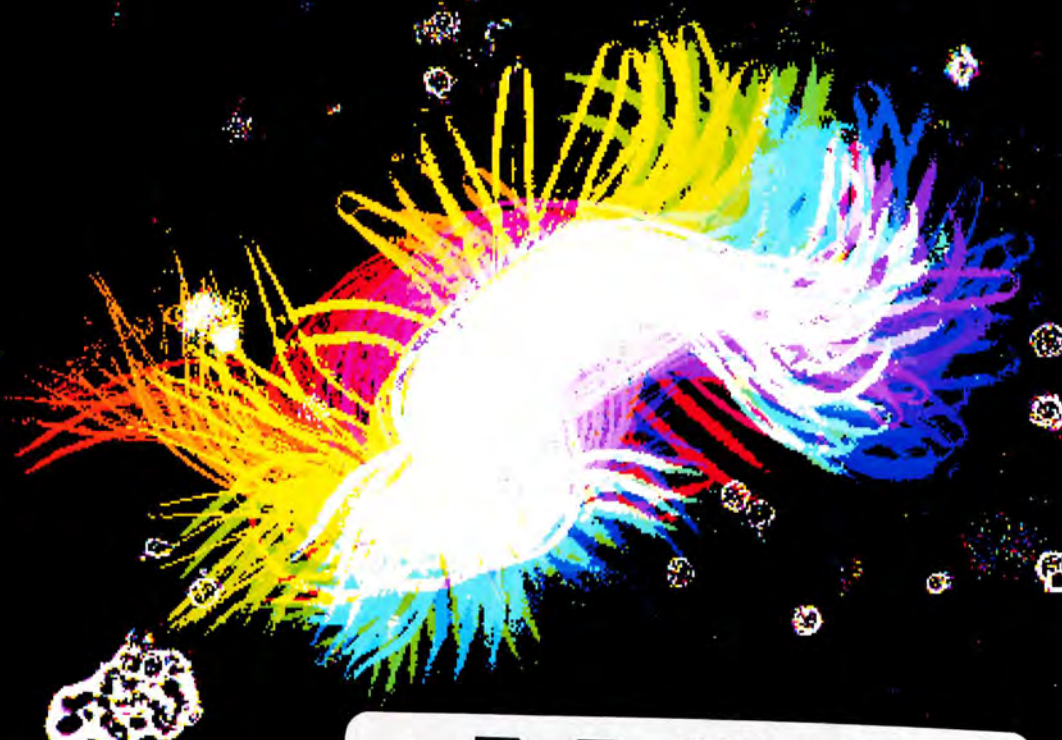


Journal of immunology.  
v. 194, no. 3 (Feb. 1 2015)  
General Collection  
W1 JO677  
2015-01-26 08:27:53



# Journal of Immunology

VOLUME 194, NUMBER 3 • FEBRUARY 1, 2015 • WWW.JIMMUNOL.ORG



3



PROPERTY OF THE  
NATIONAL  
LIBRARY OF  
MEDICINE

Genome & Co. v. Univ. of Chicago  
PGR2019-00002  
UNIV. CHICAGO EX. 2021

**DOCKET**  
**ALARM**

Find authenticated court documents without watermarks at [docketalarm.com](http://docketalarm.com).



## IN THIS ISSUE

- 845 **Driving CARs over the Threshold** *See article p. 911*  
**Finding Friends for AIRE** *See article p. 921*  
**Thymocyte Peer Pressure** *See article p. 1057*  
**One More Reason To Take Your Vitamins** *See article p. 1090*  
**The Skin-ny on Secondary Lymphoid Organs in Transplantation** *See article p. 1364*

## PILLARS OF IMMUNOLOGY

- 847 Laying Bare the Nude Mouse Gene  
*Graham Anderson and Nicholas I. McCarthy*
- 849 Pillars Article: New Member of the Winged-Helix Protein Family Disrupted In Mouse And Rat Nude Mutations. *Nature*. 1994. 372: 103–107  
*Michael Nehls, Dietmar Pfeifer, Michael Schorpp, Hans Hedrich, and Thomas Boehm*

## BRIEF REVIEWS

- 855 The Acute Respiratory Distress Syndrome: From Mechanism to Translation  
*SeungHye Han and Rama K. Mallampalli*

## CUTTING EDGE

- 863 Cutting Edge: Maresin-1 Engages Regulatory T Cells To Limit Type 2 Innate Lymphoid Cell Activation and Promote Resolution of Lung Inflammation  
*Nandini Krishnamoorthy, Patrick R. Burkett, Jesmond Dalli, Raja-Elie E. Abdunour, Romain Colas, Sesquile Ramon, Richard P. Phipps, Nicos A. Petasis, Vijay K. Kuchroo, Charles N. Serhan, and Bruce D. Levy*
- 868 Cutting Edge: Critical Role for C5aRs in the Development of Septic Lymphopenia in Mice  
*Jamison J. Grailler, Fatemeh Fattahi, Rachel S. Dick, Firas S. Zetoune, and Peter A. Ward*
- 873 Cutting Edge: AIM2 and Endosomal TLRs Differentially Regulate Arthritis and Autoantibody Production in DNase II-Deficient Mice  
*Rebecca Baum, Shruti Sharma, Susan Carpenter, Quan-Zhen Li, Patricia Busto, Katherine A. Fitzgerald, Ann Marsbak-Rothstein, and Ellen M. Gravallese*

On the cover: Motility of the infective larval stage of the intestinal helminth *Heligmosomoides polygyrus bakeri* shown in temporal color code (120 frames, 60 seconds). Esser-von Bieren, J., B. Volpe, M. Kulagin, D. B. Sutherland, R. Guiet, A. Seitz, B. J. Marsland, J. S. Verbeek, and N. L. Harris. 2015. Antibody-mediated trapping of helminth larvae requires CD11b and Fcγ receptor I. *J. Immunol.* 194: 1154–1163.

*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. © 2015 by The American Association of Immunologists, Inc.



- 878 Cutting Edge: Epigenetic Regulation of *Foxp3* Defines a Stable Population of CD4<sup>+</sup> Regulatory T Cells in Tumors from Mice and Humans  
*Jeremy D. Waigh, Shinji Takai, Bo Marelli, Guozhong Qin, Kenneth W. Hance, Dong Zhang, Robert Tighe, Yan Lan, Kin-Ming Lo, Helen Sabzevari, Robert Hofmeister, and Nicholas S. Wilson*
- 883 Cutting Edge: Progesterone Directly Upregulates Vitamin D Receptor Gene Expression for Efficient Regulation of T Cells by Calcitriol  
*Shankar Thangamani, Myughoon Kim, Youngmin Son, Xinxin Huang, Heejoo Kim, Jee H. Lee, Jungyoon Cho, Benjamin Ulrich, Hal E. Broxmeyer, and Chang H. Kim*

## ALLERGY AND OTHER HYPERSENSITIVITIES

- 887 IL-10 and Regulatory T Cells Cooperate in Allergen-Specific Immunotherapy To Ameliorate Allergic Asthma  
*Livia Böhm, Joachim Maxeiner, Helen Meyer-Martin, Sebastian Reuter, Susetta Finotto, Matthias Klein, Hansjörg Schild, Edgar Schmitt, Tobias Bopp, and Christian Taube*

## ANTIGEN RECOGNITION AND RESPONSES

- 898 Fixed Expression of Single Influenza Virus-Specific TCR Chains Demonstrates the Capacity for TCR  $\alpha$ - and  $\beta$ -Chain Diversity in the Face of Peptide-MHC Class I Specificity  
*E. Bridie Clemens, Peter C. Doherty, Nicole L. La Gruta, and Stephen J. Turner*
- 911 Target Antigen Density Governs the Efficacy of Anti-CD20-CD28-CD3  $\zeta$  Chimeric Antigen Receptor-Modified Effector CD8<sup>+</sup> T Cells  
*Keisuke Watanabe, Seitaro Terakura, Anton C. Martens, Tom van Meerten, Susumu Uchiyama, Misa Imai, Reona Sakemura, Tatsunori Goto, Ryo Hanajiri, Nobuhiko Imahashi, Kazuyuki Shimada, Akihiro Tomita, Hitoshi Kiyoi, Tetsuya Nishida, Tomoki Naoe, and Makoto Murata*

## AUTOIMMUNITY

- 921 Homeodomain-Interacting Protein Kinase 2, a Novel Autoimmune Regulator Interaction Partner, Modulates Promiscuous Gene Expression in Medullary Thymic Epithelial Cells  
*Kristin Rattay, Janine Claude, Esmail Rezavandy, Sonja Matt, Thomas G. Hofmann, Bruno Kyewski, and Jens Derbinski*

## CLINICAL AND HUMAN IMMUNOLOGY

- 929 The V Gene Repertoires of Classical and Atypical Memory B Cells in Malaria-Susceptible West African Children  
*Severin Zinöcker, Christine E. Schindler, Jeff Skinner, Tobias Rogosch, Michael Waisberg, Jean-Nicolas Schickel, Eric Meffre, Kassoum Kayentao, Aissata Ongoïba, Boubaacar Traoré, and Susan K. Pierce*
- 940 Differential Expression of the Transcription Factor ARID3a in Lupus Patient Hematopoietic Progenitor Cells  
*Michelle L. Ratliff, Julie M. Ward, Joan T. Merrill, Judith A. James, and Carol F. Webb*
- 950 Combination Therapy with Anti-CTLA-4 and Anti-PD-1 Leads to Distinct Immunologic Changes In Vivo  
*Rituparna Das, Rakesh Verma, Mario Sznol, Chandra Sekhar Boddupalli, Scott N. Gettinger, Harriet Kluger, Margaret Callahan, Jedd D. Wolchok, Ruth Halaban, Madhav V. Dhodapkar, and Kavita M. Dhodapkar*
- 960 CD26-Mediated Induction of EGR2 and IL-10 as Potential Regulatory Mechanism for CD26 Costimulatory Pathway  
*Ryo Hatano, Kei Ohmura, Haruna Otsuka, Eriko Koiniya, Izumi Taki, Satoshi Iwata, Nam H. Dang, Ko Okumura, and Chikao Morimoto*
- 973 Sterile DJ<sub>H</sub> Rearrangements Reveal that Distance Between Gene Segments on the Human Ig H Chain Locus Influences Their Ability To Rearrange



## IMMUNE REGULATION

- 983 Immune Complexes Suppress IFN- $\gamma$ -Induced Responses in Monocytes by Activating Discrete Members of the SRC Kinase Family  
*Gunther H. Boekhoudt, Anna G. McGrath, Jennifer F. A. Swisher, and Gerald M. Feldman*
- 990 Modulating DNA Methylation in Activated CD8<sup>+</sup> T Cells Inhibits Regulatory T Cell-Induced Binding of Foxp3 to the CD8<sup>+</sup> T Cell IL-2 Promoter  
*Michelle M. Miller, Nnenna Akaronu, Elizabeth M. Thompson, Sylvia F. Hood, and Jonathan E. Fogle*
- 999 Effector T Cells Boost Regulatory T Cell Expansion by IL-2, TNF, OX40, and Plasmacytoid Dendritic Cells Depending on the Immune Context  
*Audrey Bacyens, David Saadoun, Fabienne Billiard, Angéline Rouers, Sylvie Grégoire, Bruno Zaragoza, Yenkel Grinberg-Bleyer, Gilles Marodon, Eliane Piaggio, and Benoît L. Salomon*
- 1011 Intestinal Helminths Regulate Lethal Acute Graft-versus-Host Disease and Preserve the Graft-versus-Tumor Effect in Mice  
*Yue Li, Hung-Lin Chen, Nadine Bannick, Michael Henry, Adrian N. Holm, Ahmed Metwali, Joseph F. Urban, Jr., Paul B. Rothman, George J. Weiner, Bruce R. Blazar, David E. Elliott, and M. Nedim Ince*
- 1021 Chronic Morphine-Induced MicroRNA-124 Promotes Microglial Immunosuppression by Modulating P65 and TRAF6  
*Shuwei Qiu, Yimin Feng, Gene LeSage, Ying Zhang, Charles Stuart, Lei He, Yi Li, Yi Caudle, Ying Peng, and Deling Yin*
- 1031 Survival of Human Circulating Antigen-Induced Plasma Cells Is Supported by Plasma Cell-Niche Cytokines and T Follicular Helper Lymphocytes  
*Ana Ramos-Amaya, Beatriz Rodríguez-Bayona, Rubén López-Blanco, Eloisa Andújar, Mónica Pérez-Alegre, Antonio Campos-Caro, and José A. Brieva*
- 1039 Temporal Expression of Growth Factors Triggered by Epiregulin Regulates Inflammation Development  
*Masaya Harada, Daisuke Kamimura, Yasunobu Arima, Hitoshi Kobsaka, Yuji Nakatsuji, Makoto Nishida, Toru Atsumi, Jie Meng, Hidenori Bando, Rajeev Singh, Lavannya Sabharwal, Jing-Jing Jiang, Noriko Kumai, Nobuyuki Miyasaka, Saburo Sakoda, Keiko Yamauchi-Takahara, Hideki Ogura, Toshio Hirano, and Masaaki Murakami*
- 1047 CD40L Induces Functional Tunneling Nanotube Networks Exclusively in Dendritic Cells Programmed by Mediators of Type 1 Immunity  
*Colleen R. Zaccard, Simon C. Watkins, Pawel Kalinski, Ronald J. Fecek, Aarika L. Yates, Russell D. Salter, Velpandi Ayyavoo, Charles R. Rinaldo, and Robbie B. Mailliard*

## IMMUNE SYSTEM DEVELOPMENT

- 1057 Stable Interactions and Sustained TCR Signaling Characterize Thymocyte-Thymocyte Interactions that Support Negative Selection  
*Heather J. Melichar, Jenny O. Ross, Kayleigh T. Taylor, and Ellen A. Robey*

## IMMUNOGENETICS

- 1062 The Human IL-23 Receptor rs11209026 A Allele Promotes the Expression of a Soluble IL-23R-Encoding mRNA Species  
*Raymond Y. Yu, Jonathan Brazaitis, and Grant Gallagher*

## IMMUNOTHERAPY AND VACCINES

- 1069 Induction of Potent CD8 T Cell Cytotoxicity by Specific Targeting of Antigen to Cross-Presenting Dendritic Cells In Vivo via Murine or Human XCR1  
*Evelyn Hartung, Martina Becker, Annabell Bachem, Nele Reeg, Anika Jäkel, Andreas Hutloff, Harald Weber, Christoph Weis, Claudia Giesecke, Volker Henn, Stephanie Gurka, Konstantinos Anastasiadis, Hans W. Mages, and Richard A. Kroczeck*
- 1080 CD8 T Cell Tolerance to a Tumor-Associated Self-Antigen Is Reversed by CD4 T Cells Engineered To Express the Same T Cell Receptor  
*Sara Ghorashian, Pedro Velica, Jenatius Chua, Anne-Marie McNicol, Ben Carpenter, Angelika Holler, Emma Nicholson*



## INFECTIOUS DISEASE AND HOST RESPONSE

- 1090 The  $\alpha$ -Tocopherol Form of Vitamin E Reverses Age-Associated Susceptibility to *Streptococcus pneumoniae* Lung Infection by Modulating Pulmonary Neutrophil Recruitment  
*Elsa N. Bou Ghanem, Stacie Clark, Xiaogang Du, Dayong Wu, Andrew Camilli, John M. Leong, and Simin N. Meydani*
- 1100 A Major Role for Myeloid-Derived Suppressor Cells and a Minor Role for Regulatory T Cells in Immunosuppression during *Staphylococcus aureus* Infection  
*Christina Tebartz, Sarah Anita Horst, Tim Sparwasser, Jochen Huehn, Andreas Beineke, Georg Peters, and Eva Medina*
- 1112 Atg7 Enhances Host Defense against Infection via Downregulation of Superoxide but Upregulation of Nitric Oxide  
*Xuefeng Li, Yan Ye, Xikun Zhou, Canhua Huang, and Min Wu*
- 1122 IRAK4 as a Molecular Target in the Amelioration of Innate Immunity-Related Endotoxic Shock and Acute Liver Injury by Chlorogenic Acid  
*Sun Hong Park, Seung-Il Baek, Jieun Yun, Seungmin Lee, Da Young Yoon, Jae-Kyung Jung, Sang-Hun Jung, Bang Yeon Hwang, Jin Tae Hong, Sang-Bae Han, and Youngsoo Kim*
- 1131 Diverse Roles for T-bet in the Effector Responses Required for Resistance to Infection  
*Gretchen Harms Pritchard, Aisling O'Hara Hall, David A. Christian, Sagie Wagage, Qun Fang, Gaia Muallem, Beena John, Arielle Glatman Zaretsky, William G. Dunn, Jacqueline Perrigoue, Steven L. Reiner, and Christopher A. Hunter*
- 1141 CD8<sup>+</sup> T Cells Complement Antibodies in Protecting against Yellow Fever Virus  
*Maria R. Bassi, Michael Kongsgaard, Maria A. Steffensen, Christina Fenger, Michael Rasmussen, Karsten Skjodt, Bente Finsen, Anette Stryhn, Soren Buus, Jan P. Christensen, and Allan R. Thomsen*
- 1154 Antibody-Mediated Trapping of Helminth Larvae Requires CD11b and Fc $\gamma$  Receptor I  
*Julia Esser-von Bieren, Beatrice Volpe, Manuel Kulagin, Duncan B. Sutherland, Romain Guiet, Arne Seitz, Benjamin J. Marsland, J. Sjeff Verbeek, and Nicola L. Harris*
- 1164 Complement Component C5 Recruits Neutrophils in the Absence of C3 during Respiratory Infection with Modified Vaccinia Virus Ankara  
*Philip J. R. Price, Zoltán Bánki, Angelika Scheideler, Heribert Stoiber, Admar Verschoor, Gerd Sutter, and Michael H. Lehmann*

## INNATE IMMUNITY AND INFLAMMATION

- 1169 TRIF-Dependent Innate Immune Activation Is Critical for Survival to Neonatal Gram-Negative Sepsis  
*Alex G. Cuenca, Dallas N. Joiner, Lori F. Gentile, Angela L. Cuenca, James L. Wynn, Kindra M. Kelly-Scumpia, Philip O. Scumpia, Kevin E. Behrns, Philip A. Efron, Dina Nacionales, Chao Lui, Shannon M. Wallet, Westley H. Reeves, Clayton E. Mathews, and Lyle L. Moldawer*
- 1178 Radiation Exposure Induces Inflammasome Pathway Activation in Immune Cells  
*Veit M. Stoecklein, Akinori Osuka, Shizu Ishikawa, Madeline R. Lederer, Lorenz Wanke-Jellinek, and James A. Lederer*
- 1190 TLR2 Modulates Antibodies Required for Intestinal Ischemia/Reperfusion-Induced Damage and Inflammation  
*Michael R. Pope and Sherry D. Fleming*
- 1199 A Second Stimulus Required for Enhanced Antifungal Activity of Human Neutrophils in Blood Is Provided by Anaphylatoxin C5a  
*Kerstin Hünninger, Kristin Bieber, Ronny Martin, Teresa Lehnert, Marc Thilo Figge, Jürgen Löffler, Ren-Feng Guo, Niels C. Riedemann, and Oliver Kurzai*
- 1211 Neutrophil Priming Occurs in a Sequential Manner and Can Be Visualized in Living Animals by Monitoring IL-1 $\beta$  Promoter Activation  
*Yi Yao, Hironori Matsushima, Jennifer A. Ohtola, Shuo Geng, Ran Lu, and Akira Takashima*
- 1225 Zebrafish IRF1 Regulates IFN Antiviral Response through Binding to IFN $\phi$ 1 and IFN $\phi$ 3 Promoters Downstream of MvD88 Signaling

# 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.