

upstream of exon 1a. The proximal promoter has multiple transcription start sites, but the distal promoter only has a single start site. Culturing NK cells with IL-2 leads to a significant increase in the proportion of transcripts initiated from the distal promoter suggesting that the distal promoter may be more IL-2 responsive.

CD8 $\alpha\beta$ T cell clones were identified that were negative for cell surface and intracellular expression of CD94 protein, yet positive for CD94 transcripts. Transcripts with and without exon 1a were observed. CD94 cell surface expression was induced after culturing with IL-2, IL-15 and PHA but not in T cells that lacked CD94 transcripts, suggesting that CD94 protein expression in such T cells is controlled at both the transcriptional and post-transcriptional levels.

We identified three new alternatively spliced transcripts of CD94. One of these transcripts lacks part of exon 3 (T3) and another lacks exon 4 (CD94B-T2), while the third lacks part of exon 5 (T4) that encodes the β region of the protein. Protein expression studies show that T4 encoded protein preferentially dimerizes with NKG2B compared to NKG2A.

67.5

The proto-oncogene and Th2 transcription factor c-Maf modulates interleukin-10 gene expression in macrophages

Shanjin Cao, Xiaojing Ma. Microbiology and Immunology, Weill Medical College of Cornell University, 1300 York Avenue, New York, NY 10021

The appropriate balance between pro- and anti-inflammatory responses is essential for the establishment of homeostasis. Among the various mechanisms conducted to control the inflammatory processes, the activities of IL-10 play a fundamental and most important role. However, the molecular mechanisms whereby the expression of IL-10 gene is regulated in macrophages are poorly understood. Our study has identified the proto-oncogene c-Maf as a critical regulator of IL-10 gene expression. We have made the following novel observations: (1) c-Maf is constitutively expressed in macrophages. (2) IL-10 production stimulated by LPS in macrophages derived from c-Maf knockout mice is severely impaired. (3) Adenovirus-mediated c-Maf gene transduction into human macrophages can induce both the mRNA and protein expression of IL-10. (4) Overexpression of c-Maf in monocytic cells strongly induces IL-10 promoter activity. (5) The potential c-Maf response element has been mapped to within 129 bp upstream of the transcription start site of the human IL-10 promoter, where a c-Maf-induced perturbation of nuclear DNA-binding activity is noted. We are also investigating under which physiological (e.g. the establishment of homeostasis) and/or pathophysiological circumstances this transcriptional pathway is invoked.

This work is supported by National Institutes of Health Grants AI-45899 and CA-79772 (X.M.), and Susan G. Komen Breast Cancer Foundation Postdoctoral Fellowship (S.C).

67.6

Beryllium-induced gene changes in a mouse alveolar macrophage cell line

Melanie Sarah Flint, Sally S Tinkle. Toxicology & Molecular Biology Branch, CDC/NIOSH, 1095 Willowdale road, Morgantown, WV 26505

Chronic Beryllium Disease (CBD) is an occupationally acquired lung disease that occurs as a cell mediated immune response to beryllium, resulting in the development of noncaseating granulomas. We hypothesized that the identification of early genes associated with beryllium exposure may give important insights into the role of macrophages in CBD. We investigated gene expression in a mouse alveolar macrophage cell line incubated in the presence of absence of 10 μ M BeSO₄ for 4 hours. We utilized Affymetrix oligonucleotide arrays consisting of approximately 12000 genes to detect differential changes in gene expression in beryllium-treated cells compared to controls. We found that beryllium caused significant changes in the expression of numerous genes encoding; heat shock proteins, cytokines, adhesion molecules, cytokine receptors, signalling molecules and transcriptional activators and repressors. HSP70 and MHC class III region were elevated 10-fold in BeSO₄ treated macrophages. However, IL-1[β], ICAM-1 and IL-10R were all decreased by beryllium. We verified

beryllium-modulation of these genes by real time quantification (TaqmanTMPCR). Our studies identify beryllium-regulated genes and suggest that HSPs and cytokine genes play pivotal roles in an early immune response to beryllium. This work is supported by CDC/NIOSH.

67.7

Up-regulation of MHC Class II Transactivator (CIITA) expression in B lymphocytes by IFN- γ

Janet F. Piskurich¹, Carolyn A. Gilbert¹, Brittany D. Ashley¹, Jian Wu², Kenneth L. Wright². ¹Department of Basic Medical Sciences, Mercer University School of Medicine, 1550 College St., Macon, GA 31207, ²Department of Biochemistry and Molecular Biology, University of South Florida, Tampa, FL

Class II transactivator (CIITA), the master regulator of MHC class II (MHC II) expression, is a co-activator that controls MHC II transcription. Additionally, CIITA can activate MHC class I expression. B lymphocytes express MHC II constitutively because CIITA promoter III (pIII), one of the multiple promoters (pI-pIV) of this gene, is constitutively expressed. Increases in MHC II expression in B cells in response to cytokines have been observed. Although IFN- γ induces expression of MHC II and CIITA in many cell types, the effect of this cytokine on CIITA expression in B cells has not been previously studied. RT-PCR analyses demonstrate that MHC II and CIITA pIV-specific RNAs are increased in Raji B cells in response to IFN- γ treatment. Functional promoter analyses confirm that pIV is the IFN- γ -inducible promoter of CIITA in these cells and reveal that the IRF-1-binding site is required for induction. In vivo genomic footprint analysis demonstrates protections at the Stat1 and IRF-1-binding and E-box sites. Since B cells exhibit both constitutive transcription of CIITA via pIII and also inducible transcription via pIV, it may be possible to use IFN- γ to activate CIITA and MHC expression in myeloma cells where BLIMP-1 represses the activity of CIITA pIII.

This investigation was supported (in part) by research grants from the National Multiple Sclerosis Society and the MEDCEN Community Health Foundation of Central Georgia.

67.8

DNA Methylation and Chromatin Structure Suppress Perforin Expression in Normal T Cells, and Contribute to its Overexpression in CD4+ Lupus T Cells

Qianjin Lu¹, Ailing Wu¹, Mariana Kaplan¹, Mathias Lichtenheld², Bruce Richardson¹. ¹Medicine, University of Michigan, 5431 CCGCB, Ann Arbor, MI 48109-0940, ²Immunology, University of Miami, Miami, FL

The mechanisms regulating perforin expression are incompletely understood. Treating T cells with the DNA methylation inhibitor 5-azacytidine (5-azaC) increased perforin ~4-fold, so we examined the methylation and chromatin structure of its promoter and upstream enhancer. The entire region was unmethylated in NK cells and methylated in fibroblasts. In contrast, only the promoter was unmethylated in CD4+ and CD8+ cells, and expression correlated with hypomethylation of an area flanking the enhancer. 5-azaC selectively demethylated this area and increased perforin expression. Selective methylation of this region suppressed promoter function. Finally, perforin expression was associated with sensitivity of the region to DNase I digestion. CD4+ T cells from lupus patients have hypomethylated DNA, so we asked if they aberrantly express perforin. Normal CD4+ T cells did not express perforin, while 7-10% of CD8+ cells expressed the protein. CD4+ T cells from patients with active lupus expressed perforin, and the number increased with disease activity. Expression correlated with demethylation of the same region affected by 5-azaC. In contrast, CD8+ T cells from patients with active lupus did not express perforin, and the methylation sensitive region was hypermethylated. Concanamycin A, a perforin inhibitor, suppressed lupus T cell killing of autologous monocyte by ~75% (p<0.05), indicating that the perforin expression was functionally significant. We conclude that DNA methylation and chromatin structure regulate perforin expression in T cells, and that abnormal DNA methylation contributes to aberrant perforin expression in CD4+ lupus T cells. AG014783, AR42525, and AI42753 and the VA.

The American Association of Immunologists
90th Anniversary Annual Meeting

Immunology 2003
Denver, Colorado
May 6 – 10, 2003

APR 23 2003

ABSTRACTS 29.1 – 162.31

Indexes
Key Word
Author

The American Association of Immunologists

American Association of Veterinary
Immunologists

American Society of Transplantation
Association of Medical Laboratory
Immunologists

Canadian Society for Immunology
Clinical Immunology Society

International Society for Interferon and Cytokine
Research

International Society for
NeuroImmunoModulation

International Society of Neuroimmunology
PsychoNeuroImmunology Research Society
Society for Leukoctye Biology
Society for Mucosal Immunology
Society for Natural Immunity

THE FASEB JOURNAL

Volume 17, Number 7

April 14, 2003

ABSTRACTS

WEDNESDAY May 7, 2003

T Cell Development	C1
Signaling and Costimulation in Allergic Inflammation	C9
Immunopathogenesis of Infection	C15
Vaccine and Immunotherapeutic Strategies against Pathogens	C23
Pathogenic Mechanisms in Autoimmune Disease	C31
Animal Models of Autoimmune Disease	C38
Regulation of Leukocyte Migration and Inflammation in Disease	C43
Host Defense and Innate Immunity	C50
Transplantation Immunology I	C58
Signaling of Chemokines and Cytokines	C65
Molecular Regulation of Inflammation	C70
Anti-tumor Effector Cells and Regulation of Tumor Immunity	C73
Effector Mechanisms and Regulation of Effector Cells	C79
Protective Mucosal Immune Responses	C85

THURSDAY May 8, 2003

B Cell Development and Activation	C88
Transcriptional Regulation of the Immune System	C97
Regulation of Lymphocyte Migration and Tissue Localization	C104
Fc Receptors, Complement and Acute Phase Proteins	C106
Transplantation Immunology II	C111
The Role of Chemokines and Cytokines	C116
Class I Pathway and CD8 T Cell Recognition	C119
Immunotherapy of Cancer	C122
Non-classical Antigen Presentation Pathways ..	C129
Role of Modulatory Cytokines in Disease Models	C130
Immunomodulation I: Cytokines and Chemokines	C139

Immunomodulation II: Cytokines and Chemokines	C142
Hematopoiesis and Mechanisms of Cell Survival	C147
Innate Immunity against Pathogens	C153
Lymphocyte Responses to Pathogens	C162
Tolerance and Autoimmunity	C174
Costimulation and Autoimmunity	C177
Genetics and Autoimmune Disease	C179
B Cells and Autoantibodies in Pathogenesis of Autoimmunity	C182

FRIDAY May 9, 2003

Molecular Aspects of Repertoire Formation (Recombination, Isotype Switching, Somatic Mutation)	C190
Host Defense against Parasitic and Fungal Infections	C193
Macrophages and Dendritic Cells	C197
Immune System Regulation: Signal Pathways in B Cell Development, Regulation and Activation	C202
Mechanisms of Costimulation and Tolerance ...	C210
Immune System Regulation: Signaling Pathways in T Cell Development, Regulation, and Activation	C218
Influences on Mucosal Immunity	C230
Mechanisms of Tumor Rejection and Modulation of Anti-tumor Responses	C235
T Cell Memory and Homeostasis	C240
Development and Regulation of Allergic Disease and Asthma	C248
Anchoring Immunity: Interactions of Pathogens with Antigen Presenting Cells	C255
Regulatory T Cells in Autoimmunity	C258
Regulation of Signal Pathways in Immune Cells	C260
Cytokines and Autoimmune Disease	C269
Immunotherapy	C275

The abstracts on pages C1–C334 were prepared by the authors and printed by photo-offset without change. Abstracts are not subject to scientific review; therefore, the scientific validity of the results reported is the responsibility of the authors and sponsors. **Accuracy, form of citation, designation of materials,**

acknowledgment of coauthors and of grant support, terminology, nomenclature, and the like, remain the responsibility of the authors and sponsors. The appearance of an abstract in this issue does not necessarily imply future publication of a scientific paper.

Editor-in-Chief
Vincent T. Marchesi

Editorial Associate
Claire S. Veilleux

Associate Editors
Edward J. Goetzl
Yusuf A. Hannun
Joseph A. Madri

Publications and Communications Committee
Alan G. Goodridge (ASBMB)
Sandra R. Wolman (ASIP)
Susan S. Percival (ASNS)
Eleanor S. Metcalf (AAI)
Suse B. Broyde (BPS)
Donald A. Fischman Chair (AAA)
Mark A. Hermodson (Protein)
Marc K. Drezner (ASBMR)
Stephen J. Weiss (ASCI)
Peter H. Byers (ASHG)
Thomas D. Sargent (SDB)
Sidney H. Golub (non-voting)

Ex Officio
Steven L. Teitelbaum
Vincent T. Marchesi
FASEB Society
Executive Officers

Director, FASEB Office of Publications
Nancy J. Rodnan

Senior Editor
Lynn Willis

Copy Editor
Kendall Sites

FJ Express
Production Coordinator
Mary Kiorpes Eig

Marketing/Advertising Manager
Jennifer L. Pesanelli

Advertising Account Manager
Susan J. Mergenhagen
301-634-7103
Fax: 301-634-7153

Subscription Manager
Eleanor B. Peebles
301-634-7029
Fax: 301-634-7099

Editorial Board

Kari Alitalo
Mina J. Bissell
Meredith Bond
David A. Brenner
H. Franklin Bunn
George H. Caughey
Pierre Chambon
Thomas O. Daniel
Balz Frei
Martin E. Hemler
Timothy Hla
Tadamitsu Kishimoto
Hynda K. Kleinman
John S. Lazo
John J. Lemasters
George M. Martin

Mark P. Mattson
Linda C. McPhail
Hideaki Nagase
Lina M. Obeid
Jordan S. Pober
Robert E. Pollack
Stanley B. Prusiner
Russel J. Reiter
Noel R. Rose
Charles N. Serhan
William C. Sessa
Solomon H. Snyder
Andrew P. Somlyo
William G. Stetler-Stevenson
Makoto M. Taketo
George D. Yancopoulos

Editor-in-Chief
Boyer Center for Molecular Medicine
Yale University School of Medicine
295 Congress Avenue, (P.O. Box 9812)
New Haven, CT 06519-1418, USA
Phone: 203-737-2334 Fax: 203-737-2267
email: vincent.marchesi@yale.edu

Editorial Office
Boyer Center for Molecular Medicine
Yale University School of Medicine
295 Congress Avenue (P.O. Box 9812)
New Haven, CT 06519-1418, USA
Phone: 203-737-2334 Fax: 203-737-2267
Email: faseb@yale.edu

Publications Office
The FASEB Journal
9650 Rockville Pike
Bethesda, MD 20814-3998, USA
Phone: 301-634-7100
Fax: 301-634-7809
Email: ksites@faseb.org

The FASEB Journal (ISSN-0892-6638) is published 15 times a year (monthly except three times in March and two times in April) by the Federation of American Societies for Experimental Biology, 9650 Rockville Pike, Bethesda, MD 20814-3998, U.S.A. Copyright © 2003 by FASEB. All rights reserved. Requests for copyrighted material should be made in writing to the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, USA. Periodicals postage paid at Bethesda, Maryland, and at additional mailing offices. **Postmaster:** Send change of address to *The FASEB Journal*, 9650 Rockville Pike, Bethesda, MD 20814-3998. The views expressed in articles are those of the authors and not necessarily those of the Federation. Send manuscripts and proposals to the Editor-in-Chief. See **Instructions for Authors** online at <http://www.fasebj.org>.

2003	United States	Canada/Mexico	Rest of World	Online Only
INSTITUTION	\$648.	\$672.	\$710.	\$648.
MEMBER	\$93.	\$113.	\$146.	N/A
INDIVIDUAL	\$159.	\$179.	\$212.	N/A
STUDENT	\$45.	\$65.	\$97.	N/A

Corporate members of FASEB

The American Physiological Society • American Society for Biochemistry and Molecular Biology • American Society for Pharmacology and Experimental Therapeutics
American Society for Investigative Pathology • American Society for Nutritional Sciences • The American Association of Immunologists • Biophysical Society
American Association of Anatomists • The Protein Society • The American Society for Bone and Mineral Research • American Society for Clinical Investigation
The Endocrine Society • The American Society of Human Genetics • Society for Developmental Biology