T Lymphocyte Activation Threshold is Increased in Reduced Gravity
CL Adams, M Gonzalez, CF Sams, Cellular and Molecular Research, Johnson Space Center, Houston, TX, 77058

Reorganization of membrane microdomains during T cell activation mediates the costimulatory effect of CD28 and efficiently lowers the stimulation threshold for activation. T cells stimulated in space flight or during clinorotation are dramatically inhibited in their activation response. Clinorotation is a ground-based culture model of reduced gravity that provides a vector-averaged reduction of the apparent gravity of cells without significant shear force. Our laboratory has thus used clinorotation as a noninvasive tool to study cellular and biochemical events regulating T cell activation and the effects of gravitational forces on these systems. Here we demonstrate that purified T cells exhibit a dramatic increase in their activation threshold during clinorotation when stimulated with bead-immobilized antibodies to CD3 and CD28. This change in threshold involves a mechanism independent of TCR triggering as T cells stimulated during clinorotation require 2- to 3-fold higher levels of TCR internalization than in static to achieve 50% activation. Current studies are underway to investigate the role of membrane reorganization in the change of threshold during clinorotation. Preliminary evidence suggests that recruitment of lipid rafts to the contact site during T cell activation is significantly impaired during clinorotation and may account for the increased activation threshold. This is consistent with the hypothesis that lipid rafts function as preformed signal transduction platforms that provide efficient costimulation by lowering the stimulation threshold for T cell activation. This work is supported by a National Research Council Associateship (CL Adams) and NASA Grants 121-10-30-10 and 121-10-90-13.

Charley Adams
281-483-7198
Meeting B4
Poster session 1
T Lymphocyte Activation, Differentiation and Death (B4)

Organizers: Laurie H. Glimcher, William E. Paul, Gerald R. Crabtree and Harvey I. Cantor

January 28 - February 3, 2000
Keystone Resort, Keystone, Colorado

Abstract Deadline: September 28, 1999   Early Registration: November 29, 1999

There have been substantial advances in molecular and cellular biology that have provided new insight into the biochemical and genetic basis of lymphocyte recognition, activation and expression of distinct functional phenotypes. It has now become evident that for both T and B cells, stimuli delivered through their receptors can result in either clonal expansion or apoptosis. In the case of T cells, clonal expansion of helper cells is accompanied by differentiation into two major functional subsets which regulate the immune response. The pathways between the membrane and the nucleus and their molecular components are an area of very active investigation. This meeting will draw together scientists working on diverse aspects of this problem, including receptor ligand interactions, intracellular pathways that transmit receptor mediated signals and the effect of such signal transduction pathways on gene regulation. The aim of this meeting is to integrate the information from these various experimental approaches into a new synthesis and molecular explanation of T cell activation, differentiation and death.

On-line Registration & Abstract Submission

Friday, January 28

2:00 PM - 7:00 PM  Registration
6:30 PM - 7:30 PM  Welcome
7:30 PM - 8:00 PM  Orientation
8:00 PM - 9:00 PM  Keynote Address

Rolf M. Zinkernagel, University Hospital Zurich
On T Cell Selection and Induction

Saturday, January 29

7:00 AM - 8:00 AM  Breakfast
8:00 AM - 11:00 AM  Structural Basis of Receptor Specificity

John W. Kappler, National Jewish Medical and Research Center
MHC Class II Mutations Affecting Peptide Exchange Rates

Don C. Wiley, Harvard University
Structural Studies of Antigen Presentation and Recognition by T-Cells

Kristin Hogquist, University of Minnesota Health Center
Interaction of the TCR With Self Peptides During Thymic Development

* Paul M. Allen, Washington University Medical School
Formation and Function of the Immunological Synapse

Jianzhu Chen, Massachusetts Institute of Technology
Short Talk: Homeostasis and Memory T Cell Development

9:00 AM - 9:20 AM  Coffee Break
11:00 AM - 1:00 PM  Poster Setup

POSTER SESSION 1: Structural Basis of Receptor Specificity/Coreceptor Modulation of T Cell Responses

Social Hour

Coreceptor Modulation of T Cell Responses

* Ellen A. Robey, University of California-Berkeley
  Regulation of T Cell Development by Notch

Mark M. Davis, Stanford University
  Deciphering the Cell Surface and Cytoskeletal Choreography of T Cell Recognition and Costimulation

Gerald J. Siu, Columbia University
  Transcriptional Control of CD4 Expression

Sunday, January 30

7:00 AM - 8:00 AM
  Breakfast

8:00 AM - 11:00 AM
  Intracellular Signaling in T Cells, I

* Gerald R. Crabtree, Stanford University Medical School
  The BAF Chromatin Remodeling Complex in TCR Gene Rearrangement and Lymphocyte Activation

Lawrence E. Samelson, National Institutes of Health
  Signaling Events Mediated by the T Cell Antigen Receptor

Anjana Rao, Harvard University
  Regulation of Cytokine Gene Expression

Rose Zamoyska, National Institute for Medical Research
  The Role of Lck in T Cell Lineage Decisions and Cell Survival

Steven J. Burakoff, Dana Farber Cancer Institute
  Short Talk: Novel Adaptor Proteins in T Cell Signaling

9:00 AM - 9:20 AM
  Coffee Break

11:00 AM - 1:00 PM
  Poster Setup

2:00 PM - 4:00 PM
  WORKSHOP 1: Structural Considerations and Transcription in T Cell Development, Activation and Death

* Stephen C. Jameson, University of Minnesota
* Dinah S. Singer, National Institutes of Health

2:00 PM - 4:00 PM
  WORKSHOP 2: Intracellular Signaling Pathways in Thymocytes and T Cells

* Leslie J. Berg, University of Massachusetts
* B. J. Fowlkes, National Institutes of Health

4:00 PM - 6:00 PM
  POSTER SESSION 2: Intracellular Signaling in T Cells

5:00 PM - 6:00 PM
  Social Hour

8:00 PM - 9:30 PM
  Coffee Available

8:00 PM - 10:00 PM
  Intracellular Signaling in T Cells, II

* Arthur Weiss, University of California-San Francisco
  Regulators of TCR Signal Transduction

Doreen A. Cantrell, Imperial Cancer Research Fund
  Spatial and Temporal Regulation of Serine Kinases by Antigen Receptors

Tadatsugu Taniguchi, University of Tokyo
  The IRF and STAT Transcription Factors in T Cell Signaling

Hua Gu, National Institutes of Health
  Short Talk: A Novel Role of the Adaptor Molecule Cbl-b in CD28 Dependence of T Cell Activation and Autoimmunity

http://www.symposia.com/MeetingDetail.cfm?MeetingNumber=B4&Year=2000

11/8/1999
### Monday, January 31

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<th>Time</th>
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<tr>
<td>7:00 AM - 8:00 AM</td>
<td>Breakfast</td>
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<tr>
<td>8:00 AM - 11:00 AM</td>
<td>Transcription in T Cell Activation and Differentiation</td>
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<tr>
<td></td>
<td>* Laurie H. Glimcher, Harvard School of Public Health</td>
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<td>* Subset-Specific Transcription Factors That Direct Cytokine Expression</td>
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<td>* Jeffrey M. Leiden, Harvard School of Public Health</td>
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<td>* Transcriptional Regulation of T Cell Development</td>
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<td>* Hans C. Clevers, University Hospital-Utrecht</td>
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<td>* TCF Factors, Mediators of Wnt Signaling</td>
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<td>* Anuradha Ray, Yale University</td>
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<td>* Short Talk: GATA-3, Th2 Differentiation and Asthma</td>
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<td>* Jeffrey M. Leiden, Harvard School of Public Health</td>
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<td>4:00 PM - 6:00 PM</td>
<td>POSTER SESSION 3: Transcription in T Cell Activation and Differentiation/Molecular Aspects of Thymocyte Development</td>
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<td>5:00 PM - 6:00 PM</td>
<td>Social Hour</td>
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<td>8:00 PM - 9:30 PM</td>
<td>Coffee Available</td>
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<td>8:00 PM - 10:00 PM</td>
<td>Molecular Aspects of Thymocyte Development</td>
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<td>* Ada M. Kruisbeek, Netherlands Cancer Institute</td>
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<td>* Regulation of Cell-Fate Decisions in Early T Cell Development by the pre-TCR</td>
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<td>* Stephen M. Hedrick, University of California-San Diego</td>
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<td>* Control of Lymphocyte Survival and Immune Memory</td>
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<td>* Irving L. Weissman, Stanford University Medical School</td>
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<td>* Development of T Cells and Dendritic Cells from HSC and Other Progenitors</td>
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### Tuesday, February 1

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<tr>
<td>7:00 AM - 8:00 AM</td>
<td>Breakfast</td>
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<td>8:00 AM - 11:00 AM</td>
<td>Tolerance and Autoimmunity</td>
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<td>* Harvey I. Cantor, Dana Farber Cancer Institute</td>
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<td>* Molecular Mimicry in Autoimmune Disease</td>
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<td>* Christophe O. Benoist, Institut de Genetique et de Biologie Moleculaire et Cellulaire</td>
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<td>* Models of Autoimmune Diabetes</td>
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<td>* Emil R. Unanue, Washington University</td>
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<td>* Central Tolerance: Specificity of T Cells That are Negatively Selected or Escape Deletion</td>
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<td>* Terri M. Laufer, University of Pennsylvania</td>
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<td>* Development of a TCR Transgenic Model of Autoimmune Skin Disease</td>
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<td>9:00 AM - 9:20 AM</td>
<td>Coffee Break</td>
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<td>11:00 AM - 1:00 PM</td>
<td>Poster Setup</td>
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<tr>
<td>2:00 PM - 4:00 PM</td>
<td>WORKSHOP 3: Differentiative and Apoptotic Pathways in Mature T Cells</td>
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<td>* Philippa C. Marrack, National Jewish Medical and Research Center</td>
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<tr>
<td>2:00 PM - 4:00 PM</td>
<td>WORKSHOP 4: Tolerance, Autoimmunity and their Clinical Implications</td>
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**Hugh Auchincloss**, Massachusetts General Hospital

*David D. Lo*, Scripps Research Institute

4:00 PM - 6:00 PM

POSTER SESSION 4: Tolerance and Autoimmunity/Death in T Cells/Genetic Programs in T Helper Cell Differentiation/Therapeutic Implications of T Cell Signaling

5:00 PM - 6:00 PM

Social Hour

8:00 PM - 9:30 PM

Coffee Available

8:00 PM - 10:00 PM

Death in T Cells

Stanley J. Korsmeyer, Dana Farber Cancer Institute

Activation of Death Agonists

*Frederick W. Alt*, Children's Hospital, Boston Role of NHEJ Proteins in Lymphogenesis and Neurogenesis

Andreas E. Strasser, Walter and Eliza Hall Institute

BH3-only Members of the Bcl-2 Family are Critical Inducers of Apoptosis

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**Wednesday, February 2**

7:00 AM - 8:00 AM

Breakfast

8:00 AM - 11:00 AM

Genetic Programs in T Helper Cell Differentiation

*William E. Paul*, National Institutes of Health

Allelic Bias in the Regulation of IL-4 Expression

Anne O'Garra, DNAX Research Institute

Checkpoints for Regulation of Th1 Responses

Kenneth M. Murphy, Washington University Medical School

IL-12 and Th1 Development

Muriel Moser, University of Brussels

Role of Dendritic Cell Subsets in T Helper Cell Differentiation

9:00 AM - 9:20 AM

Coffee Break

3:00 PM - 4:00 PM

Coffee Available

3:00 PM - 5:00 PM

Therapeutic Implications of T Cell Signaling

Leonard Chess, Columbia University

Strategies for Immunotherapeutic Intervention: The CD40L Model

James P. Allison, University of California-Berkeley

T Cell Costimulation, Autoimmunity and Tumor Immunotherapy

Jeffrey A. Bluestone, Ben May Labs, University of Chicago CD28/CTLA4: Pathways to Tolerance

7:00 PM - 8:00 PM

Social Hour

8:00 PM - 10:00 PM

Banquet

9:00 PM - 12:00 AM

Entertainment

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**Thursday, February 3**

- Departure

* Chair

** Invited, not yet responded

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11/8/1999