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

John A. Todd, Timothy J. Atamian, Richard J. Cornel, Soumitra Ghosh, Jennifer R. S. Hall, Catherine M. Hearne, Andrew M. Knight, Jennifer M. Love, Marcia A. McAlister, 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. Spidole, 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

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. Gedla, 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 Pyshtchep, Veronika I. Zarnitsyna, Jin Sung Hong, Brian D. Evavold, and Cheng Zhu

AUTOIMMUNITY

96 The Thyroxine-Containing Thyroglobulin Peptide (aa 2549–2560) Is a Target Epitope in Iodide-Accelerated Spontaneous Autoimmune Thyroiditis

Panayota Kolypetri, Karen Carayanniotis, Shofiur 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 IL-1β Promotes the Differentiation of Polyfunctional Human CCR6+CXCR3+ Th1/17 Cells That Are Specific for Pathogenic and Commensal Microbes

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

IMMUNE REGULATION

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

Nuclear Role of WASp in Gene Transcription Is Uncoupled from Its ARP2/3-Dependent Cytoplasmic Role in Actin Polymerization
Sanjoy Sadhukhan, Konstav Sarkar, Matthew Taylor, Fabio Candotti, and Yatin M. Vyas

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 Taturn, Henry P. Adams, Filemon Tan, and Yabuan Lou

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

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 Grimmon, and Brian D. Rudd

Modeling the Clinical Phenotype of BTK Inhibition in the Mature Murine Immune System
Michal J. Benson, Varenka Rodriguez, David von Schack, Sean Keegan, Tim A. Cook, Jason Edmonds, Stephen Benoit, Nilufer Seth, Sarah Du, Dean Meseng, Cheryl L. Nickerson-Nutter, Kyri Dunussi-Joannopoulos, Andrew L. Rankin, Melanie Ruzek, Mark E. Schmute, and John Douhan, III

BCL6 Controls Th9 Cell Development by Repressing Il9 Transcription
Ribal Basil, William Orent, Marta Olah, Ahmed T. Kurdi, Michael Frangieh, Thomas Buttrick, Samia J. Khoury, and Wassim Elyaman

Bovine γδ T Cells Are a Major Regulatory T Cell Subset
Efrain Guzman, Jayne Hope, Geraldine Taylor, Adrian L. Smith, Carolina Cubillo-Zapata, and Bryan Charleston

Inhibition of Bone Remodeling in Young Mice by Bisphosphonate Displaces the Plasma Cell Niche into the Spleen
Stefan Teufel, Bettina Grotsch, Julia Luther, Anja Derer, Thorsten Schinke, Michael Amling, Georg Schett, Dirk Mielenz, and Jean-Pierre David

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

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

Binding of AID to DNA Does Not Correlate with Mutator Activity
Allysia J. Matthews, Solomon Husain, and Jayanta Chaudhuri

Membrane Association of the CD3ε Signaling Domain Is Required for Optimal T Cell Development and Function
Matthew L. Bettini, Clifford Guy, Pradyot Dash, Kate M. Vignali, David E. Hamn, Jessica Dobbins, Etienne Gagnon, Paul G. Thomas, Kai W. Wucherpfennig, and Dario A. A. Vignali
The Role of the Syk/Shp-1 Kinase-Phosphatase Equilibrium in B Cell Development and Signaling
Ameera Alsadeq, Elias Hobeika, David Medgyesi, Kathrin Kläser, and Michael Reth

INFECTIONOUS DISEASE AND HOST RESPONSE

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 Wietgrefe, Mary Zupancic, Peter J. Southern, Katherine Mask-Hammerman, R. Keith Reeves, R. Paul Johnson, and Ashley T. Haase

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

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 Kirdorlang Dkhar, Ravikanth Nanduri, Sahil Mahajan, Sandeep Dave, Ankita Saini, Arun Kumar Somavarapu, Ashish Arora, Raman Parkesh, Krishan Gopal Thakur, Shanmugam Mayilraj, and Pawan Gupta

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

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

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

A Critical Role for Human Caspase-4 in Endotoxin Sensitivity
Yuji Kajiwara, Tamar Schiff, Georgios Voloudakis, Miguel A. Gama Soa, Gregory Elder, Ozlem Bozdagi, and Joseph D. Buxbaum

Infiltrating Monocyte-Derived Macrophages and Resident Kupffer Cells Display Different Ontogeny and Functions in Acute Liver Injury
Ehud Zigmond, Shany Samia-Grinberg, Metsada Pasmanik-Chor, Eli Brazowski, Oren Shibolet, Zamir Halpern, and Chen Varol

Proliferation Conditions Promote Intrinsic Changes in NK Cells for an IL-10 Response
Margaret L. Tarrio, Seung-Hwan Lee, Maria F. Fragsos, Hong-Wei Sun, Yuka Kanno, John J. O’Shea, and Christine A. Biron

Porcine Cathelicidins Efficiently Complex and Deliver Nucleic Acids to Plasmacytoid Dendritic Cells and Can Thereby Mediate Bacteria-Induced IFN-α Responses
Arnaud Baumann, Thomas Démoulins, Sylvie Python, and Artur Summerfield

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

Signal Transduction by Different Forms of the γδ T Cell–Specific Pattern Recognition Receptor WC1
Chuang Chen, Huoting Hsu, Edward Hudgens, Janice C. Telfer, and Cynthia L. Baldwin

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
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

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 Gojekishvili, Guy N. Brock, Matthew Cave, Craig J. McClain, and Shirish S. Barve

T Cell–Intrinsic Function of the Noncanonical NF-κB Pathway in the Regulation of GM-CSF Expression and Experimental Autoimmune Encephalomyelitis Pathogenesis
Jiayi Yu, Xiaofei Zhou, Mako Nakaya, Wei Jin, Xabong Cheng, and Shao-Cong Sun

MUCOSAL IMMUNOLOGY
Specific Microbiota-Induced Intestinal Th17 Differentiation Requires MHC Class II but Not GALT and Mesenteric Lymph Nodes

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

AUTHOR INDEX

INFORMATION FOR AUTHORS