LncRNA *SNHG12* promotes the malignant progression of melanoma by targeting *miR-199b*

Yijie Xie, Guangxiong Chen

Department of Dermatology, The Affiliated People's Hospital of Ningbo University, Ningbo, China

Contributions: (I) Conception and design: Y Xie; (II) Administrative support: G Chen; (III) Provision of study materials or patients: Both authors; (IV) Collection and assembly of data: Both authors; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

Correspondence to: Yijie Xie, Department of Dermatology, The Affiliated People's Hospital of Ningbo University, Ningbo, Zhejiang 315040, China. Email: xieyijie120@163.com.

Background: Melanoma is a type of tumor caused by the malignant transformation of melanocytes, and has a high degree of malignancy. *Small nucleolar RNA host gene 12* (*SNHG12*) plays an important role in a variety of cancers, but its role in melanoma and its mechanisms are still unclear. In this study, we measured the expression of *SNHG12* and explored the molecular mechanisms involved in melanoma.

Methods: We detected the expression level of *SNHG12* in melanoma cell lines, and explored the effect of *SNHG12* on the proliferation, migration, and invasion of melanoma cells *in vitro*. Mechanistic studies explored the regulation of downstream genes by *SNHG12*.

Results: Overexpression of *SNHG12* was found in melanoma cell lines, and *SNHG12* promoted the proliferation, migration, and invasion of melanoma cells. *MiR-199b* is a target gene of *SNHG12*, which was expressed at low levels in melanoma cell lines, and *SNHG12* regulated melanoma cell proliferation, migration, and invasion through *miR-199b*. We also revealed that *SNHG12* promoted the expression of the target genes of *miR-199b*, namely *ETS1*, *PXN*, *JAG1*, and *DDR1*.

Conclusions: *SNHG12* is highly expressed in melanoma, and promotes the expression of *ETS1*, *PXN*, *JAG1*, and *DDR1* through targeted regulation of *miR-199b*, thereby promoting the proliferation, migration, and invasion of melanoma cells.

Keywords: Melanoma; lncRNA; *SNHG12*; *miR-199b*

Submitted Mar 10, 2021. Accepted for publication Feb 16, 2022.
doi: 10.21037/atm-22-214
View this article at: https://dx.doi.org/10.21037/atm-22-214

Introduction

Melanoma is a malignant tumor caused by the malignant transformation of melanocytes. It is very aggressive and has a high mortality rate (1). Recently, the incidence of melanoma has steadily increased worldwide (2). Although the current combination of surgery, chemotherapy, targeted therapy, and immunotherapy has made great progress in the treatment of melanoma, the therapeutic effect for some melanomas is still not ideal, especially for patients with distant metastases (3). The abnormal regulation of a variety of genes and signaling pathways has been associated with the occurrence of melanoma (4). Hence, it is urgent to understand the molecular mechanisms of malignant processes in melanoma and design new targets for the treatment of melanoma.

Long non-coding RNAs (lncRNAs) are non-coding RNAs with a length of at least 200 nucleotides (5). Although they do not have the ability to encode proteins, they perform a variety of biological functions (6). LncRNAs participate in a variety of carcinogenic processes such as tumor proliferation, metastasis, apoptosis inhibition, and drug resistance (7). More and more studies have shown

© Annals of Translational Medicine. All rights reserved.

that *small nucleolar RNA host gene 12* (*SNHG12*) plays an important role in a variety of cancers. For instance, in diffuse large B-cell lymphoma, a high level of *SNHG12* is closely associated with the poor prognosis of patients, and can accelerate tumor progression by regulating *miR-195* (8). In pancreatic cancer, *SNHG12* is highly expressed in cancer cell lines and tissues, and promotes the proliferation, invasion, and epithelial-mesenchymal transition of pancreatic cancer cells through regulating *miR-320b* (9). In breast cancer, the expression of *SNHG12* is up-regulated, which can up-regulate the expression of *SALL4* by inhibiting *miR-15a-5p*, and promotes breast cancer cell proliferation, migration, and invasion, and inhibits cell apoptosis (10). However, the role of *SNHG12* in melanoma and its mechanisms remain unclear.

In the present research, we detected the expression levels of *SNHG12* in melanoma cell lines. In addition, this study explored the influence of *SNHG12* on the proliferation, migration, and invasion of melanoma cells *in vitro*. Through further research, we explained the molecular mechanisms by which *SNHG12* exerts its corresponding biological functions. This study is the first to explore the role and the corresponding mechanisms of *SNHG12* in melanoma, which will provide necessary theoretical basis for designing therapeutic target. We present the following article in accordance with the MDAR reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-214/rc).

Methods

Cell culture and transfection

Human melanoma cell lines (A2058, SK-MEL-28, CHL-1, and A375) and the human epidermal melanocyte cell line HEMa-LP were all from ATCC (ATCC, USA). Human melanoma cell lines were cultured in DMEM medium (Gibco, USA) containing 10% fetal bovine serum (FBS) (Invitrogen, USA). HEMa-LP cells were maintained in 254 medium (Cascade Biologics, USA). All cell lines were maintained in a 37 ℃ cell incubator containing 5% CO_2. Cell transfection was performed with Lipofectamine 3000 (Invitrogen).

Quantitative real-time PCR (qRT-PCR) experiment

TRIzol reagent (Invitrogen) was used to isolate RNA from cells. Subsequently, ribonucleic acid (RNA) was reverse transcribed into cDNA using a cDNA synthesis kit (Takara Biotechnology, Japan). The PCR reaction was then conducted on the ABI 7500 rapid PCR system (Applied Biosystems, USA) using a SYBR Green Master Mix (Takara Biotechnology). The internal references of *SNHG12* and *miR-199b* were *GAPDH* and *U6*, respectively. All reactions were repeated at least 3 times. Finally, the $2^{-\Delta\Delta Cq}$ method was applied to analyze the results, and the relative levels of *SNHG12* and *miR-199b* were calculated.

CCK-8 experiment

Cell proliferation ability was measured with a CCK-8 kit (Beyotime, China). A total of 5×10^3 cells were seeded in a 96-well plate and cultured for 24 hours before transfection. After transfecting for 24, 48, and 72 hours, 10 µL CCK-8 solution was added into each well and incubated for an appropriate time. Subsequently, a spectrophotometer was used to detect the absorbance at 450 nm.

EdU experiment

Cells were seeded and cultured for 24 hours before transfection. An EdU imaging kit (Life Technologies, USA) was used to detect DNA synthesis in melanoma cells. Cell immunostaining was observed with a fluorescence microscope, and the cells positive for EdU staining were counted.

Scratch test

Cells were seeded and cultured for 24 hours before transfection. When the cells reached approximately 90% confluence, the cell monolayer was scratched with a 10 µl pipette tip to form a uniform scratch, and the cells were rinsed twice with serum-free DMEM. The cells were then cultured in serum-free DMEM for 24 hours. Subsequently, an optical microscope (Olympus, Japan) was used to take pictures of the scratches, the fusion of the scratches was recorded, and the cell migration rate was calculated.

Transwell experiment

The Transwell test was performed using an 8.0 µm Transwell plate (Corning, USA) covered with a matrix gel. The cells were resuspended in 200 µL of serum-free DMEM medium and put into the upper chamber of the Transwell, and 500 µL of DMEM medium containing 10% FBS was put into the lower chamber. The cells above the

© Annals of Translational Medicine. All rights reserved.

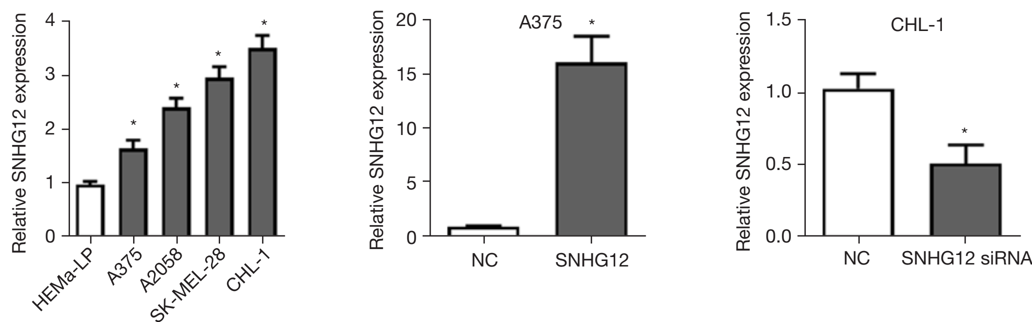

Figure 1 *SNHG12* is highly expressed in melanoma cell lines. (A) The qRT-PCR assay was performed to detect the level of SHNG12 in melanoma cell lines and human epidermal melanocytes. (B,C) *SNHG12* overexpression and silencing efficiency verification. *, P<0.05. *SNHG12*, small nucleolar RNA host gene 12; qRT-PCR, quantitative real-time PCR; NC, normal control.

membrane were wiped off with a cotton swab after culturing for 24 hours, and cells under the membrane were fixed with methanol at room temperature and stained with 0.1% crystal violet solution. The invading cells in 5 random fields were then observed with an optical microscope and counted.

Luciferase reporter gene experiment

The *SNHG12* and *ETS1* 3'UTR fragments containing *miR-199b* binding sites were constructed into the pMIR-REPORT reporter gene vector, and the mutant plasmid served as a control. The *miR-199b* mimics were co-transfected into melanoma cells together with luciferase reporter gene plasmids. The luciferase activity was detected with the dual luciferase reporter gene detection system (Promega, USA).

Western blotting

After the cells were transfected, the cells were lysed with RIPA buffer (Cell Signaling Technology, USA), and the protein concentration was measured using the BCA protein quantification kit (Thermo Fisher Scientific, USA). The same amount of protein (20 µg) was separated by SDS-PAGE electrophoresis and then transferred to the polyvinylidene fluoride (PVDF) membrane. After blocking with 5% skimmed milk at room temperature for 1 hour, the membrane was incubated with the primary antibody at 4 ℃ overnight, and then with the secondary antibody at room temperature for 2 hours. Finally, the ECL Luminescence Kit (Invitrogen) and gel imaging system (Bio-Rad Laboratories, USA) were used for imaging. The antibodies used in this experiment were anti-*ETS1* antibody (ab26096, Abcam, USA), anti-*Paxillin* antibody (ab32084, Abcam), anti-*Jagged1* antibody (ab7771, Abcam), and anti-*DDR1* antibody (#5583, Cell Signaling Technology). *GAPDH* was used as the protein internal control.

Statistical analysis

SPSS 13.0 was used to analyze the data, and all experiments were repeated independently no less than 3 times. All data were presented as mean ± standard deviation. The Student's *t*-test was performed to analyze the differences between the 2 groups, and comparisons between 3 or more groups were carried out by one-way analysis of variance. P value <0.05 indicated that the difference was statistically significant.

Results

SNHG12 is highly expressed in melanoma cell lines

First, qRT-PCR was used to detect the expression levels of *SHNG12* in melanoma cell lines. Compared with HEMa-LP cells, melanoma cell lines also showed higher *SNHG12* expression levels (*Figure 1A*). Since the expression of *SNHG12* in A375 cells was lower while *SNHG12* expression in CHL-1 cells was higher, an *SNHG12* expression plasmid was transfected in A375 cells to overexpress *SNHG12*, and siRNA was transfected in CHL-1 cells to silence *SNHG12* (*Figure 1B,1C*).

SNHG12 promotes the proliferation, migration, and invasion of melanoma cells

In order to study the biological functions of *SNHG12*,

© Annals of Translational Medicine. All rights reserved.

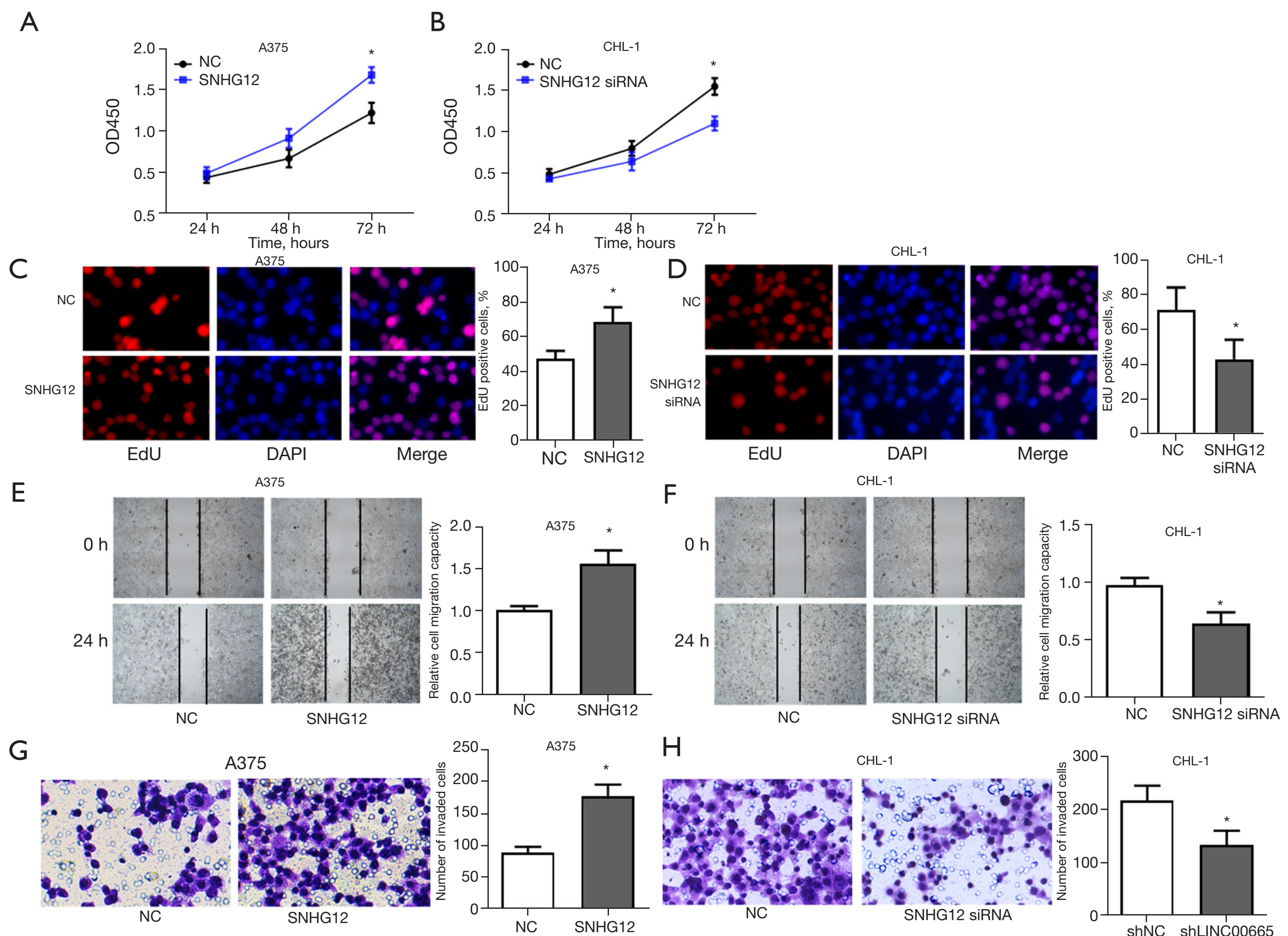

Figure 2 *SNHG12* promotes the proliferation, migration, and invasion of melanoma cells. *SNHG12* was overexpressed in A375 cells and *SNHG12* was silenced in CHL-1 cells. (A,B) The CCK-8 experiment and (C,D) EdU experiment (red: EdU, blue: DAPI, purple: merge; 100×) were conducted to study the influence of *SNHG12* on cell proliferation, (E,F) the scratch experiment (40×) was performed to evaluate the influence of *SNHG12* on cell migration, and the (G,H) Transwell experiment (crystal violet; 100×) was used to assess the effect of *SNHG12* on cell invasion. *, P<0.05. *SNHG12*, small nucleolar RNA host gene 12; CCK-8, Cell-Counting-Kit-8; EdU, 5-ethynyl-2'-deoxyuridine; NC, normal control.

after overexpressing *SNHG12* in A375 cells and silencing *SNHG12* in CHL-1 cells, CCK-8 and EdU experiments were performed to study the influence of *SNHG12* on cell proliferation (*Figure 2A-2D*), the scratch assays were applied to study the influence of *SNHG12* on cell migration (*Figure 2E,2F*), and the Transwell experiment was conducted to study the influence of *SNHG12* on cell invasion (*Figure 2G,2H*). The results demonstrated that after overexpressing *SNHG12* in A375 cells, cell proliferation was significantly accelerated (*Figure 2A,2C*), and the migration and invasion capabilities were significantly enhanced (*Figure 2E,2G*). Correspondingly, after silencing *SNHG12* in CHL-1 cells, the proliferation of the cells was significantly slowed down (*Figures 2B,2D*), and the migration and invasion capabilities were significantly weakened (*Figures 2F,2H*). These results demonstrated that *SNHG12* was able to promote the proliferation, migration, and invasion of melanoma cells *in vitro*.

MiR-199b is the target gene of SNHG12

Through the starbase database, we speculated that *miR-199b* might be the target gene of *SNHG12* (*Figure 3A*). According to this predicted site, pMIR-*SNHG12*-wt and

© Annals of Translational Medicine. All rights reserved.

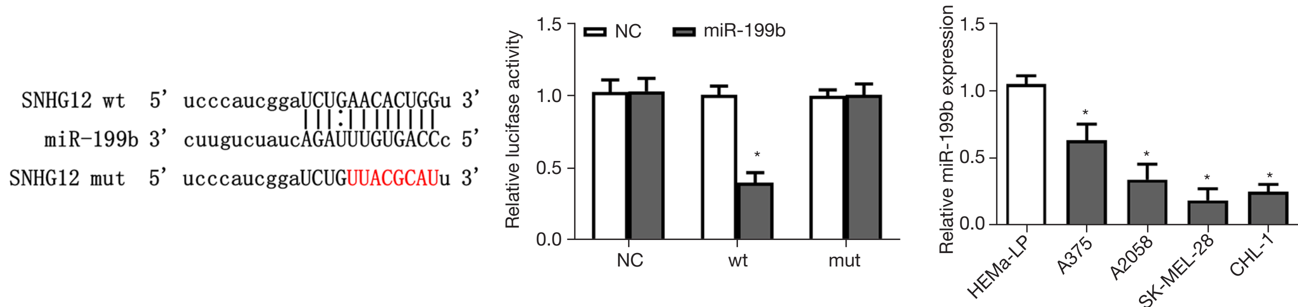

Figure 3 *MiR-199b* is the target gene of *SNHG12*. (A) Binding site prediction of *miR-199b* and *SNHG12*. (B) Experimental verification of the binding site of *miR-199b* in *SNHG12* by the luciferase assay. (C) The qRT-PCR assay was performed to detect the level of *miR-199b* in melanoma cell lines and human epidermal melanocytes. *, P<0.05. *SNHG12*, small nucleolar RNA host gene 12; qRT-PCR, quantitative real-time PCR; NC, normal control; wt, wild type; mut, mutation.

pMIR-*SNHG12*-mut luciferase reporter gene plasmids were constructed respectively, and co-transfected with NC or *miR-199b* mimics into melanoma cells. The results showed that when *miR-199b* mimics were co-transfected with pMIR-*SNHG12*-wt, the relative activity of luciferase was significantly reduced (*Figure 3B*), which indicated that *miR-199b* was the target gene of *SNHG12*. Moreover, our results showed that *miR-199b* was under-expressed in melanoma cell lines (*Figure 3C*).

SNHG12 regulates the proliferation, migration, and invasion of melanoma cells through miR-199b

CCK-8 assays, EdU assays, scratch assays and Transwell assays were performed to study the influence of *SNHG12* and *miR-199b* on cell proliferation, migration and invasion (*Figure 4A-4H*). Transfection of *miR-199b* mimics in A375 cells overexpressing *SNHG12* attenuated the promotive effect of *SNHG12* on cell proliferation, migration, and invasion (*Figure 4A,4C,4E,4G*). Transfection of an *miR-199b* inhibitor in *SNHG12*-silenced CHL-1 cells restored the reduced cell proliferation, migration, and invasion ability caused by *SNHG12* knockdown (*Figure 4B,4D,4F,4H*). The above results suggested that *SNHG12* regulates the proliferation, migration, and invasion of melanoma cells through *miR-199b*.

SNHG12 regulates the expression of miR-199b target genes

Through the starbase database, it was found that the 3'UTR of *ETS1* has a binding site for *miR-199b* (*Figure 5A*). According to this predicted site, pMIR-*ETS1* 3'UTR-wt and pMIR-*ETS1* 3'UTR-mut luciferase reporter gene plasmids were constructed respectively, and co-transfected with NC or *miR-199b* mimics into melanoma cells. The results showed that the activity of the wild-type luciferase plasmid was inhibited by *miR-199b* mimics (*Figure 5B*). At the same time, overexpression of *miR-199b* could inhibit the expression of *ETS1* at the protein level, while silencing *miR-199b* promoted the expression of *ETS1* protein (*Figure 5C,5D*). The above results suggested that *ETS1* was the target gene of *miR-199b*, and *SNHG12* regulated the expression of *ETS1* through *miR-199b* (*Figure 5E,5F*). Moreover, *SNHG12* could regulate the expression of other proven target genes of *miR-199b* such as *PXN*, *JAG1*, and *DDR1* (*Figure 5E,5F*).

Discussion

Recent studies have shown that lncRNA-miRNA regulatory networks are widely implicated in the pathogenesis of tumors (11). LncRNAs become key regulators of malignant tumors by combining with miRNAs to regulate gene expression, which is a common process of regulation (12). More and more studies have proven that lncRNAs and miRNAs play vital roles in the occurrence and development of melanoma, and may be useful biomarkers and therapeutic targets in the future (13). For example, the expression of lncRNA *FGD5-AS1* in melanoma tissue was significantly up-regulated, and its high expression was significantly related to tumor thickness, tumor stage, and overall survival rate, and may be a potential independent prognostic factor for melanoma (14). LncRNA *FOXC2-AS1* is up-regulated

© Annals of Translational Medicine. All rights reserved.

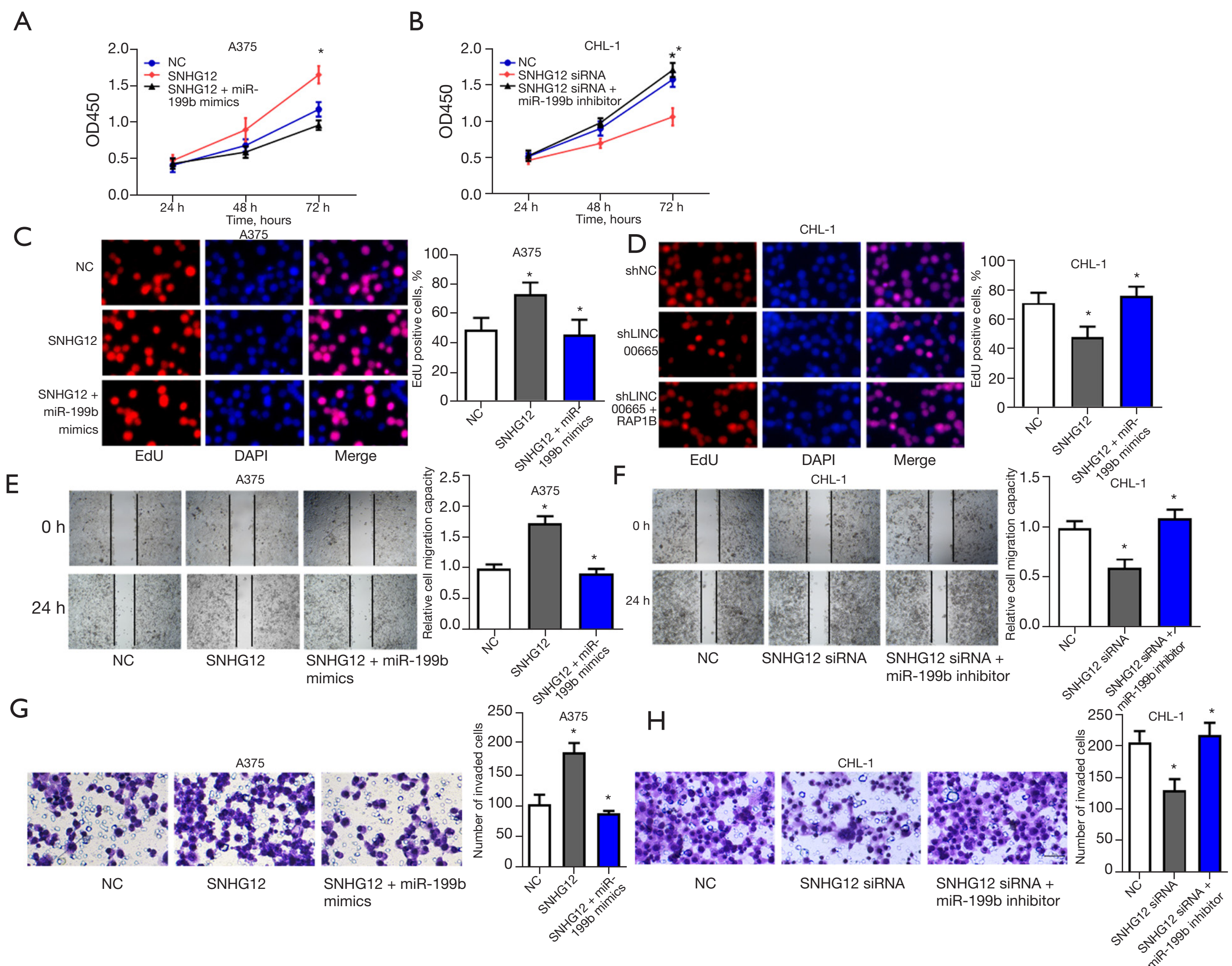

Figure 4 *SNHG12* regulates the proliferation, migration, and invasion of melanoma cells through *miR-199b*. Transfection of *miR-199b* mimics in A375 cells overexpressing *SNHG12*, and transfection of an *miR-199b* inhibitor in *SNHG12*-silenced CHL-1 cells. (A,B) The CCK-8 experiment and (C,D) EdU experiment (red: EdU, blue: DAPI, purple: merge; 100×) were carried out to study the roles of *SNHG12* and *miR-199b* on cell proliferation, (E,F) the scratch experiment (40×) was performed to study the effects of *SNHG12* and *miR-199b* on cell migration, and (G,H) the transwell experiment (crystal violet; 100×) was conducted to study the roles of *SNHG12* and *miR-199b* on cell invasion. *, P<0.05. *SNHG12*, small nucleolar RNA host gene 12; CCK-8, Cell-Counting-Kit-8; EdU, 5-ethynyl-2'-deoxyuridine; NC, normal control.

in melanoma tissues, especially in patients with metastasis or stage II-IV melanoma, and patients with high *FOXC2-AS1* expression levels have lower survival rates. *FOXC2-AS1* can stimulate the proliferation of melanoma by silencing *p15* through recruiting *EZH2* (15). Moreover, lncRNA *SNHG16* is highly expressed in melanoma and facilitates melanoma cell proliferation and migration by regulating *miR-132* (16).

LncRNA *SNHG12* is located on chromosome 1p35.3 and is related to a variety of cancers. However, its biological role and related mechanisms in melanoma are still unclear. In this study, it was confirmed that the expression of *SNHG12* in melanoma cell lines was obviously up-regulated, suggesting that *SNHG12* may play vital roles in the progression of melanoma. Subsequently, the biological functions of *SNHG12* in melanoma were evaluated, and the results showed that overexpressing the *SNHG12* gene obviously facilitated the proliferation, migration, and

© Annals of Translational Medicine. All rights reserved.

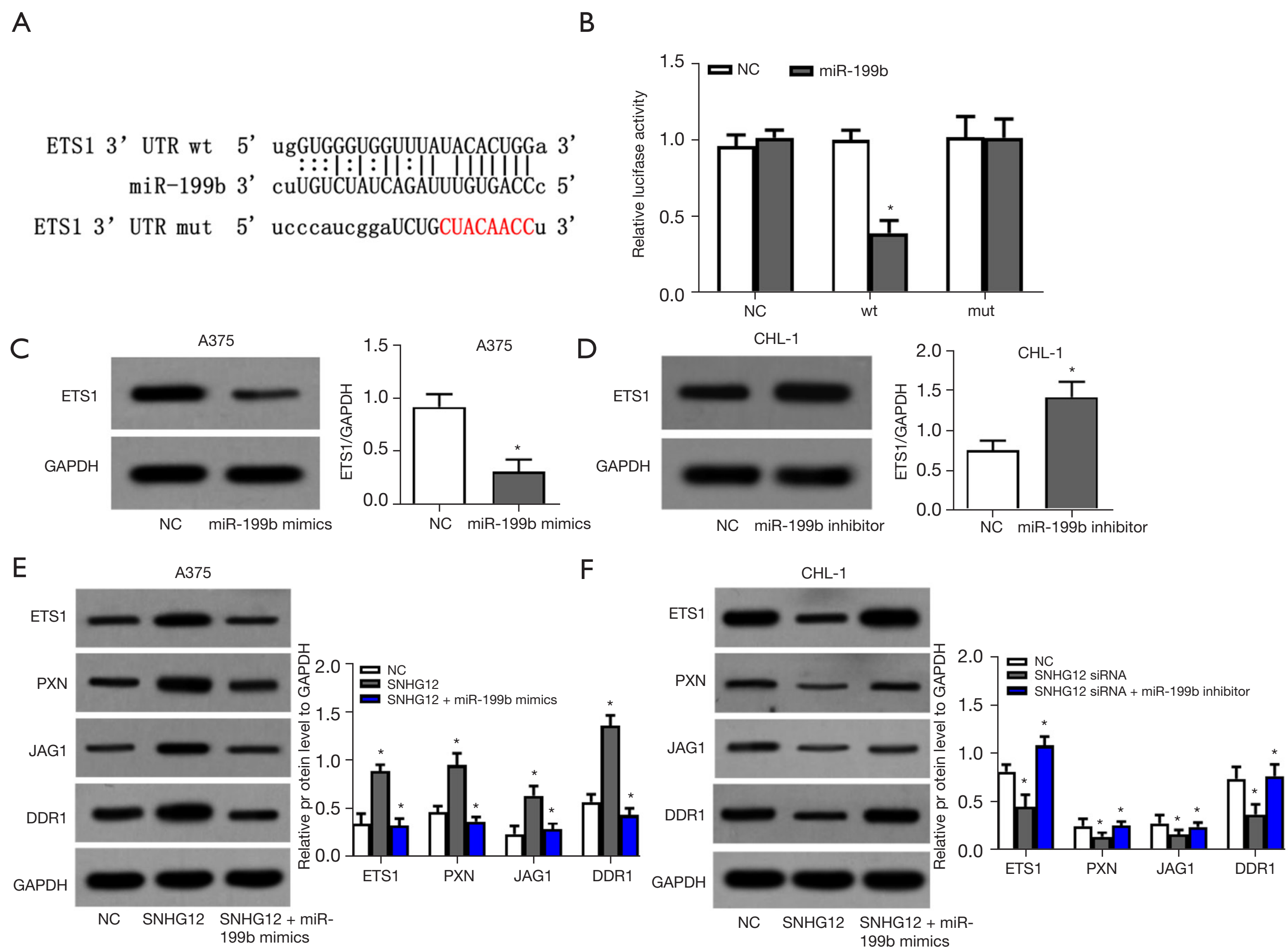

Figure 5 *SNHG12* regulates the expression of *miR-199b* target genes. (A) The binding site prediction of *miR-199b* and *ETS1* 3'UTR. (B) Experimental verification of the binding site of *miR-199b* in *ETS1* 3'UTR by the luciferase assay. (C,D) Western blot was carried out to assess the effect of *miR-199b* on the expression of *ETS1* protein. (E,F) Western blot was carried out to assess the effect of *SNHG12* and *miR-199b* on the expression of *ETS1*, *PXN*, *JAG1*, and *DDR1*. *, P<0.05. *SNHG12*, small nucleolar RNA host gene 12; NC, normal control.

invasion of melanoma cells. In contrast, silencing *SNHG12* impeded the proliferation, migration, and invasion of melanoma cells. Therefore, it is believed that *SNHG12* plays an oncogenic role in melanoma.

Bioinformatics analysis was then used to find a binding site of *miR-199b* in *SNHG12*, and further study the regulatory mechanism of *SNHG12* on *miR-195*. It was confirmed for the first time that *miR-199b* is a target gene of *SNHG12*, and *SNHG12* can affect the proliferation, migration, and invasion of melanoma cells via regulating *miR-199b*. According to reports, *miR-199b* is related to a variety of cancers, and can inhibit cancer progression by directly targeting and regulating certain oncogenes such as *PXN*, *JAG1*, and *DDR1* (17-19). In melanoma, *miR-199b* is very effective in inhibiting the proliferation and viability of melanoma cells, affecting key signaling pathways related to melanoma cell survival, and enhancing the efficacy of drugs to inhibit BRAF and MEK (20). Furthermore, this study found that *ETS1* was a new target gene of *miR-199b*, and *miR-199b* was able to directly target and reduce the expression of *ETS1* in melanoma. *ETS1* is a member of the ETS transcription factor family, and acts as a transcriptional activator and suppressor of many genes, participating in the development of stem cells, cell senescence, and death, as well as tumorigenesis (21). In most cancers, the expression of *ETS1* is related to low survival rates. *ETS1* helps to

© Annals of Translational Medicine. All rights reserved.

enhance the invasiveness of cancer cells, promote the transformation of epithelial cells to mesenchymal cells, and promote drug resistance and angiogenesis (22). This study further validated that *SNHG12* can promote the expression of *miR-199b* target genes (*ETS1*, *PXN*, *JAG1*, and *DDR1*) by regulating *miR-199b*.

This study found that *SNHG12* can promote the malignant progression of melanoma as an oncogene. Therefore, drugs targeting *SNHG12* may have potential application value for the clinical treatment and prognosis of melanoma. However, there are still many deficiencies in this study. For example, this study did not involve *in vivo* data and signaling pathways, which might be very promising in this field.

Conclusions

LncRNA *SNHG12* is overexpressed in melanoma cell lines, and can promote the expression of *miR-199b* target genes *ETS1*, *PXN*, *JAG1*, and *DDR1* through targeted regulation of *miR-199b*, thereby promoting the proliferation, migration, and invasion of melanoma cells.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the MDAR reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-214/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-214/dss

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-214/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Rebecca VW, Somasundaram R, Herlyn M. Pre-clinical modeling of cutaneous melanoma. Nat Commun 2020;11:2858.
2. Schadendorf D, van Akkooi ACJ, Berking C, et al. Melanoma. Lancet 2018;392:971-84.
3. Grob JJ, Garbe C, Ascierto P, et al. Adjuvant melanoma therapy with new drugs: should physicians continue to focus on metastatic disease or use it earlier in primary melanoma? Lancet Oncol 2018;19:e720-e725.
4. Bai X, Fisher DE, Flaherty KT. Cell-state dynamics and therapeutic resistance in melanoma from the perspective of MITF and IFNγ pathways. Nat Rev Clin Oncol 2019;16:549-62.
5. Nair L, Chung H, Basu U. Regulation of long non-coding RNAs and genome dynamics by the RNA surveillance machinery. Nat Rev Mol Cell Biol 2020;21:123-36.
6. Yao RW, Wang Y, Chen LL. Cellular functions of long noncoding RNAs. Nat Cell Biol 2019;21:542-51.
7. Tan H, Zhang S, Zhang J, et al. Long non-coding RNAs in gastric cancer: New emerging biological functions and therapeutic implications. Theranostics 2020;10:8880-902.
8. Chen LY, Zhang XM, Han BQ, et al. Long Noncoding RNA SNHG12 Indicates the Prognosis and Accelerates Tumorigenesis of Diffuse Large B-Cell Lymphoma Through Sponging microR-195. Onco Targets Ther 2020;13:5563-74.
9. Cao W, Zhou G. LncRNA SNHG12 contributes proliferation, invasion and epithelial-mesenchymal transition of pancreatic cancer cells by absorbing miRNA-320b. Biosci Rep 2020;40:BSR20200805.
10. Yuan JH, Li WX, Hu C, et al. Upregulation of SNHG12 accelerates cell proliferation, migration, invasion and restrain cell apoptosis in breast cancer by enhancing regulating SALL4 expression via sponging miR-15a-5p. Neoplasma 2020;67:861-70.
11. Fu S, Wang Y, Li H, et al. Regulatory Networks of LncRNA MALAT-1 in Cancer. Cancer Manag Res 2020;12:10181-98.

© Annals of Translational Medicine. All rights reserved.

12. Yang Y, Wang Y, Wang F, et al. The roles of miRNA, lncRNA and circRNA in the development of osteoporosis. Biol Res 2020;53:40.
13. Safa A, Gholipour M, Dinger ME, et al. The critical roles of lncRNAs in the pathogenesis of melanoma. Exp Mol Pathol 2020;117:104558.
14. Gao Y, Zhu H, Mao Q. Expression of lncRNA FGD5-AS1 correlates with poor prognosis in melanoma patients. J Gene Med 2020;22:e3278.
15. Xu DF, Tao XH, Yu Y, et al. LncRNA FOXC2-AS1 stimulates proliferation of melanoma via silencing p15 by recruiting EZH2. Eur Rev Med Pharmacol Sci 2020;24:8940-6.
16. Bi LL, Hua XQ, Li WH, et al. SNHG16 promotes cell proliferation and migration through sponging miR-132 in melanoma. J Biol Regul Homeost Agents 2020;34:1307-16.
17. Du C, Wang Y, Zhang Y, et al. LncRNA DLX6-AS1 Contributes to Epithelial-Mesenchymal Transition and Cisplatin Resistance in Triple-negative Breast Cancer via Modulating MiR-199b-5p/Paxillin Axis. Cell Transplant 2020;29:963689720929983.
18. Chen LY, Zhi Z, Wang L, et al. NSD2 circular RNA promotes metastasis of colorectal cancer by targeting miR-199b-5p-mediated DDR1 and JAG1 signalling. J Pathol 2019;248:103-15.
19. Wu A, Chen Y, Liu Y, et al. miR-199b-5p inhibits triple negative breast cancer cell proliferation, migration and invasion by targeting DDR1. Oncol Lett 2018;16:4889-96.
20. Fattore L, Campani V, Ruggiero CF, et al. In Vitro Biophysical and Biological Characterization of Lipid Nanoparticles Co-Encapsulating Oncosuppressors miR-199b-5p and miR-204-5p as Potentiators of Target Therapy in Metastatic Melanoma. Int J Mol Sci 2020;21:1930.
21. Shaikhibrahim Z, Wernert N. ETS transcription factors and prostate cancer: the role of the family prototype ETS-1. Int J Oncol 2012;40:1748-54.
22. Dittmer J. The role of the transcription factor ETS1 in carcinoma. Semin Cancer Biol 2015;35:20-38.

Cite this article as: Xie Y, Chen G. LncRNA *SNHG12* promotes the malignant progression of melanoma by targeting *miR-199b*. Ann Transl Med 2022;10(4):226. doi: 10.21037/atm-22-214

(English Language Editor: C. Betlazar-Maseh)

© Annals of Translational Medicine. All rights reserved.