

BLOOD

JOURNAL OF
THE AMERICAN
SOCIETY OF
HEMATOLOGY
VOLUME 114
NUMBER 24
3 DECEMBER 2009

An epigenetic
signature for primitive
hematopoietic cells
(p 4968)

FLT3-ITD up-regulates
MCL-1 and leukemia
stem cell survival
(p 5034)

Production of
human platelets in
immunodeficient mice
(p 5044)

Pericyte recruitment
and endothelial matrix
deposition (p 5091)

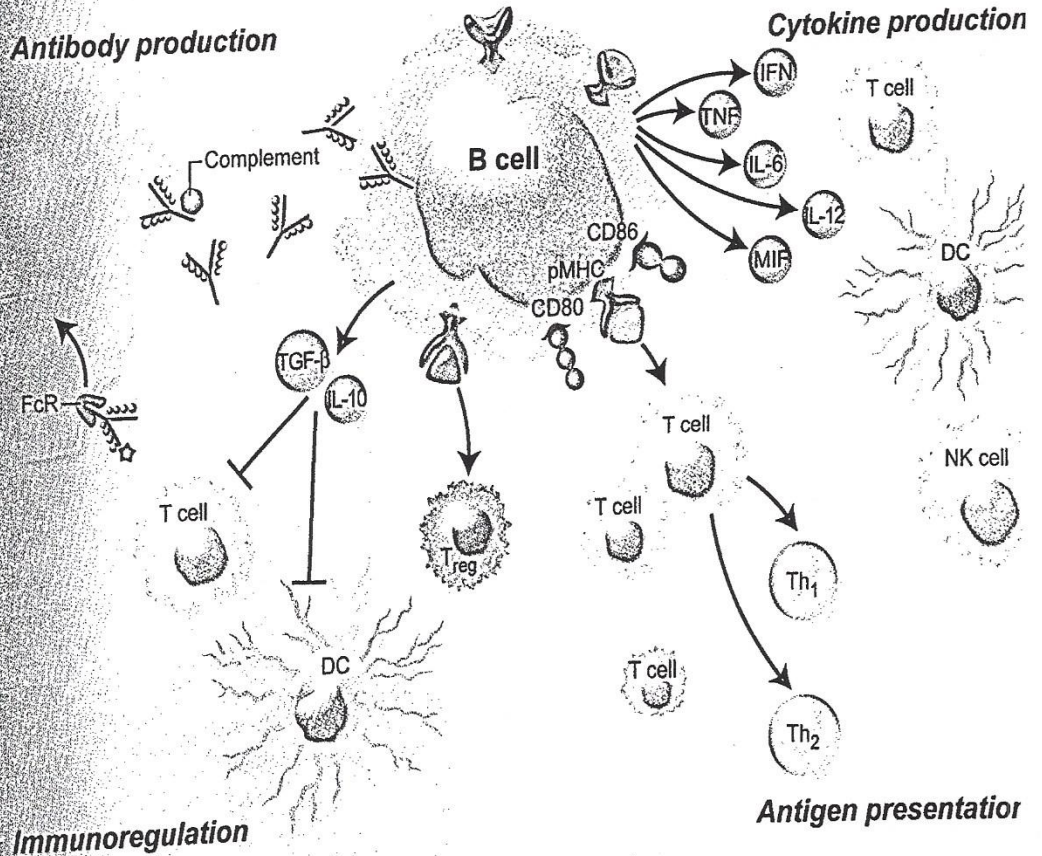
Classification of
amyloidosis by laser
microdissection and
proteomics (p 4957)

Cover:
The role of B cells in
the pathogenesis of
GVHD (p 4919)

www.bloodjournal.org

Antibody production

Cytokine production



Immunoregulation

Antigen presentation



PROPERTY OF THE
NATIONAL
LIBRARY OF
MEDICINE

blood

JOURNAL OF
THE AMERICAN
SOCIETY OF
HEMATOLOGY

Blood, Journal of The American Society of Hematology (print ISSN 0006-4971, online ISSN 1528-0020), is published weekly every Thursday, except for the last week in December, (52 times weekly), plus the ASH annual meeting abstracts in November, by the American Society of Hematology (ASH), 1900 M Street, NW, Suite 200, Washington, DC 20036. Printed in the United States of America. Periodicals postage paid at Washington, DC, and additional mailing offices.

Postmaster: Send change-of-address information to *Blood, Journal of the American Society of Hematology*, Subscription Office, 1900 M Street, NW, Suite 200, Washington, DC 20036.

Canadian regulations: Publications Mail Agreement No: 40038947. Return undeliverable Canadian addresses to: Circulation Dept. or DPGM, 4960-2 Walker Road, Windsor, ON N9A 6J3.

Manuscript submissions

Consult the Author Guide printed in each issue of *Blood* (and posted on the Web site at www.bloodjournal.org) before submitting your manuscript online at <http://submit.bloodjournal.org>.

2009 subscription rates

Institution, Worldwide Online Only: \$1,245 (Tier 2); \$1,355 (Tier 3)

US Institution, Online plus Print: \$1,400 (Tier 2); \$1,510 (Tier 3)

International Institution, Online plus Print: \$1,610 (Tier 2); \$1,720 (Tier 3)

US Individual, Online plus Print: \$840

International Individual, Online plus Print: \$1,050

*All issues shipped via expedited service at no additional charge.

Multiple Site Subscriptions: Contact bloodsubs@hematology.org.

Price for single/back issues: \$37 (US)/\$42 (international). Single issues, both current and back, exist in limited quantities and are offered for sale subject to availability.

Pay-per-view: Full-text online access to all articles is free one year after publication. Nonsubscribers may purchase 24-hour access to the full text of any article published in the preceding 12 months through the pay-per-view option on the *Blood* website.

Subscription information, claims, and changes of address

Customer service for subscribers: 1-866-328-8560 (US and Canada); 1-202-292-0280 (outside US and Canada); fax: 1-202-292-6010; e-mail: bloodsubs@hematology.org. Correspondence regarding subscriptions and changes of address should be addressed to *Blood* Journal Subscription Office, 1900 M Street, NW, Suite 200, Washington, DC 20036. Checks should be made payable to "Blood Subscriptions."

ASH Members should send their change-of-address information to the ASH Membership Department, 1900 M Street, NW, Suite 200, Washington, DC 20036.

All change-of-address notices should be sent at least 6 weeks before the first issue is to be mailed to the new address. Provide both old and new addresses.

Claims: Claims must be submitted within 4 months of the publication date (6 months for international subscribers).

Internet

Blood Home Page: www.bloodjournal.org.

ASH Home Page: www.hematology.org.

Manuscript Submission: submit.bloodjournal.org.

Copyright

Copyright © 2009 by The American Society of Hematology. All rights reserved. No part of this publication may be reproduced (see exception below), stored in a retrieval system, translated, or transmitted in any form or by any means now or hereafter known, electronic or mechanical, without permission in writing from the Publisher, The American Society of Hematology. Address for correspondence: Blood Publishing Office, 1900 M Street, NW, Suite 200, Washington, DC 20036. Important notice: Authors retain certain nonexclusive copyrights. For further information on rights and permissions, see www.bloodjournal.org/misc/rights.shtml.

The copyright owner consents that copies of articles may be made for personal or internal use, or for the personal or internal use of specific clients, for those registered with the Copyright Clearance Center, Inc (222 Rosewood Drive, Danvers, MA 01923; (978) 750-8400; www.copyright.com). This consent is given on the condition that the copier pay the stated per-copy fees through the Copyright Clearance Center, Inc, for copying beyond that permitted by Sections 107 and 108 of the US Copyright Law (Fair Use). This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For those kinds of purposes, permission must be sought from the Publisher (see above).

Advertising representation

To place orders for product advertisements, classifieds, or commercial reprints, contact Kevin Dunn, Cunningham Associates, 180 Old Tappan Road, Old Tappan, NJ 07675. Telephone: 201-767-4170; fax: 201-767-8065; e-mail: kdunn@cunnasso.com.

Disclaimer

The ideas and opinions expressed in *Blood* do not necessarily reflect those of The American Society of Hematology or the Editors of *Blood*. Publication of an advertisement or other product mention in *Blood* should not be construed as an endorsement of the product or the manufacturer's claims. Readers are encouraged to contact the manufacturer with any questions about the features or limitations of the products mentioned. The American Society of Hematology does not assume any responsibility for any injury and/or damage to persons or property arising from or related to any use of the material contained in this periodical. The reader is advised to check the appropriate medical literature and the product information currently provided by the manufacturer of each drug to be administered to verify the dosage, the method and duration of administration, or contraindications. It is the responsibility of the treating physician or other health care professional, relying on his or her independent experience and knowledge of the patient, to determine drug dosages and the best treatment for the patient.

Indexing & abstracting

Blood is indexed and abstracted by Index Medicus, Excerpta Medica, Current Contents/Life Sciences, Current Contents/Clinical Medicine, Science Citation Index, SCISEARCH, Automatic Subject Citation Alert, ISI/BIOMED, and BIOSIS.

The American Society of Hematology
1900 M Street, NW, Suite 200
Washington, DC 20036



COVER LEGEND

B cells are central players of humoral immune responses. After binding to their antigens, humoral antibodies can lead to complement activation, antibody-mediated cellular cytotoxicity, and Fc-mediated endocytosis. Besides producing antibodies, B cells exert several other important antibody-independent functions such as antigen presentation, cytokine production, and immunoregulation. Professional illustration by A. Y. Chen. See the article by Shimabukuro-Vornhagen et al on page 4919.

INSIDE BLOOD

- 4913 **Why some cells are “more equal” than others**
M. Z. Ratajczak and D.-M. Shin
- 4914 **Fine-tuning targeted therapy of CML**
N. P. Shah
- 4915 **Ready to analyze genetically modified human platelets**
M. Gawaz

BLOOD WORK

- 4917 **Blast crisis**
A. Prasad and A. Asija

REVIEW ARTICLE

- 4919 **The role of B cells in the pathogenesis of graft-versus-host disease**
A. Shimabukuro-Vornhagen, M. J. Hallek, R. F. Storb, and M. S. von Bergwelt-Baildon

**CLINICAL TRIALS AND
OBSERVATIONS**

- 4928 **Evidence of serum immunoglobulin abnormalities up to 9.8 years before diagnosis of chronic lymphocytic leukemia: a prospective study**
H.-T. Tsai, N. E. Caporaso, R. A. Kyle, J. A. Katzmann, A. Dispenzieri, R. B. Hayes, G. E. Marti, M. Albitar, P. Ghia, S. V. Rajkumar, and O. Landgren
- 4933 **Nilotinib for the frontline treatment of Ph⁺ chronic myeloid leukemia**
G. Rosti, F. Palandri, F. Castagnetti, M. Breccia, L. Levato, G. Gugliotta, A. Capucci, M. Cedrone, C. Fava, T. Intermesoli, G. Rege Cambrin, F. Stagno, M. Tiribelli, M. Amabile, S. Luatti, A. Poerio, S. Soverini, N. Testoni, G. Martinelli, G. Alimena, F. Pane, G. Saglio, and M. Baccarani, for the GIMEMA CML Working Party
- 4939 **Chronic myeloid leukemia: a prospective comparison of interphase fluorescence in situ hybridization and chromosome banding analysis for the definition of complete cytogenetic response: a study of the GIMEMA CML WP**
N. Testoni, G. Marzocchi, S. Luatti, M. Amabile, C. Baldazzi, M. Stacchini, M. Nanni, G. Rege-Cambrin, E. Giugliano, U. Giussani, E. Abruzzese, S. Kerim, M. G. Grimoldi, A. Gozzetti, B. Crescenzi, C. Carcassi, P. Bernasconi, A. Cuneo, F. Albano, G. Fugazza, A. Zaccaria, G. Martinelli, F. Pane, G. Rosti, and M. Baccarani

- 4944 **Dasatinib treatment of chronic-phase chronic myeloid leukemia: analysis of responses according to preexisting *BCR-ABL* mutations**
M. C. Müller, J. E. Cortes, D.-W. Kim, B. J. Druker, P. Erben, R. Pasquini, S. Branford, T. P. Hughes, J. P. Radich, L. Ploughman, J. Mukhopadhyay, and A. Hochhaus
- 4954 **Brief report Abnormal serum free light chain ratio in patients with multiple myeloma in complete remission has strong association with the presence of oligoclonal bands: implications for stringent complete remission definition**
C. Fernández de Larrea, M. T. Cibeira, M. Elena, J. I. Arostegui, L. Rosiñol, M. Rovira, X. Filella, J. Yagüe, and J. Bladé
- 4957 **Brief report Classification of amyloidosis by laser microdissection and mass spectrometry-based proteomic analysis in clinical biopsy specimens**
J. A. Vrana, J. D. Gamez, B. J. Madden, J. D. Theis, H. R. Bergen III, and A. Dogan

**HEMATOPOIESIS AND
STEM CELLS**

- 4960 **Induction of B-cell development in adult mice reveals the ability of bone marrow to produce B-1a cells**
S. Düber, M. Hafner, M. Krey, S. Lienenklaus, B. Roy, E. Hobeika, M. Reth, T. Buch, A. Waisman, K. Kretschmer, and S. Weiss
- 4968 **Undifferentiated hematopoietic cells are characterized by a genome-wide undermethylation dip around the transcription start site and a hierarchical epigenetic plasticity**
Y. S. Chung, H. J. Kim, T.-M. Kim, S.-H. Hong, K.-R. Kwon, S. An, J.-H. Park, S. Lee, and I.-H. Oh

IMMUNOBIOLOGY

- 4979 **Cell-cell cooperation at the T helper cell/mast cell immunological synapse**
N. Gaudenzio, N. Espagnolle, L. T. Mars, R. Liblau, S. Valitutti, and E. Espinosa
- 4989 **B-cell follicle development remodels the conduit system and allows soluble antigen delivery to follicular dendritic cells**
M. Bajénoff and R. N. Germain
- 4998 **Brief report Appearance of peripheral blood plasma cells and memory B cells in a primary and secondary immune response in humans**
G. Blanchard-Rohner, A. S. Pulickal, C. M. Jol-van der Zijde, M. D. Snape, and A. J. Pollard
- 5003 **Brief report ATG-induced expression of FOXP3 in human CD4⁺ T cells in vitro is associated with T-cell activation and not the induction of FOXP3⁺ T regulatory cells**
R. Broady, J. Yu, and M. K. Levings

**LYMPHOID
NEOPLASIA**

- 5007 **Characterization of a rituximab variant with potent antitumor activity against rituximab-resistant B-cell lymphoma**
B. Li, L. Zhao, H. Guo, C. Wang, X. Zhang, L. Wu, L. Chen, Q. Tong, W. Qian, H. Wang, and Y. Guo

- 5016 **TC-PTP is required for the maintenance of MYC-driven B-cell lymphomas**
R. M. Young, A. Polsky, and Y. Refaeli

**MYELOID
NEOPLASIA**

- 5024 **Cotreatment with panobinostat and JAK2 inhibitor TG101209 attenuates JAK2V617F levels and signaling and exerts synergistic cytotoxic effects against human myeloproliferative neoplastic cells**
Y. Wang, W. Fiskus, D. G. Chong, K. M. Buckley, K. Natarajan, R. Rao, A. Joshi, R. Balusu, S. Koul, J. Chen, A. Savoie, C. Ustun, A. P. Jillella, P. Atadja, R. L. Levine, and K. N. Bhalla
- 5034 **FLT3-ITD up-regulates MCL-1 to promote survival of stem cells in acute myeloid leukemia via FLT3-ITD-specific STAT5 activation**
G. Yoshimoto, T. Miyamoto, S. Jabbarzadeh-Tabrizi, T. Iino, J. L. Rocnik, Y. Kikushige, Y. Mori, T. Shima, H. Iwasaki, K. Takenaka, K. Nagafuji, S.-i. Mizuno, H. Niuro, G. D. Gilliland, and K. Akashi

**PLATELETS AND
THROMBOPOIESIS**

- 5044 **Human platelets produced in nonobese diabetic/severe combined immunodeficient (NOD/SCID) mice upon transplantation of human cord blood CD34⁺ cells are functionally active in an ex vivo flow model of thrombosis**
I. I. Salles, T. Thijs, C. Brunaud, S. F. De Meyer, J. Thys, K. Vanhoorelbeke, and H. Deckmyn

**THROMBOSIS AND
HEMOSTASIS**

- 5052 **Urokinase-type plasminogen activator increases hepatocyte growth factor activity required for skeletal muscle regeneration**
T. H. Sisson, M.-H. Nguyen, B. Yu, M. L. Novak, R. H. Simon, and T. J. Koh

TRANSPLANTATION

- 5062 **Inducing the tryptophan catabolic pathway, indoleamine 2,3-dioxygenase (IDO), for suppression of graft-versus-host disease (GVHD) lethality**
L. K. Jaspersen, C. Bucher, A. Panoskaltis-Mortari, A. L. Mellor, D. H. Munn, and B. R. Blazar
- 5071 **The transfer of adaptive immunity to CMV during hematopoietic stem cell transplantation is dependent on the specificity and phenotype of CMV-specific T cells in the donor**
P. Scheinberg, J. J. Melenhorst, J. M. Brenchley, B. J. Hill, N. F. Hensel, P. K. Chattopadhyay, M. Roederer, L. J. Picker, D. A. Price, A. J. Barrett, and D. C. Douek

VASCULAR BIOLOGY

- 5081 **An impaired transendothelial migration potential of chronic lymphocytic leukemia (CLL) cells can be linked to ephrin-A4 expression**
E. M. Trinidad, M. Ballesteros, J. Zuloaga, A. Zapata, and L. M. Alonso-Colmenar
- 5091 **Pericyte recruitment during vasculogenic tube assembly stimulates endothelial basement membrane matrix formation**
A. N. Stratman, K. M. Malotte, R. D. Mahan, M. J. Davis, and G. E. Davis
- 5102 **Endothelial cell ADAMTS-13 and VWF: production, release, and VWF string cleavage**
N. A. Turner, L. Nolasco, Z. M. Ruggeri, and J. L. Moake

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.