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Human Minor Histocompatibility Antigens: Targets of Graft-versus-Host Disease and Graft-versus-Leukemia Responses

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Minor histocompatibility antigens (mHAg) consist of HLA bound peptides derived from cellular proteins encoded by polymorphic genes that differ between transplant donor and recipient. T cell responses to the mHAg broadly expressed in nonhematopoietic tissues are responsible for graft-versus-host disease (GVHD), while the mHAg selectively expressed in hematopoietic cells have been proposed as potential targets for a graft-versus-leukemia (GVL) response. Thus, identification and characterization of the genes encoding mHAg contribute to improve the outcome of allogeneic hematopoietic stem cell transplantation (HSCT). Human mHAg that have been molecularly characterized include those encoded by the Y chromosome genes SMCY, UTY, DFFRY, DBY, and RPS4Y, which are polymorphic with homologues on the X chromosome and are recognized by donor T cells after sex mismatched HSCT. Autosomal genes identified to encode mHAg include KIAA0223 (HA-1), Myosin1G (HA-2), Lymphoid blast crisis (HA-3), KIAA0020 (HA-8), HB-1, BCL2A1 (ACC-1 and -2), and UGT2B17. All human mHAg but UGT2B17 have polymorphism in their amino acid sequences which may alter the processing of recipient and donor peptides, the ability of the peptide to bind HLA, or the ability of T cells to recognize the HLA/peptide complex. UGT2B17 is immunogenic because of differential expression of the protein in donor and recipient cells as a consequence of a homozygous gene deletion in the donor. SMCY, DFFRY, HA-8, and UGT2B17 are expressed in both hematopoietic and nonhematopoietic tissues suggesting these mHAg may mediate GVHD in addition to GVL activity. HA-1, HB-1, and ACC-1 are selectively expressed in hematopoietic cells suggesting these mHAg may provide targets for immunotherapy after allogeneic HSCT. This presentation will summarize the characteristics of human mHAg and detail the UGT2B17 mHAg we recently identified.