Original Article

MiR-1271-5p promotes the growth and migration of neuroblastoma cells by regulating ACY-1

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Background: Aminoacylase 1 (ACY-1) has been found to be a tumor suppressor gene in neuroblastoma (NB). This study aimed to identify and verify the microRNAs (miRNAs) that may regulate ACY-1 through database prediction analysis, and verify the mutual regulatory effect of miRNA and ACY-1 in NB through cell experiments.

Methods: The miRNAs that might bind ACY-1 were predicted and selected by TargetScan, miRTarBase and four other databases, the expression of the predicted miRNAs and ACY-1 was detected by reverse transcription-quantitative polymerase chain reaction (RT-qPCR) in four groups of clinical samples, and the differentially expressed miRNAs were screened. Then, luciferase vector was constructed according to the *ACY-1* gene sequence to detect whether ACY-1 binds to the selected miRNA. Then, miR-1271-5p expression was silenced to detect miR-1271-5p function in the growth and migration of NB. Finally, ACY-1 and miR-1271-5p were silenced to change ACY-1 expression, and ACY-1 function in NB and the regulatory role of miR-1271-5p were explored.

Results: ACY-1 was downregulated in NB, miR-1271-5p was upregulated in NB, and miR-1271-5p could be targeted to ACY-1. Silencing miR-1271-5p expression can reduce cell viability and inhibit tumor progression. After interfering with ACY-1 expression in cells, cell viability was enhanced, apoptosis was significantly decreased, and migration and invasion were enhanced. After partially restoring ACY-1 expression, the effect of si-ACY-1 on cells was weakened. In SK-N-SH and SH-SY-5Y cells, the miR-1271-5p inhibitor restored ACY-1 expression and improved ACY-1 function.

Conclusions: MiR-1271-5p can promote the growth and migration of tumor cells by inhibiting ACY-1 expression in NB.

Keywords: Neuroblastoma (NB); miR-1271-5p; aminoacylase 1 (ACY-1); cell proliferation; cell migration

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Introduction

Neuroblastoma (NB) is a childhood malignant tumor originating from the sympathetic nervous system that accounts for 8–10% of malignant tumors in young children. Moreover, NB accounts for 15% of all pediatric cancer deaths (1,2). It is estimated that there are 3,000 new cases in China every year. Approximately 30% of patients with NB are less than 1 year old, and another 50% of patients are between 1 and 4 years old. Most children under 1 year old can recover spontaneously, while children over 1 year old have a high degree of malignancy. Most children have advanced cancer at the time of treatment, and even after treatment, the prognosis is still very poor, and the 5-year

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survival rate of patients after treatment is less than 40% (3,4). The current treatment methods have greatly improved with the development of clinical experiments and basic science; yet, NB is still a complex medical problem due to its unpredictable clinical course and poor prognosis.

The exact pathogenesis of NB is still unclear, and may be related to genetic and environmental factors. The possible mechanism of NB is currently explained by the theory of "secondary mutation", that is, the occurrence of NB requires two mutations (5). The incidence of NB in children who had exposed to hydantoin, phenobarbital and ethanol before birth is greater than that in children who had not been exposed to (6). Other chemicals, drugs and radiation are not significantly related to the occurrence of NB, and the exact potential role of environmental exposure is still unclear (7). However, recent studies have shown that the genetic factors leading to the occurrence of NB are very complex and heterogeneous, and mainly include the following mechanisms (8,9): (I) proto-oncogene activation and amplification; (II) loss of heterozygosity or inactivation of tumor suppressor genes; (III) abnormal expression of certain genes, such as abnormal expression of nerve growth factor; and (IV) abnormal regulation of apoptosis. Therefore, it is popular to explore the pathogenesis of NB from the perspective of genetic factors.

MicroRNAs (miRNAs) are involved in various physiological activities of the body and are associated with tumor development and patient prognosis (10,11). The biological functions of only a small number of miRNAs, which regulate tumor-related processes such as cell growth and tissue differentiation, have been elucidated (10). Chen *et al.* first reported that miRNAs may play a role in NB. By comparison, *in-vitro* cell experiments revealed that the expression of 157 miRNAs significantly changed in NB specimens and demonstrated the inhibitory effect of miR-184 on the development of NB cells (12). Afanasyeva *et al.* identified 29 new miRNAs in 13 NB tissue specimens and two NB cell lines (13). Schulte *et al.* analyzed the expression of 430 miRNAs in 69 NB patient samples and demonstrated that the miRNA expression profile could predict the prognosis of patients in combination (14). Therefore, miRNAs have great potential in the treatment and prognosis of NB.

Aminoacylase 1 (ACY-1; EC 3.5.1.14) is a zinc-binding enzyme that hydrolyzes N-acetyl amino acids into free amino acids and acetic acid, and ACY-1 is present in various tissues, is widely involved in the hydrolysis of n-acetylated amino acids, and is considered to be a tumor suppressor in many tumors (15,16). Studies have shown that ACY-1 plays a crucial role in the pathogenesis of numerous tumor diseases, such as colorectal, liver, small cell lung cancers and renal cell carcinoma (16-18). In NB, high ACY-1 expression is associated with a good prognosis (19). Previous study (20) has shown that ACY-1 can effectively inhibit the proliferation, migration and invasion of human NB cell lines by activating the extracellular regulated protein kinases (ERK) 1/2 and transforming growth factor beta 1 (TGF-β1) signaling pathways; that is, ACY-1 acts as a tumor suppressor gene in NB. This study aimed to identify and verify the miRNAs that may regulate ACY-1 through database prediction analysis and to verify the mutual regulatory effect of miRNAs and ACY-1 in NB through cell experiments. We present this article in accordance with the MDAR reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-25/rc).

Highlight box

Key findings

- MiR-1271-5p promotes the growth and migration of tumor cells by inhibiting aminoacylase 1 (ACY-1) expression in neuroblastoma (NB).

What is known and what is new?

- ACY-1 inhibits the proliferation and migration of NB cells by regulating the downstream signaling pathway extracellular regulated protein kinases/transforming growth factor beta (ERK/TGF-β).
- This study further explored the upstream regulatory gene miRNA of ACY-1.

What is the implication, and what should change now?

- MiR-1271-5p was an upstream target gene of ACY-1, and miR-1271-5p could affect the growth and migration of NB cells by inhibiting ACY-1 expression.

Methods

Clinical specimens

Four pairs of tumor/paracancer samples were collected during surgical resection. The approximate size of each sample was 0.5 cm × 0.5 cm × 0.5 cm. Paracancer samples were obtained from the marginal area surrounding the tumor. All fresh tissue specimens were immediately transferred to liquid nitrogen after collection. The study was conducted in accordance with the Declaration of

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Table 1 Gene interference sequence

Gene	Sequence (5'–3')
MiR-1271-5p inhibitor	ACGUGACACGUUCGGAGAATT
NC inhibitor	CAGUACUUUUGUGUAGUACAA
siRNA-ACY-1	UCAACACGGUCACCACAUAGCCAGG
si-NC	ACGUGACACGUUCGGAGAATT

NC, negative control; siRNA-ACY-1, small interfering RNA fragments of aminoacylase 1; si-NC, small interfering RNA fragments of NC.

Table 2 RT-qPCR primers for gene detection

Gene	Primer sequence (5'–3')
ACY-1	Forward: CCTACACTCTCCTCCATCTTGC
	Reverse: CCTGGCATAGATGTAGCCCTCA
GAPDH	Forward: GAGTCAACGGATTTGGTCGT
	Reverse: GACAAGCTTCCCGTTCTCAG
hsa-miR-1271-5p	Forward: AACAAGCTTGGCACCTAGC
	Reverse: GTCGTATCCAGTGCAGGGTCCG AGGTATTCGCACTGGATACGACTGAGTG
U6	Forward: CTCGCTTCGGCAGCACA
	Reverse: AACGCTTCACGAATTTGCGT

RT-qPCR, reverse transcription-quantitative polymerase chain reaction; ACY-1, aminoacylase 1; GAPDH, glyceraldehyde-3-phosphate dehydrogenase.

Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of Shenzhen Children's Hospital (No. 202105802, 23rd July 2021), and informed consent was obtained from the legal guardians of all individual participants.

Cell culture and transfection

NB cancer tissues and adjacent tissues were collected from NB patients at Shenzhen Children's Hospital and stored at −80 ℃. The human NB cell lines SH-SY-5Y (CC2101) and SK-N-SH (CC2103) were purchased from Cellcook (Guangzhou, China) and cultured in matching complete medium (Cellcook).

Small interfering RNA (siRNA)-ACY-1, the miR-1271-5p inhibitor and other gene primers were designed and synthesized by Jimma (Shanghai, China) (*Table 1*). Cells were transfected using a Lipofectamine 2000 kit (Invitrogen, Waltham, MA, USA).

Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) assay

Complementary DNA (cDNA) was obtained following the instructions of the PrimeScript™ RT reagent kit (Takara, Kusatsu, Japan) after RNA isolation using TRIzol (Invitrogen). PCR was conducted according to the manufacturer's instructions for the SYBR Green Premix Kit (Takara, Kusatsu, Japan). The sequences of primers used for experimental detection are shown in *Table 2* below.

Western blot (WB)

SK-N-SH and SH-SY-5Y cells were transfected with si-ACY-1 or miR-1271-5p inhibitor for the time indicated following washing with phosphate buffered saline (PBS) twice. Radio immunoprecipitation assay (RIPA) lysis buffer (Beyotime Biotechnology, Shanghai, China) was added to the cells following centrifugation. The protein in the cell supernatant was further separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) gel and then transferred to a polyvinylidene fluoride membrane (Sangon Biotech, Shanghai, China). After that, the membrane was incubated with ACY-1 antibody (1:2,000, AB133635, Abcam, Cambridge, UK) or glyceraldehyde-3-phosphate dehydrogenase (GAPDH) antibody (1:1,000, 60004-1-LG, Proteintech, Chicago, USA) overnight followed by incubation with horseradish peroxidase (HRP) conjugated secondary antibody (1:2,000, Jackson ImmunoResearch, West Grove, PA, USA) for 2 hours. The enhanced chemiluminescence (ECL) reagent (Thermo Fisher Scientific, Massachusetts, USA) was used to visualize protein bands.

Cell proliferation assay [cell counting kit-8 (CCK-8) assay]

The cell density was adjusted, and the cells were then added to a 96-well plate at a density of 5,000 cells/well. At 24, 48, and 72 hours, CCK-8 reagent was added to the wells, and the spectrophotometric value at 450 nm was detected using CCK-8 (Beyotime).

Cell migration and invasion assays

Before conducting the invasion experiment, Matrigel (BD Biosciences, Shanghai, China) was added to a 24-

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well transwell plate (the upper chamber) to precoat the membrane. SH-SY-5Y and SK-N-SH cells were suspended in serum-free medium and seeded into the upper chamber at 100 µL per well. Then 600 µL of complete medium was added to the bottom chamber. After they had incubated for 48 hours, the migrating and invading cells were fixed with paraformaldehyde (Solarbio, Beijing, China) at 25 ℃ for 30 minutes. Afterwards, the cells were stained with 0.1% crystal violet (Sangon Biotech) for 20 minutes. We counted the number of migrating and invading cells under a microscope (Olympus, Tokyo, Japan).

Cell apoptosis assays

After SH-SY-5Y and SK-N-SH cells were transfected with interference fragments, trypsin was added to culture, and then added to binding buffer to prepare cell suspension. Cells were mixed with 10 µL annexin V-allophycocyanin (annexin V-APC) and 5 µL 7-aminoactinomycin D (7-AAD) (Invitrogen), and reacted for 15 minutes in the dark. After staining, 300 µL binding buffer was added into the cells, and the apoptosis rate was detected by flow cytometry after 1 hour of culture.

Dual luciferase reporter assay

The pmirGLO luciferase vector (Promega Corporation, Fitchburg, WI, USA) harboring ACY-1 3'-untranslated region (3'-UTR)-wild type (WT) and ACY-1 3'-UTR-mutant (MUT) was constructed, and then transfected with miR-1271 mimics or negative control (NC) into cells using Lipofectamine 2000 (Thermo Fisher Scientific). After 48 hours, the cells were assayed for luciferase activity (Promega Corporation).

Statistical analysis

GraphPad Prism Software 8.0 (San Diego, CA, USA) was used for the statistical tests in this study. The results were presented as mean ± standard deviation (SD). Differences in the data were analyzed using Student's *t*-test or one-way analysis of variance (ANOVA)/two-way ANOVA. All tests were repeated three times, and P<0.05 was considered to indicate statistical significance.

Results

Identification of miRNAs that bind to ACY-1

We screened and predicted miRNAs that may bind to ACY-1 from the miRDB, TargetScan, miRTarBase, and StarBase databases, and selected eight miRNAs that recurred in at least three databases (*Figure 1A*). The expression of these eight miRNAs and ACY-1 was detected in clinical samples, and miR-1271-5p was highly expressed in NB, while ACY-1 was expressed at low levels (*Figure 1B*). MiR-1271-5p gene sequence was predicted using TargetScan database, and dual luciferase assay was subsequently performed to verify that miR-1271-5p bound to ACY-1 and regulated luciferase activity (*Figure 1C*), suggesting that miR-1271-5p may regulate ACY-1 function.

MiR-1271-5p inhibits the function of NB cells

According to the results of previous studies, we silenced miR-1271-5p expression in cells to explore the function of miR-1271-5p in NB. MiR-1271-5p expression was decreased in the miR-1271-5p inhibition group (*Figure 2A*). In SH-SY-5Y and SK-N-SH cells, reduced expression of miR-1271-5p significantly inhibited cell proliferation (*Figure 2B,2C*). Apoptosis detection also showed that apoptosis increased after transfection with miRNA interference fragments (*Figure 2D*), and the invasion and migration ability of NB cells decreased (*Figure 2E,2F*), demonstrating that miR-1271-5p could regulate the function of NB cells.

MiRNA-1271-5p affects the growth and migration of NB cells by regulating ACY-1

We transfected SK-N-SH and SH-SY-5Y cells with an ACY-1 interference fragment (si-ACY-1), which could stably reduce the expression of ACY-1 (*Figure 3A*). In NB cells transfected with si-ACY-1, the expression of ACY-1 decreased, while the expression of ACY-1 increased after miR-1271-5p was inhibited (*Figure 3B,3C*). WB assays also showed the same results, indicating that miR-1271-5p negatively regulated ACY-1 expression (*Figure 3D*). Inhibiting the expression of ACY-1 increased cell proliferation, while restoring ACY-1 expression through a miR-1271-5p inhibitor reduced cell proliferation (*Figure 3E*). Reducing miR-1271-5p expression also increased the ability of ACY-1 to induce apoptosis (*Figure 3F*). Moreover, si-ACY-1 transfection increased cell invasion and migration, and decreased miR-1271-5p expression increased ACY-1 function in NB cells and inhibited NB progression (*Figure 3G,3H*). Therefore, miR-1271-5p can affect the growth of NB cells by regulating ACY-1 expression.

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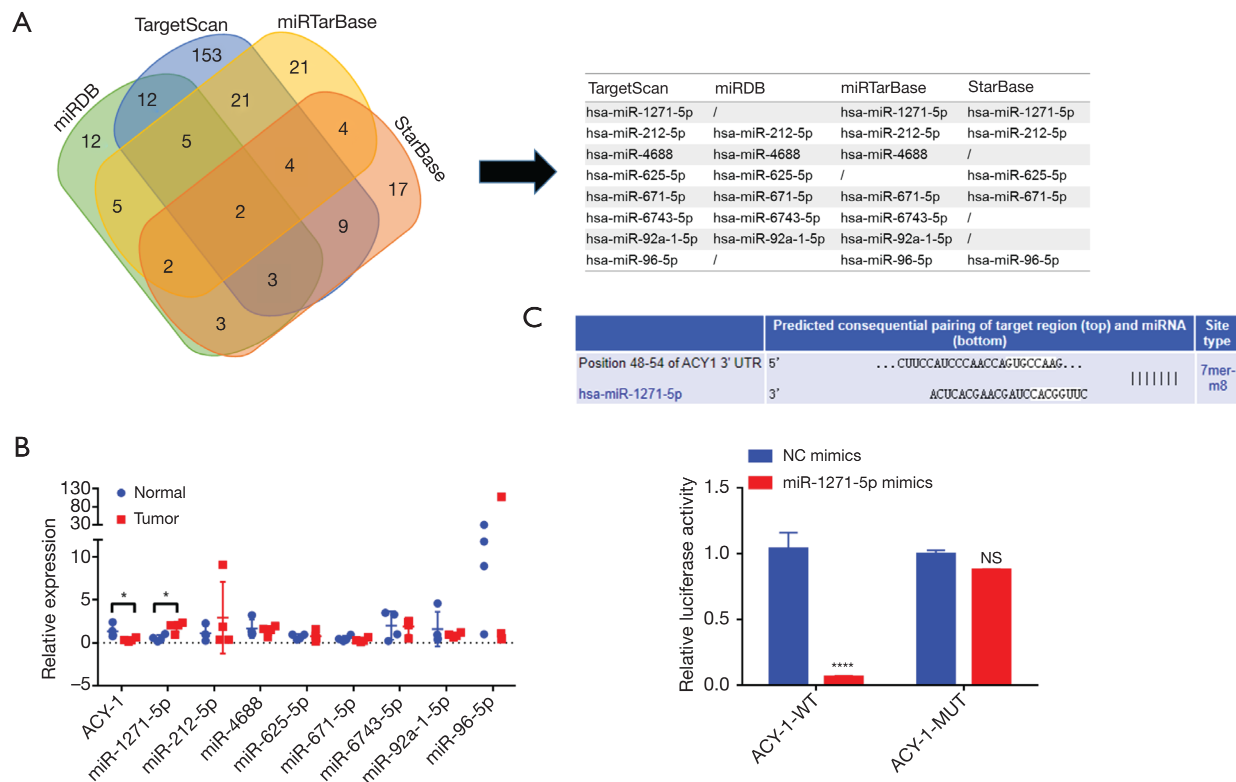

Figure 1 Screening and validation of ACY-1 binding miRNAs. (A) MiRNAs that may bind ACY-1 were predicted from miRDB, TargetScan, miRTarBase and StarBase databases, and miRNAs that had intersections in three or more databases were selected for subsequent screening and verification. (B) The expression of eight miRNAs predicted and ACY-1 in four groups of clinical tissues was detected by qPCR. (C) MiR-1271-5p was selected according to the screening results, and dual-luciferase assay was performed to verify that ACY-1 was regulated by miR-1271-5p. *, P<0.05; ****, P<0.0001. ACY-1, aminoacylase 1; miRNAs, microRNAs; qPCR, quantitative polymerase chain reaction; WT, wild type; MUT, mutant; NC, negative control; NS, no significance.

Discussion

NB is a malignant embryonic tumor originating from the sympathetic nervous system in childhood. Since NB can occur at various sites, with strong invasiveness and high degree of malignancy, its clinical manifestations are diverse, and the prognostic factors of NB are more abundant than those of other pediatric malignant tumors; thus, it is particularly important to emphasize individualized treatment (21). For the low-risk group, surgical resection is generally adopted; for the medium-risk group, surgery combined with chemotherapy is generally adopted; and for the high-risk group, surgery, chemotherapy, radiotherapy and differentiation induction therapy are often combined (22). With the progress of medical technology, many new treatments have been developed in clinical practice. Research shows that myeloablative chemotherapy with stem cell transplantation support technology can slightly improve the survival rate of children with cancer (23). The combined use of topotecan and ring phosphoric acid amine as induction chemotherapy, specific or nonspecific immunotherapy and gene therapy in primary treatment cases is still in the clinical research stage (24,25). However, in general, the treatment efficacy for NB is still poor. Therefore, it is very important to elucidate the process of tumorigenesis and metastasis and to find new therapeutic methods.

MiR-1271-5p is involved in the induction of apoptosis in acute myeloid leukemia (AML), and can reduce cardiac injury caused by acute myocardial infarction (26,27). Moreover, miR-1271-5p is significantly under-expressed in a variety of tumors, and has a significant anticancer effect, making it a potential molecular therapeutic target (28,29). However, at present, it is necessary to explore the regulatory

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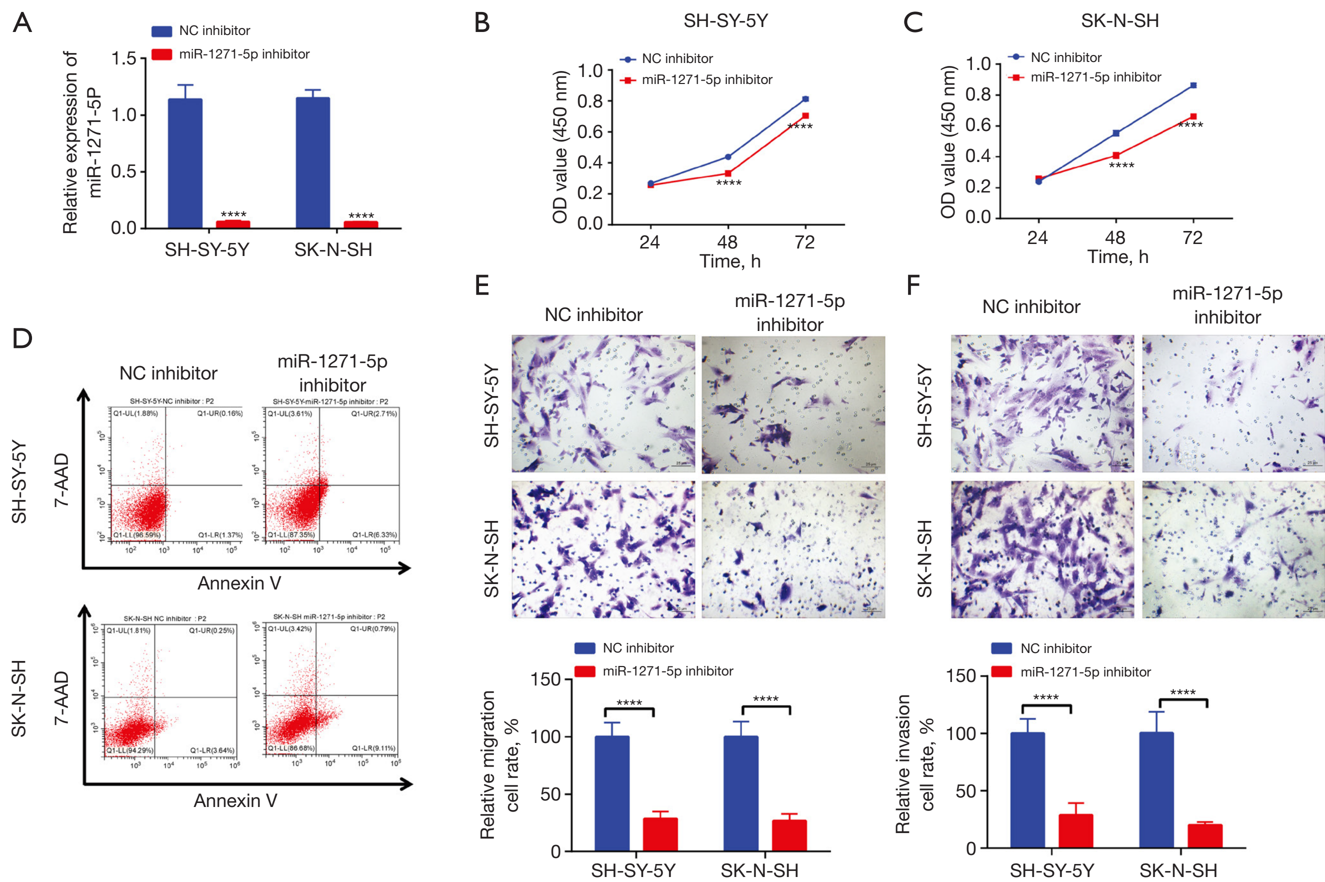

Figure 2 Effects of miR-1271-5p on physiological functions of SH-SY-5Y and SK-N-SH cells. (A) After transfection with miR-1271-5p inhibitor, miR-1271-5p expression efficiency was detected by qPCR at 48 hours. At 24, 48 and 72 hours, the cell viability of SH-SY-5Y (B) and SK-N-SH (C) was detected by CCK-8 method. (D) Cell apoptosis after 48 hours was detected by flow cytometry. Inhibition of miR-1271-5p reduced the number of cell migration (E) and invasion (F) by transwell. Transwell chamber was placed under a ×200 microscope to count the number of cells in each field of view. Staining method: crystal violet staining. Scale bar =25 μm. ****, P<0.0001. NC, negative control; OD, optical density; AAD, aminoactinomycin D; qPCR, quantitative polymerase chain reaction; CCK-8, cell counting kit-8.

role of miR-1271-5p in NB.

Previous study (20) has shown that *ACY-1* gene plays a role as a tumor suppressor gene in NB and that ACY-1 inhibits the proliferation and migration of NB cells by regulating the downstream signaling pathway ERK/TGF-β. This study further explored the upstream regulatory gene miRNA of ACY-1. At present, a common way to screen abnormally expressed genes and their related miRNA molecules is through database analysis. For example, data downloaded from the Gene Expression Omnibus (GEO) database can be used to construct volcano plots and heatmaps to identify differentially expressed genes (DEGs) (30). Network tools such as miWalk or TargetScan can also be used to identify differentially expressed miRNA molecules corresponding to target genes (31). Bioinformatics methods are widely used to explore new DEGs or screen miRNA-regulated genes corresponding to target genes. In this study, miRNAs that might bind ACY-1 were predicted and selected by TargetScan, miRTarBase and four other databases, and the expression of miRNAs and ACY-1 was detected in four groups of clinical samples. The results showed that miR-1271-5p was highly expressed in tumors and could be targeted.

Next, we found that the downregulation of miR-1271-5p expression in NB inhibited cell growth and migration. Finally, the expression of ACY-1 first decreased in SK-N-SH and SH-SY-5Ycells but was then partially restored by the miR-1271-5p inhibitor. After the expression

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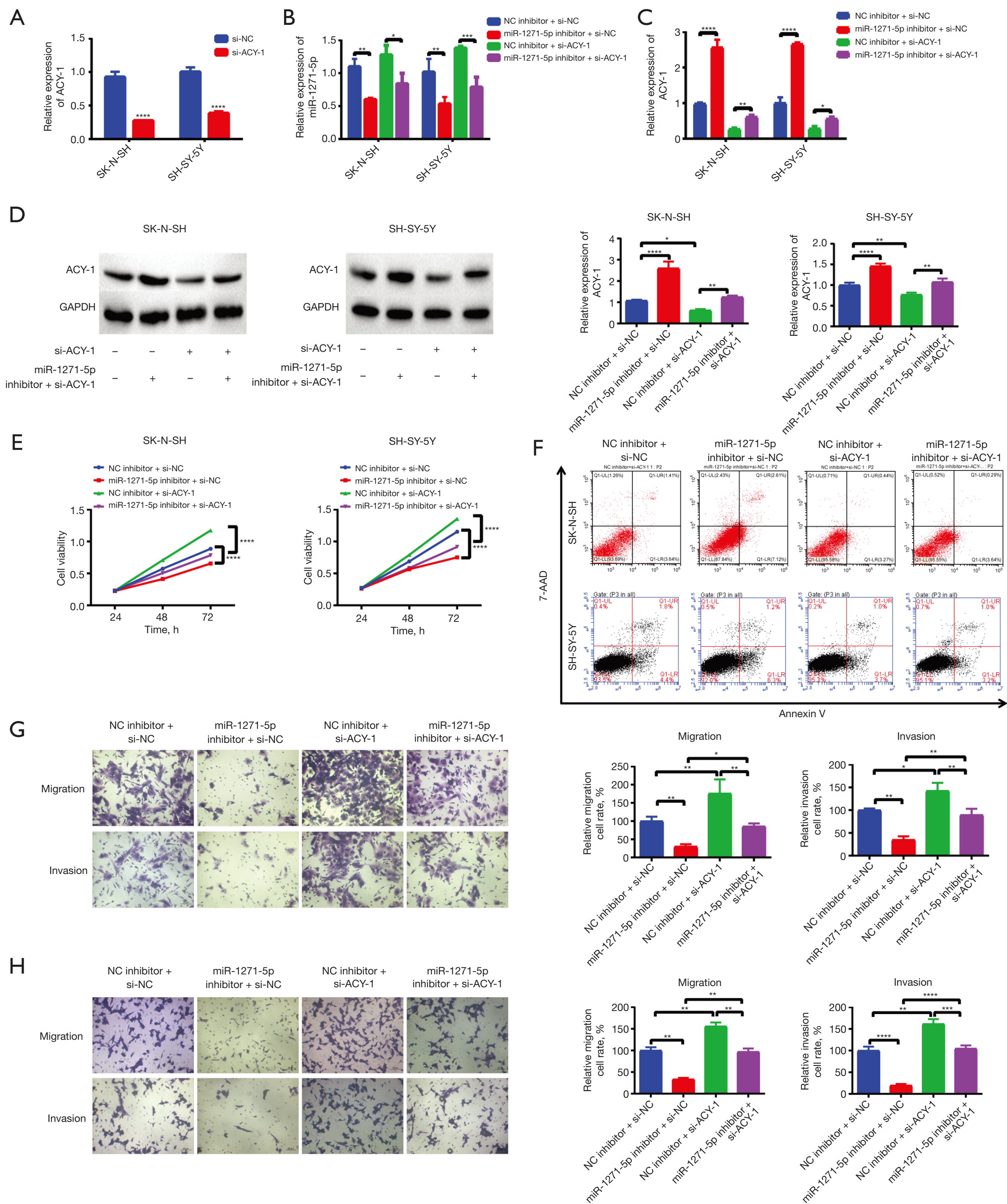

Figure 3 MiRNA-1271-5p can inhibit the cells growth and migration of neuroblastoma by regulating ACY-1. (A) 48 hours after transfection of ACY-1 gene interference sequence into human neuroblastoma cells, the expression effect of interference sequence was detected by qPCR. Cells containing ACY-1 interference fragment were further transfected with miR-1271-5p inhibitor, and the RNA levels of miR-1271-

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5p (B) and ACY-1 (C) were detected by qPCR. (D) Downregulation of miR-1271-5p can increase the level of ACY-1 protein. (E) The cell proliferation was evaluated using a CCK-8 assay. (F) The cell apoptosis level of each group was evaluated using flow cytometry. Increasing ACY-1 expression inhibited SK-N-SH cell (G) and SH-SY-5Y cell (H) migration and invasion by transwell. Transwell chamber was placed under a ×200 microscope to count the number of cells in each field of view. Staining method: crystal violet staining. Scale bar =25 μm. *, P<0.05; **, P<0.01; ***, P<0.001; ****, P<0.0001. ACY-1, aminoacylase 1; NC, negative control; si-NC, small interfering RNA fragments of NC; si-ACY-1, small interfering RNA fragments of ACY-1; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; AAD, aminoactinomycin D; qPCR, quantitative polymerase chain reaction; CCK-8, cell counting kit-8.

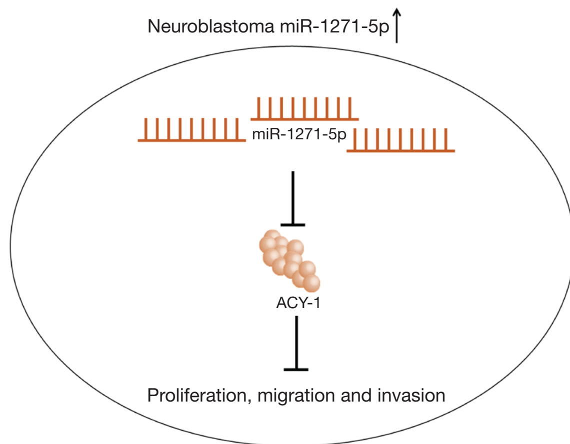

Figure 4 Mechanistic diagram of miR-1271-5p promotion of tumor proliferation, migration and invasion in neuroblastoma. ACY-1, aminoacylase 1.

of ACY-1 was inhibited, cell viability increased, indicating that proliferation accelerated. When the expression of ACY-1 was partially restored, the cell activity was significantly reduced, indicating that proliferation was inhibited. The apoptosis of SK-N-SH and SH-SY-5Y were significantly decreased after ACY-1 expression was disrupted, and the numbers of apoptotic cells were significantly increased after ACY-1 expression was partially restored. The SK-N-SH and SH-SY-5Y cells migration and invasion were also enhanced after ACY-1 expression was disrupted, and these effects were weakened after ACY-1 expression was partially restored. Specifically, in NB cells, the miR-1271-5p inhibitor restored the effect of the si-ACY-1 interference fragment on SK-N-SH and SH-SY-5Y cells proliferation, migration and invasion. These results indicate that miR-1271-5p can negatively regulate ACY-1 expression, thereby affecting the growth and migration of tumor cells.

Conclusions

We determined that miR-1271-5p was an upstream target gene of ACY-1 through data screening and experiments, and subsequent experiments also proved that miR-1271-5p could affect the growth and migration of NB cells by inhibiting ACY-1 expression (*Figure 4*). However, the mechanism by which ACY-1 affects the growth of NB cells in this study is still unclear and needs to be explored in the future.

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Footnote

Reporting Checklist: The authors have completed the MDAR reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-25/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-25/dss

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Project of Medicine in Shenzhen and the Shenzhen Fund for Guangdong Provincial High-level Clinical Key specialties. The authors have no other 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of Shenzhen Children's Hospital (No. 202105802, 23rd July 2021), and informed consent was obtained from the legal guardians of all individual participants.

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References

1. Zafar A, Wang W, Liu G, et al. Molecular targeting therapies for neuroblastoma: Progress and challenges. Med Res Rev 2021;41:961-1021.
2. Guan Q, Lin H, Hua W, et al. Variant rs8400 enhances ALKBH5 expression through disrupting miR-186 binding and promotes neuroblastoma progression. Chin J Cancer Res 2023;35:140-62.
3. Davidoff AM. Neonatal Neuroblastoma. Clin Perinatol 2021;48:101-15.
4. Almstedt E, Elgendy R, Hekmati N, et al. Integrative discovery of treatments for high-risk neuroblastoma. Nat Commun 2020;11:71.
5. Tsubota S, Kadomatsu K. Origin and initiation mechanisms of neuroblastoma. Cell Tissue Res 2018;372:211-21.
6. Heck JE, Ritz B, Hung RJ, et al. The epidemiology of neuroblastoma: a review. Paediatr Perinat Epidemiol 2009;23:125-43.
7. Patton T, Olshan AF, Neglia JP, et al. Parental exposure to medical radiation and neuroblastoma in offspring. Paediatr Perinat Epidemiol 2004;18:178-85.
8. Aygun N. Biological and Genetic Features of Neuroblastoma and Their Clinical Importance. Curr Pediatr Rev 2018;14:73-90.
9. Mugishima H. Current status of molecular biology and treatment strategy for neuroblastoma. Int J Clin Oncol 2012;17:189.
10. Wang C, Wang X, Zhang D, et al. The macrophage polarization by miRNAs and its potential role in the treatment of tumor and inflammation (Review). Oncol Rep 2023;50:190.
11. Pal A, Ojha A, Ju J. Functional and Potential Therapeutic Implication of MicroRNAs in Pancreatic Cancer. Int J Mol Sci 2023;24:17523.
12. Chen Y, Stallings RL. Differential patterns of microRNA expression in neuroblastoma are correlated with prognosis, differentiation, and apoptosis. Cancer Res 2007;67:976-83.
13. Afanasyeva EA, Hotz-Wagenblatt A, Glatting KH, et al. New miRNAs cloned from neuroblastoma. BMC Genomics 2008;9:52.
14. Schulte JH, Schowe B, Mestdagh P, et al. Accurate prediction of neuroblastoma outcome based on miRNA expression profiles. Int J Cancer 2010;127:2374-85.
15. Welberry Smith MP, Zougman A, Cairns DA, et al. Serum aminoacylase-1 is a novel biomarker with potential prognostic utility for long-term outcome in patients with delayed graft function following renal transplantation. Kidney Int 2013;84:1214-25.
16. Chen H, Wang W, Xiao C, et al. ACY1 regulating PTEN/PI3K/AKT signaling in the promotion of non-small cell lung cancer progression. Ann Transl Med 2021;9:1378.
17. Xu Z, Hu Y, Yu Z. Effect of the ACY-1 gene on HER2 and TRAIL expression in rectal carcinoma. Exp Ther Med 2021;22:817.
18. Shan W, Dai C, Zhang H, et al. ACY1 Downregulation Enhances the Radiosensitivity of Cetuximab-Resistant Colorectal Cancer by Inactivating the Wnt/β-Catenin Signaling Pathway. Cancers (Basel) 2022;14:5704.
19. Long PM, Stradecki HM, Minturn JE, et al. Differential aminoacylase expression in neuroblastoma. Int J Cancer 2011;129:1322-30.
20. Chen Z, Gao J, Sun J, et al. Aminoacylase 1 (ACY-1) Mediates the Proliferation and Migration of Neuroblastoma Cells in Humans Through the ERK/Transforming Growth Factor β (TGF-β) Signaling Pathways. Med Sci Monit 2021;27:e928813.
21. Wang H, Wang X, Xu L. Chromosome 1p36 candidate gene ZNF436 predicts the prognosis of neuroblastoma: a

bioinformatic analysis. Ital J Pediatr 2023;49:145.
22. Gustafson WC, Matthay KK. Progress towards personalized therapeutics: biologic- and risk-directed therapy for neuroblastoma. Expert Rev Neurother 2011;11:1411-23.
23. Chung C, Boterberg T, Lucas J, et al. Neuroblastoma. Pediatr Blood Cancer 2021;68 Suppl 2:e28473.
24. Castel V, Segura V, Berlanga P. Emerging drugs for neuroblastoma. Expert Opin Emerg Drugs 2013;18:155-71.
25. Kholodenko IV, Kalinovsky DV, Doronin II, et al. Neuroblastoma Origin and Therapeutic Targets for Immunotherapy. J Immunol Res 2018;2018:7394268.
26. Chen X, Yang S, Zeng J, et al. miR-1271-5p inhibits cell proliferation and induces apoptosis in acute myeloid leukemia by targeting ZIC2. Mol Med Rep 2019;19:508-14.
27. Long R, Gao L, Li Y, et al. M2 macrophage-derived exosomes carry miR-1271-5p to alleviate cardiac injury in acute myocardial infarction through down-regulating SOX6. Mol Immunol 2021;136:26-35.
28. Wei D, Tian M, Fan W, et al. Circular RNA circ_0000043 promotes endometrial carcinoma progression by regulating miR-1271-5p/CTNND1 axis. Arch Gynecol Obstet 2021;303:1075-87.
29. Fan G, Jiao J, Shen F, et al. Upregulation of lncRNA ZFAS1 promotes lung adenocarcinoma progression by sponging miR-1271-5p and upregulating FRS2. Thorac Cancer 2020;11:2178-87.
30. Shi J, Zhang P, Su H, et al. Bioinformatics Analysis of Neuroblastoma miRNA Based on GEO Data. Pharmgenomics Pers Med 2021;14:849-58.
31. Chava S, Reynolds CP, Pathania AS, et al. miR-15a-5p, miR-15b-5p, and miR-16-5p inhibit tumor progression by directly targeting MYCN in neuroblastoma. Mol Oncol 2020;14:180-96.

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