

Abstract

Viral infections and reactivations remain a serious obstacle to successful hematopoietic stem cell transplantation (HSCT). When antiviral drug treatment fails, adoptive virus-specific T-cell transfer provides an effective alternative. Assuming that naive T cells (TN) are mainly responsible for GvHD, methods were developed to generate naive T-cell-depleted products while preserving immune memory against viral infections. We compared two major strategies to deplete potentially alloreactive T cells: CD45RA and CD62L depletion and analyzed phenotype and functionality of the resulting CD45RA⁻/CD62L⁻ naive T-cell-depleted as well as CD45RA⁺/CD62L⁺ naive T-cell-enriched fractions in the CMV pp65 and IE1 antigen model. CD45RA depletion resulted in loss of terminally differentiated effector memory T cells re-expressing CD45RA (TEMRA), and CD62L depletion in loss of central memory T cells (TCM). Based on these differences in target cell-dependent and target cell-independent assays, antigen-specific T-cell responses in CD62L-depleted fraction were consistently 3–5 fold higher than those in CD45RA-depleted fraction. Interestingly, we also observed high donor variability in the CD45RA-depleted fraction, resulting in a substantial loss of immune memory. Accordingly, we identified donors with expected response (DER) and unexpected response (DUR). Taken together, our results showed that a naive T-cell depletion method should be chosen individually, based on the immunophenotypic composition of the T-cell populations present.