



wicklung in der Klinik erwarten: Neue Substanzen können die Stammzellmobilisation verbessern. Die Stammzell dosis und zelluläre Komposition von Transplantaten wird optimiert. Mögliches Transdifferenzierungspotential von Stammzellen aus dem Knochenmark weckt die Hoffnung auf neue Anwendungen dieser Stammzellen in der regenerativen Medizin. Nabelschnurblut ist eine weitere Stammzellquelle, sowohl für die klassische hämatopoetische Stammzelltransplantation als auch für neue Indikationen, welche weiter exploriert werden. Die Manipulation von immunologisch aktiven Zellen, sei es durch Depletion entsprechender Zellen zur Vermeidung einer GvHD, oder zur gezielten Anreicherung und Differenzierung in der adoptiven Immuntherapie, können zu einer Verbesserung der Transplantatsergebnisse beitragen. Schließlich spielen die hämatopoetischen Stammzellen als Zielzellen von Gentransfer oder Genkorrektur eine wichtige Rolle bei der Entwicklung innovativer Therapieansätze für bisher unheilbare Erkrankungen.

- (1) Cai J, Weiss ML, Rao MS. In search of „stemness“. *Exp Hematol.* 2004; 32: 585-598.
- (2) Scholer HR. (The potential of stem cells. A status update). *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz.* 2004; 47: 565-577.
- (3) Thomson JA, Itskovitz-Eldor J, Shapiro SS et al. Embryonic stem cell lines derived from human blastocysts. *Science.* 1998; 282: 1145-1147.
- (4) Grove JE, Bruscia E, Krause DS. Plasticity of bone marrow-derived stem cells. *Stem Cells.* 2004; 22: 487-500.
- (5) Wagers AJ, Weissman IL. Plasticity of adult stem cells. *Cell.* 2004; 116: 639-648.
- (6) Anderson DJ, Gage FH, Weissman IL. Can stem cells cross lineage boundaries? *Nat Med.* 2001; 7: 393-395.
- (7) Graf T. Differentiation plasticity of hematopoietic cells. *Blood.* 2002; 99: 3089-3101.
- (8) McGuckin CP, Pearce D, Forraz N et al. Multiparametric analysis of immature cell populations in umbilical cord blood and bone marrow. *Eur J Haematol.* 2003; 71: 341-350.
- (9) Sutherland HJ, Hogge DE, Lansdorp PM et al. Quantitation, mobilization, and clinical use of long-term culture-initiating cells in blood cell autografts. *J Hematother.* 1995; 4: 3-10.
- (10) Bhatia M, Bonnet D, Murdoch B, Gan OI, Dick JE. A newly discovered class of human hematopoietic cells with SCID-repopulating activity. *Nat Med.* 1998; 4: 1038-1045.
- (11) Serke S, Johnsen HE. A European reference protocol for quality assessment and clinical validation of autologous haematopoietic blood progenitor and stem cell grafts. *Bone Marrow Transplant.* 2001; 27: 463-470.
- (12) Metcalf D. In vitro cloning techniques for haematopoietic cells: Clinical applications (abstract). *Annals of Internal Medicine.* 1977; 87: 483-488.
- (13) Wang JC, Doedens M, Dick JE. Primitive human hematopoietic cells are enriched in cord blood compared with adult bone marrow or mobilized peripheral blood as measured by the quantitative in vivo SCID-repopulating cell assay. *Blood.* 1997; 89: 3919-3924.
- (14) Lapidot T, Petit I. Current understanding of stem cell mobilization: the roles of chemokines, proteolytic enzymes, adhesion molecules, cytokines, and stromal cells. *Exp Hematol.* 2002; 30: 973-981.
- (15) Cottler-Fox MH, Lapidot T, Petit I et al. Stem cell mobilization. *Hematology (Am Soc Hematol Educ Program).* 2003; 419-37.
- (16) Levesque JP, Liu F, Simmons PJ et al. Characterization of hematopoietic progenitor mobilization in protease-deficient mice. *Blood.* 2004; 104: 65-72.





- (17) Roberts AW, DeLuca E, Begley CG et al. Broad inter-individual variations in circulating progenitor cell numbers induced by granulocyte colony-stimulating factor therapy. *Stem Cells*. 1995; 13: 512-516.
- (18) Johnsen HE, Lanza F, Fruehauf S et al. Sources and Procurement of Haemopoetic Stem Cells. In: Apperley J, Carreras E, Gluckman E, Gratwohl A, Masszi T, eds. *The EBMT Handbook: Haemopoetic Stem Cell Transplantation*. Paris: European School of Hematology; 2004: 79-89.
- (19) Wahlin A, Eriksson M, Hultdin M. Relation between harvest success and outcome after autologous peripheral blood stem cell transplantation in multiple myeloma. *Eur J Haematol*. 2004; 73: 263-268.
- (20) Dreger P, Haferlach T, Eckstein V et al. G-CSF-mobilized peripheral blood progenitor cells for allogeneic transplantation: safety, kinetics of mobilization, and composition of the graft. *Br J Haematol*. 1994; 87: 609-613.
- (21) Wiesneth M, Schreiner T, Friedrich W et al. Mobilization and collection of allogeneic peripheral blood progenitor cells for transplantation. *Bone Marrow Transplant*. 1998; 21 Suppl 3: S21-4.: S21-S24.
- (22) Desikan KR, Tricot G, Munshi NC et al. Preceding chemotherapy, tumour load and age influence engraftment in multiple myeloma patients mobilized with granulocyte colony-stimulating factor alone. *Br J Haematol*. 2001; 112: 242-247.
- (23) Clark RE, Brammer CG. Previous treatment predicts the efficiency of blood progenitor cell mobilisation: validation of a chemotherapy scoring system. *Bone Marrow Transplant*. 1998; 22: 859-863.
- (24) Sugrue MW, Williams K, Pollock BH et al. Characterization and outcome of „hard to mobilize“ lymphoma patients undergoing autologous stem cell transplantation. *Leuk Lymphoma*. 2000; 39: 509-519.
- (25) Stiff PJ. Management strategies for the hard-to-mobilize patient. *Bone Marrow Transplant*. 1999; 23 Suppl 2: S29-33.: S29-S33.
- (26) Fruehauf S, Schmitt K, Veldwijk MR et al. Peripheral blood progenitor cell (PBPC) counts during steady-state haemopoiesis enable the estimation of the yield of mobilized PBPC after granulocyte colony-stimulating factor supported cytotoxic chemotherapy: an update on 100 patients. *Br J Haematol*. 1999; 105: 786-794.
- (27) Schwella N, Beyer J, Schwane I et al. Impact of preleukapheresis cell counts on collection results and correlation of progenitor-cell dose with engraftment after high-dose chemotherapy in patients with germ cell cancer. *J Clin Oncol*. 1996; 14: 1114-1121.
- (28) Demirel T, Ilhan O, Ayli M et al. Monitoring of peripheral blood CD34⁺ cell counts on the first day of apheresis is highly predictive for efficient CD34⁺ cell yield. *Ther Apher*. 2002; 6: 384-389.
- (29) Fontao-Wendel R, Lazar A, Melges S, Altobeli C, Wendel S. The absolute number of circulating CD34⁺ cells as the best predictor of peripheral hematopoietic stem cell yield. *J Hematother*. 1999; 8: 255-262.
- (30) Couban S, Simpson DR, Barnett MJ et al. A randomized multicenter comparison of bone marrow and peripheral blood in recipients of matched sibling allogeneic transplants for myeloid malignancies. *Blood*. 2002; 100: 1525-1531.
- (31) Bensinger WI, Martin PJ, Storer B et al. Transplantation of bone marrow as compared with peripheral-blood cells from HLA-identical relatives in patients with hematologic cancers. *N Engl J Med*. 2001; 344: 175-181.
- (32) Schmitz N, Bacigalupo A, Hasenclever D et al. Allogeneic bone marrow transplantation vs filgrastim-mobilised peripheral blood progenitor cell transplantation in patients with early leukaemia: first results of a randomised multicentre trial of the European Group for Blood and Marrow Transplantation. *Bone Marrow Transplant*. 1998; 21: 995-1003.





- (33) Blaise D, Kuentz M, Fortanier C et al. Randomized trial of bone marrow versus lenograstim-primed blood cell allogeneic transplantation in patients with early-stage leukemia: a report from the Societe Francaise de Greffe de Moelle. *J Clin Oncol.* 2000; 18: 537-546.
- (34) Akizuki S, Mizorogi F, Inoue T, Sudo K, Ohnishi A. Pharmacokinetics and adverse events following 5-day repeated administration of lenograstim, a recombinant human granulocyte colony-stimulating factor, in healthy subjects. *Bone Marrow Transplant.* 2000; 26: 939-946.
- (35) Carlo-Stella C, Di Nicola M, Milani R et al. Use of recombinant human growth hormone (rhGH) plus recombinant human granulocyte colony-stimulating factor (rhG-CSF) for the mobilization and collection of CD34⁺ cells in poor mobilizers. *Blood.* 2004; 103: 3287-3295.
- (36) Wiesneth M. Gewinnung und Präparation von peripheren Blutstammzellen. In: Mueller-Eckhardt C, Kiefel V, eds. *Transfusionsmedizin.* Springer; 2004: 272-286.
- (37) Tichelli A., Passweg J., Hoffmann T., Gregor M., Kühne T., Favre G., Wodnar-Filipowicz A., Gratwohl A.: Repeated peripheral stem cell mobilization in healthy donors: time-dependent changes in mobilization efficiency. *Brit. J. Haematol.* 1999; 106: 152-158
- (38) Muller S, Schulz A, Reiss U et al. Definition of a critical T cell threshold for prevention of GVHD after HLA non-identical PBPC transplantation in children. *Bone Marrow Transplant.* 1999; 24: 575-581.
- (39) Sputtek A, Gutensohn K, Hummel K, Löliger C, Kühnl P. Zur Kryokonservierung von Blutstammzellen. *J Lab Med* 1996; 20 (2): 70-77
- (40) Ottinger HD, Beelen DW, Scheulen B, Schaefer UW, Grosse-Wilde H. Improved immune reconstitution after allotransplantation of peripheral blood stem cells instead of bone marrow. *Blood.* 1996; 88: 2775-2779.
- (41) Schrezenmeier H, Bredesen DE, Bruno B et al. Comparison of Allogeneic Bone Marrow and Peripheral Blood Stem Cell Transplantation for Aplastic Anemia: Collaborative Study of European Blood and Marrow Transplant Group (EBMT) and International Bone Marrow Transplant Registry (IBMTR) [abstract]. *Blood.* 2003 ;102: 267.
- (42) Urbano-Ispizua A, Schmitz N, De Witte T et al. Allogeneic and autologous transplantation for haematological diseases, solid tumours and immune disorders: definitions and current practice in Europe. *Bone Marrow Transplant.* 2002; 29: 639-646.
- (43) In: Apperley J, Carreras E, Gluckman E, Gratwohl A, Masszi T, eds. *The EBMT Handbook: Haematopoietic Stem Cell Transplantation.* Paris: European School of Haematology; 2004.
- (44) Heldal D, Brinch L, Tjønnfjord G et al. Fewer relapses and increased chronic GVHD in patients transplanted with blood stem cells: a 5-year follow-up in a single centre study. *Bone Marrow Transplant.* 2003; 32: 257-264.
- (45) Powles R, Mehta J, Kulkarni S et al. Allogeneic blood and bone-marrow stem-cell transplantation in haematological malignant diseases: a randomised trial. *Lancet.* 2000; 355: 1231-1237.
- (46) Vigorito AC, Azevedo WM, Marques JF et al. A randomised, prospective comparison of allogeneic bone marrow and peripheral blood progenitor cell transplantation in the treatment of haematological malignancies. *Bone Marrow Transplant.* 1998; 22: 1145-1151.