

DAAM2 Polymorphism and Allogeneic Hematopoietic Stem Cell Transplantation

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WNT signaling pathway is known to have important functions in oncogenesis, cellular proliferation and regeneration, embryogenesis, stem cell renewal and leukemogenesis. DAAM2 is one of the key protein of WNT/PCP signaling pathway. This study examines the association of DAAM2 genetic polymorphism and the clinical outcomes in patients treated with allogeneic stem cell transplantation. Candidate SNPs associated with acute GVHD were selected using 100K DNA chip analysis in 15 patients who treated with allogeneic stem cell transplantation for various hematologic and oncologic diseases with or without acute GVHD. Six SNPs (rs2504787, rs2504086, rs2504082, rs3004067, rs882559, and rs3004070) on DAAM2 were proven to be associated with acute GVHD occurrence in this small group of patients, and extended genotyping was executed by TaqmanTM protocol in more large population of 239 patients in single institute. Retrospective analysis for medical records was performed to define correlation of these SNPs with clinical outcomes of the patients. rs882559, which is intron mutation forward to exon 24, was proven to be associated with acute GVHD incidence. Acute GVHD incidence was significant lower for the patients with CC genotype of rs882559 than other genotypes (adjusted Odds ratio 0.466, 95% CI 0.224~0.969, p=0.0409). Multivariate analyses, which included sex, age, transplant method (reduced intensity conditioning vs. conventional conditioning), stem cell source, risk group, and DAAM2 genotypes, as parameters, identified high-risk group, age over 50 years old, and codominant genotype of rs2504082, which is an intron mutation forward to exon 15, as risk factors for a shorter survival. This is the first clinical study for the DAAM2 genetic polymorphism, furthermore, and its association with clinical outcomes of allogeneic stem cell transplantation. The effects of rs882559 and rs2504082 were not identified by now, but its mutation might affect to the transcription of following coding genes causing the changes of its functions. This study suggested the clinical value of DAAM2 polymorphism as a predictive parameter of clinical outcomes of allogeneic HSCT, and its role in WNT signaling pathway.

HLA typing of A33, B58 or DR7 decreases treatment-related mortality in allogeneic stem cell transplantation in association with HSP70-hom polymorphism

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Background : Human leukocyte antigens(HLA) typing was expected to influence outcomes or adverse effects in allogeneic hematopoietic stem cell transplantation through its immunologic function. It was previously reported that HLA typing was associated with polymorphisms of Heat shock protein 70-hom (HSP70-hom) in other diseases. **Methods :** We analyzed the DNA of patients and donors who underwent allogeneic hematopoietic stem cell transplantation from HLA-matched sibling donors at single institute between 1998 and 2005 for malignancy or aplastic anemia. HLA typing was conducted and HSP70-hom polymorphisms was genotyped in patients and donors. Individual haplotypes were estimated from genotype data of the two HSP70-hom polymorphisms using the expectation maximization algorithm. **Results :** The HSP70-hom polymorphisms, rs2227956 and rs2075800, were genotyped and HLA typing was conducted in 141 patients and their donors. The HSP70-hom polymorphisms of patients were completely identical to those of their donors. Patients(101) with TG haplotype (TG/TA, TG/TG or TG/CG) did not only show less treatment-related mortality but also had longer overall survival compared with those(40) with non-TG haplotype (TA/TA or TA/CG). (P=0.011,P=0.013,respectively) TG haplotype was associated with HLA typing of A33, B58 and DR7.(P<0.001,P=0.002,P=0.039, respectively) Patients without HLA typing of A33, B58 and DR7 showed the more treatment-related mortality compared with patients with the other HLA typing.(P=0.034, HR=2.519, 95% CI:1.075-5.906) **Conclusion :** In association with HSP70-hom polymorphisms, HLA typing of A33, B58 or DR7 in HLA-matched sibling hematopoietic stem cell transplantation was protective for treatment-related mortality.