

MICA and MICB allele frequencies in a Southeast US cohort

Yasmeen Jilani¹, Grace Tabazi³, Jeane Silva³ and Valia Bravo-Egana^{1,2,3} Histocompatibility/Immunology Laboratory Wellstar Medical Center¹, Medical College of Georgia² and School of Public Health of the Augusta University³



Background

Major Histocompatibility complex class I chain-related genes A (MICA) and B (MICB) exhibit polymorphisms that make them important histocompatibility targets. Yet some populations have not been well characterized. Even less studies have explored MICB allele distribution in populations. We report the MICA and MICB allele distribution in a US population residing in Georgia and South Carolina. Notably, only one other study has used NGS to type MICA.

Methods

DNA from 190 buccal swabs or whole blood samples were extracted using EZ1 kit (QIAGEN). MICA, MICB, and HLA-B typing were obtained using NGS (CareDx Alloseg Tx17). Results were analyzed using AlloSeg Assign software, version 1.0.5. Hemizygosity was assess using CareDx Copy Number software. Table 1 shows demographics of the subjects in the study. 96 African Americans (AFA) and 74 Caucasians (CAU) make up the majority of the cohort.

Conclusions

- 28 MICA and 14 MICB alleles were identified (table 2).
- No significant differences were found in allele distribution between patients and healthy subjects.
- Percentages of homozygosis were 10% and 30% for MICA and MICB, respectively.
- 21 and 20 MICA alleles were detected in AFA and CAU, respectively (table 3).
- The most common alleles in AFA and CAU were MICA*002:01 and MICA*008:01 with frequencies of 9.4% and 5.6%, respectively. In both populations, MICA*004:01 and MICA*008:04 were the following two more common alleles.
- 9 and 11 MICB alleles were detected in AFA and CAU, respectively
- In both populations, the most common alleles were MICB*005:02 and MICB*002:01 with 35% and 27% frequencies in AFA and 17% and 12% in CAU.
- Interestingly, the percentages of homozygosity for MICA and MICB were double in AFA than in CAU. Historical restrictions on migration of AFA in this region may help explain this finding.
- The most common HLA-B/MICA associations in AFA were MICA*002:01 with B*53:01 and B*58:01, and MICA*008:04 with B*15:03 while in CAU were MICA*010:01 with B*15:10, MICA*004:01 with B44:03, MICA*008:01 with B44:02, and MICA*008:04 with B*07:02.
- The most common HLA-B/MICA associations previously described are consistent with our findings. However, none include allele MICA*008:04, likely because the methods used to type these genes did not examine exon 1 where MICA*008:01 and MICA*008:04 differ.
- We found two independent subjects hemizygous for MICA and none for MICB in our cohort.
- 1 novel allele was identified for MICA and 4 for MICB. Figure 1 shows the regions of the genes where the mutations were found.

References

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Results

Allele

Table 1. Cohort demographics.

Total	190		
Gender			
Male	95		
Female	95		
Race			
African Americans (AFA)	96		
Caucasians (CAU)	74		
Hispanics	4		
Asians	1		
Mixed Races	15		
Age (years)			
Average	51		
<16	3		
16-25	10		
26-35	20		
36-45	24		
46-55	42		
56-65	51		
>66	38		
Unknown	2		
Health Status			
Renal transplant candidates	112		
Stem cell transplant candidates (SCT)	17		
Healty subjects	61		
Other demographics (Relations)			
unrelated subjects	176		
related subjects: 4 families	14		
family 1	1 SCT candidate with 2 siblings		
family 2	1 SCT candidate with 4 siblings		
family 3	1 SCT candidate with 3 siblings		
family 4	1 SCT candidate with 1 sibling		

Table 3. MICA Allele frequencies in AFA and CAU

AA=96		CAU=74	
MICA allele	Allele Frequency %	MICA allele	Allele Frequency %
002:01	9.38	008:01	5.63
004:01	7.88	008:04	4.13
008:04	4.69	004:01	3.56
008:01	3.38	010:01	3.38
015:01	2.44	002:01	2.63
008:13	1.13	009:01	1.88
018:01	1.13	007:01	0.94
009:02	0.75	012:01	0.75
011:01	0.75	018:01	0.75
110:01	0.75	001:01	0.56
001:01	0.56	015:01	0.56
012:01	0.56	017:01	0.56
041:01	0.56	011:01	0.38
008:02	0.38	008:02	0.19
030:01	0.38	009:02	0.19
006:01	0.19	012:03	0.19
007:01	0.19	016:01	0.19
009:01	0.19	019:01	0.19
019:01	0.19	027:01	0.19
045:01	0.19	049:01	0.19
068:01	0.19	006:01	0.00
010:01	0.00	008:13	0.00
012:03	0.00	030:01	0.00
016:01	0.00	041:01	0.00
017:01	0.00	045:01	0.00
027:01	0.00	068:01	0.00
049:01	0.00	110:01	0.00

Table 2. MICA and MICB allele frequencies expressed in percentages.

Allele Frequency %

Allele	Allele Frequency %		
MICA*002:01	13.51		
MICA*004:01	12.01		
MICA*008:04	10.13		
MICA*008:01	9.94		
MICA*010:01	4.50		
MICA*015:01	3.00		
MICA*009:01	2.25		
MICA*018:01	2.06		
MICA*011:01	1.69		
MICA*001:01	1.31		
MICA*007:01	1.31		
MICA*012:01	1.31		
MICA*008:13	1.13		
MICA*009:02	0.94		
MICA*016:01	0.75		
MICA*019:01	0.75		
MICA*027:01	0.75		
MICA*110:01	0.75		
MICA*008:02	0.56		
MICA*041:01	0.56		
MICA*030:01	0.38		
MICA*049:01	0.38		
MICA*006:01	0.19		
MICA*012:03	0.19		
MICA*017:01	0.19		
MICA*045:01	0.19		
MICA*068:01	0.19		
MICA*009:02	0.19		
MICB*005:02	70.85		
MICB*002:01	29.96		
MICB*004:01	20.65		
MICB*008:01	16.60		
MICB*003:01	3.24		
MICB*024:01	2.43		
MICB*014:01	2.02		
MICB*028:01	2.02		
MICB*005:06	0.81		
MICB*005:11	0.81		
MICB*033:01	0.81		
MICB*005:01	0.40		
MICB*005:03	0.40		
MICB*013:01	0.40		

Figure 1. Location of the mutations identified in the novel alleles (red/brown arrows) in a schematic representation of the MIC

genes. (Figure modified from Wang, J, et al. Biomolecules. Vol 10, 2020).

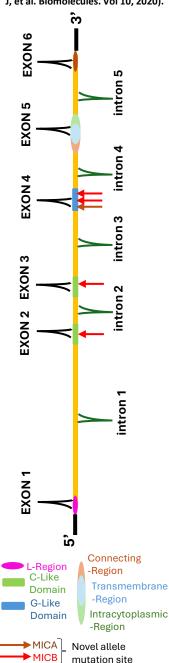


Table 4. MICB Allele frequencies in AFA and CAU						
AA=96			CAU=74			
MICB allele	Allele Frequency %		MICB allele	Allele Frequency %		
005:02	35.22		005:02	26.72		
002:01	17.00		002:01	11.74		
008:01	10.93		004:01	8.91		
004:01	7.69		008:01	5.67		
024:01	2.43		014:01	1.62		
003:01	1.21		003:01	1.21		
005:06	0.40		005:01	0.40		
014:01	0.40		005:03	0.40		
033:01	0.40		005:06	0.40		
005:01	0.00		013:01	0.40		
005:03	0.00		028:01	0.40		
013:01	0.00		024:01	0.00		
028:01	0.00		033:01	0.00		