534e Negative Selection of Blood Progenitor Cells by Continuous Magnetophoresis

Ying Jing, Lee R. Moore, Jeffrey Chalmers, and Maciej Zborowski

Enrichment of blood progenitor cells and depletion of unwanted cells, such as immunocompetent cells or tumor cells improves patient recovery in autologous and allogeneic hematopoietic stem cell (HSC) transplantations. During the purification process of the graft, it is preferred to keep the target HSCs unmanipulated. In this work, a technique is evaluated for enrichment of the blood progenitors from the clinical apheresis product (leukocytes from therapeutic leukuapheresis) using a negative selection strategy. The apheresis product was labeled with tetrameric antibody cocktail (TAC) and magnetic colloid against mature leukocytes but excluding HSC (StemSep™, Stem Cell Technologies, Vancouver, Canada). The separation of blood progenitor cells was performed by flow-through magnetophoresis in an annular channel placed coaxially with a quadrupole magnetic field, in a thin-flow split (SPLITT) configuration developed in-house. The maximum field intensity was 1.42 T, the total flow rate was 10 mL/min, the total cell number processed was 1.0E8 cells. The enriched cell fraction was characterized by flow cytometry and automated cell counting. The HSC content was determined using established CD34 cell marker measurement protocols. The recovery, purity and throughput of the isolated blood progenitors were optimized by adjusting cell suspension concentration and the SPLITT operating parameters following published SPLITT separation algorithms. The TAC progenitor enrichment cocktail and magnetic colloid were titrated to determine minimum effective antibody and magnetic reagent concentrations by measuring cell magnetophoretic mobility distribution using Cell Tracking Velocimetry (CTV). To test the reproducibility, apheresis products from different donors with an initial CD34 purity between 0.3% and 10% were evaluated. With this method, the blood progenitors are enriched with the purity of 40% to 90%, recovery of 40% to 80% and throughput of 4.0E5 cells/s(n = 12). T lymphocytes are depleted more than 3.5 log10. The negative selection method of HSC by continuous magnetophoresis holds promise for scaled-up, clinical applications.