Cancer Screening and Prevention **2023** vol. 2(3) | 149–153
DOI: 10.14218/CSP.2023.00035

Original Article

miR-618 rs2682818 C>A Polymorphism Decreases Neuroblastoma Risk in Tumors Originating from the Adrenal Gland

Li-Li Xie[1#], Chang-Mi Deng[1#], Jia-Ming Chang[1], Xin-Xin Zhang[1], Chun-Lei Zhou[2], Hai-Yan Wu[2*] and Jing He[1*]

[1]*Department of Pediatric Surgery, Guangzhou Institute of Pediatrics, Guangdong Provincial Key Laboratory of Research in Structural Birth Defect Disease, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangdong Provincial Clinical Research Center for Child Health, Guangzhou, Guangdong, China;* [2]*Department of Pathology, Children's Hospital of Nanjing Medical University, Nanjing, Jiangsu, China*

Received: July 31, 2023 | **Revised:** August 31, 2023 | **Accepted:** September 06, 2023 | **Published online:** September 25, 2023

Abstract

Background and objectives: and aims MicroRNAs (miRNAs) are endogenous small noncoding RNAs that regulate gene expression by either degrading or inhibiting the translation of mRNAs and have significant roles in the development of various tumors. A polymorphism (rs2682818) in *miR-618* has been confirmed to be correlated with susceptibility to various cancers. Nonetheless, its role has not been investigated in neuroblastoma to date. Therefore, we assessed whether the *miR-618* rs2682818 C>A polymorphism was correlated with neuroblastoma risk in the Chinese population.

Methods: We performed this case-control study with 402 neuroblastoma patients and 473 cancer-free controls from Jiangsu Province, China. The TaqMan method was used to genotype the *miR-618* rs2682818 polymorphism. We evaluated the strength of the correlation between this polymorphism and susceptibility to neuroblastoma based on the odds ratios (ORs) and 95% confidence intervals (CIs), which were calculated by logistic regression models.

Results: Overall, no significant correlation was observed between the rs2682818 C>A polymorphism and the risk of neuroblastoma. Nevertheless, we conducted a further stratification analysis and discovered that, compared to the CC genotype of rs2682818, the subjects with CA/AA genotypes had a lower risk to neuroblastoma developing in the adrenal gland (adjusted OR = 0.57, 95% CI: 0.35–0.91, $p = 0.018$).

Conclusions: We first discovered that the *miR-618* rs2682818 C>A polymorphism had an essential role in significantly decreasing susceptibility to neuroblastoma in the adrenal gland.

Keywords: *miR-618*; Neuroblastoma; Polymorphism; Susceptibility.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; HWE, Hardy-Weinberg equilibrium; miRNA, microRNA; mRNA, messenger RNA; OR, odds ratio; pre, precursor; pri, primary; SNP, single nucleotide polymorphism; UTR, untranslated region.

***Correspondence to:** Jing He, Department of Pediatric Surgery, Guangzhou Institute of Pediatrics, Guangdong Provincial Key Laboratory of Research in Structural Birth Defect Disease, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangdong Provincial Clinical Research Center for Child Health, 9 Jinsui Road, Guangzhou, Guangdong 510623, China. ORCID: https://orcid.org/0000-0002-1954-2892. Tel: +86-20-38076560, E-mail: hejing198374@gmail.com; Haiyan Wu, Department of Pathology, Children's Hospital of Nanjing Medical University, 72 Guangzhou Road, Nanjing, Jiangsu 210008, China. ORCID: https://orcid.org/0000-0002-4708-3697. Tel: +86-25-83117311, E-mail: nchwhy@163.com

[#]Contributed equally to this work.

How to cite this article: Xie LL, Deng CM, Chang JM, Zhang XX, Zhou CL, Wu HY, *et al*. *miR-618* rs2682818 C>A Polymorphism Decreases Neuroblastoma Risk in Tumors Originating from the Adrenal Gland. *Cancer Screen Prev* 2023;2(3):149–153. doi: 10.14218/CSP.2023.00035.

Introduction

Neuroblastoma, which appears during the development of the sympathetic nervous system, is a frequently occurring pediatric solid tumor.[1] With a comparatively low morbidity and affecting approximately 10.2 per million children younger than 15 years of age, neuroblastoma accounts for approximately 10% of all childhood cancers.[2,3] However, neuroblastoma, a frequently fatal form of malignancy, is the third most common cause of childhood cancer-related mortality.[4] Both in terms of prognosis and clinical presentation, neuroblastoma exhibits significant heterogeneity.[5] It is well recognized that spontaneous regression is routinely observed in localized neuroblastoma and is not limited to stage 4S.[6] Neuroblastoma, on the other hand, can be classified into different subgroups with varying survival rates based on clinical and bio-

logical characteristics.[3,7] The long-term survival of neuroblastoma with low risk is approximately 90%, whereas survival in high-risk neuroblastoma is less than 40%, even with aggressive and comprehensive therapy.[8,9] Neuroblastoma not only can have a devastating impact on the family, but it also poses a severe threat to public health and is a global burden.[10,11]

Unfortunately, the exact etiology of neuroblastoma continues to be incompletely determined.[12] Potential environmental exposure, including parental exposure to hydrocarbons, turpentine, lacquer thinner, wood dust, solder, sources of radiation, and electrical devices, have been reported to alter neuroblastoma susceptibility in descendants, although the reasons are not entirely clear.[13,14] On the other hand, increasing verification regarding studies in molecular epidemiology demonstrates that genetic polymorphisms associated with genetic risk factors may have an essential impact on susceptibility to neuroblastoma.[15,16] A multitude of susceptibility genes for neuroblastoma have been discovered based on previous genome-wide association studies, including *CASC15*, *DUSP12*, *DDX4*, *IL31RA*, *HSD17B12*, *BARD1*, *LMO1*, *MLF1*, *CPZ*, *HACE1*, *LIN28B*, and *RSRC1*.[17–22] In addition to genome-wide association studies, candidate gene methods have also served as powerful tools to identify potential inherited genetic variants that are related to neuroblastoma. Indeed, several previous studies have revealed the susceptibility of genes such as *NEFL*, *CDKN1B*, *TP53*, *BARD1*, and *ALKBH5* to neuroblastoma.[15,23–26]

MicroRNAs (miRNAs) are endogenous small noncoding RNAs with approximately 19–25 nucleotides.[27] miRNA bind to the 3′-untranslated region (UTR) of targeted messenger RNAs (mRNAs) and regulate gene expression post-transcriptionally by either degrading or inhibiting the translation of corresponding mRNAs.[28,29] With the discovery of miRNAs, evidence that they have significant and diverse roles in multiple biological processes, including cell proliferation, development, differentiation, and apoptosis, as well as their crucial implication in cancer development has accumulated.[30–32] Single nucleotide polymorphisms (SNPs) within miRNAs influence the ways in which miRNAs function. They have an impact on primary transcription, the procedure for processing and maturation of precursor (pre)-miRNAs and primary (pri)-miRNAs, as well as the interactions between miRNAs and their targets, thereby modulating gene expression.[33] Based on the type of cancer, the region, and the ethnicity, polymorphisms may have a variety of genetic impacts on cancer risk. In recent years, the correlation between *miR-618* rs2682818 and cancer risk has been extensively studied in a variety of malignancies, including breast cancer, follicular lymphoma, colorectal cancer, and acute lymphocytic leukemia,[34–37] but not in neuroblastoma. To evaluate the relevance of the rs2682818 polymorphism to the risk of neuroblastoma in Chinese children, we conducted research involving 402 neuroblastoma patients and 473 control individuals.

Methods

Study subjects

The individuals involved were selected from the Nanjing Medical University Children's Hospital in Jiangsu Province, as previously mentioned in our investigations.[38,39] All the included individuals were unrelated ethnic Chinese who came from Jiangsu Province, China. The study included 402 individuals with neuroblastoma who were diagnosed histopathologically and 473 cancer-free controls (Table S1). The institutional review board of the Children's Hospital of Nanjing Medical University approved the study protocol. All participants signed a written informed consent form for our research with the signature of their parent or legal guardian.

SNP screening and genotyping

In a previous study, we provided a detailed description regarding the selection of potentially functioning polymorphisms.[40] Briefly, to screen for any potentially functioning polymorphisms of *miR-618*, we selected the 3′ UTR, 5′ UTR, 5′-flanking region, exons, and intron of the *miR-618* according to the criteria. The rs2682818 polymorphism in the *miR-618* was available and ultimately chosen. As previously mentioned in our study, TaqMan real-time polymerase chain reaction was performed to accurately genotype *miR-618* rs2682818 C>A using the 7900 Sequencing Detection System from Applied Biosystems (Foster City, CA, USA).[40,41] To ensure accurate genetic typing of the results, we randomly selected 10% of the DNA samples for further confirmation, and the results were 100% concordant. A goodness-of-fit chi-square test was performed to test for deviations from Hardy-Weinberg equilibrium (HWE) for the genotype frequencies in control subjects. Differences in the distribution of selected demographic variables and genotypes between neuroblastoma cases and control individuals were assessed with two-sided chi-square tests. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated by multivariate logistic regression and were used to estimate the correlation of the rs2682818 C>A polymorphism with neuroblastoma risk. In addition, analysis was performed after stratification by age, sex, tumor origin, and clinical stage. SAS (version 9.4; SAS Institute, Cary, NC, USA) was used to perform the statistical analysis, and *p*-values <0.05 were considered statistically significant.

Results

Association of miR-618 rs2682818 C>A with neuroblastoma risk

Table 1 shows the genotype distribution of *miR-618* rs2682818 C>A in all participants and the association with the risk of neuroblastoma. In the controls, the data were in accord with the HWE ($p = 0.358$). No significant correlation was detected between *miR-618* rs2682818 C>A polymorphism and neuroblastoma.

Stratification analyses

To further investigate the relationship between the rs2682818 C>A polymorphism and neuroblastoma susceptibility under different stratification conditions, we analyzed the results following stratification by age, sex, site of tumor origin, and clinical stage (Table 2). Compared with the CC genotype, the CA/AA genotypes had a lower risk of neuroblastoma developing in the adrenal gland (AOR = 0.57, 95% CI: 0.35–0.91, $p = 0.018$). No other significant correlations with the risk of neuroblastoma were found.

Discussion

In this study, we investigated the association between *miR-618* rs2682818 C>A polymorphism and neuroblastoma predisposition in 402 cases and 473 controls. The rs2682818 C>A polymorphism CA/AA genotypes were associated with a reduced risk of neuroblastoma in the adrenal gland compared with the CC genotype.

In a variety of cancers, *miR-618* is an oncogene or a tumor-suppressing gene. The deregulation of *miR-618*, as described in previous studies, is directly correlated with tumorigenesis in breast cancer, esophageal Barrett's cancer, bladder cancer, pros-

Table 1. ***miR-618*** **rs2682818 C>A polymorphism and neuroblastoma risk in children from Jiangsu Province**

Genotype	Cases, *n* = 400	Controls, *n* = 473	*p*[a]	Crude OR (95% CI)	*p*	Adjusted OR (95% CI)[b]	*p*[b]
rs2682818 (HWE = 0.358)							
CC	234 (58.50)	252 (53.28)		1.00		1.00	
CA	132 (33.00)	181 (38.27)		0.79 (0.59–1.05)	0.098	0.78 (0.59–1.05)	0.097
AA	34 (8.50)	40 (8.46)		0.92 (0.56–1.50)	0.724	0.92 (0.56–1.50)	0.729
Additive			0.239	0.88 (0.72–1.09)	0.239	0.88 (0.72–1.09)	0.239
Dominant	166 (41.50)	221 (46.72)	0.122	0.81 (0.62–1.06)	0.122	0.81 (0.62–1.06)	0.121
CC/CA	366 (91.50)	433 (91.54)		1.00		1.00	
AA	34 (8.50)	40 (8.46)	0.982	1.01 (0.62–1.62)	0.982	1.01 (0.62–1.62)	0.979

CI, confidence interval; HWE, Hardy-Weinberg equilibrium; OR, odds ratio. [a]Chi-square test for genotype distributions between neuroblastoma cases and cancer-free controls; [b] Adjusted for age and sex.

tate cancer, hepatocellular carcinoma, and thyroid cancer.[36,42–46] The rs2682818 polymorphism, which is found in the stem-loop sequence of *premiR-618* may disrupt the structural development of the secondary stem-loop and consequently affect the further transformation of the precursor *miR-618* into the mature form, which may have an impact on *miR-618* expression.[34]

Fu *et al*.[34] described a variant rs2682818 T allele that interfered with pri-miR-618 stem-loop generation as well as the progress of interactions of *miR-618* with its targets, caused lower levels of mature *miR-618* and increased the risk of follicular lymphoma. In addition, *miR-618* rs2682818 was related to increased breast cancer susceptibility.[36] In contrast, as reported by Chen *et al*.,[37] rs2682818 polymorphism participated the development of colorectal cancer. They discovered that, compared with the CC genotype, the AA or AC/AA genotype of rs2682818 in the Chinese population was correlated with a decreased susceptibility to colorectal cancer. In addition, Shao *et al*.[47] reported that the rs2682818 polymorphism influenced on the degree of expression of mature *miR-618* in colorectal cancer cells, which in turn affected the capacity of *miR-618* to target *TIMP1* expression and inhibited the development of colorectal cancer. As mentioned above, these findings indicate that rs2682818 polymorphism may affect cancer susceptibility. Nevertheless, previous studies reported the association of *miR-618* rs2682818 with neuroblastoma susceptibility. Our results indicate that the rs2682818 polymorphism decreases the susceptibility to neuroblastoma in tumors originating from the adrenal gland.

Although this is the first study to find an association of the *miR-618* rs2682818 C>A polymorphism with susceptibility to neuroblastoma. Some limitations of these preliminary findings must be recognized. First, some important environmental factors, including parental exposure, dietary habits, and living conditions, were not taken into consideration. Second, the study subjects only included Chinese individuals from Jiangsu Province, and the conclusion may not be generalized to the Chinese and other ethnic populations. Finally, only the rs2682818 C>A polymorphism was investigated. Other SNPs that may be functional need to be evaluated in the future.

Table 2. Stratification analysis for the association between ***miR-618*** **rs2682818 C>A polymorphism and neuroblastoma susceptibility**

Variable	rs2682818, cases/controls		OR (95% CI)	*p*	AOR (95% CI)[a]	*p*[a]
	CC	CA/AA				
Age, months						
≤18	83/70	54/69	0.66 (0.41–1.06)	0.088	0.66 (0.41–1.06)	0.088
>18	151/182	112/152	0.89 (0.64–1.23)	0.475	0.89 (0.64–1.23)	0.479
Sex						
Female	117/130	74/95	0.87 (0.58–1.28)	0.472	0.87 (0.58–1.28)	0.472
Male	117/122	92/126	0.76 (0.53–1.10)	0.148	0.76 (0.53–1.10)	0.145
Site of origin						
Adrenal gland	62/252	31/221	0.57 (0.36–0.91)	0.019	0.57 (0.35–0.91)	0.018
Retroperitoneal	91/252	75/221	0.94 (0.66–1.34)	0.732	0.94 (0.66–1.35)	0.749
Mediastinum	68/252	51/221	0.86 (0.57–1.28)	0.450	0.85 (0.57–1.28)	0.442
Other	10/252	8/221	0.91 (0.35–2.35)	0.849	0.92 (0.36–2.37)	0.859
Clinical stage						
I+II+4s	94/252	77/221	0.93 (0.66–1.33)	0.703	0.96 (0.67–1.36)	0.811
III+IV	93/252	70/221	0.86 (0.60–1.23)	0.404	0.84 (0.59–1.21)	0.348

AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio. [a]Adjusted for age and sex, omitting the corresponding stratification factor.

Conclusions

In summary, the *miR-618* rs2682818 C>A polymorphism was significantly associated with decreased risk of neuroblastoma in tumors originating from the adrenal gland. Our findings indicate that *miR-618* rs2682818 may be a neuroblastoma susceptibility gene. Large multiregional and multicenter studies with populations of various ethnicities are required to verify our results.

Supporting information

Supplementary material for this article is available at https://doi.org/10.14218/CSP.2023.00035.

Table S1. Demographic characteristics of neuroblastoma patients and cancer-free controls from Jiangsu province.

Acknowledgments

None.

Funding

This work was conducted with financial support from the Guangzhou Science and Technology Project (No: 202201020622), the Postdoctoral Science Foundation of China (No: 2021M691649), and the Postdoctoral Science Foundation of Jiangsu Province (No: 2021K524C).

Conflict of interest

One of the authors, Jing He has been an editorial board member of *Cancer Screening and Prevention* since April 2023. The authors have no other conflict of interest.

Author contributions

Designed the study (HYW, JH), wrote the paper (LLX, CMD, JH), performed the experiments (JMC, XXZ), collected the clinical information and samples (CLZ, HYW), provided the data analysis and prepared the tables (CMD, JH). All authors approved this version to be published.

Ethical statement

This study was performed in accordance with the ethical principles of Declaration of Helsinki (as revised in 2013). The institutional review board of the Children's Hospital of Nanjing Medical University approved the study protocol (202112141-1). All participants signed a written informed consent form for our research with the signature of their parent or legal guardian.

Data sharing statement

The corresponding author will make the datasets produced during the study and used to support the conclusions accessible on reasonable request.

References

[1] Cheung NK, Dyer MA. Neuroblastoma: developmental biology, cancer genomics and immunotherapy. Nat Rev Cancer 2013;13(6):397–411. doi:10.1038/nrc3526, PMID:23702928.
[2] Maris JM, Hogarty MD, Bagatell R, Cohn SL. Neuroblastoma. Lancet 2007;369(9579):2106–2120. doi:10.1016/s0140-6736(07)60983-0, PMID:17586306.
[3] Maris JM. Recent advances in neuroblastoma. N Engl J Med 2010;362(23):2202–2211. doi:10.1056/NEJMra0804577, PMID:20558371.
[4] Smith MA, Seibel NL, Altekruse SF, Ries LA, Melbert DL, O'Leary M, *et al*. Outcomes for children and adolescents with cancer: challenges for the twenty-first century. J Clin Oncol 2010;28(15):2625–2634. doi:10.1200/jco.2009.27.0421, PMID:20404250.
[5] Zhou C, Tang Y, Zhu J, He L, Li J, Wang Y, *et al*. Association of miR-146a, miR-149 and miR-196a2 polymorphisms with neuroblastoma risk in Eastern Chinese population: a three-center case-control study. Biosci Rep 2019;39(6):BSR20181907. doi:10.1042/bsr20181907, PMID:31123171.
[6] Hero B, Simon T, Spitz R, Ernestus K, Gnekow AK, Scheel-Walter HG, *et al*. Localized infant neuroblastomas often show spontaneous regression: results of the prospective trials NB95-S and NB97. J Clin Oncol 2008;26(9):1504–1510. doi:10.1200/jco.2007.12.3349, PMID:18349403.
[7] Li Y, Zhuo ZJ, Zhou H, Liu J, Xiao Z, Xiao Y, *et al*. miR-34b/c rs4938723 T>C Decreases Neuroblastoma Risk: A Replication Study in the Hunan Children. Dis Markers 2019;2019:6514608. doi:10.1155/2019/6514608, PMID:31583029.
[8] Bernstein ML, Leclerc JM, Bunin G, Brisson L, Robison L, Shuster J, *et al*. A population-based study of neuroblastoma incidence, survival, and mortality in North America. J Clin Oncol 1992;10(2):323–329. doi:10.1200/jco.1992.10.2.323, PMID:1732433.
[9] Spix C, Pastore G, Sankila R, Stiller CA, Steliarova-Foucher E. Neuroblastoma incidence and survival in European children (1978-1997): report from the Automated Childhood Cancer Information System project. Eur J Cancer 2006;42(13):2081–2091. doi:10.1016/j.ejca.2006.05.008, PMID:16919772.
[10] Kaatsch P. Epidemiology of childhood cancer. Cancer Treat Rev 2010;36(4):277–285. doi:10.1016/j.ctrv.2010.02.003, PMID:20231056.
[11] Zhang Z, Chang Y, Jia W, Zhang J, Zhang R, Zhu J, *et al*. LINC00673 rs11655237 C>T confers neuroblastoma susceptibility in Chinese population. Biosci Rep 2018;38(1):BSR20171667. doi:10.1042/BSR20171667, PMID:29339420.
[12] He J, Wang F, Zhu J, Zhang Z, Zou Y, Zhang R, *et al*. The TP53 gene rs1042522 C>G polymorphism and neuroblastoma risk in Chinese children. Aging (Albany NY) 2017;9(3):852–859. doi:10.18632/aging.101196, PMID:28275206.
[13] De Roos AJ, Olshan AF, Teschke K, Poole C, Savitz DA, Blatt J, *et al*. Parental occupational exposures to chemicals and incidence of neuroblastoma in offspring. Am J Epidemiol 2001;154(2):106–114. doi:10.1093/aje/154.2.106, PMID:11447042.
[14] De Roos AJ, Teschke K, Savitz DA, Poole C, Grufferman S, Pollock BH, *et al*. Parental occupational exposures to electromagnetic fields and radiation and the incidence of neuroblastoma in offspring. Epidemiology 2001;12(5):508–517. doi:10.1097/00001648-200109000-00008, PMID:11505168.
[15] Capasso M, Diskin S, Cimmino F, Acierno G, Totaro F, Petrosino G, *et al*. Common genetic variants in NEFL influence gene expression and neuroblastoma risk. Cancer Res 2014;74(23):6913–6924. doi:10.1158/0008-5472.Can-14-0431, PMID:25312269.
[16] Capasso M, Diskin SJ. Genetics and genomics of neuroblastoma. Cancer Treat Res 2010;155:65–84. doi:10.1007/978-1-4419-6033-7_4, PMID:20517688.
[17] McDaniel LD, Conkrite KL, Chang X, Capasso M, Vaksman Z, Oldridge DA, *et al*. Common variants upstream of MLF1 at 3q25 and within CPZ at 4p16 associated with neuroblastoma. PLoS Genet 2017;13(5):e1006787. doi:10.1371/journal.pgen.1006787, PMID:28545128.
[18] Oldridge DA, Wood AC, Weichert-Leahey N, Crimmins I, Sussman R, Winter C, *et al*. Genetic predisposition to neuroblastoma mediated by a LMO1 super-enhancer polymorphism. Nature 2015;528(7582):418–421. doi:10.1038/nature15540, PMID:26560027.
[19] Diskin SJ, Capasso M, Schnepp RW, Cole KA, Attiyeh EF, Hou C, *et al*. Common variation at 6q16 within HACE1 and LIN28B influences

susceptibility to neuroblastoma. Nat Genet 2012;44(10):1126–1130. doi:10.1038/ng.2387, PMID:22941191.
[20] Nguyen le B, Diskin SJ, Capasso M, Wang K, Diamond MA, Glessner J, *et al*. Phenotype restricted genome-wide association study using a gene-centric approach identifies three low-risk neuroblastoma susceptibility Loci. PLoS Genet 2011;7(3):e1002026. doi:10.1371/journal.pgen.1002026, PMID:21436895.
[21] Capasso M, Devoto M, Hou C, Asgharzadeh S, Glessner JT, Attiyeh EF, *et al*. Common variations in BARD1 influence susceptibility to high-risk neuroblastoma. Nat Genet 2009;41(6):718–723. doi:10.1038/ng.374, PMID:19412175.
[22] Maris JM, Mosse YP, Bradfield JP, Hou C, Monni S, Scott RH, *et al*. Chromosome 6p22 locus associated with clinically aggressive neuroblastoma. N Engl J Med 2008;358(24):2585–2593. doi:10.1056/NEJMoa0708698, PMID:18463370.
[23] Cimmino F, Avitabile M, Diskin SJ, Vaksman Z, Pignataro P, Formicola D, *et al*. Fine mapping of 2q35 high-risk neuroblastoma locus reveals independent functional risk variants and suggests full-length BARD1 as tumor-suppressor. Int J Cancer 2018;143(11):2828–2837. doi:10.1002/ijc.31822, PMID:30132831.
[24] Capasso M, McDaniel LD, Cimmino F, Cirino A, Formicola D, Russell MR, *et al*. The functional variant rs34330 of CDKN1B is associated with risk of neuroblastoma. J Cell Mol Med 2017;21(12):3224–3230. doi:10.1111/jcmm.13226, PMID:28667701.
[25] Diskin SJ, Capasso M, Diamond M, Oldridge DA, Conkrite K, Bosse KR, *et al*. Rare variants in TP53 and susceptibility to neuroblastoma. J Natl Cancer Inst 2014;106(4):dju047. doi:10.1093/jnci/dju047, PMID:24634504.
[26] Guan Q, Lin H, Hua W, Lin L, Liu J, Deng L, *et al*. Variant rs8400 enhances ALKBH5 expression through disrupting miR-186 binding and promotes neuroblastoma progression. Chin J Cancer Res 2023;35(2):140–162. doi:10.21147/j.issn.1000-9604.2023.02.05, PMID:37180836.
[27] Veeraraghavan VP, Jayaraman S, Rengasamy G, Mony U, Ganapathy DM, Geetha RV, *et al*. Deciphering the Role of MicroRNAs in Neuroblastoma. Molecules 2021;27(1):99. doi:10.3390/molecules27010099, PMID:35011335.
[28] Bartel DP. MicroRNAs: genomics, biogenesis, mechanism, and function. Cell 2004;116(2):281–297. doi:10.1016/s0092-8674(04)00045-5, PMID:14744438.
[29] Lu TX, Rothenberg ME. MicroRNA. J Allergy Clin Immunol 2018;141(4):1202–1207. doi:10.1016/j.jaci.2017.08.034, PMID:29074454.
[30] Xu P, Guo M, Hay BA. MicroRNAs and the regulation of cell death. Trends Genet 2004;20(12):617–624. doi:10.1016/j.tig.2004.09.010, PMID:15522457.
[31] Cheng AM, Byrom MW, Shelton J, Ford LP. Antisense inhibition of human miRNAs and indications for an involvement of miRNA in cell growth and apoptosis. Nucleic Acids Res 2005;33(4):1290–1297. doi:10.1093/nar/gki200, PMID:15741182.
[32] Calin GA, Croce CM. MicroRNA signatures in human cancers. Nat Rev Cancer 2006;6(11):857–866. doi:10.1038/nrc1997, PMID:17060945.
[33] Ryan BM, Robles AI, Harris CC. Genetic variation in microRNA networks: the implications for cancer research. Nat Rev Cancer 2010;10(6):389–402. doi:10.1038/nrc2867, PMID:20495573.
[34] Fu A, Hoffman AE, Liu R, Jacobs DI, Zheng T, Zhu Y. Targetome profiling and functional genetics implicate miR-618 in lymphomagenesis. Epigenetics 2014;9(5):730–737. doi:10.4161/epi.27996, PMID:24503492.
[35] Dzikiewicz-Krawczyk A. MicroRNA polymorphisms as markers of risk, prognosis and treatment response in hematological malignancies. Crit Rev Oncol Hematol 2015;93(1):1–17. doi:10.1016/j.critrevonc.2014.08.006, PMID:25217091.
[36] Morales S, Gulppi F, Gonzalez-Hormazabal P, Fernandez-Ramires R, Bravo T, Reyes JM, *et al*. Association of single nucleotide polymorphisms in Pre-miR-27a, Pre-miR-196a2, Pre-miR-423, miR-608 and Pre-miR-618 with breast cancer susceptibility in a South American population. BMC Genet 2016;17(1):109. doi:10.1186/s12863-016-0415-0, PMID:27421647.
[37] Chen Y, Du M, Chen W, Zhu L, Wu C, Zhang Z, *et al*. Polymorphism rs2682818 in miR-618 is associated with colorectal cancer susceptibility in a Han Chinese population. Cancer Med 2018;7(4):1194–1200. doi:10.1002/cam4.1409, PMID:29533012.
[38] Chang J, Lin L, Zhou C, Zhang X, Yang T, Wu H, *et al*. Functional polymorphisms of the TET1 gene increase the risk of neuroblastoma in Chinese children. J Cell Mol Med 2023;27(15):2239–2248. doi:10.1111/jcmm.17820, PMID:37347215.
[39] Lin L, Deng C, Zhou C, Zhang X, Zhu J, Liu J, *et al*. NSUN2 gene rs13181449 C>T polymorphism reduces neuroblastoma risk. Gene 2023;854:147120. doi:10.1016/j.gene.2022.147120, PMID:36529349.
[40] He J, Qiu LX, Wang MY, Hua RX, Zhang RX, Yu HP, *et al*. Polymorphisms in the XPG gene and risk of gastric cancer in Chinese populations. Hum Genet 2012;131(7):1235–1244. doi:10.1007/s00439-012-1152-8, PMID:22371296.
[41] Chen YP, Liao YX, Zhuo ZJ, Yuan L, Lin HR, Miao L, *et al*. Association between genetic polymorphisms of base excision repair pathway and glioma susceptibility in Chinese children. World J Pediatr 2022;18(9):632–635. doi:10.1007/s12519-022-00562-0, PMID:35543809.
[42] Fassan M, Volinia S, Palatini J, Pizzi M, Baffa R, De Bernard M, *et al*. MicroRNA expression profiling in human Barrett's carcinogenesis. Int J Cancer 2011;129(7):1661–1670. doi:10.1002/ijc.25823, PMID:21128279.
[43] Abdalla MA, Haj-Ahmad Y. Promising Urinary Protein Biomarkers for the Early Detection of Hepatocellular Carcinoma among High-Risk Hepatitis C Virus Egyptian Patients. J Cancer 2012;3:390–403. doi:10.7150/jca.4280, PMID:23074380.
[44] Tölle A, Jung M, Rabenhorst S, Kilic E, Jung K, Weikert S. Identification of microRNAs in blood and urine as tumour markers for the detection of urinary bladder cancer. Oncol Rep 2013;30(4):1949–1956. doi:10.3892/or.2013.2621, PMID:23877086.
[45] Cheng Q, Zhang X, Xu X, Lu X. MiR-618 inhibits anaplastic thyroid cancer by repressing XIAP in one ATC cell line. Ann Endocrinol (Paris) 2014;75(4):187–193. doi:10.1016/j.ando.2014.01.002, PMID:25145559.
[46] Song XL, Tang Y, Lei XH, Zhao SC, Wu ZQ. miR-618 Inhibits Prostate Cancer Migration and Invasion by Targeting FOXP2. J Cancer 2017;8(13):2501–2510. doi:10.7150/jca.17407, PMID:28900488.
[47] Shao W, Xia H, Lan Q, Gu J, Huang H, Zheng F, *et al*. Polymorphism rs2682818 participates in the progression of colorectal carcinoma via miR-618-TIMP1 regulatory axis. Sci Rep 2021;11(1):23186. doi:10.1038/s41598-021-02613-4, PMID:34848810.