Towards the genetic treatment of Hematopoietic stem cell mobilization

Roberto M. Lemoli and Alessandra D'Addio

There are advantages from reinfusing autologous mobilized peripheral blood stem cells rather than bone marrow hematopoietic stem cells. This article focuses on the biomolecular mechanisms underlying the release of hematopoietic stem cells from the bone marrow to help the understanding of novel strategies to make stem cell collection more effective. See related article on page 347.

Towards the genetic treatment of β-thalassemia: new disease models, new vectors, new cells

Paolo Moi and Michel Sadelain

The transfer of a regulated globin gene in autologous hematopoietic stem cells is an attractive therapeutic approach to β-thalassemia, since, in principle, it is applicable to all patients. This commentary reviews recent advances in animal models, globin vector design and stem cell isolation. See related article on page 356.

Prevention of thrombosis in polycythemia vera and essential thrombocythemia

Raffaele Landolfi and Leonardo Di Gennaro

Thrombotic events are a dominant clinical feature of polycythemia vera and essential thrombocythemia. Estimating the vascular risk and choosing the best antithrombotic strategy are crucial issues in the management of these disorders. This article reviews the most important risk factors for thrombosis and focuses on the available therapeutic strategies for reducing the vascular risk. See related article on page 372.

Secondary malignancies after therapy of indolent non-Hodgkin’s lymphoma

Jonathan W. Friedberg

Over the past decade the survival of patients with indolent non-Hodgkin’s lymphoma has improved significantly. As a consequence, patients have more time to develop secondary effects of chemotherapy and radiation therapy. This perspective article focuses on risks and risk factors for the development of solid tumors in patients with such lymphomas. See related article on page 398.

Hematopoietic Stem Cells

Pegylated granulocyte colony-stimulating factor mobilizes CD34+ cells with different stem and progenitor subsets and distinct functional properties in comparison with unconjugated granulocyte colony-stimulating factor

Ingmar Bruns, Ulrich Steidl, Johannes C. Fischer, Akos Czibere, Guido Koble, Sascha Raschke, Raminder Singh, Roland Fenk, Michael Rosskopf, Sabrina Pechtel, Arndt von Haeusler, Peter Wernet, Daniel G. Tenen, Rainer Haas, and Ralf Kronenwett

Stem cells can be mobilized into the peripheral blood using cytokines, cytotoxic chemotherapy or a combination of both. Stimulation with pegylated-granulocyte colony-stimulating factor or granulocyte colony-stimulating factor results in different expression of key regulatory genes and different functional properties of mobilized hematopoietic stem and progenitor cells.

Thalassemia Syndrome

A novel transgenic mouse model produced from lentiviral germline integration for the study of β-thalassemia gene therapy

Wei Li, Shuyang Xie, Xinbing Guo, Xiuli Gong, Shu Wang, Dan Liu, Jingzhi Zhang, Zhaorui Ren, Shuzhen Huang, Fanzy Zeng, and Yitao Zeng

Lentiviral-mediated gene therapy has been successfully applied in the treatment of β-thalassemia. In this study transgenic mice with stable expression of a lentivirus carrying the human β-globin gene were obtained. These animals provide a useful model to investigate the stable effect of gene therapy in β-thalassemia.

Bone Marrow Failure

SBDS-deficient cells undergo accelerated apoptosis through the Fas-pathway

Piya Ruijikyanont, Ken-ichiro Watanabe, Chhaya Ambekar, Hamming Wang, Aaron Schimmer, Joseph Beyene, and Yigal Dror

Ninety percent of patients with Shwachman-Diamond syndrome, an inherited bone marrow dysfuncion, have mutations in the Shwachman-Bodian-Diamond syndrome.


FDG-PET imaging has been proven to be more accurate than conventional imaging for assessment of lymphoma response to therapy. This study evaluates the usefulness of FDG-PET for predicting response to radioimmunotherapy in patients with refractory lymphoma. The results suggest that positive FDG-PET findings 6 weeks after radioimmunotherapy predict significantly earlier relapse.


Stefano Sacchi, Luigi Marcheselli, Alessia Barri, Raffaella Marcheselli, Samantha Pozzi, Stefano Luminari, Marco Lombardo, Gabriele Buda, Antonio Lazzeri, Paolo G. Golbi, Caterina Stelitano, Fortunato Morabito, Giovanni Quarta, and Maura Brugiatelli.

There is relatively little information on secondary cancers after non-Hodgkin’s lymphomas. This long-term follow-up study determines the incidence rate and identifies subgroups of non-Hodgkin’s lymphoma patients with increased incidences of secondary malignancy.

405 A phase 2 pilot study of pegfilgrastim and filgrastim for mobilizing peripheral blood progenitor cells in patients with non-Hodgkin’s lymphoma receiving chemotherapy.

Nigel Russell, Rolf Mesters, Joerg Schubert, Marc Boogerts, Hans E. Johnsen, Consuelo del Canizo, Nigel Baker, Philippa Barker, Tomas Skacel, and Norbert Schnitz.

This phase 2 randomized, double-blind trial examines the efficacy of pegfilgrastim and filgrastim for mobilizing peripheral blood progenitors cells following chemotherapy in patients with non-Hodgkin’s lymphoma. The results of the study suggest that pegfilgrastim may provide a suitable alternative to filgrastim in this setting.

413 Clonal heterogeneity in chronic lymphocytic leukemia cells: superior response to surface IgM cross-linking in CD38, ZAP-70-positive cells.

Giovanna Cutrona, Monica Colombo, Serena Matis, Marina Fabbi, Mauro Spriano, Vincenzo Callea, Ernesto Vigna, Massimo Gentile, Simonetta Zupo, Nicholas Chiorazzi, Fortunato Morabito, and Manlio Ferrari.

The reasons why immunoglobulin gene mutation status and expression of ZAP-70 and CD38 influence disease progression in chronic lymphocytic leukemia are still undefined. This study shows that CD38+, ZAP-70+ cells have a greater capacity for signalling through the B-cell receptor and suggests a function for B-cell receptor signalling in promoting cell expansion.
cyte subsets in myeloma patients treated with allogeneic stem cell transplantation, and shows that donor-derived regulatory T cells expand faster than conventional CD4+ T cells and have a strong inhibitory function.

Decision Making and Problem Solving

Multiple Myeloma

Report of the European Myeloma Network on multiparametric flow cytometry in multiple myeloma and related disorders

Andy C. Rawstroun, Alberto Orfao, Meral Bekesac, Ludmila Bezliickova, Rik A. Brownman, Horia Bumbea, Klara Dalva, Gwenny Fuhler, Ian Grattana, Dirk Hose, Lucie Kovarova, Michael Lioznov, Gema Mateo, Ricardo Morilla, Anne K. Mylin, Paola Omede, Catherine Pellat-Deceunynck, Martin Perez Andres, Maria Petracci, Marina Ruggeri, Grzegorz Rymkiewicz, Alexander Schnitz, Martin Schreder, Carine Seynaeve, Martin Spacek, Ruth M. de Tiete, Els Van Valckenborgh, Nicky Weston-Bell, Roger G. Owen, Jesús San Miguel, Pieter Sonneveld, and Hans E. Johnson on behalf of the European Myeloma Network

In multiple myeloma, the use of multiparametric flow cytometry in many laboratories is currently restricted to clinical research studies and the differential diagnosis of unusual cases. This article reports the indications of the European Myeloma Network for flow cytometry in patients with monoclonal gammopathies, and the technical recommendations for the analysis of plasma cells.

Brief Reports

Acute Myeloid Leukemia

NPM1 mutations and cytoplasmic nucleophosmin are mutually exclusive of recurrent genetic abnormalities: a comparative analysis on 2,562 patients with acute myeloid leukaemia

Brunangelo Falini, Cristina Mecucci, Giuseppe Saglio, Francesca Lo Coco, Daniela Diverio, Patrick Brown, Fabrizio Pane, Marco Mancini, Maria Paola Martelli, Stefano Pileri, Torsten Haferlach, Claudia Haferlach, and Susanne Schnittger

NPM1 mutations, causing aberrant cytoplasmic expression of nucleophosmin, are the most frequent genetic alteration in acute myeloid leukaemia with a normal karyotype. This study confirms in a large series of patients that NPM1 mutations and cytoplasmic nucleophosmin are mutually exclusive of recurrent genetic abnormalities.

Acute Myeloid Leukemia

Histone deacetylase inhibitor treatment downregulates VLA-4 adhesion in hematopoietic stem cells and acute myeloid leukemia blast cells

Ulrich Mahlknecht and Christine Schönbein

Malignant Lymphomas

Autoimmune thrombocytopenia in non-Hodgkin lymphomas

Alexander W. Hauswirth, Cathrin Skrels, Christian Schützinger, Markus Raderer, Andreas Chott, Peter Valent, Klaus Lechner, and Ulrich Jäger

Autoimmune thrombocytopenia is a potentially life-threatening complication in non-Hodgkin’s lymphomas. This study focuses on the temporal relationship between autoimmune thrombocytopenia and lymphoma, the frequency in lymphoma subtypes, laboratory data and treatment outcome.

Multiple Myeloma

Normalization of the serum angiopoietin-1 to angiopoietin-2 ratio reflects response in refractory/resistant multiple myeloma patients treated with bortezomib

Konstantinos Avargyrou, Evangelos Terpos, Theodoros P. Vassilakopoulos, Anastasia Pouli, Sothiris Sachanas, Tatiana Tsou, Stavroula Masouridis, Dimitrios Christoulas, Maria K. Angelopoulou, Evangelia M. Dimitriadou, Christina Kalpadakis, Konstantinos Tsions, Panayiotis Panayiotidis, Meletios A. Dimopoulos, Gerassimos A. Pangalis, and Marie-Christine Kyrtonis on behalf of the Greek Myeloma Study Group

Bortezomib is a proteasome inhibitor producing high response rates in patients with relapsed/resistant multiple myeloma patients. This study investigates the effect of bortezomib on circulating angiopoietins levels, and shows that the normalization of the angiopoietin-1/angiopoietin-2 ratio reflects the response to treatment.

Multiple Myeloma

High response rate and improved graft-versus-host disease following bortezomib as salvage therapy after reduced intensity conditioning allogeneic stem cell transplantation for multiple myeloma

Jean El-Cheikh, Mauricette Michallet, Arnon Nagler, Hugues de Lavallade, Franck E. Nicolini, Patrick Brown, Fabrizio Pane, Marco Mancini, Maria Paola Martelli, Stefano Pileri, Torsten Haferlach, Claudia Haferlach, and Susanne Schnittger

This study assesses the use of bortezomib as a salvage therapy in myeloma patients who relapse after allogeneic transplantation with reduced intensity conditioning. Bortezomib treatment is associated with a high response rate and improved graft-versus-host disease, suggesting that it is a safe and efficient therapeutic option.
Amyloidosis

459 Evaluation of the serum-free light chain test in untreated patients with AL amyloidosis
Tilmann Bochtler, Ute Hegenerbart, Christiane Heiss, Axel Benner, Friedrich Cremer, Martin Volkmann, Jochen Ludwig, Jolanta B. Perz, Anthony D. Ho, Hartmut Goldschmidt, and Stefan O. Schonland

The diagnostic value of serum electrophoresis and urinary light chain excretion in AL amyloidosis is poor due to the usually low amount of monoclonal protein. This study evaluates immunoglobulin light chains in the serum of a large series of untreated patients with systemic AL amyloidosis, and proves that free light chain levels reflect disease severity.

Letters to the Editor

Sickle Cell Disease

463 Hospitalization of children with sickle cell disease in a region with increasing immigration rates
Raffaella Colombatti, Laura Visonà Dalla Pozza, Monica Mazzucato, Laura Sainati, Maria Pierobon, and Paola Facchin

Bone Marrow Failure

465 Cytokines in combination to treat radiation-induced myelosuppression: evaluation of SCF + glycosylated EPO + pegylated G-CSF as an emergency treatment in highly irradiated monkeys
Michel Drolet, Christophe Delaunay, Nancy Greener, Philippe Garrigou, Jean-François Mayol, and Francis Hérodin

Chronic Lymphocytic Leukemia

473 Recurrent cytogenetic findings in subsets of patients with chronic lymphocytic leukemia expressing IgG-switched stereotyped immunoglobulins
Anastasia Athanassiadou, Kostas Stamatopoulos, Maria Gaitatzis, Niki Stavroyianni, Athanasios Fassas, and Achilles Anagnostopoulos

Chronic Lymphocytic Leukemia

475 High dose methylprednisolone and rituximab is an effective therapy in advanced refractory chronic lymphocytic leukemia resistant to fludarabine therapy
Moëz Dungarwalla, Steve O. Evans, Unell Riley, Daniel Catovsky, Clare E. Dearden, and Estella Mattutes

Disorders of Hemostasis

477 Evaluation of factor V mRNA to define the residual factor V expression levels in severe factor V deficiency
Barbara Lunghi, Mirko Pinotti, Iva Maestri, Angelika Batorova, and Francesco Bernardi

Thrombosis

479 Thrombophilia as a predictor of persistent residual vein thrombosis
Luca Spiezia, Daniele Tormene, Raffaella Pesavento, Laura Salmass, Paolo Simonini, and Paolo Prandoni

Errata

480 Erratum in the article by Lokhorst HM et al. Thalidomide in induction treatment increases the very good partial response rate before and after high-dose therapy in previously untreated multiple myeloma. Haematologica 2008; 93:124-127

Online Only Articles

e32 Successful heart transplantation following melphalan plus dexamethasone therapy in systemic AL amyloidosis
Aude Mignot, Frank Bridoux, Antoine Thierry, Shaida Varnous, Myriam Pujo, Annick Delcourt, Jean Marc Gombert, Jean-Michel Goujon, Frédéric Favreau, Guy Touchard, Daniel Herpin, and Arnaud Jaccard

e36 Transient global amnesia associated with the infusion of DMSO-cryopreserved autologous peripheral blood stem cells
Zaher K. Otrock, Ahmad Beydoun, Wissam M. Barada, Rami Masrouje, Rola Hourani, and Ali Bazarkachi

e38 Central nervous system relapse occurs in about 5% of cases of acute promyelocytic leukaemia
Shailendra Kapoor