Cancer Screening and Prevention **2024** vol. 3(1) | 47–51
DOI: 10.14218/CSP.2024.00006

Original Article

miR-146a rs2910164 C>G Polymorphism and Wilms Tumor Susceptibility in Eastern Chinese Children

Huimin Yin[1#], Shouhua Zhang[2#], Haixia Zhou[3#], Changmi Deng[1], Yizhen Wang[4], Hongting Lu[5], Shaohua He[6], Ruixi Hua[1*] and Chunlei Zhou[7*]

[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, Guangzhou, Guangdong, China; [2]Department of General Surgery, Jiangxi Provincial Children's Hospital, Nanchang, Jiangxi, China; [3]Department of Hematology, The Key Laboratory of Pediatric Hematology and Oncology Diseases of Wenzhou, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China; [4]Department of Pathology, Anhui Provincial Children's Hospital, Hefei, Anhui, China; [5]Department of Pediatric Surgery, Qingdao Women and Children's Hospital, Qingdao, Shandong, China; [6]Department of Pediatric Surgery, Shengli Clinical Medical College of Fujian Medical University, Fuzhou, Fujian, China; [7]Department of Pathology, Children's Hospital of Nanjing Medical University, Nanjing, Jiangsu, China

Received: February 18, 2024 | **Revised:** March 18, 2024 | **Accepted:** March 22, 2024 | **Published online:** March 25, 2024

Abstract

Background and objectives: Wilms tumor is the most common renal malignancy in children. *miR-146a*, a highly conserved small noncoding RNA, plays a critical role in various human diseases. Increasing studies have suggested that rs2910164 C>G polymorphism in *miR-146a* is associated with susceptibility to cancers. However, *miR-146a* rs2910164 C>G polymorphism influence on Wilms tumor remains unknown. The aim of this study was to evaluate the relationship between *miR-146a* rs2910164 C>G polymorphism and Wilms tumor susceptibility in Chinese children.

Methods: In the six-center case-control study, we enrolled 1,352 subjects from East China (416 cases and 936 healthy controls). The TaqMan method was adopted to genotype the *miR-146a* rs2910164 C>G polymorphism. Logistic regression models were utilized to assess the correlation between this polymorphism and the risk of Wilms tumor.

Results: No significant association was observed between *miR-146a* rs2910164 C>G polymorphism and the susceptibility to Wilms tumor. Further stratification analysis also did not detect a significant relationship.

Conclusions: The present study showed no association of *miR-146a* rs2910164 C>G polymorphism with the risk of Wilms tumor in the Eastern Chinese population. Subsequent studies with a larger sample size will be required to validate these results.

Keywords: Wilms tumor; *miR-146a*; Polymorphism; Susceptibility; Eastern Chinese population; Children.

Abbreviations: miRNA, microRNA; UTR, untranslated region; SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval; HWE, Hardy-Weinberg equilibrium; CRC, colorectal cancer.

[*]**Correspondence to**: Chunlei Zhou, Department of Pathology, Children's Hospital of Nanjing Medical University, 72 Guangzhou Road, Nanjing, Jiangsu 210008, Jiangsu, China. ORCID: https://orcid.org/0000-0002-0862-2184. Tel: +86-25-52865959, Fax: +86-25-52865959, E-mail: chunlei1064@sina.cn; Ruixi Hua, 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/0000-0001-5319-656X. Tel: +86-020-38076560, Fax: +86-020-38076560, E-mail: huaruix@mail.sysu.edu.cn

[#]These authors contributed equally to this work.

How to cite this article: Yin H, Zhang S, Zhou H, Deng C, Wang Y, Lu H, *et al*. *miR-146a* rs2910164 C>G Polymorphism and Wilms Tumor Susceptibility in Eastern Chinese Children. *Cancer Screen Prev* 2024;3(1):47–51. doi: 10.14218/CSP.2024.00006.

Introduction

Wilms tumor is the most common type of renal malignant tumor in young children, accounting for over 90% of all renal tumors.[1,2] Wilms tumor often occurs unilaterally, with 5–10% occurring bilaterally.[3] The incidence has been reported to vary geographically and ethnically. It is higher in black populations in the USA and white populations of North America and Europe, while relatively lower in Asian populations. In China, the annual incidence of Wilms tumor is estimated to be 3.3 cases per million children.[4,5] With recent integration of surgery, radiation therapy, and chemotherapy, the overall survival rate of Wilms tumor is above 90%.[6] Although most children with Wilms tumor have a favorable prognosis, about 20% relapse within 2 years of diagnosis, and the survival rate for recurrent Wilms tumor is only 50%.[7–9] In addition, nearly 25% of Wilms tumor survivors develop chronic health prob-

lems such as subsequent malignant neoplasms, intestinal obstruction, kidney/heart failure, and premature ovarian insufficiency.[10] Therefore, uncovering the biology and genetics of Wilms tumor to better understand the pathogenesis of the disease and develop more effective treatments is of great importance.

MicroRNAs (miRNAs) are a group of highly conserved small noncoding RNA molecules, approximately 18–24 nucleotides in length.[11] They act as post-transcriptional regulators by binding to the 3′ untranslated region (UTR) of targeted mRNAs, resulting in the degradation or repression of mRNAs and inhibiting gene expression.[12,13] *miR-146a* is a hot topic in recent research on miRNAs. Located on chromosome 5,[14] it is known to be essential for regulating inflammatory and immune responses.[15,16] According to current studies, *miR-146a* also plays pivotal roles in some cancers, such as chronic myeloid leukemia,[17] glioblastoma,[18] ovarian cancer,[19] and breast cancer.[20]

Single nucleotide polymorphisms (SNPs) are the most common type of genetic variation. SNPs can modulate the expression of miRNAs, which in turn influences certain aspects of disease, like individual susceptibility.[21] A series of SNPs in *miR-146a* have been reported to be associated with disease risk. Qiao *et al*.[22] observed a strong correlation between the *miR-146a* rs2910164 C>G polymorphism and the incidence of acute coronary syndromes in the Chinese Han population. A meta-analysis showed that the C allele of *miR-146a* rs2910164 was related to a decreased risk of gynecological cancers.[23] Although there is increasing evidence linking *miR-146a* rs2910164 C>G polymorphism to tumors, the association between this polymorphism and Wilms tumor susceptibility has not yet been confirmed. Therefore, we conducted a case-control study to evaluate the role of *miR-146a* rs2910164 C>G polymorphism on Wilms tumor risk in an Eastern Chinese population.

Materials and methods

Study subjects

In this study, 416 children with Wilms tumor and 936 healthy controls were recruited from six hospitals located in six different provinces of East China (Jiangsu, Anhui, Zhejiang, Fujian, Shandong, and Jiangxi). Recruitment details of the subjects were as previously described.[24,25] Information on age, gender, and clinical stage of patients was collected. This study received was performed in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of the Children's Hospital of Nanjing Medical University gave its approval to the study protocol (Approval No.: 202210185-1). All participants signed a written informed consent form for our research with the signature of their parent or legal guardian.

Genotyping

Total genomic DNA was extracted from paraffin-embedded tissues and peripheral blood samples using QIAamp DNA FFPE Tissue Kit (Qiagen, Valencia, CA) and TIANGEN Blood DNA Extraction Kit (TianGen Biotech, Beijing) according to the manufacturer's protocol respectively. The samples were genotyped using TaqMan real-time PCR. To ensure the accuracy of the results, 10% of the samples were randomly selected for repeated testing and negative controls (water) were also included as reported previously.[26–28]

Statistical analysis

Clinical variables between Wilms tumor patients and control samples were analyzed by *t*-test or two-sided χ^2 test as appropriate. The goodness-of-fit χ^2 test was used to assess whether the selected SNPs in the controls were consistent with Hardy-Weinberg equilibrium (HWE). Using unconditional logistic regression adjusted for age and gender, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to investigate Wilms tumor risk. Further stratified analysis was performed according to age, gender, and clinical stages. A two-sided $P < 0.05$ was considered as statistically significant. SAS v9.4 (SAS Institute, Cary, NC, USA) was used to perform all the analyses.

Results

Population characters

The frequency distribution of selected variables of all the participants is shown in Table S1. No significant difference in age and gender between Wilms tumor patients and controls was observed ($P = 0.898$ for age and $P = 0.742$ for gender). The mean age of cases and controls were 34.09 ± 26.35 and 33.87 ± 30.88 months old, respectively. Among all 416 cases, 29.81% were classified as clinical stage I, 34.86% were stage II, 18.51% were stage III, 9.13% were stage IV, and 7.69% as not available.

miR-146a rs2910164 C>G polymorphism and Wilms tumor susceptibility

In this study, 416 cases and 936 controls were successfully genotyped. As shown in Table 1, *miR-146a* rs2910164 C>G obeyed the HWE in controls (HWE = 0.965). Genotype frequencies of CC, CG, and GG genotypes among cases were 36.78%, 47.12%, and 16.11%, while the controls were 35.26%, 48.18%, and 16.56% respectively. No significant differences were observed between cases and controls (CG vs. CC: adjusted OR = 0.94, 95% CI = 0.73–1.21, $P = 0.619$; GG vs. CC: adjusted OR = 0.93, 95% CI = 0.66–1.32, $P = 0.693$; CG/GG vs. CC: adjusted OR = 0.94, 95% CI = 0.74–1.19, $P = 0.591$; GG vs. CC/CG: adjusted OR = 0.97, 95% CI = 0.71–1.32, $P = 0.839$; and G vs. C: adjusted OR = 0.96, 95% CI = 0.81–1.13, $P = 0.632$), even adjusted for age and gender. No significant association was ascertained between *miR-146a* rs2910164 C>G polymorphism and Wilms tumor susceptibility.

Stratification analysis

To further explore whether *miR-146a* rs2910164 C>G polymorphism was related to Wilms tumor risk under certain conditions, we stratified participants by age, gender, and clinical stage. Similarly, no significant correlation was observed (Table 2).

Discussion

In this six-center case-control study, we genotyped 416 cases and 936 controls from East China to elucidate the role of *miR-146a* rs2910164 C>G polymorphism on Wilms tumor risk. To our knowledge, this is the first case-control study on the association of *miR-146a* rs2910164 C>G polymorphism with Wilms tumor risk. However, we found that this polymorphism was not relevant to the risk of Wilms tumor in children from East China.

miR-146a is a highly conserved small noncoding RNA, which is located on chromosome 5q33.3.[14] And the rs2910164 C>G polymorphism is located within the mature *miR-146a* seed regions.[29] As noted previously, SNPs in miRNAs can affect the expression of mature miRNAs which, in turn, affect the progression of various diseases.[30–32] The role of *miR-146a* rs2910164 C>G polymorphism in cancer risk has attracted great attention recently. A

Table 1. Association between *miR-146a* rs2910164 C>G polymorphism and Wilms tumor susceptibility

Genotype	Cases (N = 416)	Controls (N = 936)	P^a	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)[b]	P^b
rs2910164 (HWE = 0.965)							
CC	153 (36.78)	330 (35.26)		1.00		1.00	
CG	196 (47.12)	451 (48.18)		0.94 (0.73–1.21)	0.619	0.94 (0.73–1.21)	0.619
GG	67 (16.11)	155 (16.56)		0.93 (0.66–1.32)	0.690	0.93 (0.66–1.32)	0.693
Additive			0.630	0.96 (0.81–1.13)	0.630	0.96 (0.81–1.13)	0.632
Dominant	263 (63.22)	606 (64.74)	0.590	0.94 (0.74–1.19)	0.590	0.94 (0.74–1.19)	0.591
CC/CG	349 (83.89)	781 (83.44)		1.00		1.00	
GG	67 (16.11)	155 (16.56)	0.835	0.97 (0.71–1.32)	0.836	0.97 (0.71–1.32)	0.839
C	502 (60.34)	1,111 (59.35)		1.00		1.00	
G	330 (39.66)	761 (40.65)	0.629	0.96 (0.81–1.13)	0.629	0.96 (0.81–1.13)	0.632

[a]χ^2 test for genotype distributions between Wilms tumor patients and controls. [b]Adjusted for age and gender. CI, confidence interval; OR, odds ratio.

meta-analysis including 6506 cases and 6,576 controls showed that *miR-146a* rs2910164 C>G polymorphism significantly correlates to the susceptibility of lung cancer, and this polymorphism may be a risk factor of lung cancer.[33] By genotyping 295 patients with breast cancer and 295 healthy subjects, Rahim *et al*.[34] observed that *miR-146a* rs2910164 C>G was associated with an increased risk of breast cancer in Pakistani female population. Additionally, Hashemi *et al*.[35] found that the *miR-146a* rs2910164 polymorphism had no significant impact on conferring to risk of prostate cancer in an Iranian population. A study in Mexican patients failed to detect any significant contribution of the *miR-146a* rs2910164 C>G polymorphism to colorectal cancer (CRC) risk,[36] whereas another analysis suggested that rs2910164 may decrease the risk of CRC among Europeans, but not among Asians.[37] The above conclusions collectively indicate that *miR-146a* rs2910164 polymorphism may play different roles in different cancers, possibly due to differences in sample sizes, population sources, and living conditions. Therefore, it is necessary to validate the exact role of *miR-146a* rs2910164 C>G polymorphism in particular cancer type under specific population.

The etiology of Wilms tumor is not precisely known, and the onset and progression of Wilms tumor is closely connected to various genetic alterations. *WT1*, a tumor suppressor gene, was the first gene implicated in Wilms tumor tumorigenesis.[38] With the rapid development of biotechnology, an increasing number of genetic markers associated with Wilms tumor have been identified, including mutations in *CTNNB1* and *WTX*, as well as the loss of *IGF2/H19* imprinting.[39,40] In addition, multiple genetic variants have been identified as Wilms tumor risk loci.[41] In previous case-control studies, we also revealed some Wilms tumor susceptibility genes including *hOGG1*,[42] *FEN1*,[42] *XPD*,[43] *TRMT6*,[44] and *METTL14*.[45] However, these are not sufficient to explain the tumorigenesis of Wilms tumor. It is necessary to validate more genetic variants to better understand the pathogenesis of Wilms tumor to identify the underlying biomarkers as well as therapeutic targets. To date, the role of *miR-146a* rs2910164 C>G polymorphism with Wilms tumor susceptibility remains largely unknown. To elucidate the exact role of this polymorphism on Wilms tumor risk, we undertook a case-control study focused on the Chinese population. Unexpectedly, we did not observe any association of rs2910164 with susceptibility to Wilms tumor.

Several possible limitations should be addressed in this study. First, the relatively small sample size may be insufficient to establish a solid connection between genetic variations and Wilms tumor risk. Increased sample size may lead to better statistical power and more reliable results. Furthermore, all participants were

Table 2. Stratification analysis for the association of *miR-146a* rs2910164 C>G polymorphism with Wilms tumor susceptibility

Variables	rs2910164 (cases/controls)		Crude OR (95% CI)	*P*	Adjusted OR[a] (95% CI)	P^a
	CC	CG/GG				
Age, month						
≤18	48/149	94/255	1.14 (0.77–1.71)	0.511	1.16 (0.77–1.73)	0.483
>18	105/181	169/351	0.83 (0.61–1.12)	0.227	0.83 (0.61–1.12)	0.229
Gender						
Female	67/146	117/259	0.98 (0.69–1.41)	0.932	0.99 (0.69–1.42)	0.957
Male	86/184	146/347	0.90 (0.65–1.24)	0.521	0.90 (0.66–1.25)	0.537
Clinical stage						
I+II	104/330	165/606	0.86 (0.65–1.14)	0.305	0.87 (0.66–1.15)	0.319
III+IV	40/330	75/606	1.02 (0.68–1.53)	0.920	1.01 (0.67–1.52)	0.975

[a]Adjusted for age and gender, omitting the corresponding stratify factor. CI, confidence interval; OR, odds ratio.

enrolled from the Chinese Han population. Therefore, the conclusions reached in this study may not be applicable to other ethnic groups. Lastly, we only evaluated one SNP in this research. Many other potential *miR-146a* polymorphisms should be investigated in the future.

Conclusions

This six-center case control study illustrated that *miR-146a* rs2910164 C>G polymorphism was not relevant to Wilms tumor susceptibility in Chinese children. Further studies should be conducted with larger sample sizes, considering genetic factors and environmental factors.

Acknowledgments

None.

Funding

This study was funded by grants from the National Natural Science Foundation of China (No: 82003523), Science and Technology Planning Project of Guangzhou (No: 202102010291), and Natural Science Foundation of Zhejiang Province (No: LGF21H260012).

Conflict of interest

None.

Author contributions

CZ and RH designed this study. HY, CZ and RH wrote the paper. JC and HY performed the experiments. SZ, HZ, YW, HL, SH and CZ collected the clinical information and samples. CD and RH provided the data analyses and prepared the tables. All authors approved this version to be published.

Ethical statement

This study received was performed in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of the Children's Hospital of Nanjing Medical University gave its approval to the study protocol (Approval No.: 202210185-1). All participants signed a written informed consent form for our research with the signature of their parent or legal guardian.

Data sharing statement

All the data are available upon request from the correspondence authors.

References

[1] Pastore G, Znaor A, Spreafico F, Graf N, Pritchard-Jones K, Steliarova-Foucher E. Malignant renal tumours incidence and survival in European children (1978-1997): report from the Automated Childhood Cancer Information System project. Eur J Cancer 2006;42(13):2103–2114. doi:10.1016/j.ejca.2006.05.010, PMID:16919774.

[2] Servaes SE, Hoffer FA, Smith EA, Khanna G. Imaging of Wilms tumor: an update. Pediatr Radiol 2019;49(11):1441–1452. doi:10.1007/s00247-019-04423-3, PMID:31620845.

[3] Maciaszek JL, Oak N, Nichols KE. Recent advances in Wilms' tumor predisposition. Hum Mol Genet 2020;29(R2):R138–R149. doi:10.1093/hmg/ddaa091, PMID:32412586.

[4] Nakata K, Colombet M, Stiller CA, Pritchard-Jones K, Steliarova-Foucher E, IICC-3 Contributors. Incidence of childhood renal tumours: An international population-based study. Int J Cancer 2020;147(12):3313–3327. doi:10.1002/ijc.33147, PMID:32902866.

[5] Cunningham ME, Klug TD, Nuchtern JG, Chintagumpala MM, Venkatramani R, Lubega J, *et al*. Global Disparities in Wilms Tumor. J Surg Res 2020;247:34–51. doi:10.1016/j.jss.2019.10.044, PMID:31810638.

[6] Dome JS, Graf N, Geller JI, Fernandez CV, Mullen EA, Spreafico F, *et al*. Advances in Wilms Tumor Treatment and Biology: Progress Through International Collaboration. J Clin Oncol 2015;33(27):2999–3007. doi:10.1200/JCO.2015.62.1888, PMID:26304882.

[7] Brok J, Lopez-Yurda M, Tinteren HV, Treger TD, Furtwängler R, Graf N, *et al*. Relapse of Wilms' tumour and detection methods: a retrospective analysis of the 2001 Renal Tumour Study Group-International Society of Paediatric Oncology Wilms' tumour protocol database. Lancet Oncol 2018;19(8):1072–1081. doi:10.1016/S1470-2045(18)30293-6, PMID:29960848.

[8] Mullen EA, Chi YY, Hibbitts E, Anderson JR, Steacy KJ, Geller JI, *et al*. Impact of Surveillance Imaging Modality on Survival After Recurrence in Patients With Favorable-Histology Wilms Tumor: A Report From the Children's Oncology Group. J Clin Oncol 2018;36(34):JCO1800076. doi:10.1200/JCO.18.00076, PMID:30335557.

[9] Pinkerton CR, Groot-Loonen JJ, Morris-Jones PH, Pritchard J. Response rates in relapsed Wilms' tumor. A need for new effective agents. Cancer 1991;67(3):567–571. doi:10.1002/1097-0142(19910201)67:3<567::aid-cncr2820670307>3.0.co;2-2, PMID:1845951.

[10] Weil BR, Murphy AJ, Liu Q, Howell RM, Smith SA, Weldon CB, *et al*. Late Health Outcomes Among Survivors of Wilms Tumor Diagnosed Over Three Decades: A Report From the Childhood Cancer Survivor Study. J Clin Oncol 2023;41(14):2638–2650. doi:10.1200/JCO.22.02111, PMID:36693221.

[11] Grosshans H, Filipowicz W. Molecular biology: the expanding world of small RNAs. Nature 2008;451(7177):414–416. doi:10.1038/451414a, PMID:18216846.

[12] Guo H, Ingolia NT, Weissman JS, Bartel DP. Mammalian microRNAs predominantly act to decrease target mRNA levels. Nature 2010;466(7308):835–840. doi:10.1038/nature09267, PMID:20703300.

[13] Lin S, Gregory RI. MicroRNA biogenesis pathways in cancer. Nat Rev Cancer 2015;15(6):321–333. doi:10.1038/nrc3932, PMID:25998712.

[14] Lagos-Quintana M, Rauhut R, Lendeckel W, Tuschl T. Identification of novel genes coding for small expressed RNAs. Science 2001;294(5543):853–858. doi:10.1126/science.1064921, PMID:11679670.

[15] Saba R, Sorensen DL, Booth SA. MicroRNA-146a: A Dominant, Negative Regulator of the Innate Immune Response. Front Immunol 2014;5:578. doi:10.3389/fimmu.2014.00578, PMID:25484882.

[16] Marschner D, Falk M, Javorniczky NR, Hanke-Müller K, Rawluk J, Schmitt-Graeff A, *et al*. MicroRNA-146a regulates immune-related adverse events caused by immune checkpoint inhibitors. JCI Insight 2020;5(6):132334. doi:10.1172/jci.insight.132334, PMID:32125286.

[17] Chen X, Chen Y, Zhang M, Cheng H, Mai H, Yi M, *et al*. HucMSC exosomes promoted imatinib-induced apoptosis in K562-R cells via a miR-145a-5p/USP6/GLS1 axis. Cell Death Dis 2022;13(1):92. doi:10.1038/s41419-022-04531-3, PMID:35091542.

[18] Cui T, Bell EH, McElroy J, Liu K, Sebastian E, Johnson B, *et al*. A Novel miR-146a-POU3F2/SMARCA5 Pathway Regulates Stemness and Therapeutic Response in Glioblastoma. Mol Cancer Res 2021;19(1):48–60. doi:10.1158/1541-7786.MCR-20-0353, PMID:32973101.

[19] Chen R, Coleborn E, Bhavsar C, Wang Y, Alim L, Wilkinson AN, *et al*. miR-146a inhibits ovarian tumor growth in vivo via targeting immunosuppressive neutrophils and enhancing CD8(+) T cell infiltration. Mol Ther Oncolytics 2023;31:100725. doi:10.1016/j.omto.2023.09.001, PMID:37781339.

[20] Tordonato C, Marzi MJ, Giangreco G, Freddi S, Bonetti P, Tosoni D, *et al*. miR-146 connects stem cell identity with metabolism and pharmacological resistance in breast cancer. J Cell Biol 2021;220(5):e202009053.

doi:10.1083/jcb.202009053, PMID:33819341.
[21] Shastry BS. SNPs: impact on gene function and phenotype. Methods Mol Biol 2009;578:3–22. doi:10.1007/978-1-60327-411-1_1, PMID:19768584.
[22] Qiao XR, Zheng T, Xie Y, Yao X, Yuan Z, Wu Y, *et al*. MiR-146a rs2910164 (G/C) polymorphism is associated with the development and prognosis of acute coronary syndromes: an observational study including case control and validation cohort. J Transl Med 2023;21(1):325. doi:10.1186/s12967-023-04140-4, PMID:37189131.
[23] Bastami M, Choupani J, Saadatian Z, Zununi Vahed S, Ouladsahebmadarek E, Mansoori Y, *et al*. Evidences from a Systematic Review and Meta-Analysis Unveil the Role of MiRNA Polymorphisms in the Predisposition to Female Neoplasms. Int J Mol Sci 2019;20(20):5088. doi:10.3390/ijms20205088, PMID:31615040.
[24] Fu W, Zhu J, Xiong SW, Jia W, Zhao Z, Zhu SB, *et al*. BARD1 Gene Polymorphisms Confer Nephroblastoma Susceptibility. EBioMedicine 2017;16:101–105. doi:10.1016/j.ebiom.2017.01.038, PMID: 28161399.
[25] Hua RX, Fu W, Lin A, Zhou H, Cheng J, Zhang J, *et al*. Role of FTO gene polymorphisms in Wilms tumor predisposition: A five-center case-control study. J Gene Med 2021;23(8):e3348. doi:10.1002/jgm.3348, PMID:33894035.
[26] Wang WJ, Zhou CL, Zhang XX, Zhao YM, Deng CM, Wu HY, *et al*. Association Between miR-492 rs2289030 G>C and Susceptibility to Neuroblastoma in Chinese Children from Jiangsu Province. Cancer Screen Prev 2023;2(4):199–203. doi:10.14218/csp.2023.00025.
[27] 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.
[28] 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.
[29] Kogo R, Mimori K, Tanaka F, Komune S, Mori M. Clinical significance of miR-146a in gastric cancer cases. Clin Cancer Res 2011;17(13):4277–4284. doi:10.1158/1078-0432.CCR-10-2866, PMID:21632853.
[30] Jazdzewski K, Murray EL, Franssila K, Jarzab B, Schoenberg DR, de la Chapelle A. Common SNP in pre-miR-146a decreases mature miR expression and predisposes to papillary thyroid carcinoma. Proc Natl Acad Sci U S A 2008;105(20):7269–7274. doi:10.1073/pnas.0802682105, PMID:18474871.
[31] Forloni M, Dogra SK, Dong Y, Conte D Jr, Ou J, Zhu LJ, *et al*. miR-146a promotes the initiation and progression of melanoma by activating Notch signaling. Elife 2014;3:e01460. doi:10.7554/eLife.01460, PMID:24550252.
[32] Wang M, Chu H, Li P, Yuan L, Fu G, Ma L, *et al*. Genetic variants in miRNAs predict bladder cancer risk and recurrence. Cancer Res 2012;72(23):6173–6182. doi:10.1158/0008-5472.CAN-12-0688, PMID:22846912.
[33] Wang D, Wang Y, Lin Z, Cai L. Association between miRNA-146a polymorphism and lung cancer susceptibility: A meta-analysis involving 6506 cases and 6576 controls. Gene 2020;757:144940. doi:10.1016/j.gene.2020.144940, PMID:32640303.
[34] Rahim A, Afzal M, Naveed AK, Naeem M. Association of miR-146α gene polymorphism and expression levels of its target protein RhoA in Pakistani breast cancer patients. J Pak Med Assoc 2021;71(2(B):686–690. doi:10.47391/JPMA.825, PMID:33941959.
[35] Hashemi M, Moradi N, Ziaee SA, Narouie B, Soltani MH, Rezaei M, *et al*. Association between single nucleotide polymorphism in miR-499, miR-196a2, miR-146a and miR-149 and prostate cancer risk in a sample of Iranian population. J Adv Res 2016;7(3):491–498. doi:10.1016/j.jare.2016.03.008, PMID:27222754.
[36] Trujillo-Fernández YGV, Yzabal-Barbedillo C, Saucedo-Sarinaña AM, Tovar-Jácome CJ, Godínez-Rodríguez MY, Barros-Núñez P, *et al*. Functional Variants in MicroRNAs (rs895819, rs11614913 and rs2910164) Are Associated with Susceptibility and Clinicopathological Features in Mexican Patients with Colorectal Cancer. Arch Iran Med 2023;26(8):439–446. doi:10.34172/aim.2023.67, PMID:38301106.
[37] Alidoust M, Hamzehzadeh L, Rivandi M, Pasdar A. Polymorphisms in non-coding RNAs and risk of colorectal cancer: A systematic review and meta-analysis. Crit Rev Oncol Hematol 2018;132:100–110. doi:10.1016/j.critrevonc.2018.09.003, PMID:30447914.
[38] Haber DA, Buckler AJ, Glaser T, Call KM, Pelletier J, Sohn RL, *et al*. An internal deletion within an 11p13 zinc finger gene contributes to the development of Wilms' tumor. Cell 1990;61(7):1257–1269. doi:10.1016/0092-8674(90)90690-g, PMID:2163761.
[39] Ruteshouser EC, Robinson SM, Huff V. Wilms tumor genetics: mutations in WT1, WTX, and CTNNB1 account for only about one-third of tumors. Genes Chromosomes Cancer 2008;47(6):461–470. doi:10.1002/gcc.20553, PMID:18311776.
[40] Okamoto K, Morison IM, Taniguchi T, Reeve AE. Epigenetic changes at the insulin-like growth factor II/H19 locus in developing kidney is an early event in Wilms tumorigenesis. Proc Natl Acad Sci U S A 1997;94(10):5367–5371. doi:10.1073/pnas.94.10.5367, PMID:9144243.
[41] Turnbull C, Perdeaux ER, Pernet D, Naranjo A, Renwick A, Seal S, *et al*. A genome-wide association study identifies susceptibility loci for Wilms tumor. Nat Genet 2012;44(6):681–684. doi:10.1038/ng.2251, PMID:22544364.
[42] Zhu J, Jia W, Wu C, Fu W, Xia H, Liu G, *et al*. Base Excision Repair Gene Polymorphisms and Wilms Tumor Susceptibility. EBioMedicine 2018;33:88–93. doi:10.1016/j.ebiom.2018.06.018, PMID:29937070.
[43] Zhu J, Fu W, Jia W, Xia H, Liu GC, He J. Association between NER Pathway Gene Polymorphisms and Wilms Tumor Risk. Mol Ther Nucleic Acids 2018;12:854–860. doi:10.1016/j.omtn.2018.08.002, PMID:30161024.
[44] Chang X, Zhu J, Hua RX, Deng C, Zhang J, Cheng J, *et al*. TRMT6 gene rs236110 C>A polymorphism increases the risk of Wilms tumor. Gene 2023;882:147646. doi:10.1016/j.gene.2023.147646, PMID:37473973.
[45] Zhuo Z, Hua RX, Zhang H, Lin H, Fu W, Zhu J, *et al*. METTL14 gene polymorphisms decrease Wilms tumor susceptibility in Chinese children. BMC Cancer 2021;21(1):1294. doi:10.1186/s12885-021-09019-5, PMID:34863142.