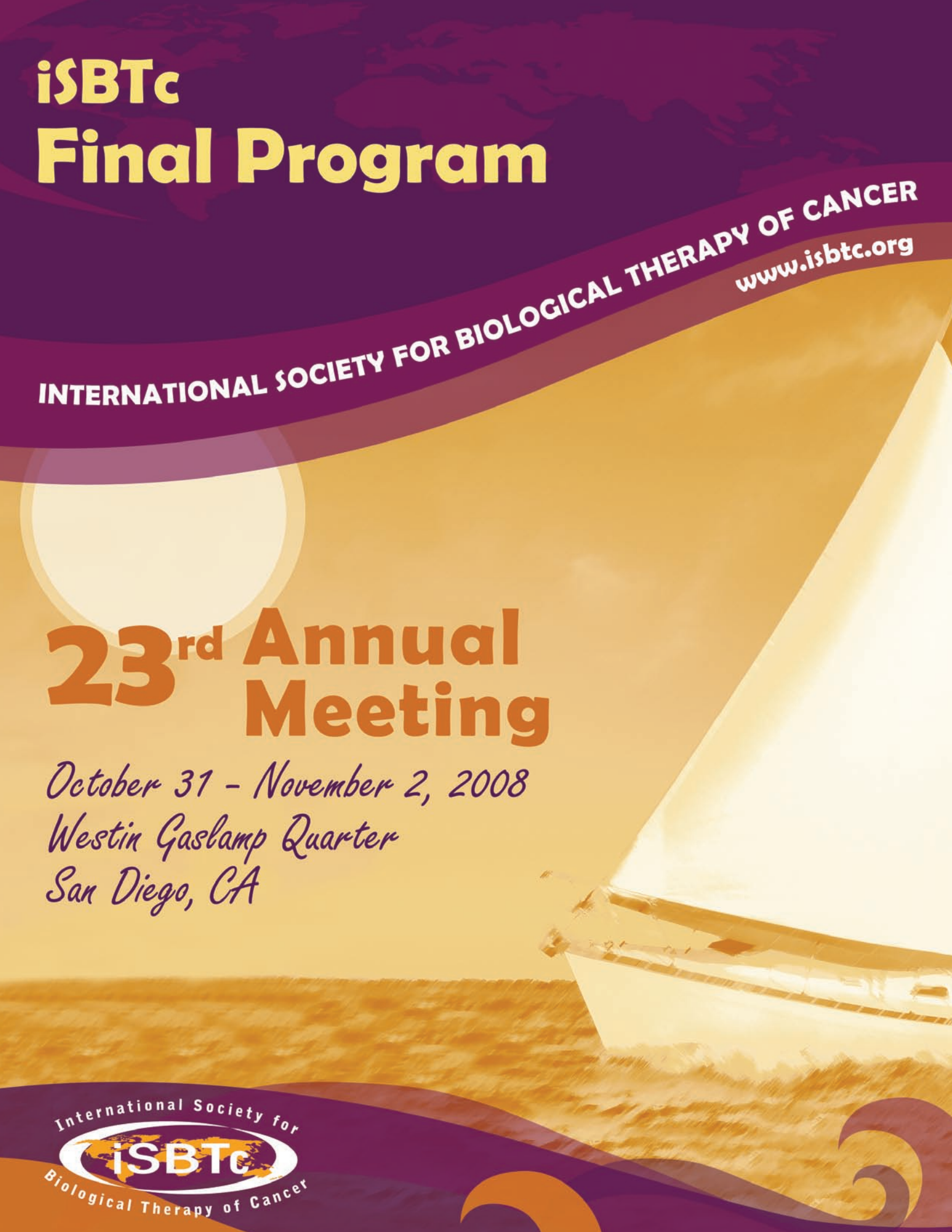
iSBTc
Final Program

INTERNATIONAL SOCIETY FOR BIOLOGICAL THERAPY OF CANCER

www.isbtc.org



23rd Annual Meeting

October 31 – November 2, 2008
Westin Gaslamp Quarter
San Diego, CA

International Society for Biological Therapy of Cancer
iSBTc

2008 Supporters

General Support: MERCK ONCOLOGY

Annual Meeting Educational Support:

Bronze: biogen idec

Bristol-Myers Squibb Company

MEDAREX

Takeda MILLENNIUM THE TAKEDA ONCOLOGY COMPANY

Eisai

Copper: ANTIGENICS

AMGEN

Annual Meeting Promotional Support:

Silver: EMD SERONO

Center for Cancer Research, National Cancer Institute

Copper: CURAGEN

Alnylam PHARMACEUTICALS

Patron: BioLegend The path to legendary discovery™

immatics

Other: Celldex therapeutics

NOVARTIS ONCOLOGY

gsk GlaxoSmithKline Biologicals

MannKind Corporation

Primer Educational Support: nventa insight to impact

Program at a Glance

Wednesday, October 29, 2008

11:00 AM – 7:00 PM	Registration Open	California Foyer
1:00 PM – 8:00 PM	Global Regulatory Summit: Considerations in the Development of Oncology Biologics Products for the Treatment of Cancer*	California B-C

Thursday, October 30, 2008

6:30 AM – 6:00 PM	Registration Open	California Foyer
7:00 AM – 8:00 AM	Continental Breakfast	California A
7:45 AM – 5:45 PM	Workshop on Cancer and Inflammation: Promise for Biological Therapy*	California B-C
8:00 AM – 5:00 PM	Primer on Tumor Immunology and Biological Therapy of Cancer *	Plaza Room

Friday, October 31, 2008

6:30 AM – 5:00 PM	Registration Open	California Foyer
7:00 AM – 8:00 AM	Continental Breakfast	California A
7:50 AM – 8:00 AM	23rd Annual Meeting Begins / President's Welcome	California B-C
8:00 AM – 8:45 AM	Richard V. Smalley, MD Memorial Lectureship: Giorgio Parmiani, MD	California B-C
8:45 AM – 11:30 AM	Plenary Session: Enhancing Cancer Vaccines	California B-C
11:30 AM – 1:00 PM	Lunch / Exhibits	California A
12:00 PM – 1:00 PM	Poster Presentations: Session I	Garden Pavilion, 4th Floor
1:00 PM – 3:00 PM	Plenary Session: Adoptive Transfer	California B-C
3:15 PM – 4:45 PM	Concurrent Session I: TH-17, Cytokines and T Cell Subsets	California B-C
3:15 PM – 4:45 PM	Concurrent Session II: Endpoints, Response Criteria for Clinical Trial Design	Plaza Room
5:00 PM – 5:30 PM	iSBTc Membership Business Meeting	California B-C
5:30 PM – 7:30 PM	Reception/Poster Presentations: Session I	Garden Pavilion, 4th Floor

Saturday, November 1, 2008

7:00 AM – 5:00 PM	Registration Open	California Foyer
7:00 AM – 8:00 AM	Continental Breakfast	California A
8:00 AM – 8:45 AM	Keynote Address: Robert D. Schreiber, PhD	California B-C
8:45 AM – 11:30 AM	Plenary Session: Tumor Escape / Tumor Microenvironment	California B-C
11:30 AM – 1:00 PM	Lunch / Exhibits	California A
12:00 PM – 1:00 PM	Poster Presentations: Session II	Garden Pavilion, 4th Floor
1:00 PM – 2:20 PM	iSBTc Presidential Abstract Session	California B-C
2:45 PM – 4:15 PM	Concurrent Session I: Tumor Targeting Monoclonal Antibodies	Plaza Room
2:45 PM – 4:15 PM	Concurrent Session II: Innate Immunity to Tumors	California B-C
4:30 PM – 5:00 PM	Update: 2007 Workshop on Future Opportunities for Combination Biological Therapy of Cancer	California B-C
5:00 PM – 5:15 PM	Award Presentations	California B-C
5:15 PM – 7:15 PM	Presidential Reception / Poster Presentations: Session II	Garden Pavilion, 4th Floor

Sunday, November 2, 2008

7:00 AM – 11:00 AM	Registration Open	California Foyer
7:00 AM – 8:00 AM	Continental Breakfast	California A
8:00 AM – 10:15 AM	Plenary Session: Cancer Stem Cells and the Host Response	California B-C
10:15 AM	Annual Meeting Adjourns	
10:30 AM – 12:00 PM	Hot Topic Symposium: Anti-CTLA-4: Issues in Development and Regulatory Approval*	California B-C

**denotes Associated Program with separate registration required*

President's Message

photo courtesy of Michael Hoetzel ©

Dear iSBTc Members and Colleagues,

Welcome to San Diego and the 23rd Annual Meeting of the International Society for Biological Therapy of Cancer (iSBTc)!

This year's programming promises to expand iSBTc's tradition of providing high-quality, cutting-edge education and networking in the field of biological therapy of cancer. In addition to our yearly Primer on Tumor Immunology, interactive Workshop and Annual Meeting program, we are excited to offer new initiatives such as the "Global Regulatory Summit: Considerations in the Development of Oncology Biologics Products for the Treatment of Cancer" and a Hot Topic Symposium on "Anti-CTLA-4: Issues in Development and Regulatory Approval."

With the addition of these programs, the iSBTc Annual Meeting and Associated Programs strengthens its reputation as the premier venue for scientific exchange and collaborative interaction among investigators from academia, industry, and regulatory agencies in the U.S. and abroad with a specific focus on tumor immunology and the biological therapy of cancer.

For our returning members and attendees, you will find new features within the program to enhance your experience. For those attending for the first time, we would like to welcome you and hope that you have an informative and productive meeting.

Highlights of the program include:

- *NEW* - Global Regulatory Summit on Wednesday
- *NEW* - Poster Presentation Receptions on Friday and Saturday evening
- Richard V. Smalley, MD Memorial Lectureship by Giorgio Parmiani, MD on Friday
- iSBTc Presidential (Young Investigator) Abstract Session on Saturday
- *NEW* - Hot Topic Symposium on Anti-CTLA-4 on Sunday

As President of the iSBTc, I would like to extend my gratitude to the program organizers who developed and organized these outstanding programs and the distinguished faculty who have offered their knowledge, expertise and time. Additionally, thank you to our exhibitors and industry supporters for their participation and generosity in supporting the programs this year.

Sincerely,

Jon M. Wigginton, MD
iSBTc President

Table of Contents

International Society for Biological Therapy of Cancer

555 East Wells Street, Suite 1100
Milwaukee, WI 53202-3823
Phone: 414-271-2456
Fax: 414-276-3349
info@isbtc.org
www.isbtc.org

iSBTc Information and Leadership

iSBTc Profile

The International Society for Biological Therapy of Cancer (iSBTc) was established in 1984 to facilitate the exchange and promotion of scientific information about the use of biological cancer therapies. iSBTc defines biological cancer therapies as those based on host response mechanisms used to control or prevent tumor growth. iSBTc is a 501 (c)(3) not for profit organization of medical professionals with a constituency of academic, government, industry, clinical, and basic scientists from around the world. The Society was founded on the belief that new systemic therapeutic treatments would continue to complement chemotherapies and move into the mainstream in the fight against cancer. To aid in this effort, iSBTc provides channels for the constructive discussion of current clinical trial results and methodologies, as well as a means to collaborate on new initiatives in tumor immunology and biological therapy. It is these key interactions and innovations that help advance the progress of cancer research and therapies and ultimately lead to better patient outcomes.

Core Purpose

To improve cancer patient outcomes by advancing the development and application of biological therapy.

Core Values

- **Interaction** – exchange of information and education among basic researchers and clinicians
- **Innovation** – development and application of biological therapy; seeking the best research and thinking related to the Society's purpose and vision
- **Leadership** – defining what is new and important

iSBTc Composition

Disease States – iSBTc programming and membership covers the full spectrum of both solid tumors and hematologic malignancies including:

- Breast
- Colorectal
- Head & Neck
- Hepatocellular
- Kidney
- Leukemia
- Lung
- Lymphoma
- Melanoma
- Neuroblastoma
- Ovarian
- Prostate
- Renal Cell

Medical Specialties – iSBTc members and delegates represent many areas of biological science including:

- Cell Biology
- Dermatology
- Genetics
- Gynecologic Oncology
- Hematology
- Immunotherapy
- Internal Medicine
- Medical Oncology
- Microbiology
- Molecular Biology
- Pediatric Oncology
- Pharmacology / Toxicology
- Radiation Oncology
- Radiology
- Stem Cell Biology
- Surgical Oncology
- Transplantation

iSBTc Leadership

Officer Directors

President
Jon M. Wigginton, MD
Merck & Co., Inc.

Vice President
Bernard A. Fox, PhD
Earle A. Chiles Research Institute

Immediate Past President
Ulrich Keilholz, MD
Charité CBF

Treasurer
Mario Sznol, MD
Yale University School of Medicine

At-Large Directors

Lisa H. Butterfield, PhD
University of Pittsburgh

William E. Carson, III, MD
Ohio State University

George Coukos, MD, PhD
University of Pennsylvania Medical Center

Mary L. Disis, MD
University of Washington

Thomas F. Gajewski, MD, PhD
University of Chicago

Jared A. Gollob, MD
Alnylam Pharmaceuticals

Rachel W. Humphrey, MD
Bristol-Myers Squibb

Patrick Hwu, MD
MD Anderson Cancer Center

Pedro J. Romero, MD
Ludwig Institute of Cancer Research

iSBTc Staff

Tara Withington, CAE
Executive Director

Angela Kilbert
Associate Director of Education and Meetings

Chloe Surinak
Senior Project Manager

Roseann Marotz
Meetings Manager

MelissaKaye Shekoski
Administrative Coordinator

Erin Hankey
Administrative Assistant

General Meeting Information

Welcome to the 23rd Annual Meeting and Associated Programs of the International Society for Biological Therapy of Cancer (iSBTc) held October 29 – November 2, 2008 at the Westin Gaslamp Quarter Hotel in San Diego, California. The Annual Meeting offers delegates an international forum where immunologic and biologic approaches to cancer treatment are showcased, discussed, and critically evaluated. This year's program features two exceptional keynote speakers: Giorgio Parmiani, MD from San Raffaele Foundation and Robert D. Schreiber, PhD from Washington University in St. Louis. Dr. Parmiani's keynote presentation is also a part of the *Richard V. Smalley, MD Memorial Award and Lectureship*.

iSBTc is proud to present the 4th Annual *Richard V. Smalley, MD Memorial Award* to Dr. Giorgio Parmiani. The *Smalley Award* serves as recognition of excellence in the field of therapeutic research with biological agents and is represented by a commemorative statue and accompanied by an honorarium of $5,000. The presentation of the award coincides with Saturday's Presidential / Poster Reception. More information about the *Richard V. Smalley, MD Memorial Award and Lectureship* can be found on page 9.

In addition to the featured keynote presentations, the iSBTc Annual Meeting sessions include presentations from both invited speakers and abstract presenters. For additional interaction and networking, iSBTc hosts poster presentation receptions on Friday and Saturday evenings. These events provide all iSBTc Annual Meeting delegates with opportunities to view and discuss posters and connect with iSBTc leadership, program faculty, and other researchers and clinicians interested in biological therapy and tumor immunology.

Exhibits

The 23rd Annual Meeting showcases a number of exhibitors whose products and services are on display for all meeting attendees to view. Exhibit booths are open on Friday and Saturday and are staffed throughout the day including during all breaks and lunches. For a complete exhibitor map and listing, please refer to pages 14-15.

Exhibit Hours	
Friday, October 31	10:00 AM – 4:00 PM
Saturday, November 1	10:00 AM – 4:00 PM

Membership

Meeting attendees who are members of iSBTc are designated by red "Member" ribbons on their name badges. Information on membership classifications, benefits, and dues can be found on page 70. All non-members are invited to complete the membership application form on page 71 and return it to the iSBTc Registration Desk.

Registration

Registration packets are ready for pick up at the iSBTc Registration Desk located in the California Foyer of the Westin Gaslamp Quarter Hotel for those who are pre-registered for the Annual Meeting and/or Associated Programs. On-site registration for the Annual Meeting and Associated Programs is accepted, space permitting. Separate registration fees are required for the Global Regulatory Summit on Wednesday, October 29 and the Primer and Workshop on Thursday, October 30. Although Sunday's Hot Topic Symposium requires a separate registration, there is no fee for attending.

Registration Desk Hours	
Wednesday, October 29	11:00 AM – 7:00 PM
Thursday, October 30	6:30 AM – 6:00 PM
Friday, October 31	6:30 AM – 5:00 PM
Saturday, November 1	7:00 AM – 5:00 PM
Sunday, November 2	7:00 AM – 11:00 AM

Session and Poster Topics

- Adoptive Transfer
- Cancer and Inflammation +
- Cancer Stem Cells and the Host Response
- Co-Stimulation / Immunoregulation *
- Dendritic Cells *
- Endpoints, Response Criteria for Clinical Trial Design
- Enhancing Cancer Vaccines
- Infectious Agent Vectors *
- Innate Immunity to Tumors
- New Agents *
- TH-17, Cytokines and T Cell Subsets
- Trafficking and *in vivo* Imaging *
- Tumor Escape / Tumor Microenvironment
- Tumor Targeting Monoclonal Antibodies
- Late-Breaking Abstracts

(*) *Presentations for these categories are posters only*

(+) *Oral presentations for this category are presented at Thursday's Workshop; posters are available for viewing on Saturday.*

General Meeting Information

Oral Abstracts

The iSBTc has selected the highest scoring abstract entries for oral presentations within the various meeting sessions. Each oral abstract presentation is followed by a five-minute question and answer period. For a complete listing of the selected oral abstract presenters, please see page 25.

Poster Abstracts

Abstracts selected for poster presentation for the 23rd Annual Meeting are on display at various times on the 4th Floor in the Garden Pavilion.

Posters in the categories of: Adoptive Transfer; Dendritic Cells; Endpoints, Response Criteria for Clinical Trial Design; Enhancing Cancer Vaccines; and TH-17, Cytokines and T Cell Subsets (#1-72) will be presented from 12:00 PM – 1:00 PM and 5:30 PM – 6:30 PM on Friday and available for viewing from 10:00 AM – 7:30 PM on Friday.

Posters in the categories of: Cancer and Inflammation; Cancer Stem Cells and the Host Response; Co-stimulation / Immunoregulation; Infectious Agent Vectors; Innate Immunity to Tumors; New Agents; Trafficking and *in vivo* Imaging; Tumor Escape / Tumor Microenvironment; Tumor Targeting Monoclonal Antibodies; and Late-Breaking Abstracts (#73-141) will be presented from 12:00 PM – 1:00 PM and 5:30 PM – 6:30 PM on Saturday and available for viewing from 10:00 AM – 7:15 PM on Saturday. Please see page 54 or the Poster Abstract Book for this year's poster listings. During the presentation times listed, designated posters are staffed by their respective authors, allowing for information exchange and interaction between researchers and attendees.

Poster Hall Hours

Friday Posters **10:00 AM – 7:30 PM**

Adoptive Transfer
Dendritic Cells
Endpoints, Response Criteria for Clinical Trial Design
Enhancing Cancer Vaccines
TH-17, Cytokines and T Cell Subsets

Saturday Posters **10:00 AM – 7:15 PM**

Cancer and Inflammation
Cancer Stem Cells and the Host Response
Co-stimulation / Immunoregulation
Infectious Agent Vectors
Innate Immunity to Tumors
New Agents
Trafficking and *in vivo* Imaging
Tumor Escape / Tumor Microenvironment
Tumor Targeting Monoclonal Antibodies
Late-Breaking Abstracts

Late-Breaking Abstracts

To fulfill iSBTc's commitment to the most cutting-edge science, late-breaking abstract submission was offered from August – September. The abstracts submitted were not available in time for printing in the *Journal of Immunotherapy* or consideration for oral presentation, but are available for viewing as posters on Saturday, November 1 in the "Late-Breaking Abstract" category. Copies of the late-breaking abstracts are also available in the Poster Abstract Book distributed with the meeting materials.

Poster Presentations/Staffing Hours

Friday Presentations: 12:00 PM - 1:00 PM & 5:30 PM - 6:30 PM

Poster Numbers 1-72 *(authors must be present)*
Adoptive Transfer (1-13)
Dendritic Cells (14-21)
Endpoints, Response Criteria for Clinical Trial Design (22-24)
Enhancing Cancer Vaccines (25-59)
TH-17, Cytokines and T Cell Subsets (60-72)

Saturday Presentations: 12:00 PM - 1:00 PM & 5:30 PM - 6:30 PM

Poster Numbers 73-141 *(authors must be present)*
Cancer and Inflammation (73-77)
Cancer Stem Cells and the Host Response (78)
Co-stimulation / Immunoregulation (79-84)
Infectious Agent Vectors (85-87)
Innate Immunity to Tumors (88-94)
New Agents (95-104)
Trafficking and *in vivo* Imaging (105)
Tumor Escape / Tumor Microenvironment (106-125)
Tumor Targeting Monoclonal Antibodies (126-129)
Late-Breaking Abstracts (130-141)

Continuing Medical Education

The iSBTc provides interested physicians the opportunity to earn Continuing Medical Education (CME) credits for attending the iSBTc Annual Meeting, Primer and Workshop. For more information on Workshop and Primer CME, please reference the iSBTc website at www.isbtc.org or the meeting materials provided to all registered attendees of those programs.

(Please note that CME credits are NOT offered for the Global Regulatory Summit or the Sunday Hot Topic Symposium).

Accreditation Statement

The iSBTc Annual Meeting has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Institute for the Advancement of Human Behavior, A Medical Education Company (IAHB-AMEDCO) and the International Society for Biological Therapy of Cancer (iSBTc). IAHB-AMEDCO is accredited by the ACCME to provide continuing medical education for physicians.

Designation Statement

The IAHB-AMEDCO designates the iSBTc Annual Meeting for a maximum of ***15.08 AMA PRA Category 1 Credits™***. Physicians should only claim credit commensurate with the extent of their participation in the activity.

- Friday: 6.5 *AMA PRA Category 1 Credits™*
- Saturday: 6.33 *AMA PRA Category 1 Credits™*
- Sunday: 2.25 *AMA PRA Category 1 Credits™*

Intended Audience

Basic and clinical investigators involved in cancer research comprising members of academic, pharmaceutical, and regulatory agencies including basic scientists, clinicians, graduate students and post-doctoral fellows, as well as allied health professionals.

Program Goals

- Promote scientific exchange of the most recent advances and data in the biological treatment of cancer, as well as advances in basic cancer biology with relevance for anti-tumor immunity
- Promote the generation of new ideas incorporating these advances and explore their potential for impact on treatment outcomes
- Discuss the latest clinical developments regarding application of biologic approaches and establish dialogue between academia, government and industry regarding implications as well as future directions
- Educate and provide perspective to the audience on the broad range of scientific developments in cancer and biological approaches to therapy
- Discuss therapeutic approaches to cancer immunotherapy including: cancer vaccines, adoptive T cell transfer, monoclonal antibodies, gene therapy, and use of cytotoxic or molecular targeting agents in combination with immune therapy
- Discuss current approaches to immunological monitoring
- Discuss current regulatory guidelines and how they impact clinical trials as well as resource availability

Expected Learner Outcomes

Upon completion of this meeting, participants will be able to:

- Summarize the most recent advances in cancer biology, how they intersect with the immune system, and how these considerations are relevant for the biologic therapy of cancer. These include but are not limited to: cancer stem cells, inflammation and cancer, cancer dormancy, and angiogenesis
- Discuss the latest information about clinical/translational work in cancer immunotherapy
- Establish how to solidify collaborations among the various members of academia, industry, and clinical practices to initiate clinical evaluation of these advances in more efficient trials
- Compare options available in trial design including immune monitoring techniques and compliance with regulatory guidelines
- Locate resources available through government agencies (funds, data-bases, tissue banks, etc.) that can facilitate translational research

Obtaining Your CME Certificates

To obtain your CME certificate for the iSBTc Primer, Workshop and/or Annual Meeting, go to **www.CmeCertificateOnline.com**. Scroll down to the iSBTc listing and click on the program for which you are claiming credit. Please note that each of the iSBTc programs have separate links and you will need to repeat the process in each program for which you are claiming credit.

On the certificate site, enter the password **ISBTC08CAMP**, select the sessions/presentations you attended and evaluate various aspects of the program. Your hours will be automatically calculated based on the sessions and programs you attend. It is recommended that you immediately print your certificate directly from this site. A copy of the certificate will also be e-mailed to you in case you need to print additional copies.

The online certificate site will only be available through **December 31, 2008**. After that date, the site and certificates will no longer be available. Please address any questions about the process to: Jay Parker; AMEDCO, LLC; Tel: 651-789-3716. For iSBTc staff assistance, please contact Angela Kilbert at akilbert@isbtc.org or call 414-271-2456.

Financial Disclosure Information

Please see the "Disclosures" section on page 26 for complete information regarding faculty disclosure of financial relationships.

Presidential and Travel Awards

iSBTc Presidential Awards

Four abstracts submitted in any category and authored by young investigators have been selected for 20-minute oral presentations during the Presidential Session from 1:00 PM – 2:20 PM on Saturday, November 1 in California B-C. Of those abstract presenters, all will receive Presidential Travel Awards and one will be selected as the 2008 Presidential Award winner. Judging of the presentations will be done by a committee of iSBTc leadership.

(1) Presidential Award winner receives:

- $1,000 Honorarium
- Up to $1,000 in Travel Reimbursement
- 1-Year Membership in iSBTc
- Commemorative Presidential Award Plaque

(3) Presidential Travel Award winners receive:

- Up to $750 in Travel Reimbursement
- 1-Year Membership in iSBTc
- Presidential Award Candidate Certificate

iSBTc Travel Awards

iSBTc has offered six travel awards to selected young investigators presenting posters at the iSBTc 23rd Annual Meeting. Judging was done by a committee of iSBTc leadership.

(6) iSBTc Travel Award winners receive:

- Up to $750 in Travel Reimbursement
- iSBTc Travel Award Winner Certificate
- "iSBTc Travel Award Winner" Ribbon

Previous iSBTc Award Winners

Presidential Award

2007 - Boston, MA
Amy Wesa, PhD
University of Pittsburgh School of Medicine
Pittsburgh, PA

Susanne Wilde
GSF National Center for Environment and Health
Munich, Germany

Presidential Travel Awards

Talya Schwarzberg, MD
Beth Israel Deaconess Medical Center
Boston, MA

Laura Strauss, PhD
San Raffaele Telethon Institute for Gene Therapy
Milan, Italy

iSBTc Travel Awards

Arvind Chhabra, PhD
University of Connecticut Health Center
Farmington, CT

Hideo Komita, MD
University of Pittsburgh
Pittsburgh, PA

Kerrington Molhoek, PhD
University of Virginia
Charlottesville, VA

Marta Santisteban, MD, PhD
Mayo Clinic
Rochester, MN

James Thompson, PhD
Earle A. Chiles Research Institute
Portland, OR

Meghaan Walsh
National Cancer Institute
Bethesda, MD

Presidential Award

2006 - Los Angeles, CA
Ulf Petrausch, MD
Earle A. Chiles Research Institute
Portland, OR

2005 - Alexandria, VA
Anne Letsch, MD
Charité - Campus Benjamin Franklin
Berlin, Germany

Ainhoa Pérez-Diez, PhD
National Institutes of Health
Bethesda, MD

2004 - San Francisco, CA
Luca Gattinoni, MD
National Cancer Institute - Surgery Branch
Bethesda, MD

Jiali Li, PhD
Stanford University
Stanford, CA

2003 - Bethesda, MD
Steven E. Finkelstein, MD
National Cancer Institute - Surgery Branch
Bethesda, MD

Christian Poehlein, MD
Earle A. Chiles Research *Institute*
Portland, OR

2002 - San Diego, CA
Erin B. Dickerson, PhD
University of Wisconsin-Madison - School of Veterinary Medicine
Madison, WI

2001 - Bethesda, MD
Julia A. Coronella, PhD
University of Arizona - Arizona Cancer Center
Tucson, AZ

2000 - Berlin, Germany
Annette Paschen, MD
University Clinics of Mannheim
Mannheim, Germany

2000 - Seattle, WA
Robbie Malliard
University of Pittsburgh
Pittsburgh, PA

1999 - Boston, MA
Roopa Srinivasan, PhD
Memorial Sloan Kettering Cancer Center
New York, NY

1998 - Pittsburgh, PA
Clemens Esche, MD
University of Pittsburgh
Pittsburgh, PA

1997 - Pasadena, CA
Pia M. Challita-Eid, PhD
University of Rochester Cancer Center
Rochester, NY

Tadashi Osaki, MD, PhD
University of Pittsburgh
Pittsburgh, PA

1996 - Washington, DC
Carmen Scheibenbogen, MD
University Hospital Benjamin Franklin Free University Berlin
Berlin, Germany

1995 - Williamsburg, VA
Jon M. Wigginton, MD
National Cancer Institute
Frederick, MD

1994 - Napa, CA
Laurence Zitvogel, MD, PhD
University of Pittsburgh
Pittsburgh, PA

1993 - Nashville, TN
David G. Maloney, MD, PhD
Stanford University
Stanford, CA

1992 - Williamsburg, VA
Carol A. Nieroda, MC
National Cancer Institute
Bethesda, MD

1991 - Pittsburgh, PA
Judith Kantor, PhD
National Cancer Institute
Bethesda, MD

Richard V. Smalley, MD Memorial Award and Lectureship

In memory of his many wonderful achievements, both professionally and personally, the International Society for Biological Therapy of Cancer (iSBTc) established the annual *Richard V. Smalley, MD Memorial Award* in 2005. The Smalley Award serves as recognition of excellence in the field of therapeutic research with biological agents and is accompanied by an honorarium of $5,000. The Smalley Award winner also provides an informative scientific lecture at the Annual Meeting as part of his/her acceptance.

2008 Richard V. Smalley, MD Memorial Award Winner

Giorgio Parmiani, MD

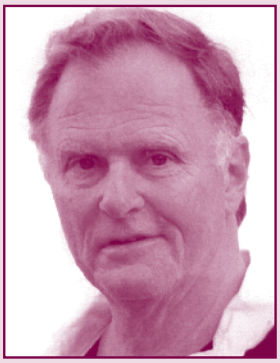
San Raffaele Foundation

In recognition of his outstanding research, work, and achievements in cancer therapy, the International Society for Biological Therapy of Cancer (iSBTc) proudly presents the 2008 *Richard V. Smalley, MD Memorial Award* to Giorgio Parmiani, MD. Dr. Parmiani presents the keynote address on Friday, October 31 from 8:00 AM – 8:45 AM in California B-C.

Giorgio Parmiani holds an MD from the University of Milan. He was trained in Tumor Immunology at the Institute for Cancer Research of Philadelphia (1970-71) under the supervision of Richmond T. Prehn, one of the founders of Modern Tumor Immunology. In Italy he worked at the Instituto Nazionale Tumori where, in 1984, he was appointed Director of the Division of Experimental Oncology and, in 1998, as Deputy Scientific Director and Head of the Department of Innovative Therapies. In 1994, he started the PhD Program in Molecular Oncology at the same institution. In January 2007, he moved to the San Raffaele Foundation Scientific Institute, where he is currently the Head of the Unit of Immuno-Biotherapy of Melanoma and Solid Tumors.

Dr. Parmiani's research interests have been focused on the study of Molecular Characterization of Human Tumor Antigens and the T-cell response to them, particularly in melanoma patients. His interests have also focused on studies of immunotherapy in melanoma, colorectal, and prostate cancer patients, primarily with gene-modified cellular vaccines, along with peptide or heat-shock protein-based vaccines.

Dr. Parmiani has published over 400 papers in the field of tumor immunology, mostly in internationally peer-reviewed journals. He has been awarded several national and international prizes. Dr. Parmiani has participated as invited speaker in many international meetings and has served as expert in several scientific committees and scientific advisory boards.



Richard V. Smalley, MD (1932 – 2004)

As one of the Society's charter members, Dr. Richard Smalley was an integral part of the iSBTc fabric from its inception. Dr. Smalley served on the original Board of Directors from 1984 – 1990, where he also served as the Society's third President from 1988 – 1990, leading the Society through some of its most formative years. In 1994 – 1998, while serving as iSBTc Treasurer, the environment for biological therapy began to change and the Society faced many challenges. During this time, Dr. Smalley showed inspirational devotion by meeting these challenges and administering the Society from his own home and nurturing its continued growth. iSBTc's success is due, in large part, to the consummate dedication and leadership of Dr. Richard Smalley.

Richard Vincent Smalley was born in New York City on June 21, 1932 and grew up in Larchmont, NY. He graduated from Hamilton College in 1953 and from the Temple University School of Medicine in 1957. After serving as a lieutenant in the United States Navy, he completed his residency at Temple University Hospital and his fellowship at Ohio State University.

Dr. Smalley was Professor of Medicine and Head of the Section of Medical Oncology at Temple University until 1981. He served as Branch Chief of the Biological Response Modifiers Program at the National Cancer Institute from 1982 – 1984. He worked in the Department of Human Oncology at the University of Wisconsin Cancer Center from 1984 – 1991, prior to starting his own cancer clinical trials management company, Synertron, Inc. A seven-year survivor of chronic lymphocytic leukemia, Dr. Smalley died of an unrelated brain tumor at his home in Edgewater, MD on January 17, 2004 at the age of 71.

Previous iSBTc Smalley Award Winners

2007 Recipient
Ernest Borden, MD
Cleveland Clinic Foundation

2006 Recipient
Ronald Levy, MD
Stanford University School of Medicine

2005 Recipient
Steven A. Rosenberg, MD, PhD
National Cancer Institute

Associated Programs

In association with the Annual Meeting, iSBTc holds several highly regarded educational programs: the Global Regulatory Summit on Wednesday, October 29; the Workshop and Primer on Thursday, October 30; and the Hot Topic Symposium on Sunday, November 2. These programs all require separate registration and some offer the opportunity to earn Continuing Medical Education (CME) credit. For more information about these associated programs, please visit the iSBTc Registration Desk located in the California Foyer.

Global Regulatory Summit

Wednesday, October 29 ~ 1:00 PM – 8:00 PM

The Wednesday program entitled "Global Regulatory Considerations in the Development of Oncology Biologics Products for the Treatment of Cancer," was developed to bring together the knowledge and insight of thought leaders at regulatory agencies from around the world to give a global perspective on regulatory considerations in the development of oncology biologics products for the treatment of cancer. Representatives from regulatory agencies in the United States, Europe, Germany, Japan, India, Canada, China and others will contribute to this program as faculty members and will discuss their country's regulatory perspectives and requirements as well as address audience questions. The Global Regulatory Summit is organized by Ulrich Kalinke, PhD and Raj K. Puri, MD, PhD.

Workshop on Cancer and Inflammation: Promise for Biological Therapy

Thursday, October 30 ~ 7:45 AM – 5:45 PM

This year's Workshop is a small group, interactive seminar that assembles leading experts in the field to discuss inflammation and its role in cancer. The program will cover the most recent data using inhibition of inflammation to both prevent cancer development and also increase the efficacy of cancer treatments. The goal for the Workshop is to provide a unique venue for scientific dialogue that ultimately results in a published manuscript that will outline the crucial outcomes formulated through the program's constructive discourse. The Workshop is organized by Lisa M. Coussens, PhD; Steven Dubinett, MD; Michael Karin, PhD; Michael T. Lotze, MD; and George J. Weiner, MD.

Primer on Tumor Immunology and Biological Therapy of Cancer

Thursday, October 30 ~ 8:00 AM – 5:00 PM

This year's Primer provides attendees a current overview of immunology as it applies to cancer etiology, biology, and therapy by leaders in the field and seeks to educate the audience on both the biologic underpinnings of the field, as well as recent basic science and clinical developments. Attendees will learn the current status and the most recent advances in biologic therapies including cancer vaccines, vaccine adjuvants, host-tumor interactions and the role of the innate and adaptive immune systems in tumor immunology and therapy. The Primer is organized by Patrick Hwu, MD and Kim Margolin, MD.

Hotel Information

The Westin Gaslamp Quarter Hotel San Diego serves as the headquarters for the iSBTc 23rd Annual Meeting and Associated Programs. It is located adjacent to the Horton Plaza Shopping and Entertainment mall, one of the nation's premier shopping centers and is just a short walk away from the historic San Diego Gaslamp District.

Transportation Options

Taxis, whether the traditional kind or "pedicabs," are readily available within the city. The Red Trolley is a public transit system which offers transportation from the Mexican border through downtown and Mission Valley to parts of the East County. The Old Town Trolley offers a stop just outside of the hotel and offers tours throughout San Diego's Old Town and Coronado Island. See the Westin Gaslamp Quarter Hotel's concierge for details about times and pricing.

Business Services

- Free Wireless High Speed Internet Access in Lobby

Recreation & Entertainment

- Running Maps by Runner's World with 3-mile and 5-mile jogging/walking routes
- WestinWORKOUT® Gym – open 24 hours a day
- Outdoor Swimming Pool
- In-room Spa
- Shopping at Horton Plaza

Hotel Dining

Cafe Express

For lighter fare and Starbucks coffee, visit our stylish café with comfortable leather chairs and bar stools, for surfing the web, reading the paper, or enjoying a light snack anytime. Complimentary wireless high speed internet access is available.

Hours: Monday - Friday, 6:30 AM - 9:00 PM
Saturday - Sunday, 6:30 AM - 6:00 PM

Café San Diego

Café San Diego is the ideal setting for a delicious and revitalizing breakfast. Choose from a menu or select from the buffet. Elevate your senses with an espresso, cappuccino, imported tea of your choice, or Starbucks coffee to go.

Hours: Monday - Friday, 6:30 AM - 10:30 AM
Saturday & Sunday, 6:30 AM - 11:30 AM

Horton's Bar & Grill

Offering a regionally-inspired menu in a casual, contemporary setting, Horton's Bar & Grill is the perfect place for lunch or dinner. On game night, we feature major sporting events on one of our numerous flat screen televisions.

Hours: Monday - Sunday, 11:30 AM - 1:30 AM

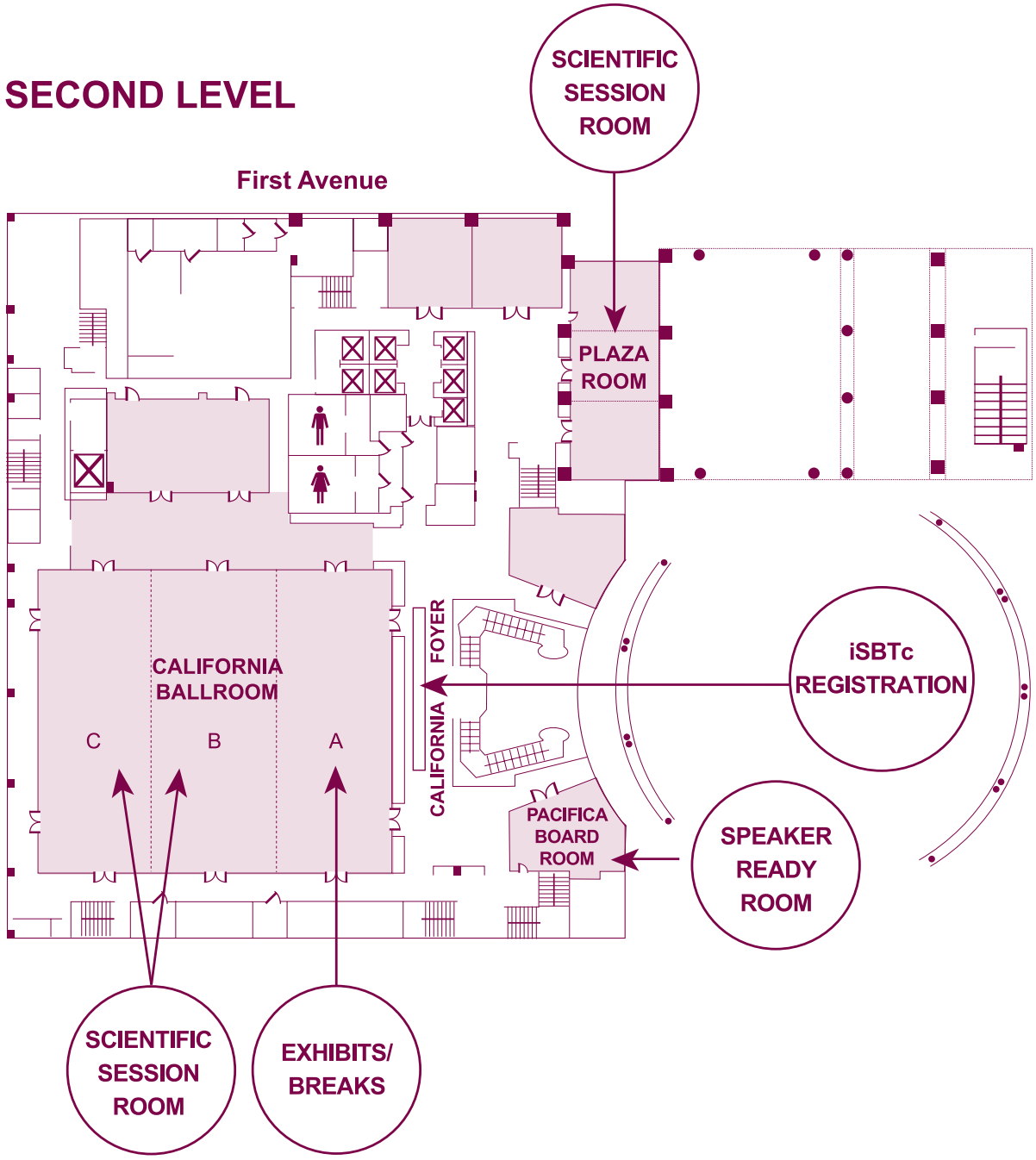
The Lobby Lounge

Relax and experience, unwind, a nightly Westin ritual, in the Lobby Lounge, with culturally distinctive beverage and food pairings.

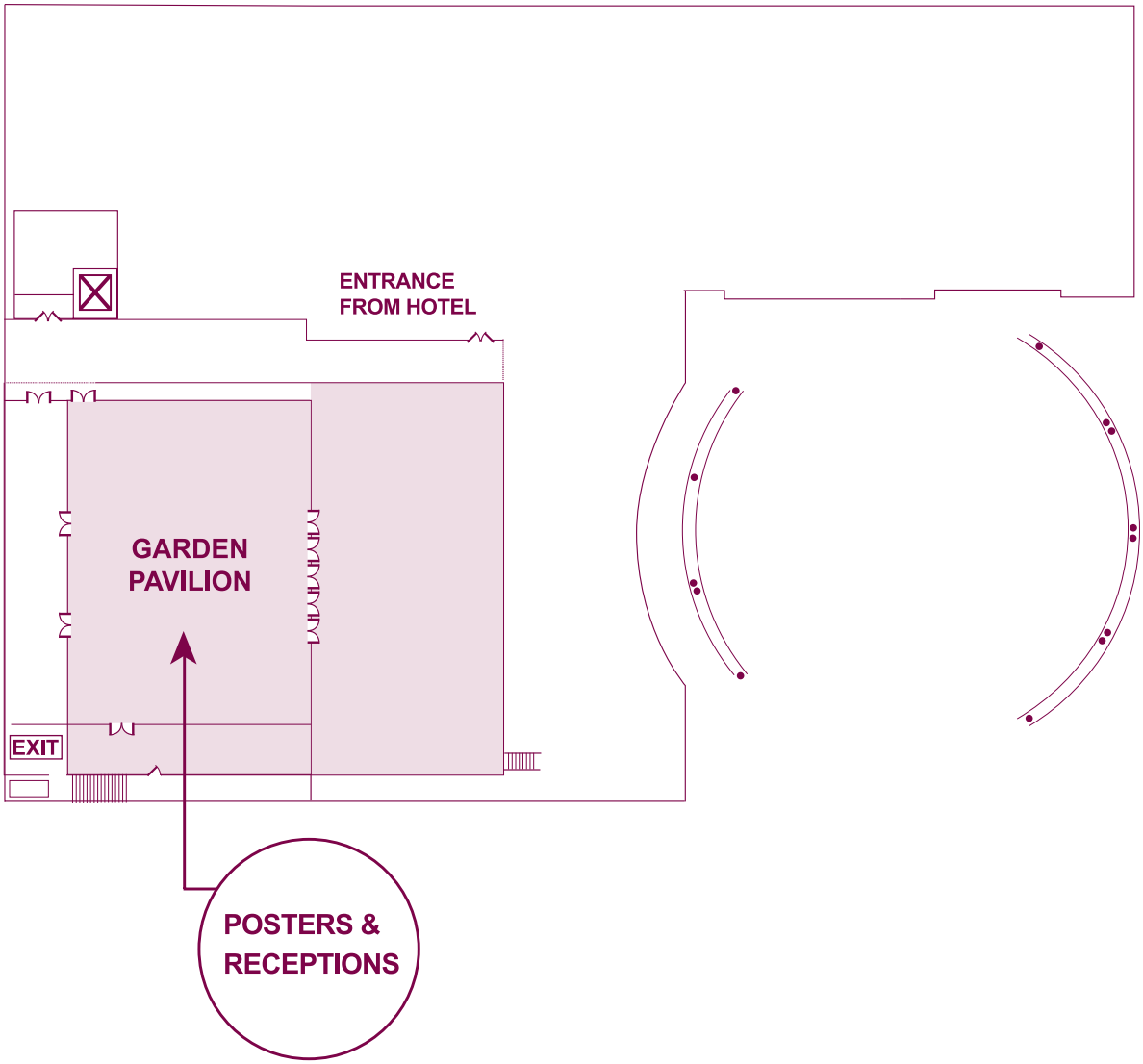
Hours: Monday - Sunday, 5:00 PM - 10:00 PM

Hotel Maps and Floor Plans

SECOND LEVEL

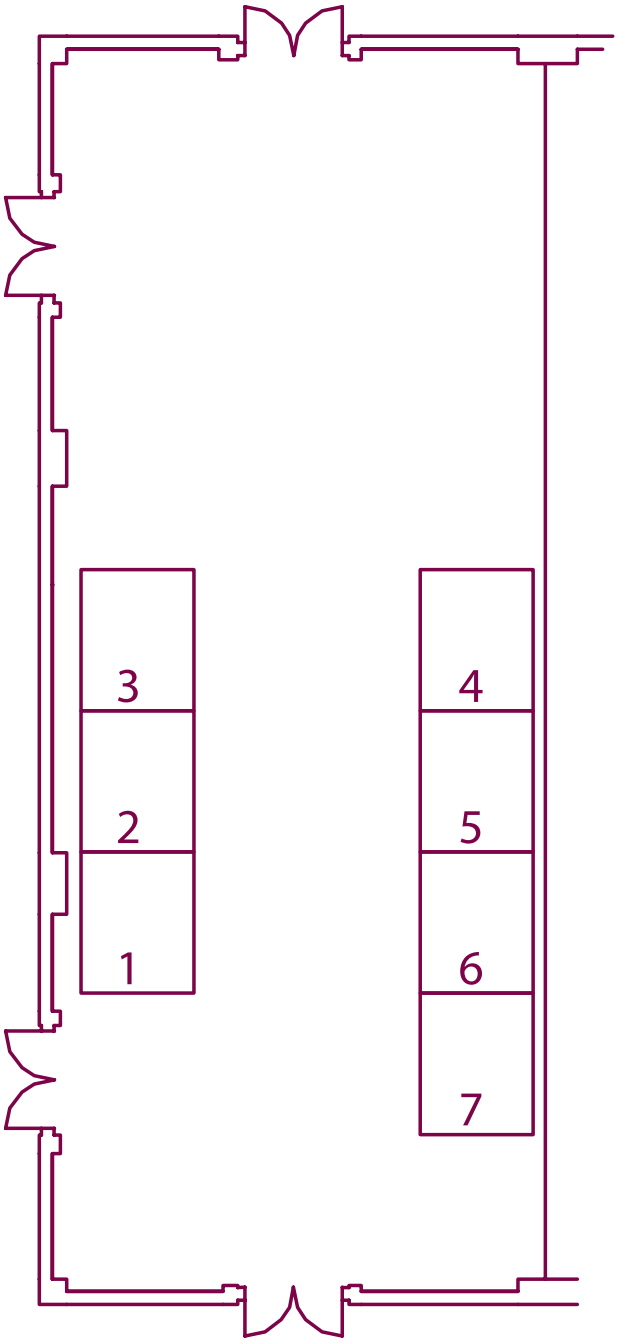


FOURTH LEVEL



Exhibitor Map

California A



Exhibitors:
Booth 1. CellGenix
Booth 2. Accuri Cytometers, Inc.
Booth 3. Novartis
Booth 4. Seppic, Inc.
Booth 5. BioLegend, Inc.
Booth 6. NeoMPS, Inc.
Booth 7. Novartis

Exhibitor Listing

Premier Exhibitors:

Novartis Oncology **Booth # 7**
One Health Plaza
East Hanover, NJ 07936-1080
Tel: 888-669-6682
www.TargetmTOR.com

At Novartis Oncology, our mission is to become the world's premier oncology company by consistently discovering, developing, and producing broadly available novel therapies that improve and extend the lives of cancer patients. Novartis Oncology offers treatments for breast cancer, leukemia, bone cancer, carcinoid tumors, kidney cancer and melanoma.

Novartis Oncology **Booth # 3**
180 Park Avenue
Florham Park, NJ 07932
Tel: 1-888-NOW-NOVA (1-888-669-6682)
Web: www.novartisoncology.us

Novartis Oncology delivers a broad range of innovative therapies to potentially improve and extend the lives of patients. These include Gleevec® (imatinib mesylate), Exjade® (deferasirox), Zometa® (zoledronic acid), Proleukin® (aldesleukin for injection), Sandostatin LAR® Depot (octreotide acetate for injectable suspension) and Femara® (letrozole tablets). Novartis Oncology has a robust pipeline capitalizing on recent discoveries in molecular genomics, rational drug design and state-of-the-art drug discovery technologies.

Basic Exhibitors:

Accuri Cytometers, Inc. **Booth #2**
173 Parkland Plaza
Ann Arbor, MI 48103
Tel: 734-994-8000
Fax: 734-994-8002
Web: www.AccuriCytometers.com

Accuri Cytometers introduces the full-featured C6 Flow Cytometer® System. Simple, affordable and powerful - the two-laser, six-detector C6 has capabilities similar to the market leader but is priced at 1/3 the market leader's price. The C6 collects six decades of dynamic range, all the time, eliminating errors involving incorrect gain or voltage settings. Plus, CFlow® software is so intuitive that you can be up and running within an hour of receiving your Accuri C6 Flow Cytometer System.

BioLegend, Inc. **Booth #5**
101080 Roselle Street
San Diego, CA 92121
Tel: 858-455-9588
Fax: 858-455-9587
Web: www.biolegend.com

Optimal Immunological Reagents, Outstanding Value. New Th17, Treg, Stem Cell, Cancer Biology, Innate Immunity Research Tools. Hot Products: IL-32, IL-17, VEGF-A, FOXP3, CXCR3, RORγt. New IHC-Validated Antibodies. More Colors: PerCP, PerCP/Cy5.5, Alexa Fluor®, Pacific Blue™… Flexible Sizes, Bulk Discounts. Low Endotoxin, Azide-Free (LEAF™) Antibodies for Functional Analyses. Complete ELISA kits.

CellGenix Technologie Transfer, GmbH **Booth #1**
16 Am Flughafen
Freiburg, Germany D-79108
49-761-88889-100

US Operations:
Richard Neubiser, VP GM
602 Hillside Ave.
Antioch, IL 60002
Tel: 847-395-7277
Fax: 847-395-0808
Web: www.cellgenix.com

CellGenix manufactures high quality cGMP produced cytokines and cell culture medium for ex-vivo dendritic, stem, NK, and T cell expansion and maturation protocols. We also offer research grade cytokines and distribute a line of GMP culture bags made from clear, inert, gas permeable FEP plastic used in expansion and maturation protocols. CellGenix is an innovative biotech company focusing on individualized cell and protein therapeutics for cancer treatment and orthopedic surgery. cGMP contract services are available.

NeoMPS, Inc. **Booth #6**
9395 Cabot Drive
San Diego, CA 92126
Tel: 800-338-4965/ 858-408-0808
Fax: 800-654-5592/ 858-408-0799
Web: www.mps-sd.com

NeoMPS is very excited to announce its recent merger with PolyPeptide Laboratories. NeoMPS/PolyPeptide is a leading provider of GMP and research grade peptides. With corporate roots that began in the 1950's, the group now has 6 GMP facilities located across 3 continents. Its world-class chemists and support personnel offer an unparalleled range of services for clients of every size and stage of development.

Seppic, Inc. **Booth #4**
30 Two Bridges Road, Suite 210
Fairfield, NJ 07004
Tel: 973-882-5597
Fax 973-992-5178
Web: www.seppic.com www.montanide.com

For more than 25 years, Seppic has developed vaccine adjuvants for human use. These adjuvants known under the name Montanide ISA 51 VG and Montanide ISA 720, have been used widely in immunotherapy against cancer with Phase III clinical trials in progress. Please visit us in our booth to get more information.

Program Schedule

Friday, October 31, 2008

6:30 AM - 5:00 PM	**Registration Open**	**California Foyer**
10:00 AM - 4:00 PM	**Exhibit Hall Open**	**California A**
10:00 AM - 7:30 PM	**Poster Hall Open**	**Garden Pavilion, 4th Floor**
7:00 AM - 8:00 AM	**Continental Breakfast**	**California A**
7:50 AM - 8:00 AM	**President's Welcome** Jon M. Wigginton, MD *Merck & Co., Inc.*	**California B-C**
8:00 AM - 8:45 AM	**Richard V. Smalley, MD Memorial Lectureship: Different Tumor Antigens in the Immunotherapy of Cancer: Are We Selecting the Right Target?** Giorgio Parmiani, MD *San Raffaele Foundation*	**California B-C**
8:45 AM - 11:30 AM	**Plenary Session: Enhancing Cancer Vaccines** Co-Chairs: Glenn Dranoff, MD - *Dana-Farber Cancer Institute* W. Martin Kast, PhD - *University of Southern California*	**California B-C**
8:45 AM - 9:15 AM	**Enhancing Cancer Vaccines Through Heterologous Prime Boost Strategies that Include VRP and that Induce Lifelong Protection from Prostate Cancer and Therapy of Cervical Cancer in Mice and Robust Cell-Mediated Immunity in Rhesus Macaques** W. Martin Kast, PhD *University of Southern California*	
9:15 AM - 9:30 AM	**Interleukin-15 and its Receptor Enhance Antitumor Activity Following a Genetically-Modified Dendritic Cell Vaccine** Jason C. Steel, PhD *National Cancer Institute, Metabolism Branch, NIH*	
9:30 AM - 9:45 AM	**T Cell Receptor-Dependent and Independent Pathways Control PD-1 Expression on CD8+ T cells Generated upon Intra Lymph Node Immunization** Adrian Bot, MD, PhD *MannKind Corporation*	
9:45 AM - 10:00 AM	**Cellular Immunotherapy and Immune Regulation in Ovarian Cancer** Martin J. Cannon, PhD *University of Arkansas for Medical Sciences*	
10:00 AM - 10:15 AM	**Intra-Lymphatic Continuous Infusion of Dendritic Cells in Patients with Advanced Melanoma: Early Indication of Clinical Efficacy** Pawel Kalinski, MD, PhD *University of Pittsburgh Cancer Institute*	
10:15 AM - 10:45 AM	**Refreshment Break**	**California A**

Friday, October 31, 2008 (continued)

10:45 AM - 11:00 AM	**Clinical Response to the MAGE-A3 Immunotherapeutic in Metastatic Melanoma Patients is Associated with a Specific Gene Expression Profile Present at the Tumor Site** Jamila Louahed, PhD *GlaxoSmithKline Biologicals SA*	
11:00 AM - 11:30 AM	**Balancing Tumor Immunity and Inflammation** Glenn Dranoff, MD *Dana-Farber Cancer Institute*	
11:30 AM - 1:00 PM	**Lunch and Exhibits**	**California A**
12:00 PM - 1:00 PM	**Poster Presentations: Session I** *(authors must be present)* **Poster Topics:** Adoptive Transfer Dendritic Cells Endpoints, Response Criteria for Clinical Trial Design Enhancing Cancer Vaccines TH-17, Cytokines and T Cell Subsets	**Garden Pavilion, 4th Floor**
1:00 PM - 3:00 PM	**Plenary Session: Adoptive Transfer** Co-Chairs: Helen E. Heslop, MD - *Baylor College of Medicine* William J. Murphy, PhD - *University of California Davis, School of Medicine*	**California B-C**
1:00 PM - 1:30 PM	**Three Ways to Enhance the Destructive Power of Tumor-Specific T Cells** Nicholas P. Restifo, MD *National Cancer Institute, NIH*	
1:30 PM - 2:00 PM	**Engineering GVL by T-Cell Genetic Modification** Michael C.V. Jensen, MD *City of Hope / Beckman Research Institute*	
2:00 PM - 2:15 PM	**Targeted Elimination of Brain Tumor Stem Cells with T Cell Therapies** Christine Brown, PhD *City of Hope National Medical Center*	
2:15 PM - 2:30 PM	**Intralesional Placement of Lymphokine-Activated Killer Cells After Resection of Primary Glioblastoma** Robert O. Dillman, MD *Hoag Cancer Center*	
2:30 PM - 2:45 PM	**Provision of CD4+ T Cell Help Prevents Tolerization of Tumor-Specific CTLs and Enhances Tumor Immunity in a Murine Model of Prostate Cancer** Kimberly Shafer-Weaver *SAIC/National Cancer Institute-Frederick, NIH*	
2:45 PM - 3:00 PM	**Rapid Expansion of Melanoma TIL in Adoptive Cell Therapy Leads to Loss of CD28 and Reduced Proliferative Potential in the MART-1-Specific T Cell Population** Yufeng Li *MD Anderson Cancer Center*	
3:00 PM - 3:15 PM	**Refreshment Break**	**California A**

Program Schedule

Friday, October 31, 2008 (continued)

3:15 PM - 4:45 PM	**Concurrent Session I: TH-17, Cytokines and T Cell Subsets** Co-Chairs: Martin Oft - *Schering-Plough Biopharma (formerly DNAX)* Hideaki Tahara, MD, PhD - *University of Tokyo*	**California B-C**
3:15 PM - 3:40 PM	**IL-23 Promotes Tumor Associated Inflammation and Subverts Immune Surveillance** Martin Oft *Schering-Plough Biopharma (formerly DNAX)*	
3:40 PM - 4:05 PM	**Potent Anti-Tumor Immunity and Both TH-1 and TH-17 Promotion Associated with IL-23 Administration** Hideaki Tahara, MD, PhD *University of Tokyo*	
4:05 PM - 4:30 PM	**TH-17 Cells in Ovarian Cancer Patients** Ilona Kryczek, PhD *University of Michigan*	
4:30 PM - 4:45 PM	**CD40 Dependent Induction of TH-17 Effector Cells from T Regulatory Cells Using the Immune Modulator B7-DC XAb** Suresh Radhakrishnan, PhD *Mayo Clinic, College of Medicine*	
3:15 PM - 4:45 PM	**Concurrent Session II: Endpoints, Response Criteria for Clinical Trial Design** Co-Chairs: Thomas A. Davis, MD - *Celldex Therapeutics, Inc.* Jeffrey Schlom, PhD - *National Cancer Institute, NIH*	**Plaza Room**
3:15 PM - 3:35 PM	**Immunotherapies in Combination with Other Therapeutic Modalities: New Paradigms for Clinical Trial Design** Jeffrey Schlom, PhD *National Cancer Institute, NIH*	
3:35 PM - 3:50 PM	**Overall Survival and New Patterns of Response in Patients with Advanced Melanoma Treated with Ipilimumab** Steven J. O'Day, MD *The Angeles Clinic and Research Institute*	
3:50 PM - 4:05 PM	**Identification of Antibody Responses Induced in Patients with Castration-Resistant Prostate Cancer Receiving GVAX Immunotherapy for Prostate Cancer** Karin Jooss, PhD *Cell Genesys, Inc.*	
4:05 PM - 4:25 PM	**Endpoints for Biologic Therapeutics in Oncology** Peter Bross, MD *FDA- Office of Cellular, Tissue, and Gene Therapies*	
4:25 PM - 4:45 PM	**Panel Discussion**	
5:00 PM - 5:30 PM	**iSBTc Membership Business Meeting** (iSBTc Members Only)	**California B-C**
5:30 PM - 7:30 PM	**Reception with Poster Viewing**	**Garden Pavilion, 4th Floor**

Friday, October 31, 2008 (continued)

5:30 PM - 6:30 PM	**Poster Presentations: Session I** *(authors must be present)* **Poster Topics:** Adoptive Transfer Dendritic Cells Endpoints Response Criteria for Clinical Trial Design Enhancing Cancer Vaccines TH-17, Cytokines and T Cell Subsets	**Garden Pavilion, 4th Floor**

Saturday, November 1, 2008

7:00 AM - 5:00 PM	**Registration Open**	**California Foyer**
10:00 AM - 4:00 PM	**Exhibit Hall Open**	**California A**
10:00 AM - 7:15 PM	**Poster Hall Open**	**Garden Pavilion, 4th Floor**
7:00 AM - 8:00 AM	**Continental Breakfast**	**California A**
8:00 AM - 8:45 AM	**Saturday Keynote Address:** **Cancer Immunoediting: Distinct Roles for Innate and Adaptive Immunity in Cancer Control and Promotion** Robert D. Schreiber, PhD *Washington University in St. Louis*	**California B-C**
8:45 AM - 11:30 AM	**Plenary Session: Tumor Escape / Tumor Microenvironment** Co-Chairs: Thomas F. Gajewski, MD, PhD - *University of Chicago* Weiping Zou, MD, PhD - *University of Michigan*	**California B-C**
8:45 AM - 9:15 AM	**Innate Immune Signals that Mediate Host Awareness of Tumor and Promote Adaptive Immune Responses Against Tumor Antigens** Thomas F. Gajewski, MD, PhD *University of Chicago*	
9:15 AM - 9:30 AM	**Persistent High Grade Cervical Dysplasia Excludes CD8+ T Cells** Cornelia L. Trimble, MD *Johns Hopkins University School of Medicine*	
9:30 AM - 10:00 AM	**Inhibitory B7 Family Members (B7-H1 and B7-H4) in the Tumor Microenvironment** Weiping Zou, MD, PhD *University of Michigan*	
10:00 AM - 10:15 AM	**L-Arginine Availability Regulates Cyclin D3 mRNA Stability in Human T Cells by Controlling HuR Expression** Paulo C. Rodriguez, PhD *Louisiana State University Health Science Center*	
10:15 AM - 10:45 AM	**Refreshment Break**	**California A**
10:45 AM - 11:15 AM	**Correcting the Anergy of Human Tumor-Infiltrating Lymphocytes?** Pierre van der Bruggen, PhD *Ludwig Institute for Cancer Research*	
11:15 AM - 11:30 AM	**Evidence for Selection of a Resistant Tumor Microenvironment Following Successful Clinical Response to a Multi-Peptide + IL-12 Melanoma Vaccine** Yuanyuan Zha, PhD *Human Immunologic Monitoring Facility, University of Chicago*	

Program Schedule

Saturday, November 1, 2008 (continued)

11:30 AM - 1:00 PM	**Lunch and Exhibits**	**California A**
12:00 PM - 1:00 PM	**Poster Presentations: Session II** *(authors must be present)* **Poster Topics:** Cancer and Inflammation Cancer Stem Cells and the Host Response Co-stimulation / Immunoregulation Infectious Agent Vectors Innate Immunity to Tumors New Agents Trafficking and *in vivo* Imaging Tumor Escape / Tumor Microenvironment Tumor Targeting Monoclonal Antibodies Late-Breaking Abstracts	**Garden Pavilion, 4th Floor**
1:00 PM - 2:20 PM	**Presidential Abstract Session** Chair: Jon M. Wigginton, MD - *Merck & Co., Inc.*	**California B-C**
1:00 PM - 1:20 PM	**Increasing Immunostimulatory Ability of Tolerogenic APCs Enhances Anti-Tumor Immunity** Stephanie K. Watkins, PhD *National Cancer Institute - Frederick, NIH*	
1:20 PM - 1:40 PM	**CCL28 a New Link Between Hypoxia Angiogenesis and Tumor Immune Evasion** Andrea Facciabene, PhD *University of Pennsylvania*	
1:40 PM - 2:00 PM	**Cytotoxic T Lymphocyte-associated Antigen 4 Blockade Enhances Polyfunctional NY-ESO-1 Specific T Cell Responses in Metastatic Melanoma Patients with Tumor Regression** Jianda Yuan, MD, PhD *Memorial Sloan-Kettering Cancer Center*	
2:00 PM - 2:20 PM	**Radiofrequency Ablation with KS-IL2 Immunocytokine (EMD 273066) Results in an Enhanced Antitumor Effect Against Murine Colon Adenocarcinoma** Erik Johnson, MD *University of Wisconsin-Madison*	
2:20 PM - 2:45 PM	**Refreshment Break**	**California A**
2:45 PM - 4:15 PM	**Concurrent Session I: Tumor Targeting Monoclonal Antibodies** Co-Chairs: Greg Lazar, PhD - *Xencor, Inc.* Helen Chen, MD - *National Cancer Institute, CTEP, NIH*	**Plaza Room**
2:45 PM - 3:15 PM	**Antibody and Small Moldular Immune Pharmaceutical Therapies for Patients with Chronic Lymphocytic Leukemia: A Major Step Forward** John C. Byrd, MD *The Ohio State University*	
3:15 PM - 3:30 PM	**Phase I/II Study of CR011-vcMMAE, an Antibody-Drug Conjugate Targeting GPNMB, for the Treatment of Patients with Advanced Melanoma** Patrick Hwu, MD *MD Anderson Cancer Center*	

Saturday, November 1, 2008 (continued)

3:30 PM - 4:00 PM	**Optimizing Engagement of the Immune System by Anti-Tumor Antibodies** John R. Desjarlais, PhD *Xencor, Inc.*	
4:00 PM - 4:15 PM	**Cetuximab Mediated Antibody Dependent Cellular Cytotoxicity by NK Cells Expressing Polymorphic Fc Gamma Receptor IIIa** Robert L. Ferris, MD, PhD *University of Pittsburgh Cancer Institute*	
2:45 PM - 4:15 PM	**Concurrent Session II: Innate Immunity to Tumors** Co-Chairs: Giorgio Trinchieri, MD - *National Cancer Institute, NIH* David Raulet, PhD - *University of California Berkeley*	**California B-C**
2:45 PM - 3:15 PM	**Innate Resistance, Inflammation, and Cancer** Giorgio Trinchieri, MD *National Cancer Institute, NIH*	
3:15 PM - 3:45 PM	**Role of NKG2D in Tumor Surveillance** David Raulet, PhD *University of California Berkeley*	
3:45 PM - 4:00 PM	**Innate Immunity Can Contribute to the Shaping of Tumor Immunogenicity in the Absence of Adaptive Immunity** Jack D. Bui, MD, PhD *University of California San Diego*	
4:00 PM - 4:15 PM	**Spontaneous CTL-mediated Rejection of GP33-positive Lewis Lung Carcinoma is Dependent on an IFNAR Competent Environment** Ulrich Kalinke, PhD *TWINCORE, Centre for Experimental and Clinical Infection Research*	
4:30 PM - 5:00 PM	**Update: 2007 Workshop on Future Opportunities for Combination Biological Therapy of Cancer** Jon M. Wigginton, MD *Merck & Co., Inc.*	**California B-C**
5:00 PM - 5:15 PM	**Awards Presentation**	**California B-C**
5:15 PM - 7:15 PM	**Presidential Reception with Poster Viewing**	**Garden Pavilion, 4th Floor**
5:30 PM - 6:30 PM	**Poster Presentations: Session II** *(authors must be present)* **Poster Topics:** Cancer and Inflammation Cancer Stem Cells and the Host Response Co-stimulation / Immunoregulation Infectious Agent Vectors Innate Immunity to Tumors New Agents Trafficking and *in vivo* Imaging Tumor Escape / Tumor Microenvironment Tumor Targeting Monoclonal Antibodies Late-Breaking Abstracts	**Garden Pavilion, 4th Floor**

Program Schedule

Sunday, November 2, 2008

7:00 AM - 11:00 AM	**Registration Open**	**California Foyer**
7:00 AM - 8:00 AM	**Continental Breakfast**	**California A**
8:00 AM - 10:15 AM	**Plenary Session: Cancer Stem Cells and the Host Response** Co-Chairs: Madhav Dhodapkar, MD - *The Rockefeller University* Max Wicha, MD - *University of Michigan*	**California B-C**
8:00 AM - 8:42 AM	**Regulation of Breast Cancer Stem Cells by the Microenvironment** Max Wicha, MD *University of Michigan*	
8:42 AM - 9:24 AM	**Harnessing the Immune System to Target Stem Cell Genes in Myeloma** Madhav Dhodapkar, MD *The Rockefeller University*	
9:24 AM - 9:49 AM	**Characterization of the Immune Profile of Cancer Stem Cells Isolated from Human Glioblastoma** Cristina Maccalli, PhD *San Raffaele Foundation Scientific Institute*	
9:49 AM - 10:15 AM	**CD133 as a Potential Target of Anti-cancer Stem Cell Immunotherapy: Identification of a HLA-A*02 Restricted CD133 Epitope** John S. Yu, MD *Cedars Sinai Medical Center*	
10:15 AM	**Annual Meeting Adjourns**	
10:15 AM - 10:30 AM	**Refreshment Break**	**California A**
10:30 AM - 12:00 PM	**Sunday Hot Topic Symposium:** **Anti-CTLA-4: Issues in Development and Regulatory Approval** See following page for a detailed schedule	**California B-C**

Hot Topic Symposium Schedule

Hot Topic Symposium: Anti-CTLA-4: Issues in Development and Regulatory Approval

Sunday, November 2 ~ 10:30 AM – 12:00 PM

Co-Chairs: Michael B. Atkins, MD – *Beth Israel Deaconess Medical Center*
Ulrich Keilholz, MD – *Charité CBF*

Program Goals

- Describe and discuss the development strategies for two antibodies aiming at the same immune checkpoint molecule CTLA-4 and the current status of these agents in comparison to the experience interleukin-2
- Create a forum to discuss complex clinical outcome issues such as tumor response after initial progression, durable response ("tail of the curve") in small subsets of patients without other treatment options, selection of responding patients that are commonly seen with active immunotherapies
- Discuss regulatory issues including the definition of patient benefit, optimal endpoints for single agent trials, design and conduct of enrichment studies and steps to combination therapy that are critical to the development of active immunotherapies
- Educate those new to the iSBTc community– students, faculty and industry representatives– regarding clinical development issues and strategies for immunologic agents

Expected Learner Outcomes

After attending the symposium, participants will be able to:

- Summarize the current results of clinical developments of anti-CTLA-4 antibodies
- Understand the complexity of regulatory issues and definition of outcome measures in cancer clinical trials utilizing biologicals
- Improve the design and implementation of their own research-aimed preclinical or clinical development of immunological agents and biomarkers

Sunday Hot Topic Schedule

10:30 AM - 10:35 AM	**Introduction** Ulrich Keilholz, MD *Charité CBF*
10:35 AM - 10:45 AM	**Review of Ipilmumab Development Program and Data** Jeffrey S. Weber, MD, PhD *H. Lee Moffitt Cancer Center and Research Institute*
10:45 AM - 10:55 AM	**Review of Tremilmumab Development Program and Data** Antoni Ribas, MD *UCLA Medical Center*
10:55 AM - 11:05 AM	**Comparison of Development Plans of IL2 and CTLA-4** Mario Sznol, MD *Yale University School of Medicine*
11:05 AM - 11:15 AM	**Evaluation of IL2/Anti-CTLA-4 Type Activity Data** Steven Hirschfeld, MD, PhD *National Institute of Child Health and Human Development*
11:15 AM - 12:00 PM	**Panel Discussion/Audience Questions** Moderator: Michael B. Atkins, MD *Beth Israel Deaconess Medical Center*
12:00 PM	**Closing Remarks** Ulrich Keilholz, MD *Charité CBF*

Faculty Listing

Annual Meeting Organizers

Thomas A. Davis, MD
Celldex Therapeutics, Inc.

Thomas F. Gajewski, MD, PhD
University of Chicago

William J. Murphy, PhD
University of California Davis, School of Medicine

Hideaki Tahara, MD, PhD
University of Tokyo

Richard V. Smalley, MD Memorial Lectureship Award Recipient

Giorgio Parmiani, MD
San Raffaele Foundation

Keynote Speaker

Robert D. Schreiber, PhD
Washington University in St. Louis

Session Co-Chairs / Moderators

Michael B. Atkins, MD*
Beth Israel Deaconess Medical Center

Helen Chen, MD
National Cancer Institute, CTEP

Thomas A. Davis, MD
Celldex Therapeutics, Inc.

Madhav Dhodapkar, MD
The Rockefeller University

Glenn Dranoff, MD
Dana-Farber Cancer Institute

Thomas F. Gajewski, MD, PhD
University of Chicago

Helen E. Heslop, MD
Baylor College of Medicine

W. Martin Kast, PhD
University of Southern California

Ulrich Keilholz, MD*
Charité CBF

Greg Lazar, PhD
Xencor, Inc.

William J. Murphy, PhD
University of California Davis, School of Medicine

Martin Oft
Schering-Plough Biopharma (formerly DNAX)

David Raulet, PhD
University of California Berkeley

Jeffrey Schlom, PhD
National Cancer Institute, NIH

Hideaki Tahara, MD, PhD
University of Tokyo

Giorgio Trinchieri, MD
National Cancer Institute, NIH

Max Wicha, MD
University of Michigan

Jon M. Wigginton, MD
Merck & Co., Inc.

Weiping Zou, MD, PhD
University of Michigan

Invited Speakers

Peter Bross, MD
FDA – Office Cellular, Tissue, and Gene Therapies

John C. Byrd, MD
Ohio State University

John R. Desjarlais, PhD
Xencor, Inc.

Madhav Dhodapkar, MD
The Rockefeller University

Glenn Dranoff, MD
Dana-Farber Cancer Institute

Thomas F. Gajewski, MD, PhD
University of Chicago

Steven Hirschfeld, MD, PhD*
National Institute of Child Health and Human Development

Michael C.V. Jensen, MD
City of Hope / Beckman Research Institute

W. Martin Kast, PhD
University of Southern California

Ilona Kryczek, PhD
University of Michigan

Martin Oft
Schering-Plough Biopharma (formerly DNAX)

David Raulet, PhD
University of California Berkeley

Nicholas P. Restifo, MD
National Cancer Institute, NIH

Antoni Ribas, MD*
UCLA Medical Center

Jeffrey Schlom, PhD
National Cancer Institute, NIH

Mario Sznol, MD*
Yale University School of Medicine

Hideaki Tahara, MD, PhD
University of Tokyo

Giorgio Trinchieri, MD
National Cancer Institute, NIH

Pierre van der Bruggen, PhD
Ludwig Institute for Cancer Research

Jeffrey S. Weber, MD, PhD*
H. Lee Moffitt Cancer Center and Research Institute

Max Wicha, MD
University of Michigan

Jon M. Wigginton, MD
Merck & Co., Inc.

Weiping Zou, MD, PhD
University of Michigan

***denotes Hot Topic Symposium Faculty**

Oral Abstract Presenter Listing

Adrian Bot, MD, PhD
MannKind Corporation

Christine Brown, PhD
City of Hope National Medical Center

Jack D. Bui, MD, PhD
University of California San Diego

Martin J. Cannon, PhD
University of Arkansas for Medical Sciences

Robert O. Dillman, MD
Hoag Cancer Center

Andrea Facciabene, PhD
University of Pennsylvania

Robert L. Ferris, MD, PhD
University of Pittsburgh Cancer Institute

Patrick Hwu, MD
MD Anderson Cancer Center

Erik Johnson, MD
University of Wisconsin - Madison

Karin Jooss, PhD
Cell Genesys, Inc.

Ulrich Kalinke, PhD
Twincore, Centre for Experimental and Clinical Infection Research

Pawel Kalinski, MD, PhD
University of Pittsburgh Cancer Institute

Yufeng Li
MD Anderson Cancer Center

Jamila Louahed, PhD
GlaxoSmithKline Biologicals SA

Cristina Maccalli, PhD
San Raffaele Foundation Scientific Institute

Steven O'Day, MD
The Angeles Clinic and Research Institute

Suresh Radhakrishnan, PhD
Mayo Clinic, College of Medicine

Paulo C. Rodriguez, PhD
Louisiana State University Health Science Center

Kimberly Shafer-Weaver
SAIC/National Cancer Institute - Frederick, NIH

Jason C. Steel, PhD
National Cancer Institute, Metabolism Branch, NIH

Cornelia L. Trimble, MD
Johns Hopkins University School of Medicine

Stephanie K. Watkins, PhD
National Cancer Institute - Frederick, NIH

John S. Yu, MD
Cedars Sinai Medical Center

Jianda Yuan, MD, PhD
Memorial Sloan-Kettering Cancer Center

Yuanyuan Zha, PhD
Human Immunologic Monitoring Facility, University of Chicago

Disclosures

Participant Financial Disclosure Information

It is the policy of iSBTc to ensure balance, independence, objectivity and scientific rigor in all educational activities. All presenters participating in any iSBTc-sponsored CME activity are required to disclose to iSBTc any real or potential conflict of interest that may have a direct bearing on the subject matter of the CME activity. This pertains to relationships with pharmaceutical companies, device manufacturers, or other corporations whose products or services are related to the subject matter of the presentation topic.

In accordance with the Accreditation Council for Continuing Medical Education (ACCME) standards and policies, the disclosures are critically reviewed to ensure any conflicts of interest are resolved prior to the educational program taking place.

The disclosures provided are inclusive of all faculty, organizers and planners for this educational intervention. In addition to the individual presenters, those that may be in a position of influence over the program such as the iSBTc Board of Directors, Scientific Program Committee and Staff are also listed here.

Disclosure Listing *(alphabetical)*

Jacques Banchereau
No relevant financial relationships

Adrian Bot
No relevant financial relationships

Peter Bross
No relevant financial relationships

Christine Brown
No relevant financial relationships

Jack Bui
No relevant financial relationships

Lisa H. Butterfield
No relevant financial relationships

John C. Byrd
No relevant financial relationships

Martin Cannon
DCV Technologies - Major Stockholder

William Carson
No relevant financial relationships

Helen Chen
No relevant financial relationships

George Coukos
No relevant financial relationships

Thomas A. Davis
No relevant financial relationships

John R. Desjarlais
Xencor, Inc. - Employee

Madhav Dhodapkar
No relevant financial relationships

Robert Dillman
No relevant financial relationships

Mary Disis
No relevant financial relationships

Glenn Dranoff
Novartis Pharmaceuticals - Grant/ Research Support
Novartis Pharmaceuticals - Consultant/ Scientific Advisor

Andrea Facciabene
No relevant financial relationships

Robert Ferris
No relevant financial relationships

Bernard A. Fox
No relevant financial relationships

Thomas Gajewski
No relevant financial relationships

Jared Gollob
No relevant financial relationships

Helen E. Heslop
No relevant financial relationships

Rachel Humphrey
Bristol-Myers Squibb - Employee

Patrick Hwu
No relevant financial relationships

Michael C.V. Jensen
No relevant financial relationships

Erik Johnson
No relevant financial relationships

Karin Jooss
Cell Genesys, Inc. - Employee

Ulrich Kalinke
No relevant financial relationships

Pawel Kalinski
No relevant financial relationships

W. Martin Kast
AlphaVax - Grant/Research Support
Wyeth - Grant/Research Support

Ulrich Keilholz
No relevant financial relationships

Angela Kilbert
No relevant financial relationships

Julian Kim
No relevant financial relationships

Ilona Kryczek
No relevant financial relationships

Disclosures

Greg Lazar
Xencor, Inc. - Employee

Yufeng Li
No relevant financial relationships

Jamila Louahed
GlaxoSmithKline Biologicals - Employee

Cristina Maccalli
No relevant financial relationships

Francesco Marincola
No relevant financial relationships

William J. Murphy
No relevant financial relationships

Steven O'Day
Bristol-Myers Squibb - Grant/Research Support
Bristol-Myers Squibb - Speaker's Bureau
Bristol-Myers Squibb - Consultant/Scientific Advisor

Martin Oft
Schering-Plough - Employee

Giorgio Parmiani
No relevant financial relationships

Suresh Radhakrishnan
No relevant financial relationships

David Raulet
Innate Pharma - Consultant/Scientific Advisor
Novo Nordisk - Grant/Research Support

Nicholas Restifo
No relevant financial relationships

Paulo Rodriguez
No relevant financial relationships

Pedro Romero
No relevant financial relationships

Jeffrey Schlom
No relevant financial relationships

Robert D. Schreiber
No relevant financial relationships

Kimberly Shafer-Weaver
No relevant financial relationships

Jason Steel
No relevant financial relationships

Chloe Surinak
No relevant financial relationships

Mario Sznol
Bayer - Consultant/Scientific Advisor
Schering-Plough - Grant/Research Support
Bristol-Myers Squibb - Consultant/Scientific Advisor
Curagen - Grant/Research Support
Medarex -Grant/Research Support
Pfizer - Consultant/Scientific Advisor

Hideaki Tahara
No relevant financial relationships

Cornelia Trimble
No relevant financial relationships

Giorgio Trinchieri
No relevant financial relationships

Pierre van der Bruggen
No relevant financial relationships

Stephanie Watkins
No relevant financial relationships

Max Wicha
No relevant financial relationships

Jon M. Wigginton
No relevant financial relationships

Tara Withington
No relevant financial relationships

John Yu
Immunocellular Therapeutics, Ltd. - Major Stockholder

Jianda Yuan
No relevant financial relationships

Arnold H. Zea
No relevant financial relationships

Yuanyuan Zha
No relevant financial relationships

Weiping Zou
No relevant financial relationships

Presentation Abstracts – Friday

(primary authors listed in italics)

Richard V. Smalley, MD Memorial Lectureship

DIFFERENT TUMOR ANTIGENS IN THE IMMUNOTHERAPY OF CANCER: ARE WE SELECTING THE RIGHT TARGET?

Giorgio Parmiani
Oncology, San Raffaele Scientific Institute, Milan, Italy

Human tumor antigens (Ags) include peptides recognized by T cells in the context of class I or class II HLA. These Ags have been grouped according to their molecular characterization and tissue distribution. Among them we described new mutation-derived Ags in melanoma cells and a new ubiquitary colon cancer Ag recognized by T cells of advanced but not early colon cancer patients. The group of shared/self and cancer/testis Ags have been used as vaccines in patients with different forms of cancer. While the first trials of phase I and II have been conducted with one or two such peptides, during the last few years multiple peptides have been administered simultaneously in an attempt to avoid selection of Ag-negative tumor cells by T lymphocytes elicited by vaccination. Peptide-based vaccines have been usually given emulsified in IFA-like adjuvant Montanide ISI 51 or pulsed onto autologous dendritic cells (DCs).

These phase I-II trials will be summarized that have resulted in a variable frequency (20-60%) of patients developing an anti-vaccine specific T cell response, while tumor regression have been reported in a minority of cases. An attempt to vaccinate patients with autologous tumor-derived gp96 heat shock proteins (possibly including mutation-derived Ags) led to tumor-specific T cell immune response in 50-60% of metastatic melanoma and colon carcinoma patients with evidence of better survival in immune responders as compared to non-responders. Recent experiments suggest that gp96 may work by a specific interaction with the CD91 receptor of plasmacytoid DCs.

A potential new target of immunotherapy is represented by cancer stem cells (CSC). We have evaluated the antigenic profile of glioblastoma CSC which showed impaired expression of HLA as compared with non-CSC counterparts; susceptibility to T and NKT cytotoxicity was also reduced. Several studies have addressed the reasons of the limited clinical outcome of vaccination. In addition to the previously defined escape mechanisms (e.g. down-regulation of HLA/peptide complexes by tumor cells), it has recently been shown that new factors may prevent tumor rejection even in the presence of an ongoing tumor-specific immune reaction induced by the vaccine. These are the activation of T regulatory lymphocytes and of myeloid-derived suppressor cells (MDSCs). We have found MDSC both in the blood and tumor tissue of patients with metastatic melanoma and colorectal cancer. Mechanisms underlying such suppressive activity, including the release of microvescicles, will be described. These principles have now been incorporated in designing new vaccination protocols with multipeptides in melanoma patients and early prostate cancer patients. Preliminary data of these trials will be presented.

Enhancing Cancer Vaccines

ENHANCING CANCER VACCINES THROUGH HETEROLOGOUS PRIME BOOST STRATEGIES THAT INCLUDE VRP AND THAT INDUCE LIFELONG PROTECTION FROM PROSTATE CANCER AND THERAPY OF CERVICAL CANCER IN MICE AND ROBUST CELL-MEDIATED IMMUNITY IN RHESUS MACAQUES

W. Martin Kast
Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA

HPV vaccines, based upon platforms of Venezuelan equine encephalitis virus replicon particles (VRP) and attenuated recombinant Vesicular Stomatitis Virus (VSV) vectors, both expressing mutated E7-E6 fusion proteins from the high-risk HPV16 and 18 genotypes, were tested in various homologous or heterologous prime-boost regimens in mice and in Rhesus macaques to assess levels of immunogenicity and anti-tumor immunity. Anti-tumor immunity was assessed by prophylactic and therapeutic vaccination with the HPV16 E7-E6 coding vectors in mice against HPV16-transformed tumors. Full protection from tumor challenge was observed after immunization with all three VRP/VRP, VSV/VSV, and VRP/VSV regimens. Therapeutic immunization of tumor-bearing mice showed 75% rejection of tumors in mice treated with VRP/VRP or VSV/VSV regimens and 100% rejection in mice treated with VRP/VSV combination strategies. Rhesus macaques vaccinated intramuscularly with three doses of VRP four weeks apart and boosted once with VSV showed very robust and sustained antigen-specific IFN gamma and IL-2 ELISPOT responses against HPV E6 and E7 peptides. In contrast to mice, only modest responses were detected after three doses of VRP alone or two doses of VSV alone in the macaques. In a separate TRAMP mouse prostate cancer model VRP in combination with DNA based vaccines both coding for the prostate cancer associated antigens PSCA or STEAP were able to induce lifelong protection against prostate cancer development when the male mice were vaccinated at an age of 8 weeks, which is the stage at which they have developed prostate intraepithelial neoplasia. All control vaccinated mice had succumbed of prostate cancer within a year but of the DNA prime VRP boost immunized mice 90% were alive and apparently healthy at month 12 and 65% at month 18. In conclusion, these strong in vivo anti-tumor responses both in cervical cancer and prostate cancer models and the unprecedented high cellular immune responses in non-human primates after heterologous VRP prime and VSV boost or in mice DNA prime and VRP boost provide strong justification for further development of the VRP platform and including it in heterologous prime-boost strategies especially for therapeutic anti-tumor vaccines that are used in a preventive setting.

Presentation Abstracts – Friday

(primary authors listed in italics)

INTERLEUKIN-15 AND ITS RECEPTOR ENHANCE ANTITUMOR ACTIVITY FOLLOWING A GENETICALLY-MODIFIED DENDRITIC CELL VACCINE

Jason C. Steel, Charmaine A. Ramlogan, Ping Yu, Thomas A. Waldmann, John C. Morris
Metabolism Branch, National Cancer Institute, Bethesda, MD

Background: Interleukin-15 (IL-15) has been shown to induce T and NK cell proliferation and differentiation, enhance cytolytic effector cells including antigen-experienced CD44hi CD8+ T memory cells, and enhance B-cell stimulation. Unlike IL-2, IL-15 does this without inducing T-regulatory cells or stimulating activation-induced cell death (AICD) thus making IL-15 an ideal adjuvant candidate for cancer vaccines. IL-15 functions through interaction with its receptor (IL-15Rα), presenting IL-15 in *trans* to immune effectors cells. The efficacy of exogenously administered IL-15 may be limited by the availability of IL-15Rα therefore a genetic vaccine expressing both the cytokine and its receptor may be advantageous. BALB-neuT transgenic mice develop breast cancers as a consequence of mammary gland-specific expression of an activated *neu* oncogene. We examined the antitumor effect of adenoviral-mediated gene transfer of the combination of IL-15 and IL-15Rα to augment a dendritic cell (DC) vaccine directed against the *neu* oncoprotein in these mice.

Methods: Bone marrow-derived DCs were generated from BALB/c mice and transduced with recombinant adenoviruses expressing a non-signaling truncated *neu* antigen, murine IL-15 and its receptor, IL-15Rα. Transgenic BALB-neuT mice at 10-12 weeks of age were subcutaneously vaccinated with four weekly injections of 1 x 10^6 genetically-modified DCs and followed for tumor development and immune response.

Results: Mice vaccinated with IL-15, IL-15Rα and the *neu* antigen, were protected from the onset of mammary carcinomas with 70% of animals tumor free at 25 weeks compared to 10% of animals treated with DC expressing the *neu* antigen alone, and none of the unvaccinated control mice. These mice also exhibited greater tumor protection than mice vaccinated with *neu* and either IL-15 (30% tumor free) or IL-15Rα (40% tumor free) alone. The combination of IL-15 and IL-15Rα lead to significantly greater antibody responses to the *neu* antigen compared to mice treated with DCs expressing *neu* alone, or *neu* combined with IL-15 or IL-15Rα alone. Serum from vaccinated mice exhibited antibody-dependant cellular cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) against *neu*-expressing target cells and induced down-regulation of *neu* signaling *in vitro*.

Conclusion: Co-expression of IL-15 in combination with its receptor augments antitumor vaccination with genetically-modified DCs expressing the neu antigen highlighting the potential for the use of IL-15 and IL-15Rα gene transfer as an adjuvant for anticancer vaccination.

Presentation Abstracts – Friday

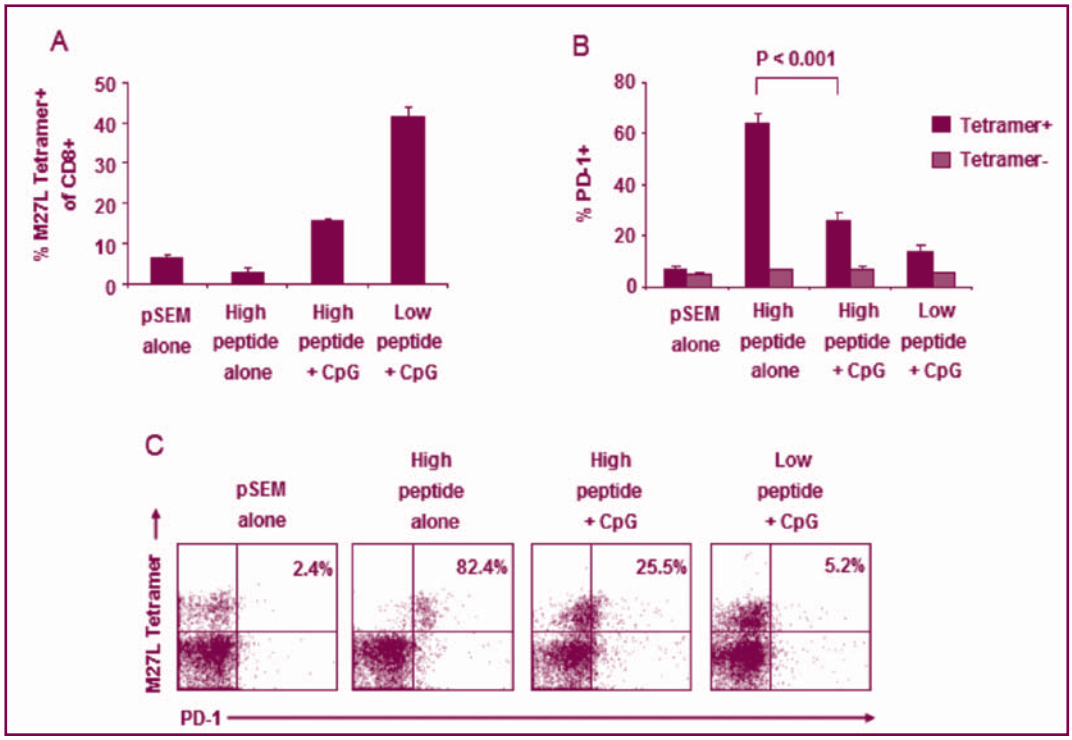
(primary authors listed in italics)

T CELL RECEPTOR-DEPENDENT AND INDEPENDENT PATHWAYS CONTROL PD-1 EXPRESSION ON CD8+ T CELLS GENERATED UPON INTRA LYMPH NODE IMMUNIZATION

Adrian Bot, *Raymond Wong*, Victor Tam, Brenna Meisenburg, Angeline Quach, Mayra Carrillo
MannKind Corp, Valencia, CA

Programmed Death-1 (PD-1) has been shown to be a marker for T cell activation; however, persistently elevated PD-1 expression is associated with T cell exhaustion, potentially a barrier to achieve optimal immunity against viruses and cancer antigens. Using a direct lymph node-targeted vaccination procedure that allows uncoupling of signal 1 (TCR-mediated) versus signal 2 (non TCR-mediated), we evaluated the impact of antigen-dependent and -independent signals on epitope-specific CD8+ T cell - associated PD-1 expression. The level of antigen exposure and costimulation mediated by CpG oligodeoxynucleotide (ODN) TLR9 agonist respectively, had dramatic yet opposite effects on overall PD-1 acquisition by specific CD8+ T cells. For example, high dose antigen exposure with minimal immune costimulation yielded CD8+ T cells with significantly elevated PD-1 expression. This was associated with impairment of IFN-γ secretion and proliferation in vitro, reversible upon antibody-mediated PD-1 blockade. By comparison, low antigen exposure in context of increased immune costimulatory signals - for example low dose peptide + CpG ODN adjuvant or DNA plasmid vaccination respectively - yielded CD8+ T cells with low PD-1 expression, greater in vitro proliferative capacity and increased IFN-γ secretion upon stimulation with cognate antigen. These findings shed light on molecular mechanisms involved with the homeostasis of CD8+ T cells and elucidate key features of DNA and similar vaccines that are currently investigated in several clinical trials.

Figure legend. PD-1 expression profile of peripheral blood epitope-specific CD8+ T cells elicited by DNA and peptide vaccination in HLA-A*0201 transgenic HHD-1 mice. A) M27L-specific immune response magnitude. B) PD-1 expression on M27L tetramer+ and tetramer- CD8+ T cells. C) Representative dot plots for M27L-specific CD8+ T cells. Upper right quadrants display percent of tetramer+ cells that are PD-1+. All data are representative of ≥ two independent studies. N = 10 per group. pSEM; DNA plasmid encoding human Melan A. M27L; human MelanA26-35(27L). Error bars; SEM.



Presentation Abstracts – Friday

(primary authors listed in italics)

CELLULAR IMMUNOTHERAPY AND IMMUNE REGULATION IN OVARIAN CANCER

Martin J. Cannon, Kellie L. Kozak, Timothy J. O'Brien
University of Arkansas for Medical Sciences, Little Rock, AR

While there is an increasing consensus that active immunotherapy or anti-tumor vaccination should be supported by selective and efficient prior depletion of tumor-associated regulatory T cells (Treg), there is also a new appreciation that DC vaccination itself may induce or expand Treg, promoting tumor-specific tolerance. Supporting the clinical observation that vaccination with cytokine-matured DC expands Treg in myeloma patients, we have found that ovarian tumor antigen-loaded DC matured with a standard cytokine cocktail (TNF, IL-1 and PGE2) activate and expand CD4+foxp3+ Treg in vitro. It is thus probable that DC activation of anti-tumor effector T cell responses would be seriously compromised. For DC vaccination to be clinically effective, the new challenge is to identify alternative pathways of DC and T cell differentiation that bias T cell responses away from Treg homeostasis and in favor of active anti-tumor immunity.

We have found that IL-15 treatment of DC and/or responder CD4+ T cells specific for serine protease ovarian tumor antigens diminishes T cell foxp3 expression and Treg activity, with resultant reciprocal enhancement of helper T cell function and tumor antigen-specific CD8+ cytotoxic T cell responses. We have also shown that IL-1 can antagonize IL-2-driven human Treg expansion, subverting responses to the reciprocally regulated Th17 phenotype. IL-1 conditioning also diminished CD4+ T cell CCR4 expression. As CCR4 is the receptor for CCL22, which is responsible for Treg homing in ovarian cancer, these results suggest that IL-1 would not only reduce Treg function, but also inhibit trafficking of foxp3+ Treg in the tumor microenvironment. Both IL-15 and IL-1 may thus regulate key points of cellular immune differentiation that are critical for the success of DC vaccination or adoptive T cell immunotherapy. Collectively, these results support the developing consensus that Treg and Th17 differentiation and expansion are reciprocally regulated, and suggest that subversion of Treg responses in favor of Th17 responses may have therapeutic benefit for cellular immunotherapy of ovarian cancer. Apart from inhibition of Treg activation, other benefits may accrue. First, IL-15 conditioning yields a dramatic increase in T cell expression of IL-17F, which has anti-angiogenic activity, and may thus have therapeutic value. Second, IL-15 IL-15-driven CD4+ Th17 responses correlate with enhancement of CD8+ T cell cytotoxicity. Third, Th17 responses are less sensitive than Th1 responses to Treg suppression, which may remain a barrier to immunotherapy in ovarian cancer patients, even in those pre-treated with cyclophosphamide or ONTAK to deplete tumor-associated Treg.

INTRA-LYMPHATIC CONTINUOUS INFUSION OF DENDRITIC CELLS IN PATIENTS WITH ADVANCED MELANOMA: EARLY INDICATION OF CLINICAL EFFICACY

Pawel Kalinski, Howard Edington, Lisa Butterfield, Theresa Whiteside, David Bartlett, John Kirkwood
University of Pittsburgh, Pittsburgh, PA

Therapeutic cancer vaccines need to function in the presence of suppressive T*regs* and $CD8^+$ CTLs present in peripheral tissues of cancer patients. In order to assure rapid delivery of "non-exhausted" dendritic cells (DCs) to the lymph nodes and to avoid their inactivation/elimination by peripheral T*regs* and CTLs, we have developed a semi-continuous intralymphatic mode of vaccine delivery, using implantable lymphatic cannulas. This approach allows the efficient and rapid delivery of vaccines to draining lymph nodes without disruption of the nodal structure. It also allows for repeated/semi-continuous delivery of vaccines over prolonged time periods, mimicking the kinetics of the migration and persistence of functional DCs during physiologic immune responses.

We have completed the initial safety evaluation of standard DC-based and αDC1-based semi-continuous intralymphatic vaccines (25,000 DC per injection; 12 injections over 4 days; a total of 300,000 DCs) in six patients with stage IIIb-IV melanoma in trial UPCI 03-118 and are now proceeding to the comparative evaluation of "high" doses (250,000 DC per injection) in additional 14 patients. Four of the initial six patients successfully completed the protocol and received two courses of the intralymphatic DC infusions. Two patients dropped out before the second course of treatment for the reasons unrelated to the protocol. Prolonged lymphatic cannulations and semi-continuous DC delivery were feasible and safe.

Unexpectedly, already at this ultra-low dose-level (10-100 fold fewer DCs than routinely-used doses of intradermal or intranodal vaccines) we have observed evidence of clinical efficacy of vaccination in 3/6 patients, including three of the four patients who received both courses of vaccination.

Among the four patients who successfully completed the protocol, progressive disease was observed only in one patient (stage IV). In the remaining three patients, we observed one stabilization of stage IV disease (lung; > 6 months long), and two partial antitumor responses in patients with stage IIIb disease (one near-complete and ongoing for >12 months; another ongoing for >2 months).
The current data demonstrate the feasibility of prolonged intralymphatic delivery of biotherapeutic agents in patients with advanced cancer and provide preliminary indication that DC-based cancer vaccines can be clinically effective at ultra-low doses, up to 100-fold lower than the doses currently considered as necessary.

Presentation Abstracts – Friday

(primary authors listed in italics)

CLINICAL RESPONSE TO THE MAGE-A3 IMMUNOTHERAPEUTIC IN METASTATIC MELANOMA PATIENTS IS ASSOCIATED WITH A SPECIFIC GENE EXPRESSION PROFILE PRESENT AT THE TUMOR SITE

Jamila Louahed[1], Olivier Gruselle[1], Swann Gaulis[1], Thierry Coche[1], Alexander M. Eggermont[2], Wim Kruit[2], Brigitte Dréno[3], Vanna Chiarion-Sileni[4], Laurent Mortier[5], Frederic F. Lehmann[1], Vincent G. Brichard[1]

[1]*GSK Biologicals, Rixensart, Belgium*

[2]*Erasmus Medical Center, Rotterdam, Netherlands*

[3]*C.H.R. Hotel Dieu, Nantes, France*

[4]*Azienda Ospedaliera, Padova, Italy*

[5]*C.H.R., Lille, France*

Background: This study was designed to select the optimal combination of MAGE-A3 recombinant protein with an Adjuvant System (EORTC 16032-18031/NCT00086866). In addition, gene expression profiling was used to identify markers predictive of the clinical activity of the MAGE-A3 ASCI recorded in this Phase II study.

Methods: 75 patients (pts) with progressive, unresectable stage III or stage IV M1a MAGE-A3 (+) melanomas, were randomized as 1st line therapy between immunization with MAGE-A3 protein and Adjuvant Systems AS15 or AS02B (GSK proprietary). Gene expression profiling (Affymetrix) was performed on tumor biopsies taken pre-immunization.

Results: 4 Objective responses (OR) were reported in the AS15 arm vs 1 OR in the AS02B arm. Stable disease (SD) ≥ 16 wk was reported in 5 pts in each arm and several mixed response (MxR) were reported in each arm.

Initial analysis using supervised hierarchical clustering of 2 OR with 7 non-responders identified 2 gene clusters based on differential expression. The correlation of this gene expression signature (GS) and OR was further confirmed on 22 pts. MxR and SD clustered with OR, suggesting a strong association between the identified signature and the MAGE-A3-induced clinical benefit. Independent validation on additional 30 pts confirmed the association of clinical benefit and GS. Most of the identified genes are immune-related, defining a particular biological context in the tumor environment before immunization. The signature was randomly distributed in the 2 study arms and identified all pts with clinical benefit (OR, MxR, SD). Selection of pts with the GS results in increased clinical efficiency as illustrated by the median time to treatment failure: 2.3 months in the GS (-) and 10.3 months in the GS (+) population (HR = 0.31; 95% CI: 0.13-0.76).

Conclusions: The AS15 arm has shown to induce a higher MAGE-A3 immune response and more frequent clinical activity. The gene expression in metastatic melanoma is strongly correlated with clinical activity to the MAGE-A3 ASCI treatment. This signature reflects an immune microenvironment in the tumor prior to MAGE-A3 ASCI treatment. Interestingly, this signature has also been independently reported to be correlated with clinical activity to MAGE-A3 treatment in a randomized double-blind Phase II study in resected NSCLC. In this setting, increased activity is also reported in the enriched populations. This predictive gene signature will be prospectively validated in future Phase III trials.

Presentation Abstracts – Friday

(primary authors listed in italics)

BALANCING TUMOR IMMUNITY AND INFLAMMATION

Glenn Dranoff
Dana-Farber Cancer Institute, Boston, MA

We demonstrated that vaccination with irradiated tumor cells engineered to secrete granulocyte-macrophage colony stimulating factor (GM-CSF) generates potent, specific, and long-lasting anti-tumor immunity in murine models through improved tumor antigen presentation by mature CD11b+ dendritic cells and macrophages. The coordinated activities of CD4+ and CD8+ T cells, CD1d-restricted invariant NKT cells, and antibodies accomplish protective immunity. Several Phase I clinical trials evaluating this immunization scheme in patients with disseminated tumors revealed the consistent elicitation in distant metastases of dense T and B cell infiltrates that effectuated substantial tumor necrosis and fibrosis. Moreover, the subsequent administration of a humanized blocking antibody against cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) accomplished additional tumor destruction with lymphocyte and granulocyte infiltrates in a majority of stage IV patients, in the absence of serious autoimmune toxicities. Detailed study of blood and tumor samples from patients on these trials revealed the induction of a broad cellular and humoral response to multiple tumor-associated antigens, including melanoma inhibitor of apoptosis protein (ML-IAP) and MHC class I chain-related protein A (MICA). Pathologic examination of tumor infiltrates following immunotherapy revealed a linear relationship between the extent of tumor necrosis and the natural logarithm of the ratio of CD8+ cytotoxic T cells to FoxP3 expressing regulatory T cells (Tregs).

Our recent investigations of GM-CSF deficient mice uncovered an unexpected critical role for this cytokine in Treg homeostasis. GM-CSF is required for the expression of the phosphatidylserine binding protein milk fat globule EGF-8 (MFG-E8) in antigen presenting cells, whereas the uptake of apoptotic cells by phagocyte-derived MFG-E8 stimulates peripheral Treg maintenance through TGF-β, MHC class II, and CCL22. In wild type mice, MFG-E8 limits the potency of GM-CSF secreting B16 melanoma vaccines through Treg induction, while a dominant negative MFG-E8 mutant (RGE) potentiates therapeutic immunity through Treg inhibition, resulting in the regression of established tumors. Together, these findings suggest that combinations of GM-CSF and MFG-E8 inhibition might improve the efficacy of cancer vaccines and complement the activity of CTLA-4 antibody blockade. Efforts to translate this combinatorial strategy involving MFG-E8 blockade into early stage clinical testing in advanced melanoma patients are underway.

(primary authors listed in italics)

Presentation Abstracts – Friday

Adoptive Transfer

THREE WAYS TO ENHANCE THE DESTRUCTIVE POWER OF TUMOR-SPECIFIC T CELLS

Nicholas P. Restifo
NCI, NIH, Bethesda, MD

Our goal is to design new immunotherapies for patients with advanced cancer using an iterative process of mouse and human studies. In studies performed at the NCI, Bethesda, we have observed that a variety of immunotherapies can induce objective response rates (ORR) in patients with metastatic melanoma. Cancer vaccines can induce ORR ranging from 3-7%, while ORR using IL-2 or anti-CTLA-4 range from 13-17%. ORR using adoptive cell therapy (ACT) plus IL-2 is higher at 34%, and this is in the absence of a lymphodepleting preparative regimen. However, three maneuvers might improve the function of adoptively transferred T cells.

1. Adding lymphodepleting chemotherapy prior to ACT improved ORR to 49% and adding radiotherapy has improved ORR to 72% (JCO, In Press): Some of these responses are complete and long-lasting. We have learned that total body irradiation (TBI) augments the function of adoptively transferred cells by depleting regulatory T cells (Treg), by removing immune cells that act as "sinks" for homeostatic cytokines, and by the activating the innate immune system.

2. The use of "young" T cells with stem cell-like properties in ACT enhances their effectiveness: Much progress has been made in identifying the phenotypic and functional characteristics of cells that are associated with successful ACT of large, established tumors in mice and in humans. We have found that the acquisition of effector function of CD8+ cells is associated with senescence and can limit anti-tumor efficacy upon adoptive transfer. Conversely, we have described that developmental arrest of CD8+ cells can be achieved using IL-21 and that this is associated with the enhanced function of anti-tumor T cell. Unpublished findings from the laboratory indicate that the developmental arrest of CD8+ T cells can be achieved at an even earlier stage, that of the "T memory stem cell" by pharmacologically simulating Wnt signaling.

3. CD4+ T cells can be powerful anti-tumor effector cells. "Polarization," rather than maturation, may be a major determinant of anti-tumor efficacy of CD4+ T cells. Skewing CD4+ T cells towards a "Th17" phenotype has recently been found to be highly effective in the treatment of large established tumors. Efforts to translate the use of "younger" cells are currently underway in the clinic, while work with CD4+ T cell polarization remains at an early stage of preclinical development. In conclusion, ACT represents the most effective immunotherapy for patients with metastatic melanoma and patients with bulky metastatic disease achieve an objective response. Lessons learned from this work on the use of lymphodepleting preparative regimens and an understanding of T cell differentiation are being applied to genetically engineered T cells. ACT using with peripheral lymphocytes genetically engineered to express anti-tumor T cell receptors hold promise for extending ACT therapy to patients with common epithelial cancers.

Additional reading: 1. Description of the pmel-1 (CD8+) TCR transgenic T cell model: WW Overwijk, et al. J Exp Med, 198 (4): 569, 2003. 2. How T regulatory and T helper cells influence tumor immunity: PA Antony, et al. J Immunol, 174(5): 2591, 2005. 3. An up-to-date description of the basic science of ACT: Gattinoni L, et al. Nat Rev Immunol. 2006 May;6(5):383. 4. Activating innate immunity: CM Paulos, et al. J Clin Invest. 2007 Aug;117(8):2197. 5. How IL-21 halts the differentiation of CD8+ T cells: CS Hinrichs, et al. Blood. 2008 Jun 1;111(11):5326-33. 6. Th17-polarized CD4+ T cells in a new TCR transgenic mouse model (called TRP-1): P Muranski, et al. Blood. 2008 Jul 15;112(2):362. 7. The challenge of targeting tumor-associated antigens: DC Palmer, et al. Proc Natl Acad Sci U S A. 2008 Jun 10;105(23):8061-6.

Presentation Abstracts – Friday

(primary authors listed in italics)

ENGINEERING GVL BY T-CELL GENETIC MODIFICATION

Michael Jensen
City of Hope/Beckman Research Institute, Duarte, CA

Disease relapse is a major contributor to treatment failure of hematopoietic stem cell transplantation for hematologic malignancy. Targeting post-transplant minimal residual disease with antigen-specific immunologic effector cells is a conceptually attractive strategy to consolidate the anti-tumor effect of the transplant preparative regimen by the selective augmentation of the GVL effect in the allogeneic setting. Endowing T cells with tumor specificity by genetic modification is one approach to generating effector cells for post-transplant cellular immunotherapy. In order to target malignant B-cells of lymphoma and leukemia, we have constructed chimeric immunoreceptors specific for B-cell lineage markers by fusing CD20- and CD19-specific single chain antibody (scFvFc) domains to the intracellular sequence of the T cell receptor complex's zeta chain (scFvFc:zeta). These antibody-based chimeric receptors bind to epitopes on native cell-surface CD20 and CD19 and thus are non-MHC restricted and universal. Our laboratory has focused on studying the immunobiology of T-cells engineered to express these receptors, as well as, on the development of these technologies for clinical deployment.

Our initial clinical trials applying autologous CD20-specific CD8+ CTL clone adoptive transfer for intermediate grade CD20+ diffuse large cell lymphomas and CD19-specific polyclonal T-cell autografts for follicular lymphoma have revealed a significant obstacle to therapeutic efficacy: that being limited in vivo persistence. In order to address this, our group in collaboration with Dr Stanley Riddell's lab have sought to identify T-cell subsets that have the intrinsic capacity to persist following adoptive transfer and to couple the use of these cells with ex vivo culture systems for human T cell gene transfer and expansion that preserve this function. To this end we have identified anti-viral Tcm's as intrinsically programmed for in vivo persistence. We have developed an ex vivo platform system for rapid acquisition of CMV-specific Tcm's through CD62L selection followed by CMV pp65 activation/IFN-gamma capture/SIN lentiviral transduction and expansion in IL-15 that permits the isolation of therapeutically relevant numbers of bispecific pp65xCD19 Tcm's in 21-days.

Our group is in the final stages of manufacturing and release testing the clinical-grade reagents to make this platform operational in IND-supported clinical applications. A major new application of this technology will be towards the augmentation of GVL effect following allogeneic HSCT for CD19+ acute lymphoblastic leukemias and to explore the therapeutic application of autologous HSCT in combination with adoptive transfer of CD19-specific effectors for engineered autologous GVL for those patients without donors or who have contraindications for allografting.

TARGETED ELIMINATION OF BRAIN TUMOR STEM CELLS WITH T CELL THERAPIES

Christine E. Brown[1], Renate Starr[1], Catalina Martinez[1], Stanley R. Riddell[3], Behnam Badie[2], Michael C. Jensen[1]
[1]Div. of Cancer Immunotherapeutics and Tumor Immunology, City of Hope, Duarte, CA
[2]Dept. of Neurosurgery, City of Hope, Duarte, CA
[3]Div. of Allergy and Infectious Diseases, Fred Hutchinson Cancer Research Center, Seattle, WA

Human brain tumors have been shown to consist of a subset of cells which exhibit stem cell-like properties and can drive tumor formation. Brain tumor stem/progenitor cells (BTSCs) are a formidable cellular target for current therapeutic regimens, and have been shown to be chemo- and radio-resistant due to the high expression of multi-drug resistant pumps, anti-apoptotic genes, and preferential activation of the DNA damage response pathway. We hypothesize that the glioma-cancer stem cell population represents a clinical entity that is attractive for cellular immunotherapeutic intervention. However, at present little is known regarding the immunobiology of BTSCs, including their intrinsic ability to be recognized by cytolytic T lymphocytes (CTLs) based on antigen presentation and antigen processing, their sensitivity to CTL mediated effector mechanisms such as perforin/granzyme lytic pathways, or their employment of potential escape mechanisms that render CTLs anergic or apoptotic.

We have expanded the CD133+ cancer stem cell population from primary human brain tumors and have demonstrated that these cells do exhibit stem cell like properties: they 1) grow in neurosphere-like clusters; 2) self-renew in vitro to reform secondary neurospheres; 3) express stem cell markers; 4) differentiate to express lineage specific markers; and 5) form tumors in nod-SCID mice. We are currently evaluating the utility of T cells for BTSC elimination. Using target populations that are either loaded with a CMV pp65 immunodominant peptide or engineered to express CMV pp65, we show that BTSCs are killed by CMV-specific T cells as efficiently as matched differentiated tumor lines in vitro; and CMV-specific CTL are capable of ablating the in vivo tumor initiation of ex vivo expanded pp65+ BTSC tumor spheres. Furthermore, we demonstrate that chimeric immunoreceptor redirected IL13Rα2-specific CTL, presently being evaluated in an FDA-approved pilot Phase I trail, can kill IL13Rα2-expressing BTSCs in vitro, and reduce the engrafted potential of this population in an orthotopic murine tumor model. Current models now predict that curative therapies for many cancers will require the elimination of the stem/progenitor population, and our studies lay the foundation for an immunotherapy approach to achieve this goal.

Presentation Abstracts – Friday

(primary authors listed in italics)

INTRALESIONAL PLACEMENT OF LYMPHOKINE-ACTIVATED KILLER (LAK) CELLS AFTER RESECTION OF PRIMARY GLIOBLASTOMA (GBM)

Robert O. Dillman, Christopher Duma, Robin Ellis, Andrew N. Cornforth, Patric M. Schiltz, Shari Sharp, Carol DePriest
Hoag Cancer Center, Newport Beach, CA

Background: Median survival for resectable GBM patients GBM is still only 12 to 15 months, even with the addition of intraoperative BCNU chemotherapy wafers or adjuvant temozolomide; so an additional effective adjuvant treatment would be desirable. We previously observed minimal toxicity and an encouraging 9.0 month median survival and 34% 1-year survival from the date of treatment with intra-lesional autologous LAK cells in 40 patients with recurrent GBM (J Immunother 27:398-404, 2004). The purpose of the current study was to obtain safety and efficacy data for the use of LAK cells placed intralesionally in patients with surgically proven GBM as part of primary therapy rather than after disease progression.

Methods: Eligible patients had completed primary therapy for GBM per their managing physician without disease progression. LAK cells were produced by incubating peripheral blood mononuclear cells after Ficoll-hypaque separation with 6,000 IU/ml IL-2 in AIM-V media in culture bags at a cell concentration of 3 x 106/ml for 3-5 days. The harvested LAK were then suspended in autologous plasma with 1 MIU IL-2, to which calcium was added to produce a fibrin clot. The LAK preparation was then transported to the operating room where the surgeon placed the cells into the surgically exposed tumor cavity. Results: LAK cell production was satisfactory for all 36 patients, including 22 men and 14 women aged 35 to 78 years with a median age of 57. All but one had undergone prior neurosurgery (18 had near complete resection; 13 had a partial resection). All patients had received partial brain radiation and a gamma knife boost except for one patient who had only undergone a near complete resection and gamma knife therapy and another who had only received irradiation via gamma knife. 24 had received chemotherapy (92% temozolomide) prior to LAK. LAK Treatment was well-tolerated. Average length of hospitalization was three days and median two days. Median time from diagnosis to LAK cell therapy was 5.0 months (range 3 to 11). At the time of this analysis 25 patients have died, but the median survival from the date of original diagnosis is 22.5 months with a 1-year survival rate of 79%. From the time of LAK cell placement, 1-year survival is 67% with a median survival of 14.6 months.

Conclusions: This treatment is feasible, safe, and the survival encouraging. Our intent is to conduct a randomized phase II trial of intralesional therapies with LAK in one arm and BCNU wafers in the other arm.

PROVISION OF CD4+ T CELL HELP PREVENTS TOLERIZATION OF TUMOR-SPECIFIC CTLS AND ENHANCES TUMOR IMMUNITY IN A MURINE MODEL OF PROSTATE CANCER

Kimberly A. Shafer-Weaver[1,2], Stephanie K. Watkins[2], Anatoli Malyguine[1], Arthur A. Hurwitz[2]
[1]*Laboratory of Cell-Mediated Immunity, Clinical Services Program, SAIC-Frederick, Inc., Frederick, MD*
[2]*Tumor Immunity and Tolerance Section, Laboratory of Molecular Immunoregulation, Cancer and Inflammation Program, NCI-Frederick, Frederick, MD*

In this study, we investigated T cell tolerance to tumor antigens using the TRansgenic Adenocarcinoma of the Mouse Prostate (TRAMP) model in combination with adoptive transfer of T cell receptor (TcR) transgenic T cells with specificity for a TRAMP tumor antigen. We previously reported that adoptive transfer of CD8+ (TcR-I) cells into TRAMP mice resulted in rapid tolerization of the cells. The objective of the current study was to test the ability of CD4+ helper T cells to enhance anti-tumor immunity by preventing or reversing TcR-I cell tolerance. Naïve tumor-specific CD4+ (TcR-II) T cells adoptively transferred into TRAMP mice became activated in LN, trafficked to the prostate, and initially functioned as T helper-1 cells, as measured by their ability to proliferate and secrete IL-2 and IFN-γ in response to their cognate tumor antigen. However, by ten days after transfer, the TcR-II cells became tolerant of tumor antigen. We next tested whether this transient activation of TcR-II cells was sufficient to prevent TcR-I cell tolerization. Co-transfer of naïve TcR-II and TcR-I cells initially enhanced the frequency, activation, survival and function of TcR-I cells and increased expression of co-stimulatory molecules on dendritic cells in the tumor-draining lymph nodes and tumor, improving their ability to stimulate naive T cell proliferation. While a single co-transfer of TCR-II cells only delayed tolerization of TcR-I cells, we have observed that repeated transfer of TcR-II cells prevented tolerization of TcR-I cells and ultimately slowed tumor progression. These data demonstrate that while tumor-specific CTL may be primed in the absence of CD4 help, maintenance anti-tumor CTL activity is profoundly enhanced by the sustained provision of activated CD4+ T cells. Our current studies are aimed at understanding how provision of CD4 help reverses the immunosuppressive tumor microenvironment to assist in the design of more effective immunotherapeutic approaches for treating cancer.

(primary authors listed in italics)

RAPID EXPANSION OF MELANOMA TIL IN ADOPTIVE CELL THERAPY LEADS TO LOSS OF CD28 AND REDUCED PROLIFERATIVE POTENTIAL IN THE MART-1-SPECIFIC T CELL POPULATION

Yufeng Li, Shujuan Liu, Jessica Hernandez, Patrick Hwu, Laszlo Radvanyi
Melanoma Medical Oncology, MDACC, Houston, TX

Adoptive T-cell therapy (ACT) of expanded tumor-infiltrating lymphocytes (TIL) has shown great promise in the treatment of metastatic melanoma. However, a critical problem in ACT is a lack of long-term TIL persistence in many patients required for durable clinical responses. The maintenance of an effector-memory phenotype characterized by the expression of key costimulatory molecules, especially CD28 and CD27, is associated with long-term persistence of transferred TIL. In this project, we have tracked the phenotypic and functional changes in CD8+ TIL, and their tumor-antigen-specific proliferation, after long-term culture in IL-2. Isolated TIL were initially expanded with IL-2 from tumor fragments and then subjected to rapid expansion protocol (REP), which is the current protocol used to generate the large numbers of cells for ACT. We found that melanoma antigen-reactive TIL (MART-1-reactive) lose their capacity to proliferate after the REP when re-stimulated with mature dendritic cells (mDC) pulsed with MART-1 peptide. In contrast, MART-1-specific TIL before REP (pre-REP TIL) proliferated well. Pre-REP TIL continued to expand with IL-2 for a minimum of a month after antigenic restimulation, while no similar expansion of post-REP TIL was found. However, analysis of CTL function by IFN-g staining and killing assays showed that post-REP TIL were superior effector cells. Staining for both TILs revealed that CD28 expression was significantly down-regulated during the REP, while no significant decrease in CD27 occurred. TIL were sorted based on CD27 and CD28, and re-stimulated. Both CD27+ and CD27- TIL expanded equally well over a 7-day period when re-stimulated. However, restimulated sorted CD27- TIL exhibited greater rates of MART-1-specific T-cell loss after the initial 7 day period. When sorted CD28+ and CD28- were compared, only CD28+ TIL could be induced to divide, with CD28- TIL failed to enter cell cycle and had increased apoptosis. These results indicate that loss of CD28, and not CD27, occurs during the REP and that the absence of CD28 costimulation leads to a loss of short-term proliferative potential. In contrast, CD27 costimulation seems to be required only for the longer-term survival of expanded antigen-specific CD8+ clones. Our results also help explain why the persistence of TIL expressing both CD27 and CD28 is associated with long-term complete responses in ACT patients. Highly differentiated CD28- TIL may only mediate short-term tumor eradication and can not expand and persist for long periods of time in vivo to mediate long-term durable clinical responses. This may explain why the majority of ACT patients receiving TIL therapy exhibit only partial and not complete clinical responses.

TH-17, Cytokines and T Cell Subsets

IL-23 PROMOTES TUMOR ASSOCIATED INFLAMMATION AND SUBVERTS IMMUNE SURVEILLANCE

Martin Oft
Oncology, Schering-Plough Biopharma (formerly DNAX), Palo Alto, CA

Human tumor cells acquire and accumulate mutations and transcriptional changes that provide sufficient clues for the mammalian immune system to distinguish tumor from normal cells. Immune surveillance is indeed able to protect from certain types of malignancies. Immune mediated inflammation increases however tumor incidence and progression. The cytokines IL-12 and IL-23 control the decision between immune surveillance and inflammation. IL-23, but bot IL-12, is highly prevalent in human tumors. In the presence of IL-23 inflammatory responses replace tumor immune surveillance. IL-23 stimulates myeloid inflammatory cells and metalloprotease activation, resulting in angiogenesis and tumor progression. The immune mediated elimination of the tumor cells, stimulated by IL-12 and IFNg. is simultaneously lost.

POTENT ANTI-TUMOR IMMUNITY AND BOTH TH1 AND TH17 PROMOTION ASSOCIATED WITH IL-23 ADMINISTRATION

Hideaki Tahara
Surgery and Bioengineering, Institute of Medical Science, University of Tokyo, Tokyo, Japan

Interleukin-23 (IL-23) is a cytokine composed of the p40 subunit shared with IL-12 and the IL-23-specific p19 subunit. The IL-23 has been shown to induce proliferation and IFN-g production of Th1 effecter/memory CD4+ T-cells and involved in inducing tissue injury through the stimulation on Th17. We have recently shown that systemic administration of IL-23 in mouse tumor system is associated with significant suppression of the growth of pre-existing MCA205 fibrosarcoma and prolongation of the survival of treated mice. In these animals, obvious toxicity or the significant elevation of IFN-g concentration were not seen in the treated animals. Furthermore, IL-23-treatment induced characteristic immune responses which can be abrogated with in vivo depletion of CD4+ T-cells or CD8+ T-cells. Detailed examination of the immune reaction of the treated animals has shown that significant IFN-g- and IL-17-responses were shown by the lymphoid cells upon anti-CD3 mAb stimulation in vitro. Thus, both Th1- and Th17- responses appear to be promoted in the animals treated with IL-23. However, the anti-tumor effects of IL-23 treatment were absent in the IFN-g- or IL-12-gene knock-out mice. These results and additional results including the ones with IL-17-gene knock-out mice will be discussed to define the role of IL-23 in Th1/Th17 promotion and anti-tumor effects.

Presentation Abstracts – Friday

(primary authors listed in italics)

TH17 CELLS IN OVARIAN CANCER PATIENTS

Ilona Kryczek[1], Rebecca Liu[1], Mousumi Banerjee[1], Wojciech Szeliga[1], Linhua Vatan[1], Shuang Wei[1], Pui Cheng[3], George Coukos[2], Weiping Zou[1]
[1]*University of Michigan, Ann Arbor, MI*
[2]*University of Pennsylvania, Philadelphia, PA*
[3]*Tulane University, New Orleans, LA*

We studied Th17 cells in 127 cancer patients. Tumor infiltrating Th17 cells exhibit a polyfunctional effector T cell phenotype with high expression of IL-2, IFNγ and TNF-α, and limited expression of IL-10, PD-1 and FOXP3; are positively associated with IFNγ+ T cells and negatively associated with regulatory T (Treg) cells in the same tumor. Tumor associated macrophages promote, while tumor and tumor associated Treg cells inhibit Th17 cell development. The levels of IL-17 released by Th17 cells in ovarian cancer ascites positively predict patient outcome. Furthermore, we observed enhanced tumor growth and lung tumor colonization in IL-17-deficient mice, associated with decreased IFNγ+ NK and T cells in the tumor draining lymph nodes. Altogether, our work has characterized the nature of Th17 cells in the tumor microenvironment and indicates that Th17 cells play a protective role in human tumor immunity. Inhibition of Th17 cell development represents a novel immune evasion mechanism.

CD40 DEPENDENT INDUCTION OF TH17 EFFECTOR CELLS FROM T REGULATORY CELLS USING THE IMMUNE MODULATOR B7-DC XAB

Suresh Radhakrishnan, Rosalyn Cabrera, Kristina Bruns, Larry R. Pease
Immunology, Mayo Clinic and College of Medicine, Rochester, MN

B7-DC XAb is a human IgM antibody isolated from the serum of a patient diagnosed with Waldenstrom's macroglobulinemia. The antibody binds to B7-DC/ PD-L2 molecules on the surface of murine and human DCs and stimulates the DCs to become potent activators of naïve T cells. Binding of pentameric B7-DC XAb results in cell surface cross-linking and activation of multiple signaling cascades in DCs downstream of an assembled molecular cap. Recently, we have documented that the co-culturing of CD25 + T regulatory cells with the antigen pulsed B7-DC XAb treated DCs results in the conversion of T regulatory cells into Th17 cells. The Treg conversion to T effector cells is dependent on IL-6. We have shown that cross-linking B7-DC on DCs leads to the activation of NFkB through the PI3K-Akt pathway and IL-6 secretion. Activation of NFkB leads to the protection of DCs against cell death upon cytokine withdrawal or upon induction of apoptosis by Vitamin D3 analog. We have identified TREM-2 as one of the proteins recruited by B7-DC cross-linking. In the absence of TREM-2, B7-DC XAb mediated induction of antigen uptake in the mature DCs is compromised. However, TREM-2 was not found to be necessary for the activation of NFkB or for the conversion of Tregs. Therefore, we sought to delineate the upstream molecules regulating the ability of activated DC to promote DC survival in response to apoptotic signals and to convert T regulatory cells into IL-17+ effectors. Here we show by FRET and co-immunoprecipitation that CD40 is also recruited into the macromolecular cap. DCs that lack the expression of CD40 molecule did not activate Akt or NFkB in response to B7-DC XAb. Moreover, B7-DC XAb treatment failed to protect the DC from cytokine withdrawal or Vitamin D3 induced cell death. The presence of CD40 is necessary for the secretion of IL-6 as CD40-/- DCs activated with B7-DC XAb do not secrete IL-6. The CD40 deficient DC were unable to convert T regulatory cells into IL-17+ effector T cells. Finally, the presence of CD40 on the DCs in vitro and in vivo is important for the generation of T effector cells capable of providing tumor protection against B16 melanoma or WEHI-3.

(primary authors listed in italics)

Endpoints, Response Criteria for Clinical Trial Design

IMMUNOTHERAPIES IN COMBINATION WITH OTHER THERAPEUTIC MODALITIES: NEW PARADIGMS FOR CLINICAL TRIAL DESIGN

Jeffrey Schlom
Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, MD

The field of cancer vaccines is currently in an active state of preclinical and clinical investigations. Several new paradigms are emerging from recent clinical findings both in the use of combination therapy approaches and, perhaps more importantly, in clinical trial design and end point analyses. Data are emerging from recent clinical trials involving several different cancer vaccines contrasting classic "tumor response" (Response Evaluation Criteria in Solid Tumors) criteria with "patient response" in the manifestation of increased patient survival post-vaccine therapy. Several strategies in which cancer vaccines can be exploited in combination with other agents and therapeutic modalities are quite unique when compared with "conventional" combination therapies. This is most likely due to the phenomena that (a) cancer vaccines initiate a dynamic immune process that can be exploited in subsequent therapies and (b) both radiation and certain chemotherapeutic agents have been shown to alter the phenotype of tumor cells as to render them more susceptible to T-cell-mediated killing. Consequently, evidence is emerging from several studies in which patient cohorts who first receive a cancer vaccine (as contrasted with control cohorts) benefit clinically from subsequent therapies.

Reference:

J. Schlom, P.M. Arlen, J.L. Gulley. 2007. Cancer vaccines: moving beyond current paradigms. Clin. Cancer Res. 13:3776-3782.

OVERALL SURVIVAL (OS) AND NEW PATTERNS OF RESPONSE IN PATIENTS (PTS) WITH ADVANCED MELANOMA TREATED WITH IPILIMUMAB

Steven O'Day[1], Ramy Ibrahim[2], Veerle De Pril[3], Michele Maio[4], Vanna Chiarion Sileni[5], Thomas F. Gajewski[6], Hubert Pehamberger[7], Igor N. Bondarenko[8], Paola Queirolo[9], Lotta Lundgren[10], Sergey Mikhailov[11], Laslo Roman[12], Claire Verschraegen[13], Axel Hoos[2], Rachel Humphrey[2], Jedd Wolchok[14]
[1]*The Angeles Clinic and Research Inst, Santa Monica, CA*
[2]*Bristol-Myers Squibb, Wallingford, CT*
[3]*Bristol-Myers Squibb, Braine-l'Alleud, Belgium*
[4]*Univ. Hosp. of Siena, Siena, Italy*
[5]*IOV-IRCCS, Padova, Italy*
[6]*Univ. of Chicago, Chicago, IL*
[7]*Univ. of Vienna, Vienna, Austria*
[8]*City Clinical Hosp. #4, Dniptopetrovsk, Ukraine*
[9]*Ist. Nazionale per la Ricerca sul Cancro, Genova, Italy*
[10]*Lund Univ. Hosp., Lund, Sweden*
[11]*Stavropol Regional Clinical Onc. Ctr., Stavropol, Russian Federation*
[12]*Leningrad Regional Onc. Ctr., St. Petersburg, Russian Federation*
[13]*UNM Cancer Ctr., Albuquerque, NM*
[14]*MSKCC, New York, NY*

Ipilimumab, a cytotoxic T lymphocyte antigen-4 (CTLA-4) monoclonal antibody, administered at 10 mg/kg to 155 melanoma pts (Phase II trial CA184-008) resulted in modified World Health Organization (mWHO)-classified tumor responses and a median OS of 10.2 months (95% CI 7.3, not reached). mWHO criteria may not capture its full clinical benefit. OS by response per mWHO or novel efficacy endpoints was examined. Previously-treated advanced melanoma pts received 10 mg/kg ipilimumab every 3 weeks (Q3W)x4; eligible pts received 10mg/kg maintenance ipilimumab Q12W starting at Week 24. The primary objective was best overall response rate. OS was a secondary endpoint. Response was assessed using mWHO (complete/partial response [CR/PR], stable/progressive disease [SD/PD]) by an Independent Review Committee. Efficacy was measured in some pts after mWHO PD if they did not receive other therapies. Novel response endpoints (Hodi FS et al. ASCO 2008:abst3008) tracked total tumor burden over time when tumor shrinkage occurred after mWHO PD and captured 4 response patterns: 1)response in baseline lesions; 2)'stable disease' with slow, steady decline in total tumor burden; 3)response after initial increase in total tumor burden; 4)response in index+new lesions after the appearance of new lesions. There were no mWHO CRs. Median OS follow-up was 9.5 months. Median OS for pts with mWHO PR/SD (n=42) has not been reached with only 5 deaths (11.9%). Pts with mWHO PD who then experienced tumor shrinkage per the new efficacy endpoints (n=16) have not reached a median OS; 2 (12.5%) died. Median OS for pts with PD by both endpoints (n=60) was 6.8 months (95% CI 5.5, 9.3); 42 pts (70%) died. OS follow-up is ongoing. Similar OS benefit was observed in pts with mWHO PR/SD and pts with tumor shrinkage per the novel response endpoints (despite being assessed as mWHO PD). These data suggest PD by mWHO in ipilimumab-treated pts may not indicate drug failure. The 4 response patterns likely contribute to OS.

Presentation Abstracts – Friday

(primary authors listed in italics)

IDENTIFICATION OF ANTIBODY RESPONSES INDUCED IN PATIENTS WITH CASTRATION-RESISTANT PROSTATE CANCER (CRPC) RECEIVING GVAX IMMUNOTHERAPY FOR PROSTATE CANCER

Thomas Harding[1], Minh Nguyen[1], Kathryn Koprivnikar[1], Guang Huan-Tu[1], Natalie Sacks[1], Eric J. Small[2], *Karin Jooss*[1]
[1]*Cell Genesys, Inc., South San Francisco, CA*
[2]*Comprehensive Cancer Center, University of California, San Francisco, CA*

Introduction: GVAX immunotherapy for prostate cancer is comprised of 2 allogeneic prostate carcinoma cell lines (PC-3 and LNCaP) that have been modified to secrete GM-CSF. Completed phase 2 trials include a multicenter Phase 2 trial, G-0010, in patients (pts) with CRPC. The subset of pts in G-0010 who received doses comparable to the dose used in ongoing Phase 3 trials (n=22) showed median survival of 35.0 m.

Methods: Immunotherapy-induced antibody (Ab) responses were evaluated in 14 pts from G-0010 whose actual survival exceeded that predicted by the Halabi nomogram using 3 methods: i) serological analysis of gene expression (SEREX), ii) protein chip analysis, iii) screening pre-defined prostate cancer antigens (Ags). Ab responses observed in at least 2 of these 14 pts were then further examined in all evaluable G-0010 pts (n=65). Ab responses were evaluated for potential association with survival using the Cox regression model, adjusted for prognostic factors and dose group.

Results: Analysis of Ab responses in 14 CRPC pts yielded 411 candidate Ags of which 93 were seen in ≥ 2 pts. Preliminary data from all evaluable G-0010 pts suggests that Abs to protein FLJ14668, neuronatin, cardiolipin and the PC-3-derived HLA-A24 may be associated with survival independently of treatment duration and prognostic factors. For example, pts with Ab to protein FLJ14668 (n=34) had a median survival of 43 m vs. 21 m in Ab negative pts (n=31), HR=0.34, p=0.002. Among HLA-A24 haplotype-negative pts, the HLA-A24 Ab-positive pts (n=30) had a median survival of 43 m vs. 18 m in Ab-negative pts (n=28), HR=0.53, p=0.05.

Conclusions: GVAX immunotherapy for prostate cancer induces a polyvalent IgG Ab response to a broad panel of immunotherapy-derived antigens. The majority of proteins targeted are pt-specific; however, a smaller group of higher frequency Ab targets were identified. Abs to HLA-A24, neuronatin, cardiolipin and FLJ14668-specific IgG may be associated with observed survival. Phase II immunomonitoring studies are designed to identify Ab candidates that will be evaluated prospectively in 2 on-going 600 pt phase 3 trials of GVAX immunotherapy for prostate cancer with the goal of identifying potential biomarkers of response.

ENDPOINTS FOR BIOLOGIC THERAPEUTICS IN ONCOLOGY

Peter Bross
Food and Drug Administration, Office Cellular, Tissue, and Gene Therapies

Abstract not available

(primary authors listed in italics)

Saturday Keynote Address

CANCER IMMUNOEDITING: DISTINCT ROLES FOR INNATE AND ADAPTIVE IMMUNITY IN CANCER CONTROL AND PROMOTION

Robert D. Schreiber
Washington University in St. Louis, St. Louis, MO

We have shown that (a) mice lacking an intact immune system form more spontaneous and chemically induced tumors than wild type mice and (b) tumors from immunodeficient mice are more immunogenic than those from immunocompetent mice. Based on these observations we proposed the term "cancer immunoediting" to describe the dual host-protective and tumor-promoting actions of immunity on developing tumors. We now think of cancer immunoediting as a process comprised of three phases: Elimination—the host-protective phase comparable to cancer immunosurveillance; Equilibrium—a phase where residual tumor cells circumventing elimination may persist in the host and undergo immunologic sculpting; and Escape—the phase in which immunity can no longer restrain tumor growth permitting emergence of clinically-apparent, progressively-growing tumors. A large body of data now exists demonstrating the existence of the elimination phase and identifying several innate and adaptive immune components that play obligate roles in the process. Similarly, a significant amount is known about mechanisms of tumor escape involving alterations of either the tumor cells themselves (via loss of immune recognition structures) or the host immune system (through induction of potent immunosuppressive activities). However, until recently, no experimental data existed to document the existence of the equilibrium phase. We injected wild type mice with a limited dose of the carcinogen methylcholanthrene (MCA) and during the next 200 days, removed from the experiment any mouse that developed a clinically apparent, progressively growing tumor. At day 200 (when the rate of new tumor formation dropped off significantly) the remaining "tumor free mice" were placed on weekly injections of either control monoclonal antibody (mAb) or mAbs that deplete or block components of adaptive and/or innate immunity. The mice were then followed for appearance of progressively growing tumors. Nearly half of the tumor-free mice originally exposed to low-dose MCA harbored fully transformed tumor cells whose outgrowth was controlled by both cytostatic and cytocidal effects of adaptive immunity. In contrast, innate immunity was not required for maintenance of the equilibrium state. Tumor cells held in equilibrium were highly immunogenic (i.e. were unedited) while tumor cells that spontaneously advanced from equilibrium to escape showed attenuated immunogenicity (i.e., were edited). These results thus demonstrate that the equilibrium phase indeed occurs during immunoediting of primary tumors. Our findings suggest that a therapeutically induced equilibrium state may someday represent a novel mechanism to convert some cancers into chronic controllable diseases.

Tumor Escape/Tumor Microenvironment

INNATE IMMUNE SIGNALS THAT MEDIATE HOST AWARENESS OF TUMOR AND PROMOTE ADAPTIVE IMMUNE RESPONSES AGAINST TUMOR ANTIGENS

Thomas Gajewski, Justin Kline, Long Zhang, Aalok Kacha
University of Chicago, Chicago, IL

The rationale behind active immunization against cancer is to overcome theoretical defects in natural T cell priming in response to tumor antigens. However, recent clinical observations have suggested that tumor antigen-specific T cell and antibody responses are frequently detected in patients with advanced cancer. In addition, activated T cells can be found infiltrating metastatic tumor sites, particularly in melanoma, a phenomenon that has provided a source of T cells for expansion and adoptive transfer as a therapeutic approach. These observations have prompted a new fundamental question, namely, how is it possible for a spontaneous adaptive immune response to develop against a tumor that lacks obvious infection or pathogen-associated innate immune ligands? Gene expression profiling of human melanoma metastases revealed the presence of an interferon signature in tumors that contained T cells. Based on this correlation, mechanistic experiments were performed in murine models studying the role of host type I interferons in bridging to T cell priming. Following subcutaneous implantation of transplantable tumors, interferon-β (IFN-β) was induced in the tumor draining lymph nodes within 3-5 days. This preceded detection of a tumor antigen-specific CD8+ T cell response, which occurred at 6-8 days. Using Stat1 knockout mice that are defective in IFN-based signaling, we found that T cell priming, as well as rejection of immunogenic tumors, was abolished. This was recapitulated using type I IFNR-deficient but not IFN-γR-deficient mice. Bone marrow chimera experiments revealed a requirement for IFN signaling in the hematopoietic compartment. Adoptive transfer of wildtype TCR Tg T cells revealed that the host IFN requirement was upstream, presumably at the level of antigen-presenting cells. Immunization with wildtype dendritic cells pulsed with antigen led to successful T cell priming even in Stat1 knockout mice. Together, these results indicate that rapid induction of host IFN-β is part of the innate immune recognition of a growing tumor, which is a necessary step in spontaneous priming of anti-tumor T cells. Exploitation of the IFN-β system could lead to improved anti-tumor immunity in vivo by augmenting spontaneous adaptive immune responses. Use of these model systems is enabling characterization of additional factors required in the innate immune recognition of tumors.

Presentation Abstracts – Saturday

(primary authors listed in italics)

PERSISTENT HIGH GRADE CERVICAL DYSPLASIA EXCLUDES CD8+ T CELLS

Cornelia L. Trimble[1], Christopher J. Thoburn[1], Shiwen Peng[1], Ferdynand Kos[1], Achim A. Jungbluth[2]
[1]*The Johns Hopkins Medical Institutions, Baltimore, MD*
[2]*Ludwig Institute for Cancer Research at Memorial Sloan-Kettering Cancer Center, New York, NY*

Persistent mucosal infection with human papillomavirus (HPV) is the cause of virtually all squamous cervical cancer (SCC). High grade cervical dysplasia (CIN3), the lesion which is the immediate precursor to SCC, is associated with integration of the HPV genome into the host genome, and subsequent constitutive expression of the HPV E6 and E7 oncoproteins. Because both E6 and E7 are functionally required for disease, they present compelling targets for immunotherapeutic strategies. We have established a prospective cohort of subjects with CIN3, who are followed conservatively for a brief 15-week observational protocol prior to undergoing standard therapeutic resection. In this window, no subject has had progression of disease. Neither have we identified occult, unsuspected invasive disease in any subject at the time of resection at week 15 (Tweek15). In fact, up to 25% of high grade lesions associated with HPV16 undergo complete regression in this window, which is presumably immunologically mediated. We measured CD8 T cell responses to HPV16 antigens in peripheral blood specimens obtained longitudinally from study participants, and were unable to identify responses that correlated with disease outcome. Therefore we examined the cervical compartment to determine the extent to which lesions contained immune cells.

In normal cervical mucosa, CD8+ cell infiltrates were detectable in low numbers, predominantly distributed along the superficial lamina propria immediately subtending the epithelial basement membrane. Immune cells isolated from normal cervix were overwhelmingly comprised of antigen-experienced T cells which expressed epithelial addressins CLA and CCR4. Compared to the peripheral blood compartment, very few B cells or NK cells were detected. Compared to normal cervical mucosa, CIN3 lesions were associated with a higher intensity of CD8+ infiltrates ($p<0.0001$), which were greater in the lamina propria compared to the epithelial compartment ($p<0.0001$). Both the higher density and the localization of CD8+ cells in the lesional tissue compared to immediately adjacent normal mucosa suggest recruitment of this population. Moreover, in lesions which were still present (persistent CIN3) at the time of resection (Tweek15), we observed higher intensity of CD8+ infiltrates localized to the lesion site compared to baseline (T0). In contrast to the lamina propria infiltrates, in persistent CIN3 lesions, infiltration of the epithelial compartment with CD8 cells did not change appreciably. This constellation of findings suggests that persistent CIN3, despite expression of potentially immunogenic viral proteins, excludes CD8 T cells.

Presentation Abstracts – Saturday

(primary authors listed in italics)

INHIBITORY B7 FAMILY MEMBERS (B7-H1 AND B7-H4) IN THE TUMOR MICROENVIRONMENT

Ilona Kryczek[1], Lieping Chen[2], *Weiping Zou*[1]
[1]*University of Michigan, Ann Arbor, MI*
[2]*Johns Hopkins University, Baltimore, MD*

The B7 family consists of activating and inhibitory co-stimulatory molecules that positively and negatively regulate immune responses. In this talk, we focus on their expression, regulation and function in the tumor microenvironment. We also discuss novel therapeutic strategies that target these inhibitory B7 molecules and their signaling pathways to treat human cancer.
Expression: The expression of B7-H1 and B7-H4 mRNA, but not the protein is abundant in many tissues and organs in humans. However, B7-H1 and B7-H4 proteins are highly expressed in the human cancer microenvironment including ovarian cancers. Tumor cells, tumor associated APCs and stromal cells express B7-H1 and B7-H4.

Regulation: B7-H1 expression can be induced or maintained by many cytokines. IFNgamma is the most potent stimulator for inducing B7-H1 expression. It remains unknown which factor(s) can downregulate B7-H1 expression. The regulation of B7-H4 expression has only been studied in the human system. IL-6 and IL-10 stimulate B7-H4 expression on monocytes, macrophages and myeloid DCs. GM-CSF and IL-4, decrease B7-H4 expression on these cells induced by IL-6 and IL-10. IL-4, IL-6, IL-10 and GM-CSF have no regulatory effects on B7-H4 expression on tumor cells.

Role of inhibitory B7 molecules: The physiological functions of inhibitory B7-family members are to limit, terminate and attenuate T-cell responses, by which they avoid tissue and organ damage during immune responses. However, these inhibitory B7 molecules could suppress ongoing or induced tumour immunity.

Mechanisms of inhibitory B7 molecules in evading T-cell immunity: B7-H1-expressing cells use at least six distinct mechanisms to evade T-cell immunity: inducing apoptosis, anergy or exhaustion of T cells, forming a molecular shield to protect tumor cells from lysis, inducing production of the immunosuppressive cytokine IL-10, and promoting Treg-cell-mediated suppression. B7-H4 has been studied in less detail than B7-H1 in the context of tumor immune evasion, but evidence indicates that B7-H4 might act through myeloid APCs and Treg cells to mediate T-cell suppression in the tumor microenvironment. For example, tumor associated B7-H4 expressing macrophages induce T cell cycle arrest in B7-H4 dependent manner.

Inhibitory B7 molecules in cancer progression and cancer treatment: Many tumor-associated APCs and tumor cells express B7-H1 and B7-H4, which mediate T-cell suppression. Clinical data have documented that the expression of inhibitory B7 molecules correlates with poor prognosis of various types of human cancer. Therefore, the manipulation of B7-induced immune suppression might be a broadly applicable therapeutic modality to treat human cancers.

L-ARGININE AVAILABILITY REGULATES CYCLIN D3 MRNA STABILITY IN HUMAN T CELLS BY CONTROLLING HUR EXPRESSION

Paulo C. Rodriguez[1], Claudia P. Hernandez[2], Augusto C. Ochoa[2]
[1]*Department of Microbiology, Immunology and Parasitology, Louisiana State University, New Orleans, LA*
[2]*Department Pediatrics, Louisiana State University, New Orleans, LA*

Depletion of extra cellular levels of L-Arg by arginase I-producing MDSC inhibit CD3z expression and blocked T cell proliferation, which may impair the potential therapeutic benefit of immunotherapy. L-Arg starvation impairs T cell proliferation by arresting cells in G0-G1 phase of the cell cycle, which is associated with an inability to upregulate cyclin D3. The regulation of cyclin D3 by L-Arg starvation included a low rate of transcription, a decreased mRNA stability and an impaired translation. We aimed to determine the post-transcriptional mechanisms leading to a decreased stability of cyclin D3 mRNA in T cells cultured under L-Arg starvation. We found that 3'UTR within the cyclin D3 mRNA contains response elements, which inhibit mRNA stability in the absence of L-Arg. The increased cyclin D3 mRNA stability observed in T cells cultured in the presence of L-Arg was associated with a higher cytoplasmic expression of RNA binding protein (RBP) HuR. Furthermore, HuR binds cyclin D3 mRNA in vitro and endogenously in T cells cultured in the presence of L-Arg, but not in T cells cultured in the absence of L-Arg. Silencing HuR expression in primary T cells using siRNA leads to a decreased cyclin D3 mRNA stability and a lower expression of cyclin D3 protein. We have previously shown that T cells from GCN2 knockout mice proliferate in the absence of L-Arg. As expected, T cells from GCN2 knockout mice, but not from wild type mice, cultured in the absence of L-Arg upregulated HuR and did not show a decreased cyclin D3 mRNA stability. These results therefore suggest that in T cells cultured in the absence of L-Arg, GCN2 impairs cyclin D3 mRNA stability by blocking the expression of HuR. These data contribute to understand a central mechanism by which cancer and other diseases characterized by high arginase I production may cause T cell dysfunction.

Presentation Abstracts – Saturday

(primary authors listed in italics)

CORRECTING THE ANERGY OF HUMAN TUMOR-INFILTRATING LYMPHOCYTES ?

Nathalie Demotte[1,2], Vincent Stroobant[1,2], Pierre J. Courtoy[3], Patrick Van Der Smissen[3], Didier Colau[1,2], Danièle Godelaine[1,2], Thierry Boon[1,2], Pierre van der Bruggen[1,2]

[1]*Ludwig Institute for Cancer Research, Brussels, Belgium*

[2]*Cellular Genetics Unit, de Duve Institute, Université catholique de Louvain, Brussels, Belgium*

[3]*Cell Biology Unit, de Duve Institute, Université catholique de Louvain, Brussels, Belgium*

After antigenic stimulation, human CTL clones exhibit for several days a decrease in their effector activity and in their binding to HLA-peptide tetramers. We observed that CTL in that state had lost the colocalization of TCR and CD8. Effector function and TCR-CD8 colocalization were restored with galectin disaccharide ligands, suggesting that the binding of TCR to galectin plays a role in the distancing of TCR from CD8. These findings appear to be applicable in vivo, as TCR were distant from CD8 on human tumor-infiltrating lymphocytes which were anergic. These lymphocytes recovered effector functions and TCR-CD8 colocalization after ex vivo treatment with galectin disaccharide ligands.

EVIDENCE FOR SELECTION OF A RESISTANT TUMOR MICROENVIRONMENT FOLLOWING SUCCESSFUL CLINICAL RESPONSE TO A MULTI-PEPTIDE + IL-12 MELANOMA VACCINE

Yuanyuan Zha[1], Thomas F. Gajewski[2]

[1]*Human Immunologic Monitoring Facility, Office of Shared Research, University of Chicago, Chicago, IL*

[2]*Section of Hematology and Oncology, Department of Medicine, University of Chicago, Chicago, IL*

We recently have identified a gene expression signature in melanoma metastases that correlates with clinical response to a melanoma vaccine utilizing 4 tumor antigen peptides and IL-12. When feasible, patients in this trial are being followed longitudinally to monitor the evolution of the T cell response and changes in tumor biology. Here we describe the features a patient who initially responded then recurred 3 years after vaccination. In 2004, a 51-year-old male diagnosed with melanoma was recruited to participate in this vaccine trial. He was immunized subcutaneously with irradiated (2000 rad) autologous PBMCs pulsed with Melan-A, gp-100, NA-17, and MAGE-3 peptides along with rhIL-12 every 3 weeks for 6 months. A pre-treatment tumor biopsy revealed a tumor microenvironment that was "favorable", containing transcripts for T cell-recruiting chemokines. Following the 3rd immunization, robust T cell responses were observed against all 4 peptides. Clinically he experienced a durable partial response. He was then monitored by routine follow-up until 2007 when a clinical recurrence was detected in the form of a new pelvic mass. Analysis of the T cell response in the peripheral blood at that time revealed persistent reactivity against Melan-A and NA-17. Biopsy and gene expression profiling of the recurrent tumor, however, revealed a significant down-regulation of transcripts encoding key chemokines, as well as up-regulation of transcripts linked to more aggressive tumor biology. Immunohistochemistry revealed exclusion of CD8+ T cells from the center of the tumor mass. Our results suggest that metastatic melanoma may have the potential to become selected under immune pressure to develop a tumor microenvironment that is resistant to the effector phase of the anti-tumor T cell response.

(primary authors listed in italics)

Presentation Abstracts – Saturday

iSBTc Presidential Abstract Session

INCREASING IMMUNOSTIMULATORY ABILITY OF TOLEROGENIC APCS ENHANCES ANTI-TUMOR IMMUNITY

Stephanie K. Watkins[1], Kimberly A. Shafer-Weaver[2], Arthur A. Hurwitz[1]
[1]*Laboratory of Molecular Immunoregulation, NCI-Frederick, Frederick, MD*
[2]*Laboratory of Cell-Mediated Immunity, Clinical Services Program SAIC-Frederick, Frederick, MD*

One obstacle in adoptive immunotherapy of cancer is the loss of effector function by tumor-specific CD8+ T cells. Our lab previously demonstrated that following adoptive transfer into prostate tumor-bearing mice, CD8+ tumor-specific T cells become activated in the periphery and traffic to the tumor. However, upon infiltration into the prostate tumor microenvironment, the cells were observed to be functionally tolerant of their cognate antigen. Because the potency of tumor-specific T cells is regulated by many factors, including tumor-associated tolerogenic antigen presenting cells (APCs), in the current study, we examined the function and phenotype of the APCs present in both the prostate tumor microenvironment as well as the tumor draining lymph node. Using the Transgenic Adenocarcinoma of the Mouse Prostate (TRAMP) model, we have observed that the largest population of APCs within the prostate tumor microenvironment were CD11cint/B220+/mPDCA-1+ which are reportedly characteristic of APCs that are poor presenters of Ag. Furthermore, we noted that these APCs produced elevated levels of molecules that are known to suppress T cell responses including indoleamine 2, 3 dioxygenase (IDO) and Arginase I (ARG 1), as well as ligands such as PDL-1 and FASL, which can induce anergy, exhaustion, and programmed cell death in T cells that express the PD-1 and FAS receptors. Interestingly, we demonstrate that by inhibiting the activity of the tolerogenic enzymes IDO and ARG 1, or by blocking receptor ligation of PD-1, tolerance induction of tumor specific T cells was delayed in vivo. Further studies revealed that providing tumor-specific CD4+ T cell help enhanced APC expression of co-stimulatory molecules and increased their ability to stimulate proliferation of naïve CD8+ T cells in vitro. Our data demonstrate that the tolerization of tumor-infiltrating CD8+ T cells may be dependent upon the phenotype, activation, and function of the APCs within the tumor microenvironment. These findings have critical importance for the design of novel immunotherapies that sustain T cell responses to tumor antigens to elicit more potent, long-lasting tumor immunity.

CCL28 A NEW LINK BETWEEN HYPOXIA ANGIOGENESIS AND TUMOR IMMUNE EVASION

Andrea Facciabene, Xiahoui Peng, Klara Balint, Andrea Barchetti, George Coukos
Center for Research on Women's Health, University of Pennsylvania, Philadelphia, PA

Hypoxia is now recognized as one of the major contributors to cancer progression and to treatment failure. The precise role of hypoxia signaling in modulating the tumor microenvironment and cancer outcome still needs to be defined. In this work, we sought to understand the effect of hypoxia in immune regulation in the tumor microenvironment. We characterized the expression profile of genes implicated in immune response by real-time quantitative PCR low density microarray in 17 human ovarian cancer cell lines in vitro. CCL28 was one of the most up-regulated genes identified in 9 out of 17 ovarian cancer cell lines. Migration assays with peripheral blood mononuclear cells (PBMC) using supernatants from hypoxic ovarian cancer lines showed a preferential migration of CD4+, CD25+ FoxP3+ T cells, suggesting a link of hypoxia to regulatory T cells. Because we have previously shown that increased Treg infiltration is associated with short survival in ovarian cancer, we also explored the relationship between CCL28 expression and disease outcome. Results showed that survival for patients with high CCL28 expression was short in comparison with patients with low expression of CCL28. Next, to investigate the role of CCL28 in ovarian cancer in vivo, we transfected the well-characterized mouse ovarian cancer model ID8 with CCL28. ID8-CCL28 or wild type ID8 cells were injected intraperitoneally into the C57Bl/6. Stable expression of CCL28 in ID8 tumor cells resulted in a faster tumor and ascites progression in comparison with the parental ID8 cells. Next, we characterized the cell infiltrate and cytokine profile of the ascites of animals injected with ID8-CCL28. In these animals, we found a higher number of CD4+, CD25+, FoxP3+ cells and a higher expression of IL-10, VEGF, MCP-1, MCP-2 and MCP-3. To investigate the role of the CD4+, CD25+, FoxP3+ cells in the progression of ID8-CCL28 tumors in vivo, we depleted the CD25+ cells 4 days before the tumor challenge. CD25 depletion resulted in a partial decrease of the tumor growth suggesting a role of T regulatory cells in the CCL28-mediated tumor progression. To our knowledge, these results provide the first evidence establishing a link between hypoxia and cancer immune evasion and could lead to alternative and more efficient therapeutic approaches.

Presentation Abstracts – Saturday

(primary authors listed in italics)

CYTOTOXIC T LYMPHOCYTE-ASSOCIATED ANTIGEN 4 BLOCKADE ENHANCES POLYFUNCTIONAL NY-ESO-1 SPECIFIC T CELL RESPONSES IN METASTATIC MELANOMA PATIENTS WITH TUMOR REGRESSION

Jianda Yuan[1,4], Sacha Gnjatic[2], Hao Li[1,4], Sarah Powel[4], Humilidad Gallardo[4], Erika Ritter[2], Teresa S. Rasalan[4], Gregor Manukian[1,4], Yinyan Xu[1,4], Stephanie Terzulli[4], Gerd Ritter[2], Lloyd Old[2], James P. Allison[1,3], Jedd D. Wolchok[1,4]

[1]*Ludwig Center for Cancer Immunotherapy, Memorial Sloan Kettering Cancer Center, New York, NY*

[2]*Ludwig Institute for Cancer Research, New York Branch, Memorial Sloan Kettering Cancer Center, New York, NY*

[3]*Howard Hughes Medical Institute, Memorial Sloan Kettering Cancer Center, New York, NY*

[4]*Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY*

Blockade of the inhibitory signals mediated by cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) has been shown to enhance T cell responses and induce objective, durable clinical responses in patients with metastatic melanoma. The functional impact of anti-CTLA-4 therapy on human immune responses is still unclear. To explore this, we analyzed immune-related adverse events and immune responses in metastatic melanoma patients treated with ipilimumab, a fully human anti-CTLA-4 monoclonal antibody. We have treated a large cohort of refractory metastatic melanoma patients enrolled on two phase II trials of Ipilimumab, sponsored by Bristol-Meyers Squibb. Patients had received a variety of prior chemotherapies and immunotherapies, including one patient who was previously immunized with a NY-ESO-1 protein vaccine. Patients received an induction regimen with 4 doses of Ipilimumab at 10 mg/kg given every 3 weeks or a blinded dose (0.3, 3 or 10 mg/kg) given along the same schedule. Patients were eligible for maintenance doses every three months if clinical benefit was observed in the absence of significant toxicity. Fifteen Ipilimumab-treated patients were selected on the basis of availability of a suitable panel of specimens for immunologic monitoring, and eight of these showed evidence of clinical benefit (partial or complete responses or stable disease for > 24 weeks). Five of the eight clinical responders had NY-ESO-1 antibody, whereas none of seven clinical non-responders were seropositive for NY-ESO-1. All five NY-ESO-1 seropositive patients had clearly detectable CD4+ and CD8+ T cells against NY-ESO-1; One NY-ESO-1 seronegative clinical responder also had a NY-ESO-1 CD4+ and CD8+ T cell response, possibly related to prior vaccination with NY-ESO-1. Among five clinical non-responders analyzed, only one had a NY-ESO-1 CD4+ T cell response and this patient did not have detectable anti-NY-ESO-1 antibody. Overall, NY-ESO-1-specific T-cell responses increased in frequency and quality during anti-CTLA-4 treatment, revealing a polyfunctional response pattern of IFN-γ, MIP-1β and TNF-α. We therefore suggest that CTLA-4 blockade enhanced NY-ESO-1 antigen-specific B cell and T cell immune responses in patients with durable objective clinical responses.

RADIOFREQUENCY ABLATION WITH KS-IL2 IMMUNOCYTOKINE (EMD 273066) RESULTS IN AN ENHANCED ANTITUMOR EFFECT AGAINST MURINE COLON ADENOCARCINOMA

Erik Johnson[1], Brett Yamane[1], Alexander Rakhmilevich[2,4], David Mahvi[1,4], Stephen Gillies[5], Paul Sondel[2,3,4]

[1]*Surgery, University of Wisconsin, Madison, WI*

[2]*Human Oncology, University of Wisconsin, Madison, WI*

[3]*Pediatrics, University of Wisconsin, Madison, WI*

[4]*Paul P. Carbone Comprehensive Cancer Center, University of Wisconsin, Madison, WI*

[5]*EMD-Serono Lexigen Research Center, Billerica, MA*

Background: Radiofrequency ablation (RFA) is a common treatment modality for surgically unresectable tumors. In this pre-clinical work, we sought to enhance the antitumor effect from RFA by adding immunotherapy in the form of the huKS-IL2 immunocytokine (EMD 273066) given to mice bearing CT26-KS colon adenocarcinoma. The huKS-IL2 immunocytokine (huKS-IL2) is an experimental immunotherapeutic reagent, comprised of a humanized IgG1 antibody that detects the KS-antigen (an epitope on the human Epithelial Cell Adhesion Molecule), that is over-expressed on most epithelial carcinomas, including colon cancer.

Results: The addition of huKS-IL2 treatment to RFA-treated mice resulted in a significantly greater antitumor response as measured by suppression of tumor growth, compared to untreated animals and those treated with RFA or huKS-IL2 alone. Animals treated with huKS-IL2 + RFA also had significantly enhanced survival compared to all other treatment groups. Further, after conditions were optimized, treatment with RFA + huKS-IL2 resulted in complete tumor resolution of established disease in 50% of mice, whereas under these conditions no mice in other groups resolved tumors. When immunological memory was tested in tumor-bearing mice that resolved smaller tumors, RFA + huKS-IL2 resulted in significantly more animals rejecting both CT26-KS and more aggressive CT26 tumors on rechallenge, compared to animals treated with RFA alone. This memory response was found to be tumor-specific, as animals which previously rejected CT26-KS and CT26 did not reject an unrelated Meth A sarcoma. Treatment of a local tumor with RFA + huKS-IL2 also demonstrated anti-tumor effects against a distant untreated tumor. Flow cytometry analysis of T-cells from mice from all treatment groups demonstrated that treatment with RFA + huKS-IL2 results in a greater proportion of cytokine producing (interferon and GM-CSF) CD4 T-cells and CD8 T-cells than all other treatment groups.

Conclusion: These results show that the addition of huKS-IL2 to RFA significantly enhances the anti-tumor response, resulting in complete tumor resolution and induction of immunological memory.

(primary authors listed in italics)

Tumor Targeting Monoclonal Antibodies

ANTIBODY AND SMALL MODULAR IMMUNE PHARMACEUTICAL THERAPIES FOR PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA: A MAJOR STEP FORWARD

John C. Byrd

Internal Medicine, The Ohio State University, Columbus, OH

Chronic lymphocytic leukemia (CLL) is the most common type of adult leukemia and is currently not curable with available therapy. For several decades different cytotoxic therapies have been introduced with only modest improvement in observed response and time of treatment remission. The introduction of the two therapeutic monoclonal antibodies rituximab and alemtuzumab has greatly impacted the therapy of CLL. Rituximab when combined with fludarabine or fludarabine and cyclophosphamide increases the complete remission rate significantly, promotes remissions lasting greater than 5 years in a subset of patients and may prolong survival. Similar promising results have been observed with alemtuzumab when applied as a consolidation therapy for eliminating minimal residual disease. Given the success of therapeutic antibodies in CLL, we have taken an active role in exploring several new therapeutic antibodies in the laboratory and clinic. Our laboratory interest has recently transitioned to studying a different class of drugs, small modular immune pharmaceuticals (SMIP). Several SMIP agents have been constructed using a single chain variable region (scFv) linked to a modified human IgG1 hinge, CH2 and CH3 domains. CD37 SMIP is one such agent that targets CD37, a lineage-specific B-cell antigen that represents an attractive target for immunotherapy in B-cell malignancies. We have demonstrated that CD37 SMIP promotes significant induction of apoptosis and antibody dependent cellular cytotoxicity (ADCC) but not complement mediated cytotoxicity by CD37-SMIP against B-cell lymphoma/leukemia cell lines and primary chronic lymphocytic leukemia (CLL) cells. The apoptosis induced by CD37-SMIP was correlated with levels of CD37 surface expression and occurred independent of caspase activation. Most notably, CD37 SMP mediates apoptosis and ADCC significantly better than alternative antibodies used for CLL including alemtuzumab and rituximab. We have examined which effector cells are responsible for ADCC and have identified that natural killer (NK) cells but not naïve or activated monocytes mediate CD37-SMIP dependent ADCC function in vitro. Interestingly, CD37-SMIP conferred significant protection from disease progression in vivo in a Raji cell xenograft SCID mouse model of disseminated leukemia/lymphoma with a dramatic improvement in survival following treatment. Depletion of NK cells in mice resulted in diminished efficacy of CD37-SMIP further supporting the in vivo importance of NK cells in SMIP-mediated therapeutic efficacy. Overall our data suggest that the CD37-SMIP is a promising therapeutic agent against CD37+ B-cell malignancies that warrants further clinical development. This talk will focus on new antibody and SMIP based therapies coming forward for the treatment of CLL and related lymphoproliferative disorders.

Presentation Abstracts – Saturday

(primary authors listed in italics)

PHASE I/II STUDY OF CR011-VCMMAE, AN ANTIBODY-DRUG CONJUGATE TARGETING GPNMB, FOR THE TREATMENT OF PATIENTS WITH ADVANCED MELANOMA

Patrick Hwu[1], M. Sznol[2], A. Pavlick[3], H. Kluger[2], K. B. Kim[1], W. J. Hwu[1], N. Papadopoulos[1], D. Sanders[1], P. Boasberg[4], R. Simantov[5], O. Hamid[4]
[1]*MD Anderson Cancer Center, Houston, TX*
[2]*Yale Cancer Center, New Haven, CT*
[3]*New York University Medical Center, New York, NY*
[4]*The Angeles Clinic, Santa Monica, CA*
[5]*CuraGen Corporation, Branford, CT*

Background: Glycoprotein NMB (GPNMB) is expressed by a number of tumor types including melanoma, breast cancer, and glioma, and has been shown to promote the invasion and metastasis of cancer cells. CR011-vcMMAE is a fully-human monoclonal antibody directed against the extracellular domain of GPNMB conjugated to the tubulin-stabilizing agent monomethyl auristatin E (MMAE) via an enzyme-cleavable valine-citrulline (vc) linker. The antibody-drug conjugate is designed to bind GPNMB and undergo internalization, which leads to intracellular cleavage of the vc linker by endosomal proteases, releasing the cytotoxic MMAE.

Methods: The study objectives are to determine the safety, establish the maximum tolerated dose, and assess the activity of CR011-vcMMAE administered iv once every 3 weeks in patients with unresectable stage III or stage IV melanoma. Eligible patients have progressive disease at study entry and may have received prior cytokine, immune, or vaccine therapies, but no more than one prior cytotoxic therapy. Phase II uses a Simon 2-stage design with the primary endpoint of objective response rate.

Results: Thirty-two patients (26 (81%) stage IV; 11 M1b, 12 M1c) in Phase I received doses of 0.03-2.63 mg/kg iv q 3 wks. Dose-limiting toxicities at 2.63 mg/kg were rash with desquamation (n=2). The recommended Phase II dose was 1.88 mg/kg iv q 3 wks. Preliminary adverse event data at this dose (n=15) included: fatigue (n=10), rash (n=9, one grade 3), diarrhea (n=8), and nausea (n=8). Neutropenia was observed in nine patients at 1.88 mg/kg; five were grade 2, two were grade 3 and two were grade 4. Pharmacokinetic analysis showed terminal half-life for total antibody of 38 hours with less than 1% free MMAE. Tumor shrinkage, including one PR by RECIST, was observed in Phase I and appeared to be dose-dependent. In the ongoing Phase II study, 18 patients (8 women; 10 men), median age 58 years (range 38-70) were evaluable for response as of 01 July 2008. Three ongoing patients had PR (1 confirmed, 2 unconfirmed); 12 patients had SD (median 9 wks, range 7+ to 20+ wks) with 10 continuing on study.

Conclusions: The antibody-drug conjugate CR011-vcMMAE is active and well-tolerated in heavily pretreated patients with advanced melanoma. The Phase II portion of the study has met the criteria for advancement into the second stage of accrual. Updated Phase II data will be presented.

OPTIMIZING ENGAGEMENT OF THE IMMUNE SYSTEM BY ANTI-TUMOR ANTIBODIES

John R. Desjarlais, John Richards, Greg Lazar, Sher Karki
Research, Xencor, Inc., Monrovia, CA

Antibody-dependent cellular killing is considered one of the primary modes of action of anti-tumor antibodies. Numerous in vitro and in vivo studies on the role of Fc γ receptors (FcγR) support this premise, which is further supported by observed correlations between FcγR polymorphisms and clinical efficacy of antibodies such as Rituxan and Herceptin. Considerable effort has therefore been applied to modify the Fc domains of therapeutic antibodies to enhance their interactions with one or more FcγRs and further promote engagement of immune effector cells. However, several related FcγRs and immune effector cells are capable of mediating killing through a variety of mechanisms, and careful review of the available literature on which of these dominates in humans is inconclusive. Although many engineering efforts have been aimed at enhancing FcγRIIIa interactions, a growing body of evidence suggests that FcγRIIa may be of equal or greater importance. In our efforts to better understanding of the impact of Fc engineering on antibody efficacy, we have engineered a series of Fc domain variants that have diverse affinities for human FcγRIIIa, FcγRIIa, and FcγRIIb and have characterized their abilities to promote targeted in vitro killing of tumor cells by human NK cells, macrophage, and neutrophils. We find that while NK-mediated killing is mediated by FcγRIIIa, macrophage- and neutrophil-mediated killing are dominated by FcγRIIa, and that these latter cell types are more efficiently activated by Fc modifications that enhance FcγRIIa affinity. Finally, we demonstrate in mouse and non-human primate pharmacology studies that Fc engineering can dramatically enhance the in vivo efficacy of antibodies.

(primary authors listed in italics)

CETUXIMAB MEDIATED ANTIBODY DEPENDENT CELLULAR CYTOTOXICITY (ADCC) BY NK CELLS EXPRESSING POLYMORPHIC FC GAMMA RECEPTOR (FCγR)IIIA

Robert L. Ferris, Andres Lopez-Albaitero, Steve Lee, William Gooding
University oif Pittsburgh Cancer Institute, Pittsburgh, PA

Despite cetuximab's clinical efficacy against squamous cell carcinoma of the head and neck (SCCHN) only 10-20% of the patients receiving it demonstrate responses. We previously demonstrated that the EGFR-specific mAb cetuximab can mediate antibody dependent cell cytotoxicity (ADCC) against squamous cell carcinoma of the head and neck (SCCHN) cells, but factors responsible for variability between donors, such as polymorphisms in Fcγ receptor (FcγR) and level of EGFR expression have not been determined. ADCC assays were performed using cetuximab treated SCCHN cell lines expressing different levels of EGFR and enriched NK cells or unfraccionated PBMC from SCCHN patients or healthy donors. Effector cells were characterized for their FcγRIIIa-158 genotype and analyzed by flow cytometry for CD69 and CD107a expression. Supernatants from these assays were analyzed using multiplexed ELISA for their cytokine and chemokine secretion. NK cells and SCCHN patients PBMC with poor ADCC responses were treated with IL-2 or IL-15 and used in ADCC assays. Cetuximab mediated ADCC against SCCHN cell lines varied with the NK cell FcγRIIIa-158 polymorphisms (VV>VF>FF, $p<0.001$) and was dependent of antibody concentration and level of EGFR expression. Furthermore, these polymorphisms correlated with CD69 and CD107a expression by effector cells and their secretion of IFN-γ, TNF-α, IL-8, MIP-1α and MIP-1β. Treatment of effector PBMC with IL-2 or IL-15 enhanced ADCC activity in both poor responder PBMC, leading to increased effector cell activation phenotype and cytokine secretion genotype.

The importance of FcγRIIIa polymorphisms in cytotoxicity of NK cells against SCCHN cells supports a potential role for immune activation in variability of cetuximab mediated clinical responses. Additionally, these polymorphisms correlated with NK cell activation and cytokine secretion. ADCC activity by PBMC from SCCHN patients and poor responder genotypes can be improved with IL-2 or IL-15 treatment. Serum cytokine levels, cellular immune profiles or FcγR genotypes from patients' peripheral blood may provide clinically useful biomarkers of immune activation in cetuximab treated patients. Prospective clinical trials are necessary to validate these findings in SCCHN.

Innate Immunity to Tumors

INNATE RESISTANCE, INFLAMMATION, AND CANCER

Giorgio Trinchieri
Cancer and Inflammation Program, Center for Cancer Research, NCI, Frederick, MD

The interaction of the inflammatory mediators and innate and immune effector cells with carcinogenesis and tumor progression is complicated and results in effects that either favor or impede tumor progression. The simple concept that early inflammation is necessary for carcinogenesis whereas inflammatory and immune response would prevent, when successful, tumor progression has been replaced by a more subtle understanding that the degree of inflammation and the type of inflammatory/immune response are responsible for tilting the balance between tumor progression and regression. Furthermore, it is becoming evident that the processes that the organisms use for resistance to infections are derived and shared with the mechanisms essential for tissue homeostasis and morphogenesis. Innate resistance is mediated not only by specialized cells but most stromal and parenchyma cells participate in the process and they may express and utilize many of the receptors also utilized by "immune" cells with similar signaling and physiological responses. Similarly, in cancer biology, it is becoming manifest that what used to be considered the defensive mechanisms of innate resistance and inflammation are indeed manifestations of tissue homeostasis and control of cellular proliferation that have many pleiotropic effects on carcinogenesis as well as on tumor progression and dissemination. The understanding of the cross-talk between inflammation and tumorigenesis may open new opportunities for the planning of therapeutic intervention for tumor prevention and treatment.

Presentation Abstracts – Saturday

(primary authors listed in italics)

ROLE OF NKG2D IN TUMOR SURVEILLANCE

David Raulet
Molecular and Cell Biology, UC Berkeley, Berkeley, CA

Natural killer (NK) cell receptors regulate the capacity of NK cells and in some cases T cells to attack tumor cells and infected cells. Diseased cells in the body become susceptible to NK cells by down-regulating inhibitory ligands such as MHC class I molecules, and/or up-regulating stimulatory ligands, such as the Raet1 family proteins recognized by the NKG2D receptor. This presentation will discuss the role of NKG2D in tumor surveillance in vivo and the molecular mechanisms and signaling pathways responsible for induction of NKG2D ligands in cancer cells and their relationship to major pathways regulating tumorigenesis. Supported by grants from NCI, NIAID and Prostate Cancer Foundation.

INNATE IMMUNITY CAN CONTRIBUTE TO THE SHAPING OF TUMOR IMMUNOGENICITY IN THE ABSENCE OF ADAPTIVE IMMUNITY

Jack D. Bui[1], William Vermi[2], Cora Arthur[2], J. Michael White[2], Ravindra Uppaluri[3], Robert D. Schreiber[2]
[1]*Pathology, University of California, La Jolla, CA*
[2]*Pathology and Immunology, Washington University, St. Louis, MO*
[3]*Otolaryngology, Washington University, St. Louis, MO*

Although components of innate and adaptive immunity have been shown to work together to protect the host against cancer development and sculpt tumor immunogenicity (i.e., promote cancer immunoediting), it remains unclear whether innate immunity is capable of manifesting tumor-editing functions on its own. In particular, whereas natural killer (NK) cells can promote tumor surveillance of methylcholanthrene (MCA)-induced sarcomas in the context of an intact immune system, it has not been shown whether NK cells can impact on cancer immunoediting without subsequent contributions from T cells. To address this question, we compared the immunogenicities of sarcoma cells derived from MCA-treated wild type (WT) immunocompetent mice, RAG2-/- mice lacking adaptive immunity, or RAG2-/- x IL-2Rgc-/-mice which lack NK cells and adaptive immunity. To measure immunogenicity, MCA-sarcoma cell lines were transplanted into naive, syngeneic WT or RAG2-/- mice to assess their ability to grow in the presence of the full immune system or solely the innate immune system. Consistent with our previous reports, all sarcoma cell lines from MCA-treated WT mice were poorly immunogenic and grew progressively when transplanted into syngeneic WT recipients. In addition, 40% of sarcoma cell lines from MCA-treated RAG2-/- mice displayed high immunogenicity and were rejected. Interestingly, MCA-sarcoma cells from RAG2-/- x IL-2Rgc-/- mice were highly likely to be immunogenic since 60% were rejected when transplanted into WT mice. When these cell lines were transplanted into RAG2-/- mice, all cell lines were able to grow. However, the RAG2-/- x IL-2Rgc-/- MCA-sarcomas displayed delayed growth compared to MCA-sarcomas from RAG2-/- and WT mice. Furthermore, RAG2-/- x IL-2Rgc-/- tumors that were transplanted into RAG2-/- mice became heavily infiltrated with innate immune cells that expressed high levels of MHC class II. This infiltration required IL-2Rgc function, suggesting that NK cells are important in the recruitment of class II+ cells into highly immunogenic tumors. Finally, the infiltration of innate cells into highly immunogenic tumors resulted in tumor editing, since highly immunogenic tumor cells that were passaged through RAG2-/- but not RAG2-/- x IL-2Rgc-/- mice became poorly immunogenic. Our results conclusively show that innate immunity can manifest IL-2Rgc-dependent tumor editing function in the absence of adaptive immunity.

(primary authors listed in italics)

Presentation Abstracts – Saturday

SPONTANEOUS CTL-MEDIATED REJECTION OF GP33-POSITIVE LEWIS LUNG CARCINOMA IS DEPENDENT ON AN IFNAR COMPETENT ENVIRONMENT

Patricia Bach[1], Susanne Roederstein[1], Peter Aichele[2], Ulrike Blohm[3], Thomas Hinz[1], Hanspeter Pircher[2], *Ulrich Kalinke*[1]
[1]Immunology, Paul-Ehrlich-Institut, Langen, Germany
[2]Institute of Medical Microbiology and Hygiene, Freiburg, Germany
[3]Friedrich-Loeffler Institute, Insel Riems, Germany

Recent evidence accumulated that interferon-alpha/beta (IFN-a/b) can support anti-tumor activity by stimulating host cells instead of exhibiting anti-proliferative effects on tumor cells. We addressed the role of the IFN-a/b system in a model of a spontaneous tumor regression, i.e. Lewis lung carcinoma expressing the cytotoxic T cell (CTL) epitope 33 of lymphocytic choriomeningitis virus glycoprotein as a tumor associated neo-antigen (A9GP33). In A9GP33 treated wild-type (WT) mice, small tumors developed within 5 to 8 days that usually were rejected by GP33-specific CTL around day 14. In contrast, mice devoid of a functional IFN-a/b receptor (IFNAR-/-) showed progressive A9GP33 growth. The analysis of such tumor cells in a GP33-specific in vitro CTL assay revealed that tumor cells were still GP33-positive. Furthermore, approximately 20% of A9GP33 tumors grown in IFNAR-/- mice were still rejected when re-injected into WT mice. Interestingly, T cell priming was not impaired in IFNAR-/- mice as indicated by similar cytolytic activities in spleen cells of A9GP33 treated IFNAR-/- and WT mice in a secondary 51Cr release assay. Nevertheless, reduced in vivo killing of GP33 positive target cells was observed in A9GP33 treated IFNAR-/- mice when compared to WT mice. The analysis of conditional mice with a lymphocyte-specific IFNAR ablation indicated that direct IFNAR trigging of B and/or T cells did not play a crucial role in A9GP33 tumor rejection, whereas stimulation of dendritic cells was critical. Thus, our data indicate that tumor-induced CTL priming was overall normal in IFNAR-/- mice, whereas an IFNAR competent environment was required to promote efficient tumor lysis.

Presentation Abstracts – Sunday

Cancer Stem Cells and the Host Response

REGULATION OF BREAST CANCER STEM CELLS BY THE MICROENVIRONMENT

Max S. Wicha, L. Liu, C. Ginestier, H. Korkaya
University of Michigan Comprehensive Cancer Center, Ann Arbor, MI

There is increasing evidence that breast cancers may be driven and maintained by a cellular subcomponent that exhibits stem cell properties. These properties include self-renewal which drives tumorigenesis and differentiation which generates the cellular heterogeneity found in the tumor bulk. These "tumor stem cells" mediate invasion and metastasis and may contribute to treatment resistance. We have developed *in vitro* and mouse models to investigate the influence of cells in the tumor microenvironment on cancer stem cell behavior. Humanization of NOD/SCID mouse breasts by introduction of normal mammary fibroblasts facilitates mammary gland development from normal human breast stem cells. In breast tumors, breast cancer stem cell self-renewal is stimulated by mesenchymal stem cells which may be recruited from the bone marrow. This regulation of breast cancer stem cells by the mesenchyme is mediated by cytokines including IL6, IL8, CCL5 and CCL6. Inhibition of IL8 signaling induces apoptosis in breast tumor cells, a process mediated by the FAS pathway. These studies demonstrate that the tumor microenvironment plays a crucial role in the regulation of breast stem cells. Interventions aimed at dysregulating microenvironmental signals may provide a novel approach to targeting cancer stem cells. Since these cells drive tumorigenesis, metastasis and mediate treatment resistance, these approaches may improve outcome for patients with advanced metastatic cancers.

Presentation Abstracts – Sunday

(primary authors listed in italics)

HARNESSING THE IMMUNE SYSTEM TO TARGET STEM CELL GENES IN MYELOMA

Madhav Dhodapkar
Yale University, New Haven, CT

Immune system has long been thought as a potential barrier to cancer, and can represent a useful approach for early detection and prevention of cancer. However, while the nature of antigens recognized by the immune system in cancer patients have been extensively studied, less is known of the targets of immune response in the preclinical stages of cancer. Understanding which targets correlate with improved outcome also has major implications for immune therapy and prevention of cancer. Monoclonal gammopathy of undetermined significance (MGUS) represents a precursor lesion to myeloma and is much more common than its malignant counterpart. In spite of the high degree of genomic changes in tumor cells, most MGUS lesions do not progress to MM. Recently, we developed the tools to evaluate the nature of antigenic targets in preneoplasia. Our studies suggest that the targets of spontaneous immune response in preneoplastic MGUS may differ from those in MM. Majority of MGUS patients, but not MM or healthy donors, mount an immune response against SOX2, a gene critical for pluripotency in human embryonal stem cells. The detection of intranuclear SOX2 marks the putative clonogenic compartment in MGUS, and anti-SOX2 T cells effectively inhibit the growth of these tumors. The detection of these T cells predicts exceptionally good clinical outcome and prolonged survival in patients with early plasma cell tumors. These data support the hypothesis that immune targeting of critical stem cell associated pathways may be of therapeutic benefit in myeloma and other tumors.

CHARACTERIZATION OF THE IMMUNE PROFILE OF CANCER STEM CELLS ISOLATED FROM HUMAN GLIOBLASTOMA

Cristina Maccalli[1], Stefania Mazzoleni[2], Samantha Scaramuzza[1], Gloria Sovena[1], Soldano Ferrone[3], Rossella Galli[2], Parmiani Giorgio[1]
[1]*Oncology, Unit of Immuno-Biotherapy of Solid Tumors, San Raffaele Foundation Scientific Institute, Milan, Italy*
[2]*Stem Cell Research Institute, San Raffaele Foundation Scientific Institute, Milan, Italy*
[3]*Hillman Cancer Center, University of Pittsburgh Cancer Institute, Pittsburgh, PA*

Cancer Stem cells (CSCs) represent the most aggressive component of tumors and have been proposed as elective cellular target in the context of biological therapies such as immunotherapy. The main objectives of our project are represented by the identification of markers with immunological relevance expressed by CSCs and the validation of their role as target molecule to design immunotherapeutic protocols for GBM.

We carried out a set of experiments using IF and cytofluorimetric or confocal microscopy analysis aimed at the immunological characterization of CSCs isolated from human GBM and in vitro cultured either in the presence or absence of mitogens. We found that GBM CSCs were negative or weakly positive for the expression of MHC class I or class II molecules, with only 1 out of 8 GBM CSC lines expressing high level of HLA molecules. Along this line, NKG2D ligands (MICA/B or ULBPs) were weakly or not expressed by most GBM CSCs with only one cell line being positive for all these molecules while significant expression of these molecules was detected on GBM tumor cell lines (grown in vitro under standard culture conditions (FBS)). Moreover, defective expression of MHC antigen processing machinery (APM) by GBM CSC lines was observed. Up-regulation of MHC class I and of most of APM molecules was achieved after IFN-γ treatment of CSCs, while weak or no modulation of MHC class II molecules was observed. Heterogeneous expression of MHC molecules or NKG2D ligands was also observed in tumors generated by intracranial or subcutaneous trasplantation of GBM CSCs in immunodeficient mice. Notably, cancer-testis TAAs, such as NY-ESO or MAGE were weakly or not expressed by GBM CSC lines while survivin and COA-1 were detected in all these cell lines (N=8). We carried out in vitro stimulation of PBMCs isolated from two GBM patients with autologous CSCs and the specific reactivity of T lymphocytes against GBM CSCs was evaluated by IFN-γ release (ELISPOT) or cytotoxic activity (CD107a mobilization). We found that GBM CSCs, following IFN-γ treatment, can elicit an efficient CSC-specific T cell-mediated immune response.

Taken together, these results indicate that MHC molecules and NKG2D ligands are expressed heterogeneously by both in vitro established CSC lines and in tumors transplanted in immunodeficient mice. In addition, though the expression of APM is defective in these cells, we found that GBM CSCs can be exploited to generate T cell-mediated immune responses in at least some GBM patients.

Presentation Abstracts – Sunday

CD133 AS A POTENTIAL TARGET OF ANTI-CANCER STEM CELL IMMUNOTHERAPY: IDENTIFICATION OF A HLA-A*02 RESTRICTED CD133 EPITOPE

John S. Yu[1,2], Gentao Liu[2], Aki Hoji[1], Minlin Xu[2], Mia Mazer[2], Keith Black[2]
[1]*Immunocellular Therapeutics, Woodland Hills, CA*
[2]*Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, CA*

Recently, we have found a small population of cells in malignant glioblastoma multiforme (GBM), that resemble cancer stem cells (CSCs). These putative GBM CSCs appear to express high levels of CD133, a surface protein that is normally absent from neuronal cells. This raises a possibility that CD133 could serve as a potential target of cytotoxic T cells (CTLs) in future GBM CSC immunotherapy. In order to find potential CTL epitopes for masses, we sought immunogenic HLA-A*0201 restricted CD133 epitopes in this study. Based on an epitope prediction, five potential HLA-A*02 restricted CD133 epitopes were selected for further immunologic characterizations. Among these epitopes, a ninemer demonstrated the strongest binding to HLA-A*0201 molecules. To further test the immunogenecity of this epitope, we were able to generate peptide-specific CD8+ cytotoxic T cells (CTLs) from a normal donor by using autologous monocyte derive dendritic cells (MoDC) pulsed with ILS. Moreover, MoDC loaded with irradiated CD133 positive CSCs were to prime ILS-specific CTLs in vitro. These in vitro generated CTLs only recognized CD133 expressing HLA-A*0201+ GBM CSCs but not CD133 expressing normal neural stem cells which lack expression of MHC class I molecules. Overall, our findings show natural processing and subsequent presentation of immunodominant CD133 epitopes in GBM CSCs, and the presence of CD8+ T cells specific for such epitope in the periphery. The results of this study have an enormous impact on current and future GBM immunotherapy since successful immunotherapy depends largely on discovery of CTL epitopes that can specifically target GBM CSCs.

Posters – Friday

(primary authors listed in bold italics)

Poster #:

Adoptive Transfer

1 **SELECTIVE EXPANSION OF HUMAN T REGULATORY CELL SUBSETS AND T CELL DEPLETION: ROLE OF RAPAMYCIN (SIROLIMUS)**
Christoph Bergmann[1,2], *Laura Strauss[2], Stephan Lang[1], Magis Mandapathil[2,1], Theresa L. Whiteside[2]*
[1]Department of Otorhinolaryngology, University of Duisburg-Essen, Essen, Germany
[2]Department of Pathology, University of Pittsburgh Cancer Institute, Pittsburgh, PA

2 **ADOPTIVE TRANSFER OF "YOUNG" MART1/MELAN-A CTL GENERATED WITH ARTIFICIAL APC AND IL-2/IL-15: EMERGENCE AND PERSISTENCE OF A MEMORY/EFFECTOR PHENOTYPE**
Marcus O. Butler, *Philip A. Friedlander, Mary Mooney, Alla Berezovskaya, Linda Drury, Marisa Flavin, Andrew Murray, Osamu Imataki, Makito Tanaka, Heather Daley, Myriam Armant, Grace Kao, F. Stephen Hodi, Lee M. Nadler, Naoto Hirano*
Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA

3 **INSERTION OF AN MHC CLASS I-RESTRICTED T CELL RECEPTOR (TCR) SKEWS THE PHENOTYPE OF GENETICALLY ENGINEERED HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMCS) FOR ADOPTIVE T CELL THERAPY**
Thinle Chodon[1], *Erika M. von Euw[1], Richard C. Koya[2], Begonya Comin-Anduix[2], Paul Tumeh[2], Antoni Ribas[1,2]*
[1]Dept. of Medicine, Div. of Hem/Onc, UCLA, Los Angeles, CA
[2]Dept. of Surgery, UCLA, Los Angeles, CA

4 **MYCOPHENOLATE MOFETIL SELECTION OF GENE MODIFIED T CELLS WITH AN ENGINEERED HUMAN INOSINE MONOPHOSPHATE DEHYDROGENASE II (IMPDH2)**
Mahesh Jonnalagadda, *Wen-Chung Chang, Michael C. Jensen*
Cancer Immunotherapeutics and Tumor Immunology, BRI, City of Hope National Medical Center, Duarte, CA

5 **MAINTENANCE OF TUMOR ANTIGEN-SPECIFIC CYTOLYTIC T CELLS DURING EXPANSION OF TIL FOR ADOPTIVE IMMUNOTHERAPY**
Shujuan Liu[1], *Tamara Etto[1], Pariya Sukhumalchandra[2], Tania Rodriguez-Cruz[1], Yufeng Li[1], Jeffrey J. Molldren[2], Patrick Hwu[1], Laszlo Radvanyi[1], Gregory Lizee[1]*
[1]Melanoma Medical Oncology, UT MD Anderson Cancer Center, Houston, TX
[2]Stem Cell Transplantation and Cellular Therapy, UT MD Anderson Cancer Center, Houston, TX

6 **ENGINEERING TUNABLE HOMEOSTATIC SIGNALING RECEPTORS BASED ON IL-7R FOR REGULATION OF PROLIFERATION, SURVIVAL, AND DIFFERENTIATION STATUS OF CD8+ CYTOLYTIC T CELLS**
Michelle Malbon, *Michael C. Jensen*
Cancer Immunotherapeutics and Tumor Immunology, BRI, City of Hope National Medical Center, Duarte, CA

7 **GENETIC APPROACHES FOR COMBINATORIAL RESISTANCE TO PD-1 AND TGF-β MEDIATED T CELL DYSFUNCTION IN THE TUMOR MICROENVIRONMENT**
Megan Prosser, *Michael C. Jensen, John J. Rossi*
Cancer Immunotherapeutics & Tumor Immunology, BRI, City of Hope National Medical Center, Duarte, CA

8 **NOVEL METHODS FOR THE GENERATION AND CHARACTERIZATION OF MELANOMA-SPECIFIC T CELLS FROM TUMOR-INFILTRATING LYMPHOCYTES**
Sachin Puri[1], *James A. Thompson[1], Tarsem L. Moudgil[1], Elisa Cardenas[1,2], Nick Morris[1], William Miller[1], Kevin Floyd[1], Andy Weinberg[1,2], Sidney H. Rosenheim[1], Christian H. Poehlein[1], Walter J. Urba[1], Edwin Walker[1], Bernard A. Fox[1,2]*
[1]Molecular And Tumor Immunology, Earle A Chiles Research Institute, Portland, OR
[2]Molecular Microbiology and Immunology, Oregon Health and Science University, Portland, OR

9 **ADOPTIVE T-CELL THERAPY AT THE MD ANDERSON CANCER CENTER: EARLY RESULTS AND A PROMISING FUTURE**
Laszlo Radvanyi, *Vijay Peddareddigari, Kathryn Bushnell, Rahmatu Bassie, Orenthial Fulbright, Marissa Gonzalez, Priscilla Miller, Patrick Hwu Melanoma Medical Oncology, UT MD Anderson Cancer Center, Houston, TX*

10 **A PHASE I/II TRIAL OF COMBINATION THERAPY OF TUMOR LYSATE-PULSED DENDRITIC CELLS AND ADOPTIVE TRANSFER OF ANTI-CD3 ACTIVATED T CELLS (ATVAC) IN PATIENTS WITH ADVANCED GASTROINTESTINAL (GI) CANCERS**
Koichi Shimizu[1,2,3], *Keishi Tanigawa[3,2], Nobuhiro Takeshita[2], Toshimi Fujisawa[2], Ken Takasaki[3,2], Masakazu Yamamoto[2], Atsuhi Aruga[2]*
[1]Chemoimmunotherapy Center, Shin-Itabashi Clinic, Tokyo, Japan
[2]Department of Gastroenterological Surgery, Tokyo Women's Medical University (TWMU), Tokyo, Japan
[3]J. B. Therapeutics. Inc., Japan, Tokyo, Japan

(primary authors listed in bold italics)

Posters – Friday

11 PHASE II TRIAL OF COMBINATION THERAPY OF TUMOR LYSATE-PULSED DENDRITIC CELLS AND ADOPTIVE TRANSFER OF ANTI-CD3 ACTIVATED T CELLS (ATVAC) TO LOWER POSTSURGICAL RECURRENCE RATES OF CHOLANGIOCELLULAR CARCINOMA (CCC)
Koichi Shimizu[1,2,3], *Nobuhiro Takeshita[2], Yoshihito Kotera[2], Kenji Yoshitoshi[2], Syunichi Ariizumi[2], Satoshi Katagiri[2], Yoshihito Otsubo[2], Keishi Tanigawa[3,2], Ken Takasaki[3,2], Masakazu Yamamoto[2], Atsushi Aruga[2,3]*
[1]Chemoimmunotherapy Center, Shin-Itabashi Clinic, Tokyo, Japan
[2]Department of Gastroenterology, Tokyo Women's Medical University (TWMU), Tokyo, Japan
[3]J. B. Therapeutics inc., Japan, Tokyo, Japan

12 THE CD19 CHIMERIC ANTIGEN RECEPTOR RE-DIRECTS CMV SPECIFIC T CELLS DERIVED FROM CENTRAL MEMORY T CELLS (BI-SPECIFIC T CELLS) AGAINST HUMAN ACUTE LYMPHOID LEUKEMIA (ALL)
Xiuli Wang, *Winnie Wong, Wen-Chung Chang, Julie R. Ostberg, David DiGiusto, Michael C. Jensen*
Cancer Immunotherapeutics and Tumor Immunology, BRI, City of Hope National Medical Center, Duarte, CA

13 ISOLATING HIGH-AFFINITY T CELL RECEPTORS FOR ADOPTIVE THERAPY OF TUMORS
Susanne Wilde[1], *Bernhard Frankenberger[1], Daniel Sommermeyer[3], Wolfgang Uckert[3], Slavoljub Milosevic[1], Stefani Spranger[1], Heike Pohla[2,4], Matthias Schiemann[5], Dirk H. Busch[5], Dolores J. Schendel[1,2]*
[1]Institute of Molecular Immunology, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich, Germany
[2]Institute of Molecular Immunology and Clinical Cooperation Group Immune Monitoring, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich, Germany
[3]Max-Delbrueck-Center for Molecular Medicine, Berlin, Germany
[4]Laboratory of Tumor Immunology, LIFE-Center, Ludwig-Maximilians-University, Munich, Germany
[5]Institute of Microbiology, Immunology and Hygiene, Technical University Munich, Munich, Germany

Poster #:

Dendritic Cells

14 AUTOLOGOUS DENDRITIC CELL IMMUNOTHERAPY INDUCED INCREASES IN SERUM TARC/CCL17 LEVELS ARE ASSOCIATED WITH PROGRESSION-FREE SURVIVAL IN ADVANCED MELANOMA PATIENTS
Andrew N. Cornforth, *Gregory Lee, William McRorie, Abner Fowler, Deneysha Carbonell, Beatty Andrea, Tillman Sarah, Senthamil R. Selvan, Robert O. Dillman*
Cell Biology Lab, Hoag Cancer Center, Newport Beach, CA

15 TUMOR LYSATE CAPTURE AND PROCESSING BY DENDRITIC CELLS: A KINETIC AND AN IMMUNOFLUORESCENCE STUDY BY FLOW CYTOMETRY AND CONFOCAL MICROSCOPY IMAGING
Granato[1], Elena Pancisi[1], Laura Ridolfi[1], Ruggero Ridolfi[1], Jay R. Knutson[2], Tilman Rosales[2], ***Paolo Neyroz[3]***
[1]Immunotherapy and Somatic Cell Therapy, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola-Forlì, Italy
[2]Laboratory of Molecular Biophysics, National Heart, Lung and Blood Institute,, National Institutes of Health, Bethesda MD 20892-1412, MD
[3]Department of Biochemistry, University of Bologna, Bologna, Italy

16 IL-12 AS AN IMMUNOPOTENCY MARKER FOR FULLY AUTOLOGOUS DENDRITIC CELL IMMUNOTHERAPEUTICS
Don G. Healey, *David Calderhead, Helen Ketteringham, Alicia Gamble, Joe Horvatinovich, Irina Tcherepanova, Charles Nicolette, Mark DeBenedette*
Immunology, Argos Therapeutics, Durham, NC

17 THE EVALUATION OF MONOCYTE DERIVED MATURE DENDRITIC CELLS WITH GENE AND MICRORNA EXPRESSION MICROARRAYS
Tae Hee Han[1,2], *Ping Jin[1], Jiaqiang Ren[1], Stefanie Slezak[1], Francesco M. Marincola[1], David F. Stroncek[1]*
[1]DTM, NIH, Bethesda, MD
[2]Inje University, Sanggye Paik Hospital, Seoul, South Korea

18 INFLUENCE OF PLATELETS ON THE ACTIVATION AND FUNCTION OF SIPULEUCEL-T, AN INVESTIGATIONAL CELLULAR IMMUNOTHERAPY FOR THE TREATMENT OF PROSTATE CANCER
Joseph B. Marino, *L. A. Jones, N. A. Sheikh, N. R. Chu*
Dendreon Corporation, Seattle, WA

19 PHENOTYPIC AND FUNCTIONAL ANALYSIS OF STANDARD AND FAST DENDRITIC CELLS (DC)FOR DC-BASED CANCER IMMUNOTHERAPY
Carlos A. Parra-Lopez[1], *Diana R. Tovar Murillo[1,2]*
[1]Microbiology and Immunology Department, Universidad Nacional de Colombia, Medical School, Bogotá, Colombia
[2]Group of Immunotherapy at PREVIMEDIC S. A., Center for Immunological Studies on Clinical Onco-Immunology, Bogotá, Colombia

Poster Listing

(primary authors listed in bold italics)

Posters – Friday

20 BLOCKADE OF TRANSFORMING GROWTH FACTOR BETA RECEPTOR I ENHANCES THE EFFICACY OF DENDRITIC CELL-BASED IMMUNOTHERAPY OF ESTABLISHED BREAST TUMORS
***Matthew P. Rausch*[1]**, *Lalitha Ramanathapuram[1], Tobias Hahn[2], Deborah Bradley-Dunlop[1], Daruka Mahadevan[3], David G. Besselsen[4], Xiamei Zhang[5], H. Kam Cheung[5], Wen Cherng Lee[5], Leona E. Ling[5], Emmanuel T. Akporiaye[2]*
[1]Immunobiology, University of Arizona, Tucson, AZ
[2]Robert W. Franz Cancer Research Center, Providence Portland Medical Center, Portland, OR
[3]The Arizona Cancer Center, University of Arizona, Tucson, AZ
[4]University Animal Care and Department of Veterinary Sciences/Microbiology, The University of Arizona, Tucson, AZ
[5]Oncology Cell Signaling, Biogen Idec, Cambridge, MA

21 INTRATUMORAL INJECTION OF IMMATURE DENDRITIC CELLS (DCI) AGAINST GASTROINTESTINAL (GI) CANCERS: A PHASE I STUDY IN PATIENTS WITH METASTATIC GI CANCERS
***Keishi Tanigawa*[2,1]**, *Koichi Shimizu[3,1], Toshimi Fujisawa[1], Nobuhiro Takeshita[1], Ken Takasaki[2,1], Masakazu Yamamoto[1], Atsushi Aruga[1]*
[1]Department of Suergery, Institute of Gastroenterology, Tokyo Women's Medical University, Tokyo, Japan
[2]J. B. Therapeutics, Inc., Japan, Tokyo, Japan
[3]Chemoimmunotherapy Center, Shin-Itabashi Clinic, Tokyo, Japan

Poster #: Endpoints, Response Criteria for Clinical Trial Design

22 MGMT PROMOTER METHYLATION IN SPORADIC COLORECTAL CANCER
Fatemeh Khatami, *Reza Mohebbi, Fatemeh Nemati Malek, Somayeh Ghiasi, Mahdi Montazer Haghighi, Mahammad R. Zali*
Research Center for Gastroenterology and Liver Diseases, Taleghani Hospital, Tehran, Iran

23 IMPROVING T CELL ASSAYS USING HLA CLASS I OR CLASS II MONO-SPECIFIC APCS/TARGETS
Philip Savage
Medical Oncology, Charing Cross Hospital, London, United Kingdom

24 MONITORING IMMUNE RESPONSES IN CLINICAL TRIALS AND ANIMAL STUDIES
Kimberly A. Shafer-Weaver, *Susan Strobl, Luibov Zaritskaya, Melissa Gregory, Michael Baseler, Anatoli Malyguine*
Laboratory of Cell-Mediated Immunity, Clinical Services Program, SAIC-Frederick, Inc., Frederick, MD

Poster #: Enhancing Cancer Vaccines

25 SELECTION OF IDEAL PARTICLE SIZE FOR W/O EMULSIONS BASED VACCINE
Stephane Ascarateil, *Fabien Bonhoure*
AVI, SEPPIC, Paris La Defense, France

26 THE IMMUNE SYSTEM STRIKES BACK: CELLULAR IMMUNE RESPONSES AGAINST INDOLEAMINE 2,3-DIOXYGENASE
***Rikke Bæk Sørensen*[1]**, *Inge Marie Svane[1], Ton Schumacher[2], Sine R. Hadrup[2], Tania M. Kollgaard[1], Jurgen C. Becker[3], Per thor Straten[1], Mads H. Andersen[1]*
[1]Center for Cancer Imune Therapy (CCIT), University Hospital Herlev, Herlev, Denmark
[2]Department of Immunology, The Netherlands Cancer Institute, Amsterdam, Netherlands
[3]Department of Dermatology, University Hospital Würzburg, Würzburg, Germany

27 MECHANICAL DISRUPTION OF THE PRIMARY TUMOR USING BIOCOMPATIBLE MAGNETIC BEADS IN COMBINATION WITH IMMUNOTHERAPY ALLOWS FOR SYSTEMIC ANTI-TUMOR RESPONSES IN METASTATIC BREAST CANCER
***Myriam N. Bouchlaka*[1]**, *Alan Fuchs[2], Cahit A. Evrensel[3], Lisbeth A. Welniak[1], William J. Murphy[1]*
[1]Immunology and Molecular Biology, University of Nevada Reno, Reno, NV
[2]Chemical Engineering, University of Nevada Reno, Reno, NV
[3]Biomedical and Mechanical Engineering, University of Nevada Reno, Reno, NV

28 IMPACT OF TUMOR ANTIGEN LOADING OF DENDRITIC CELLS ON CD8+ AND CD4+ T CELL AND NK CELL RESPONSES
Sarah Bray[1], Jun Eun Park[1], Jian Shi[1], Jason C. Tse[1], Simon C. Watkins[2], Nikola L. Vujanovic[3], Lazar N. Vujanovic[1], ***Lisa H. Butterfield*[1,3,4]**
[1]Medicine, University of Pittsburgh, Pittsburgh, PA
[2]Cell Biology and Physiology, University of Pittsburgh, Pittsburgh, PA
[3]Pathology, University of Pittsburgh, Pittsburgh, PA
[4]Immunology and Surgery, University of Pittsburgh, Pittsburgh, PA

29 SHIKONIN ENHANCES THE EFFICIENCY OF GENE-BASED VACCINE VIA INDUCTION OF RANTES AND RECRUITMENT OF DENDRITIC CELLS
***Huiming Chen*[1,2]**, *Ningsun Yang [2]*
[1]Department of Pharmacology, School of Medicine, National Yang-Ming University, Taipei, Taiwan, Taipei, Taiwan
[2]Agricultural Biotechnology Research center, Academia Sinica, Taipei, Taiwan, Taipei, Taiwan

(primary authors listed in bold italics)

Posters – Friday

30 EVALUATION OF INTERLEUKIN-13 RECEPTOR (IL-13R) OVEREXPRESSION IN HUMAN THYROID CANCERS
***Ritika S. Dogra*[1]**, *Bharat H. Joshi*[1], *Ricardo Lloyd*[2], *Jan L. Kasperbauer*[3], *Raj K. Puri*[1]
[1]*Tumor Vaccine and Biotechnology Branch, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, FDA, Bethesda, MD*
[2]*Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN*
[3]*Department of Otolaryngology, Head and Neck Surgery, Mayo Clinic, Rochester, MN*

31 ENHANCEMENT OF ANTITUMOR ACTIVITY USING CETUXIMAB AND NOVEL EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) PEPTIDE-SPECIFIC T CELLS
Robert L. Ferris, *Pedro A. Andrade Filho, Andres Lopez-Albaitero*
University of Pittsburgh Cancer Institute, Pittsburgh, PA

32 CYCLOPHOSPHAMIDE AND FLUDARABINE TREATMENT PRIOR TO RECONSTITUTION WITH PBMC AND IMMUNOTHERAPY IMPROVES PSA-DT IN MEN WITH ANDROGEN-INDEPENDENT PROSTATE CANCER
Brendan D. Curti[1], *James A. Thompson*[1], *Sachin Puri*[1], *Tarsem L. Moudgil*[1], *Ilka Assmann*[1], *Theresa Ratzow*[1], *Shawn M. Jensen*[1], *Hong-Ming Hu*[1,3,4], *Michael LaCelle*[1], *Daniel P. Haley*[1], *Christian H. Poehlein*[1], *Edwin B. Walker*[1], *Natalie Sacks*[2], *Kristen Hege*[2], *Walter J. Urba*[1], ***Bernard A. Fox*[1,4,5]**
[1]*Earle A. Chiles Research Institute, Portland, OR*
[2]*Cell Genesys, Inc, San Francisco, CA*
[3]*Department of Radiation Oncology, Portland, OR*
[4]*OHSU Cancer Institute, Portland, OR*
[5]*Departments of Molecular Microbiology and Immunology; and Environmental and Biomolecular Systems OHSU, Portland, OR*

33 INTERLEUKIN 13 (IL-13) MEDIATES SIGNALING THROUGH IL-13Rα2: TARGETING OF THE RECEPTORS BY IL-13 PSEUDOMONAS EXOTOXIN (IL-13PE) FOR PANCREATIC CANCER THERAPY
***Toshio Fujisawa*[1]**, *Takeshi Shimamura*[1], *Syed R. Husain*[1], *Bharat H. Joshi*[1], *Atsushi Nakajima*[2], *Raj K. Puri*[1]
[1]*Center for Biologics Evaluation & Research/Office of Cellular Tissue and Gene Therapy/Division of Cellular Gene Therapy, Food and Drug Administration, Bethesda, MD*
[2]*Gastroenterology Division, Yokohama City University School of Medicine, Yokohama, Japan*

34 REGULATORY T CELLS IN MOUSE MODELS OF HUMAN PROSTATE CANCER
Andrew Gray, *W. Martin Kast*
Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA

35 CANCER VACCINES REGULATE THE LYMPHOID/MEMORY VERSUS PERIPHERAL/EFFECTOR PATHWAY OF DIFFERENTIATION OF CD8+ T CELLS
Payal Watchmaker, Errik Berk, Ravikumar Muthuswamy, ***Pawel Kalinski***
Surgery, University of Pittsburgh, Pittsburgh, PA

36 ENHANCED DEPOT VACCINE FORMULATIONS FOR TARGETED PEPTIDE-BASED CANCER IMMUNOTHERAPY
***Mohan Karkada*[1]**, *G. Sinnathamby*[2], *Genevieve Weir*[1], *Leelahdar Sammatur*[1], *Ramila Philip*[2], *Marc Mansour*[1]
[1]*ImmunoVaccine Technologies Inc, Halifax, NS, Canada*
[2]*Immunotope Inc, Doylestown, PA*

37 IMMUNIZATION OF A RECOMBINANT PLASMID ENCODING HEPATITIS C VIRUS CORE PROTEIN
Fatemeh Khatami, *Nasrin Rastgoo, Ali Karami, Mohammad R. Zali*
Research Center for Gastroenterology and Liver Diseases,, Tehran, Iran

38 DEVELOPMENT OF AN EFFECTIVE CANCER IMMUNE THERAPY BY CBL-B SILENCING
***Guenther Lametschwandtner* [1]**, *Gottfried Baier*[2], *Thomas Gruber*[2], *Sabine Gruenaug*[1], *Bettina Wagner*[1], *Manfred Schuster*[1], *Hans Loibner*[1]
[1]*Apeiron Biologics, Vienna, Austria*
[2]*Experimental Cell Genetics Unit, Innsbruck Medical University, Innsbruck, Austria*

39 IDENTIFICATION OF MHC CLASS II RESTRICTED EPITOPES IN THE TUMOR ASSOCIATED ANTIGEN BCL-X(L)
Stine K. Larsen, *Per T. Straten, Mads H. Andersen*
Department of Hematology, Center for Cancer ImmuneTherapy, University Hospital Herlev, Herlev, Denmark

40 DIFFERENT QUALITY OF T CELL RESPONSES TO WT1 PEPTIDE VACCINATION IN PATIENTS WITH AML/MDS AND PATIENTS WITH SOLID TUMORS
***Anne Letsch*[1]**, *Anne Marie Asemissen*[1], *Kaja Zimmermann*[1], *Sandra Bauer*[2], *David Stather*[1], *Marcel Völker-Call*[1], *Eckhard Thiel*[1], *Carmen Scheibenbogen*[2], *Ulrich Keilholz*[1]
[1]*Hematology and Oncology, Charité, Campus Benjamin Franklin, Berlin, Germany*
[2]*Medical Immunology, Charité, Campus Mitte, Berlin, Germany*

Poster Listing

Posters – Friday

(primary authors listed in bold italics)

41 LOW LYMPHOCYTE AND NEUTROPHIL COUNTS AT START OF VACCINATIONS WITH THE CANCER VACCINE IGN101 PREDICT IMPROVED RELAPSE-FREE SURVIVAL - RESULTS OF A RANDOMIZED PHASE II/III TRIAL IN ADJUVANT NSCLC

***Hans Loibner*[1]**, *Franz Groiss[1], Helmut Eckert[3], Wolfgang Stoiber[3], Erich Stoelben[2]*
[1]HL Bioscience Research, Vienna, Austria
[2]Krankenhaus Merheim, Cologne, Germany
[3]Altropus GmbH, Arlesheim, Switzerland

42 INDUCTION OF ANTI-TUMOR ACTIVITY IN HER-2 TOLERANT MICE AND OF ANTIGEN SPREADING BY MVA-BN®-HER2

***Stefanie Mandl*[1]**, *Ryan Rountree[1], Ellen Cheang[1], Katie Dal Pozzo[1], James Nachtwey[1], Robin Steigerwald[2], Reiner Laus[1], Alain Delcayre[1]*
[1]BN ImmunoTherapeutics, Mountain View, CA
[2]Bavarian Nordic, Martinsried, Germany

43 POST-APOPTOTIC TUMORS ARE EFFICIENTLY ENGULFED BY DENDRITIC CELLS AND ENHANCE THEIR ANTIGEN CROSS-PRESENTATION ACTIVITY

Davide Brusa[1], Stefano Garetto[1], Giovanna Chiorino[2], Maria Scatolini[2], Elisa Migliore[1], ***Lina Matera*[1]**
[1]Laboratory of Tumor Immunology Department of Internal Medicine, University of Turin, Turin, Italy
[2]Cancer Genomics Lab, Fondo Edo Tempia, Biella, Italy

44 TREATMENT OF LATE STAGE CANCER PATIENTS WITH CYCLOPHOSPHAMIDE IN COMBINATION WITH ZYC300 RESULTS IN A DECREASE IN TREG MEDIATED IMMUNO-SUPPRESSION AND AN INCREASE IN T-CELL IMMUNE RESPONSES TO CYP1B1

***Mark Matijevic*[1]**, *Radha Ramesh[1], Mary Lynne Hedley[2], Thomas M. Luby[1]*
[1]EISAI Research Institute, Andover, MA
[2]EISAI Corp. of North America, Woodcliff Lake, NJ

45 PHASE I CLINICAL RESULTS COMPARING LOCAL AND SYSTEMIC ADMINISTRATION OF AN APC-TARGETED CANCER VACCINE

***Michael Morse*[1]**, *Robert Chapman[2], John Powderly[3], Tibor Keler[4], He Lizhen[4], Venky Ramakrishna[4], Laura Vitale[4], Timothy Clay[1], Thomas Davis[4]*
[1]Duke University Medical Center, Durham, NC
[2]Henry Ford Health System, Detroit, MI
[3]Carolina BioOncology Institute, Huntersville, NC
[4]Celldex Therapeutics, Inc., Phillipsburg, NJ

46 ENHANCING IMMUNOGENICITY OF THERAPEUTIC VACCINES IN THE IMMUNOTHERAPY OF OVARIAN CANCER

C. F. Nicodemus, *L. Wang, B. C. Schultes*
Advanced Immune Therapeutics, Wellesley, MA

47 INDUCTION OF TYPE-1 CTL RESPONSES AGAINST NOVEL GLIOMA-ASSOCIATED ANTIGEN (GAA)-DERIVED EPITOPES EPHA2 (883-891) AND IL-13RALPHA2 (345-353) IN PATIENTS WITH RECURRENT MALIGNANT GLIOMA RECEIVING TYPE-1 DENDRITIC CELL (DC) VACCINES IN COMBINATION WITH POLY-ICLC

***Hideho Okada*[1,2,4]**, *Frank S. Lieberman[4], Ryo Ueda[1,4], Pawel Kalinski[2,4], David L. Bartlett[2,4], Theresa L. Whiteside[4], Lisa H. Butterfield[2,4], Andres M. Salazar[3], Ian F. Pollack[1,4]*
[1]Neurological Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA
[2]Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA
[3]Oncovir, Inc, Washington, DC
[4]University of Pittsburgh Cancer Institute, Pittsburgh, PA

48 CD8+ T CELLS ACTIVATED USING A LOW AFFINITY MHC CLASS I LIGAND FROM TYROSINASE RELATED PROTEIN 1 LEAD TO TUMOR REJECTION

Kevin D. Pavelko, *Michael J. Hansen, Larry R. Pease*
Immunology, Mayo Clinic, Rochester, MN

49 A CLINICAL PHASE I TRIAL WITH AN ALLOGENEIC GENE-MODIFIED TUMOR CELL VACCINE (RCC-26/CD80/IL-2) IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA

***Heike Pohla*[1,3]**, *Alexander Buchner[1,2], Bernhard Frankenberger[3], Andrea Baur[4], Christian Stief[2], Alfons Hofstetter[1], Ralph Oberneder[5], Joachim Kopp[6], Antonio Pezzutto[7], Thomas Blankenstein[8], Dolores J. Schendel[3]*
[1]Laboratory of Tumor Immunology, Ludwig-Maximilians-University, Munich, Germany
[2]Department of Urology, Ludwig-Maximilians-University, Munich, Germany
[3]Institute of Molecular Immunology and Clinical Cooperation Group Immune Monitoring, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich, Germany
[4]Department of Radiology, Ludwig-Maximilians-University, Munich, Germany
[5]Urological Clinic, Munich-Planegg, Germany
[6]Charité-University Medicine, Campus Berlin-Buch, Berlin, Germany
[7]Department of Hematology, Oncology and Tumor Immunology, Charité-University Medicine, Campus Virchow, Berlin, Germany
[8]Institute of Immunology, Charité-University Medicine, Berlin, Germany

Posters – Friday

(primary authors listed in bold italics)

50 ALLOGENEIC RETROVIRALLY-TRANSDUCED, IL-2 AND IFN-GAMMA SECRETING TUMOR CELL VACCINE IN PATIENTS WITH HORMONE-REFRACTORY PROSTATE CANCER (HRPC) - A PHASE I/II TRIAL

Heike Pohla[1,2], *Thomas Brill[3], Hubert Kübler[4], Alexander Buchner[1], Heiner van Randenborgh[4], Roger Paul[4], Michael Osthoff[1], Bernd Eisele[5], Falko Fend[6], Rudolf Hartung[4], Dolores J. Schendel[2], Bernd Gansbacher[3]*
[1]Laboratory of Tumor Immunology, LIFE-Center, Ludwig-Maximilians-University, Munich, Germany
[2]Institute of Molecular Immunology and Clinical Cooperation Group Immune Monitoring, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich, Germany
[3]Institute for Experimental Oncology and Therapeutic Research, Technical University, Munich, Germany
[4]Department of Urology, Technical University, Munich, Germany
[5]VPM GmbH, Hannover, Germany
[6]Department of Pathology, Technical University, Munich, Germany

51 TELOMERASE-TRANSFECTED LYMPHOCYTES STIMULATE ANTIGEN-SPECIFIC CD8 T CELL RESPONSES IN PATIENTS WITH STAGE III MELANOMA

Caridad Rosette, *Fernando B. Laysa, Mary K. Mascarenas, Seema Patkar, Jon Berglin, Mara Gerloni*
Cosmo Bioscience, San Diego, CA

52 CONTRIBUTION OF THE MVA-BN® VECTOR TO THE ANTI-TUMOR ACTIVITY OF MVA-BN®-HER2, A VACCINE CANDIDATE IN DEVELOPMENT FOR THE TREATMENT OF BREAST CANCER

Ryan Rountree[1], *Stefanie Mandl[1], Katie Dal Pozzo[1], Dyan Curry[1], Ellen Cheang[1], James Nachtwey[1], Robin Steigerwald[2], Reiner Laus[1], Alain Delcayre[1]*
[1]BN ImmunoTherapeutics, Mountain View, CA
[2]Bavarian Nordic, Martinsried, Germany

53 ESTABLISHMENT OF MELANOMA CELL LINES FOR AUTOLOGOUS VACCINE THERAPY: COMPREHENSIVE ANALYSIS OF SEVEN YEAR FEASIBILITY

Senthamil R. Selvan, *Denysha J. Carbonell, Abner W. Fowler, Andrea R. Beatty, Robert O. Dillman*
Cell Biology, Hoag Cancer Center of Excellence, Newport Beach, CA

54 INTERLEUKIN-15 AND ITS RECEPTOR ENHANCE ANTITUMOR ACTIVITY FOLLOWING A GENETICALLY-MODIFIED DENDRITIC CELL VACCINE

Jason C. Steel, *Charmaine A. Ramlogan, Ping Yu, Thomas A. Waldmann, John C. Morris*
Metabolism Branch, National Cancer Institute, Bethesda, MD

55 IN VIVO APPLICATION OF BIODEGRADABLE ARTIFICIAL ANTIGEN-PRESENTING CELLS

Erin Steenblock[1], *Stephen Wrzesinski[2], Richard Flavell[3], Tarek Fahmy[1,4]*
[1]Biomedical Engineering, Yale University, New Haven, CT
[2]Yale Cancer Center, Yale School of Medicine, New Haven, CT
[3]Immunobiology, Yale University, New Haven, CT
[4]Chemical Engineering, Yale University, New Haven, CT

56 NEUTROPHIL-LIKE MYELOID DERIVED SUPPRESSOR CELLS ARE INCREASED IN HEAVY TUMOR BURDEN AND UPREGULATE MHC CLASS II EXPRESSION IN RESPONSE TO TOLL-LIKE RECEPTOR STIMULATION

William W. Tseng[1,2], *Edgar G. Engleman[1]*
[1]Pathology, Stanford University School of Medicine, Palo Alto, CA
[2]Surgery, UCSF, San Francisco, CA

57 DEVELOPMENT OF MULTIPLE LISTERIA MONOCYTOGENES BASED CONSTRUCTS FOR THE THERAPEUTIC TREATMENT OF PROSTATE CANCER

Anu Wallecha[1], *Paulo C. Maciag[1], Kyla D. Carroll[1], Sandra Rivera[1], Yvonne Paterson[2], Vafa Shahabi[1]*
[1]Reseach and Development, Advaxis Inc, North Brunswick, NJ
[2]Microbiology, University of Pennsylvania, Philadelphia, PA

58 THE 1170 A-P SMALL NUCLEAR POLYMORPHISM (SNP) IN THE HER-2/NEU PROTEIN (HER2) AS A MINOR HISTOCOMPATIBILITY ANTIGEN (MHAG)

Lynn Wenandy[1], *Tania M. Kollgaard[1], Rikke Sick[1], Tina Seremet[1], Inge Marie Svane[1,2], Lars Vindeløv[1], Mads H. Andersen[3], Per thor Straten[1]*
[1]Center for Cancer Immune Therapy (CCIT), University Hospital Herlev, Herlev, Denmark
[2]Department of Oncology, University Hospital Herlev, Herlev, Denmark
[3]The Hematopoietic Cell Transplantation Laboratory, State University Hospital, Copenhagen, Denmark

Posters – Friday

(primary authors listed in bold italics)

59 **MELCANCERVAC®: AUTOLOGOUS DENDRITIC CELLS PULSED WITH AN ALLOGENEIC TUMOR LYSATE FOR THE TREATMENT OF COLORETAL CANCER AND NON SMALL CELL LUNG CANCER**
Ayako W. Pedersen[1], Christian M. Bechmann[1], Pia Kvistborg[1], Brian T. Weinert[1], Stefan Burgdorf[4], Han Toh Chong[3], Anders Mellemgaard[5], Mogens H. Claesson[2], ***Mai-Britt Zocca[1]***
[1]DanDrit Biotech A/S, Copenhagen, Denmark
[2]The Panum Institute, University of Copenhagen, Copenhagen, Denmark
[3]Medical Oncology, National Cancer Center, Singapore, Singapore
[4]Surgical Gastroenterology, University Hospital of Copenhagen, Copenhagen, Denmark
[5]Herlev University Hospital, Copenhagen, Denmark

Poster #:

TH-17, Cytokines and T Cell Subsets

60 **CRITICAL ROLE OF TNFα IN THE EXPANSION OF REGULATORY T CELLS AND AGE RELATED TOXICITY FOLLOWING IMMUNOTHERAPY**
Kory L. Alderson[1]*, Myriam N. Bouchlaka[1], Danice E. Wilkins[1], Doug Redelman[2], Lisbeth A. Welniak[1], William J. Murphy[1]*
[1]Immunology and Molecular Biology, University of Nevada Reno, Reno, NV
[2]Department of Physiology, University of Nevada Reno, Reno, NV

61 **SENSITIVITY TO APOPTOSIS OF THE CD8+CD45RA+CCR7- T-CELL SUBSET IN THE BLOOD DISCRIMINATES CANCER PATIENTS FROM HEALTHY CONTROLS**
Malgorzata Czystowska*, William Gooding, Miroslaw Szczepanski, Jonas T. Johnson, Theresa L. Whiteside*
University of Pittsburgh Cancer Institute, Pittsburgh, PA

62 **AMPLIFIED AND TARGETED IL-15 EXPRESSION VECTOR FOR CANCER IMMUNO-GENE THERAPY**
Xianghui He*, Weidong Li, Linan Hou, Na Zhao, Yujie Qiu, Liwei Zhu*
Department of Surgery, Tianjin General Surgery Institute, Tianjin Medical University General Hospital, Tianjin, China

63 **THE ANTITUMOR EFFECTS OF COX-2 INHIBITORS IN TUMOR MICROENVIRONMENT ARE MEDIATED BY THE INHIBITION OF TH17 CELLS**
Sung Yong Lee*, Hye Kyoung Choi, Kyoung Ju Lee, Sang Yeub Lee, Je Hyeong Kim, Chol Shin, Jae Jeong Shim, Kwang Ho In, Kyung Ho Kang, Se Hwa Yoo*
Department of Internal Medicine, Korea University Medical Center, Korea University, Seoul, South Korea

64 **GENE EXPRESSION PROFILING SIGNATURES ASSOCIATED WITH RCC RESPONSE TO IL-2 THERAPY**
Towia A. Libermann[1,5,6]*, Manoj Bhasin[1,5,6], Marie G. Joseph[1,6], Sabina Signoretti[3,5], Marc S. Ernstoff[4], David F. McDermott[2,5], Michael B. Atkins[2,5]*
[1]Division of Interdisciplinary Medicine and Biotechnology, Beth Israel Deaconess Medical Center, Boston, MA
[2]Division of Hematology/Oncology, Beth Israel Deaconess Medical Center, Boston, MA
[3]Department of Pathology, Brigham and Women's Hospital, Boston, MA
[4]Division of Hematology/Oncology, Dartmouth Hitchcock Medical Center, Lebanon, NH
[5]Kidney Cancer Program, Dana Farber/Harvard Cancer Center, Boston, MA
[6]Cancer Proteomics Core, Dana Farber/Harvard Cancer Center, Boston, MA

65 **OVEREXPRESSION OF CD39 AND CD73 AND THE LACK OF CD26 IN HUMAN REGULATORY T CELLS LEAD TO ENDOGENOUS ADENOSINE PRODUCTION AND INDUCE IMMUNOSUPPRESSION**
Magis Mandapathil[1,3]*, Ben Hilldorfer[1], Miroslaw J. Szczepanski[1], Malgorzata Czystowska[1], Martha Szajnik[1], Jin Ren[2], Edwin K. Jackson[2], Stephan Lang[3], Elieser Gorelik[1], Theresa L. Whiteside[1]*
[1]Departments of Pathology, University of Pittsburgh Cancer Institute, Pittsburgh, PA
[2]Department of Pharmacology, University of Pittsburgh, Pittsburgh, PA
[3]Department of Otorhinolaryngology, University of Duisburg-Essen, Essen, Germany

66 **HIGH DOSE CONTINUOUS INFUSION + PULSE INTERLEUKIN-2 WITH FAMOTIDINE HAS ACTIVITY IN METASTATIC KIDNEY CANCER**
Walter D. Quan, Jr[3]*, Francine M. Quan[1], Paul R. Walker[1], Darla K. Liles[2]*
[1]Division of Medical Oncology and Hematology, University of Toledo College of Medicine, Toledo, OH
[2]Division of Hematology/Oncology, East Carolina University, Greenville, NC
[3]Division of Hematology/Oncology, Loma Linda University School of Medicine, Loma Linda, CA

(primary authors listed in bold italics)

Posters – Friday

67 INDUCTION OF CD56 POSITIVE LYMPHOCYTES BY PULSE INTERLEUKIN-2 AND FAMOTIDINE IN PERIPHERAL BLOOD OF PATIENTS WITH MELANOMA OR KIDNEY CANCER
Walter D. Quan, Jr.[1,3], *Francine M. Quan[2]*
[1]Division of Hematology/Oncology, Loma Linda University, Loma Linda, CA
[2]Division of Hematolgy/Oncology, East Carolina University, Greenville, NC
[3]Division of Medical Oncology, University of Toledo, Toledo, OH

68 IL-7 AND IL-15 DIFFERENTIALLY REGULATE CD8+ T CELL SUBSETS DURING CONTRACTION OF THE IMMUNE RESPONSE
Mark P. Rubinstein[1], *Nicholas A. Lind[1], Jared F. Purton[2], Pauline Filippou[1], J. A. Best[1], Patrick A. McGhee[1], Charles D. Surh[2], Ananda W. Goldrath[1]*
[1]Biological Sciences, University of California, San Diego, La Jolla, CA
[2]Immunology, Scripps Research Institute, La Jolla, CA

69 SERUM VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AND FIBRONECTIN AS A POTENTIAL PREDICTOR OF RESPONSIVENESS TO HIGH-DOSE INTERLEUKIN (IL)-2 THERAPY
Marianna Sabatino[1], *Seunghee Kim-Schulze[2], Dae Won Kim[2], Monica C Panelli[3], David Stroncek[1], Ena Wang[1], Francesco M. Marincola[1], Howard L. Kaufman[2]*
[1]Infectious Disease and Immunogenetics Section (IDIS), Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD
[2]Department of Surgery, Columbia University, New York, NY
[3]Department of Medicine, University of Pittsburgh Cancer Institute, Pittsburgh, PA

70 CTLA-4 BLOCKADE INCREASES INTERFERON-GAMMA-PRODUCING CD4+ICOSHI CELLS TO SHIFT THE RATIO OF EFFECTOR TO REGULATORY T CELLS IN CANCER PATIENTS
Padmanee Sharma[1,2], *Chrysoula Liakou[1], Ashish Kamat[3], Derek Ng Tang[1], Hong Chen[1], Jingjing Sun[1], Patricia Troncoso[4], Christopher Logothetis[1]*
[1]Genitourinary Medical Oncology, M. D. Anderson Cancer Center, Houston, TX
[2]Immunology, M. D. Anderson Cancer Center, Houston, TX
[3]Urology, M. D. Anderson Cancer Center, Houston, TX
[4]Pathology, M. D. Anderson Cancer Center, Houston, TX

71 EXPANSION OF FUNCTIONAL CD4(+)CD25(HIGH)FOXP3(+) TREG IS MEDIATED BY TUMOR-DERIVED MICROVESICLES
Marta Szajnik, *Malgorzata Czystowska, Magis Mandapathil, Miroslaw J. Szczepanski, Theresa L. Whiteside*
University of Pittsburgh Cancer Institute, Pittsburgh, PA

72 INTERLEUKIN-15 ENHANCES NK-CELL CYTOTOXICITY IN PATIENTS WITH ACUTE MYELOID LEUKEMIA BY UPREGULATING THE ACTIVATING NK-CELL RECEPTORS
Miroslaw J. Szczepanski[1,2], *Malgorzata Czystowska[2], Marta Szajnik[2], Magis Mandapathil[2], Benedict Hilldorfer[2], Ann Welsh[1,2], Kenneth Foon[1,2], Theresa L. Whiteside[2,1], Michael Boyiadzis[1,2]*
[1]University of Pittsburgh, School of Medicine, Pittsburgh, PA
[2]University of Pittsburgh Cancer Institute, Pittsburgh, PA

Posters – Saturday

Poster #:

Cancer and Inflammation

73 IL-29 INDUCES JAK-STAT SIGNAL TRANSDUCTION AND CAN SYNERGIZE WITH TEMOZOLOMIDE AND BORTEZOMIB IN HUMAN MELANOMA CELL LINES
Kristan Guenterberg, *Ene Raig, Jason Zimmerer, Greg Lesinski, William Carson*
Comprehensive Cancer Center, The Ohio State University, Columbus, OH

74 BORTEZOMIB (B) ACTIVITY IN PLASMA CELL DYSCRASIA (PCD) WITH POEMS LIKE SYNDROME SUPPORTS AN ETIOLOGIC UNDERLYING NF-κB INFLAMMATORY PATHWAY
Philip A. Haddad
Medicine, LSU-HSC, Overton Brooks VAMC, Feist-Weiller Cancer Treatment Center, Shreveport, LA

75 MAST CELLS ARE ESSENTIAL FOR POLYP FORMATION AND COLON CANCER PROGRESSION
Khashayarsha Khazaie
Medicine/Microbiology-Immunology, Northwestern Universtiy, Chicago, IL

76 THE ROLE OF α5β1 INTEGRINS AND MYCOBACTERIAL PROTEIN PHOSPHATASES IN RESPONSES OF BLADDER CANCER CELL LINES TO BCG THERAPY
Juwita N. Rahmat, *Kesavan Esuvaranathan, Ratha Mahendran*
Surgery, National University of Singapore, Singapore, Singapore

(primary authors listed in bold italics)

Posters – Saturday

77 **THE ANTIPROLIFERATIVE CYTOSTATIC EFFECTS OF A SELF-ACTIVATING VIRIDIN PRODRUG**
Ralph A. Smith[1], *Joe Blois*[1], *Hushan Yuan*[1], *Elena Aikawa*[1], *Christopher Ellson*[4], *Jose-Luiz Figueiredo*[1], *Ralph Weissleder*[1], *Lewis Cantley*[2,3], *Lee Josephson*[1]
[1]*Center for Molecular Imaging Research, Massachusetts General Hospital/Harvard Medical School, Charlestown, MA*
[2]*Department of Systems Biology, Harvard Medical School, Boston, MA*
[3]*Division of Signal Transduction, Beth Israel Deaconness Medical Center, Boston, MA*
[4]*Department of Biology, Massachusetts Institute of Technology, Cambridge, MA*

Poster #:

Cancer Stem Cells and the Host Response

78 **UPREGULATION OF STEM CELL-RELATED GENES IN HYPOXIC MAMMOSPHERE CULTURES**
Norazizah Shafee[1], *Shu-Yuan Liao*[2], *Eric J Stanbridge*[2]
[1]*Department of Microbiology, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia, Serdang, Malaysia*
[2]*Department of Microbiology and Molecular Genetics, University of California, Irvine, CA*

Poster #:

Co-stimulation / Immunoregulation

79 **INFLUENCE ON THE MUTUAL EXPRESSION OF COSTIMULATORY MOLECULES ON RENAL CELL CARCINOMA LINES FOLLOWING STABLE AND TRANSIENT TRANSFECTION OF CD80, CD86 AND B7-H1**
Bernhard Frankenberger, *Stefani Spranger, Dolores J. Schendel*
Helmholtz Zentrum München, German Research Center for Environmental Health, Institute of Molecular Immunology, Munich, Germany

80 **CLINICAL ACTIVITY AND SAFETY OF IPILIMUMAB IN COMBINATION WITH PLACEBO OR PROPHYLACTIC BUDESONIDE IN PATIENTS (PTS) WITH ADVANCED MELANOMA AND BRAIN METASTASES (METS)**
Omid Hamid[1], *David Berman*[2], *Jonathan Siegel*[2], *David Minor*[3], *Asim Amin*[4], *John A. Thompson*[5], *Ilan G. Ron*[6], *Ruggero Ridolfi*[7], *Hazem Assi*[8], *Jeffrey S. Weber*[9]
[1]*The Angeles Clinic and Research Institute, Santa Monica, CA*
[2]*Bristol-Myers Squibb, Wallingford, CT*
[3]*California Pacific Medical Center, San Francisco, CA*
[4]*Blumenthal Cancer Center, Charlotte, NC*
[5]*Seattle Cancer Care Alliance, Seattle, WA*
[6]*Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*
[7]*IRST, Meldola, Italy*
[8]*The Moncton Hosp, Moncton, QC, Canada*
[9]*H Lee Moffitt Cancer Ctr. and Research Inst., Tampa, FL*

81 **LATE-STAGE TUMORS ARE ENRICHED IN T CELLS BEARING A GITRHI/OX40+ PHENOTYPE AND ARE EFFECTIVELY TREATED WITH GITR AND OX40 AGONISTS**
Angela D. Pardee[1], *Alan L. Epstein*[2], *Sean Alber*[3], *Simon C. Watkins*[3], *Amy K. Wesa*[4], *Walter J. Storkus*[1,4]
[1]*Department of Immunology, University of Pittsburgh, Pittsburgh, PA*
[2]*Department of Pathology, University of Southern California, Los Angeles, CA*
[3]*Center for Biologic Imaging, University of Pittsburgh, Pittsburgh, PA*
[4]*Department of Dermatology, University of Pittsburgh, Pittsburgh, PA*

82 **AUTOIMMUNITY IS ASSOCIATED WITH CLINICAL BENEFIT IN METASTATIC MELANOMA TREATED WITH COMBINATION BIOTHERAPY OF IFNA-2B AND ANTI-CTLA4 BLOCKADE**
Ahmad A. Tarhini, *Monica Panelli, C. Sander, John M. Kirkwood*
Hematology/Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA

83 **IMPAIRMENT OF SECONDARY ANTITUMOR RESPONSES AFTER IL-2/ANTI CD40 IMMUNOTHERAPY: A PUTATIVE ROLE FOR NATURAL KILLER CELLS AND PERFORIN**
Jonathan M. Weiss[1], *Myriam Bouchlaka*[2], *Jeff Subleski*[1], *Tim Back*[1], *Danice Wilkins*[2], *Kory Alderson*[2], *Lisbeth Welniak*[2], *Doug Redelman*[2], *William J. Murphy*[2], *Robert H. Wiltrout*[1]
[1]*Cancer and Inflammation Program, NCI Frederick, Frederick, MD*
[2]*Department of Microbiology and Immunology, University of Nevada School of Medicine, Reno, NV*

84 **IMMUNOTHERAPY WITH ANTI-CD40 AND IL-2 RESULTS IN ANTIGEN INDEPENDENT CD8+ T CELL ACTIVATION IN VIVO**
Danice E. Wilkins[1], *Kory L. Alderson*[1], *Jonathan M. Weiss*[2], *Myriam Bouchlaka*[1], *Doug Redelman*[3], *Lisbeth A. Welniak*[1], *William J. Murphy*[1]
[1]*Microbiology and Immunology, University of Nevada School of Medicine, Reno, NV*
[2]*Cancer and Inflammation Program, National Cancer Institute, Frederick, MD*
[3]*Department of Physiology, University of Nevada School of Medicine, Reno, NV*

(primary authors listed in bold italics)

Posters – Saturday

Poster #:

Infectious Agent Vectors

85 A PHASE I STUDY TO EVALUATE SYSTEMIC WILD-TYPE REOVIRUS (REOLYSIN®) IN COMBINATION WITH DOCETAXEL IN PATIENTS WITH ADVANCED MALIGNANCIES

Charlie Comins[1], *James Spicer*[2], *Andrew Protheroe*[5], *D. Mukherji*[2], *Matt Coffey*[4], *Brad Thompson*[4], *Kevin Harrington*[3], *Hardev Pandha*[1]
[1]*Oncology, University of Surrey Postgraduate Medical School, Guildford, United Kingdom*
[2]*Oncology, Guy's Hospital, London, United Kingdom*
[3]*Head and Neck Unit, Royal Marsden Hospital, London, United Kingdom*
[4]*Oncolytics Biotech, Calgary, BC, Canada*
[5]*Oncology, Churchill Hospital, Oxford, United Kingdom*

86 SYNERGISTIC ANTI-TUMOUR ACTIVITY OF ONCOLYTIC REOVIRUS AND DOCETAXEL IN A PC-3 PROSTATE CANCER MOUSE MODEL

Lucy Heinemann[1], *Tim Kottke*[5], *Richard Vile*[5], *Kevin Harrington*[3], *Alan Melcher*[2], *Matt Coffey*[4], *Hardev Pandha*[1]
[1]*Oncology, University of Surrey, Postgraduate Medical School, Guildford, United Kingdom*
[2]*Oncology, USt James University Hopsital, Leeds, United Kingdom*
[3]*Head and Neck Unit, Royal Marsden Hospital, London, United Kingdom*
[4]*Oncolytics Biotech, Calgary, BC, Canada*
[5]*Mayo Clinic, Rochester, MN*

87 PHASE I TRIAL OF ONCOLYTIC REOVIRUS (REOLYSIN) IN COMBINATION WITH CARBOPLATIN/PACLITAXEL IN PATIENTS WITH ADVANCED SOLID CANCERS

Eleni Karapanagiotou[1], *Hardev Pandha*[2], *Geoff Hall*[3], *John Chester*[3], *Alan Melcher*[3], *Johann De Bono*[1], *Martin Gore*[1], *Christopher Nutting*[1], *Kevin Harrington*[1]
[1]*The Royal Marsden Hospital/The Institute of Cancer Research, London, United Kingdom*
[2]*University of Surrey, Guildford, United Kingdom*
[3]*Leeds Institute of Molecular Medicine, Leeds, United Kingdom*

Poster #:

Innate Immunity to Tumors

88 INNATE IMMUNITY CAN CONTRIBUTE TO THE SHAPING OF TUMOR IMMUNOGENICITY IN THE ABSENCE OF ADAPTIVE IMMUNITY

Jack D. Bui[1], *William Vermi*[2], *Cora Arthur*[2], *J. Michael White*[2], *Ravindra Uppaluri*[3], *Robert D. Schreiber*[2]
[1]*Pathology, University of California, La Jolla, CA*
[2]*Pathology and Immunology, Washington University, St. Louis, MO*
[3]*Otolaryngology, Washington University, St. Louis, MO*

89 COMPLETION OF TAXANE TREATMENT IN BREAST CANCER PATIENTS AND THE EFFECT ON CELLULAR IMMUNITY

Kalpana Dhungel[1,2], *Ram Shrestha*[1,2]
[1]*Medicine and Research, Tribhuwan University Teaching Hospital, Kathmandu, Nepal*
[2]*Tribhuwan University Teaching Hospital, Kathmandu, Nepal*

90 BREAST TUMOR GROWTH AND MACROPHAGE: THE EFFECT OF DIAZEPAM

Kalpana Dhungel[1,2], *Sita Guragain*[2,1]
[1]*medicine and research, Tribhuwan University Teaching Hospital, Kathmandu, Nepal*
[2]*Research, TUTH, Kathmandu, Nepal*

91 GAUGING INNATE IMMUNITY IN HIV-INFECTION

Alessandro Monaco[1,2], *F. M. Marincola*[1], *M. Sabatino*[1], *Zoltan Pos*[1], *Maria Lina Tornesello*[3], *David F. Stroncek*[1], *Ena Wang*[1], *Robert C. Gallo*[4], *George K. Lewis*[4], *Franco M. Buonaguro*[3], *Luigi Buonaguro*[3,4]
[1]*DTM, NIH, Bethesda, MD*
[2]*CEO Lab, IRCCS "Giovanni Paolo II", Bari, Italy*
[3]*Lab of Mol Biol Viral Oncogen, Ist Naz Tumori, Naples, Italy*
[4]*Inst Human Virol, U. Maryland, Baltimore, MD*

92 TLR ENGAGEMENT AS A MECHANISM OF PREVENTION OF TUMOROGENENSIS

Subhadra Nandakumar, *Stacie N. Woolard, Uday Kumaraguru*
Dept. of Microbiology, Quillen College of Medicine, East Tennessee State University, Johnson City, TN

93 ENHANCED T CELL-INDEPENDENT ANTI-TUMOR EFFECT OF CYCLOPHOSPHAMIDE COMBINED WITH ANTI-CD40 MAB AND CPG

Erik E. Johnson, Ilia N. Buhtoiarov, Julie B. Waisbren, Paul M. Sondel, ***Alexander L. Rakhmilevich***
University of Wisconsin-Madison, Madison, WI

(primary authors listed in bold italics)

Posters – Saturday

94 **PREDICTING THE IMMUNOLOGIC CONSTANT OF REJECTION**
Andrea Worschech[1,2,3], *Nanhai Chen[1], Yong Yu[1], Qian Zhang[1], Marianna Sabatino[3], Alessandro Monaco[3], Zoltan Pos[3], Hui Lui[3], Mark R. Buller[4], Ena Wang[3], Aladar A. Szalay[1,2], Francesco M. Marincola[3]*
[1]Genelux Corp., San Diego, CA
[2]Virchow Center for Experimental Biomedicine and Department for Biochemistry, University of Wuerzburg, Wuerzburg, Germany
[3]Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD
[4]Department of Molecular Microbiology and Immunology, Saint Louis University School of Medicine, St. Louis, MO

Poster #:

New Agents

95 **BIOCHEMICAL AND IMMUNOMODULATORY PROPERTIES FROM CONCHOLEPAS HEMOCYANIN (CCH) AND THEIR ISOLATED SUBUNITS**
María I. Becker[1], *Miguel Del Campo[1], Augusto Manubens[3], Esteban Nova[1], Marcelo Campos-Vallete[2], Jorge Ferreira[2], Pablo De Ioannes[1], Bruno Moltedo[1], Alfredo E. De Ioannes[3]*
[1]Fundación Ciencia y Tecnología para el Desarrollo, Santiago, Chile
[2]Universidad de Chile, Santiago, Chile
[3]BIOSONDA S.A., Santiago, Chile

96 **FUNCTIONAL MODULATION OF DENDRITIC CELLS BY MILATUZUMAB, A HUMANIZED ANTI-CD74 MONOCLONAL ANTIBODY**
Xiaochuan Chen[1], *Ken Chang[2], David M. Goldenberg[1]*
[1]Garden State Cancer Center, Center for Molecular Medicine and Immunology, Belleville, NJ
[2]Immunomedics, Inc., Morris Plains, NJ

97 **BCL-2 SMALL HAIRPIN RNAS ENHANCE ARA-C-INDUCED APOPTOS IN RAJI CELLS**
He Dongmei, *Fang Baoying*
Jinan University, Guangzhou, China

98 **BCL-2 SMALL INTERFERING RNA INHIBITS THE GROWTH OF HUMAN LYMPHOMA TRANSPLANTED SUBCUTANEOUSLY IN NUDE MICE**
He Dongmei, *Zou Fanyan, Fang Baoying*
Jinan University, Guangzhou, China

99 **PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTIPLE-DOSE, DOSE-ESCALATION STUDY OF IMPRIME PGG® INJECTION (IMPRIME PGG) IN HEALTHY SUBJECTS**
Charles Halstenson[2], *Michele Gargano[1], Michael Kurman[3], Richard Walsh[1], Nathaniel Theoharis[1], Myra Patchen[1]*
[1]Biothera, Eagan, MN
[2]Prism Research, St. Paul, MN
[3]MKConsulting, Upper Saddle River, NJ

100 **PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE-DOSE, DOSE-ESCALATION STUDY OF IMPRIME PGG® INJECTION (IMPRIME PGG) IN HEALTHY SUBJECTS**
Charles Halstenson[2], *Michele Gargano[1], Michael Kurman[3], Richard Walsh[1], Nathaniel Theoharis[1], Myra Patchen[1]*
[1]Biothera, Eagan, MN
[2]Prism Research, St. Paul, MN
[3]MKConsulting, Upper Saddle River, NJ

(primary authors listed in bold italics)

Posters – Saturday

101 PHASE I STUDY OF BMS-663513, A FULLY HUMAN ANTI-CD137 AGONIST MONOCLONAL ANTIBODY, IN PATIENTS(PTS) WITH ADVANCED CANCER (CA)

***T. Logan*[1]**, *F. S. Hodi[2], K. Margolin[3], D. F. McDermott[4], M. S. Ernstoff[5], J. M. Kirkwood[6], A. Oza[7], E. Pujade-Lauraine[8], C. Lhomme[9], F. Rolland[10], J. Medioni[11], N. Houede[12], Z. Tsuchihashi[13], B. Hu[13], D. Wu[13], L. Patti-Diaz[13], L. Lang[13], S. Huang[13], J. S. Platero[13], A. Shah[13], C. Wojtaszek[13], S. Goldberg[13], D. Feltquate[13], M. Sznol[14]*

[1]Indiana University Cancer Center, Indianapolis, IN
[2]Dana Farber Cancer Institute, Boston, MA
[3]City of Hope Medical Center, Los Angeles, CA
[4]Beth-Israel Deaconess Medical Center, Boston, MA
[5]Dartmouth-Hitchcock Medical Center, Lebanon, NH
[6]University of Pittsburgh, Pittsburgh, PA
[7]Princess Margaret Hospital, Toronto, ON, Canada
[8]Hopital Hotel-Dieu, Paris, France
[9]Institut Gustave Roussy, Villejuif, France
[10]Centre Rene Gauducheau, Saint Herblain, France
[11]Hopital Europeen Pompidou, Paris, France
[12]Institut Bergonie, Bordeaux, France
[13]Bristol-Myers Squibb, Princeton, NJ
[14]Yale University, New Haven, CT

102 DEVELOPMENT OF A NOVEL MULTIPLEX CANCER VACCINE FOR THE THERAPY OF PATIENTS WITH MELANOMA

***Anthony E. Maida*[1]**, *Amanda Enstrom[1], Kit S. Lam[1], Jianhua Ye[2], Miguel Castro[2]*

[1]Internal Medicine, UD Davis Cancer Center, Sacramento, CA
[2]N/A, Biosynthesis, Inc., Lewisville, TX

103 CHARACTERIZATION OF A HUMANIZED ANTI-HGITR MONOCLONAL ANTIBODY (MAB), TRX518

Joe Ponte, *Irina Apostolou, Daniel Doty, Daron Forman, Justin Guild, Reema Gulati, Devangi Mehta, Michael Slavonic, Paul Ponath, Lou Vaickus, Michael Rosenzweig*

Tolerx, Inc, Cambridge, MA

104 TARGETING PROTEIN TYROSINE PHOSPHATASES TO ENHANCE IMMUNE TARGETING AGAINST RECEPTOR TYROSINE KINASE-OVEREXPRESSING CANCERS

***Amy Wesa*[1]**, *Maja Mandic[1], Jennifer Taylor[1], Robert Ferris[1,2], Walter Storkus[1,2]*

[1]University of Pittsburgh School of Medicine, Pittsburgh, PA
[2]University of Pittsburgh Cancer Institute, Pittsburgh, PA

Poster #:

Trafficking and *in vivo* Imaging

105 EVALUATION OF ANGIOGENESIS USING MICRO-COMPUTED TOMOGRAPHY IN A XENOGRAFT MOUSE MODEL OF LUNG CANCER

***Rajkumar Savai*[1]**, *Alexander C. Langheinrich[2], Ralph T. Schermuly[3,5], Soni S. Pullamsetti[3,5], Rio Dumitrascu[3], Horst Traupe[4], Wigbert S. Rau[2], Werner Seeger[3,5], Friedrich Grimminger[1,3], Gamal A. Banat[1]*

[1]Department of Hematology and Oncology, University Hospital Giessen and Marburg GmbH, Giessen, Germany
[2]Department of Radiology, University Hospital Giessen and Marburg GmbH, Giessen, Germany
[3]Department of Internal Medicine, University Hospital Giessen and Marburg GmbH, Giessen, Germany
[4]Department of Neuroradiology, University Hospital Giessen and Marburg GmbH, Giessen, Germany
[5]Department of Lung Development and Remodelling, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany

Poster #:

Tumor Escape / Tumor Microenvironment

106 MECHANISM OF MEMBRANE-BOUND TGF-β1 REGULATION IN HNSCC CELL LINES

***Yong-Oon Ahn*[1]**, *Myung Whun Sung[1,3], Dae Seog Heo[1,2]*

[1]Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea
[2]Department of Internal Meidicine, Seoul National University College of Medicine, Seoul, South Korea
[3]Otolaryngology, Seoul National University College of Medicine, Seoul, South Korea

107 A NOVEL MECHANISM OF LATE GENE SILENCING DRIVES SV40 TRANSFORMATION OF HUMAN MESOTHELIAL CELLS

***Michele Carbone*[1]**, *Antonio Pannuti[1], Lei Zhang[1], Joseph R. Testa[3], Maurizio Bocchetta[2]*

[1]University of Hawaii, Honolulu, HI
[2]Loyola University Chicago, Chicago, IL
[3]Fox Chase Cancer Center, Philadelphia, PA

Poster Listing

(primary authors listed in bold italics)

Posters – Saturday

108 ALTERED GENE EXPRESSION PATTERNS IN PRIMARY-VERSUS-METASTATIC MELANOMA: IMPACT OF INTERACTIONS WITH STROMAL CELL COMPONENTS
***Evelyna Derhovanessian*[1]**, *Dawn Mazzatti*[2], *Graham Pawelec*[1]
[1]*Second Department of Internal Medicine, University of Tuebingen Medical School, Tuebingen, Germany*
[2]*Unilever Corporate Research, Sharnbrook, United Kingdom*

109 DOXORUBICIN SELECTIVELY DOWN-REGULATES B7-H1 SURFACE EXPRESSION IN BREAST CANCER CELLS
***Hazem Ghebeh*[1]**, *Cynthia Lehe*[1], *Eman Barhoush*[1], *Taher Al-Tweigeri*[3], *Abdelilah Aboussekhra*[2], *Said Dermime*[1]
[1]*Immunology/Stem Cell Therapy Program, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia*
[2]*Biological and Medical Research, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia*
[3]*King Faisal Cancer Center, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia*

110 HUMAN ACTIVATED T LYMPHOCYTES MODULATE INDOLEAMINE 2,3-DIOXYGENASE EXPRESSION IN TUMORS THROUGH TH1/TH2 BALANCE
***Jessica Godin-Ethier*[1]**, *Sandy Pelletier*[1], *Laïla-Aïcha Hanafi*[1], *Philippe O. Gannon*[1], *Marie-Andrée Forget*[1], *Simon Tanguay*[2], *Nathalie Arbour*[1], *Réjean Lapointe*[1]
[1]*Oncology department, Research Center, Centre Hospitalier de l'Université de Montréal (CRCHUM) and Institut du cancer de Montréal, Montreal, QC, Canada*
[2]*McGill University Health Center, Montreal, QC, Canada*

111 EXPANSION OF TUMOR CELLS DEFICIENT IN CXCL9/MIG PRODUCTION DURING GROWTH OF CUTANEOUS TUMORS
Anton Gorbachev, *Robert Fairchild*
Immunology, Cleveland Clinic, Cleveland, OH

112 CELL SURFACE BOUND MUC16 (CA125) SHIELDS OVARIAN TUMOR CELLS FROM NATURAL KILLER CELL MEDIATED ATTACK
***Jennifer A. Gubbels*[1]**, *Mildred Felder*[1], *Jennifer A. Belisle*[1], *Helen Holden*[1], *Sarah Petrie*[1], *Martine Migneault*[2], *Claudine Rancourt*[2], *Joseph Connor*[1], *Manish S. Patankar*[1]
[1]*OB-GYN, University of Wisconsin-Madison, Madison, WI*
[2]*Microbiology and Infectiology, Universite de Sherbrooke, Sherbrooke, QC, Canada*

113 MOLECULAR MECHANISMS FOR GENERATION OF IMMUNOSUPPRESSIVE MICROENVIROMENT BY CANCER CELLS
Yutaka Kawakami, *Chie Kudo-Saito, Hidetoshi Sumimoto, Nobuo Tsukamoto, Tomonori Yaguchi*
Division of Cellular Signaling, Institute for Advanced Medical Research, Keio University School of Medicine, Tokyo, Japan

114 CENTRAL ROLE OF TUMOR-ASSOCIATED CD8+ T-EFFECTOR/MEMORY CELLS IN RESTORING SYSTEMIC ANTI-TUMOR IMMUNITY
Mehmet O. Kilinc, *Tao Gu, Virtuoso P. Lauren, Nejat K. Egilmez*
Dept of Microbiology and Immunology, University at Buffalo, Buffalo, NY

115 PROPORTION OF REGULATORY T LYMPHOCYTES AND MYELOID-DERIVED SUPPRESSOR CELLS IN PERIPHERAL BLOOD OF PATIENTS WITH UTERINE CERVICAL CANCER
***Yong-Man Kim*[1]**, *Shin Wha Lee*[1], *Ha-Young Lee*[2], *Dae-Yeon Kim*[1], *Jong-Hyeok Kim*[1], *Young-Tak Kim*[1], *Joo-Hyun Nam*[1]
[1]*Department of obstetrics & gynecology, University of Ulsan, Asan Medical Center, Seoul, South Korea*
[2]*Department of Medicine, the Graduate school, University of Ulsan, Seoul, South Korea*

116 IMMUNOGLOBULIN-LIKE TRANSCRIPT 3 (ILT3) IS EXPRESSED BY MYELOID DERIVED SUPPRESSOR CELLS IN THE TUMOR MICROENVIRONMENT OF MELANOMA PATIENTS
Seunghee Kim-Schulze, *Dae Won Kim, Dorota Moroziewicz, Gail DeRaffele, Bret Taback, Howard L. Kaufman*
Surgery, Columbia University, New York, NY

117 HEMOGLOBIN-BETA AS A TUMOR-REJECTION ANTIGEN ALLOWING IMMUNE TARGETING OF THE TUMOR-ASSOCIATED STROMA
Hideo Komita, *Andrew A. Amoscato, Sean M. Alber, Amy K. Wesa, Walter J. Storkus*
Dermatology and Immunology, University of Pittsburgh, Pittsburgh, PA

118 TUMOR TREG POTENTLY ABROGATE IN VIVO ANTITUMOR T CELL PRIMING
***Zuqiang Liu*[1]**, *Hae S. Noh*[1], *Janet Chen*[1], *Jin H. Kim*[1], *Louis D. Falo, Jr.*[1,3], *Zhaoyang You*[1,2,3]
[1]*Dermatology, Univ. of Pittsburgh School of Medicine, Pittsburgh, PA*
[2]*Immunology, Univ. of Pittsburgh School of Medicine, Pittsburgh, PA*
[3]*The University of Pittsburgh Cancer Institute, Univ. of Pittsburgh School of Medicine, Pittsburgh, PA*

(primary authors listed in bold italics)

Posters – Saturday

119 EXPRESSING TH1 OR TH2 CYTOKINES IN THE BLADDER AND THEIR EFFECTS ON TUMOR GROWTH IN A MURINE ORTHOTOPIC BLADDER TUMOR MODEL
Ratha Mahendran, *Shih Wee Seow, Chen Zhang, Sin Mun Tham, Kesavan Esuvaranathan*
Surgery, National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore

120 SOLUBLE VEGF RECEPTOR PRODUCTION FROM GM-CSF-STIMULATED HUMAN MONOCYTES IS ENHANCED UNDER HYPOXIC CONDITIONS
Julie M. Roda, *Tim D. Eubank, Clay B. Marsh*
Department of Internal Medicine, Ohio State University, Columbus, OH

121 EPITHELIAL-MESENCHYMAL TRANSITION IN RENAL CELL CARCINOMA (RCC): INFLUENCE ON ANTIGEN EXPRESSION AND IMMUNE RECOGNITION
Markus Schmid[1], *Bernhard Frankenberger[1], Heinz Höfler[2], Gregor Weirich[2], Dolores J. Schendel[1]*
[1]Institute of Molecular Immunology, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich, Germany
[2]Institute of Pathology, Technical University, Munich, Germany

122 INDOLEAMINE 2,3-DIOXYGENASE EXPRESSION IN RENAL CELL CARCINOMA
Ellen T. Scholnicoff[1], *Amy Wesa[2], Walter J. Storkus[3]*
[1]Pediatrics, Division of Pulmonary Medicine, Allergy & Immunology, Children's Hospital/University of Pittsburgh Medical Center, Pittsburgh, PA
[2]Dermatology, University of Pittsburgh Medical Center, Pittsburgh, PA
[3]Immunology, University of Pittsburgh Medical Center, Pittsburgh, PA

123 MOLECULAR REGULATION OF MDSCS BY COX-2 AND TK INHIBITORS IN A TRANSGENIC MURINE MAMMARY CANCER MODEL
James E. Talmadge, *Sherry Westphal, Alicia Dafferner, Moses Donkor, Traci Hoke, Fuminori Abe*
U of Neb Med Ctr, Omaha, NE

124 EFFECT OF ARGINASE II ON L-ARGININE DEPLETION AND CELL GROWTH IN MURINE CELL LINES OF RENAL CELL CARCINOMA
David J. Tate[1], *Derek J. Vonderhaar[1], John R. Patterson[1], Arnold H. Zea[1,2]*
[1]Stanley S. Scott Cancer Center, LSUHSC, New Orleans, LA
[2]Microbiology Immunology and Parasitology, LSUHSC, New Orleans, LA

125 BLOCKADE OF PD-1/PD-L1 INTERACTIONS IS PARADOXICALLY DETRIMENTAL IN A T CELL ADOPTIVE TRANSFER TUMOR THERAPY MODEL
Long Zhang, *Thomas F. Gajewski, Justin Kline*
Department of Medicine, University of Chicago, Chicago, IL

Poster #:

Tumor Targeting Monoclonal Antibodies

126 TARGETING HUMAN B CELL CHRONIC LYMPHOCYTIC LEUKEMIA WITH A MONOCLONAL ANTIBODY SPECIFIC FOR THE RECEPTOR TYROSINE KINASE ROR1
Sivasubramanian Baskar, *Jiahui Yang, Christoph Rader*
Experimental Transplantation and Immunology Branch, National Cancer Institute, Bethesda, MD

127 IMMUNOCYTOKINE KS-IL2 INCREASES NATURAL KILLER (NK) CELL IMMUNE SYNAPSE FORMATION AND CONJUGATES EFFECTOR AND TARGET CELLS VIA THE IL-2 RECEPTOR
Jennifer A. Gubbels[1], *Mildred Felder[1], Helen Holden[1], Zane Neal[2], Jackie Hank[2], Paul Sondel[2], Manish S. Patankar[1], Joseph P. Connor[1]*
[1]OB-GYN, University of Wisconsin-Madison, Madison, WI
[2]Human Oncology, University of Wisconsin-Madison, Madison, WI

128 CYTOKINES ENHANCE THE ANTI-TUMOR EFFECTS OF FOLATE CONJUGATED IMMUNOGLOBULIN
Sri Vidya Kondadasula[1], *Aruna Mani[2], Natalie Jones[3], Julie Roda[2], Yanhui Lu[4], Hong Li[4], Xiaoli Zhang[4], David Jarjoura[5], Robert J. Lee[4], William E. Carson[3]*
[1]Department of Molecular Virology, Immunology and Medical Genetics, The Ohio State University, Columbus, OH
[2]Internal Medicine, The Ohio State University, Columbus, OH
[3]Surgery, The Ohio State University, Columbus, OH
[4]Pharmacy, The Ohio State University, Columbus, OH
[5]Biostatistics, The Ohio State University, Columbus, OH

129 ADCC-MEDIATED LYSIS OF KRAS-MUTATED COLON CANCER CELLS BY ANTI-EPCAM ANTIBODY ADECATUMUMAB
Dominik Rüttinger[1,2], *Christian Brandl[1,2], Christiane Simmich[1,2], Anja Brandl[1,2], Patrick A. Baeuerle[1,2], Andreas Wolf[1,2]*
[1]Micromet AG, Munich, Germany
[2]Micromet Inc, Bethesda, MD

Posters – Saturday

(primary authors listed in bold italics)

Poster #:

Late-Breaking Abstracts

130 NUCLEOTIDES-BASED IMMUNIZATION: COMPARISON OF WATER-IN-OIL LIPOSOME-BASED DELIVERY OF NUCLEOTIDES WITH IN VIVO ELECTROPORATION

Pirouz Daftarian[1,3], *Marc Mansour[2], Raquibul Chowdhury[1], Robert G. Brown[2], Jose Da Silva[1], Vance Lemmon[4], Norma Kenyon[1,5]*
[1]Biological Modifiers Laboratory of the Wallace H. Coulter Center for Translational Research, University of Miami, Miami, FL
[2]Research and Developement, ImmunoVaccine Technologies Inc, Halifax, NS, Canada
[3]Miami Project to Cure Paralysis, Miller School of Medicine,, University of Miami, Miami, FL
[4]Department of Microbiology & Immunology, University of Miami, Miami, FL
[5]Diabetes Research Institute, University of Miami, Miami, FL

131 DEVELOPMENT OF AN RNAI THERAPEUTIC FOR SOLID TUMORS: ESTABLISHMENT OF EFFICACY IN AN ORTHOTOPIC LIVER TUMOR MODEL

I. Toudjarska[1], A. Judge[2], J. Brodsky[1], K. McClintock[2], E. Ambegia[2], T. Buck[1], L. Jeffs[2], E. Yaworski[2], I. MacLachlan[2], ***J. Gollob[1]****, D. Sah[1], D. Bumcrot[1]*
[1]Alnylam Pharmaceuticals, Inc., Cambridge, MA
[2]Tekmira Pharmaceuticals Corp., Vancouver, BC, Canada

132 EXPLORING THE ROLE OF INFLAMMATION IN PANCREATIC CANCER DEVELOPMENT

Reginald Hill*, Harvey Herschman, Hong Wu*
Molecular and Medical Pharmacology, UCLA, Los Angeles, CA

133 PHASE I CLINICAL TRIAL OF EPITOPE PEPTIDES BASED VACCINE TARGETING TUMOR VASCULAR ENDOTHELIAL CELLS AGAINST ADVANCED CANCER PATIENTS

Akira Kanamoto*, Marimo Sato, Masahisa Jinushi, Akihiko Ito, Hideaki Tahara*
Department of Surgery and Bioengineering, Institute of Medical Science, University of Tokyo, Tokyo, Japan

134 INHIBITORY EFFECTS OF QUEERCETIN AND ITS METHYLETHERS ON LIPOPOLYSACCHARIDE-INDUCED NO PRODUCTION IN RAW 264.7 CELLS AND THEIR STRUCTURE-ACTIVITY RELATIONSHIPS

Agnes L.-F. Chan[1], Chwen-Ming Shih[2], Tzu-Ting Chen[3], Chi-Ming Chen[4], ***Wun-Chang Ko[3]***
[1]Pharmacy Department, Chi Mei Medical Center, Tainan, Taiwan
[2]Department of Biochemistry, Taipei Medical University, Taipei, Taiwan
[3]Graduate Institute of Pharmacology, Taipei Medical University, Taipei, Taiwan
[4]Department of Medicinal Chemistry, Taipei Medical University, Taipei, Taiwan

135 RECOMBINANT HUMAN ANGIOTENSIN CONVERTING ENZYME 2 AS NOVEL BIOLOGIC FOR CANCER THERAPY

Hans Loibner*, Evelyne Janzek, Bernhard Peball, Guenter Lametschwandtner, Manfred Schuster*
Apeiron, Vienna, Austria

136 AUTOLOGOUS HUMAN IMMUNE/ CYTOKINES AND RELATED EFFECTORS THERAPY FOR BREAST CANCER

Konstantinos Papapolychroniadis[1]*, John Anthopoulos[2], P. Makrantonakis[3], Vasilis Papadopoulos[1], Julia Papapolychroniadi[1], Epaminondas Fahantidis[1]*
[1]First Propedeutic Surgical Clinic Of Aristotle University Of Thessaloniki Greece, Aristotle University Of Thessaloniki, Thessaloniki, Greece
[2]Clinical Biochemical Institute for Cellbiotechnology and Immunology, K-BIO, Munchen, Germany
[3]Department of Medical Oncology - First Medical Clinic, Aristotle University Of Thessaloniki, Thessaloniki, Greece

137 A CLOSED AND AUTOMATED SYSTEM FOR THE GENERATION OF MELANOMA ANTIGEN-SPECIFIC CYTOTOXIC T LYMPHOCYTES FOR THE TREATMENT OF METASTATIC MELANOMA

Karen Stegman*, Wei-Xing Shi, Xilian Yue, Ann Moriarty, Didier Leturcq*
Cell Therapy, Johnson & Johnson Pharmaceutical R&D, La Jolla, CA

138 INDUCTION OF CELLULAR AND HUMORAL IMMUNE RESPONSES TO TUMOR CELLS AFTER CRYOABLATION

Archana Thakur*, Elyse N. Paul, Peter Littrup, Lawrence G. Lum*
Karmanos Cancer Institute, Detroit, MI

139 INCREASED TH17 CELLS IN PATIENTS WITH MELANOMA TREATED WITH THE ANTI-CTLA4 BLOCKING ANTIBODY TREMELIMUMAB

Erika M. von Euw[1]*, Thinle Chodon[1], Jason Jalil[2], Richard C. Koya[2], Begonya Comin-Anduix[2], Antoni Ribas[1,2]*
[1]Medicine, UCLA, Los Angeles, CA
[2]Surgery, UCLA, Los Angeles, CA

(primary authors listed in bold italics)

Posters – Saturday

140 REDUCTION OF AKT2 EXPRESSION INHIBITS CHEMOTAXIS SIGNAL TRANSDUCTION IN HUMAN BREAST CANCER CELLS

*Wuzhou Wan[1], Ronghua Sun[1], Ying Liu[1], Xiangjun Sun[3], Ning Zhang[2], **Jingna Wang[3]***
[1]Peking University, Beijing, China
[2]Tianjin Medical University Cancer Institute and Hospital, Tianjin, China
[3]College of Agriculture and Biotechnology, Shanghai Jiao Tong University, Shanghai, China

141 AGONISTIC ANTIBODY TO CD40 INDUCES CCR2-DEPENDENT ANTI-TUMOR RESPONSES WHEREAS IL-2/ANTI-CD40 SYNERGY INVOLVES MULTIPLE CHEMOKINES AND EFFECTOR LEUKOCYTE MECHANISMS

***Jonathan M. Weiss[1]**, Timothy C. Back[1], Perwez Hussain[2], Peijun He[2], Eilene Gruys[1], Jimmy K. Stauffer[1], Veronica L. Hall[1], Jeff J. Subleski[1], Dejan Micic[1], Curtis C. Harris[2], William J. Murphy[3], Robert H. Wiltrout[1]*
[1]Cancer and Inflammation Program, NCI Frederick, Frederick, MD
[2]Laboratory of Human Carcinogenesis, NCI, Bethesda, MD
[3]Microbiology and Immunology, University of Nevada School of Medicine, Reno, NV

iSBTc Membership Information

iSBTc Profile

The International Society for Biological Therapy of Cancer (iSBTc) was established in 1984 to facilitate the exchange and promotion of scientific information about the use of biological cancer therapies. iSBTc is a 501(c)(3) not for profit organization of medical professionals with a constituency of academic, government, industry, clinical, and basic scientists from around the world. The Society was founded on the belief that new systemic therapeutic treatments would continue to complement chemotherapies and move into the mainstream in the fight against cancer. To aid in this effort, iSBTc provides intimate channels for the discussion of current clinical trial results and methodologies, as well as means to collaborate on new initiatives in tumor immunology and biological therapy. It is these key interactions and innovations that help advance the progress of cancer research and therapies and lead to better patient outcomes.

Core Purpose

To improve cancer patient outcomes by advancing the development and application of biological therapy.

Core Values

- **Interaction** - exchange of information and education among basic researchers and clinicians
- **Innovation** - development and application of biological therapy; seeking the best research and thinking related to the Society's purpose and vision
- **Leadership** - defining what is new and important

Membership

The International Society for Biological Therapy of Cancer invites your support for our organization, its activities, and events, by becoming a member of the Society. iSBTc fills its membership with those from industry, academia, and government, serving as clinical and basic scientists and industry representatives. Your contributions as a member can help shape iSBTc policy as we continue in our efforts to advance the development and application of biological therapy.

Through membership in iSBTc, you will be a member of an organization that is actively engaged in facilitating the implementation of timely, cutting-edge translational clinical research in cancer biotherapy.

What iSBTc Membership Offers

- Access to the best science in the field
- Early access to timely information on what is new and relevant to biologic approaches for the treatment of cancer
- Opportunities to participate in and shape discussions that guide progress in the field
- Opportunities to network with colleagues to develop new ideas, establish new collaborations to advance your work, and participate in active scientific exchange
- Access to leaders in the field, including leading scientists and clinical researchers
- Guidance on relevant and timely issues
- The opportunity to advance your career

Additional Benefits

- One year subscription to *Journal of Immunotherapy*, the official journal of iSBTc
- One year, online full-text access to *Journal of Immunotherapy*
- Early registration opportunities for Society programs
- Reduction in program registration fees
- Online directory of iSBTc members
- Access to Members Only section of iSBTc web site: www.isbtc.org
- Eligibility to serve on iSBTc Committees
- Eligibility to serve on iSBTc Board of Directors (Regular members)

Membership Types

Regular Membership ($220 annual dues): Available to individuals with an MD or PhD in a biological science or the equivalent who are active, bona fide representatives of the international scientific community with a specialty or interest in a field related to the biological therapy of cancer. Regular membership includes the right to vote.

Affiliate Membership ($220 annual dues): Available to individuals active or otherwise interested in the biological therapy of cancer. Affiliate membership does not include the right to vote.

Scientist-in-Training (Student) Membership ($50 annual dues): Available to individuals enrolled in MD or PhD academic programs or those participating in post-doctoral fellowships and residency programs who show a demonstrated interest in biological therapy of cancer. Student membership includes an online only subscription to the *Journal*, but does not include the right to vote.

Application Requirements

Regular applicants:
- Curriculum Vitae or educational resumé
- $50 application fee

Affiliate applicants:
- Business or educational resumé or Curriculum Vitae
- $50 application fee

Student applicants:
- Proof of enrollment
- Letter of Recommendation or Curriculum Vitae
- $50 application fee

iSBTc • 555 E. Wells St., Suite 1100 • Milwaukee, WI 53202-3823
Tel: 414-271-2456 • Fax: 414-276-3349 • E-mail: info@isbtc.org • Web: www.isbtc.org

iSBTc Membership Application

Applicant Category

Please check the membership category you are applying for:

☐ Regular ☐ Affiliate ☐ Scientist-in-Training (Student)

Applicant Information

Name: _____

Academic Degree: *(please circle)* MD PhD RN MS NP Other: _____

Institution/Company: _____

Position/Title: _____ Dept: _____

Mailing Address: _____

City: _____ State: _____ Zip: _____

Country: _____ E-mail: _____

Phone: _____ Fax: _____

Please check your field(s) of specialty:

- ☐ Cell Biology
- ☐ Dermatology
- ☐ Genetics
- ☐ Gynecologic Oncology
- ☐ Hematology
- ☐ Immunotherapy
- ☐ Internal Medicine
- ☐ Medical Oncology
- ☐ Microbiology
- ☐ Molecular Biology
- ☐ Pediatric Oncology
- ☐ Pharmacology/ Toxicology
- ☐ Radiation Oncology
- ☐ Radiology
- ☐ Stem Cell Biology
- ☐ Surgical Oncology
- ☐ Transplantation
- ☐ Other _____

Please check the disease state(s) most affiliated with your research or practice:

- ☐ Breast
- ☐ Colorectal
- ☐ Head & Neck
- ☐ Hepatocellular
- ☐ Kidney
- ☐ Leukemia
- ☐ Lung
- ☐ Lymphoma
- ☐ Melanoma
- ☐ Neuroblastoma
- ☐ Ovarian
- ☐ Prostate
- ☐ Renal Cell
- ☐ Other _____

Application Requirements

Regular applicants:

- ☐ I will e-mail my CV or educational resumé to info@isbtc.org.
- ☐ My CV or educational resumé is enclosed.

Affiliate applicants:

- ☐ I will e-mail my business or educational resumé to info@isbtc.org.
- ☐ My business or educational resumé is enclosed.

Student applicants:

- ☐ I will e-mail my letter of recommendation and proof of enrollment to info@isbtc.org.
- ☐ My letter of recommendation and proof of enrollment are enclosed.

Application Fee $50.00 USD

☐ Check (enclosed) ☐ VISA ☐ MasterCard ☐ American Express

An application fee of $50 is required to complete this application. Upon approval for membership, this $50 application fee will be credited toward annual membership dues and the remaining dues balance will be invoiced.

Membership applications are reviewed throughout the year. Applicants will be contacted upon acceptance. Membership is valid from the date dues are paid in full until the end of that calendar year.

Card Holder: _____

Card Number: _____ Exp.: _____

Signature: _____ Date: _____

Return this form to: iSBTc • 555 E. Wells St., Suite 1100 • Milwaukee, WI 53202-3823
Tel: 414-271-2456 • Fax: 414-276-3349 • E-mail: info@isbtc.org • Web: www.isbtc.org

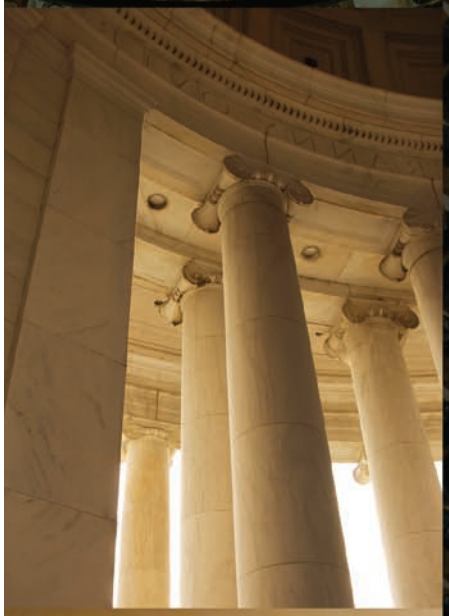
Notes

International Society for Biological Therapy of Cancer
555 East Wells Street, Suite 1100
Milwaukee, Wisconsin 53202-3823
Tel: 414-271-2456 Fax: 414-276-3349
E-Mail: info@isbtc.org
Web site: www.isbtc.org

Save the Date

iSBTc 2009 Annual Meeting and Associated Programs

October 29 - November 1, 2009
Washington, D.C.



International Society for Biological Therapy of Cancer
iSBTc

24th Annual Meeting