



The Journal of **Immunology**

VOLUME 193, NUMBER 2 • JULY 15, 2014 • WWW.JIMMUNOL.ORG

IN THIS ISSUE

- 465 **Migration May Matter in MS** See articles p. 555 and 564
Fibroblasts Modulate Macrophages See article p. 597
T Cells Taxi with Autotaxin See article p. 617
CD70 Modulates MCMV Responses See article p. 871
ERAPs Enhance Epitopes See article p. 901
Editing Ets1 Expression See article p. 909

LETTERS TO THE EDITOR

- 467 Comment on “Tim-3 Directly Enhances CD8 T Cell Responses to Acute *Listeria monocytogenes* Infection”
Vijay K. Kuchroo, Ana C. Anderson, and Gordon J. Freeman
- 467 Response to Comment on “Tim-3 Directly Enhances CD8 T Cell Responses to Acute *Listeria monocytogenes* Infection”
Jacob V. Gorman and John D. Colgan

BRIEF REVIEWS

- 469 Influenza-Specific Antibody-Dependent Cellular Cytotoxicity: Toward a Universal Influenza Vaccine
Sinthujan Jegaskanda, Patrick C. Reading, and Stephen J. Kent

ALLERGY AND OTHER HYPERSENSITIVITIES

- 477 Elevated Levels of Mast Cells Are Involved in Pruritus Associated with Polycythemia Vera in JAK2V617F Transgenic Mice
Xi Jin, Wanke Zhao, Annet Kirabo, Sung O. Park, Wanting T. Ho, Peter P. Sayeski, and Zhizhuang J. Zhao
- 485 The Wnt/ β -Catenin Pathway Attenuates Experimental Allergic Airway Disease
Sebastian Reuter, Helen Martin, Hendrik Beckert, Matthias Bros, Evelyn Montermann, Christina Belz, Anke Heinz, Svetlana Ohngemach, Ugur Sabin, Michael Stassen, Roland Buhl, Leonid Eshkind, and Christian Taube

On the cover: The digital image shows a tangential section of a colon biopsy from a patient with ulcerative colitis. The section was immunohistochemically stained for one of the prostaglandin D₂ receptors, chemoattractant receptor homologous molecule expressed on Th2 cells (CRTH2; brown), and counterstained with hematoxylin. Abundant staining can be seen in the inflammatory infiltrates and epithelial cells of the crypts. Sturm, E. M., B. Radnai, K. Jandl, A. Stančić, G. P. Parzmair, C. Högenauer, P. Kump, H. Wenzl, W. Petritsch, T. R. Pieber, R. Schuligoi, G. Marsche, N. Ferreira, A. Heinemann, and R. Schicho. 2014. Opposing roles of prostaglandin D₂ receptors in ulcerative colitis. *J. Immunol.* 193: 827–839.

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). 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 © 2014 by The American Association of Immunologists, Inc.

496 GM-CSF–Licensed CD11b⁺ Lung Dendritic Cells Orchestrate Th2 Immunity to *Blomia tropicalis*
Qian Zhou, Adrian W. S. Ho, Andreas Schlitzer, Yafang Tang, Kenneth H. S. Wong, Fiona H. S. Wong, Yen Leong Chua, Veronique Angeli, Alessandra Mortellaro, Florent Ginhoux, and David M. Kemeny

510 High Proportion of CD5⁺ B Cells in Infants Predicts Development of Allergic Disease
Anna-Carin Lundell, Susanne Johansen, Ingegerd Adlerberth, Agnes E. Wold, Bill Hesselmar, and Anna Rudin

ANTIGEN RECOGNITION AND RESPONSES

519 Real-Time Detection of CTL Function Reveals Distinct Patterns of Caspase Activation Mediated by Fas versus Granzyme B
Jinzhu Li, Sarah K. Figueira, Alexandra C. A. Vrazo, Brock F. Binkowski, Braeden L. Butler, Yasuhiro Tabata, Alexandra Filipovich, Michael B. Jordan, and Kimberly A. Risma

529 B Cells Regulate CD4⁺ T Cell Responses to Papain following B Cell Receptor–Independent Papain Uptake
Daniel F. Dwyer, Matthew C. Woodruff, Michael C. Carroll, K. Frank Austen, and Michael F. Gurish

AUTOIMMUNITY

540 IL-17 Promotes Murine Lupus
Gil Amarilho, Elaine V. Lourenço, Fu-Dong Shi, and Antonio La Cava

544 Inhibition of PI3K δ Reduces Kidney Infiltration by Macrophages and Ameliorates Systemic Lupus in the Mouse
Abel Suárez-Fueyo, José M. Rojas, Ariel E. Cariaga, Esther García, Bart H. Steiner, Domingo F. Barber, Kamal D. Puri, and Ana C. Carrera

555 Cytokine-Regulated Neutrophil Recruitment Is Required for Brain but Not Spinal Cord Inflammation during Experimental Autoimmune Encephalomyelitis
Sarah B. Simmons, Denny Liggitt, and Joan M. Goverman

564 Site-Specific Chemokine Expression Regulates Central Nervous System Inflammation and Determines Clinical Phenotype in Autoimmune Encephalomyelitis
Joshua S. Stoolman, Patrick C. Duncker, Amanda K. Huber, and Benjamin M. Segal

571 TCR Affinity and Tolerance Mechanisms Converge To Shape T Cell Diabetogenic Potential
Maria Bettini, Lori Blanchfield, Ashley Castellaw, Qianxia Zhang, Maki Nakayama, Matthew P. Smeltzer, Hui Zhang, Kristin A. Hogquist, Brian D. Evavold, and Dario A. A. Vignali

CLINICAL AND HUMAN IMMUNOLOGY

580 Rituximab Efficiently Depletes Increased CD20-Expressing T Cells in Multiple Sclerosis Patients
Arumugam Palanichamy, Sarah Jahn, Dorothee Nickles, Mia Derstine, Aya Abounasr, Stephen L. Hauser, Sergio E. Baranzini, David Leppert, and H.-Christian von Büdingen

587 Humanized Mice as a Model for Aberrant Responses in Human T Cell Immunotherapy
Nalini K. Vudattu, Frank Waldron-Lynch, Lucy A. Truman, Songyan Deng, Paula Preston-Hurlburt, Richard Torres, Maurice T. Raycroft, Mark J. Mamula, and Kevan C. Herold

IMMUNE REGULATION

597 Adventitial Fibroblasts Induce a Distinct Proinflammatory/Profibrotic Macrophage Phenotype in Pulmonary Hypertension
Karim C. El Kasmi, Steven C. Pugliese, Suzette R. Riddle, Jens M. Poth, Aimee L. Anderson, Maria G. Frid, Min Li, Soni S. Pullamsetti, Rajkumar Savai, Maria A. Nagel, Mehdi A. Fini, Brian B. Graham, Rubin M. Tuder, Jacob E. Friedman, Holger K. Eltzschig, Ronald J. Sokol, and Kurt R. Stenmark

610 Human NKG2E Is Expressed and Forms an Intracytoplasmic Complex with CD94 and DAP12
Gerasim A. Orbelyan, Fangning Tang, Benjamin Sally, Jason Solus, Bertrand Meresse, Cezary Ciszewski, Jean-Christophe Grenier, Luis B. Barreiro, Lewis L. Lanier, and Bana Jabri

- 617 Autotaxin Produced by Stromal Cells Promotes LFA-1–Independent and Rho-Dependent Interstitial T Cell Motility in the Lymph Node Paracortex
Tomoya Katakai, Naoyuki Kondo, Yoshihiro Ueda, and Tatsuo Kinashi
- 627 Targeting of TLRs Inhibits CD4⁺ Regulatory T Cell Function and Activates Lymphocytes in Human Peripheral Blood Mononuclear Cells
Kui Shin Voo, Laura Bover, Megan Lundell Harline, Jinsheng Weng, Naoshi Sugimoto, and Yong-Jun Liu
- 635 gp49B-Mediated Negative Regulation of Antibody Production by Memory and Marginal Zone B Cells
Saori Fukao, Kei Haniuda, Takuya Nojima, Toshiyuki Takai, and Daisuke Kitamura
- 645 Human Th2 but Not Th9 Cells Release IL-31 in a STAT6/NF- κ B–Dependent Way
Elisabeth Maier, Dagmar Werner, Albert Duschl, Barbara Bohle, and Jutta Horejs-Hoeck
- 655 Regulatory T Cells Restrain CD4⁺ T Cells from Causing Unregulated Immune Activation and Hypersensitivity to Lipopolysaccharide Challenge
Emeka B. Okeke, Ifeoma Okwor, and Jude E. Uzonna

IMMUNE SYSTEM DEVELOPMENT

- 663 Id1 Expression Promotes T Regulatory Cell Differentiation by Facilitating TCR Costimulation
Chen Liu, Hong-Cheng Wang, Sen Yu, Rong Jin, Hui Tang, Yuan-Feng Liu, Qing Ge, Xiao-Hong Sun, and Yu Zhang
- 673 Innate PLZF⁺CD4⁺ $\alpha\beta$ T Cells Develop and Expand in the Absence of Itk
Amanda L. Prince, Levi B. Watkin, Catherine C. Yin, Liisa K. Selin, Joonsoo Kang, Pamela L. Schwartzberg, and Leslie J. Berg
- 688 Development of Innate CD4⁺ and CD8⁺ T Cells in Itk-Deficient Mice Is Regulated by Distinct Pathways
Amanda L. Prince, Zachary Kraus, Shannon A. Carty, Caleb Ng, Catherine C. Yin, Martha S. Jordan, Pamela L. Schwartzberg, and Leslie J. Berg
- 700 Themis2 Is Not Required for B Cell Development, Activation, and Antibody Responses
Harald Hartweiger, Edina Schweighoffer, Sophia Davidson, Matthew J. Peirce, Andreas Wack, and Victor L. J. Tybulewicz

IMMUNOTHERAPY AND VACCINES

- 708 Metabolic Engineering of *Salmonella* Vaccine Bacteria To Boost Human V γ 2V δ 2 T Cell Immunity
Grefachew Workalemahu, Hong Wang, Kia-Joo Puan, Mohanad H. Nada, Tomohisa Kuzuyama, Bradley D. Jones, Chenggang Jin, and Craig T. Morita
- 722 CD40 Ligand Preferentially Modulates Immune Response and Enhances Protection against Influenza Virus
Anwar M. Hashem, Caroline Gravel, Ze Chen, Yinglei Yi, Monika Tocchi, Bozena Jaentschke, Xingliang Fan, Changgui Li, Michael Rosu-Myles, Alexander Pereboev, Runtao He, Junzhi Wang, and Xuguang Li
- 735 Autologous Tumor Vaccine Modified with Recombinant New Castle Disease Virus Expressing IL-7 Promotes Antitumor Immune Response
Lixiang Zhao, Yu Mei, Qing Sun, Linghua Guo, Yan Wu, Xiao Yu, Bo Hu, Xiufan Liu, and Haiyan Liu
- 746 Acute and Chronic B Cell Depletion Disrupts CD4⁺ and CD8⁺ T Cell Homeostasis and Expansion during Acute Viral Infection in Mice
Jacquelyn M. Lykken, David J. DiLillo, Eric T. Weimer, Susanne Roser-Page, Mark T. Heise, Jason M. Grayson, M. Neale Weitzmann, and Thomas F. Tedder

INFECTIOUS DISEASE AND HOST RESPONSE

- 757 Immune Memory–Boosting Dose of Rapamycin Impairs Macrophage Vesicle Acidification and Curtails Glycolysis in Effector CD8 Cells, Impairing Defense against Acute Infections
Emily L. Goldberg, Megan J. Smithey, Lydia K. Lutes, Jennifer L. Uhrlaub, and Janko Nikolich-Zugich

- 764 Macrophage Migration Inhibitory Factor Promotes Clearance of Pneumococcal Colonization
Rituparna Das, Meredith I. LaRose, Christopher B. Hergott, Lin Leng, Richard Bucala, and Jeffrey N. Weiser
- 773 The Peritrophic Matrix Mediates Differential Infection Outcomes in the Tsetse Fly Gut following Challenge with Commensal, Pathogenic, and Parasitic Microbes
Brian L. Weiss, Amy F. Savage, Bridget C. Griffith, Yineng Wu, and Serap Aksoy
- 783 Ficolin-2 Inhibits Hepatitis C Virus Infection, whereas Apolipoprotein E3 Mediates Viral Immune Escape
Yinglan Zhao, Yushan Ren, Xuping Zhang, Ping Zhao, Wanyin Tao, Jin Zhong, Qiao Li, and Xiao-Lian Zhang
- 797 Early Lymphoid Responses and Germinal Center Formation Correlate with Lower Viral Load Set Points and Better Prognosis of Simian Immunodeficiency Virus Infection
Jung Joo Hong, Praveen K. Amancha, Kenneth A. Rogers, Cynthia L. Courtney, Colin Havenar-Daughton, Shane Crotty, Aftab A. Ansari, and Francois Villinger
- 807 Tryptophan Catabolism Restricts IFN- γ -Expressing Neutrophils and *Clostridium difficile* Immunopathology
Mohamad El-Zaatari, Yu-Ming Chang, Min Zhang, Matthew Franz, Andrew Shreiner, Andrew J. McDermott, Koenraad F. van der Sluijs, René Lutter, Helmut Grasberger, Nobuhiko Kamada, Vincent B. Young, Gary B. Huffnagle, and John Y. Kao
- 817 Adrenocortical Scavenger Receptor Class B Type I Deficiency Exacerbates Endotoxic Shock and Precipitates Sepsis-Induced Mortality in Mice
Sophie Gilbert, Lauriane Galle-Treger, Martine Moreau, Flora Saint-Charles, Sara Costa, Raphaëlle Ballaire, Philippe Couvert, Alain Carrié, Philippe Lesnik, and Thierry Huby

INNATE IMMUNITY AND INFLAMMATION

- 827 Opposing Roles of Prostaglandin D₂ Receptors in Ulcerative Colitis
Eva M. Sturm, Balazs Radnai, Katharina Jandl, Angela Stančić, Gerald P. Parzmair, Christoph Högenauer, Patrizia Kump, Heimo Wenzl, Wolfgang Petritsch, Thomas R. Pieber, Rufina Schuligoi, Gunther Marsche, Nerea Ferreira, Akos Heinemann, and Rudolf Schicho
- 840 DOK3 Is Required for IFN- β Production by Enabling TRAF3/TBK1 Complex Formation and IRF3 Activation
Susana Soo-Yeon Kim, Koon-Guan Lee, Ching-Siang Chin, Say-Kong Ng, Natasha Ann Pereira, Shengli Xu, and Kong-Peng Lam
- 849 GM-CSF but Not IL-17 Is Critical for the Development of Severe Interstitial Lung Disease in SKG Mice
Aoi Shiomi, Takashi Usui, Yuki Ishikawa, Masakazu Shimizu, Kosaku Murakami, and Tsuneyo Mimori
- 860 PILR α Negatively Regulates Mouse Inflammatory Arthritis
Yonglian Sun, Patrick Caplazi, Juan Zhang, Anita Mazloom, Sarah Kummerfeld, Gabriel Quinones, Kate Senger, Justin Lesch, Ivan Peng, Andrew Sebrell, Wilman Luk, Yanmei Lu, Zhonghua Lin, Kai Barck, Judy Young, Mariela Del Rio, Sophie Lehar, Vida Asghari, WeiYu Lin, Sanjeev Mariathasan, Jason DeVoss, Shahram Misaghi, Mercedesz Balazs, Tao Sai, Benjamin Haley, Philip E. Hass, Min Xu, Wenjun Ouyang, Flavius Martin, Wyne P. Lee, and Ali A. Zarrin
- 871 Dual Function of CD70 in Viral Infection: Modulator of Early Cytokine Responses and Activator of Adaptive Responses
Atef Allam, Melissa Swiecki, William Vermi, Jonathan D. Ashwell, and Marco Colonna
- 879 Cellular Stress Amplifies TLR3/4-Induced CXCL1/2 Gene Transcription in Mononuclear Phagocytes via RIPK1
Chenyang Zhao, Paul G. Pavicic, Jr., Shyamasree Datta, Dongxu Sun, Michael Novotny, and Thomas A. Hamilton

MOLECULAR AND STRUCTURAL IMMUNOLOGY

- 889 Investigation of Soluble and Transmembrane CTLA-4 Isoforms in Serum and Microvesicles
Laura Esposito, Kara M. D. Hunter, Jan Clark, Daniel B. Rainbow, Helen Stevens, Jennifer Denesha, Simon Duley, Sarah Dawson, Gillian Coleman, Sarah Nutland, Gwynneth L. Bell, Carla Moran, Marcin Pekalski, John A. Todd, and Linda S. Wicker

- 901 ERAP1–ERAP2 Dimerization Increases Peptide-Trimming Efficiency
Irini Evmouchidou, Mirjana Weimershaus, Loredana Saveanu, and Peter van Endert
- 909 A Balance between B Cell Receptor and Inhibitory Receptor Signaling Controls Plasma Cell Differentiation by Maintaining Optimal Ets1 Levels
Wei Luo, Jessica Mayeux, Toni Gutierrez, Lisa Russell, Andrew Getahun, Jennifer Müller, Thomas Tedder, Jane Parnes, Robert Rickert, Lars Nitschke, John Cambier, Anne B. Satterthwaite, and Lee Ann Garrett-Sinha
- 921 Molecular Determinants of Agonist and Antagonist Signaling through the IL-36 Receptor
Sebastian Günther and Eric J. Sundberg
- 931 Apurinic/Apyrimidinic Endonuclease 2 Regulates the Expansion of Germinal Centers by Protecting against Activation-Induced Cytidine Deaminase–Independent DNA Damage in B Cells
Jeroen E. J. Guikema, Erin K. Linehan, Nada Esa, Daisuke Tsuchimoto, Yusaku Nakabeppu, Robert T. Woodland, and Carol E. Schrader

MUCOSAL IMMUNOLOGY

- 940 Human NK Cells Licensed by Killer Ig Receptor Genes Have an Altered Cytokine Program That Modifies CD4⁺ T Cell Function
Lin Lin, Chao Ma, Bo Wei, Najib Aziz, Raja Rajalingam, Susy Yusung, Henry A. Erlich, Elizabeth A. Trachtenberg, Stephan R. Targan, Dermot P. B. McGovern, James R. Heath, and Jonathan Braun

TUMOR IMMUNOLOGY

- 950 Reactive Oxygen Species– and DNA Damage Response–Dependent NK Cell Activating Ligand Upregulation Occurs at Transcriptional Levels and Requires the Transcriptional Factor E2F1
Alessandra Soriani, Maria Luisa Iannitto, Biancamaria Ricci, Cinzia Fionda, Giulia Malgarini, Stefania Morrone, Giovanna Peruzzi, Maria Rosaria Ricciardi, Maria Teresa Petrucci, Marco Cippitelli, and Angela Santoni

NOVEL IMMUNOLOGICAL METHODS

- 961 Targeted Delivery of α -Galactosylceramide to CD8 α ⁺ Dendritic Cells Optimizes Type I NKT Cell–Based Antitumor Responses
Elodie Macho-Fernandez, Luis Javier Cruz, Reem Ghinnagow, Josette Fontaine, Emilie Bialecki, Benoit Frisch, François Trottein, and Christelle Faveeuw

- 970 AUTHOR INDEX