457g The Scale-up of T Cell Depletion for Mismatched Bone Marrow Transplants

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Graft-versus-host disease (GVHD) is the major limitation preventing allogeneic stem cell transplantation (SCT) in a clinical setting; however SCT is the only curative option, to date, for a variety of hematological malignancies. It is generally believed that GVHD can be prevented by the use of large doses of CD34+ progenitor cells in a sample which has had a significant depletion of T cells. A subset of T-cells mediate GVHD. The number of progenitor cells necessary for safe engraftment may depend on several factors. Generally, 1x10E7 CD34+ progenitor cells/kg body weight is required, while a certain threshold of less than 2x10e5 T-cells (CD3+)/kg body weight renders the patients at increased risk for graft rejection/failure. This level of performance standards for a typical clinical transplantation requires approximately 0.5 to 1 x 10E10 peripheral blood leukocytes (PBLs) to be processed with a 80-90% recovery of the stem cells and a 4 to 5 log10 depletion of the T-cells. There are a number of technologies used with respect to T cell depletion and stem cell enrichment, the most efficient of which is immunomagnetic separation. Immunomagnetic separation is a promising technology using magnetism to purify cells and biological compounds. The most popular system employed for immunomagnetic cell separation that can select CD34+ cells positively is the commercial, batch MACS system. While promising, significant limitations exit with this system. A high-throughput, continuous immunomagnetic cell sorting system, Quadrupole Magnetic Cell Sorter, QMS, is being developed in our lab for a number applications including T cell depletion. We have demonstrated on small samples of human blood a (n-16) 4 log10 T cell depletion and a 60% recovery of CD34+ cells after the separation of 10E7 PBLs. At present the research, supported by the National Cancer Institute, is focused on scaling up to be able to process on the order of 2,,e108 PBLs from one buffy in an economical manner. This requires several studies to be conduced simultaneously, namley 1) Optimizing the immunomagnetic labeling of T cells, 2) Optimizing the separation of the labeled T cells in QMS, 3) Improving the models of the separation process. This presentation will present the current standing of this process.