Keystone 2000

T Lymphocyte Activation Threshold is Increased in Reduced Gravity

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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 signficant 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 I

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**

4:00 PM - 6:00 PM	**POSTER SESSION 1: Structural Basis of Receptor Specificity/Coreceptor Modulation of T Cell Responses**
5:00 PM - 6:00 PM	**Social Hour**
8:00 PM - 9:30 PM	**Coffee Available**
8:00 PM - 10:00 PM	**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*

Monday, January 31

7:00 AM - 8:00 AM	**Breakfast**
8:00 AM - 11:00 AM	**Transcription in T Cell Activation and Differentiation**
	* **Laurie H. Glimcher** , Harvard School of Public Health *Subset-Specific Transcription Factors That Direct Cytokine Expression* **Jeffrey M. Leiden** , Harvard School of Public Health *Transcriptional Regulation of T Cell Development* **Hans C. Clevers** , University Hospital-Utrecht *TCF Factors, Mediators of Wnt Signaling* **Anuradha Ray** , Yale University *Short Talk: GATA-3, Th2 Differentiation and Asthma* **Barry P. Sleckman** , Washington University Medical School *Short Talk: Targeting Rearrangement by RSSs: Beyond the 12/23 Rule*
9:00 AM - 9:20 AM	**Coffee Break**
11:00 AM - 1:00 PM	**Poster Setup**
4:00 PM - 6:00 PM	**POSTER SESSION 3: Transcription in T Cell Activation and Differentiation/Molecular Aspects of Thymocyte Development**
5:00 PM - 6:00 PM	**Social Hour**
8:00 PM - 9:30 PM	**Coffee Available**
8:00 PM - 10:00 PM	**Molecular Aspects of Thymocyte Development**
	* **Ada M. Kruisbeek** , Netherlands Cancer Institute *Regulation of Cell-Fate Decisions in Early T Cell Development by the pre-TCR* **Stephen M. Hedrick** , University of California-San Diego *Control of Lymphocyte Survival and Immune Memory* **Irving L. Weissman** , Stanford University Medical School *Development of T Cells and Dendritic Cells from HSC and Other Progenitors*

Tuesday, February 1

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

	* **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*

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**

Thursday, February 3

-	**Departure**

*** Chair**
**** Invited, not yet responded**

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