HLA-DPB1 mismatching between patients and unrelated donors is known to increase the risk of acute graft-versus-host-disease (GvHD) after hematopoietic stem cell transplantation. If only HLA-DPB1 mismatched donors are available, the genotype defined by the Single Nucleotide Polymorphism (SNP) rs9277534 can be used to select mismatched donors that are well-tolerated. [1]

However, since rs9277534 resides within the 3' untranslated region (UTR), it usually is not analyzed during DPB1 routine typing.

To verify whether rs9277534 can be inferred from standard DPB1 typing, we analyzed 37,261 samples of mostly Caucasian origin for their linkage between rs9277534 and HLA-DPB1 typing results based on sequencing exons 2 and 3. rs9277534 located in the 3' UTR was amplified by PCR and sequenced on Illumina MiSeq or Hiseq instruments. SNP calling was performed with FasType (DKMS Life Science Lab). DPB1 was typed based on sequencing exons 2 and 3 as described before [2, 3]. All samples with unclear results were reanalyzed using PacBio SMRT sequencing.

After primary analysis of 37,261 samples, 19 showed an unexpected rs9277534. SMRT sequencing disproved all of these as artefacts.

In 100% of samples linkage was in full concordance with the expectation derived from the DPB1 genotyping result.

We conclude that HLA-DPB1 typing of exons 2 and 3 is sufficient to infer the DPB1 expression marker rs9277534 with very high accuracy. This information could be used to select HLA-DPB1-mismatched donors that do not increase the risk of GvHD, without the need for an additional pretransplantation screening for SNP rs9277534.

References