Anoikis is a specific form of programmed cell death that is induced by the loss of cell contact with the extracellular matrix, which plays a key role in the maintenance of tissue homeostasis[9]. However, tumor cells can evade cell death and are typically resistant to anoikis; this can lead to tumor progression and the metastatic spread of cancer cells[10]. An increasing number of studies have confirmed the involvement of anoikis in non-small cell lung cancer (NSCLC)-related biological processes. For example, Liu et al.[11] showed that silencing of Zic family member 2 (ZIC2) could decrease migration, invasion and anoikis resistance in NSCLC cells by inhibiting Src/FAK signaling. In addition, McCarroll et al.[12] found that βIII-tubulin induced NSCLC development and anoikis resistance through the PTEN/AKT signaling axis. Furthermore, Jang et al.[13] demonstrated that knockdown of FAM188B decreased the activity of various antianoikis signaling pathways downstream of epidermal growth factor receptor (EGFR), sensitizing NSCLC cells to anoikis and inhibiting tumor metastasis. Anoikis resistance is known to be regulated by multiple signaling pathways in NSCLC cells, and 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]. Thus, β-elemene may exert anti-NSCLC effects by regulating anoikis-related pathways, and the targets of β-elemene may play key roles in anoikis.

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]. Additionally, extensive interactions occur between ncRNAs. lncRNAs typically 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 play key roles in NSCLC and influence NSCLC development through various mechanisms[18-20]. In particular, anoikis-associated ncRNAs are key markers for metastasis and progression in various cancers, including breast cancer[21], hepatocellular carcinoma[22], and prostate cancer[23]. Recent studies have shown 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 investigating the regulatory roles of anoikis-related ncRNAs in NSCLC have been reported less frequently. 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 in NSCLC may improve our understanding of the mechanism by which β-elemene affects anoikis and reveal new therapeutic strategies for NSCLC.

In this study, we explored the expression patterns 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 the identified molecular clusters. In addition, a lncRNA–miRNA-mRNA network of anoikis- and β-elemene-related targets was constructed to clarify the regulatory effects of anoikis-associated ncRNAs on β-elemene targets. Finally, potential targets were identified by constructing a prognostic regression model, and the binding stability of

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the predicted targets and β-elemene was evaluated via molecular docking, providing a theoretical foundation and new possibilities for the diagnosis and treatment of NSCLC.