Anoikis is a specific form of programmed cell death induced by the loss of cellular exposure to the extracellular matrix, which plays a key role in the maintenance of tissue homeostasis[9]. However, tumor cells have the ability to evade cell death and are usually resistant to anoikis, with tumor progression and the metastatic spread of cancer cells[10]. An increasing number of studies have confirmed the involvement of anoikis in NSCLC-related biological processes: Liu et al. [11] showed that silencing Zic family member 2 (ZIC2) could decrease the migration, invasion and anoikis resistance ability of NSCLC cells by inhibiting Src/FAK signaling; McCarroll et al.[12] found that βIII-tubulin induced NSCLC development and anoikis resistance through the PTEN/AKT signaling axis; and Jang et al.[13] demonstrated that knockdown of FAM188B decreased the activity of various signaling pathways involved in antianoikis effects downstream of EGFR (epidermal growth factor receptor), sensitizing NSCLC cells to anoikis and inhibiting tumor metastasis. It is evident that anoikis resistance is regulated by multiple signaling pathways in NSCLC cells. Several studies have shown that the main pathways associated with the anti-NSCLC effects of β-elemene include the AMPK/MAPK, PI3K/AKT/mTOR and FAK-Src pathways[6,8,14]. It is thus evident that β-elemene may exert anti-NSCLC effects by participating in the regulation of anoikis-related pathways, and that the targets of β-elemene may play key roles in the anoikis process.

Noncoding RNAs (ncRNAs) are unique RNA transcripts that are widely found in eukaryotes, and a variety of ncRNAs, including long noncoding RNAs (lncRNAs), microRNAs (miRNAs), and circular RNAs (circRNAs), are oncogenic drivers and tumor suppressors of major cancers[15]. Extensive interactions between ncRNAs also occur, with lncRNAs usually acting as specific competing endogenous RNAs (ceRNAs), competing for complementary miRNA binding sites and influencing and regulating the expression of cancer target genes[16,17]. A variety of ncRNAs have been found to play key roles in NSCLC and can influence NSCLC development through various mechanisms[18-20]. In particular, anoikis-associated ncRNAs have been shown to be key markers for tumor metastasis and progression, including for breast cancer[21], hepatocellular carcinoma [22], and prostate cancer[23]. The latest research shows that lncRNA-miRNA interactions can be successfully predicted via multiple network algorithms, providing novel and important insights into the value of ncRNAs for predicting the prognosis of NSCLC. However, studies involving the regulatory roles of anoikis-related ncRNAs in NSCLC have been less frequently reported. Additionally, it is not yet known whether the target of β-elemene interacts with anoikis-related ncRNAs. Thus, elucidating the roles of anoikis-related ncRNAs ingold NSCLC may improve our understanding of the mechanism by which β-elemene affects anoikis, as well as reveal new therapeutic strategies for NSCLC.

In this study, we explored the expression pattern of anoikis-related prognostic factors in NSCLC patients by mining data from the Cancer Genome Atlas (TCGA) database and investigated the biological functions and prognostic significance of these molecular clusters. In addition, by constructing a lncRNA–miRNA-mRNA network of anoikis- and β-elemene-related targets, the regulatory effects of anoikis-associated ncRNAs on β-elemene targets were clarified. Finally, potential targets were obtained by constructing a prognostic regression model, and the binding stability of the targets

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and β-elemene was evaluated through molecular docking, providing a theoretical basis and new possibilities for the diagnosis and treatment of NSCLC.