Introduction

Avoidance of HLA-E*01:03 homozygous donors has been reported to improve the outcome of hematopoietic stem cell transplantations (HSCT) in certain settings (C. Tsamadou et al., BBMT 2019). Consequently, DKMS implemented a short amplicon based Next-Generation Sequencing (NGS) high-throughput workflow for HLA-E donor registry typing. Our approach provides resolution of the clinically relevant antigen recognition domain (ARD) level for all currently (IMGT/HLA version 3.36) known HLA-E alleles. In July 2017, DKMS added HLA-E to the default typing profile for newly enrolled potential donors for HSCT. Since then, more than 1,800,000 samples have been typed for HLA-E at DKMS donor centers in Germany, Poland, the United Kingdom, the United States, Chile, and India.

Methods

HLA-E is typed by our well-establish high-throughput approach relying on an amplicon spanning exons 2 and 3. Amplicons are sequenced by Illumina MiSeq or HiSeq 2500 instruments without fragmentation, preserving phase information. Reads are analysed by our in-house typing software nXyte. Primary typing results comprise the high-resolved alleles HLA-E*01:01, 01:03-03, 01:04, 01:05, 01:07 and 01:08N and three G-groups: HLA-E*01:01G, 01:03:01G and 01:03:02G. For this analysis, typing results have been translated to their respective 2-field equivalent. Upon enrollment with a DKMS donor center, potential stem cell donors provide information on their self-assessed ethnic background. Ethnic groups have been considered only, if typing results were available for at least 100 individuals.

Results

HLA-E is dominated by two allele groups, HLA-E*01:01 and HLA-E*01:03, rendering this locus almost bi-allelic. For ethnic groups with sample sizes of at least 100 individuals, we observed frequencies for HLA-E*01:01g from $f_{\text{min}}=40.1\%$ (Thailand) to $f_{\text{max}}=63.1\%$ (Kenya). Accordingly, we observed a frequency range from $f_{\text{min}}=35.6\%$ (Kenya) to $f_{\text{max}}=59.9\%$ (Thailand) for HLA-E*01:03. While in most East Asian countries HLA-E*01:03 is dominant, in Kenya, Morocco, and Chile HLA-E*01:01 is the most frequent allele.

HLA-E*01:05 has been observed most frequently in individuals with an ethnic background from the Democratic Republic of Congo ($f=2.5\%$), Kenya ($f=1.4\%$), and Ghana ($f=1.0\%$). Conclusions: We observed the highest deviation from bi-allelic behavior as reflected in the share of HLA-E*01:05 in samples from African countries. Also, a considerable shift between the two dominating allele groups was seen. Alleles 01:04 und 01:08N are not observed in any sample.