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ORIGINAL ARTICLE

Low frequency of *MLLT10* risk SNPs in Korean meningiomas: an exploratory analysis highlighting population-specific difference

Jae Young HUR[1,2], Yhong-Hee SHIM[3], Jeong Hoon KIM[4], Kyung Rae CHO[5], Wan Seop KIM[1], Soo Nyung KIM[6], So Dug LIM[1,*]

[1]Department of Pathology, Konkuk University School of Medicine, Konkuk University Medical Center, Seoul, Republic of Korea; [2]Precision Medicine Lung Cancer Center, Konkuk University Medical Center, Seoul, Republic of Korea; [3]Department of Bioscience and Biotechnology, Konkuk University, Seoul, Republic of Korea; [4]Department of Neurosurgery, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea; [5]Department of Neurosurgery, Konkuk University School of Medicine, Konkuk University Medical Center, Seoul, Republic of Korea; [6]Department of Obstetrics and Gynecology, Konkuk University School of Medicine, Konkuk University Medical Center, Seoul, Republic of Korea

Abstract

Introduction: Several *MLLT10*-associated single-nucleotide polymorphisms (SNPs) have been identified by genome-wide association studies (GWASs) as germline risk variants for meningioma in predominantly European cohorts, but their relevance in Koreans remains uncertain. We investigated these *MLLT10* risk SNPs in Korean meningiomas, assessing differences across two time cohorts and comparing allele frequencies with those observed in other populations. *Materials and Methods*: Three *MLLT10* SNPs (rs12770228, rs11012732, and rs1243180) were examined in 143 meningiomas from patients aged ≤50 years, comprising 62 fresh-frozen tissues collected during 1999–2003 (Period 1) and 81 formalin-fixed paraffin-embedded tissues from 2006–2023 (Period 2). *Results*: Three SNPs were detected in 9 of 143 meningiomas (6.3%). While the differences did not reach statistical significance ($p > 0.05$), minor allele frequencies of all three SNPs were reduced two- to four-fold in Period 2 compared with Period 1. The observed frequencies were similar to those reported in Japanese cohorts but substantially lower than the ≥30% reported in European populations. *Conclusion*: Despite the limitation of using tumour-derived DNA to assess germline variants, our findings consistently showed that *MLLT10* risk SNPs occur at very low frequencies in Koreans, similar to Japanese data and in contrast to Europeans. These results highlight the population-specific nature of *MLLT10* variants and underscore the need for large-scale Asian studies for risk SNP analysis in meningiomas.

Keywords: Meningioma; Single nucleotide polymorphism; *MLLT10*

INTRODUCTION

Meningiomas account for approximately 35–40% of primary central nervous system tumours, making them the most common type, followed by gliomas, pituitary tumours, and nerve sheath tumours.[1-4] Although most meningiomas are benign, about 20% are classified as high-grade[5], and their incidence has steadily increased in recent decades, as consistently demonstrated in several epidemiological studies worldwide.[3,6] The incidence of meningiomas is consistently higher in women, and African Americans show elevated rates compared to other ethnic groups, suggesting contributions from both genetic and environmental factors.[3,6]

Meningioma is considered a representative tumour influenced by both genetic predisposition and environmental factors. Genetic risk factors for meningioma include high-penetrance germline mutations such as *NF2* in neurofibromatosis type 2[7,8], as well as low-penetrance susceptibility loci identified by genome-wide association studies (GWASs), most consistently at the *MLLT10* (*Myeloid/Lymphoid or Mixed-Lineage Leukaemia*

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*Address for correspondence: Prof So Dug Lim. Department of Pathology, Konkuk University School of Medicine, Konkuk University Medical Center, 120-1 Hwayang-dong, Gwangjin-Gu, Seoul, 05030 Republic of Korea. Tel: 82-2-2030-5643 (SDL); Email: *sdlim@kuh.ac.kr*

Translocated To 10) locus.[9-12] There are a limited number of GWAS investigated in meningioma risk, almost exclusively in European populations. Among the loci identified, the *MLLT10* locus at 10p12 has emerged as one of the most consistently replicated germline susceptibility loci[9-11,13], with risk SNPs such as rs12770228[9,14], rs11012732[9,10,13], and rs1243180[9,10] reported across multiple independent studies.

MLLT10, located at 10p12**,** encodes a transcriptional regulator that plays a key role in chromatin remodelling, transcriptional activation, and the DNA damage response.[9,13] Functionally, *MLLT10* interacts with multiple transcriptional complexes, including those involved in histone modification and epigenetic regulation**,** thereby influencing cell fate decisions and stem cell maintenance, particularly during the development and maintenance of hematopoietic stem cells.[9,13] *MLLT10* appears to act as both a fusion partner driving somatic oncogenesis in leukaemia and a germline susceptibility locus contributing to inherited cancer risk in meningioma and possibly other tumours.[13,15] These findings demonstrate the dual role of *MLLT10* in cancer biology, bridging both oncogenic translocation events and inherited risk predisposition. In contrast, GWAS targeting Asian meningioma populations are exceedingly rare, and the first investigation was only recently reported in Japan.[12] They reported that risk variants identified in previous European GWASs were difficult to replicate in the Japanese population, likely due to inter-ethnic differences in allele frequencies.[12] To date, no independent GWAS of meningiomas has been conducted in other Asian countries, including Korean or Chinese cohorts, except within the context of meta-analyses.

Meanwhile, ionizing radiation such as therapeutic exposure during childhood leukaemia or brain tumour treatment remains the most established environmental risk factor for meningiomas.[16-18] Hormonal influences, family history, and high body mass index (BMI) have also been implicated[19], whereas evidence for other exposures, including head trauma, occupational factors, and mobile phone use, remains inconclusive.[18,20,21] However, over the past three decades, lifestyle changes such as increased mobile phone use, greater reliance on hormone therapy, and rising BMI have likely amplified the contribution of environmental factors to meningioma risk. Although many studies have examined these associations, the limitations of epidemiological research make it difficult to draw firm conclusions.[21] From an epidemiological perspective, if differences in environmental factors across two time cohorts stratified by collection period are accompanied by variations in the frequency of meningioma risk SNPs, this may suggest that environmental factors should be given greater weight in interpreting meningioma risk.

On the other hand, treatment decisions for meningiomas are typically based on tumour location, radiologic findings, and WHO histopathologic grade.[22] While most meningiomas generally respond well to surgical treatment, however, skull base meningiomas such as those located in the sphenoid wing, petroclival region, tuberculum sellae, and cerebellopontine angle, etc pose significant surgical challenges[22,23], are associated with higher recurrence rates and may negatively impact quality of life.[22,23] Clinical presentation varies by tumour site, but symptoms are often subtle or absent, leading to delayed diagnosis until tumours reach considerable size.[22,23] Thus, timely detection is critical for enabling early intervention, improving treatment efficacy, and enhancing survival and quality of life.[23-25] Currently, there are no standardised biomarkers used in clinical practice for meningiomas, and biomarkers for the early diagnosis of meningiomas are still in the research phase.[26,27] Studying risk SNPs for meningioma development can help identify high-risk individuals, and incorporating them into polygenic risk scores could enable targeted surveillance, contributing to earlier detection and improved outcomes.

Therefore, the present study examined three representative risk SNPs in *MLLT10* (rs12770228, rs11012732, and rs1243180) at 10p12.31 in meningiomas, comparing differences across two time cohorts defined by sample collection period, and further assessed allele frequencies against other populations to clarify the population-specific relevance of these variants in Koreans.

MATERIALS AND METHODS

Study Design

A total of 143 meningioma cases from patients younger than 50 years in a Korean cohort were included in the risk SNP analysis for meningiomas. All procedures were conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Konkuk University Medical Center (KUMC IRB

2025-03-048).

Data collection and processing

A total of 299 pathologically confirmed meningiomas resected at Konkuk University Hospital (Seoul, Republic of Korea) between 2006 and 2023, and 161 fresh-frozen meningioma specimens collected at Asan Medical Center (Seoul, Republic of Korea) between 1999 and 2003 were identified. Patients younger than 50 years were selected to minimize environmental confounders and highlight potential genetic predispositions, while cases with poor DNA quality or non-Korean origin were excluded. In total, 143 meningiomas were analysed for risk SNPs, including 62 fresh-frozen tissues from period 1 (≤2003) and 81 formalin-fixed paraffin-embedded (FFPE) tissues from period 2 (≥2006).

For Period 1, only diagnostic information, including patient age, sex, and WHO grade, was available. In contrast, for Period 2, medical record review enabled the assessment of imaging findings, including tumour location. Tumour locations were classified as skull base, such as lesions in the olfactory groove, planum sphenoidale, cavernous sinus, sphenoid wing, clinoidal portion, tuberculum sellae, clivus, and petrous bone, etc, and non-skull base, following prior studies.[23,28]

We referenced allele frequency data from the Allele Frequency Aggregator (ALFA), a population-scale database curated by NCBI.[29]

SNP Selection

We performed a literature search to identify GWAS for meningioma risk and related papers. Three SNPs within the *MLLT10* locus, including rs12770228, rs11012732, and rs1243180, were selected, as these variants have been repeatedly implicated in meningioma susceptibility through previous GWASs, subsequent replication studies, and meta-analyses, thereby supporting their potential relevance as risk-associated loci.[9,10,14]

DNA Extraction & SNP Genotyping

Genomic DNA was extracted from each meningioma tissue using the PANAMAX™ Tissue/Cultured Cells DNA Extraction Kit or Panamax™ FFPE Plus DNA Extraction Kit (HLB Panagene, Daejeon, Korea), following the manufacturer's protocol. DNA concentration and purity were measured using a NanoDrop spectrophotometer (Thermo Scientific, Waltham, MA, USA). DNA quality and fragment length were further assessed with the 4200 TapeStation system and Genomic DNA ScreenTape (Agilent Technologies, Santa Clara, CA, USA) to ensure sufficient quality for downstream applications.

SNP genotyping for rs1243180, rs11012732, and rs12770228 was performed using the TaqMan® SNP Genotyping Assay (Life Technologies, Carlsbad, CA, USA) on a 7500 Fast Real-Time PCR Instrument System (Applied Biosystems, Foster City, CA, USA), according to the manufacturer's instructions. The forward and reverse primers for each SNP were designed using Primer3 v0.4.0, and the sequences used in this study are presented in Table 1. Reactions were performed in a total volume of 25µl containing 0.1µl Biofact A-Star Taq (BIOFACT, Daejeon, Korea), 2µl 10X Biofact A-Taq buffer (BIOFACT), 0.4µl dNTP (BIOFACT), 0.5 µl primer, 21µl water, and 1µl of DNA. PCR conditions were: initial denaturation at 95°C for 20 s, followed by 40 cycles of 95°C for 30 s, 60°C for 15 s, and 72°C for 25 s. Results were analysed using SDS v1.5.1 software (Applied Biosystems).

Statistical Methods

Statistical analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria; www.R-project.org) and DBSTAT version 5 (DBSTAT, Seoul, Korea; www.dbstat.com). Descriptive statistics were applied to summarise clinical characteristics. For continuous variables, the median and interquartile range (IQR) were reported when distributions were skewed. Categorical variables were summarised as frequencies. Associations between categorical variables were assessed using Fisher's exact test or the chi-square test of independence. A two-tailed *p*-value of <0.05 was considered statistically significant.

RESULTS

Clinical characteristics of 143 meningioma patients were summarised in Table 2. The cohort had a median age of 45 years (IQR 8), included 43 males (30.1%) and 100 females (69.9%), and consisted predominantly of WHO grade 1 tumour. Three risk SNPs were detected in 9 of 143 patients (6.3%), with 3 individuals harbouring two or more variants. These risk SNPs were more frequent in females (66.7%) than in males (33.3%). The rs12770228 A allele appeared as a heterozygous variant in 1 patient (0.7%). The rs11012732 A>G variant (heterozygous or homozygous) was found in 4 patients (2.8%),

TABLE 1: Forward primer, reverse primer, and TaqMan probe for each single nucleotide polymorphism (SNP)

rsID	Primer	Sequence
rs12770228	Forward	CTGGGAAAAGTCAGCTCGTACG
	Reverse	CTCCTCTGCGTCCAGGAGA
	TaqMan Probe [VIC / FAM]	CTTTCGCTTGCGGTTTGCAACCCCT [A/G] GGGTGGGTCTGACCCCGCGCGGCAC
rs11012732	Forward	GTGTGGTGGTGTGTGCACCTGTAA
	Reverse	CTTCAAGGCTGCAGTGAGCAA
	TaqMan Probe [VIC / FAM]	ACTCGTCTCACAAAAAAAGAAAGAA [A/G] TAATGGTTGAGTAACCTATAAAAAT
rs1243180	Forward	CATGAGGGTAGTAGTCCCGTAACC
	Reverse	CAAAAGGGCAGGTACCAGGTAAC
	TaqMan Probe [VIC / FAM]	TGAAGAGAGCTAGACTACTTTCTTC [T/A] GTGGCCCTCAAAGGAATAAAACTCT

SNP, single nucleotide polymorphism

and the rs1243180 T>A heterozygous genotype was found in 8 patients (5.6%) (Table 2). Of the Period 2 cases, 35 meningiomas (43.2%) were skull-based tumour, none of which carried the risk SNPs. There were three patients diagnosed with neurofibromatosis type 2, all of whom presented with multiple meningiomas at the convexity location and harboured none of the three analysed risk SNPs (Table 2).

The minor allele frequencies (MAFs) of three risk SNPs in Korean meningiomas were compared with the dbSNP data[29] of the Korean Genome Project 4K cohort (Fig. 1).[30] For rs11012732, the MAF was 1.75% in patients versus 0.77% in controls (OR = 2.28, 95% CI 0.91–5.74, *p = 0.08*). For rs12770228, the MAF was 0.35% in patients versus 0.58% in controls (OR = 0.60, 95% CI 0.08–4.38, *p = 0.62*). For rs1243180, the MAF was 2.8% in patients versus 2.5% in controls (OR = 1.12, 95% CI 0.55–2.29, *p = 0.76*). Rs11012732 demonstrated a trend toward increased frequency in meningiomas, whereas rs12770228 and rs1243180 showed no significant differences.

MAFs were compared across the two time-based cohorts (Table 3). Although no statistically significant differences were observed for rs12770228, rs11012732, or rs1243180 between the two Periods (*p > 0.05*), all three SNPs showed a decreasing trend in Period 2. In Period 1 (1999–2003), the MAF of rs12770228 (A) was 0.81%, whereas it was undetectable in Period 2 (2006–2023). The MAF of rs11012732 (G) declined from 2.42% in Period 1 to 1.23% in Period 2, representing an approximately two-fold reduction. Similarly, the MAF of rs1243180 decreased from 4.84% to 1.23%, corresponding to an approximately four-fold reduction. This pattern suggests a potential cohort effect or sampling variation over time.

MAFs of the three *MLLT*10 SNPs in Korean meningiomas were substantially lower than those reported in European cohorts but were consistent with other East Asian populations (Table 4). In the current Korean meningioma cohort, the MAFs were 0.35% for rs12770228, 1.75% for rs11012732, and 2.80% for rs1243180. By contrast, European GWAS reported frequencies exceeding 30% for all three loci, whereas Japanese GWAS data in meningioma patients showed much lower values, closely resembling the Korean findings.

TABLE 2: Clinicopathological characteristics of meningiomas carrying MLLT10 risk single nucleotide polymorphism (SNPs)

Characteristics	risk SNPs, n (%)	rs12770228 (GG)*	rs11012732 (AA)*	rs1243180 (TT)*	*p-value*
Patient n (%)	9 (6.3%)	1 (0.7%, A)	4 (2.8%, G)	8 (5.6%, A)	
Sex, n=143					
Male	43 (30.1%)	0	1 (GG)	2 (TA)	*0.85*
Female	100 (69.9%)	1 (GA)	3 (AG)	6 (TA)	
Age, n=143, median(IQR), years					
	45 (8)	49	45.5 (4.5)	41 (9)	
WHO grade, n=143					
1	128 (89.5%)	1 (100%)	4 (100%)	7 (87.5%)	*0.885*
2	13 (9.1%)			1 (12.5%)	
3	2 (1.4%)				
Location, n=81					
Non-skull base	46 (56.8%)	0	1	2	*0.255*
Skull base	35 (43.2%)	0	0	0	
NF2, n=81	3 (3.7%)	0	0	0	

*SNP, single nucleotide polymorphism; n, number; *, the dominant variant genotype; IQR, Interquartile Range; WHO, World Health Organization; NF2, Neurofibromatosis type 2*

When these three meningioma risk SNPs were examined in the NCBI dbSNP reference population database,[29] the Korean Genome Project 4K[30] and 38KJPN cohorts consistently showed low MAFs (<3%), whereas the European 1000 Genomes cohort displayed much higher values, exceeding 30% (Table 4). Moreover, ALFA data revealed striking variation within Asian populations: East Asians had very low frequencies (<1% for both rs12770228 and rs11012732, and nearly 0 for rs1243180), while South Asians showed intermediate values, more similar to Europeans (24.2% for rs12770228, 22.6% for rs11012732, and 2.0% for rs1243180).

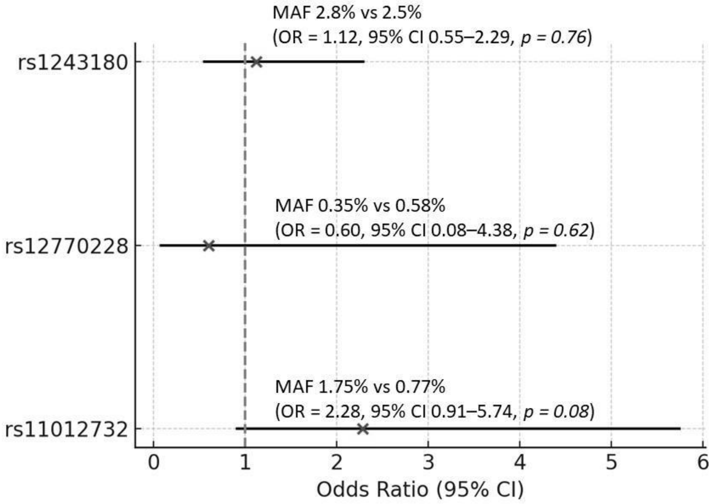

FIG. 1. Forest plot of single nucleotide polymorphism (SNP) associations between meningiomas in the current study and the Korean reference panel. *MAF, minor allele frequency; Allele counts are based on 2 alleles per individual. OR, 95% CI, and p-values represent comparisons of MAFs between meningiomas in the current study versus Korean reference panel*

TABLE 3: Period-specific genotype distributions and clinical characteristics of meningiomas carrying MLLT10 single nucleotide polymorphism (SNPs)

SNP	Group	Cases n	Genotype n$^+$	MAF (%)	*p*-value	AgeSex (Genotype)
rs12770228 (GG/GA/AA)$^+$	Period 1	62	61 / 1 / 0	0.81	0.434	49F(AG)*
	Period 2	81	81 / 0 / 0	0		
	Total	143	142 / 1 / 0	0.35		
rs11012732 (AA/AG/GG)$^+$	Period 1	62	59 / 3 / 0	2.42	0.32	41F(AG)**, 45F(AG)***, 49F(AG)*
	Period 2	81	80 / 0 / 1	1.23		46M(GG)
	Total	143	139 / 3 / 1	1.75		
rs1243180 (TT/TA/AA)$^+$	Period 1	62	56 / 6 / 0	4.84	0.081	28M, 36F, 39F, 41F**, 45F***, 49F* (all TA)
	Period 2	81	79 / 2 / 0	1.23		42F, 7M (all TA)
	Total	143	135 / 8 / 0	2.8		

*Period 1, fresh frozen tissue (1999-2003); Period 2, FFPE tissue (2006-2023); MAF, minor allele frequency; SNP, single nucleotide polymorphism;+, genotype; *,**, ***, same patients*

DISCUSSION

The first GWAS in meningioma was conducted by Dobbins *et al*[9] in a large German cohort of meningioma patients and again validated in an independent replication in a European cohort. In this GWAS, a novel susceptibility locus was identified near *MLLT10* on 10p12.31, and the genotyped SNP rs12770228 emerged as a lead variant associated with meningioma susceptibility, and the imputed SNP rs11012732, which is in strong linkage disequilibrium with rs12770228, demonstrated the most significant association with meningioma risk.[9] These results provided the first widely replicated common variant risk locus near *MLLT10* in meningiomas and served as a starting point for subsequent studies. Subsequently, Egan *et al*[10] also performed a GWAS on glioma and meningioma in a European descent cohort, and identified 22 candidate functional SNPs located at the *MLLT10*, and both rs12770228 and rs1243180

TABLE 4: The minor allele frequencies (MAFs) of three MLLT10 SNPs in meningiomas compared with reference populations

Reference & Population		**Gene**	***MLLT10***		
		rsID	**rs12770228**	**rs11012732**	**rs1243180**
		Minor alleles	G>A	A>G	T>A
			MAF % (minor allele n / total allels n)		
GWAS	Dobbins et al[9] Northern European	Meningioma	39.0 (1257/3224)	41.5 (1316/3170)	*Not tested*
		Controls	31.3 (1529/4880)	32.6 (1572/4824)	*Not tested*
	Egan et al[10] European ancestry	Meningioma	37.9 (203/536)	*Test failed*	34.7 (204/588)
		Controls	33.0 (415/1256)	*Test failed*	31.4 (404/1286)
	Yamada et al[12] Japanese	Meningioma	*Not tested*	0.87 (7/802)	*Not tested*
		Controls	*Not tested*	0.54 (549/101,752)	*Not tested*
Current study	Korean	Meningioma	0.35 (1/286)	1.75 (5/286)	2.8 (8/286)
dbSNP[29]	Korean Genome Project 4K	Korean	0.58 (42/7232)	0.77 (56/7234)	2.5 (183/7234)
	38KJPN	Japanese	0.49 (379/77444)	0.53 (407/77444)	2.2 (1689/77444)
	1000 Genomes Project phase 3	European	32.5 (391/1266)	34.1 (432/1266)	30.9 (391/1266)
	ALFA	Global	31.3 (84571/270586)	32.8 (144771/441340)	15.7 (2248/14336)
		East Asian	0.94 (10/1062)	0.83 (71/8550)	0.00 (0/84)
		South Asian	24.2 (1217/5034)	22.6 (694/3078)	2.0 (1/66)

MAF, minor allele frequency; GWAS, Genome-Wide Association Study; 38KJPN, 38,000 Japanese population reference panel; ALFA, Allele frequency aggregator were associated with an increased risk of meningioma. Interestingly, these SNPs did not show a significant association with glioma risk, highlighting their specificity for meningiomas and supporting the previously reported findings by Dobbins *et al.*[9] that germline variants at the *MLLT10* locus may play an important role in meningioma susceptibility.

Furthermore, Walsh *et al.*[13] conducted a subset-based meta-analysis of multiple diseases using GWAS-based data to investigate the genetic associations between meningioma and oestrogen-dependent cancers, including breast and ovarian cancer. The study identified shared genetic variants near the *MLLT10* at 10p12.31, and the *MLLT10* eQTL (expression Quantitative Trait Locus) rs7084454 is associated with meningioma, oestrogen receptor-positive breast cancer, ovarian cancer, and obesity. These findings support a hormonal pleiotropy between meningioma and oestrogen-related cancers.[13] They also noted racial differences in allele frequency, being higher in African Americans and lower in East Asians, underscoring the importance of race-specific risk assessment.[13] Overall, these findings strongly implicate the 10p12.31 locus at *MLLT10* in the genetic predisposition to meningiomas. A large-scale meta-analysis combining existing GWAS data and an additional independent case control study also identified a new meningioma risk locus, rs2686876 at 11p15.5. This locus included genes such as *RIC8A*, which is involved in neural crest development, suggesting the possibility of a polygenic model together with the existing *MLLT10* locus.[11]

The functional role of *MLLT10* at 10p12.31 in meningioma remains to be elucidated, and loss of chromosome 10 is known to be a feature of high-grade meningiomas in adults.[31] The *MLLT10* gene itself is involved in regulating chromatin structure and the DNA damage response, particularly during the early development, maintenance, and differentiation of haematopoietic stem cells. Cancer susceptibility variant SNPs mapped to the *MLLT10* locus at 10p12 have been implicated in the pathogenesis of several cancers, such as pituitary adenoma, leukaemia, and meningiomas, and highlight the broader role of this variant in cancer biology.[9,10] Because these risk SNPs for meningioma identified in GWAS have been studied primarily in European cohorts, confirming whether the same SNPs are valid in other populations is an important step in verifying the reproducibility and generalisability of GWAS results.[9,12,25]

The first GWAS of meningioma in Asians, conducted in Japan, failed to replicate the significant associations reported for the risk SNPs in European populations, due to their very low MAFs in the Japanese population.[12] However, the stratified analyses by sex and tumour location in the Japanese cohort suggested that certain variants, such as rs141887933 in *GREB1*, may be particularly significant in women. While Dobbins *et al.*,[9] as well as our study, found no associations with WHO grade or gender, these findings underscore the importance of subgroup analyses in interpreting GWAS results and suggest a potential role of sex-specific genetic susceptibility. Also, when comparing this aspect with a general reference cohort, East Asian general populations exhibited extremely low frequencies of these three SNPs (all <1% for rs12770228 and rs11012732, and near zero for rs1243180), while South Asians displayed intermediate values over 20%, close to the European cohort (24.2% for rs12770228, 22.6% for rs11012732) (Table 4), highlighting a clear distinction between East and South Asian populations. Hence, given the lack of prior investigations in Korea, the present work represents the first attempt to evaluate *MLLT10* risk SNPs in a Korean meningioma cohort. Further investigations are warranted not only in East Asian populations but also through large-scale cohort studies encompassing both East and South Asia to strengthen the evidence base across diverse populations.

A major limitation of this study is that germline risk SNPs were analysed using tumour-derived DNA, which carries the theoretical risk of somatic mutations confounding the interpretation of germline variants. Nevertheless, because archival tumour tissue was the only material available, this approach was unavoidable. Importantly, the risk SNPs previously reported at high frequencies in European meningioma GWAS were observed at much lower frequencies in our Korean cohort, consistent with findings from the Japanese study. This concordance suggests that the use of tumour tissue did not substantially distort the results.

We considered whether the rise in social and environmental risk factors for meningioma might be linked to changes in the distribution of risk SNPs in meningiomas. When analysing two groups from different time periods, the prevalence of three *MLLT10* SNPs was lower in the more recent cohort of Period 2. This suggests changes in allele frequency distribution over time, although not statistically significant. This decrease may suggest that recent increases in environmental factors, such as radiofrequency electromagnetic fields (RF-EMF) exposure, hormonal influences, radiation, and chemicals[20,32,33], play a greater role in the development of meningiomas than genetic predisposition. However, this difference may be more likely explained by variations in patient groups or technical issues related to tissue storage and DNA quality. Nonetheless, although exploratory, analyses of frequency differences in risk SNPs may yield new insights, particularly when they draw attention to methodological limitations in epidemiological studies, such as those investigating mobile phone use and brain tumours.[20,32,33]

In addition, this study has several limitations, including the relatively small sample size and the very low MAFs of the analysed SNPs, which reduced the statistical power. Nonetheless, we believe that validating risk SNPs identified in GWASs of other populations provides valuable insights for future study designs and for the development of risk prediction models, such as polygenic risk scores, where the incorporation of population-specific SNP frequency data is essential to ensure both accuracy and clinical applicability.[34,35] Although recent advances in medical technology have improved the survival rates of patients with brain tumours, reliable early diagnostic markers for meningiomas—the most common primary brain tumour—are still lacking. While most recent studies on meningiomas have concentrated on the application of next-generation sequencing (NGS) technologies in high-grade or advanced disease, the present study was undertaken with the recognition that early detection of high-risk meningiomas—particularly those arising at the skull base—is crucial. Therefore, identifying meningioma risk SNPs specific to Asian populations may contribute to patient stratification according to genetic predisposition and ultimately support the development of early detection and treatment strategies.

CONCLUSION

Our findings indicate that *MLLT10* risk SNPs are rare in Koreans, similar to Japanese but contrasting with Europeans, highlighting their population-specific nature and the need for large-scale Asian studies.

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Informed Consent Statement: Because of the nature of retrospective research and the analysis used anonymous data with no personal information such as name and personal identification number, informed consent from patients was waived for the present study.

Authors' contributions: SDL, WSK and JYH conceived and conducted the study, and drafted the manuscript. YHS, JHK, and KRC were responsible for clinical sample collection and processing. SDL and SNK also performed the statistical analyses. All authors reviewed and approved the final version of the manuscript.

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