

Identifying Genetic Variants Associated With Acute Graft Versus Host Disease

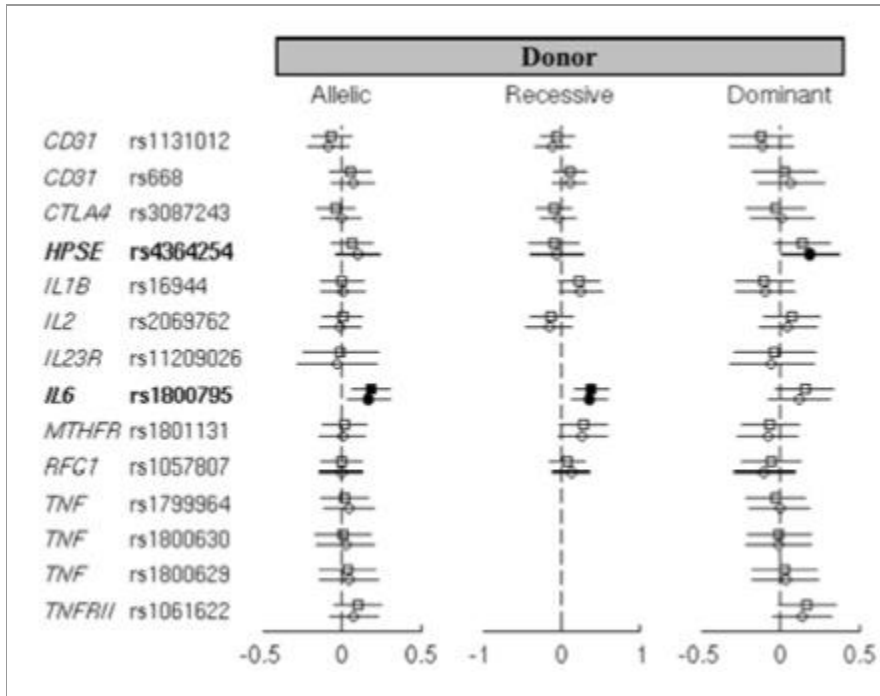
March 19, 2012

J Graham

Following allogeneic hematopoietic cell transplantation (HCT), where healthy donor cells are transferred to a patient, acute graft versus host disease (GVHD) can be a serious concern. Recently, many studies have identified genetic variants such as single nucleotide polymorphisms (SNPs), variations of single base pairs within the genome, associated with the risk of acute GVHD after transplant. A new study from the Clinical Research Division, published by lead author Dr. Jason Chien, along with Dr. John Hansen and collaborators, attempted to replicate all of the published significant candidate genetic associations with acute GVHD by using actual and imputed genome-wide SNP data from nearly 1300 allogeneic HCT donors and recipients.

The researchers performed a comprehensive literature search to identify published studies reporting an association between acute GVHD and genetic polymorphisms. Their study population included patients who received allogeneic HCT after myeloablative conditioning at Fred Hutchinson Cancer Research Center and the Seattle Cancer Care Alliance between 1992 and 2004, and included recipients with either related or unrelated donors. A genome-wide human SNP array was used with data subjected to a candidate SNP genotype determination algorithm to determine inclusion in the analysis. Of the 40 SNPs identified in the literature as gene variants potentially associated with acute GVHD, 16 could be analyzed by these methods. The researchers had previously published associations between acute GVHD risk and *IL10/IL10RB* SNPs, and the use of imputed genotypes to replicate this previous data was validated. Additionally, SNPs in the *IL6* donor genotype was associated with a 20 to 60% increased risk for acute GVHD after transplant. Additional associations were found for SNPs in other genes, but these findings proved to be inconsistent with original publications, suggesting that the majority of published associations likely represent false-positive discoveries. This study demonstrates the advantages and disadvantages of this novel approach using SNP data in genetic analysis to study genetic associations with acute GVHD, and sets clear benchmarks for replication of genetic association studies in the stem cell transplant population.

[Chien JW, Zhang XC, Fan W, Wang H, Zhao LP, Martin PJ, Storer BE, Boeckh M, Warren EH, Hansen JA.](#) 2012. Evaluation of published single nucleotide polymorphisms associated with acute graft versus host disease. *Blood*; DOI:10.1182/blood-2011-09-371153.



Plots for unadjusted (squares) and adjusted (circles) analysis of acute GVHD and candidate SNPs among HCT. X axis shows positive (increased risk for acute GVHD) or negative association (decreased risk for acute GVHD). Bolded indicates that the data exceeds the $p=0.05$ threshold (such as IL6).