



## Reporter Cell Lines

The family keeps growing

[Learn more >](#)

InvivoGen



The Journal of  
**Immunology**

**192 (1)**

*J Immunol* 2014; 192:1-535; ;  
<http://www.jimmunol.org/content/192/1>

This information is current as  
of April 18, 2019.

### Why *The JI*? [Submit online.](#)

- **Rapid Reviews! 30 days\*** from submission to initial decision
- **No Triage!** Every submission reviewed by practicing scientists
- **Fast Publication!** 4 weeks from acceptance to publication

*\*average*

**Subscription** Information about subscribing to *The Journal of Immunology* is online at:  
<http://jimmunol.org/subscription>

**Permissions** Submit copyright permission requests at:  
<http://www.aai.org/About/Publications/JI/copyright.html>

**Email Alerts** Receive free email-alerts when new articles cite this article. Sign up at:  
<http://jimmunol.org/alerts>

*The Journal of Immunology* is published twice each month by  
The American Association of Immunologists, Inc.,  
1451 Rockville Pike, Suite 650, Rockville, MD 20852  
All rights reserved.  
Print ISSN: 0022-1767 Online ISSN: 1550-6606.



## IN THIS ISSUE

- 1 **Etoposide Topples Autoimmune T Cells** *See article p. 73*  
**The Other Side of TGF- $\beta$**  *See article p. 103*  
**TRAF5 Keeps TABs on TLR Signaling** *See article p. 145*  
**Heterozygous Harm to Hematopoiesis** *See article p. 160*  
**Challenging the Canonical CD8<sup>+</sup> Antitumor Response** *See article p. 224*  
**Influenza Gives Pentraxin the Slip** *See article p. 271*

## PILLARS OF IMMUNOLOGY

- 3 A Methods Paper That Led to Much More  
*Derry Roopenian*
- 5 Pillars Article: Methods for the Study of Histocompatibility Genes. *J. Genet.* 1948. 49: 87–108  
*G. D. Snell*

## BRIEF REVIEWS

- 27 Infection-Induced Changes in Hematopoiesis  
*Arielle Glatman Zaretsky, Julie B. Engiles, and Christopher A. Hunter*

## CUTTING EDGE

- 35 Cutting Edge: Expression of Fc $\gamma$ RIIB Tempers Memory CD8 T Cell Function In Vivo  
*Gabriel R. Starbeck-Miller, Vladimir P. Badovinac, Daniel L. Barber, and John T. Harty*

## ALLERGY AND OTHER HYPERSENSITIVITIES

- 41 Munc18-2 and Syntaxin 3 Control Distinct Essential Steps in Mast Cell Degranulation  
*Cristiana Brochetta, Ryo Suzuki, Francesca Vita, Maria Rosa Soranzo, Julien Claver, Lydia Celia Madjene, Tarik Attout, Joana Vitte, Nadine Varin-Blank, Giuliano Zabucchi, Juan Rivera, and Ulrich Blank*

On the cover: CD4 T cells (red) targeting amyloid- $\beta$  (A $\beta$ ) plaques (blue) in the brain of a mouse model of Alzheimer's disease. A $\beta$ -reactive Th1 CD4 T cells were injected into the lateral ventricle of the brain and are shown within the brain parenchyma colocalized with MHCII-expressing cells (green) at sites of A $\beta$  plaques. Fisher, Y., I. Strominger, S. Biton, A. Nemirovsky, R. Baron, and A. Monsonogo. 2014. Th1 polarization of T cells injected into the cerebrospinal fluid induces brain immunosurveillance. *J. Immunol.* 192: 92–102.

*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.

## ANTIGEN RECOGNITION AND RESPONSES

- 52 Cognate Peptide–MHC Complexes Are Expressed as Tightly Apposed Nanoclusters in Virus-Infected Cells To Allow TCR Crosslinking  
*María Ferez, Mario Castro, Balbino Alarcon, and Hisse M. van Santen*

## AUTOIMMUNITY

- 59 Therapeutic Efficacy of Suppressing the JAK/STAT Pathway in Multiple Models of Experimental Autoimmune Encephalomyelitis  
*Yudong Liu, Andrew T. Holdbrooks, Patrizia De Sarno, Amber L. Rowse, Lora L. Yanagisawa, Braden C. McFarland, Laurie E. Harrington, Chander Raman, Steffanie Sabbaj, Ety N. Benveniste, and Hongwei Qin*
- 73 Eliminating Encephalitogenic T Cells without Undermining Protective Immunity  
*Jonathan P. McNally, Eileen E. Elfers, Catherine E. Terrell, Eli Grunblatt, David A. Hildeman, Michael B. Jordan, and Jonathan D. Katz*

## CLINICAL AND HUMAN IMMUNOLOGY

- 84 Etoposide Selectively Ablates Activated T Cells To Control the Immunoregulatory Disorder Hemophagocytic Lymphohistiocytosis  
*Theodore S. Johnson, Catherine E. Terrell, Scott H. Millen, Jonathan D. Katz, David A. Hildeman, and Michael B. Jordan*
- 92 Th1 Polarization of T Cells Injected into the Cerebrospinal Fluid Induces Brain Immunosurveillance  
*Yair Fisher, Itai Strominger, Shva Biton, Anna Nemirovsky, Rona Baron, and Alon Monsonego*

## IMMUNE REGULATION

- 103 TGF- $\beta$  Promotes Immune Responses in the Presence of Mesenchymal Stem Cells  
*Chunliang Xu, Pengfei Yu, Xiaoyan Han, Liming Du, Jianhe Gan, Ying Wang, and Yufang Shi*
- 110 Calcium Signaling via Orai1 Is Essential for Induction of the Nuclear Orphan Receptor Pathway To Drive Th17 Differentiation  
*Kyun-Do Kim, Sonal Srikanth, Yossan-Var Tan, Ma-Khin Yee, Marcus Jew, Robert Damoiseaux, Michael E. Jung, Saki Shimizu, Dong Sung An, Bernard Ribalet, James A. Waschek, and Yousang Gwack*
- 123 Qualitatively Different T Cell Phenotypic Responses to IL-2 versus IL-15 Are Unified by Identical Dependences on Receptor Signal Strength and Duration  
*Abhinav Arneja, Hannah Johnson, Laura Gabrovsek, Douglas A. Lauffenburger, and Forest M. White*
- 136 Leptin Metabolically Licenses T Cells for Activation To Link Nutrition and Immunity  
*Donte C. Saucillo, Valerie A. Gerriets, John Sheng, Jeffrey C. Rathmell, and Nancie J. MacIver*
- 145 TRAF5 Negatively Regulates TLR Signaling in B Lymphocytes  
*Claire M. Buchta and Gail A. Bishop*
- 151 Two Separate Defects Affecting True Naive or Virtual Memory T Cell Precursors Combine To Reduce Naive T Cell Responses with Aging  
*Kristin R. Renkema, Gang Li, Angela Wu, Megan J. Smithy, and Janko Nikolich-Zugich*

## IMMUNE SYSTEM DEVELOPMENT

- 160 Cell-Intrinsic In Vivo Requirement for the E47–p21 Pathway in Long-Term Hematopoietic Stem Cells  
*Patricia M. Santos, Ying Ding, and Lisa Borghesi*
- 169 A Novel T Cell Subset with *Trans*-Rearranged V $\gamma$ -C $\beta$  TCRs Shows V $\beta$  Expression Is Dispensable for Lineage Choice and MHC Restriction  
*Steven Bowen, Peter Sun, Ferenc Livak, Susan Sharrow, and Richard J. Hodes*
- 178 The Transcription Factor E74-like Factor 4 Suppresses Differentiation of Proliferating CD4<sup>+</sup> T Cells to the Th17 Lineage  
*Ping-Hsien Lee, Monica Puppi, Kimberly S. Schluns, Li-Yuan Yu-Lee, Chen Dong, and H. Daniel Lacorazza*

## IMMUNOGENETICS

- 189 Polymorphisms in the CD1d Promoter That Regulate CD1d Gene Expression Are Associated with Impaired NKT Cell Development  
*Zachary D. Borg, Patrick J. Benoit, Graham W. J. Lilley, Idil Aktan, Alan Chant, Victoria L. DeVault, Mercedes Rincon, and Jonathan E. Boyson*

## IMMUNOTHERAPY AND VACCINES

- 200 Inflammation and TCR Signal Strength Determine the Breadth of the T Cell Response in a Bim-Dependent Manner  
*Dietmar Zehn, Sarah Roepke, Kristin Weakly, Michael J. Bevan, and Martin Prlic*
- 206 Immunotherapy with TCR-Redirected T Cells: Comparison of TCR-Transduced and TCR-Engineered Hematopoietic Stem Cell-Derived T Cells  
*Lilian Stärck, Katja Popp, Hanspeter Pircher, and Wolfgang Uckert*
- 214 Immunization with a Recombinant Bacillus Calmette–Guérin Strain Confers Protective Th1 Immunity against the Human Metapneumovirus  
*Christian E. Palavecino, Pablo F. Céspedes, Roberto S. Gómez, Alexis M. Kalergis, and Susan M. Bueno*
- 224 CD8<sup>+</sup> T Cell-Independent Tumor Regression Induced by Fc-OX40L and Therapeutic Vaccination in a Mouse Model of Glioma  
*Katherine A. Murphy, Jami R. Erickson, Charles S. Johnson, Charles E. Seiler, Jessica Bedi, Peisheng Hu, G. Elizabeth Pluhar, Alan L. Epstein, and John R. Ohlfest*

## INFECTIOUS DISEASE AND HOST RESPONSE

- 234 The Pore-Forming Toxin Listeriolysin O Is Degraded by Neutrophil Metalloproteinase-8 and Fails To Mediate *Listeria monocytogenes* Intracellular Survival in Neutrophils  
*Eusondia Arnett, Stephen Vadia, Colleen C. Nackerman, Steve Oghumu, Abhay R. Satoskar, Kenneth R. McLeish, Silvia M. Uriarte, and Stephanie Seveau*
- 245 Neutralization of *Plasmodium falciparum* Merozoites by Antibodies against PfRH5  
*Alexander D. Douglas, Andrew R. Williams, Ellen Knuepfer, Joseph J. Illingworth, Julie M. Furze, Cécile Crosnier, Prateek Choudhary, Leyla Y. Bustamante, Sara E. Zakutansky, Dennis K. Awuah, Daniel G. W. Alanine, Michel Theron, Andrew Worth, Richard Shimkets, Julian C. Rayner, Anthony A. Holder, Gavin J. Wright, and Simon J. Draper*
- 259 Altered IFN- $\gamma$ -Mediated Immunity and Transcriptional Expression Patterns in *N*-Ethyl-*N*-Nitrosourea-Induced STAT4 Mutants Confer Susceptibility to Acute Typhoid-like Disease  
*Megan M. Eva, Kyoko E. Yuki, Shauna M. Dauphinee, Jeremy A. Schwartztruber, Michal Pyzik, Marilène Paquet, Mark Lathrop, Jacek Majewski, Silvia M. Vidal, and Danielle Malo*
- 271 A Single Amino Acid Substitution in the Hemagglutinin of H3N2 Subtype Influenza A Viruses Is Associated with Resistance to the Long Pentraxin PTX3 and Enhanced Virulence in Mice  
*Emma R. Job, Barbara Bottazzi, Kirsty R. Short, Yi-Mo Deng, Alberto Mantovani, Andrew G. Brooks, and Patrick C. Reading*
- 282 MyD88 Signaling Regulates Both Host Defense and Immunopathogenesis during *Pneumocystis* Infection  
*Sheila N. Bello-Irizarry, Jing Wang, Carl J. Johnston, Francis Gigliotti, and Terry W. Wright*
- 293 Targeting CD137 Enhances Vaccine-Elicited Anti-Respiratory Syncytial Virus CD8<sup>+</sup> T Cell Responses in Aged Mice  
*Sujin Lee, Robert S. Mittler, and Martin L. Moore*
- 300 The Role of NOD2 in Murine and Human Melioidosis  
*Nicolle D. Myers, Narisara Chantratita, William R. Berrington, Wirongrong Chierakul, Direk Limmathuwotsakul, Vanaporn Wuthiekanun, Johanna D. Robertson, H. Denny Liggitt, Sharon J. Peacock, Shawn J. Skerrett, and T. Eoin West*
- 308 Anti-HIV Antibody-Dependent Activation of NK Cells Impairs NKp46 Expression  
*Matthew S. Parsons, Chi-Chang Tang, Sinthujan Jegaskanda, Robert J. Center, Andrew G. Brooks, Ivan Stratov, and Stephen J. Kent*

- 316 *Helicobacter pylori* Cytotoxin-Associated Gene A Impairs Human Dendritic Cell Maturation and Function through IL-10–Mediated Activation of STAT3  
*Romy Kaebisch, Raquel Mejías-Luque, Christian Prinz, and Markus Gerhard*

## INNATE IMMUNITY AND INFLAMMATION

- 324  $\beta_2$  Integrin–Mediated Crawling on Endothelial ICAM-1 and ICAM-2 Is a Prerequisite for Transcellular Neutrophil Diapedesis across the Inflamed Blood–Brain Barrier  
*Roser Gorina, Ruth Lyck, Dietmar Vestweber, and Britta Engelhardt*
- 338 Thrombin-Induced CCAAT/Enhancer-Binding Protein  $\beta$  Activation and IL-8/CXCL8 Expression via MEKK1, ERK, and p90 Ribosomal S6 Kinase 1 in Lung Epithelial Cells  
*Chien-Huang Lin, Po-Ling Nai, Mauo-Ying Bien, Chung-Chi Yu, and Bing-Chang Chen*
- 349 IL-6–Mediated Induction of Matrix Metalloproteinase-9 Is Modulated by JAK-Dependent IL-10 Expression in Macrophages  
*Poonam Kothari, Roberto Pestana, Rim Mesraoua, Rim Elchaki, K. M. Faisal Khan, Andrew J. Dannenberg, and Domenick J. Falcone*
- 358 The p53 Transcription Factor Modulates Microglia Behavior through MicroRNA-Dependent Regulation of c-Maf  
*Wei Su, Stephanie Hopkins, Nicole K. Nesser, Bryce Sopher, Aurelio Silvestroni, Simon Ammanuel, Suman Jayadev, Thomas Möller, Jonathan Weinstein, and Gwenn A. Garden*
- 367 Lidocaine Reduces Neutrophil Recruitment by Abolishing Chemokine-Induced Arrest and Transendothelial Migration in Septic Patients  
*Christian Berger, Jan Rossaint, Hugo Van Aken, Martin Westphal, Klaus Habnenkamp, and Alexander Zarbock*
- 377 Soluble gC1qR Is an Autocrine Signal That Induces B1R Expression on Endothelial Cells  
*Berhane Ghebrehiwet, Yan Ji, Alisa Valentino, Lina Pednekar, Mahalakshmi Ramadass, David Habié, Richard R. Kew, Kinga H. Hosszu, Dennis K. Galanakis, Uday Kishore, and Ellinor I. B. Peerschke*
- 385 Slit2–Robo4 Pathway Modulates Lipopolysaccharide-Induced Endothelial Inflammation and Its Expression Is Dysregulated during Endotoxemia  
*Helong Zhao, Appakkudal R. Anand, and Ramesh K. Ganju*
- 394 Akt2 Deficiency Protects from Acute Lung Injury via Alternative Macrophage Activation and miR-146a Induction in Mice  
*Eleni Vergadi, Katerina Vaporidi, Emmanuel E. Theodorakis, Christina Doxaki, Eleni Lagoudaki, Eleftheria Ieronymaki, Vassilia I. Alexaki, Mike Helms, Eumorfia Kondili, Birte Soennichsen, Efsthathios N. Stathopoulos, Andrew N. Margioris, Dimitrios Georgopoulos, and Christos Tsatsanis*
- 407 A Circadian Clock Gene, Rev-erb $\alpha$ , Modulates the Inflammatory Function of Macrophages through the Negative Regulation of *Ccl2* Expression  
*Shogo Sato, Takuya Sakurai, Junetsu Ogasawara, Motoko Takahashi, Tetsuya Izawa, Kazuhiko Imaizumi, Naoyuki Taniguchi, Hideki Ohno, and Takako Kizaki*
- 418 The Response of Secondary Genes to Lipopolysaccharides in Macrophages Depends on Histone Deacetylase and Phosphorylation of C/EBP $\beta$   
*Neus Serrat, Carlos Sebastian, Selma Pereira-Lopes, Lorena Valverde-Estrella, Jorge Lloberas, and Antonio Celada*
- 427 Identification of a Unique Hybrid Macrophage-Polarization State following Recovery from Lipopolysaccharide Tolerance  
*Christine O’Carroll, Ailís Fagan, Fergus Shanahan, and Ruaidhrí J. Carmody*
- 437 Platelet-Secreted MicroRNA-223 Promotes Endothelial Cell Apoptosis Induced by Advanced Glycation End Products via Targeting the Insulin-like Growth Factor 1 Receptor  
*Yi Pan, Hongwei Liang, Huan Liu, Donghai Li, Xi Chen, Limin Li, Chen-Yu Zhang, and Ke Zen*
- 447 “Activated” STAT Proteins: A Paradoxical Consequence of Inhibited JAK-STAT Signaling in Cytomegalovirus-Infected Cells  
*Mirko Trilling, Vu Thuy Khanh Le, Jassin Rashidi-Alavijeh, Benjamin Katschinski, Jürgen Scheller, Stefan Rose-John, Gabriela Elena Androsiac, Stipan Jonjić, Valeria Poli, Klaus Pfeffer, and Hartmut Hengel*

- 459 Oposing Immunomodulatory Roles of Prostaglandin D<sub>2</sub> during the Progression of Skin Inflammation  
*Hana Sarashina, Yoshiki Tsubosaka, Keisuke Omori, Kosuke Aritake, Takayuki Nakagawa, Masatoshi Hori, Hiroyuki Hirai, Masataka Nakamura, Shuh Narumiya, Yoshihiro Urade, Hiroshi Ozaki, and Takahisa Murata*

## MOLECULAR AND STRUCTURAL IMMUNOLOGY

- 466 Demethylation of the Human Eotaxin-3 Gene Promoter Leads to the Elevated Expression of Eotaxin-3  
*Eunjin Lim and Marc E. Rothenberg*
- 475 TGF- $\beta$ -Mediated *Foxp3* Gene Expression Is Cooperatively Regulated by Stat5, Creb, and AP-1 through CNS2  
*Chihiro Ogawa, Yukiko Tone, Masato Tsuda, Christian Peter, Herman Waldmann, and Masahide Tone*

## MUCOSAL IMMUNOLOGY

- 484 T Lymphocyte-Dependent and -Independent Regulation of *Cxcl8* Expression in Zebrafish Intestines  
*Sylvia Brugman, Merlijn Witte, Rianne C. Scholman, Mark R. Klein, Marianne Boes, and Edward E. S. Nieuwenhuis*
- 492 MPYS/STING-Mediated TNF- $\alpha$ , Not Type I IFN, Is Essential for the Mucosal Adjuvant Activity of (3'-5')-Cyclic-Di-Guanosine-Monophosphate In Vivo  
*Steven M. Blaauboer, Vincent D. Gabrielle, and Lei Jin*

## TRANSPLANTATION

- 503 Expansion of CMV-Mediated NKG2C<sup>+</sup> NK Cells Associates with the Development of Specific De Novo Malignancies in Liver-Transplanted Patients  
*Abla Achour, Florence Baychelier, Caroline Besson, Armelle Arnoux, Michel Marty, Laurent Hannoun, Didier Samuel, Patrice Debré, Vincent Vieillard, and the K-GREF Study Group*

## TUMOR IMMUNOLOGY

- 512 Macrophages Are More Potent Immune Suppressors Ex Vivo Than Immature Myeloid-Derived Suppressor Cells Induced by Metastatic Murine Mammary Carcinomas  
*Melisa J. Hamilton, Momir Bosiljcic, Nancy E. LePard, Elizabeth C. Halvorsen, Victor W. Ho, Judit P. Banáth, Gerald Krystal, and Kevin L. Bennewith*
- 523 Cancer-Initiating Cells from Colorectal Cancer Patients Escape from T Cell-Mediated Immunosurveillance In Vitro through Membrane-Bound IL-4  
*Andrea Volonté, Tiziano Di Tomaso, Michela Spinelli, Matilde Todaro, Francesca Sanvito, Luca Albarello, Massimiliano Bissolati, Luca Ghirardelli, Elena Orsenigo, Soldano Ferrone, Claudio Doglioni, Giorgio Stassi, Paolo Dellabona, Carlo Staudacher, Giorgio Parmiani, and Cristina Maccalli*

## CORRECTIONS

- 533 Correction: Cutting Edge: Influence of *Tmevpg1*, a Long Intergenic Noncoding RNA, on the Expression of *Ifng* by Th1 Cells  
*Sarah P. Collier, Patrick L. Collins, Christopher L. Williams, Mark R. Boothby, and Thomas M. Aune*
- 534 Correction: Shaping of Human Germline IgH Repertoires Revealed by Deep Sequencing  
*Kevin Larimore, Michael W. McCormick, Harlan S. Robins, and Philip D. Greenberg*
- 535 Correction: Secondary Immunization Generates Clonally Related Antigen-Specific Plasma Cells and Memory B Cells  
*Daniela Frölich, Claudia Giesecke, Henrik E. Mei, Karin Reiter, Capucine Daridon, Peter E. Lipsky, and Thomas Dörner*

## 536 AUTHOR INDEX

## 538 INFORMATION FOR AUTHORS