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ARHGAP11A Promotes Lung Adenocarcinoma Proliferation and Invasion through ROCK-LIMK-Cofilin Pathway

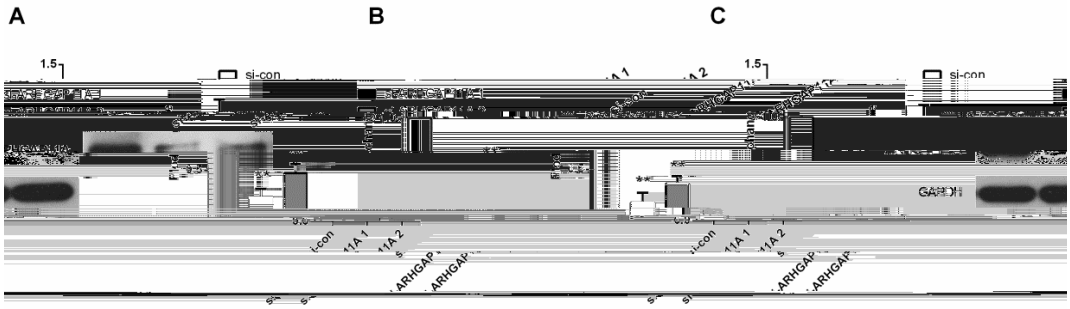
[1]

CA, US) supplemented with penicillin G (100 U/ml), streptomycin

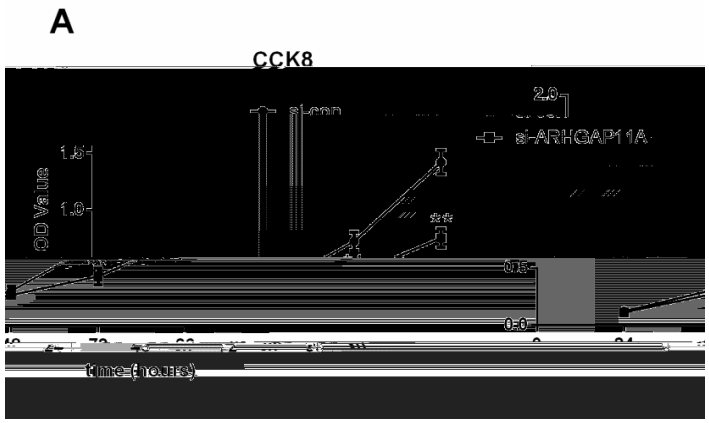
A549 was higher than that in Calu-3 cells, thus, in subsequent study, A549 cell line was used.

A HGAP11A is an independent predictor for survival in LUAD patients

e correlation between the *ARHGAP11A* expression status and the clinic pathologic characteristics of 535 LUAD tissues was further evaluated, and the results are listed in Table 1. A positive correlation was found between the *ARHGAP11A* over-expression and gender (p=0.000) and pathologic-node (p=0.040) (Table 1). Moreover, Kaplan-Meier survival analysis suggested that the survival rate was signi cantly lower in patients with *ARHGAP11A* high-expression than in the patients with lower *ARHGAP11A* expression (p=0.001, Figure 1B). Further, univariate and multivariate analysis exhibited that the up-regulation of *ARHGAP11A* (p=0.004), pathologic tumor (p=0.008), and ARHGAP11A ,hpt[r thaARHGAP11Al 82 10 42Si1 Tfrais ae tf (i)-6 (e)1.6 (of)42.5197 693.6268 T



ARHGAP11A expression, measured by qRT-PCR and western blotting, following the treatment of A549 cells with siRNA ARHGAP11A 1# and siRNA ARHGAP11A 2#.



CCK-8 assay was conducted to analyze the proliferation rate of si- ARHGAP11A-transfected A549 cells. Asterisk stands for statistically signiýcant differences relative to the negative control (˜p<0.001).

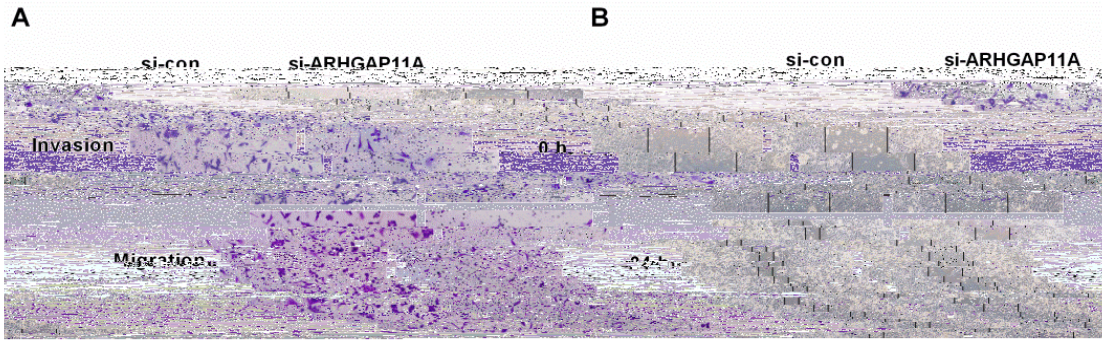
Signi cantly, *ARHGAP11A* activation has been implicated to play key roles in cancer development. Nevertheless, the potential roles and the related molecular mechanisms of *ARHGAP11A* in LUAD are yet to be clari ed.

Our study is the rst direct investigation of the relationship between *ARHGAP11A* and LUAD. In the current report, we observed that the average expression level of *ARHGAP11A* in LUAD tissues was signi cantly higher than those in adjacent normal lung tissues. Furthermore, the TCGA dataset exhibited that *ARHGAP11A* could act as a prognostic factor for LUAD. Additionally, *ARHGAP11A* knockdown signi cantly inhibited LUAD cell viability, migration, and invasion *in vitro*. In a nutshell, the observations of our study demonstrate that *ARHGAP11A* may serve as an oncogene and may exert important functions in LUAD development and progression.

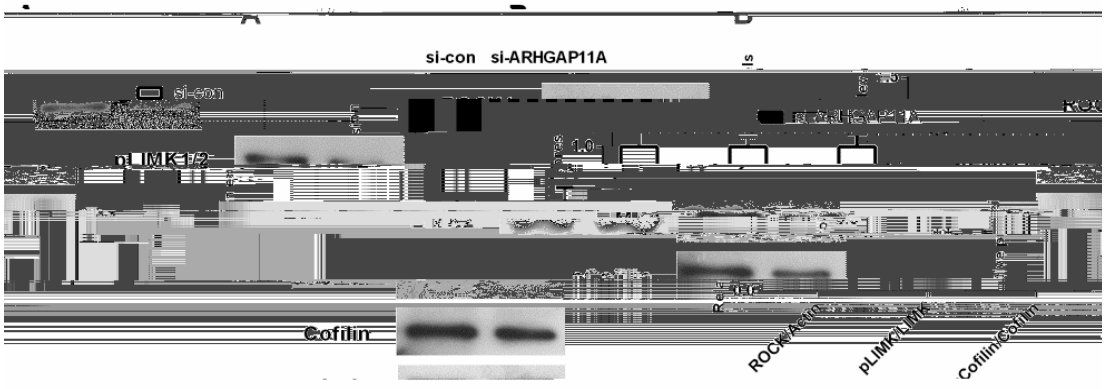
Cancer progression is a dynamic process involving adhesion, migration, invasion, as well as morphogenesis, which is controlled by the dynamics of actin cytoskeleton [13]. Co lin is a kind of actin-binding proteins that play a crucial role in mediating actin lament dynamics and reorganization via catalyzing polymerization or depolymerization of actin laments in migrating cells [14,15]. Co lin phosphorylation is needed for actin polymerization [15]. Co lin is inactivated by phosphorylation by LIMK1, and the p-co lin can in turn re ect the activity of LIMK1. LIMKs is phosphorylated and activated by Rho-associated kinase (ROCK), which facilitates actin polymerization through inactivating co lin by phosphorylation at Ser3 to prevent cleavage of actin bers [16]. In cancer cells, phosphorylation of co lin is controlled by RhoC/ROCK/LIMK pathway [17]. Abundant published evidence has demonstrated that Rho-related pathways, including that mediated by ROCK, participated in polarity control, invasion, in ltration, migration and metastasis [18-20]. Accordingly, our study highlighted the importance of the ROCK/LIMK/co lin pathway in controlling actin dynamics, which participates in invasion and metastasis of cancer cells. Signi cantly, silence of *ARHGAP11A* remarkably inhibited the expression of ROCK, pLIMK2, and pCo lin in A549 cells in the current study. Accordingly, our results suggest that the *ARHGAP11A* low-expression might be closely related with progression and prognosis of LUAD, which is mediated through the inactivation of ROCK/LIMK/co lin signaling pathway.

Conclusion

Taken together, our study identi es *ARHGAP11A* as a novel potential oncogene in LUAD that acts by in uencing the changes in action cutoskeleton. *ARHGAP11A* may serve as a prognostic factor in LUAD. e silencing of *ARHGAP11A* in LUAD cell line A549 dramatically inhibited tumor growth and migration *in vitro*, raising the possibility that *ARHGAP11A* could be a promising new therapeutic target for LUAD. However, our ndings were not veri ed using animal mode or patient tissues. us, in the late work, further studies are required to advance our understanding of the involvement of *ARHGAP11A* in LUAD progression using animal model or patient samples, because this gene is a potential candidate for LUAD diagnosis and treatment.



Effects of ARHGAP11A silence on tumor migration in vitro (A, B, C). A. Wound healing assay was used to measure the migration ability of A549 cells with or without ARHGAP11A silence. B and C. Transwell assays were conducted to determine the migratory and invasive abilities of si-ARHGAP11A-transfected A549 cells.



Analysis of ROCK1, pLIMK2, LIMK2, pCoýlin, and Coýlin expression in A549 cells treated with siRNA ARHGAP11A by western blotting. The mean content of protein was normalized with the expression of ɓ-actin. **p<0.001 compared with the respective negative control group.

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