



The Journal of Immunology

VOLUME 193, NUMBER 1 • JULY 1, 2014 • WWW.JIMMUNOL.ORG



IN THIS ISSUE

- 1 **B Cells Boost Tregs** See article p. 170
- Too Young To Remember Well** See article p. 177
- AID Needs Aid** See article p. 252
- GAS M Protein Fuels IgA Nephropathy** See article p. 317
- WC1 Domains Alter Signal Strength** See article p. 379

PILLARS OF IMMUNOLOGY

- 3 Hunting Autoimmune Disease Genes in NOD: Early Steps on a Long Road to Somewhere Important (Hopefully)
Edward K. Wakeland
- 7 Pillars Article: Genetic Analysis of Autoimmune Type 1 Diabetes Mellitus in Mice. *Nature*. 1991. 351: 542–547
John A. Todd, Timothy J. Aitman, Richard J. Cornall, Soumitra Ghosh, Jennifer R. S. Hall, Catherine M. Hearne, Andrew M. Knight, Jennifer M. Love, Marcia A. McAleer, Jan-Bas Prins, Nanda Rodrigues, Mark Lathrop, Alison Pressey, Nicole H. DeLarato, Laurence B. Peterson, and Linda S. Wicker

BRIEF REVIEWS

- 13 The Ground State of Innate Immune Responsiveness Is Determined at the Interface of Genetic, Epigenetic, and Environmental Influences
Edward Huang and Christine Anne Wells

CUTTING EDGE

- 21 Cutting Edge: Antigen-Specific Thymocyte Feedback Regulates Homeostatic Thymic Conventional Dendritic Cell Maturation
Nicholas A. Spidale, Bo Wang, and Roland Tisch
- 26 Cutting Edge: Parathyroid Hormone Facilitates Macrophage Efferocytosis in Bone Marrow via Proresolving Mediators Resolvin D1 and Resolvin D2
Laurie K. McCauley, Jesmond Dalli, Amy J. Koh, Nan Chiang, and Charles N. Serhan

On the cover: Confocal images showing increased nuclear (red) BrdU incorporation (green) of mouse colonic crypts in coculture with (white) Ly6C⁺ monocytes (yellow denotes proliferating nuclei). Skoczek, D. A., P. Walczysko, N. Horn, A. Parris, S. Clare, M. R. Williams, and A. Sobolewski. 2014. Luminal microbes promote monocyte–stem cell interactions across a healthy colonic epithelium. *J. Immunol.* 193: 439–451.

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.

30 Cutting Edge: Vitamin D Regulates Lipid Metabolism in *Mycobacterium tuberculosis* Infection
Hugh Salamon, Natalie Bruiners, Karim Lakehal, Lanbo Shi, Janani Ravi, Ken D. Yamaguchi, Richard Pine, and Maria Laura Gennaro

35 Cutting Edge: Dexamethasone Potentiates the Responses of Both Regulatory T Cells and B-1 Cells to Antigen Immunization in the ApoE^{-/-} Mouse Model of Atherosclerosis
Aoshuang Chen, Yajun Geng, Hanzhong Ke, Laura Constant, Zhaoqi Yan, Yue Pan, Patricia Lee, Isaiah Tan, Kurt Williams, Samantha George, Gnanasekar Munirathinam, Catherine A. Reardon, Godfrey S. Getz, Bin Wang, and Guoxing Zheng

ALLERGY AND OTHER HYPERSENSITIVITIES

41 Aspirin Activation of Eosinophils and Mast Cells: Implications in the Pathogenesis of Aspirin-Exacerbated Respiratory Disease
John W. Steinke, Julie Negri, Lixia Liu, Spencer C. Payne, and Larry Borish

ANTIGEN RECOGNITION AND RESPONSES

48 Tofacitinib Suppresses Antibody Responses to Protein Therapeutics in Murine Hosts
Masanori Onda, Kamran Ghoreschi, Scott Steward-Tharp, Craig Thomas, John J. O'Shea, Ira H. Pastan, and David J. FitzGerald

56 TCR Microclusters Pre-Exist and Contain Molecules Necessary for TCR Signal Transduction
Travis J. Crites, Kartika Padhan, James Muller, Michelle Krogsgaard, Prabhakar R. Gudla, Stephen J. Lockett, and Rajat Varma

68 Accumulation of Serial Forces on TCR and CD8 Frequently Applied by Agonist Antigenic Peptides Embedded in MHC Molecules Triggers Calcium in T Cells
Sergey Pryshchep, Veronika I. Zarnitsyna, Jinsung Hong, Brian D. Evavold, and Cheng Zhu

77 Superimposed Epitopes Restricted by the Same HLA Molecule Drive Distinct HIV-Specific CD8⁺ T Cell Repertoires
Xiaoming Sun, Mamoru Fujiwara, Yi Shi, Nozomi Kuse, Hiroyuki Gatanaga, Victor Appay, George F. Gao, Shinichi Oka, and Masafumi Takiguchi

85 Lysophosphatidic Acid Receptor 5 Inhibits B Cell Antigen Receptor Signaling and Antibody Response
Jiancheng Hu, Shannon K. Oda, Kristin Shotts, Erin E. Donovan, Pamela Strauch, Lindsey M. Pujanauski, Francisco Victorino, Amin Al-Shami, Yuko Fujiwara, Gabor Tigyi, Tamas Oravecz, Roberta Pelanda, and Raul M. Torres

AUTOIMMUNITY

96 The Thyroxine-Containing Thyroglobulin Peptide (aa 2549–2560) Is a Target Epitope in Iodide-Accelerated Spontaneous Autoimmune Thyroiditis
Panayota Kolypetri, Karen Carayanniotis, Shofiqur Rahman, Paris E. Georghiou, Vassiliki Magafa, Paul Cordopatis, and George Carayanniotis

CLINICAL AND HUMAN IMMUNOLOGY

102 Hemin Controls T Cell Polarization in Sickle Cell Alloimmunization
Hui Zhong, Weili Bao, David Friedman, and Karina Yazdanbakhsh

111 Endogenously Expressed IL-13R α 2 Attenuates IL-13–Mediated Responses but Does Not Activate Signaling in Human Lung Fibroblasts
Sanjay Chandriani, Daryle J. DePianto, Elsa N. N'Diaye, Alexander R. Abbas, Janet Jackman, Jack Bevers, III, Vladimir Ramirez-Carrozzi, Rajita Pappu, Steven E. Kauder, Karen Toy, Connie Ha, Zora Modrusan, Lauren C. Wu, Harold R. Collard, Paul J. Wolters, Jackson G. Egen, and Joseph R. Arron

120 IL-1 β Promotes the Differentiation of Polyfunctional Human CCR6⁺CXCR3⁺ Th1/17 Cells That Are Specific for Pathogenic and Commensal Microbes
Thomas Duhon and Daniel J. Campbell

- 130 The Inhibitory Effect of IFN- γ on Protease HTRA1 Expression in Rheumatoid Arthritis
Yuzhu Hou, Haijiang Lin, Linnan Zhu, Zhaoting Liu, Fanlei Hu, Jianfeng Shi, Tao Yang, Xiaoyun Shi, Huifang Guo, Xiaotian Tan, Lianfeng Zhang, Qiang Wang, Zhanguo Li, and Yong Zhao

IMMUNE REGULATION

- 139 Astrocytic TGF- β Signaling Limits Inflammation and Reduces Neuronal Damage during Central Nervous System *Toxoplasma* Infection
Egle Cekanaviciute, Hans K. Dietrich, Robert C. Axtell, Aaron M. Williams, Riann Egusquiza, Karen M. Wai, Anita A. Koshy, and Marion S. Buckwalter
- 150 Nuclear Role of WASp in Gene Transcription Is Uncoupled from Its ARP2/3-Dependent Cytoplasmic Role in Actin Polymerization
Sanjoy Sadhukhan, Koustav Sarkar, Matthew Taylor, Fabio Candotti, and Yatin M. Vyas
- 161 Unique Temporal and Spatial Expression Patterns of IL-33 in Ovaries during Ovulation and Estrous Cycle Are Associated with Ovarian Tissue Homeostasis
Colin I. Carlock, Jean Wu, Cindy Zhou, Kiana Tatum, Henry P. Adams, Filemon Tan, and Yahuan Lou
- 170 A Role for Intrathymic B Cells in the Generation of Natural Regulatory T Cells
Stacey N. Walters, Kylie E. Webster, Stephen Daley, and Shane T. Grey
- 177 Rapid Proliferation and Differentiation Impairs the Development of Memory CD8⁺ T Cells in Early Life
Norah L. Smith, Erin Wissink, Jocelyn Wang, Jennifer F. Pinello, Miles P. Davenport, Andrew Grimson, and Brian D. Rudd
- 185 Modeling the Clinical Phenotype of BTK Inhibition in the Mature Murine Immune System
Micah J. Benson, Varenka Rodriguez, David von Schack, Sean Keegan, Tim A. Cook, Jason Edmonds, Stephen Benoit, Nilufer Seth, Sarah Du, Dean Messing, Cheryl L. Nickerson-Nutter, Kyri Dunussi-Joannopoulos, Andrew L. Rankin, Melanie Ruzek, Mark E. Schnute, and John Douhan, III
- 198 BCL6 Controls Th9 Cell Development by Repressing *Il9* Transcription
Ribal Bassil, William Orent, Marta Olah, Ahmed T. Kurdi, Michael Frangieh, Thomas Buttrick, Samia J. Khoury, and Wassim Elyaman
- 208 Bovine $\gamma\delta$ T Cells Are a Major Regulatory T Cell Subset
Efrain Guzman, Jayne Hope, Geraldine Taylor, Adrian L. Smith, Carolina Cubillos-Zapata, and Bryan Charleston
- 223 Inhibition of Bone Remodeling in Young Mice by Bisphosphonate Displaces the Plasma Cell Niche into the Spleen
Stefan Teufel, Bettina Grötsch, Julia Luther, Anja Derer, Thorsten Schinke, Michael Amling, Georg Schett, Dirk Mielenz, and Jean-Pierre David
- 234 Podocytes Regulate Neutrophil Recruitment by Glomerular Endothelial Cells via IL-6-Mediated Crosstalk
Sahithi J. Kuravi, Helen M. McGettrick, Simon C. Satchell, Moin A. Saleem, Lorraine Harper, Julie M. Williams, George Ed Rainger, and Caroline O. S. Savage
- 244 Differential Impact of CD27 and 4-1BB Costimulation on Effector and Memory CD8 T Cell Generation following Peptide Immunization
Jane E. Willoughby, Jonathan P. Kerr, Anne Rogel, Vadim Y. Taraban, Sarah L. Buchan, Peter W. M. Johnson, and Aymen Al-Shamkhani

IMMUNE SYSTEM DEVELOPMENT

- 252 Binding of AID to DNA Does Not Correlate with Mutator Activity
Allisia J. Matthews, Solomon Husain, and Jayanta Chaudhuri
- 258 Membrane Association of the CD3 ϵ Signaling Domain Is Required for Optimal T Cell Development and Function
Matthew L. Bettini, Clifford Guy, Pradyot Dash, Kate M. Vignali, David E. Hamm, Jessica Dobbins, Etienne Gagnon, Paul G. Thomas, Kai W. Wucherpfennig, and Dario A. A. Vignali

- 268 The Role of the Syk/Shp-1 Kinase-Phosphatase Equilibrium in B Cell Development and Signaling
Ameera Alsaqeb, Elias Hobeika, David Medgyesi, Kathrin Kläsener, and Michael Reth

INFECTIOUS DISEASE AND HOST RESPONSE

- 277 NK Cell Responses to Simian Immunodeficiency Virus Vaginal Exposure in Naive and Vaccinated Rhesus Macaques
Liang Shang, Anthony J. Smith, Lijie Duan, Katherine E. Perkey, Lucy Qu, Stephen Wietgreffe, Mary Zupancic, Peter J. Southern, Katherine Masek-Hammerman, R. Keith Reeves, R. Paul Johnson, and Ashley T. Haase
- 285 IL-27 Limits Central Nervous System Viral Clearance by Promoting IL-10 and Enhances Demyelination
Maria Teresa P. de Aquino, Parul Kapil, David R. Hinton, Timothy W. Phares, Shweta S. Puntambekar, Carine Savarin, Cornelia C. Bergmann, and Stephen A. Stohlman
- 295 *Mycobacterium tuberculosis* Keto-Mycolic Acid and Macrophage Nuclear Receptor TR4 Modulate Foamy Biogenesis in Granulomas: A Case of a Heterologous and Noncanonical Ligand-Receptor Pair
Hedwin Kidorlang Dkhar, Ravikanth Nanduri, Sabil Mahajan, Sandeep Dave, Ankita Saini, Arun Kumar Somavarapu, Ashish Arora, Raman Parkesh, Krishan Gopal Thakur, Shanmugam Mayilraj, and Pawan Gupta
- 306 Tetherin Promotes the Innate and Adaptive Cell-Mediated Immune Response against Retrovirus Infection In Vivo
Sam X. Li, Bradley S. Barrett, Karl J. Heilman, Ronald J. Messer, Rachel A. Liberatore, Paul D. Bieniasz, George Kassiotis, Kim J. Hasenkrug, and Mario L. Santiago

INNATE IMMUNITY AND INFLAMMATION

- 317 The Combined Role of Galactose-Deficient IgA1 and Streptococcal IgA-Binding M Protein in Inducing IL-6 and C3 Secretion from Human Mesangial Cells: Implications for IgA Nephropathy
Roland Schmitt, Anne-lie Ståhl, Anders I. Olin, Ann-Charlotte Kristoffersson, Johan Rebetz, Jan Novak, Gunnar Lindahl, and Diana Karpman
- 327 miR-27a Regulates Inflammatory Response of Macrophages by Targeting IL-10
Na Xie, Huachun Cui, Sami Banerjee, Zheng Tan, Reinaldo Salomao, Mingui Fu, Edward Abraham, Victor J. Thannickal, and Gang Liu
- 335 A Critical Role for Human Caspase-4 in Endotoxin Sensitivity
Yuji Kajiwara, Tamar Schiff, Georgios Voloudakis, Miguel A. Gama Sosa, Gregory Elder, Ozlem Bozdagi, and Joseph D. Buxbaum
- 344 Infiltrating Monocyte-Derived Macrophages and Resident Kupffer Cells Display Different Ontogeny and Functions in Acute Liver Injury
Ehud Zigmund, Shany Samia-Grinberg, Metsada Pasmanik-Chor, Eli Brazowski, Oren Shibolet, Zamir Halpern, and Chen Varol
- 354 Proliferation Conditions Promote Intrinsic Changes in NK Cells for an IL-10 Response
Margarite L. Tarrío, Seung-Hwan Lee, Maria F. Fragosa, Hong-Wei Sun, Yuka Kanno, John J. O'Shea, and Christine A. Biron
- 364 Porcine Cathelicidins Efficiently Complex and Deliver Nucleic Acids to Plasmacytoid Dendritic Cells and Can Thereby Mediate Bacteria-Induced IFN- α Responses
Arnaud Baumann, Thomas Démoulin, Sylvie Python, and Artur Summerfeld
- 372 Gcsf-Chr19 Promotes Neutrophil Migration to Damaged Tissue through Blood Vessels in Zebrafish
Jorge A. Galdames, Constanza Zuñiga-Traslaviña, Ariel E. Reyes, and Carmen G. Feijóo

MOLECULAR AND STRUCTURAL IMMUNOLOGY

- 379 Signal Transduction by Different Forms of the $\gamma\delta$ T Cell-Specific Pattern Recognition Receptor WC1
Chuang Chen, Haoting Hsu, Edward Hudgens, Janice C. Telfer, and Cynthia L. Baldwin
- 391 T Cell Activation Regulates CD6 Alternative Splicing by Transcription Dynamics and SRSF1
Vânia G. da Glória, Mafalda Martins de Araújo, Ana Mafalda Santos, Rafaela Leal, Sérgio F. de Almeida, Alexandre M. Carmo, and Alexandra Moreira

- 400 Characterization of Conventional and Atypical Receptors for the Chemokine CCL2 on Mouse Leukocytes
Laura B. Ford, Vuk Cerovic, Simon W. F. Milling, Gerard J. Graham, Chris A. H. Hansell, and Robert J. B. Nibbs
- 412 Coordinated Histone H3 Methylation and Acetylation Regulate Physiologic and Pathologic Fas Ligand Gene Expression in Human CD4⁺ T Cells
Smita S. Ghare, Swati Joshi-Barve, Akshata Moghe, Madhuvanti Patil, David F. Barker, Leila Gobejishvili, Guy N. Brock, Matthew Cave, Craig J. McClain, and Shirish S. Barve
- 422 T Cell–Intrinsic Function of the Noncanonical NF- κ B Pathway in the Regulation of GM-CSF Expression and Experimental Autoimmune Encephalomyelitis Pathogenesis
Jiayi Yu, Xiaofei Zhou, Mako Nakaya, Wei Jin, Xuhong Cheng, and Shao-Cong Sun

MUCOSAL IMMUNOLOGY

- 431 Specific Microbiota-Induced Intestinal Th17 Differentiation Requires MHC Class II but Not GALT and Mesenteric Lymph Nodes
Duke Geem, Oscar Medina-Contreras, Michelle McBride, Rodney D. Newberry, Pandelakis A. Koni, and Timothy L. Denning
- 439 Luminal Microbes Promote Monocyte–Stem Cell Interactions Across a Healthy Colonic Epithelium
Dagmara A. Skoczek, Petr Walczysko, Nikki Horn, Alyson Parris, Simon Clare, Mark R. Williams, and Anastasia Sobolewski
- 452 AUTHOR INDEX
- 454 INFORMATION FOR AUTHORS