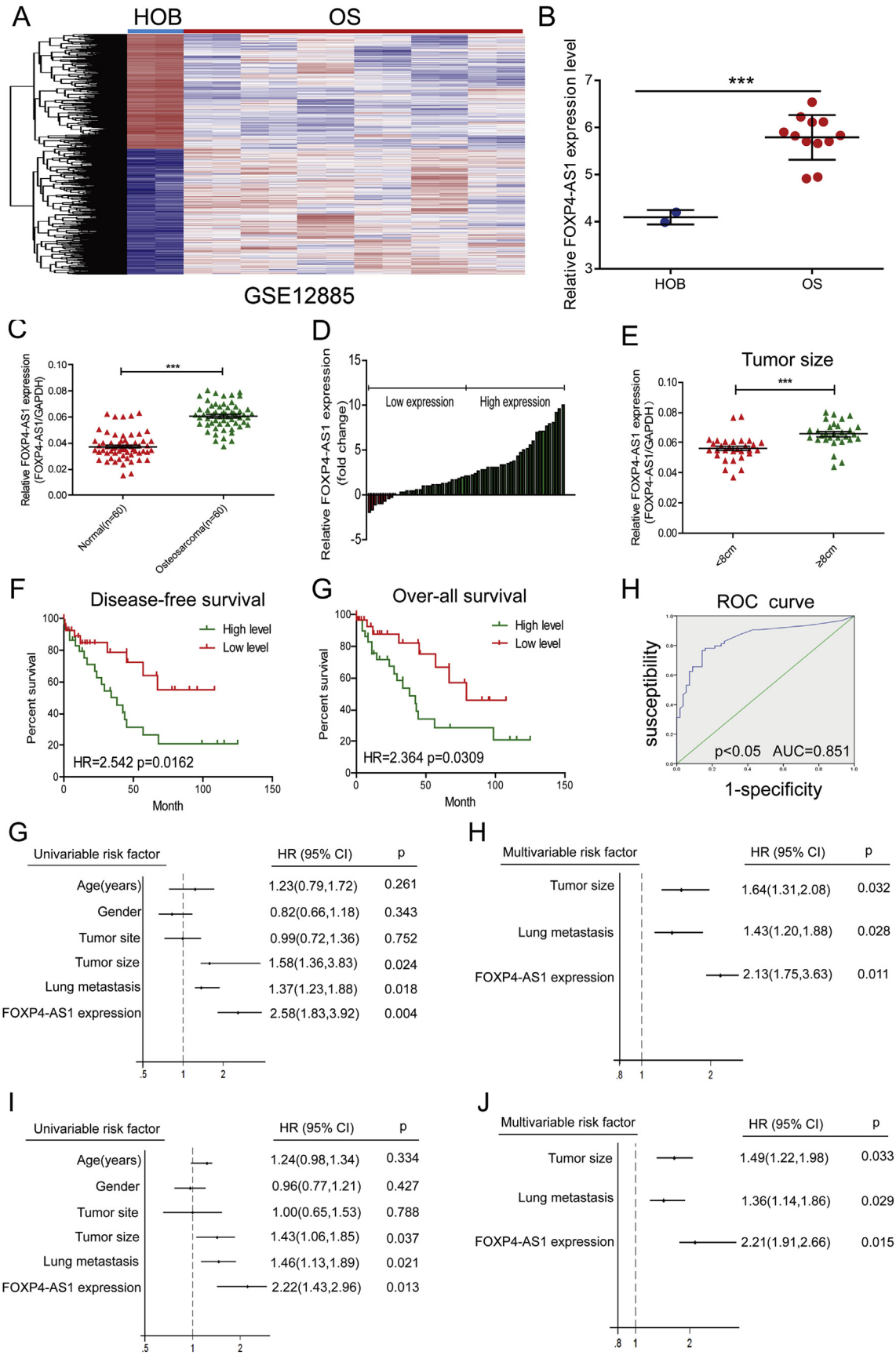

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