IMPACT OF MHC GAMMA BLOCK (GAMMA TYPE) MISMATCHING IN THE OUTCOME OF UNRELATED HEMATOPOETIC STEM CELL TRANSPLANTATION

Joselito Getz1, David C. Sayer2, Ricardo Pasquini3, Vaneuza M. Funke1, Carmem S. Bonfim1, Vergílio R. Colturato4, Hayley Hogan2, Margareth A. Torres4, Maria Elisa. Moraes4, Noemi F. Pereira1. 1-Hospital de Clínicas - UFPR, Curitiba, Brazil, 2-Conexio Genomics, Fremantle, Australia, 3-Hospital Nossa Sra das Graças, Curitiba, Brazil, 4-Hospital Amaral Carvalho, Jaú, Brazi

Matching for HLA is not enough to prevent life-threatening complications in unrelated hematopoetic stem cell transplants (HSCT). MHC has blocks of genetic diversity associated as haplotypes that can encode unidentified transplantation antigens. Previous HLA-A, B, DRB1 linkage study showed that MHC haplotype matching in HSCT lowered risk of aGVHD and increased relapse. A recent study identified single nucleotide polymorphisms (SNPs) in C4A/C4B genes (gamma block) which lie between HLA-B/C and DRB/DQB blocks, and showed that mismatching at these SNPs may occur in HLA matched unrelated individuals suggesting they are markers for partial MHC haplotype matching. This study investigated the effect of C4A/C4B SNPs mismatching on the outcome of HSCT. Cohort included 225 patients (pts) transplanted with HLA10/10 (66%) and 9/10 (34%) unrelated donors, in 3 Brazilian centers between 1996 and 2013. Pts/donors were typed by PCR-SSP using Gamma Type (GT) assay (Conexio Genomics, Australia) that detects 23 SNPs in C4A/C4B genes. Probability of GVHD occurrence and overall survival were estimated from time of Tx by Kaplan Meier, and group differences compared by Log-rank. In HLA10/10 group 77 (52%) pairs were GT Matched (GT-M) and 71 (48%) GT Mismatched (GT-MM) (1-7 SNPs); in the HLA9/10 group 16 (21%) were GT-M and 61 (79%) GT-MM (1-11 SNPs). Univariate analysis showed in HLA 10/10 matched pts that 19.7% (14/71) of GT-MM pts developed grade III-IV aGVHD in comparison to only 3.9% (3/77) of GT-M patients (p=0.008), they were also more likely to develop chronic GVHD (p=0.047) despite no significant difference was seen in survival. In the 9/10 HLA transplants the likelihood of survival at 5 years is higher when pt and donor were GT-M (65.6%) compared with GT-MM (37.1%) (p=0.074). There were no significant differences in GVHD between GT-M and GT-MM probably due to the small sample size. This study shows that GT mismatching identifies patients at risk of adverse events following unrelated HSCT. This is likely to be because GT is a haplotype marker and GT-MM results in additional incompatibilities in non-HLA MHC sequences, which may be important in unrelated HSCT immunobiology. The differences seen between the 9/10 and the 10/10 HLA matched groups may reflect the interplay between HLA matching and non-HLA MHC sequence matching in unrelated HSCT.