**Cover Figure**

The iron acquisition pathway in developing erythroblasts. This illustration is taken from the review article by Iolascon and co-workers on page 395.

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**Editorials and Perspectives**

307 Towards explaining “unexplained hyperferritinemia”  
Clara Camaschella and Erika Poggiali

Elevated serum ferritin is found in a large spectrum of conditions both genetic and acquired, associated or not with iron overload. In this perspective article, Drs. Camaschella and Poggiali examine our current knowledge of the molecular basis of inherited hyperferritinemia. See related article on page 335.

310 Immunosuppressive treatment for aplastic anemia: are we hitting the ceiling?  
Jakob R. Passweg and André Tichelli

The combination of antithymocyte globulin of horse origin and cyclosporine A is the standard treatment for aplastic anemia in patients not eligible for bone marrow transplantation. In this perspective article, Drs. Passweg and Tichelli discuss the current immunosuppressive therapy of aplastic anemia. See related article on page 348.

313 Microparticles in endothelial cell and vascular homeostasis: are they really noxious?  
Olivier Morel, Florence Tott, Nicolas Morel, and Jean-Marie Freyssinet

Endothelial damage and release of membrane microparticles are key steps in the pathogenesis of inflammation. In this perspective article, Dr. Morel and co-workers discuss the biological and clinical significance of microparticles in endothelial cells. See related article on page 387.

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**Original Articles**

318 Green fluorescent protein transgene driven by Kit regulatory sequences is expressed in hematopoietic stem cells  
Francesco Cerisoli, Letizia Cassinelli, Giuseppe Lamorte, Stefania Citterio, Francesca Bertolotti, Maria Cristina Magli, and Sergio Ottolenghi

The expression of Kit in multiple types of stem cells suggests that common transcriptional programs might regulate this gene in different stem cells. In this work, the authors used mouse lines expressing transgenic green fluorescent protein under the control of Kit promoter/first intron regulatory elements. This study provides the basis for the elucidation of DNA sequences regulating a stem cell gene in multiple types of stem cells.

326 TAM receptors and the regulation of erythropoiesis in mice  
Hongmei Tang, Song Chen, Haikun Wang, Hui Wu, Qingxian Lu, and Daishu Han

TAM receptors (Tyro3, Axl and Mer) are expressed in hematopoietic tissues, but their roles in hematopoiesis are largely unknown. This study shows that Axl and Mer play an important role in regulating erythropoiesis.

335 A new missense mutation in the L ferritin coding sequence associated with elevated levels of glycosylated ferritin in serum and absence of iron overload  

The best known type of inherited hyperferritinemia not related to iron overload is the hyperferritinemia-cataract syndrome (OMIM #600886), caused by a mutation in the iron-responsive element in the 5′-prime non-coding region of the ferritin light chain gene (FTL). This study describes a novel missense mutation of FTL responsible for genetic hyperferritinemia without iron overload. See related perspective article on page 307.

340 Elevated tricuspid regurgitant jet velocity in children and adolescents with sickle cell disease: association with hemolysis and hemoglobin oxygen desaturation  
Caterina P. Minniti, Craig Sable, Andrew Campbell, Sohail Rana, Gregory Ensing, Niti Dham, Onyinye Onyekwere, Melodi Nouraei, Gregory J. Kato, Mark T. Gladwin, Oswaldo L. Castro, and Victor R. Gordeuk

An elevated echocardiography-determined tricuspid regurgitant jet velocity predicts high systolic pulmonary artery pressure and early mortality in adults with sickle cell disease. The study provides evidence for independent associations of elevated jet velocity with hemolysis and oxygen desaturation in children and adolescents with sickle cell disease.
### Aplastic Anemia

Treatment of severe aplastic anemia with a combination of horse anti-thymocyte globulin and cyclosorine, with or without sirolimus: a prospective randomized study  
Phillip Scheinberg, Colin O. Wu, Olga Nunez, Priscila Scheinberg, Carol Boss, Elaine M. Sloand, and Neal S. Young

As mentioned above, the combination of antithymocyte globulin of horse origin and cyclosporine A is the standard treatment for aplastic anemia in patients not eligible for bone marrow transplantation. The authors hypothesized that the addition of sirolimus to standard horse antithymocyte globulin and cyclosporine A would improve response rates in severe aplastic anemia, due to its complementary and synergistic properties to cyclosporine A. Despite a theoretical rationale for its use, unfortunately sirolimus did not improve the response rate. See related perspective article on page 310.

### Hodgkin's Lymphoma

Comparative analysis of oncogenic properties and nuclear factor-kb activity of latent membrane protein 1 natural variants from Hodgkin’s lymphoma’s Reed-Sternberg cells and normal B-lymphocytes  
Nathalie Faumont, Aurélie Chanut, Alan Benard, Nadine Cogne, Georges Delsoel, Jean Feuillard, and Fabienne Meggetto

Latent membrane protein 1 (LMP1) was the first Epstein-Barr virus (EBV) latent protein found to be able to transform cell lines, and further the development of diversity. In EBV-associated Hodgkin’s lymphomas, LMP1 polymorphism participates in EBV genetic potential. LMP1 variants from Reed-Sternberg cells have enhanced proliferating and clonogenic potential.

### Chronic Lymphocytic Leukemia

A high number of losses in 13q14 chromosome is associated with a worse outcome and biological differences in patients with B-cell chronic lymphoid leukemia  
José Angel Hernández, Ana Eugenia Rodriguez, Marcos González, Rocio Benito, Celia Fontanillo, Virgilio Sandoval, Mercedes Romero, Guillermo Martín-Núñez, Alfonso García de Coca, Rosa Fiscas, Josefina Galende, Isabel Recio, Francisco Ortúñez, Juan Luis García, Javier de las Rivas, Norma Carmen Gutiérrez, Jesús F. San Miguel, and Jesús María Hernández

In B-cell chronic lymphoid leukemia, patients with 13q14 deletion generally have a favorable outcome. The findings of this study suggest that the number of malignant cells carrying the 13q14 deletion, as assessed by FISH, appears to be associated with long overall survival and time to progression.

### Multiple Myeloma

Cystatin-C is an independent prognostic factor for survival in multiple myeloma and is reduced by bortezomib administration  
Evangelos Tzifakis, Efstatios Kasbrits, Dimitrios Christoulas, Anastasia Poul, Euryaliki Michalis, Evgenia Verrou, Konstantinos Anargyrou, Konstantinos Tsonos, Meletios A. Dimopoulos, and Konstantinos Zervas, on behalf of the Greek Myeloma Study Group

Renal impairment is a common complication of multiple myeloma, and serum cystatin-C is considered an accurate marker of glomerular filtration rate. The findings of this study suggest that serum cystatin-C is not only a sensitive marker of renal impairment, but also reflects tumor burden and is of prognostic value in multiple myeloma.

### Amyloidosis

Translocation t(11;14) and survival of patients with light chain (AL) amyloidosis  
Alan H. Bryce, Rhett P. Ketterling, Morie A. Gertz, Martha Lacy, Ryan A. Knudson, Steven Zeldenrust, Shaji Kumar, Suzanne Hayman Francis Buadi, Robert A. Kyle, Philip R. Cremp, John A. Lust, Stephen Russell, S. Vincent Rajkumar, Rafael Fonseca, and Angela Dispensieri

Little is known about cytogenetic abnormalities in patients with light chain (AL) amyloidosis. The findings of this study suggest that interphase FISH coupled to cytoplasmic staining of specific Ig on bone marrow cells could be useful in light chain (AL) amyloidosis, and that t(14;14) is an adverse prognostic factor in these patients.

### Thrombosis

Microparticle-associated endothelial protein C receptor and the induction of cytoprotective and anti-inflammatory effects  
Margarita Pérez-Casas, Colin Downey, Beatriz Cutillas-Moreno, Mirko Zuzel, Kenji Fukudome, and Cheng Hock Toh

The endothelial protein C receptor plays an important role within the protein C pathway in regulating coagulation and inflammation. This study provides information on the mechanisms by which activated protein C causes the release of the endothelial protein C receptor in microparticulate form from endothelial cells. See related perspective article on page 313.

### Review Article

Red Cell Disorders

Molecular basis of inherited microcytic anemia due to defects in iron acquisition or heme synthesis  
Achille Iolascon, Luigia De Falco, and Carole Beaumont

The molecular basis of inherited microcytic anemia due to defects in iron acquisition or heme synthesis is discussed. See related perspective article on page 313.
This review article examines our present knowledge on the molecular basis of inherited microcytic anemia due to defects in iron acquisition or heme synthesis. The conditions examined include congenital sideroblastic anemias due to mutations in ALAS2, ABCB7 or GRX5, microcytic anemias due to DMT1 mutations, and the microcytic anemia associated with TMPRSS6 mutations.

**Brief Reports**

**Bone Marrow Failure**

Shwachman-Diamond syndrome neutrophils have altered chemoattractant-induced F-actin polymerization and polarization characteristics
Claudia Orelio and Taco W. Kuijpers

The findings of this study indicate that Shwachman-Diamond syndrome neutrophils have aberrant chemoattractant-induced F-actin properties that might contribute to the impaired neutrophil chemotaxis present in this syndrome.

**Myeloproliferative Neoplasms**

Detection of JAK2 exon 12 mutations in 15 patients with JAK2V617F negative polycythemia vera
Claudia Orelio and Taco W. Kuijpers

This study describes JAK2 exon 12 mutations in patients with polycythemia vera not carrying the classical JAK2 V617F mutation.

**Malignant Lymphomas**

Expression pattern of XBP1(S) in human B-cell lymphomas
Lorenza Maestre, Reuben Tooze, Marta Cañamero, Santiago Montes-Moreno, Rocio Ramos, Gina Doody, May Boll, Sharon Barrans, Sara Baena, Miguel Angel Pires, and Giovanna Roncador

The transcription factor XBP1 (X-box-binding protein 1) is essential for plasma cell differentiation and immunoglobulin secretion. This study indicates that the active form of XBP1, XBP1(S), provides a specific marker of advanced plasma cell differentiation, and in lymphoid malignancies is restricted to plasma cell-derived neoplasms and plasmablastic diffuse large B-cell lymphomas.

**Malignant Lymphomas**

CD20 mutations involving the rituximab epitope are rare in diffuse large B-cell lymphomas and are not a significant cause of R-CHOP failure
Nathalie A. Johnson, Stephen Leach, Bruce Woolcock,

**Letters to the Editor**

**Aplastic Anemia**

Increased CD4+ and CD8+ effector memory T cells in patients with aplastic anemia
Xiaojing Hu, Yan Gu, Yingxue Wang, Yaqin Cong, Xin Qu, and Conggao Xu

**Myelodysplastic Syndromes**

The response to lenalidomide of myelodysplastic syndrome patients with deletion del(5q) can be sequentially monitored in CD34+ progenitor cells
Brigitte Mohr, Uta Oelschlagele, Christian Thiede, Michelle Meredeth Stewart, Gerhard Ehniger, and Uwe Platzbecker

**Myeloproliferative Neoplasms**

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**Acute Myeloid Leukemia**

A JAK2-V617F activating mutation in addition to KIT and FLT3 mutations is associated with clinical outcome in patients with t(8;21)(q22;q22) acute myeloid leukemia
Eisaku Iwanaga, Tomoko Nunn, Naofumi Matsuno, Hiroaki Kawakita, Hiroaki Mitsuiy, and Norio Asou

**Acute Lymphoblastic Leukemia**

JAK1 mutation analysis in T-cell acute lymphoblastic leukemia cell lines
Michaël Porcu, Olga Gielen, Jan Cools, and Kim De Keersmaecker

**Amyloidosis**

A father and his son with systemic AL amyloidosis
Stina Enqvist, Ulf Henrik Mellqvist, Johan Møhne, Knut Sletten, Charles Murphy, Alan Solomon, Fred J. Stevens, and Per Westermark

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