

## INVESTIGATION OF NON-CLASSICAL HLA CLASS IB (HLA-E, -F, -G, -H, MICA AND MICB) GENES POLYMORPHISM IN HEALTHY INDIVIDUALS FROM THE BULGARIAN POPULATION

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**Aim:** HLA gene polymorphism has been investigated in many populations around the world, although the data regarding the non-classical HLA class I (E, -F, -G, H) and class I chain-related MICA and MICB genes is limited compared to classical HLAs. The present pilot study aims to analyze the allele and haplotype polymorphism of non-classical HLA class Ib genes in healthy individuals from the Bulgarian population by utilizing new technology next generation sequencing (NGS).

**Material and methods:** 63 healthy individuals from the Bulgarian population with known HLA class I and II genotypes were included in the study. Non-classical HLA class Ib genotyping was performed by new NGS methodology - AlloSeq Tx 17 (CareDx).

**Results:** As expected the highest degree of polymorphism was found for MIC genes - 16 MICA alleles, from which the most frequently observed allele is MICA\*008:01 and 13 MICB alleles, with the most frequent allele MICB\*002:01. Among the non-classical HLA genes, we identified five main allele groups: HLA-E\*01, -F\*01, -G\*01, -H\*01 and -H\*02. The highest degree of polymorphism was detected for HLA-H, with the most frequently observed allele HLA-H\*01:01:01. Statistically significant global linkage disequilibrium was found between HLA-A and non-classical HLA-E, -F, -G and H loci, and for HLA-B and class I chain-related MICA and MICB genes. Haplotype analysis was performed between non-classical HLA class Ib genes and classical HLA class I genes. Extended haplotypes are defined.

**Conclusion:** This preliminary data throw light on the HLA-E, -F, -G, -H, MICA and MICB allelic polymorphism, linkage disequilibrium, and haplotype polymorphism in the Bulgarian population. These results will allow better characterization of the clinical significance of these genes and defining their role as transplant antigens.

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