

780/l

# THE JOURNAL OF IMMUNOLOGY

Volume 190 | No. 3 | February 1, 2013



[www.jimmunol.org](http://www.jimmunol.org)

VOL. 190 | NO. 3 | February 1, 2013 | Pages 845–1386

### 845 IN THIS ISSUE

#### PILLARS OF IMMUNOLOGY

- 847 Converging Discoveries: The First Reports of IL-4  
*Robert L. Coffman*
- 849 Pillars Article: T Cell-Derived B Cell Differentiation Factor(s). Effect on the Isotype Switch of Murine B Cells. *J Exp Med.* 1982. 155: 734–748  
*Peter C. Isakson, Ellen Puré, Ellen S. Vitetta, and Peter H. Krammer*
- 864 Pillars Article: Identification of a T Cell-Derived B Cell Growth Factor Distinct from Interleukin 2. *J Exp Med.* 1982. 155: 914–923  
*Maureen Howard, John Farrar, Mary Hilfiker, Barbara Johnson, Kiyoshi Takatsu, Toshiyuki Hamaoka, and William E. Paul*

#### BRIEF REVIEWS

- 875 The Paradoxical Functions of B Cells and Antibodies in Transplantation  
*Marilia I. Cascalho, Brian J. Chen, Mandy Kain, and Jeffrey L. Platt*

#### CUTTING EDGE

- 881 Cutting Edge: IL-6-Dependent Autoimmune Disease: Dendritic Cells as a Sufficient, but Transient, Source  
*Melanie D. Leech, Tom A. Barr, Darryl G. Turner, Sheila Brown, Richard A. O'Connor, David Gray, Richard J. Mellanby, and Stephen M. Anderton*
- 886 Cutting Edge: Type I IFN Drives Emergency Myelopoiesis and Peripheral Myeloid Expansion during Chronic TLR7 Signaling  
*Matthew B. Buechler, Thomas H. Teal, Keith B. Elkon, and Jessica A. Hamerman*

On the cover: De novo-induced expression of the transcriptional autoimmune regulator Aire in purified immature Aire<sup>+</sup> medullary thymic epithelial cells after 6 d of culture in a three-dimensional organotypic coculture (OTC) model in the presence of RANKL. OTCs were labeled with anti-keratin-14 (red) and anti-Aire (green) Abs, as well as with nuclear staining (blue). Pinto, S., K. Schmidt, S. Egle, H.-J. Stark, P. Boukamp, and B. Kyewski. 2013. An organotypic coculture model supporting proliferation and differentiation of medullary thymic epithelial cells and promiscuous gene expression. *J. Immunol.* 190: 1085–1093.

*The Journal of Immunology* (ISSN 0022-1767) is published twice each month by The American Association of Immunologists, Inc., 9650 Rockville Pike, Bethesda, MD 20814-3994, Phone: 301-634-7197, Fax: 301-634-7829. Subscription terms: New subscriptions and renewals begin January 1 and expire one year later (see <http://www.jimmunol.org/subscriptions> for prices and details). A special rate is available to members of The American Association of Immunologists, Inc. (see <http://www.aai.org/membership>). The American Association of Immunologists, Inc., is not responsible for undeliverable issues. Replacement issues can be obtained, if available, at the regular price of single issues (see [http://www.jimmunol.org/pdf/single\\_issue\\_purchase.pdf](http://www.jimmunol.org/pdf/single_issue_purchase.pdf)). Reprints of individual articles are available only from authors. Periodicals postage paid at Bethesda, MD 20814-3994, and at additional mailing offices. Country of origin U.S.A. Printed on acid-free recyclable paper. Postmaster: Send address changes 60 days in advance to *The Journal of Immunology*, Subscription Department, 9650 Rockville Pike, Bethesda, MD 20814-3994. Copyright © 2013 by The American Association of Immunologists, Inc.

- 892 Cutting Edge: Endothelial-Specific Gene Ablation of CD99L2 Impairs Leukocyte Extravasation In Vivo  
*Ruth Seelige, Christiane Natsch, Sigrid März, Ding Jing, Maike Frye, Stefan Butz, and Dietmar Vestweber*

## ALLERGY AND OTHER HYPERSENSITIVITIES

- 897 Aeroallergen Challenge Promotes Dendritic Cell Proliferation in the Airways  
*Tibor Z. Veres, Sabrina Voedisch, Emma Spies, Joono Valtonen, Frauke Prenzler, and Armin Braun*
- 904 Thymic Stromal Lymphopoietin Amplifies the Differentiation of Alternatively Activated Macrophages  
*Hongwei Han, Mark B. Headley, Whitney Xu, Michael R. Comeau, Baohua Zhou, and Steven F. Ziegler*
- 913 Antigen-Specific Regulation of IgE Antibodies by Non-Antigen-Specific  $\gamma\delta$  T Cells  
*Yafei Huang, M. Kemal Aydinoglu, Joshua Loomis, Megan K. MacLeod, Amy S. McKee, Greg Kirchenbaum, Claudia V. Jakubzick, Ross M. Kedl, Deming Sun, Jordan Jacobelli, Rebecca L. O'Brien, and Willi K. Born*

## ANTIGEN RECOGNITION AND RESPONSES

- 922 Lamprey Variable Lymphocyte Receptors Mediate Complement-Dependent Cytotoxicity  
*Fenfang Wu, Liyong Chen, Xin Liu, Huaying Wang, Peng Su, Yinglun Han, Bo Feng, Xu Qiao, Jing Zhao, Ning Ma, Huijie Liu, Zhen Zheng, and Qingwei Li*
- 931 CD8 $^{+}$  TCR Repertoire Formation Is Guided Primarily by the Peptide Component of the Antigenic Complex  
*Dan Koning, Ana I. Costa, Ilka Hoof, John J. Miles, Nening M. Nanlohy, Kristin Ladell, Katherine K. Matthews, Vanessa Venturi, Ingrid M. M. Schellens, Jose A. M. Borghans, Can Kesmir, David A. Price, and Debbie van Baarle*
- 940 Transfer of CD8 $^{+}$  T Cell Memory Using Bcl-2 as a Marker  
*Alexis Dunkle, Ivan Dzhagalov, Claire Gordy, and You-Wen He*
- 948 TLR7 Triggering with Polyuridylic Acid Promotes Cross-Presentation in CD8 $\alpha^{+}$  Conventional Dendritic Cells by Enhancing Antigen Preservation and MHC Class I Antigen Permanence on the Dendritic Cell Surface  
*María I. Crespo, Estefanía R. Zacca, Nicolás G. Núñez, Romina P. Ranocchia, Mariana Maccioni, Belkys A. Maletto, María C. Pistoresi-Palencia, and Gabriel Morón*

## AUTOIMMUNITY

- 961 The B7-Independent Isoform of CTLA-4 Functions To Regulate Autoimmune Diabetes  
*Melanie Stumpf, Xuyu Zhou, and Jeffrey A. Bluestone*

## IMMUNE REGULATION

- 970 Recirculating Memory T Cells Are a Unique Subset of CD4 $^{+}$  T Cells with a Distinct Phenotype and Migratory Pattern  
*Shannon K. Bromley, Sha Yan, Michio Tomura, Osami Kanagawa, and Andrew D. Luster*
- 977 Varicella Zoster-Specific CD4 $^{+}$ Foxp3 $^{+}$  T Cells Accumulate after Cutaneous Antigen Challenge in Humans  
*Milica Vukmanovic-Stejic, Daisy Sandhu, Toni O. Sobande, Elaine Agius, Katie E. Lacy, Natalie Riddell, Sandra Montez, One B. Dintwe, Thomas J. Scriba, Judith Breuer, Janko Nikolich-Zugich, Graham Ogg, Malcolm H. A. Rustin, and Arne N. Akbar*
- 987 Mouse IgM Fc Receptor, FCMR, Promotes B Cell Development and Modulates Antigen-Driven Immune Responses  
*Seung-Chul Choi, Hongsheng Wang, Linjie Tian, Yousuke Murakami, Dong-Mi Shin, Francisco Borrego, Herbert C. Morse, III, and John E. Coligan*
- 997 Deficiency of Annexin A1 in CD4 $^{+}$  T Cells Exacerbates T Cell-Dependent Inflammation  
*Yuan H. Yang, Wuqi Song, James A. Deane, Wenping Kao, Joshua D. Ooi, Devi Ngo, A. Richard Kitching, Eric F. Morand, and Michael J. Hickey*
- 1008 Helios Induces Epigenetic Silencing of *Il2* Gene Expression in Regulatory T Cells  
*Ian Baine, Samik Basu, Rachel Ames, Rani S. Sellers, and Fernando Macian*

- 1017 Aurintricarboxylic Acid Ameliorates Experimental Autoimmune Encephalomyelitis by Blocking Chemokine-Mediated Pathogenic Cell Migration and Infiltration  
*Feifei Zhang, Wei Wei, Hui Chai, and Xin Xie*
- 1026 Mnk1 and 2 Are Dispensable for T Cell Development and Activation but Important for the Pathogenesis of Experimental Autoimmune Encephalomyelitis  
*Balachandra K. Gorenla, Sruti Krishna, Jinwook Shin, Makoto Inoue, Mari L. Shinohara, Jason M. Grayson, Rikiro Fukunaga, and Xiao-Ping Zhong*
- 1038 Chronic Exposure to *Plasmodium falciparum* Is Associated with Phenotypic Evidence of B and T Cell Exhaustion  
*Joseph Illingworth, Noah S. Butler, Sophie Roetynck, Jedida Mwacharo, Susan K. Pierce, Philip Bejon, Peter D. Crompton, Kevin Marsh, and Francis M. Ndungu*
- 1048 Inflammatory Monocytes Are Critical for Induction of a Polysaccharide-Specific Antibody Response to an Intact Bacterium  
*Quanyi Chen and Clifford M. Snapper*
- 1056 Transcription Factors GATA-3 and ROR $\gamma$ t Are Important for Determining the Phenotype of Allergic Airway Inflammation in a Murine Model of Asthma  
*Satoshi Ano, Yuko Morishima, Yukio Ishii, Keigyou Yoh, Yuichi Yageta, Shigeo Ohtsuka, Masashi Matsuyama, Mio Kawaguchi, Satoru Takahashi, and Nobuyuki Hizawa*
- 1066 Intrinsic Role of FoxO3a in the Development of CD8 $^{+}$  T Cell Memory  
*Fanny Tzelepis, Julie Joseph, Elias K. Haddad, Susanne MacLean, Renu Dudani, Fabien Agenes, Stanford L. Peng, Rafick-Pierre Sekaly, and Subash Sad*
- 1076 TNFR2 Is Critical for the Stabilization of the CD4 $^{+}$ Foxp3 $^{+}$  Regulatory T Cell Phenotype in the Inflammatory Environment  
*Xin Chen, Xueqiang Wu, Qiong Zhou, O. M. Zack Howard, Mihai G. Netea, and Joost J. Oppenheim*

## IMMUNE SYSTEM DEVELOPMENT

- 1085 An Organotypic Coculture Model Supporting Proliferation and Differentiation of Medullary Thymic Epithelial Cells and Promiscuous Gene Expression  
*Sheena Pinto, Katrin Schmidt, Stefanie Egle, Hans-Jürgen Stark, Petra Boukamp, and Bruno Kyewski*
- 1094 Focal Adhesion Kinase Regulates the Localization and Retention of Pro-B Cells in Bone Marrow Microenvironments  
*Shin-Young Park, Peter Wolfram, Kimberly Canty, Brendan Harley, César Nombela-Arrieta, Gregory Pivarnik, John Manis, Hilary E. Beggs, and Leslie E. Silberstein*
- 1103 Nck Recruitment to the TCR Required for ZAP70 Activation during Thymic Development  
*Aldo Borroto, Irene Arellano, Elaine P. Dopfer, Marek Prouza, Miloslav Suchánek, Manuel Fuentes, Alberto Orfao, Wolfgang W. Schamel, and Balbino Alarcón*

## IMMUNOTHERAPY AND VACCINES

- 1113 A Synthetic Codon-Optimized Hepatitis C Virus Nonstructural 5A DNA Vaccine Primes Polyfunctional CD8 $^{+}$  T Cell Responses in Wild-Type and NS5A-Transgenic Mice  
*Fredrik Holmström, Anna Pasetto, Veronica Nähr, Anette Brass, Malte Kriegs, Eberhard Hildt, Kate E. Broderick, Margaret Chen, Gustaf Ahlén, and Lars Frelin*
- 1125 Triggering of B7h by the ICOS Modulates Maturation and Migration of Monocyte-Derived Dendritic Cells  
*Sergio Occhipinti, Chiara Dianzani, Annalisa Chiocchetti, Elena Boggio, Nausicaa Clemente, Casimiro Luca Gigliotti, Maria Felicia Soluri, Rosalba Minelli, Roberto Fantozzi, Jungi Yagi, Josè Maria Rojo, Daniele Sblattero, Mirella Giovarelli, and Umberto Dianzani*
- 1135 Assessment of Immune Interference, Antagonism, and Diversion following Human Immunization with Biallelic Blood-Stage Malaria Viral-Vectored Vaccines and Controlled Malaria Infection  
*Sean C. Elias, Katharine A. Collins, Fenella D. Halstead, Prateek Choudhary, Carly M. Bliss, Katie J. Ewer, Susanne H. Sheehy, Christopher J. A. Duncan, Sumi Biswas, Adrian V. S. Hill, and Simon J. Draper*

## INFECTIOUS DISEASE AND HOST RESPONSE

- 1148 Macrophage-Specific TLR2 Signaling Mediates Pathogen-Induced TNF-Dependent Inflammatory Oral Bone Loss  
*George Papadopoulos, Ellen O. Weinberg, Paola Massari, Frank C. Gibson, III, Lee M. Wetzler, Elise F. Morgan, and Caroline A. Genco*
- 1158 Regulatory B Cell (B10 Cell) Expansion during *Listeria* Infection Governs Innate and Cellular Immune Responses in Mice  
*Mayuka Horikawa, Eric T. Weimer, David J. DiLillo, Guglielmo M. Venturi, Rosanne Spolski, Warren J. Leonard, Mark T. Heise, and Thomas F. Tedder*
- 1169 CD70 Deficiency Impairs Effector CD8 T Cell Generation and Viral Clearance but Is Dispensable for the Recall Response to Lymphocytic Choriomeningitis Virus  
*Ivana Munitic, Mirela Kuka, Atef Allam, Jonathan P. Scoville, and Jonathan D. Ashwell*
- 1180 Pro-Apoptotic Protein Noxa Regulates Memory T Cell Population Size and Protects against Lethal Immunopathology  
*Felix M. Wensveen, Paul L. Klarenbeek, Klaas P. J. M. van Gisbergen, Maria F. Pascutti, Ingrid A. M. Derkx, Barbera D. C. van Schaik, Anja ten Brinke, Niek de Vries, Durdica Cekinović, Stipan Jonjić, René A. W. van Lier, and Eric Eldering*
- 1192 Biphasic RLR-IFN- $\beta$  Response Controls the Balance between Antiviral Immunity and Cell Damage  
*Sun-Young Hwang, Kye-Yeon Hur, Jeong-Rae Kim, Kwang-Hyun Cho, Seung-Hwan Kim, and Joo-Yeon Yoo*
- 1201 *Salmonella* Downregulates Nod-like Receptor Family CARD Domain Containing Protein 4 Expression To Promote Its Survival in B Cells by Preventing Inflammasome Activation and Cell Death  
*Araceli Perez-Lopez, Roberto Rosales-Reyes, Celia Mercedes Alpuche-Aranda, and Vianney Ortiz-Navarrete*
- 1210 Micro-RNA 155 Is Required for Optimal CD8 $^+$  T Cell Responses to Acute Viral and Intracellular Bacterial Challenges  
*Evan F. Lind, Alisha R. Elford, and Pamela S. Ohashi*

## INNATE IMMUNITY AND INFLAMMATION

- 1217 Neutrophil Extracellular Trap-Associated Protein Activation of the NLRP3 Inflammasome Is Enhanced in Lupus Macrophages  
*J. Michelle Kahlenberg, Carmelo Carmona-Rivera, Carolyne K. Smith, and Mariana J. Kaplan*
- 1227 Rescue of Dysfunctional Autophagy Attenuates Hyperinflammatory Responses from Cystic Fibrosis Cells  
*Matthew L. Mayer, Christoph J. Blohmke, Reza Falsafi, Chris D. Fjell, Laurence Madera, Stuart E. Turvey, and Robert E. W. Hancock*
- 1239 Inflammasome-Independent NLRP3 Augments TGF- $\beta$  Signaling in Kidney Epithelium  
*Wenjie Wang, Xiangyu Wang, Justin Chun, Akosua Vilaysane, Sharon Clark, Gabrielle French, Nathan A. Bracey, Kiril Trpkov, Shirin Bonni, Henry J. Duff, Paul L. Beck, and Daniel A. Muruve*
- 1250 Regulation of TLR2-Mediated Tolerance and Cross-Tolerance through IRAK4 Modulation by miR-132 and miR-212  
*Md A. Nahid, Bing Yao, Paul R. Dominguez-Gutierrez, Lakshmyya Kesavulu, Minoru Satoh, and Edward K. L. Chan*
- 1264 Endothelial MKK3 Is a Critical Mediator of Lethal Murine Endotoxemia and Acute Lung Injury  
*Praveen Mannam, Xuchen Zhang, Peiying Shan, Yi Zhang, Amanda S. Shinn, Yitao Zhang, and Patty J. Lee*
- 1276 Flagellin Induces Myeloid-Derived Suppressor Cells: Implications for *Pseudomonas aeruginosa* Infection in Cystic Fibrosis Lung Disease  
*Nikolaius Rieber, Alina Brand, Andreas Hector, Ute Graepler-Mainka, Michael Ost, Iris Schäfer, Irene Wecker, Davide Neri, Andreas Wirth, Lauren Mays, Sabine Zundel, Jörg Fuchs, Rupert Handgretinger, Martin Stern, Michael Hogardt, Gerd Döring, Joachim Riethmüller, Michael Kormann, and Dominik Hartl*
- 1285 TLR4 Activation Under Lipotoxic Conditions Leads to Synergistic Macrophage Cell Death through a TRIF-Dependent Pathway  
*Joel D. Schilling, Heather M. Machkovech, Li He, Abhinav Diwan, and Jean E. Schaffer*

- 1297 Regulation of DNA Methylation in Rheumatoid Arthritis Synoviocytes  
*Kazuhisa Nakano, David L. Boyle, and Gary S. Firestein*

## MOLECULAR AND STRUCTURAL IMMUNOLOGY

- 1304 The Crystal Structure of Human Soluble CD14 Reveals a Bent Solenoid with a Hydrophobic Amino-Terminal Pocket  
*Stacy L. Kelley, Tiiit Lukk, Satish K. Nair, and Richard I. Tapping*
- 1312 Dynein Light Chain LC8 Inhibits Osteoclast Differentiation and Prevents Bone Loss in Mice  
*Hyeryeon Kim, Seungha Hyeon, Hojin Kim, Yoohee Yang, Ji Young Hub, Doo Ri Park, Hyojung Lee, Dong-Hyun Seo, Han-Sung Kim, Soo Young Lee, and Woojin Jeong*
- 1319 Identification of SERPINB1 As a Physiological Inhibitor of Human Granzyme H  
*Li Wang, Qian Li, Lianfeng Wu, Shengwu Liu, Yong Zhang, Xuan Yang, Pingping Zhu, Honglian Zhang, Kai Zhang, Jizhong Lou, Pingsheng Liu, Liang Tong, Fei Sun, and Zusen Fan*

## MUCOSAL IMMUNOLOGY

- 1331 Functional Characterization of T Cell Populations in a Mouse Model of Chronic Obstructive Pulmonary Disease  
*Bryan L. Eppert, Brian W. Wortham, Jennifer L. Flury, and Michael T. Borchers*

## TRANSPLANTATION

- 1341 Granzyme B-Mediated Damage of CD8<sup>+</sup> T Cells Impairs Graft-versus-Tumor Effect  
*Guanglin Bian, Xilai Ding, Nicholas D. Leigh, Youzhou Tang, Maegan L. Capitano, Jingxin Qiu, Philip L. McCarthy, Hong Liu, and Xuefang Cao*
- 1351 Graft-versus-Host Disease Impairs Vaccine Responses through Decreased CD4<sup>+</sup> and CD8<sup>+</sup> T Cell Proliferation and Increased Perforin-Mediated CD8<sup>+</sup> T Cell Apoptosis  
*Christian M. Capitini, Nicole M. Nasholm, Brynn B. Duncan, Martin Guimond, and Terry J. Fry*

## TUMOR IMMUNOLOGY

- 1360 Heat Shock Protein 90 Is Critical for Regulation of Phenotype and Functional Activity of Human T Lymphocytes and NK Cells  
*Jooeun Bae, Aditya Munshi, Cheng Li, Mehmet Samur, Rao Prabhala, Constantine Mitsiades, Kenneth C. Anderson, and Nikhil C. Munshi*
- 1372 The Receptor for Advanced Glycation End Products Promotes Pancreatic Carcinogenesis and Accumulation of Myeloid-Derived Suppressor Cells  
*Philip J. Vernon, Tara J. Loux, Nicole E. Schapiro, Rui Kang, Ravi Muthuswamy, Pawel Kalinski, Daolin Tang, Michael T. Lotze, and Herbert J. Zeh, III*

## CORRECTIONS

- 1380 Correction: GPR105 Ablation Prevents Inflammation and Improves Insulin Sensitivity in Mice with Diet-Induced Obesity  
*Jianfeng Xu, Hidetaka Morinaga, Dayoung Oh, Pingping Li, Ai Chen, Saswata Talukdar, Eduardo Lazarowski, Jerrold M. Olefsky, and Jane J. Kim*
- 1381 Correction: Cutting Edge: FcγRIII (CD16) and FcγRI (CD64) Are Responsible for Anti-Glycoprotein 75 Monoclonal Antibody TA99 Therapy for Experimental Metastatic B16 Melanoma  
*Marcello Albanesi, David A. Mancardi, Lynn E. Macdonald, Bruno Iannascoli, Laurence Zitvogel, Andrew J. Murphy, Jeanette H. Leusen, and Pierre Bruhns*
- 1382 Correction: Novel Role for Surfactant Protein A in Gastrointestinal Graft-versus-Host Disease  
*Kymberly M. Gowdy, Diana M. Cardona, Julia L. Nugent, Charles Giamberardino, Joseph M. Thomas, Sambudho Mukherjee, Tereza Martinu, W. Michael Foster, Scott E. Plevy, Amy M. Pastva, Jo Rae Wright, and Scott M. Palmer*

1383 Correction: Antibody Repertoire Development in Fetal and Neonatal Piglets. XI. The Relationship of Variable Heavy Chain Gene Usage and the Genomic Organization of the Variable Heavy Chain Locus  
*Tomoko Eguchi-Ogawa, Nancy Wertz, Xiu-Zhu Sun, Francois Puimi, Hirohide Uenishi, Kevin Wells, Patrick Chardon, Gregory J. Tobin, and John E. Butler*

1384 AUTHOR INDEX