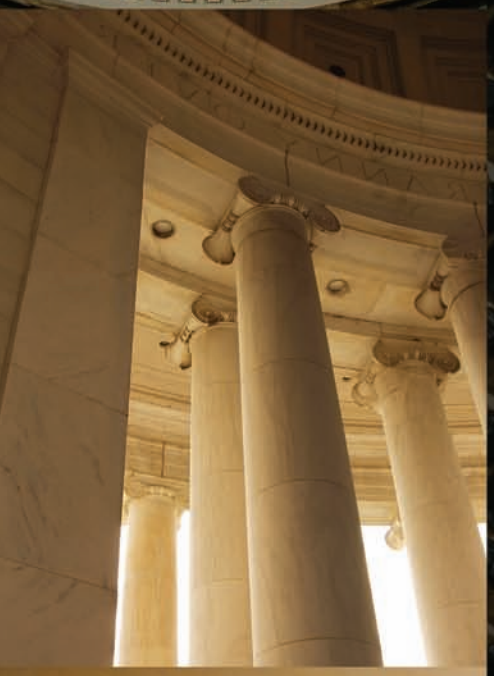
International Society for Biological Therapy of Cancer



Final Program

iSBTc
24th Annual Meeting

October 29-31, 2009

Gaylord National Hotel and Convention Center

National Harbor, MD ~ Washington, D.C.

International Society for iSBTc Biological Therapy of Cancer

www.iSBTc.org

2009 Supporters

ANNUAL MEETING

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GENERAL SOCIETY

Otsuka
Otsuka Pharmaceutical Co., Ltd.

Program at a Glance

** separate registration required*

Tuesday, October 27, 2009

5:00 pm – 8:00 pm	Registration Open	Potomac Desk C

Wednesday, October 28, 2009

6:30 am – 6:00 pm	Registration Open	Potomac Desk C
7:00 am – 8:00 am	Continental Breakfast	Exhibit Hall D
7:45 am – 7:00 pm	iSBTc-FDA-NCI Workshop on Prognostic and Predictive Immunologic Biomarkers in Cancer*	Potomac C

Thursday, October 29, 2009

6:30 am – 6:00 pm	Registration Open	Potomac Desk C
7:00 am – 7:45 am	Young Investigator "Meet-the-Expert" Breakfasts*	Exhibit Hall D
7:00 am – 8:00 am	Continental Breakfast	Exhibit Hall D
7:50 am – 8:00 am	24th Annual Meeting Begins / President's Welcome	Potomac C
8:00 am – 8:45 am	*Richard V. Smalley, MD Memorial Lectureship*: Isaiah J. Fidler, DVM, PhD	Potomac C
8:45 am – 11:30 am	Plenary Session: Human Immunology	Potomac C
11:30 am – 1:00 pm	Lunch / Exhibits	Exhibit Hall D
12:00 pm – 1:00 pm	Poster Presentations: Session I (odd numbers)	Exhibit Hall D
1:00 pm – 3:00 pm	Plenary Session: Enhancing Cancer Vaccines/Combinations	Potomac C
3:15 pm – 4:45 pm	Concurrent Session I: Regulatory & Activated T Cell Subsets	Potomac C
3:15 pm – 4:45 pm	Concurrent Session II: Monoclonal Antibodies/Combinations	Potomac 2
5:00 pm – 5:30 pm	iSBTc Membership Business Meeting	Potomac C
5:30 pm – 7:00 pm	Networking Reception	Exhibit Hall D
5:30 pm – 6:30 pm	Poster Presentations: Session I (odd numbers)	Exhibit Hall D

Friday, October 30, 2009

7:00 am – 5:00 pm	Registration Open	Potomac Desk C
7:00 am – 8:00 am	Continental Breakfast	Exhibit Hall D
8:00 am – 8:45 am	Keynote Address: Mark M. Davis, PhD	Potomac C
8:45 am – 11:30 am	Plenary Session: Viral and Cellular Proteomic Targets	Potomac C
11:30 am – 1:00 pm	Lunch / Exhibits	Exhibit Hall D
12:00 pm – 1:00 pm	Poster Presentations: Session II (even numbers)	Exhibit Hall D
1:00 pm – 2:20 pm	iSBTc Presidential Abstract Session	Potomac C
2:45 pm – 4:15 pm	Concurrent Session I: Manipulation of the Tumor Microenvironment	Potomac 2
2:45 pm – 4:15 pm	Concurrent Session II: Targeted Therapeutics and Biological Therapy	Potomac C
4:30 pm – 5:00 pm	2008 Workshop on Cancer and Inflammation Update: Promise for Biological Therapy	Potomac C
5:00 pm – 5:30 pm	Award Presentations	Potomac C
5:30 pm – 7:00 pm	Presidential Reception *supported by* NOVARTIS	Exhibit Hall D
5:30 pm – 6:30 pm	Poster Presentations: Session II (even numbers)	Exhibit Hall D

Saturday, October 31, 2009

7:00 am – 11:00 am	Registration Open	Potomac Desk C
7:00 am – 8:00 am	Continental Breakfast	Exhibit Hall D
8:00 am – 10:15 am	Plenary Session: Adoptive Transfer	Potomac C
10:15 am	Annual Meeting Adjourns	
10:20 am – 12:00 pm	Hot Topic Symposium: "Positive Immunotherapy Clinical Trial Outcomes"*	Potomac C

Message from the President

Dear iSBTc Members and Colleagues,

Welcome to Washington D.C. and the iSBTc 24th Annual Meeting and Biomarkers Workshop! We are excited that you have joined us for what promises to be a stellar week of education, networking, and partnership.

iSBTc's focus on translational science, paired with the intimate meeting environment, expert faculty, participation by the U.S. Food and Drug Administration (FDA), National Cancer Institute (NCI), and leading immunotherapy groups and delegates from around the world promises an experience like no other in the field.

On behalf of the program organizers, I invite you to take advantage of all the iSBTc Annual Meeting and Biomarkers Workshop have to offer. Some things of special note:

- NEW- Young Investigator "Meet-the-Expert" Breakfasts on Thursday
- Richard V. Smalley Lectureship by Isaiah J. Fidler, DVM, PhD on Thursday
- Poster presentations on Thursday and Friday evenings representing 26 countries
- Young Investigator Award Recipient presentations and posters
- Hot Topic Symposium on Positive Immunotherapy Clinical Trial Outcomes on Saturday

As President of iSBTc, I would like to extend a personal thank you for attending these programs to share your science and to jointly celebrate the advancement and success of the field. While it has been a financially trying year for many, you will see iSBTc's numbers are strong – reinforcing the excitement of these critical achievements in the field.

Thank you as well to our international delegates who have travelled great distances to share their research and represent the field on a global scale. And to our Young Investigators, whose enthusiasm, energy, and excellence ensure a bright future for the science.

On behalf of all the delegates and iSBTc members, my gratitude also goes to the program organizers who developed and organized these outstanding programs and the distinguished faculty who have offered their knowledge, expertise and time, as well to our exhibitors and industry supporters for their generosity in supporting the programs this year.

Welcome to the iSBTc Annual Meeting and enjoy!

Bernard A. Fox, PhD
iSBTc President

P.S. Mark your calendars now. The 2010 iSBTc Annual Meeting will be a month earlier, October 1-4, at the Hyatt Regency Washington on Capitol Hill in Washington, D.C.

Support education, research and President Bernie Fox with a "Friend of the President" ribbon (see page 5).

Table of Contents

2009 Program Organizers

24th Annual Meeting

Lieping Chen, MD, PhD
Johns Hopkins University School of Medicine

Robert Ferris, MD, PhD, FACS
University of Pittsburgh Cancer Institute

Carl H. June, MD
University of Pennsylvania

Giorgio Trinchieri, MD
National Cancer Institute

Laurence Zitvogel, MD, PhD
Institute Gustave Roussy

iSBTc-FDA-NCI Workshop on Prognostic and Predictive Immunologic Biomarkers in Cancer

Lisa H. Butterfield, PhD
University of Pittsburgh

Mary L. Disis, MD
University of Washington

Samir Khleif, MD
National Cancer Institute

Francesco Marincola, MD
National Institutes of Health

Magdalena Thurin, PhD
National Cancer Institute

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 science, development and application of biological therapy/immunotherapy

Core Values

- **Interaction/Integration** – exchange of information and education among basic and translational researchers, clinicians, and young investigators; societies and groups sharing the vision and core values of iSBTc
- **Innovation** – challenge the thinking and seek the best research in the development of biological therapy/immunotherapy
- **Translation** – promote the application and understanding of biological therapy/immunotherapy
- **Leadership** – define what is new and important and effectively communicate it to all relevant stakeholders

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

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Earle A. Chiles Research Institute

Vice President
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University of Chicago

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Bristol-Myers Squibb

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Alnylam Pharmaceuticals

Patrick Hwu, MD
MD Anderson Cancer Center

Elizabeth M. Jaffee, MD
Johns Hopkins University

Carl H. June, MD
University of Pennsylvania

Howard Kaufman, MD
Mount Sinai School of Medicine

Dolores J. Schendel, PhD
Helmholtz Center Munich - National Research Center for Environmental Health

iSBTc Staff

Tara Withington, CAE
Executive Director

Angela Kilbert
Director of Administration

Chloe Surinak
Project Manager

Roseann Marotz
Meetings Manager

Sonja Ortman
Executive Assistant

General Meeting Information

Welcome to the 24th Annual Meeting and Workshop of the International Society for Biological Therapy of Cancer (iSBTc) held October 28 – 31, 2009 at the Gaylord National Hotel and Convention Center in National Harbor, Maryland. 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: Isaiah J. Fidler, DVM, PhD from MD Anderson Cancer Center and Mark M. Davis, PhD from Stanford University School of Medicine/ Howard Hughes Medical Institute. Dr. Fidler's keynote presentation is also a part of the *Richard V. Smalley, MD Memorial Award and Lectureship*.

iSBTc is proud to present the 5th Annual *Richard V. Smalley, MD Memorial Award* to Dr. Isaiah J. Fidler. 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 Friday'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 Thursday and Friday 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 24th Annual Meeting showcases a number of exhibitors whose products and services are on display for all meeting attendees to view. Exhibit booths are located on the Atrium Level of the Gaylord National Convention Center in Exhibit Hall D. The hall is open on Thursday and Friday and booths are staffed throughout the day including during all lunches and receptions. For a complete exhibitor map and listing, please refer to pages 13-15.

Exhibit Hours

Convention Center, Atrium Level, Hall D

Thursday, October 29	10:00 am – 7:00 pm
Friday, October 30	10:00 am – 7:00 pm

Membership

Meeting attendees who are members of the iSBTc are designated by a red "Member" ribbon on their name badge. Information on membership classifications, benefits, and dues can be found on page 79. All non-members are invited to complete the membership application form on page 80 and return it to the iSBTc Registration Desk.

"Friend of the President" Ribbons

iSBTc is committed to furthering the field of cancer immunotherapy/biologic therapy by establishing a Trust to support research, training and education. In support of this Trust, iSBTc created a special opportunity to honor its President, Dr. Bernard A. Fox, through the offering of "Friend of the President" ribbons. Delegates with this special commitment to cancer immunotherapy/biological therapy and President Bernie Fox are noted by the lavender ribbons on their name badges as well as on signs throughout the conference. Show your support by purchasing a ribbon at the Registration Desk for a minimum donation of $50.

Registration

Registration packets are ready for pick up at the iSBTc Registration Desk located at the Gaylord National Convention Center Potomac Registration Desk C for those who are preregistered for the Annual Meeting. On-site registration for the Annual Meeting and Associated Programs is accepted space permitting. Separate registration and fees are required for the iSBTc-FDA-NCI Workshop on Prognostic and Predictive Immunologic Biomarkers in Cancer on Wednesday, October 28. Saturday's Hot Topic Symposium requires a separate registration, but is complimentary for Annual Meeting delegates. Symposium-only registration is $100.

Registration Desk Hours

Convention Center, Ballroom Level, Potomac Desk C

Tuesday, October 27	5:00 pm – 8:00 pm
Wednesday, October 28	6:30 am – 6:00 pm
Thursday, October 29	6:30 am – 6:00 pm
Friday, October 30	7:00 am – 5:00 pm
Saturday, October 31	7:00 am – 11:00 am

Session and Poster Topics

- Adoptive Transfer
- Clinical Trials of New Agents*
- Cytokines / Immunotherapy*
- Enhancing Cancer Vaccines / Combinations
- Human Immunology
- Manipulation of the Tumor Microenvironment
- Monoclonal Antibodies / Combinations
- Regulatory & Activated T Cell Subsets
- Targeted Therapeutics & Biological Therapy
- Viral & Cellular Proteomic Targets
- Late-Breaking Abstracts

** presentations for these categories are posters only*

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 26.

General Meeting Information

Poster Abstracts

All accepted posters for the 24th Annual Meeting are on display in Exhibit Hall D on the Atrium Level of the Convention Center and are available for viewing throughout Thursday and Friday of the Annual Meeting. Please see pages 56-78 or the Poster Abstract Book for a listing of the posters being displayed. During the presentation times below, designated posters are staffed by their respective authors, allowing for information exchange and interaction between researchers and attendees.

Poster Presentations / Staffing Hours

Odd Number Posters *(authors are present)*	
Thursday:	12:00 pm – 1:00 pm & 5:30 pm – 6:30 pm
Even Number Posters *(authors are present)*	
Friday:	12:00 pm – 1:00 pm & 5:30 pm – 6:30 pm

Poster Numbers

Adoptive Transfer	1-23
Clinical Trials of New Agents	24-30
Cytokines / Immunotherapy	31-69
Enhancing Cancer Vaccines / Combinations	70-104
Human Immunology	105-117
Manipulation of the Tumor Microenvironment	118-131
Monoclonal Antibodies / Combinations	132-135
Regulatory & Activated T Cell Subsets	136-148
Targeted Therapeutics & Biological Therapy	149-174
Viral & Cellular Proteomic Targets	175
Late-Breaking Abstracts	176-190

Poster Hall Hours

Convention Center, Atrium Level, Exhibit Hall D

Thursday:	10:00 am – 7:00 pm
Friday:	10:00 am – 7:00 pm

Late-Breaking Abstracts

To fulfill iSBTc's commitment to the most cutting-edge science, late-breaking abstract submission was offered from August to September. Due to this timeframe, these abstracts were not available for publication in the *Journal of Immunotherapy*, but are available for viewing as posters 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.

Young Investigator Meeting Features

iSBTc supports growth and achievement among young investigators in the field of cancer biologics. To this end, iSBTc has fostered the development of the Young Investigator Taskforce whose mission is to promote the career development of young scientists by utilizing the core knowledge and experience of established iSBTc members, to ensure young scientists have a voice within the iSBTc and to provide young scientists access to the support and resources they require to succeed. In fulfillment of this mission, iSBTc offers two specialized opportunities for young investigators in association with the 24th Annual Meeting, the "Meet-the-Expert" Breakfasts and the Presidential and Travel Awards.

Presidential and Travel Awards

iSBTc received a record number of entries for these competitive awards which recognize excellence in oral abstract and poster presentations. See page 8 for more information and past award recipients.

"Meet-the-Expert" Breakfasts *(Ticketed Event)*

7:00 am – 7:45 am Thursday, October 29, 2009
Exhibit Hall D, Atrium Level

The Young Investigator "Meet-the-Expert" Breakfasts focus on the unique issues related to the career development of Young Investigators. Key leaders in the field facilitate small roundtable discussions on particular topics of interest. Registered attendees of the breakfasts submit discussion questions in advance to which the experts provide responses and lead informal dialogues to help provide guidance and direction. Separate registration is required for this event.

Breakfast Topics *(Ticketed Event)*

Developing Successful Collaborations
Leader: Carl H. June, MD
University of Pennsylvania

Finding Your Niche
Leader: Jon M. Wigginton, MD
Bristol-Myers Squibb Company

Grant Writing
Leader: Mary L. Disis, MD
University of Washington

Publishing Papers
Leader: Lieping Chen, MD, PhD
Johns Hopkins University School of Medicine

Translational Research
Leaders: Robert L. Ferris, MD, PhD, facs
University of Pittsburgh Cancer Institute
Craig L. Slingluff, Jr., MD
University of Virginia

iSBTc-FDA-NCI Biomarkers Workshop

In association with the 24th Annual Meeting, iSBTc offers the highly regarded iSBTc-FDA-NCI Workshop on Prognostic and Predictive Immunologic Biomarkers in Cancer on Wednesday, October 28, 2009. Separate registration is required for this program. For more information about this Workshop, please visit the iSBTc Registration Desk located at the Potomac C Desk.

iSBTc-FDA-NCI Workshop on Prognostic and Predictive Immunologic Biomarkers in Cancer

Wednesday, October 28 ~ 7:45 am – 7:00 pm

Organizers

Lisa H. Butterfield, PhD
University of Pittsburgh

Mary L. Disis, MD
University of Washington

Samir Khleif, MD
National Cancer Institute

Francesco Marincola, MD
National Institutes of Health

Magdalena Thurin, PhD
National Cancer Institute

Participating Organizations

Association for Immunotherapy of Cancer (CIMT)
Biotherapy Development Association (BDA)
Cancer Vaccine Consortium (CVC) of the Cancer Research Institute (CRI)
Food and Drug Administration (FDA)
Italian Network for Tumor Biotherapy (NIBIT)
Japanese Society of Cancer Immunology (JSCI)
National Cancer Institute (NCI)
National Institutes of Health (NIH)
Nordic Center for Development of Antitumour Vaccines (NCV-network)

This year's Workshop is the culminating event of months of work by leading experts, global partnering organizations and collaborative programs. It is an interactive program that assembles these leading experts and global organizations in the field to focus on the unique issues related to immunologic monitoring assays as well as novel methodologies for assessing the immune landscape in cancer. Standardization of assays, assay validation, and appropriate potency assays are the subjects of one subcommittee while the other assesses the clinical utility of promising novel technologies and makes recommendations on how to incorporate these into the clinical arena.

Goals of the program include:

1. Establishing a "best practices" protocol for the collection and storage of clinical samples for the assessment of immunologic outcomes in clinical trials of immune based therapies.
2. Defining minimum quality standards for laboratories developing immunologic biomarkers to be used for clinical trial analyses.
3. Establishing a consensus for performance characteristics of the most common immunologic assays to be used for the evaluation of immune based therapies and discussing standards for the reporting of immunologic results.
4. Evaluating and determining key measures of potential potency of cell based immunotherapeutic products.

iSBTc Primer on Tumor Immunology Webinar

CDs available!

Video presentations by:

Judah Folkman
Patrick Hwu
Rakesh Jain
Kim Margolin
Franco Marincola
Polly Matzinger
Ira Pastan
Carmen Scheibenbogen
Paul Sondel
Louis Weiner

Brush up on the basics and learn what's new. Get your CD today at the iSBTc Registration Desk.

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 Friday, October 30 in Potomac C. Of those abstract presenters, all will receive Presidential Travel Awards and one will be selected as the 2009 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
- Presidential Award Plaque
- "Presidential Award Winner" Ribbon

(3) Presidential Travel Award winners receive:
- Up to $750 in Travel Reimbursement
- 1-Year Membership in iSBTc
- Presidential Travel Award Certificate
- "Presidential Travel Award Winner" Ribbon

iSBTc Travel Awards

iSBTc has offered six travel awards to selected young investigators presenting posters at the iSBTc 24th 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 Certificate
- "iSBTc Travel Award Winner" Ribbon

Previous iSBTc Presidential/Travel Award Winners

2008 - San Diego, CA

Presidential Award

Andrea Facciabene, PhD
University of Pennsylvania
Philadelphia, PA

Presidential Travel Awards

Erik Johnson, MD
University of Wisconsin-Madison
Madison, WI

Stephanie K. Watkins, PhD
National Cancer Institute – Frederick
Frederick, MD

Jianda Yuan, MD, PhD
Memorial Sloan-Kettering Cancer Center
New York, NY

iSBTc Travel Awards

Yong-Oon Ahn
Seoul National University College of Medicine
Seoul, Korea

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

Shujuan Liu, PhD
MD Anderson Cancer Center
Houston, TX

Markus Schmid
Helmholtz Zentrum Munchen, Institute of Molecular Immunology
Munich, Germany

Jason C. Steel, PhD
National Cancer Institute, Metabolism Branch
Bethesda, MD

Andrea Worschech, M.Sc.
National Institutes of Health, CC-DTM
Bethesda, MD

2007 - Boston, MA

Presidential Award

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

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.

2009 *Richard V. Smalley, MD Memorial Award* Recipient
Isaiah J. Fidler, DVM, PhD
MD Anderson Cancer Center

In recognition of his outstanding research, work, and achievements in cancer therapy, the International Society for Biological Therapy of Cancer (iSBTc) proudly presents the 2009 *Richard V. Smalley, MD Memorial Award* to Isaiah J. Fidler, DVM, PhD. Dr. Fidler presents the keynote address on Thursday, October 29 from 8:00 am – 8:45 am in Potomac C.

Dr. Isaiah Fidler, a native of Jerusalem, Israel, earned his veterinary medicine degree in 1963 from Oklahoma State University, and his doctorate in human pathology from the University of Pennsylvania School of Medicine in 1970. After serving as an Assistant and then Associate Professor of Pathology at the University of Pennsylvania, Dr. Fidler was named head of the Biology of Metastasis Section at the National Cancer Institute's Frederick Cancer Research Facility in Maryland in 1975. Four years later, he was appointed Director of the Cancer Metastasis and Treatment Laboratory. In 1983, Dr. Fidler joined the University of Texas MD Anderson Cancer Center as Professor and Chairman of the Department of Cell Biology and Director of the Program of Interferon Research; and in 1998, he was named Director of the Cancer Metastasis Research Center. In June, 2008, Dr. Fidler retired as Department Chair, but continues as Director of the CMRC.

Research in Dr. Fidler's laboratory continues to primarily focus on the biology and therapy of cancer metastasis. Additionally, recent laboratory work has included the study of angiogenesis and the development and progression of brain metastasis.

Dr. Fidler is a past President of the American Association for Cancer Research, a past President of the International Society of Differentiation, and he holds memberships in numerous professional organizations. He is the Founding Editor of Cancer and Metastasis Reviews and serves on the editorial boards of several scientific journals. He has authored or co-authored more than 794 scientific publications. Throughout his career, Dr. Fidler has been honored and recognized for his pioneering work in the field of metastasis, receiving numerous awards from national and international organizations. He is considered the premier expert in the field of cancer metastasis research.

Dr. Isaiah J. Fidler is the R. E. "Bob" Smith Distinguished Chair in Cell Biology, Professor, Department of Cancer Biology and Department of Urology, and Director, Cancer Metastasis Research Center, The University of Texas MD Anderson Cancer Center, in Houston, Texas.

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 Recipients

2008
Giorgio Parmiani, MD
San Raffaele Foundation

2007
Ernest Borden, MD
Cleveland Clinic Foundation

2006
Ronald Levy, MD
Stanford University School of Medicine

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

Hotel Information

The Gaylord National Hotel and Convention Center serves as the headquarters for the iSBTc 24th Annual Meeting and Biomarkers Workshop. It is a location ideal for enjoying the region's rich cultural and business destinations. Located in National Harbor, Maryland in Prince George's County, Gaylord National offers convenient access to Washington, D.C. with an hourly shuttle service, water taxi to Old Town Alexandria, and shuttle service to Ronald Reagan National Airport.

Business Amenities and Services

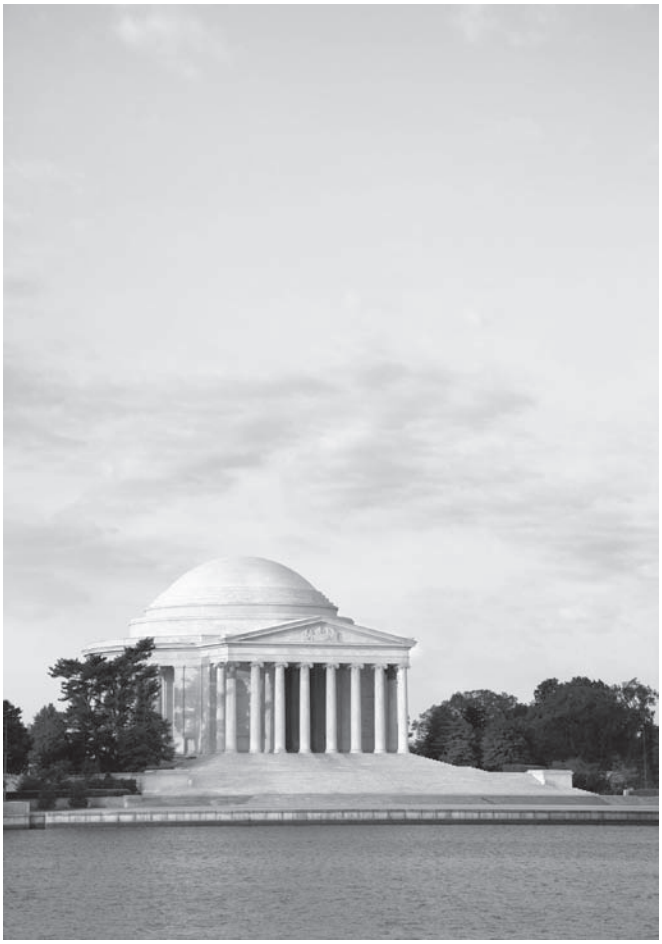
Business Center Hours of Operation
Monday – Sunday, 7:00 am – 9:00 pm
Computer Access, 24 hours

Transportation Options

Taxis are available outside the hotel's main entrance. The Hotel offers a shuttle to downtown Washington, D.C.'s Old Post Office and Union Station daily between 8:00 am – 9:00 pm. Fees apply. Consult the Gaylord National Tour Desk for exact times and fees.

Recreation

- Relâche Spa
- All-season Pool
- 24-hour Fitness Center



Hotel Dining

Java Coast Coffee Shop
Hours: Open 24 hours

Pienza Italian Marketplace
From the produce markets of Tuscany to the irresistible zest of the Veneto region, Pienza embodies the spirit, excitement and hospitality of an Italian marketplace. The ever-changing offerings of five market-inspired stations reflect seasonal changes, the passions of our culinary team, and *abbondanza*—the generosity of the Italian culture. *Open daily for: Breakfast: Monday – Saturday, 6:30 – 10:30 am; Sunday Brunch: 11:30 am – 2:30 pm; Lunch: Monday – Saturday, 11:30 am – 2:30 pm; Dinner: Friday – Saturday, 5:00 – 10:00 pm.*

Moon Bay Coastal Cuisine
Step into Moon Bay for an eclectic menu of Mid-Atlantic seafood, where chefs transform the traditional fruits of the Chesapeake Bay—including Maryland's famous crabs and oysters—into modern versions for today's culinary tastes. Gaze at sweeping views of the Potomac River as you're surrounded by the aroma of freshly prepared seafood. Dive into fresh lobster, whole fish, a variety of clams, and contemporary sushi and sashimi. Choose from a collection of fine wines from around the world, or pair your seafood selection with a cocktail from the vast menu. *Lunch, Saturday and Sunday, 11:30 am – 5:00 pm. Dinner daily, 5:00 – 10:00 pm.*

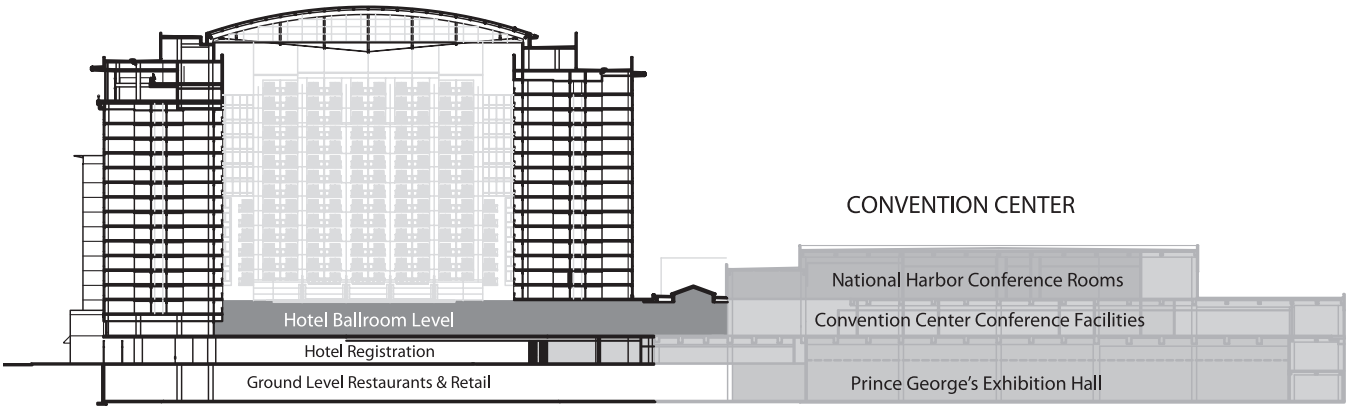
National Pastime Sports Bar
Watch your favorite sporting event on a 30-foot video wall while you drink and dine at National Pastime Sports Bar and Grill. National Pastime's cutting-edge sports-bar environment artfully blends contemporary design with sports memorabilia, fusing ageless character with charm from decades past. Curved banquets... custom sofas... individual lounge chairs... and dozens of flat screens throughout the sports bar and grill to ensure you never miss a play. *Open daily for lunch and dinner from 11:00 am until midnight.*

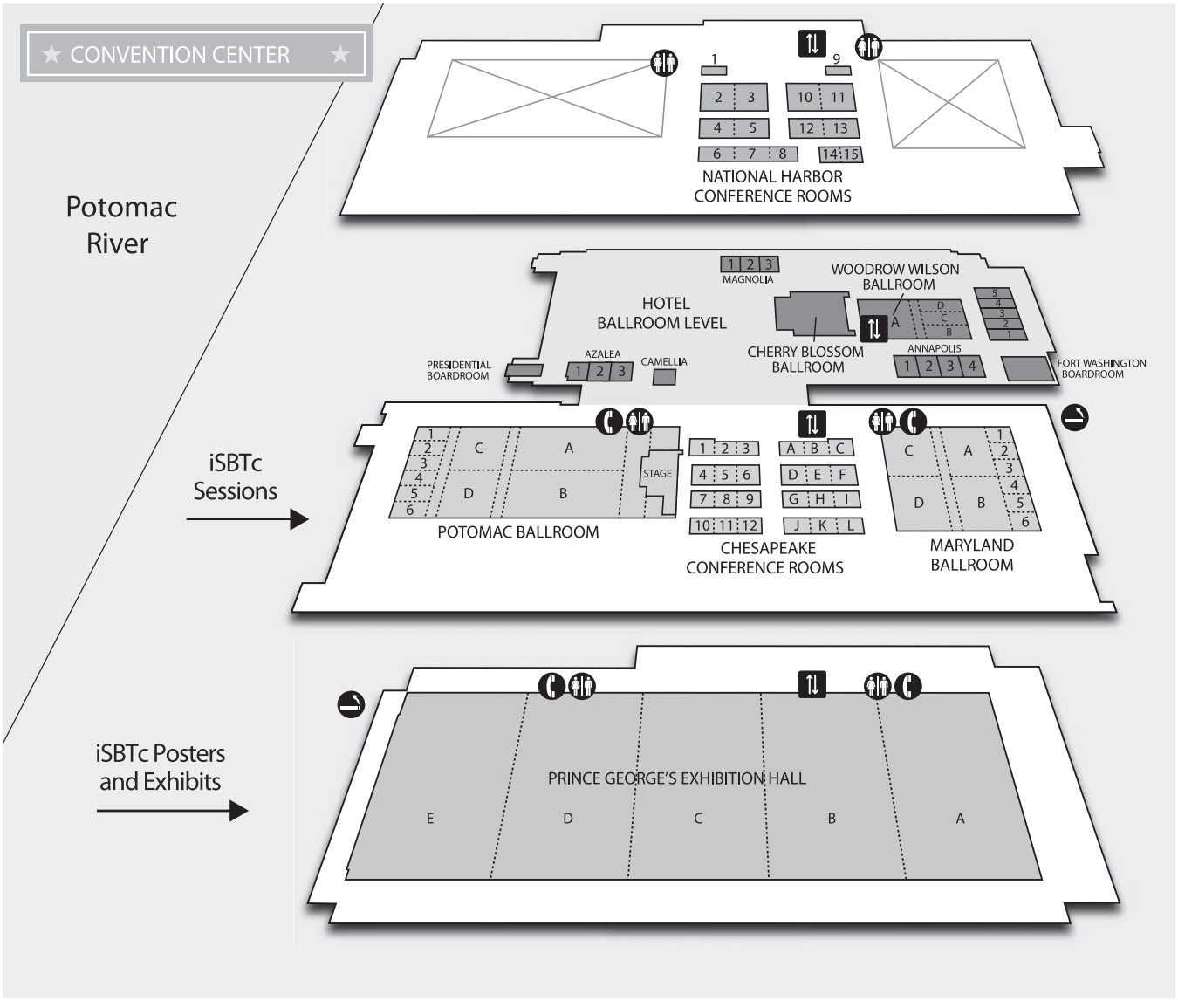
Old Hickory Steakhouse
This is the Gaylord Hotels' signature restaurant—features a stylish and contemporary design, modeled on the interior of an elegant Georgian row house. *Open for dinner daily 5:30 – 11:00 pm.*

Belvedere Lobby Lounge
Belvedere's sophisticated setting fosters a relaxing atmosphere to socialize with friends and colleagues. Located just off the main lobby, guests of Belvedere enjoy a bird's-eye view of the two-acre atrium. *Open daily from 5:00 – 10:00 pm.*

Pose Ultra Lounge
High atop Gaylord National Hotel is Pose, the DC area's only ultra lounge, featuring an exotic Infusion bar and breathtaking views from the wraparound terrace. This cutting-edge, two-story lounge that offers dramatic vistas of the nation's capital viewed through 18-foot, floor-to-ceiling windows, is National Harbor's most exclusive place to find your pose. *Open daily from 5:00 pm – 2:00 am. Hours and days may vary. Please check with the front desk for a current schedule.*

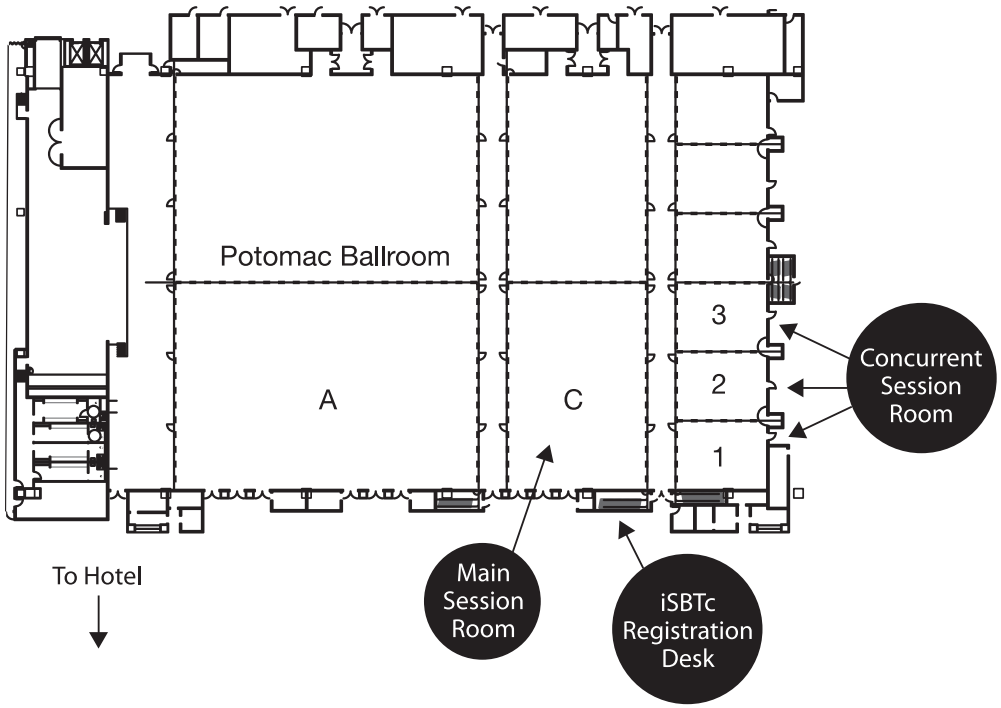
Gaylord National Hotel and Convention Center





Convention Center Maps

Convention Center, Ballroom Level, Potomac Ballroom



Convention Center, Atrium Level, Exhibit Hall

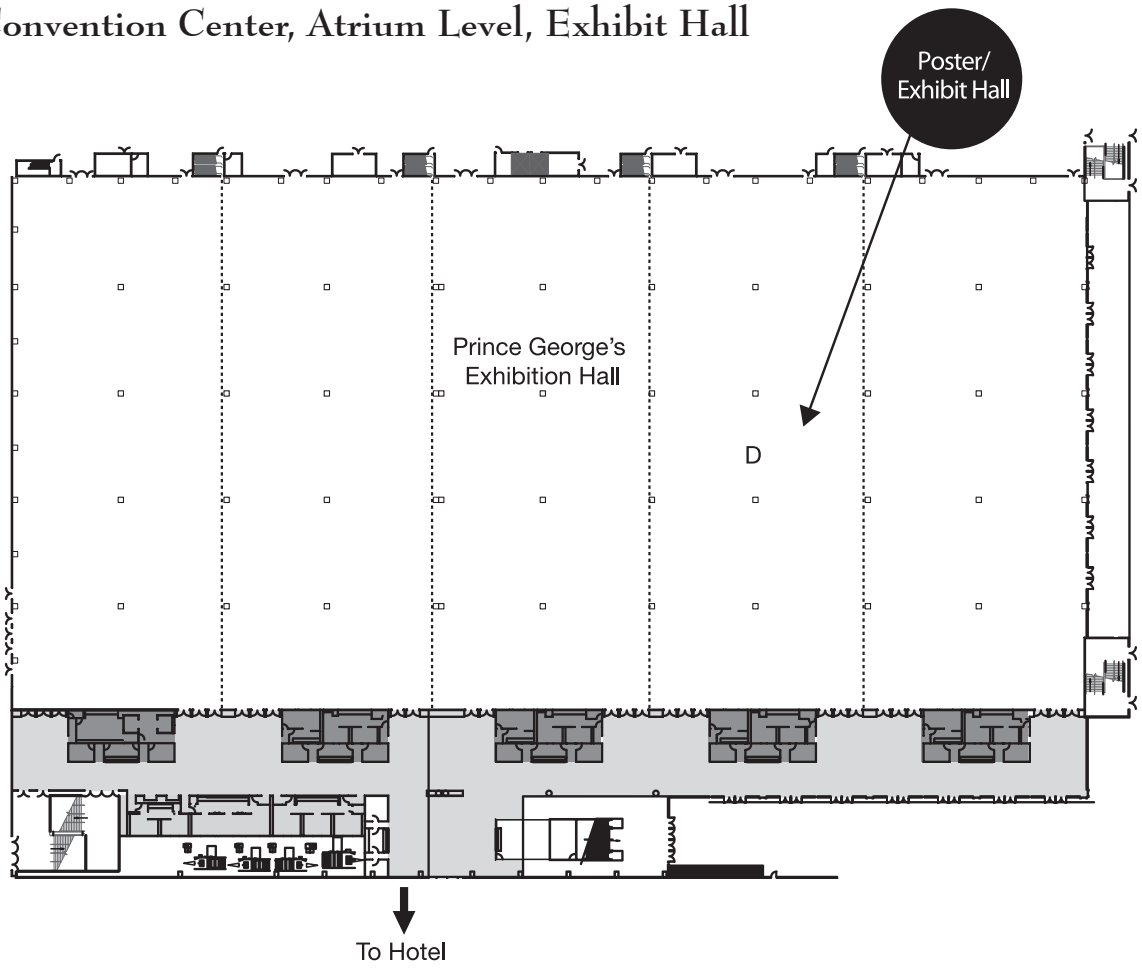
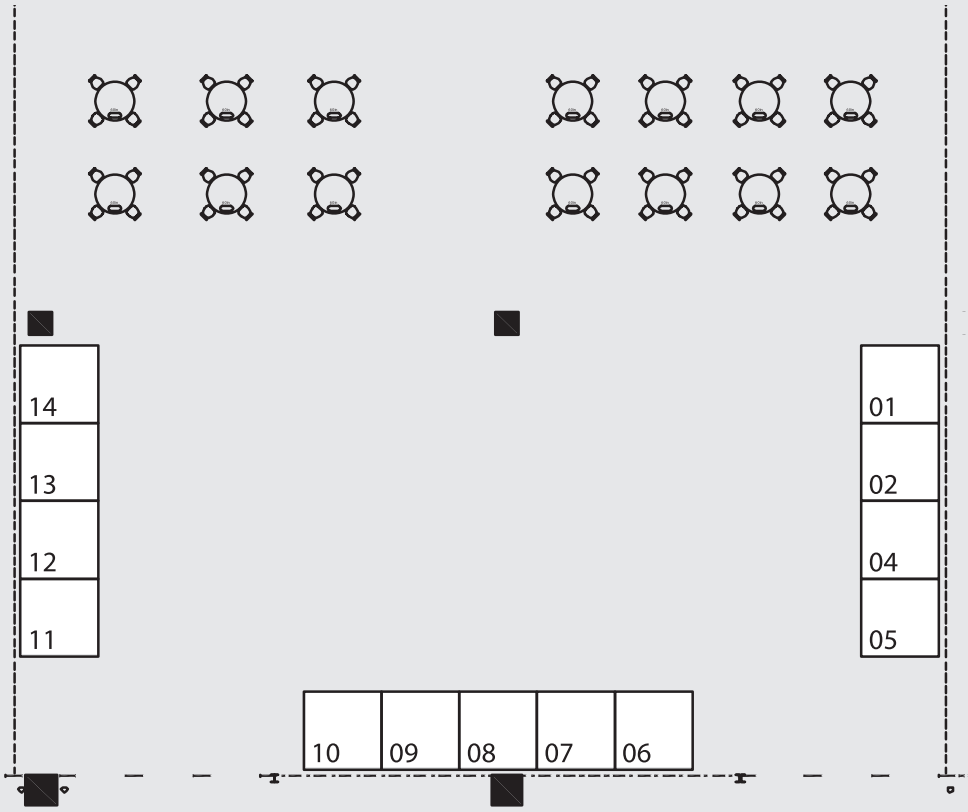


Exhibit Hall D, Atrium Level



Booth #	Exhibitor
1	EMD Serono
2	Cellular Technology Limited (C.T.L.)
4	Lippincott, Williams & Wilkins
5	Biologics Consulting Group, Inc.
6	CellGenix/American Fluoroseal
7	PGxHealth, LLC
8	Invitrogen
9	Novartis Oncology
10	Novartis Oncology
11	JPT Peptide Technologies GmbH
12	Mabtech, Inc.
13	Elsevier
14	Seppic

Exhibitor Listing

Deluxe Exhibitor

Novartis Oncology **Booth #9 & 10**
180 Park Avenue
Florham Park, NJ 07932
Tel: 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) tablets, Afinitor® (everolimus) tablets, 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

Biologics Consulting Group, Inc. **Booth #5**
1317 King Street
Alexandria, VA 22314
Tel: 800- 485-0106 (in U.S.)
Fax: 703-548-7457
Web: www.bcg-usa.com

Biologics Consulting Group, Inc. (BCG) is an international firm providing national and international regulatory and product development advice on the development and commercial production of biological, drug, and device products. Our staff consists of experts in regulatory affairs, product manufacturing and testing, pharmacology/toxicology, facility inspections, statistics, program management, and clinical trial design and evaluation. Many of our consultants are former CBER, CDER, and CDRH reviewers, certified FDA inspectors, and senior scientists from the biotechnology industry.

CellGenix / American Fluoroseal **Booth #6**
CellGenix Technologie Transfer, GmbH
16 Am Flughafen
Freiburg, Germany D-79108
Tel: 49-761-88889-100

US Operations:
303 Main St., Suite 100-C
Antioch, Illinois 60002
Tel: 847-395-7277
Fax: 847-395-0808
Web: www.cellgenix.com

American Fluoroseal Corporation
431 E. Diamond Ave.
Gaithersburg, MD 20877
Tel: 301-990-1407
Fax: 301-990-1472
Web: www.toafc.com

CellGenix manufactures both high quality GMP and research grade cytokines and GMP cell culture medium for use in ex-vivo dendritic, stem, NK, MSC, and T cell culture protocols. These products are marketed in combination with AFC's GMP closed system cell culture and unique cryopreservation containers made from clear, inert, non-leachable, gas permeable FEP film. Both CellGenix and AFC's focus is on high quality, individualized, ex-vivo, cell and gene therapeutics.

Exhibitor Listing

Cellular Technology Limited (C.T.L.) **Booth #2**
20521 Chagrin Blvd
Shaker Heights, OH 44122
Tel: 216-791-5084
Fax: 216-751-1393

The success of Cancer immunotherapy and biological therapy depends on a diversified approach. For nearly a decade, Cellular Technology Limited (CTL) has provided the necessary tools and resources to industry, government and academic institutions. CTL offers contract research services for ELISPOT, ELISA and FACS, as well as a large library of cryopreserved human PBMC, and CEF-peptide pools. In addition, CTL markets the ImmunoSpot®/BioSpot® plate reader systems for ELISPOT, viral plaque, clonogenic, genotoxic and stem cell assays.

Elsevier **Booth #13**
Saunders, Mosby, Churchill, Academic Press
Tel: 240-477-8564
Fax: 240-477-8571
Email: b.karafin@elsevier.com

As the world's leading publisher of science and health information, Elsevier serves more than 30 million scientists, students, and health and information professionals worldwide. By delivering world-class information and innovative tools to researchers, students, educators and practitioners worldwide, we help them increase their productivity and effectiveness.

EMD Serono **Booth #1**
One Technology Place
Rockland, MA 02370
Tel: 800-283-8088
Web: www.emdserono.com

EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany, is a leader in the US biopharmaceutical arena, integrating cutting-edge science with unparalleled patient support systems to improve people's lives. EMD Serono has more than 1000 employees around the country and fully integrated commercial, clinical and research operations in Massachusetts.

Invitrogen Corporation (Headquarters) **Booth #8**
5791 Van Allen Way
P.O. Box 6482
Carlsbad, CA 92008
Tel: 800-955-6288
Fax: 760-602-6500
Web: www.invitrogen.com

A provider of essential life science technologies for academic and government research, production and diagnostics. Invitrogen's efforts are focused on breakthrough innovation in all major areas of biological discovery including life sciences, cloning, stem cells, cell biology, gene therapy, molecular biology, drug discovery, cell culture, proteomics and RNAi.

JPT Peptide Technologies GmbH **Booth #11**
Volmerstrasse 5 (UTZ)
12489 Berlin, Germany
Tel: 49-30-6392-7878
US Tel: 888-578-2666
Web: www.jpt.com

JPT Peptide Technologies (JPT) is an DIN EN ISO 9000:2001 certified and GCLP compliant supplier of innovative peptide based products and services for profiling humoral and cellular immune responses and proteomics. JPT's core technologies are: Spot™and PepStar™ - peptide arrays for humoral immune response profiling; PepMix™ - peptide pools for cellular immune response monitoring; PepTrack™ peptide libraries to address the specific needs of T-cell assays and SpikeTides™ - stable isotope labeled and non modified tryptic peptides for relative and absolute protein quantification.

Mabtech, Inc. **Booth #12**
3814 West Street, Suite 220
Cincinnati, OH 45227
Tel: 866-ELI-Spot (866-354-7768)
Fax: 513-871-7353
Web: www.mabtech.com

Mabtech AB, Stockholm, Sweden with subsidiaries/offices in Australia, France, Germany and the USA, is a privately owned biotech company. We develop, manufacture and market high quality kits and reagents specifically for ELISpot, FluoroSpot and ELISA. Our portfolio also includes antibodies suited to other immunological applications. Continuous efforts to optimize existing and develop relevant and novel ELISpot and FluoroSpot systems have made us a world leader in advancing these methods. Products are for Research Use Only.

PGxHealth, LLC **Booth #7**
5 Science Park
New Haven, CT 06511
Tel: 203-786-3675
Email: kpierz@pgxhealth.com

PGxHealth, a division of Clinical Data, Inc. is a biotechnology company that leverages its expertise in biomarker discovery and late-stage drug development to deliver first-in-class or best-in-class therapeutics, as well as genetic and pharmacogenomic tests to detect serious diseases and help predict drug safety, tolerability and efficacy.

Seppic, Inc. **Booth #14**
30 Two Bridges Road, Suite 210
Fairfield, NJ 07004
Tel: 973-882-5597
Fax: 973-882-5158
Web: www.seppic.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 VG, 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

Thursday, October 29, 2009

**separate registration required*

6:30 am – 6:00 pm	Registration Open	Potomac Registration Desk C , Ballroom Level
10:00 am – 7:00 pm	Exhibit Hall Open	Exhibit Hall D, Atrium Level
10:00 am – 7:00 pm	Poster Hall Open	Exhibit Hall D, Atrium Level
7:00 am – 7:50 am	Continental Breakfast	Exhibit Hall D, Atrium Level
7:00 am – 7:45 am	**Young Investigator "Meet-the-Expert" Breakfasts***	**Exhibit Hall D, Atrium Level**
7:50 am – 8:00 am	**President's Welcome** Bernard A. Fox, PhD *Earle A. Chiles Research Institute*	**Potomac C**
8:00 am – 8:45 am	***Richard V. Smalley, MD Memorial Lectureship*:** **The Biology and Therapy of Brain Metastasis** Isaiah J. Fidler, DVM, PhD *MD Anderson Cancer Center*	**Potomac C**
8:45 am – 11:30 am	**Plenary Session: Human Immunology** Co-Chairs: Jacques Banchereau, PhD *Baylor Institute for Immunology Research* Adrian Hayday, PhD *King's College London*	**Potomac C**
8:45 am – 9:15 am	Dendritic Cells as Therapeutic Vaccines in Cancer Jacques Banchereau, PhD *Baylor Institute for Immunology Research*	
9:15 am – 9:30 am	Identification of Colon Cancer Associated Antigens which would be Key Therapeutic Targets in the Prevention of Disease Relapse or Progression Elizabeth K. Broussard, MD *University of Washington, Tumor Vaccine Group*	
9:30 am – 10:00 am	Harnessing Invariant NKT Cells to Abolish the Suppressive Activity of Myeloid Derived Suppressor Cells and Restore Melanoma Specific Immune Response Vincenzo Cerundolo, MD, PhD *University of Oxford - Institute of Molecular Medicine*	
10:00 am – 10:15 am	Identification of a Novel CD8+CD57+ T Cell Subset in Human Melanoma Exhibiting an Incompletely Differentiated CTL Phenotype Richard Wu, BS *MD Anderson Cancer Center*	
10:15 am – 10:45 am	Refreshment Break	Potomac Foyer
10:45 am – 11:00 am	A Data Analysis Method for Identifying Autoantibody Biomarkers in Cancer Patients Following Immunotherapy Janet Siebert, MS *CytoAnalytics*	
11:00 am – 11:30 am	γδ T Cells-Agents of Tissue and Tumor Immune Surveillance Adrian Hayday, PhD *King's College London*	
11:30 am – 1:00 pm	Lunch and Exhibits	Exhibit Hall D
12:00 pm – 1:00 pm	**Odd Numbered Poster Presentations** *(authors present)*	**Exhibit Hall D**

Thursday, October 29, 2009 *Continued*

1:00 pm – 3:00 pm	**Plenary Session: Enhancing Cancer Vaccines / Combinations** Co-Chairs: Jeffrey Schlom, PhD *National Cancer Institute* Laurence Zitvogel, MD, PhD *Institute Gustave Roussy*	**Potomac C**
1:00 pm – 1:25 pm	**Enhancing Cancer Vaccines as Monotherapy and in Combination Therapies** Jeffrey Schlom, PhD *National Cancer Institute*	
1:25 pm – 1:50 pm	**Defining the Role of TKIs in Reducing Immune Suppression While Improving T Cell Responsiveness and Efficacy of Immunotherapy for the Treatment of Tumors** James H. Finke, PhD *Cleveland Clinic Foundation*	
1:50 pm – 2:05 pm	**Type-1 Dendritic Cell Vaccines in Combination With Poly-ICLC - Association Between Positive Tetramer Response and 6-Month Progression-Free Survival** Hideho Okada, MD, PhD *University of Pittsburgh Cancer Institute*	
2:05 pm – 2:30 pm	**IDO/IDO2 Inhibition: A New Strategy to Drive Immunotherapeutic Responses in Cancer by Reversing Tumoral Immune Tolerance** George C. Prendergast, PhD *Lankenau Institute for Medical Research*	
2:30 pm – 2:55 pm	**How to Exploit the Immunogenicity of Chemotherapy or Radiotherapy Towards a Personalized Therapy of Cancer** Laurence Zitvogel, MD, PhD *Institute Gustave Roussy*	
3:00 pm – 3:15 pm	**Refreshment Break**	Potomac Foyer
3:15 pm – 4:45 pm	**Concurrent Session I: Regulatory & Activated T Cell Subsets** Co-Chairs: Charles G. Drake, MD, PhD *Johns Hopkins University* Giorgio Trinchieri, MD *National Cancer Institute*	**Potomac C**
3:15 pm – 3:30 pm	**CD81- A New Functional Marker for Tumor-induced Regulatory T Cells that Suppress Priming of Tumor-specific Effector T Cells in Reconstituted, Lymphopenic Hosts** Christian H. Poehlein, MD *Earle A. Chiles Research Institute*	
3:30 pm – 3:55 pm	**Regulation of Tumor Immunity by NKT Cell Subsets** Masaki Terabe, PhD *National Cancer Institute*	
3:55 pm – 4:20 pm	**IL-17 Secreting CD8 T Cells - Functional Plasticity and Potential Role in Tumor Immunity** Charles G. Drake, MD, PhD *Johns Hopkins University*	
4:20 pm – 4:45 pm	**Interleukin-1 Role in Human Th17 Responses, Dendritic Cell Activation, and Epithelial Cell Transformation** Giorgio Trinchieri, MD *National Cancer Institute*	

Program Schedule

Thursday, October 29, 2009 *Continued*

3:15 pm – 4:45 pm	**Concurrent Session II: Monoclonal Antibodies / Combinations** Co-Chairs: Glenn Dranoff, MD *Dana-Farber Cancer Institute* Robert L. Ferris, MD, PhD, FACS *University of Pittsburgh Cancer Institute*	**Potomac 2**
3:15 pm – 3:35 pm	**FcγR Mediated Regulation of Adaptive Immunity: Implications for Antibody Therapies** Madhav Dhodapkar, MD *Yale University*	
3:35 pm – 3:50 pm	**Synergy of Radiation and Immune Therapy in Tumor Eradication** Maria Grazia Ruocco, PhD *NYU - School of Medicine, Skirball Institute*	
3:50 pm – 4:10 pm	**Enhancing Cancer Vaccines** Glenn Dranoff, MD *Dana-Farber Cancer Institute*	
4:10 pm – 4:25 pm	**Antitumor Activity of Cytotoxic T-Lymphocyte Antigen-4 Blockade Alone or Combined with Paclitaxel, Etoposide, or Gemcitabine in Murine Models** Maria Jure-Kunkel, PhD *Bristol-Myers Squibb Company*	
4:25 pm – 4:45 pm	**Immune Activation by Cetuximab Involves NK Cells, CTL and DC Against EGFR in Head and Neck Cancer** Robert L. Ferris, MD, PhD, FACS *University of Pittsburgh Cancer Institute*	
4:45 pm – 5:00 pm	**Break**	
5:00 pm – 5:30 pm	**iSBTc Membership Business Meeting**	Potomac C
5:30 pm – 7:00 pm	**Reception with Poster Viewing**	Exhibit Hall D
5:30 pm – 6:30 pm	**Odd Numbered Poster Presentations** *(authors present)*	**Exhibit Hall D**

Program Schedule

Friday, October 30, 2009

7:00 am – 5:00 pm	**Registration Open**	Potomac Registration Desk C , Ballroom Level
10:00 am – 7:00 pm	**Exhibit Hall Open**	Exhibit Hall D, Atrium Level
10:00 am – 7:00 pm	**Poster Hall Open**	Exhibit Hall D, Atrium Level
7:00 am – 8:00 am	**Continental Breakfast**	Exhibit Hall D, Atrium Level
8:00 am – 8:45 am	**Friday Keynote Address:** **T Cell Recognition and the Coming Golden Age of Human Immunology and Immunotherapy** Mark M. Davis, PhD *Stanford University School of Medicine / Howard Hughes Medical Institute*	**Potomac C**
8:45 am – 11:30 am	**Plenary Session: Viral and Cellular Proteomic Targets** Co-Chairs: Lieping Chen, MD, PhD *Johns Hopkins University School of Medicine* Douglas R. Lowy, MD *National Cancer Institute, Center for Cancer Research*	**Potomac C**
8:45 am – 9:15 am	**Current and Future Preventive HPV Vaccines** Douglas R. Lowy, MD *National Cancer Institute, Center for Cancer Research*	
9:15 am – 9:45 am	**Therapeutic Strategies for Human Papillomavirus-Associated Cancers** Karl Münger, PhD *Brigham & Women's Hospital, Harvard Medical School*	
9:45 am – 10:15 am	**Targets of Protective Tumor Immunity** Glenn Dranoff, MD *Dana-Farber Cancer Institute*	
10:15 am – 10:45 am	**Refreshment Break**	Potomac Foyer
10:45 am – 11:00 am	**Definition of the Immunological Properties of Cancer Stem Cells Isolated from Human Glioblastoma** Cristina Maccalli, PhD *San Raffaele Foundation Scientific Institute*	
11:00 am – 11:15 am	**Cell-Free EBV DNA is a Specific Biomarker for Tumor Burden in EBV-Associated Lymphomas** Kimberley Jones *Queensland Institute of Medical Research*	
11:15 am – 11:30 am	**Vinorelbine Induced Angiogenesis and Metastatic Spread in NSCLC and Breast Cancer are Circumvented with Induced Pluripotent Stem Cells Encoded with Anti-GRP78 shRNA, which Induces Apoptosis After a Gene Silencing Bystander Effect** John Giannios, MD, PhD *General State Hospital of Athens*	
11:30 am – 1:00 pm	**Lunch and Exhibits**	Exhibit Hall D
12:00 pm – 1:00 pm	**Even Numbered Poster Presentations** *(authors present)*	**Exhibit Hall D**

Program Schedule

Friday, October 30, 2009 *Continued*

1:00 pm - 2:20 pm	**Presidential Abstract Session** Chair: Bernard A. Fox, PhD *Earle A. Chiles Research Institute*	**Potomac C**
1:00 pm - 1:20 pm	**T Cell Delivery of Interleukin-12 to the Tumor Microenvironment Triggers Potent Endogenous Anti-Tumor Responses** Sid Kerkar, MD *National Cancer Institute, Center for Cancer Research*	
1:20 pm - 1:40 pm	**Transduction of Tumor-Specific T Cells with the Gene Encoding CXCR2 Improves Migration to Tumor and In Vivo AntiTumor Immune Responses** Weiyi Peng, MD, PhD *MD Anderson Cancer Center*	
1:40 pm - 2:00 pm	**Cellular and Molecular Requirements for Rejection of B16 Melanoma in the Setting of Regulatory T Cell Depletion and Homeostatic Proliferation** Justin P. Kline, MD *University of Chicago*	
2:00 pm - 2:20 pm	**Eradication of Established CD19-Postive Leukemia Using a Single Injection of Chimeric Immunoreceptor Modified Lentiviral Transduced T Cells in a Xenograft Nog Mouse Model** David M. Barrett, MD, PhD *Children's Hospital of Philadelphia*	
2:20 pm - 2:45 pm	**Refreshment Break**	Potomac Foyer
2:45 pm - 4:15 pm	**Concurrent Session I: Manipulation of the Tumor Microenvironment** Co-Chairs: James P. Allison, PhD *Memorial Sloan-Kettering Cancer Center* Dmitry I. Gabrilovich, MD, PhD *H. Lee Moffitt Cancer Center and Research Institute*	**Potomac 2**
2:45 pm - 3:15 pm	**Checkpoint Blockade in Tumor Immunotherapy: New Insights and Opportunities** James P. Allison, PhD *Memorial Sloan-Kettering Cancer Center*	
3:15 pm - 3:30 pm	**Manipulation of the Tumor Microenvironment by CTLA-4 Blockade** Padmanee Sharma, MD, PhD *MD Anderson Cancer Center*	
3:30 pm - 4:00 pm	**Myeloid-Derived Suppressor Cells and Tumor Microenvironment** Dmitry I. Gabrilovich, MD, PhD *H. Lee Moffitt Cancer Center and Research Institute*	
4:00 pm - 4:15 pm	**Eosinophilic Granulocytes Modulate Tumor Microenvironment by Oxidizing Damage Associated Molecular Pattern Molecules Derived from Necrotic Tumor Cells** Ramin Lotfi, MD *University of Ulm, Institute for Transfusion Medicine*	
2:45 pm - 4:15 pm	**Concurrent Session II: Targeted Therapeutics and Biological Therapy** Co-Chairs: Richard Jove, PhD *City of Hope Cancer Institute* David H. Munn, MD *Medical College of Georgia*	**Potomac C**
2:45 pm - 3:15 pm	**Targeting Jak-Stat Signaling for Cancer Therapy** Richard Jove, PhD *City of Hope Cancer Institute*	

Program Schedule

Friday, October 30, 2009 *Continued*

**separate registration required*

3:15 pm - 3:45 pm	**Small-Molecule Inhibitors of the IDO Pathway as Immune Modulators** David H. Munn, MD *Medical College of Georgia*	
3:45 pm - 4:00 pm	**Soluble, High Affinity T Cell Receptors as Cancer Therapeutics** Rebecca Ashfield, PhD *Immunocore, Ltd.*	
4:00 pm - 4:15 pm	**Small Molecule Curcumin Analogs Induce Apoptosis in Human Melanoma Cells via STAT3 Inhibition but do not Alter the Cellular Response to Immunotherapeutic Cytokines** Gregory B. Lesinski, PhD *The Ohio State University Comprehensive Cancer Center*	
4:15 pm - 4:30 pm	**Break**	
4:30 pm - 5:00 pm	**2008 Workshop on Cancer and Inflammation Update: Promise for Biological Therapy** Michael T. Lotze, MD *University of Pittsburgh Cancer Institute*	**Potomac C**
5:00 pm - 5:30 pm	**Awards Presentation**	Potomac C
5:30 pm - 7:00 pm	**Presidential Reception**	Exhibit Hall D
5:30 pm - 6:30 pm	**Even Numbered Poster Presentations** *(authors present)*	**Exhibit Hall D**

Saturday, October 31, 2009

7:00 am – 11:00 am	**Registration Open**	Potomac Registration Desk C , Ballroom Level
7:00 am - 8:00 am	**Continental Breakfast**	Potomac Foyer
8:00 am - 10:15 am	**Plenary Session: Adoptive Transfer** Co-Chairs: Carl H. June, MD *University of Pennsylvania* Steven A. Rosenberg, MD, PhD *National Cancer Institute*	**Potomac C**
8:00 am - 8:30 am	**Cell Transfer Therapy for Patients with Metastatic Cancer** Steven A. Rosenberg, MD, PhD *National Cancer Institute*	
8:30 am - 9:00 am	**What are the Functional and Phenotypic Qualities of Therapeutically Successful Anti-Tumor T Cells?** Nicholas P. Restifo, MD *National Cancer Institute*	
9:00 am - 9:15 am	**Programming Tumor-Reactive Effector Memory CD8+ T Cells In Vitro Obivates the Requirement for In Vivo Vaccination** Christopher A. Klebanoff, MD *National Institutes of Health, Center for Cancer Research*	
9:15 am - 9:45 am	**Engineered T Cells for Cancer Therapy** Carl H. June, MD *University of Pennsylvania*	
9:45 am - 10:15 am	**Adoptive Transfer of T Cells Genetically Modified Using the Sleeping Beauty System** Laurence J.N. Cooper, MD *MD Anderson Cancer Center*	
10:15 am	**Annual Meeting Adjourns**	
10:20 am - 12:00 pm	**Hot Topic Symposium: Positive Immunotherapy Clinical Trial Outcomes*** *(see following page for detailed program schedule)*	**Potomac C**

Hot Topic Symposium

Hot Topic Symposium: Positive Immunotherapy Clinical Trial Outcomes

Saturday, October 31, 2009 - 10:20 am - 12:00 pm

Co-Chairs
Thomas F. Gajewski, MD, PhD
University of Chicago

Drew M. Pardoll, MD, PhD
Johns Hopkins University School of Medicine

This cutting-edge session presents exciting new data on recent positive phase III immunotherapy clinical trials. The session features presentations on primary data from these studies and discussion by faculty commentators. Delegates include clinical trialists, pharmaceutical representatives, and basic researchers working in the area of cancer immunology and immunotherapy.

Program Goals

1. Present the latest promising data from cancer immunotherapy clinical trials showing positive clinical outcome data.
2. Review the details of these studies in terms of clinical trial design, scientific endpoints, and specifics of the agent being investigated.
3. Discuss these data with respect to other recent clinical trials that were not successful at meeting designated endpoints.
4. Utilize these exciting new observations as a springboard for considering how to take the therapeutic approach further and move to the next steps in development.

Expected Outcomes

After attending this symposium, participants will be able to:

1. Summarize the most recent advances in the clinical application of cancer immunotherapeutics.
2. Solidify collaborations among the various members of academia and industry to consider how to build upon these data for new clinical trial concepts and initiatives.
3. Understand the key elements to achieving success with immunotherapy clinical trial approaches.
4. Generate new hypotheses generated from these clinical studies for interrogation in laboratory-based preclinical investigations.

Faculty

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Invited Speakers
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MD Anderson Cancer Center

Doug J. Schwartzentruber, MD, FACS
Goshen Center for Cancer Care

David L. Urdal, PhD
Dendreon Corporation

Oral Abstract Presenters
Matteo Vergati, MD
National Cancer Institute, Center for Cancer Research

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

Schedule

Saturday, October 31, 2009

10:20 am – 10:25 am	**Welcome & Introductions** Thomas F. Gajewski, MD, PhD *University of Chicago*
10:25 am – 10:45 am	**Therapeutic Vaccines for Lymphoma: A Tale of Bench to Bedside Translation** Larry W. Kwak, MD, PhD *MD Anderson Cancer Center*
10:45 am – 11:05 am	**A Phase III Multi-Institutional Randomized Study of Immunization with the gp100:209-217 (210M) Peptide Followed by High Dose IL-2 vs. High Dose IL-2 Alone in Patients with Metastatic Melanoma** Doug J. Schwartzentruber, MD, FACS *Goshen Center for Cancer Care*
11:05 am – 11:25 am	**Development History of Sipuleucel-T: Progress of an Active Immunotherapy for Prostate Cancer** David L. Urdal, PhD *Dendreon Corporation*
11:25 am – 11:35 am	**NY-ESO-1 Specific Responses in Patients with Advanced Prostate Cancer Treated with Ipilimumab** Jianda Yuan, MD, PhD *Memorial Sloan-Kettering Cancer Center*
11:35 am – 11:45 am	**Circulating Regulatory T Cell Function and Overall Survival in Metastatic Castration-Resistant Prostate Cancer Patients Treated with Poxviral-based Vaccine** Matteo Vergati, MD *National Cancer Institute, Center for Cancer Research*
11:45 am – 12:00 pm	**Audience Discussion** Moderator: Drew M. Pardoll, MD, PhD *Johns Hopkins School of Medicine*

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Richard V. Smalley, MD Memorial Award Recipient

Isaiah J. Fidler, DVM, PhD
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Keynote Speaker

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In assurance of independence, objectivity and balance, 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 program. 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.

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As part of my US Government supported research at the NCI/NIH, I am an inventor of technology that underlies the L1-based prophylactic virus-like particle (VLP) HPV vaccine. The NIH has licensed the technology for the L1 VLP vaccine to Merck, the manufacturer of Gardasil, and to GlaxoSmithKline, the manufacturer of Cervarix. The NIH receives royalties from both pharmaceutical companies, and US Federal law entitles me to a limited share of these royalties. The L2-based vaccine technology is the subject of a cooperative research and development agreement between the NCI, Johns Hopkins University, and Shantha Biotech.

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Presentation Abstracts – Thursday *(primary authors listed in italics)*

Richard V. Smalley, MD Memorial Lectureship

THE BIOLOGY AND THERAPY OF BRAIN METASTASIS

Isaiah J. Fidler
MD Anderson Cancer Center, Houston, TX

The major cause of death from cancer is metastasis. In the USA, more than 40% of cancer patients develop brain metastasis. The median survival for untreated patients is 1-2 months which may be extended to 6 months with conventional radiotherapy and chemotherapy. The growth and survival of metastases depends on the interaction of tumor cells with host factors in the organ microenvironment.

The brain microenvironment regulates the resistance of tumor cells to systemic therapy. The mechanism for this resistance has been under active investigation. One potential mechanism is the blood-brain barrier (BBB), which protects the normal brain parenchyma from circulating toxic substances. In brain metastases, however, the BBB is permeable. This permeability is due to increased release of vascular endothelial growth factor-vascular permeability factor (VEGF/VPF) by tumor cells growing in the brain, suggesting that the resistance of brain metastases to chemotherapy is mediated by a mechanism independent of the BBB.

Histological examination of clinical specimens of human breast, lung, melanoma, and colon brain metastases demonstrates that the lesions are surrounded and infiltrated by activated astrocytes expressing glial fibrillary acidic protein (GFAP). GFAP-positive astrocytes are also associated with experimental brain metastases produced by lung, brain, melanoma, and colon cancers. We isolated astrocytes from the brain of the "ImmortoMouse" and established the cells in culture.

Astrocytes co-cultured with melanoma, breast cancer, or lung cancer cells protect the tumor cells from all tested chemotherapeutic agents (Taxol, VCR, VGL, 5-FU, Cisplatinum, ADR). Establishment of a gap junction between the astrocytes and tumor cells is required for this chemoprotection. Coculture of tumor cells with other tumor cells or fibroblasts does not protect the cells from chemotherapeutic drugs. Microarray experiments for cross-species hybridization (human tumor cells cocultured with mouse astrocytes or mouse fibroblasts) identified upregulation of several survival genes, including GSTA5, BCL2-L1, TWIST1, and BCL-xL, in tumor cells cocultured with astrocytes, but not with fibroblasts. Once removed from astrocytes, the expression of these genes declined, and the tumor cells lost the resistance to the chemotherapeutic drugs.

These data clearly demonstrate that host cells in the microenvironment influence the biological behavior of tumor cells and reinforce the contention that the organ microenvironment must also be taken into consideration during the design of therapy.

Oral Presentation Abstracts

Presentation Abstracts – Thursday *(primary authors listed in italics)*

Human Immunology

DENDRITIC CELLS AS THERAPEUTIC VACCINES IN CANCER

Jacques Banchereau[1], Hideki Ueno[1], Joseph W. Fay[1,2], A.Karolina Palucka[1]
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Cancer immunotherapy seeks to mobilize a patient's immune system for therapeutic benefit. It can be passive, i.e., transfer of immune effector cells (T cells) or proteins (antibodies); or active, i.e., vaccination. Early clinical trials testing vaccination with ex-vivo generated dendritic cells (DCs) pulsed with tumor antigens provide a proof-of-principle that therapeutic immunity can be elicited.

In our center, between March 1999 and February 2005 sixty four patients with metastatic melanoma were treated with DCs vaccines in the course of four phase I/IIa clinical trials. DCs were generated either from CD34+ hematopoietic progenitors or from blood monocytes. Forty nine (49) HLA-A*0201+ patients received vaccines pulsed with melanoma antigen derived peptides. Twenty one (21) patients received DCs loaded with killed allogeneic tumors regardless of their HLA type. Patients received up to eight vaccinations with antigen-loaded DCs over a maximum of 7 months.

DC vaccinations were safe and tolerable. Nine of 64 patients were alive as of January 2008 from 39-105 months. Median survival was 17 (95% CI 12-26) months. Preliminary analysis demonstrated the induction of long-lived melanoma-antigen specific CD8+T cells in a patient who obtained durable complete regression of in-transit melanoma. DC vaccination expanded circulating MART-1-specific CD8+ T cells. These could be detected after the 4th and 8th DC vaccination as well as 2.5 years after the last vaccination with DCs. The T cells had predominantly effector memory phenotype.

Yet, the clinical benefit measured by regression of established tumors in patients with stage IV cancer has been observed in a fraction of patients only. Two immune parameters appear linked to clinical outcome of the patients: 1) objective clinical response is associated with induction of melanoma-specific effector cells; and 2) all patients display melanoma-specific IL-10 secreting CD4+T cells regulatory/suppressor function that may counteract effector cells. Thus, we need to identify the next generation DC vaccines able to generate large numbers of high avidity effector CD8+ T cells and to overcome regulatory T cells and suppressive environment established by tumors, a major obstacle in metastatic disease. Our pre-clinical studies actually demonstrate that Langerhans cells, a DC subset that is absent in IL-4-generated monocyte-DCs, are superior in their capacity to prime high affinity melanoma-specific CD8+T cells able to kill authentic tumor targets.

Thus, the ultimate ex vivo-generated therapeutic DC vaccine will be heterogeneous and composed of several subsets, each of which will target a specific immune effector. These ex vivo strategies should help to identify the parameters for DC targeting in vivo, which represents the next step in the development of DC-based vaccination. We have already developed a series of constructs based on anti-DC antibodies and vaccine antigens including a series of cancer antigens. Prototype vaccines with viral antigens have already been tested in non-human primates and demonstrated immunogenicity. Pre-clinical studies with cancer vaccines are ongoing. We foresee DC vaccination to be based on in vivo targeting of DCs with fusion proteins containing anti-DCs antibodies, antigens from tumor stem/propagating cells and DC activators.

Presentation Abstracts – Thursday

(primary authors listed in italics)

IDENTIFICATION OF COLON CANCER ASSOCIATED ANTIGENS WHICH WOULD BE KEY THERAPEUTIC TARGETS IN THE PREVENTION OF DISEASE RELAPSE OR PROGRESSION

Elizabeth Broussard[2], Vy Lai[1], Jennifer Childs[1], Doreen Higgins[1], Elizabeth O'Donoghue[1], Kathy Tietje[1], Hailing Lu[1], Mary L. Disis[1]
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Colon cancer is the second leading cause of cancer death in the United States. Recent studies have demonstrated that colon cancer is an immunogenic tumor and that adaptive immunity may play a role in inhibiting disease relapse. Ideally, a vaccine which could boost cellular immunity in patients with colon cancer would allow prevention ofdisease recurrence in the majority of patients. However, there have been few defined immunogenic proteins, implicated in driving the malignant phenotype, that have been identified as vaccine candidates. Our group has shown that overexpressed tumor associated proteins, those that are abundant in the cancer state but expressed at basal levels in normal cells, can be immunogenic. We questioned whether biologically relevant immunogenic proteins could be identified for a vaccine aimed at inhibiting colon cancer relapse or progression. We hypothesized that ideal candidate antigens would be ones that had already been validated as prognostic markers in multivariate analysis. To that end, we performed a directed literature review using a variety of search words e.g. colon cancer, prognostic, biomarker, etc. to identify such proteins in colon cancer. From the over 120 papers identified, we selected a panel of eight proteins based on (1) incidence of expression, (2) independent predictor of poor prognosis, (3) independent predictor of early disease recurrence, and (4) known biologic function in colon cancer pathogenesis. Two of the eight selected proteins had already been shown to be human tumor antigens. The panel includes proteins involved in cell adhesion, migration, and division, angiogenesis, inhibition of apoptosis, and the evasion of immunologic defense mechanisms. Using an algorithm program developed by our group based on widely available web based prediction methods, we identified peptides derived from each candidate protein that were predicted to be high affinity binders across multiple HLA DR alleles; characteristics we have shown to be associated with native epitopes of self tumor antigens. Data will be presented on the immunogenicity of these candidate antigens in patients with colon cancer demonstrating proteins involved in mediating disease progression can serve as immunologic targets.

HARNESSING INVARIANT NKT CELLS TO ABOLISH THE SUPPRESSIVE ACTIVITY OF MYELOID DERIVED SUPPRESSOR CELLS AND RESTORE MELANOMA SPECIFIC IMMUNE RESPONSE

Vincenzo Cerundolo
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We have previously demonstrated that activation of invariant NKT (iNKT) cells results in DC maturation and assists priming of antigen specific T lymphocytes. We have recently extended these results by assessing priming of B lymphocytes and characterizing the parameters controlling the activation of iNKT cells and binding affinity of iNKT cell T Cell Receptor (TCR) to CD1d/lipid complexes. More recently we have described that activation of iNKT cells can abolish the suppressive activity of myeloid derived suppressor cells (MDSC) during viral infection and cancer growth, restoring antigen specific immune responses. These results are clinically relevant as indicate the potential benefits of harnessing iNKT cells in cancer vaccination strategies.

Presentation Abstracts – Thursday

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IDENTIFICATION OF A NOVEL CD8+CD57+ T CELL SUBSET IN HUMAN MELANOMA EXHIBITING AN INCOMPLETELY DIFFERENTIATED CTL PHENOTYPE

Richard Wu, Shujuan L Liu, Yufeng Li, Patrick Hwu, Gregory Lizee, Laszlo Radvanyi
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A number of studies have shown a lack of full CTL differentiation in solid tumors, but the stages of differentiation affected are unclear. Mature CTL have been associated with two markers, CD57 and CD56. However, the association between their expressions on CD8+ tumor-infiltrating lymphocytes (TILs) and which of these markers is associated with mature anti-tumor CTL unknown. In this study, we used multi-color flow cytometry to track CD8+ molecular markers associated with specific stages of CTL differentiation in TILs from over 30 surgically-resected melanoma metastases. Our aim was to determine the differentiation status of CD8+ TILs and the relationship between CD57+ and CD56+ in the CD8+ subset. First, we observed a striking lack of fully mature CTL with the majority of CD8+ T cells having an early effector-memory phenotype (CD27+,CD28+,CD57-,CD56-,Granzyme B/GB+,Perforin-). Second, a significant number of freshly-isolated TILs expressed CD57, but these cells were GB+, but mostly Perforin-, a phenotype consistent with incompletely differentiated CTL. Third, CD56 expression was never found in freshly-isolated CD8+ TILs, but emerged in a subset of GB+ and Perforin+ CD8+ TILs after culture with IL-2/IL-15. CD56 and CD57 were never co-expressed, indicating that CD8+CD57+ and the CD8+CD56+ cells were unique T cell lineages in TILs. Examination of effector function found that it was the CD8+CD56+ subset that contained the most potent anti-tumor CTL population with the highest GB and Perforin expression. In contrast, the CD57+ subset has weak cytolytic, but high cytokine-secreting, function. Moreover, the CD57+ subset did not acquire potent tumor killing activity, even after long-term culture with IL-2. Closer examination of this latter subset also found that a substantial fraction of CD57+ cells expressed high levels CD27 and CD28 and were GB+, but Perforin-. This atypical, incompletely differentiatied, CTL population was not found in peripheral blood of melanoma patients or normal donors, indicating that it is unique to the tumor microenvironment. Functional analysis, however, found that the CD8+CD27+CD28+CD57+ subset was capable of further cell division and differentiation into Perforin+ T cells after TCR triggering and culture with IL-2 suggesting that they are not terminally differentiated, but incompletely differentiated CTL. These results indicate that CD8+CD57+ CTL differentiation in the melanoma microenviroment is impaired with an early EM phenotype incapable of potent anti-tumor killing activity. The appearance of the more cytolytic CD8+CD56+ subset may also be a key factor in the improved anti-tumor function of TILs used for adoptive T cell therapy after extensive expansion ex vivo with IL-2.

A DATA ANALYSIS METHOD FOR IDENTIFYING AUTOANTIBODY BIOMARKERS IN CANCER PATIENTS FOLLOWING IMMUNOTHERAPY

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Immunological monitoring following administration of allogeneic whole tumor cell vaccines is a complex challenge. Frequently, analysis is limited because autologous tumor cells are unavailable. This is particularly problematic in patients with breast and prostate cancer. One approach to overcoming this limitation is to use protein array technology to monitor the immune response generated following vaccination. However, a major limitation to performing these studies is the absence of a software package for identifying candidate antibody markers. Here we describe a method for data analysis of low frequency and diverse autoantibody profiles in complex protein array data. Serum antibody reactivity, hereinafter referred to as protein expression, with 8,217 autoantigens was measured pre- and post-treatment for 11 prostate cancer patients using Invitrogen's ProtoArray Human Protein Microarray. Patients showed diverse protein expression profiles, with the number of "hits" per patient ranging from 37 to 7,585 proteins (average=2,133). Because of this diversity of expression, we applied specialized informatic techniques to identify proteins that showed increased or decreased expression after treatment in multiple patients. First, we filtered the data on a per-treatment per-protein basis to limit the analysis to only those proteins with a credible reading in both pre- and post-treatment samples. Second, for each donor, we identified the proteins with the 50 largest post-treatment increases and the proteins with the 50 largest post-treatment decreases. Third, we consolidated these "Top 50" lists to determine which proteins increased or decreased in multiple patients. There were a total of 418 distinct proteins in the Top 50 post-treatment increase list, with 46 of those expressed by 2 or more donors, and 13 expressed by 3 or more donors. There were a total of 393 distinct proteins in the Top 50 post-treatment decrease list, with 44 of those expressed by 2 or more donors, and 14 expressed by 3 or more donors. Four of 11 patients showed increased expression of 3 different galectin clones, making galectin a candidate for further research.

Presentation Abstracts – Thursday

(primary authors listed in italics)

γδ T CELLS-AGENTS OF TISSUE AND TUMOR IMMUNE SURVEILLANCE

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The community has adopted a powerful and compelling description of immune surveillance of infected tissues, that links the activation of myeloid lineage cells (dendritic cells [DC]; monocytes, and macrophages) of the innate response to the activation of antigen-specific lymphocytes of the adaptive response. The key initiators are inherited pattern recognition receptors, such as Toll-like receptors (TLRs), and TLR agonists are therefore being applied to enhance tumor immunotherapy. However, non-microbial stress, including cell transformation, can induce or otherwise alter the expression of a variety of cell surface molecules, collectively expressed by a broad spectrum of cells but particularly epithelial cells. The receptors for these "stress-antigens" , such as MICA, are frequently found not on myeloid cells, but on "unconventional" or "innate-like" lymphocytes, of which γδ cells are the prototype. Using transgenic mouse systems, we have shown that the induced expression of these stress-antigens is sufficient to initiate a "lymphoid stress-surveillance response" that is much more rapid than conventional T cell responses, and that composes a new component of immunobiology that can limit carcinogenesis. This presentation will describe the key features of lymphoid stress-surveillance, including evidence of its capacity to regulate adaptive antigen-specific responses. In this context, we shall also review our and others' experience of the clinical application of γδ T cells against prostate cancer and other malignancies. Promising indications suggest that this may be a useful clinical strategy, possibly in combination with cancer vaccines.

Enhancing Cancer Vaccines / Combinations

ENHANCING CANCER VACCINES AS MONOTHERAPY AND IN COMBINATION THERAPIES

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We have taken the approach that vaccine efficacy can be enhanced by the use of poxviral vectors expressing transgenes encoding one or more tumor-associated antigens and three T cell costimulatory molecules (B7.1, ICAM-1, LFA-3, designated as TRICOM). A recent 43 center randomized, Phase II, vector-controlled study in patients with metastatic castrate-resistant prostate cancer demonstrated that the PSA-TRICOM vaccine increased patient survival vs vector (p=0.006). A concurrent Phase II study showed similar findings and provided evidence of immunologic and patient characteristics that are associated with clinical benefit. Preclinical data have now demonstrated, and clinical data are emerging, on the benefit of combination therapies employing chemotherapy, hormone therapy, small molecule targeted therapy and local radiation with vaccine. Several of these additional therapies, when used in appropriate dose scheduling regimens, have the ability to enhance host immune function and/or alter the phenotype of tumor cells to render them more susceptible to vaccine-mediated T cell killing.

Oral Presentation Abstracts

Presentation Abstracts – Thursday

(primary authors listed in italics)

DEFINING THE ROLE OF TKIS IN REDUCING IMMUNE SUPPRESSION WHILE IMPROVING T CELL RESPONSIVENESS AND EFFICACY OF IMMUNOTHERAPY FOR THE TREATMENT OF TUMORS

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Immunotherapy for the treatment of metastatic RCC has demonstrated a 15-20% response rate, while in a small minority of patients, treatment with interleukin-2 induced long-term survival. The relatively weak response to immunotherapy by the majority of patients is likely related to tumor-induced suppression of T cell immunity. Indeed, peripheral blood T cells from RCC patients display a diminished capacity to generate a type-1 T cell IFNγ response, which is considered critical for an antitumor immune response. Recently the small molecule receptor tyrosine kinase inhibitor, sunitinib, which targets several receptors in the vascular endothelial growth factor receptor (VEGFR) family, has become first-line treatment for patients with metatstatic RCC (mRCC). This drug has increased the response rate over that observed with cytokine therapy and has been relatively successful at extending patient survival although it is not curative. We have shown that treatment of RCC patients with sunitinib reverses T cell suppression as demonstrated by increased T cell production of IFNγ along with increased frequency of RCC-antigen-specific (EphA2 and MAGE6 peptides) T cells. The improvement in T cell response coincided with a dramatic reduction in the number of myeloid-derived suppressor cells (MDSC) and to a lesser degree in T-regulatory cells numbers. Parallel to the human findings we and others show that sunitinib inhibits MDSC accumulation and improves T cell function (enhanced proliferation and IFNγ production) in mice bearing several tumor types (4T1, RENCA, CT26 and M05B16.OVA, 40 mg/kg). Similar to in vivo treatment with sunitinib, in vitro MDSC depletion using either anti-Gr1-magnetic beads or anti-CD15 beads restored T cell function within murine splenocytes or peripheral blood mononuclear cells of RCC patients, respectively. The mechanisms by which sunitinib inhibit accumulation of MDSC in tumor bearing host is under investigation and recent findings suggest that sunitinib may significantly block the proliferation of the monocytic-MDSC subset (m-MDSC) while possibly promoting apoptosis of the neutrophilic-MDSC subset (n-MDSC), the later of which is the most prevalent subset in most mouse models and RCC patients. Additional studies show that tumor conditioned media (TCM) from RCC lines can not only induce n- MDSC from healthy donor whole blood but can also extend their survival in vitro. While treatment of whole blood with sunitinib in the presence of TCM was unable to prevent the induction of MDSC by TCM, TCM derived from sunitinib (0.1ug/mL)-treated tumor cells was less able to activate n-MDSC.

Additional experiments illustrate that sunitinib can enhance the efficacy of two different immunotherapy approaches in mouse tumor models. Treatment of Balb/c mice bearing established CT26 tumors showed that while intratumoral CpG (ODN1826, 50 ug) and/or pIC (40 ug) and/or i.p. sunitinib 40 mg/kg had minimal effectiveness, the combination of CpG, pIC and sunitinib significantly prolonged survival. This therapeutic effect persisted until treatment was stopped. We observed superior anti-tumor efficacy in mice with established M05 (B16.OVA) melanoma following treatment with sunitinib plus DC/OVA peptide-based vaccination that was paralleled by the greatest degree of specific T cell priming and CD8+ T cell infiltrate. These data support combinational therapies implementing both sunitinib and cancer-specific vaccination.

Presentation Abstracts – Thursday

(primary authors listed in italics)

TYPE-1 DENDRITIC CELL VACCINES IN COMBINATION WITH POLY-ICLC - ASSOCIATION BETWEEN POSITIVE TETRAMER RESPONSE AND 6-MONTH PROGRESSION-FREE SURVIVAL

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Our previous preclinical studies have demonstrated that intramuscular (i.m.) administration of a Toll-like receptor 3 ligand poly-ICLC remarkably enhances induction of type-1 cytotoxic T-lymphocytes (CTLs) and improves therapeutic efficacy of vaccinations against glioma-associated antigen (GAA)-derived CD8+ T cell epitopes. We have developed a phase I/II trial. Human leukocyte Antigen (HLA)-A2+ participants with recurrent malignant glioma received intra-lymph-node injections of type-1 dendritic cells (DCs) loaded with HLA-A2 binding GAA-peptides EphA2 (883-891), IL-13Ralpha2 (345-353:1A9V), YKL-40 (202-211) and GP100 (209-217: 2M) at two-week intervals. Participants also received twice weekly i.m. injections of 20 μg/kg poly-ICLC. Participants who demonstrated positive radiological response or stable disease without major adverse events were allowed to receive booster vaccines. Primary endpoints were assessments of safety and immunological responses. Clinical and radiological responses were also evaluated. To date, 15 participants (8 with glioblastoma multiforme [GBM], 5 with anaplastic astrocytoma [AA] and 2 anaplastic oligodendroglioma [AO]) have received at least 4 vaccinations with no major adverse events. Increased CD8+ cells reactive to EphA2- or IL-13Ralpha2-tetramers were detected in post-vaccine peripheral blood mononuclear cells (PBMC) in 9 of 11 participants evaluated. These patients also demonstrated up-regulation of a chemokine receptor CXCR3 on CD8+ PBMC following vaccines, indicating that the vaccine regimen induced type-1 CTL responses. Five patients achieved progression free at 6 months (2 GBM, 2AA and 1 AO). Among these, 4 patients are currently progression free at 17 (AA), 15 (GBM), 14 (AA) or 9 (AO) months after the first vaccine, and receiving booster vaccines every 3 months. Although the trial enrolled mixed tumor types, Fisher's exact test indicated an association between positive tetramer response and 6-month progression-free survival, suggesting a possible correlation between antigen-specific responses and clinical response. These interim data demonstrate preliminary safety, immunological and clinical activity of poly-ICLC-assisted type-1 DC-based vaccines.

Oral Presentation Abstracts

Presentation Abstracts – Thursday

(primary authors listed in italics)

IDO/IDO2 INHIBITION: A NEW STRATEGY TO DRIVE IMMUNOTHERAPEUTIC RESPONSES IN CANCER BY REVERSING TUMORAL IMMUNE TOLERANCE

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Small molecule inhibitors of the tryptophan catabolic enzymes IDO1 and IDO2 (indoleamine 2,3-dioxygenase-1/2) represent novel immunotherapeutic modalities to treat cancer by reversing immune tolerance. In collaboration with academic, government, and biopharmaceutical groups my laboratory has promoted preclinical and clinical development of IDO inhibitors. With our discovery that the tumor suppressor gene Bin1 supports immune surveillance by restricting IDO1, we went on to identify several classes of small molecule inhibitors of IDO1 and/or IDO2. In several preclinical models of cancer, these agents exert antitumor effects that cooperate with 'immunogenic' chemotherapeutic drugs to elicit tumor regression. Cancer relevance has been furthered with recent evidence that IDO1-deficient animals are resistant to inflammatory carcinogenesis.

Our preclinical studies provided an impetus to evaluate the D stereoisomer of the well-studied IDO inhibitor 1MT (1-methyl-tryptophan). Pharmacological and toxicological analyses revealed D-1MT to be very stable, well distributed, >90% free in blood, orally bioavailable, and essentially non-toxic in animals even at very high doses. 1MT has been widely studied as a racemic mixture of D and L stereoisomers, however, D-1MT was found to be largely responsible for anti-tumor potency and T cell stimulatory activity. The basis for D-1MT activity is complex and not fully understood. Our work indicates that IDO2 is preferentially inhibited by D-1MT with the action of both IDO2 and D-1MT linked to IDO1 action. The biochemical requirements for IDO2 catalytic activity differ from IDO1 and we find that IDO2 is post-transcriptionally regulated by IDO1, pointing toward an IDO1 > IDO2 genetic pathway that may explain the reliance of D-1MT on IDO1.

D-1MT has served as a clinical 'lead' compound in Phase I studies conducted at two U.S. sites. Initial findings suggest that orally administered D-1MT can elicit biological activity and radiological responses at safely tolerated doses. Ongoing studies focus on mechanistic questions about the regulation, function, and role of IDO1 and IDO2 in cancer and clinical responses to D-1MT.

ACKNOWLEDGEMENTS

I express gratitude for long-standing collaborations in this area with Alex Muller (Lankenau Institute for Medical Research), Andy Mellor and David Munn (Medical College of Georgia, USA), Bill Malachowski (Bryn Mawr College, USA), and Rick Metz, Chuck Link, Mario Mautino, and Nick Vahanian (New Link Genetics Corporation, USA). I declare a conflict of interest due to personal financial interests, grant support, and a consultancy role with New Link Genetics Corporation, which is developing D-1MT and other IDO inhibitors to treat cancer and other diseases.

SELECTED REFERENCES

1. Muller et al. Inhibition of indoleamine 2,3-dioxygenase, a target of the cancer suppression gene Bin1, potentiates cancer chemotherapy. Nature Med. 11, 312-319 (2005).
2. Hou et al. Inhibition of IDO in dendritic cells by stereoisomers of 1-methyl-tryptophan correlates with anti-tumor responses. Cancer Res. 67, 792-801 (2007).
3. Metz et al. Novel tryptophan catabolic enzyme IDO2 is the preferred biochemical target of the antitumor IDO inhibitory compound D-1MT. Cancer Res. 67, 7082-7087 (2007).
4. Kumar et al. Indoleamine 2,3-dioxygenase is the anticancer target for a novel series of potent naphthoquinone-based inhibitors. J. Med. Chem. 51, 1706-1718 (2008).
5. Muller et al. Chronic inflammation that facilitates tumor progression creates local immune suppression by inducing indoleamine 2,3-dioxygenase. Proc. Natl. Acad. Sci. USA 105, 17073-17078 (2008).
6. Katz et al. Indoleamine 2,3-dioxygenase in T cell tolerance and tumoral immune escape. Immunol. Rev. 222, 206-221 (2008).

Presentation Abstracts – Thursday

(primary authors listed in italics)

HOW TO EXPLOIT THE IMMUNOGENICITY OF CHEMOTHERAPY OR RADIOTHERAPY TOWARDS A PERSONALIZED THERAPY OF CANCER

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Conventional therapies of cancer rely upon radiotherapy and chemotherapy. Such treatments supposedly mediate their effects via the direct elimination of tumor cells. However, anticancer such therapies can also modulate the host immune system in several ways. Drugs can inhibit immunosuppressive pathways, or activate distinct immune effectors, or sensitize tumor target cells to CTL attack or generate an immunogenic cell death modality, all culminating in eliciting or enhancing anticancer immune responses contributing to the tumoricidal activity of the drug. Indeed, we reported that anthracycline-mediated cell death is immunogenic in tumor bearing hosts through a molecular pathway involving membrane exposure of calreticuline (CRT) by tumor cells1,2,3. CRT is mandatory for the uptake by dendritic cells of dying tumor cells. More generally, anthracyclines, X-Rays and platinum based-therapies mediate a tumoricidal activity relying on CD8+ T cells, CD11c+ DC, IFNg/IFNgR signalling pathway but not IL-12. We addressed which biochemical or metabolic components expressed or released by dying tumor cells could trigger the immune system and participate to the immunogenicity of cell death. While HMGB1/TLR4 are mandatory for the processing of dying bodies by DC and the activity of chemotherapy, other components such as the inflammasome complex NLRP3 recently unravelled will be presented at the meeting. Moreover, other innate components appear to be involved in the immunogenicity of chemotherapy such as NKT and gammadelta T cells. These results delineate a clinically relevant immunoadjuvant pathway triggered by tumor cells. Designing an algorithm of immune parameters dictating the success of chemotherapy becomes possible. The clinical implementations of this work in the management of breast cancer will be detailed.

1. Obeid M, et al. Calreticuline exposure dictates the immunogenicity of anthracyclines. Nat. Med. 2007, Jan 13 (1): 54-61.Epub, ahead offprint Dec 24, 2006
2. Zitvogel L, et al. Cancer in spite of immunosurveillance. Immunosubversion and immunosuppression Nat. Rev. Immunol. 2006 Oct 6, 715-27.
3. Casares N, et al. Caspase-dependent immunogenicity of doxorubicin-induced tumor cell death. J Exp Med. 2005 Dec 19;202(12):1691-701.
4. Apetoh L, et al. TLR4 -dependent contribution of the immune system to the antitumor effects of chemotherapy and radiotherapy. Nat. Med. Aug; 2007.

Regulatory & Activated T Cell Subsets

CD81- A NEW FUNCTIONAL MARKER FOR TUMOR-INDUCED REGULATORY T CELLS THAT SUPPRESS PRIMING OF TUMOR-SPECIFIC EFFECTOR T CELLS IN RECONSTITUTED, LYMPHOPENIC HOSTS

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We reported previously, that B16BL6-D5 (D5) systemic tumor-bearing mice (TBM) harbor CD4+CD25+ tumor-induced regulatory T cells that block vaccination-induced priming of tumor-specific T cells. Elimination of these cells restores priming and therapeutic efficacy in the reconstituted, lymphopenic mouse (RLM) model. Gene micro array analysis of purified TBM CD4+CD25+ T cells identified a number of selectively over-expressed genes, one of them was CD81. CD81 surface expression highly correlates with CD25 expression on CD4 T cells and is selectively up-regulated on TBM CD4+CD25+ T cells. Magnetic depletion of CD81+ TBM T cells prior to reconstitution successfully restored the priming of therapeutic, tumor-specific effector T cells in the RLM model as compared to naïve donor T cells. Here we show, that in vivo treatment with anti-CD81 mAb in TBM donor mice prior to reconstitution of the lymphopenic host reduces the suppressive capacity of tumor-induced regulatory T cells. Interestingly, inhibition of CD81 in RLM hosts reconstituted with un-manipulated TBM T cells does not reduce the suppressive capacity of tumor-induced regulatory T cells. Thus, depletion or in-vivo inhibition of CD81 on donor T cells prior to reconstitution reduces tumor-induced regulatory T cells and restores the priming efficacy of a successful tumor vaccine for donor T cells used in reconstitution. CD81 therefore serves as novel marker to manipulate donor T cells in the RLM model. Clinical trials using vaccination of lymphopenic cancer patients reconstituted with CD25-depleted PBMCs will allow further evaluation of CD81 as an interventional marker for tumor-induced regulatory T cells during the course of treatment. Effective markers for tumor-induced regulatory T cells will be crucial for the development of future interventional immunotherapy protocols to enhance the generation of therapeutic effector T cells by tumor vaccines. (Supported by K22CA127739, RO1CA80964, the Murdock Trust and the Chiles Foundation)

Oral Presentation Abstracts

Presentation Abstracts – Thursday

(primary authors listed in italics)

REGULATION OF TUMOR IMMUNITY BY NKT CELL SUBSETS

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NKT cells, CD1d-restricted T cells, have been shown to play critical roles in the regulation of tumor immunity. We have shown in several mouse tumor models that type I NKT cells expressing a semi-invariant TCR with Vα14Jα18 enhance tumor immunity whereas type II NKT cells suppress tumor immunity when stimulated with agonistic antigen. Furthermore, the two types of NKT cells counteract each other, forming a new immunoregulatory axis. We have reported that type II NKT cells can suppress CD8+ CTL by producing IL-13, which then induces production of TGF-β by CD11b+Gr-1+ cells. We now observed that type II NKT cells also suppress CD4+ T cells suggesting that this axis impacts a broader range of immune responses. Alpha-galactosylceramide (α-GalCer) is a prototypic glycolipid antigen recognized by type I NKT cells. It has been reported that activation of type I NKT cells by α-GalCer and its analogues such as OCH can induce strong anti-tumor immunity despite the fact that they preferentially induce different cytokine profiles in activated type I NKT cells. Although many glycolipids have been tested for their ability to induce anti-tumor responses by activating type I NKT cells, those that induce strong anti-tumor immunity have alpha-linked galactose as a sugar moiety. We tested glycosylceramides with same lipid structure with different sugar moieties and discovered that beta-mannosylceramide (β-ManCer) induces anti-tumor immunity to a similar degree as α-GalCer in a type I NKT cell-dependent manner. However, they induced protection through different mechanisms; α-GalCer-induced protection was completed abrogated in IFN-γ KO mice while β-ManCer-mediated protection partially remained in IFN-γ KO mice. This is the first evidence to our knowledge that a glycosylceramide with a beta-linked sugar moiety can induce significant anti-tumor immunity and the first description of a type I NKT cell agonistic antigen which induces protection by a mechanism(s) different from that induced by α-GalCer. We are currently investigating possible synergy between these two type I NKT cell-agonists to induce protection with the goal of developing more effective cancer immunotherapies.

IL-17 SECRETING CD8 T CELLS - FUNCTIONAL PLASTICITY AND POTENTIAL ROLE IN TUMOR IMMUNITY

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IL-17 secreting CD8 T cells have been described in several settings, but little is known regarding their functional characteristics. While Tc1 cells (CD8 T cells generated under conditions similar to classic CD4 TH1 cells) produce IFN-γ and efficiently kill targets, Tc17 cells (CD8 T cells generated under conditions similar to CD4 Th17 cells) predominantly secrete IL-17 and lack lytic function in vitro. Interestingly, the small numbers of IFN-γ secreting cells generated under Tc17 conditions also lack lytic activity and express a pattern of cell surface proteins nearly identical to IL-17 producing CD8 T cells. As is the case for IL-17 secreting CD4 T cells (TH17), STAT3 is important for Tc17 polarization, both in vitro and in vivo. Adoptive transfer of pure populations of antigen-specific IL-17 secreting Tc17 cells into antigen-bearing hosts resulted in near complete conversion to an IFN-γ secreting phenotype, demonstrating functional plasticity in this CD8 T cell subset. In addition, Tc17 accumulated to a greater extent than Tc1 cells - adoptive transfer of CD8 T cells cultured under Tc17 conditions mitigates tumor outgrowth in vivo. Taken together, these data demonstrate that CD8 T cells, like CD4 T cells, are functionally plastic and that CD8 T cells cultured in the presence of TGF-β and Il-6 may have a role in tumor immunotherapy.

INTERLEUKIN-1 ROLE IN HUMAN TH17 RESPONSES, DENDRITIC CELL ACTIVATION, AND EPITHELIAL CELL TRANSFORMATION

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We have shown that IL-1β production is essential for the induction of Th17 cell differentiation by human Dendritic Cells (DC) activated by the Dectin1 ligand β-glucan. We have now determined that a positive feedback through autocrine IL-1β and activation of NF-κB is necessary for transcription and production of late response cytokines by β-glucan activated human DCs, including the Th17 amplifying cytokine IL-23. Thus, DC-produced IL-1β favors the Th17 response by acting both on the antigen-presenting cells and on the responding CD4+ T cells.

We have identified a similar autocrine positive feedback of IL-1 with activation of NF-κB in epithelial cell transformation. The adaptor MyD88 is required for signaling through all Toll-like receptors except TLR3 and through the IL-1 receptor family. Studies by us and other have shown that expression of MyD88 is required for carcinogenesis in the skin, colon, and liver. In skin carcinogenesis, expression of MyD88 appears to be required for optimal papilloma formation in both radiosensitive hematopoietic cells and radioresistant host cells. In order to investigate whether signaling through MyD88 in keratinocytes was important for tumorigenesis, we transformed in vitro keratinocytes with oncogeneic ras and we found that MyD88 expression in these cells was necessary for production of chemokines, metalloproteases, and hematopoietic growth factors and also for optimal growth when grafted in vivo. It was identified that the lack of expression of MyD88 prevented the expression of the full transformation by blocking the ability of autocrine IL-1α to signal through the interleukin-1 receptor.

Monoclonal Antibodies / Combinations

FCγR MEDIATED REGULATION OF ADAPTIVE IMMUNITY: IMPLICATIONS FOR ANTIBODY THERAPIES

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Monoclonal antibodies (mAbs) have emerged as effective therapeutics that can mediate durable responses against cancer. Anti-tumor properties of MoAbs can be mediated by several mechanisms including direct effects on tumor cells, and induction of innate immune mechanisms such as antibody mediated cytotoxicity (ADCC). However the potential capacity of MoAbs to recruit adaptive immunity has received less attention. In prior studies, we and others have shown that uptake of tumor cells opsonized with anti-tumor MoAbs by dendritic cells (DCs) leads to greatly enhanced cross presentation and induction of T cell immunity. This process requires the engagement of Fc receptors on DCs. The capacity of DCs to induce immunity also depends on their maturation status, which in turn regulates the nature of induced immune responses. DCs are efficient not only at inducing CD4+ T helper and CD8+ killer T cells, but also FOXP3+ regulatory T cells, and IL17 producing inflammatory T cells. DCs express both activating and inhibitory Fcγ receptors and the balance of signaling via these receptors can regulate DC activation. Selective blockade of inhibitory FcγRIIB on human DCs leads to a distinct form of maturation, with the induction of type I interferon response genes and several inflammation associated cytokines and chemokines. This induction of type I interferon response is critical to FcγR mediated DC maturation. FcγR mediated activation also has a clear impact on the capacity of tumor loaded DCs to induce immunity. In particular, such DCs lead to greater activation of IFNγ producing effector T cells, with less concurrent activation of FOXP3+ Tregs. Recent studies of patients treated with anti-tumor mAbs support the concept that these agents may induce adaptive immunity. These preliminary studies also suggest that analysis of immune responses in the tumor bed may be essential to better understand the effects of mAbs on adaptive immunity in vivo. Together these data suggest that targeting tumor antigens selectively to activating FcγRs on human DCs can greatly enhance DC mediated induction of anti-tumor T cell responses. This pathway may also be exploited to enhance the efficacy of anti-tumor monoclonal antibodies in cancer.

Oral Presentation Abstracts

Presentation Abstracts – Thursday

(primary authors listed in italics)

SYNERGY OF RADIATION AND IMMUNE THERAPY IN TUMOR ERADICATION

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We have investigated the mechanism of synergy between anti-CTLA-4 immunotherapy and radiation therapy (RT) in treatment of the 4T1 mouse model of breast carcinoma. We have utilized genetically manipulated mice in which CXCR6 is replaced with GFP and intravital two-photon laser scanning microscopy with CFP expressing tumors to follow the interaction of infiltrating CD8+ T cells with tumor cells. We have found that the blocking anti-CTLA-4 antibody 9H10 increased T cell speed and effectively prevented stable interactions with tumor cells or stromal elements, critical for efficient killing. RT also increased T cell velocity, but not to the same extent as 9H10 treatment. When RT was combined with 9H10 we observed increased T cell arrest in contact with tumor cells and later on elimination of the tumor. It has been shown that CTLA-4 ligation can increase T cell motility and this can overcome a TCR mediated stop signal. We confirmed that 9H10 treatment increased T cell motility on ICAM-1 coated surfaces and 9H10 was dominant over stop signals provided by soluble anti-CD3 antibodies. However, when a 9H10 go signal was subordinated to a stronger stop signal provided by solid phase anti-CD3 T cells did stop. Based upon these observations we suggest that anti-CTLA-4 therapy may impair killing within tumors by suppressing immunological synapse formation, but this effect can be overcome by boosting tumor antigen presentation with RT.

ENHANCING CANCER VACCINES

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Efficacious cancer immunotherapies will likely require combinations of strategies that enhance tumor antigen presentation and antagonize negative immune regulatory circuits. We demonstrated that vaccination with irradiated, autologous melanoma cells engineered to secrete GM-CSF followed by antibody blockade of CTLA-4 accomplishes clinically significant tumor destruction with minimal toxicity in a majority of stage IV metastatic melanoma patients. The extent of tumor necrosis in post-treatment biopsies was linearly related to the natural logarithm of the ratio of infiltrating CD8+ effector T cells to FoxP3+ Tregs, suggesting that further Treg inhibition might increase the frequency of clinical responses. Through an analysis of cytokine deficient mice, we delineated a critical role for GM-CSF in Treg homeostasis. GM-CSF is required for the expression of the phosphatidylserine binding protein MFG-E8 in antigen presenting cells, whereas the uptake of apoptotic cells by phagocyte-derived MFG-E8 maintains peripheral Treg numbers through TGF-β, MHC class II, and CCL22. In wild type mice, MFG-E8 restrains 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. In patients, MFG-E8 is expressed at high levels in melanoma cells and/or tumor associated myeloid elements upon progression to the vertical growth phase. MFG-E8 acts as a melanoma promoter through coordinated avb3 integrin signaling in the tumor microenvironment, thereby stimulating melanoma cell resistance to apoptosis, epithelial-to-mesenchymal transition, invasion, angiogenesis, and immune suppression. Inhibition of MFG-E8 with shRNAs or systemic antibodies enhances the anti-tumor activity of cytotoxic treatments in vitro and in vivo. Together, our results suggest that MFG-E8 blockade might prove therapeutic through both immune-mediated and tumor cell autonomous pathways.

Presentation Abstracts – Thursday

(primary authors listed in italics)

ANTITUMOR ACTIVITY OF CYTOTOXIC T-LYMPHOCYTE ANTIGEN-4 (CTLA-4) BLOCKADE ALONE OR COMBINED WITH PACLITAXEL (PAC), ETOPOSIDE (ETO), OR GEMCITABINE (GEM) IN MURINE MODELS

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To determine if the antitumor activity of an anti-CTLA-4 monoclonal antibody (CTLA-4 mAb) is synergized or inhibited by the addition of chemotherapeutic agents, CTLA-4 mAb was evaluated alone and in combination with Pac, Eto, or Gem in murine tumor models. M109 lung carcinoma, SA1N fibrosarcoma, and CT26 colon carcinoma models were chosen based on different sensitivity to the chemotherapeutic agents and CTLA-4 blockade. All compounds were tested at their optimal dose and schedule. When used in combination, CTLA-4 mAb was initiated one day after the first dose of chemotherapy. Percent tumor growth inhibition and number of days to reach target tumor size were used to evaluate efficacy. Antitumor activity was scored as: complete regression (CR; non-palpable tumor for ≥ 2 assessments) or partial regression (PR; 50% reduction in tumor volume for ≥ 2 assessments). Synergy was defined as antitumor activity significantly superior ($p<0.05$) to the activity of monotherapy with each agent. In the M109 subcutaneous tumor model, which is insensitive to CTLA-4 blockade and modestly sensitive to Pac, Eto, and Gem, borderline synergy was evident with the combination of CTLA-4 mAb and Pac, whereas no effect was observed with Eto. Gem monotherapy did not produce significant M109 antitumor activity; however, combining Gem with CTLA-4 mAb resulted in synergy. In the M109 lung metastasis model, synergy was detected for CTLA-4 mAb combined with Eto, borderline synergy was found with Gem, and Pac did not enhance activity. SA1N fibrosarcoma is sensitive to CTLA-4 blockade and all three chemotherapies. Pac, Eto, and Gem enhanced the activity of CTLA-4 mAb in this model, but synergy was only observed with Eto. CTLA-4 mAb and Pac were ineffective against established CT26 colon carcinoma tumors, but synergistic when the tumor burden was minimal. Both Eto and Gem were effective as single agents in this model and the activity of both was significantly synergized by CTLA-4 mAb. In summary, addition of CTLA-4 mAb to Eto, Gem, or Pac resulted in model-dependent synergistic activities. Synergy was observed regardless of the immunogenicity of the tumor and only when at least one of the therapies was active. All combination regimens were well-tolerated and the chemotherapies did not appear to inhibit CTLA-4 mAb activity in the SA1N tumor model. Of particular importance, synergy was observed in tumors unresponsive to CTLA-4 mAb alone, suggesting that the chemotherapeutic agents might have induced immunogenic cell death. These findings provide support for the evaluation of chemoimmunotherapy combinations in clinical trials.

IMMUNE ACTIVATION BY CETUXIMAB INVOLVES NK CELLS, CTL AND DC AGAINST EGFR IN HEAD AND NECK CANCER PATIENTS

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Immunotherapy with the EGFR-specific mAb cetuximab is clinically effective in 10-20% of patients with squamous cell carcinoma of the head and neck (SCCHN). Little information is available about the mechanism(s) underlying patients' differential clinical response to cetuximab-based immunotherapy, although this information may contribute to optimizing the design of cetuximab-based immunotherapy. Our understanding of these mechanisms would benefit from the characterization of the variables which influence the extent of cell dependent-lysis of SCCHN cells incubated with cetuximab in vitro. The extent of NK cell lysis of SCCHN cells was influenced by the EGFR expression level, cetuximab concentration, and FcγR polymorphism. Effector cells expressing the FcγR IIIa-158 VV allele were significantly ($p<0.0001$) more effective than those expressing FcγR IIIa VF and FF alleles in mediating lysis of SCCHN cells, expressed higher levels of the activation markers CD69 and CD107a, and secreted significantly ($p<0.05$) larger amounts of inflammatory cytokines and chemokines. A murine SCCHN xenograft model was used to distinguish the antitumor contributions of cetuximab and FcγR IIIa expressing NK cells. Since other FcγR genotypes correlate with clinical activity of cetuximab, we also show that cetuximab induces EGFR-specific CTL in treated SCCHN patients, versus cetuximab naïve patients. Enhanced cross-presentation and DC activation were observed in the presence of NK cells and cetuximab. These results support a potential role for immune activation in SCCHN patients and may explain patient variability of cetuximab mediated clinical responses. We will discuss the role of chemoradiotherapy combinations on cetuximab-mediated antitumor immunity, since there regimens are commnoly used in the clinic. Cellular and secreted immune profiles and FcγR genotypes from patients' lymphocytes may provide clinically useful biomarkers of immune activation in cetuximab treated patients.

Oral Presentation Abstracts

Presentation Abstracts – Friday *(primary authors listed in italics)*

Friday Keynote Address

T CELL RECOGNITION AND THE COMING GOLDEN AGE OF HUMAN IMMUNOLOGY AND IMMUNOTHERAPY

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T cell recognition of specific peptide-MHC complexes is one of the key events in most successful immune responses and thus a desired outcome in many immunotherapeutic approaches to cancer. In recent work, we have investigated the basic biochemistry of αβ TCR-mediated recognition in solution and in its cellular context, the immunological synapse. We find a number of remarkable aspects -from the organization of TCRs on specific "protein islands" to the molecular dynamics of their interactions within a synapse. These features are likely to be important in the sensitivity and ligand discriminating qualities of T cell receptors. In other work, we have investigated the T cell repertoire in normal humans and find that naïve T cells to foreign antigens are present in very similar frequencies to those found in the mouse, despite having ~ 100 times more T cells, suggesting that the ligand repertoire is regulated in some way. More remarkably, we find that self-antigen reactive T cells are very abundant in peripheral blood and thus a major function of the immune system must be to keep these from causing autoimmunity. We have also begun to develop metrics of what constitutes a normal human immune response, using influenza vaccination as a model. These later efforts are based on the idea that we need to develop a much more extensive knowledge of human immunology, independent of animal models, in order to correctly navigate the challenges of developing immunotherapies.

Viral and Cellular Proteomic Targets

CURRENT AND FUTURE PREVENTIVE HPV VACCINES

Douglas R. Lowy[1], Patricia M. Day[1], Rhonda Kines[1], Jeffrey N. Roberts[1], Cynthia D. Thompson[1], Susana Pang[1], Christopher B. Buck[1], Richard Roden[2], John T. Schiller[1]
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Cervical infection by a sub-set of human papillomaviruses (HPV), especially HPV16 and HPV18, is the primary cause of virtually all cases of cervical cancer, which worldwide is the second most common cause of cancer deaths in women. HPV is also responsible for a variable proportion of several other cancers, including vulvar, vaginal, penile, anal, and oropharyngeal. Identification of HPV as the causative agent of cervical cancer has led to development of prophylactic HPV vaccines based on the observation that the L1 main structural protein of the HPV virion can self-assemble into empty virus-like particles (VLPs) which contain the conformationally-dependent neutralization epitopes of L1 and can induce high levels of neutralizing antibodies. Two pharmaceutical companies have developed commercial versions of the VLP vaccine. The one manufactured by GlaxoSmithKline (GSK) is a bivalent vaccine composed of VLPs from HPV16 and HPV18, while Merck's is a quadrivalent vaccine composed of VLPs from HPV6 and HPV11 (which together account for about 90% of genital warts) in addition to VLPs from HPV16 and HPV18. The Merck vaccine is licensed in the United States (for females 9-26 years old), the European Union, and other countries, while the GSK vaccine is licensed in Europe and other countries, but has not yet been licensed in the US. Clinical efficacy trials conducted by the companies have shown that, for fully vaccinated women, both vaccines induce almost complete protection against incident persistent genital infection attributable to the HPV types targeted by the vaccine and the associated lesions, including high-grade cervical dysplasia and, for the Merck vaccine, genital warts. Both vaccines also confer some degree of cross-protection against incident infection by closely related HPV types. The type-restricted nature of protection implies that ~30% of potentially cancer-causing infections will not be prevented by the current vaccines. Therefore, it would be beneficial to develop second generation vaccines that, ideally, could protect against a broader spectrum of serious HPV infections, were less expensive to produce and deliver, and required fewer doses. Efforts are underway to develop vaccines that meet at least some of these criteria.

To test new vaccines and other potential primary prevention approaches, as well as to gain insight into the initial steps of HPV infection in vivo, we have developed a tractable mouse cervico-vaginal challenge model in which the female mouse genital tract can be infected with HPV pseudoviruses. The pseudoviruses are composed of authentic HPV capsids that have encapsidated a reporter plasmid that can express a reporter protein (such as luciferase or Red Fluorescent Protein) when infection is successful. Results indicate that the intact genital mucosa is resistant to virion binding and, therefore, to infection. However, disruption of mucosal integrity, by gentle abrasion with a cytobrush or a detergent (nonoxynol-9), leads to the virions efficiently binding first to the basement membrane, rather than to cells, which is followed by infection of the keratinocytes in the genital tract and expression of the reporter protein. The presumed key role of epithelial disruption may also explain the high degree of protection induced by the vaccine, as microtrauma could provide a mechanism for the preferential exudation of systemic neutralizing antibodies at sites of potential infection.

Presentation Abstracts – Friday

(primary authors listed in italics)

THERAPEUTIC STRATEGIES FOR HUMAN PAPILLOMAVIRUS-ASSOCIATED CANCERS

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High-risk human papillmaviruses (HPVs) are associated with a number of cancers, most notably cervical carcinoma. Only two viral oncoproteins, High-risk human papillomaviruses (HPVs) are associated with a number of carcinomas, most notably cervical carcinoma. Only two viral oncoproteins, HPV E6 and E7 are consistently expressed in HPV-associated cancers. The E6 and E7 oncoproteins contribute to initiation and progression of HPV-associated carcinomas and their continued expression is key to the maintenance of the transformed state. Hence, HPV E6 and E7 oncoproteins are predicted to be excellent therapeutic targets. E6 and E7 are small proteins that lack intrinsic enzymatic activities and/or specific DNA binding properties but function by associating with and functionally reprogramming host cellular regulatory networks. Hence, E6 and E7 are considered poorly "druggable" directly by small molecule inhibitors. To overcome these limitations we are using a combination of proteomics, genetic screens and systems biology related approaches to identify signaling pathways that are essential in HPV oncoprotein expressing cells but are dispensable in normal cells.

TARGETS OF PROTECTIVE TUMOR IMMUNITY

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The detailed analysis of patients achieving sustained clinical benefits from irradiated, autologous GM-CSF secreting tumor cell vaccines and CTLA-4 antibody blockade affords a rich opportunity to identify antigens associated with immune-mediated tumor destruction and to delineate mechanisms of therapeutic immunity. We elucidated several of the molecular pathways that underlie this dual targeting of melanoma cells and the tumor vasculature. We established a key role for the NKG2D system, as some long-term responding patients mounted high titer antibodies to MHC class I chain-related protein A (MICA), an NKG2D ligand, and ERp5, a protein disulfide isomerase involved in MICA shedding. The anti-MICA antibodies proved functional, antagonizing the immune suppression triggered by soluble MICA, and stimulating innate and adaptive anti-tumor cytotoxicity. These results have motivated several companies to develop anti-MICA monoclonal antibodies as cancer therapy. Additionally, we uncovered a potent humoral reaction that broadly targeted the angiogenic network within the tumor microenvironment. Treatment-induced antibodies to angiopoietin-1/2 and macrophage inhibitory factor (MIF) blocked the ability of these cytokines to promote angiogenesis in several in vitro assays. These results suggest that immunotherapies might be effectively combined with anti-angiogenic strategies. We also revealed an association between coordinated humoral reactions against multiple intra-cellular proteins and immune-mediated tumor destruction in some patients. Lastly, we found that the immunogenicity of some target antigens is conserved between mice and humans.

Presentation Abstracts – Friday

(primary authors listed in italics)

DEFINITION OF THE IMMUNOLOGICAL PROPERTIES OF CANCER STEM CELLS ISOLATED FROM HUMAN GLIOBLASTOMA

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Background: The main objectives of our study were to characterize the immune profile of cancer stem cells (CSCs) isolated from glioblastoma multiforme (GBM) and to identify potential molecules for immunotherapeutic target for GBM patients.

Methods: We have assessed, by IF and cytofluorimetric or confocal microscopy analysis, the immune profile of 9 GBM CSC lines. Five of them also have parental autologous tumor cell lines in vitro cultured in the presence of fetal bovine serum (FBS). Moreover, we determined the efficiency of these CSC and FBS lines in eliciting T cell-mediated anti-GBM activity by analyzing the cytokine release (IFN-γ and IL-5) or the cytotoxic activity (CD107a mobilization) of in vitro stimulated autologous lymphocytes.

Results: Both GBM CSCs and FBS tumor cells were found to be weakly positive or negative for the expression of MHC class I or class II molecules, respectively. Moreover, we could observed in these cell lines a defective expression of a large array of molecules involved in antigen processing and trafficking (APM). Up-regulation of MHC class I and APM molecules, in contrary to MHC class II molecules, was achieved after IFN-α or -γ treatment of the cells. Along this line, weak or no expression of NKG2D ligands (MICA/B or ULBPs) was detected by most GBM CSC and FBS lines. Interestingly, Survivin, COA-1 and SOX2 were efficiently expressed by both GBM CSC and FBS tumor lines. Moreover, these GBM lines released high level of pro-angiogenic, chemotactic factors (MCP1, VEGF and Ang2) and cytokines (e.g. IL-6, IL-8 and TGF-β).

Transcriptome profile analysis revealed that 469 transcripts, including genes involved in immunological pathways, were differentially expressed between CSC and FBS tumor cell lines, the functional significance of these data is currently being evaluated.

At functional level, we found that in one GBM patient IFN-γ–treated CSCs could elicit T cell-mediated immune response specific for CSCs by stimulation of autologous PBMCs. Conversely, TH2 subset-mediated immune responses were mostly found from 3 others GBM patients. Conclusions: Taken together, these results indicate that, though the antigenic profile of GBM CSCs still needs to be better defined, these cells represent low efficient antigenic source for eliciting T cell-mediated immune responses in some GBM patients.

Presentation Abstracts – Friday

(primary authors listed in italics)

CELL-FREE EBV DNA IS A SPECIFIC BIOMARKER FOR TUMOR BURDEN IN EBV-ASSOCIATED LYMPHOMAS

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The quantity of Epstein-Barr Virus (EBV) DNA in the peripheral blood of EBV-positive lymphoma patients has the potential to be a highly specific biomarker that would assist in the clinical managements of these patients. A number of studies have shown that cell free tumor derived DNA is elevated in cancer patients. The presence of EBV within the malignant cells of EBV-associated cancers and the elevated level of EBV DNA in the blood of these patients makes it a highly attractive biomarker.

Numerous studies have illustrated that EBV DNA is elevated in the blood of certain EBV-positive lymphoma patients and that the viral load is nil at remission but elevated in refractory disease or returns at relapse. However, there is yet to be a detailed study that incorporates serial monitoring with radiographic imaging. Furthermore, EBV viral load analysis remains a controversial topic as the optimal blood compartment to analyse and the most appropriate target gene to amplify is yet to be determined.

We report the results of a multicentre, prospective study on 40 Lymphoma patients. Serial samples were taken at six fixed time points during the course of therapy. The mean age was 45 years (15F: 25M). The tumor load and response was determined by CT (+/- PET). Their plasma, serum and peripheral blood mononuclear cell (PBMC) EBV viral load was determined by Real-Time PCR. In order to establish if a multiple copy gene increases the sensitivity of the PCR, we amplified two genes; the single copy gene BALF5 and the multiple copy gene BAMH1W.

Of the 40 Lymphoma patients, 14 had EBV positive lymphomas and of these 14 paitents,11 had a positive EBV viral load in their plasma (positive viral load defined as above cut off value of 100 copies/ml of plasma). Of those patients that had a detectable viral load prior to treatment there was a tight correlation between the kinetics of the viral load and tumor burden, with viral load decreasing and remaining below threshold in sustained responders and remaining above threshold in patients with refractory disease. The BALF5 and BAMH1W results were analogous, indicating similar sensitivity.

In contrast to the plasma, there was no association between tumor burden and viral load measured from patient PBMC, and no correlation between matched PBMC and plasma samples. This suggests that the cell-free compartment is the optimal one to analyse, with PBMC (and by inference whole blood) overly sensitive due to detection of EBV in benign B cells. Our results indicate that cell-free EBV DNA is a highly sensitive and specific biomarker that reflects tumor load of patients with EBV positive lymphomas.

VINORELBINE INDUCED ANGIOGENESIS AND METASTATIC SPREAD IN NSCLC AND BREAST CANCER ARE CIRCUMVENTED WITH INDUCED PLURIPOTENT STEM CELLS (IPSCS) ENCODED WITH ANTI-GRP78 SHRNA,WHICH INDUCES APOPTOSIS AFTER A GENE SILENCING BYSTANDER EFFECT (GSBE)

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Introduction: Vinorelbine-tartrate in a small number of NSCLC and breast Ca cells induces tumor relapse with enhanced angiogenesis and metastasis by inducing an innate cancer cellular stress response,which enhances the expression of a prosurvival protein GRP78 that blocks cell death or apoptosis increasing growth,and spread of NSCLC and breast Ca due to chemoresistance.We aim to circumvent this with the use of induced pluripotent stem cells (iPSCs) encoded with antisense GRP78 shRNA.

Materials and methods:We take induced pluripotent stem cells(iPSCs),which we infected them with a DNA vector that encoded an RNA molecule of 67 nucleotides. The sequence of this small hairpin RNA (shRNA) is designed to suppress the GRP78 gene. NSCLC and breast Ca cells were obtained from patients,and they were implanted in animal models,which were treated with vinorelbine.After tumor relapse, there was induction of enhanced angiogenesis,and metastasis.These chemoresistant tumor cells were treated with the induced pluripotent stem cells,which were encoded with shRNA against GRP78.

Results: Post-treatment,stem cells encoded with anti-GRP78 shRNA converted dicer into a siRNA molecule generating a long lasting RNAi silecing effect of GRP78,which spreads to adjacent tumor cells inducing a gene silencing bystander effect (GSBE).Capillary growth into the tumors were blocked,while angiogenic growth factors VEGF and bFGF were downregulated. Furthermore,the antiangiogenic enzyme PKG was upregulated inhibiting beta-catenin.Integration of endothelial precursor cells and tumor cells was blocked inhibiting growth of mosaic blood vessels.This leads to inhibition of tumor spread or metastasis,while the existing tumors die from lack of nutrients/oxygen,and a waste disposal pathway.TEM exhibited induction of type I PCD or apoptosis in tumor cells leading to a bystander killing effect.Thus,anti-GRP78 induced pluripotent stem cells (iPSCs) circumvented vinorelbine induced angiogenesis,and metastasis eradicating chemoresistant NSCLC,and breast cancer cells.

Conclusion: Vinorelbine induced angiogenesis,and metastatic spread in NSCLC and breast Ca are circumvented with induced pluripotent stem cells (iPSCs) encoded with anti-GRP78 shRNA,which induces apoptosis after a gene silencing bystander effect (GSBE).

Oral Presentation Abstracts

Presentation Abstracts – Friday *(primary authors listed in italics)*

iSBTc Presidential Session

T CELL DELIVERY OF INTERLEUKIN-12 TO THE TUMOR MICROENVIRONMENT TRIGGERS POTENT ENDOGENOUS ANTI-TUMOR RESPONSES

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IL-12 is a well-studied heterodimeric cytokine playing a central role in bridging both innate and cell mediated immunity. Current treatments with IL-12 have not led to robust anti-tumor responses, but the effect of delivering IL-12 directly into the tumor microenvironment through a systemic approach is unknown. CD8+ pmel-1 T cells specific for the melanoma-associated antigen, glycoprotein 100 (gp100) were transduced with a retroviral vector expressing the p40 and p35 subunits of IL-12 as a single functional molecule and transferred into B16-melanoma-bearing mice following non-myeloablating total body irradiation (5-Gy). Pmel-1 cells transduced with IL-12 caused regression of large established melanomas with 100-fold fewer cells than non-transduced cells without the need for systemic IL-2 or a gp100 encoding vaccine. T cell receptor specificity allowed for delivery of IL-12 directly into the tumor microenvironment. Open repertoire CD8+ cells transduced with IL-12 did not induce tumor regression while cells double transduced with IL-12 and the pmel-1 TCR reproduced the potent anti-tumor response. Using IL-12Rβ2-/- mice, we determined that the therapeutic effect was critically dependent on the host's ability to respond to secreted IL-12 and not due to the enhanced functional quality of transferred cells. These findings reveal a key approach for systemic localization of IL-12 to the tumor site and have major implications for improving future adoptive cell therapies.

TRANSDUCTION OF TUMOR-SPECIFIC T CELLS WITH THE GENE ENCODING CXCR2 IMPROVES MIGRATION TO TUMOR AND IN VIVO ANTITUMOR IMMUNE RESPONSES

Weiyi Peng[1], Yang Ye[1], Brian A Rabinobich[2], Chenwen Liu[1], Yanyan Lou[1], Minying Zhang[1], Greg Lizee[1], Patrick Hwu[1]
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Adoptive T-cell therapy (ACT) is a promising therapeutic modality for cancer. Although tumor regression can be dramatic in some ACT treated patients, other patients do not experience any clinical responses. We hypothesize that one of the rate limiting steps in ACT is the inefficient migration of T-cells to tumors. Chemokines are secreted proteins which are essential for mediating the trafficking of immune cells towards tumor sites. Melanomas specifically express the chemokines CXCL1 and CXCL8. However, we previously demonstrated that tumor-specific T-cells fail to express the receptors for these chemokines, such as CXCR2. Therefore, we hypothesized that migration of T cells to tumors could be improved through the expression of the CXCR2 gene in T cells. In this study, we utilized transgenic Pmel T cells which recognize melanoma antigen gp100, and transduced these cells with our previously modified luciferase gene. In order to visualize luciferase-expressing T-cells within a tumor, a non-pigmented tumor is required. Therefore, we utilized the MC38 tumor model which naturally expresses CXCL1. MC38 was transduced to express gp100 so that the cells could be recognized by Pmel T cells. Mice bearing MC38/gp100 tumor cells treated with CXCR2/luciferase-transduced Pmel T cells showed enhanced tumor regression and survival compared to mice receiving control luciferase transduced Pmel T cells (median tumor size 29.12 vs 61.1mm2 on day 24 after tumor inoculation, respectively, $p < 0.001$). We also observed preferential accumulation of CXCR2-expressing Pmel T cells in the tumor sites of these mice using bioluminescence imaging (Median luciferase output of 191901 vs 83480 photons/s/cm2/sr, respectively on day 6 after T-cell transfer, $p = 0.024$).To confirm these results, we utilized B16 melanoma cells, which naturally express gp100, but do not express CXCL1. A similar enhancement in tumor regression and survival was observed when CXCR2-transduced Pmel T cells were transferred into mice bearing CXCL1-transduced B16 tumors compared to mice treated with control Pmel T cells (median tumor size 27.37 vs 95.76 mm2 on day 18 after tumor inoculation, respectively, $p < 0.001$). Based on these results, we conclude that the introduction of the CXCR2 gene into tumor-specific T cells can enhance their localization to tumors to mediate improved antitumor immune responses. This study may provide an important new avenue in 'personalized cancer therapy' based on the chemokine profile of specific tumors, and plans are underway to translate this strategy to the clinic.

Presentation Abstracts – Friday

(primary authors listed in italics)

CELLULAR AND MOLECULAR REQUIREMENTS FOR REJECTION OF B16 MELANOMA IN THE SETTING OF REGULATORY T CELL DEPLETION AND HOMEOSTATIC PROLIFERATION

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We recently have demonstrated that adoptive transfer of Treg-depleted T cells into lymphopenic mice can result in potent rejection of B16 melanoma in vivo. In the current work, we have investigated the cellular and molecular requirements for tumor rejection by CD25-depleted splenic T cells in $RAG^{-/-}$ or irradiated C57BL/6 recipient mice. Using donor T cells from $CD4^{-/-}$ or $CD8^{-/-}$ mice, we observed that both $CD4^+$ and $CD8^+$ T cells were necessary for B16.SIY rejection. The contribution of conventional $CD4^+$ T cells led us to investigate mechanisms of T cell help. Interestingly, tumor rejection still occurred in irradiated $CD40^{-/-}$ hosts, and also with transfer of $IL2^{-/-}$ CD4+CD25- T cells along with wildtype CD8+ T cells into $RAG2^{-/-}$ hosts. These results indicate that the role of $CD4^+$ T cells is not via provision of CD40L to antigen-presenting cells and not through provision of IL-2 to $CD8^+$ T cells. Consistent with the tremendous expansion of antigen-specific $CD8^+$ T cells observed, we found that host tumor antigen cross-presentation was required, as tumor rejection did not occur in irradiated $Kb^{-/-}$ or $B7.1/B7.2^{-/-}$ mice following CD25-depleted T cell transfer. At the effector phase, host IFN-γ production, and both production of and sensitivity to IFN-γ by adoptively-transferred T cells, were necessary for rejection of B16.SIY. Finally, production of TNF-α and perforin by adoptively-transferred CD25-depleted T cells was dispensable. Collectively, these results support a model in which host tumor antigen cross-presentation and B7 costimulation to $CD8^+$ T cells, along with an undefined role of $CD4^+$ T cells, generate effector cells that depend at least upon IFN-γ for tumor control. The elimination of Tregs and homeostatic proliferation maintain persistent T cell function in the context of a growing tumor. This straightforward adoptive transfer strategy has strong potential for translation to the clinic.

ERADICATION OF ESTABLISHED CD19-POSITIVE LEUKEMIA USING A SINGLE INJECTION OF CHIMERIC IMMUNORECEPTOR MODIFIED LENTIVIRAL TRANSDUCED T CELLS IN A XENOGRAFT NOG MOUSE MODEL

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CD19 is a membrane glycoprotein found on human B lymphocytes at all stages of maturation, and is not lost during malignant transformation to precursor-B cell ALL. T cells engineered with chimeric immunoreceptors (CIR) consisting of an extracellular scFv domain against CD19 fused to the T cell receptor ζ signal transduction domain represent a promising adoptive immunotherapy against leukemias refractory to traditional chemotherapy. Previous studies from our group and others have demonstrated that inclusion of signaling domains from costimulatory molecules such as CD28 or CD137 (4-1BB) can improve the antileukemic efficacy and *in vivo* persistence of CIR-modified T cells. To critically evaluate the anti-tumor efficacy of anti-CD19-targeting CIR that contained various signaling domains alone or in combination we utilized the highly immunodeficient NOG mouse model and an aggressive CD19+ leukemia cell line (Nalm-6) and then treated with primary human CD8+ and CD4+ lymphocytes gene modified to express anti-CD19-targeting CIR with TcR zeta alone, CD28-TcRzeta, CD137-TcRzeta, and CD28- CD137-TcR signalling domains.

NOG mice were injected with $1x10^6$ Nalm-6 on Day 1, a dose that produces 100% engraftment in the bone marrow by Day 7 (95% CI 0.15-1.2% of total bone marrow cells CD19+) with 100% mortality by Day 25 if untreated. T-cells were expanded *ex vivo* using CD3/CD28 beads and subjected to lentiviral gene transfer of various CIRs, and $1x10^7$ T cells were injected on Day 7 (70% CIR +). Mice were followed weekly by quantitative flow cytometric analysis of peripheral blood for CD3, CD4, CD8 and CD19 positive human cells.

Mice treated with T cells engineered to express each of the anti-CD19 CIR demonstrated statistically significant improved survival over control animals, with animals succumbing either to leukemia, or in a construct dependent manner, xenogenic GVHD. Additionally, a hierarchy of survival advantage was observed among the anti-CD19 constructs, with the CD19-CD28-CD137-ζ CIR mediating the most enhanced survival, with 37% of those mice surviving until the end of the study at Day 125.

These data indicate it is possible to eradicate established bone marrow disease with a single injection of lentiviral transduced CIR T cells. Future efforts will focus on evaluating a model where mice that appear cured will be rechallenged with leukemia to evaluate *in vivo* persistence and the surveillance capabilities of these CIR T cells.

Oral Presentation Abstracts

Manipulation of the Tumor Microenvironment

CHECKPOINT BLOCKADE IN TUMOR IMMUNOTHERAPY: NEW INSIGHTS AND OPPORTUNITIES

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It has become apparent that the effectiveness of active immunologic strategies for cancer therapy can be limited by cell intrinsic and extrinsic checkpoints that limit immune responses in order to maximize target destruction and minimize harm to normal tissues. The prototype of cell intrinsic "checkpoints" whose blockade enhances anti-tumor responses is CTLA-4, which has been extensively studied in animal models and shown to be quite effective in achieving complete tumor eradication and long lasting tumor immunity. Over 4,000 patients have been treated with an antibody to human CTLA-4 (Ipilimumab, Medarex and Bristol-Meyers Squibb). Significant responses, including complete remissions, have been observed in about 15% of metastatic melanoma patients, with effects on survival in about 40%. This has led to considerable effort to identify biomarkers that would be useful in determining the impact of CTLA-4 blockade on immune responses in order to identify changes that correlate with clinical responses, as well as to inform combinatorial strategies that might enhance the effectiveness of Ipilimumab.

We have shown in melanoma and prostate cancer models in mice that tumor rejection is closely correlated with an increase in the ratio of both CD4 and CD8 effector cells to FoxP3+ regulatory cells. In chimeric mouse experiments we have shown that the major target of CTLA-4 blockade are effector T cells. Blockade of CTLA-4 exclusively on Treg cells does not result in tumor rejection, while blockade of CTLA-4 on effector cells results in tumor rejection in about 50% of mice. However, blockade on both Treg and Teff is necessary for optimal tumor rejection. In both metastatic melanoma and prostate cancer patients, we have shown that existence of pre-existing immune responses to tumor, as indicated by high titer of serum antibodies to the cancer testis antigen NY-ESO-1, is predictive of clinical benefit of Ipilimumab treatment. In a presurgical bladder cancer trial (Sharma et al.) it was shown that Ipilimumab treatment results in an increase in the frequency of CD4 T cells that express high levels of the CD28/CTLA-4 homolog ICOS. We have shown that this is also true in metastatic melanoma and prostate cancer. In melanoma, sustained elevation of ICOS expression by CD4 T cells appears to correlate with clinical benefit. We have also shown that anti-CTLA-4 treatment is associated with elevation of the frequency of ICOShigh CD4 and CD8 T cells in mouse models, and that the size of transplantable tumors following therapy is inversely correlated with the frequency of ICOShigh T cells. Finally, we have shown that the function of tumor reactive T cells induced by anti-CTLA-4 treatment is impaired in ICOS deficient mice. Together, these data indicate an important role for ICOS in the therapeutic effect of CTLA-4 blockade.

MANIPULATION OF THE TUMOR MICROENVIRONMENT BY CTLA-4 BLOCKADE

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Biomarker studies used with immunotherapeutic strategies in the clinic have typically involved monitoring immunologic changes within the systemic circulation; however, recent data indicate that immunological changes within tumor tissues will be more likely to predict clinical responses. In several murine models, blockade of the T cell inhibitory molecule CTLA-4 has been shown to result in tumor rejection, which correlates with an increase in the ratio of effector to regulatory T cells. More than 4000 cancer patients have now been treated with anti-CTLA-4 antibody on clinical trials, but there have been limited data correlating immunological changes with clinical outcomes for two major reasons: 1) most clinical trials are conducted in the metastatic disease setting which makes it difficult to access tumor tissues for immunological studies and 2) a marker to define effector T cells in cancer patients treated with anti-CTLA-4 therapy has not been established. To obtain such data we conducted the first pre-surgical clinical trial with anti-CTLA-4 antibody in a cohort of patients with localized bladder cancer.

Our trial focused on identifying immunological changes within the tumor microenvironment that correlates with those in the systemic circulation, which can then be used to monitor patients with metastatic disease. We found an increased frequency of CD4 T cells expressing high levels of the CD28/CTLA-4 homolog ICOS as well as a decreased frequency of FOXP3-expressing CD4 T cells within tumor tissues of treated patients. The CD4+ICOShi population contained effector T cells that produced IFN-γ and recognized the cancer-testis antigen NY-ESO-1 expressed on tumor cells. We therefore identified an increase in the ratio of ICOS-expressing effector to FOXP3-expressing regulatory T cells in tumor tissues of treated patients. Real-time PCR analyses also revealed changes in tumor tissues of treated patients consisting of increased T-bet and IFN-γ mRNA. These changes led to an increase in the ratio of the Th1 cytokine IFN-γ to the Th2 cytokine IL-10, which was consistent with an increase in the ratio of effector to regulatory T cells.

Immunologic changes within tumor tissues correlated with changes within peripheral blood in that an increased frequency of CD4+ICOShi T cells was also detectable in the systemic circulation of treated patients. Therefore, we examined peripheral blood samples from metastatic melanoma patients who were treated with anti-CTLA-4 and found that sustained elevation of CD4+ICOShi T cells within the systemic circulation correlated with improved survival. These are the first results to demonstrate changes within the tumor microenvironment as a result of anti-CTLA-4 therapy that can be correlated with changes within the systemic circulation, which may potentially correlate with clinical benefit.

Presentation Abstracts – Friday

(primary authors listed in italics)

MYELOID-DERIVED SUPPRESSOR CELLS AND TUMOR MICROENVIRONMENT

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Myeloid-derived suppressor cells (MDSC) represent an intrinsic part of myeloid cell lineage and comprised of myeloid progenitors and precursors of myeloid cells. In healthy host upon generation in bone marrow immature myeloid cells (IMC) quickly differentiate into mature granulocytes, macrophages, or dendritic cells. In cancer increased production of IMC is associated with partial block of their differentiation and most importantly pathological activation of these cells manifests in up-regulation of arginase, inducible nitric oxide synthase (iNOS) and NO production, increased level of reactive oxygen species (ROS). This results in expansion of IMC with immune suppressive activity. Accumulation of MDSC was detected in practically all mouse tumor models and in patients with different types of cancer. In mice, MDSCs are characterized by the co-expression of myeloid lineage differentiation antigen Gr1 and CD11b. In humans, MDSC are currently defined as CD14-CD11b+ cells or more narrowly as cells that express the common myeloid marker CD33 but lack the expression of markers of mature myeloid and lymphoid cells and the MHC class II molecule HLA-DR. It appears that MDSC in peripheral lymphoid organs and in tumor sites utilize different mechanisms of T-cell suppression. In peripheral lymphoid organs MDSC have high level of ROS and relatively low levels of NO and arginase. MDSC cause antigen-specific tolerance of CD8+ T cells. We tried to identify the mechanism of MDSC mediated T-cell tolerance. Using double TCR CD8+ T cells we have demonstrated that MDSC induced tolerance against only the peptide, which was directly presented by MDSC. This effect was associated with nitration of the molecules on the surface of CD8+ T cells localized to the site of physical interaction between MDSC and T cells. After incubation with MDSC only nitrotyrosine (NT) positive CD8+ T cells demonstrated profound non-responsiveness to the specific peptide, whereas NT negative CD8+ T cells responded normally to that stimulation. Incubation of antigen-specific CD8+ T cells with peptide-loaded MDSC did not induce signaling downstream of TCR. However, it prevented subsequent signaling from peptide-loaded dendritic cells. MDSC caused dissociation between TCR and CD3ζ molecules disrupting TCR complexes on T cells. In contrast, MDSC from tumor site have relatively low ROS production but high level of NO and arginase. As a result MDSC inhibited T-cell function in antigen independent fashion. We have demonstrated that in tumor microenvironment splenic MDSC rapidly up-regulate iNOS and arginase and are rapidly converted to antigen non-specific suppressor cells. MDSC quickly differentiated into tumor-associated macrophages with potent T-cell suppressive activity. The potential mechanisms of this phenomenon are discussed.

EOSINOPHILIC GRANULOCYTES MODULATE TUMOR MICROENVIRONMENT BY OXIDIZING DAMAGE ASSOCIATED MOLECULAR PATTERN MOLECULES (DAMPS) DERIVED FROM NECROTIC TUMOR CELLS

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Eosinophilic granulocytes (Eos) are found at increased numbers within necrotic areas of tumors. Necrotic death is associated with release of Damage Associated Molecular Pattern Molecules (DAMPs) which influence tumor microenvironment enhancing proliferation of adjacent cells, angiogenesis and inflammation. We show that necrotic material from tumor or mesenchymal stem cell lysates containing DAMPs induce Eos degranulation (release of major basic protein and eosinophil peroxidase) and enhance Eos oxidative burst while the stimulatory capacity of cell lysates is significantly diminished following oxidation. High mobility group box 1 (HMGB1), a prototypic DAMP, released following necrosis but not apoptosis induced a similar effect on Eos. Additionally, we demonstrate that HMGB1 enhances Eos survival and acts as a chemoattractant. Consistently, we show that Eos express an HMGB1 receptor, the receptor for advanced glycation end product (RAGE), and that anti-RAGE could diminish the HMGB1-mediated effects. Of all tested biologic activities, Eos respond most sensitively to the presence of necrotic material including HMGB1 with generation of oxidants. We postulate that Eos 'sense' stressed cells, migrating to and responding to areas of tissue injury/necrosis. Oxidation of cell lysates reduces their biologic activity when compared with native lysates. We postulate that Eos-associated modulation of immunity within tumor and other damaged tissues may be primarily by promoting oxidative degradation of DAMPs. Novel therapeutic strategies may be considered by advancing oxidative denaturation of released necrotic material using Eos or other aerobic strategies.

Oral Presentation Abstracts

Presentation Abstracts – Friday *(primary authors listed in italics)*

Targeted Therapeutics and Biological Therapy

TARGETING JAK-STAT SIGNALING FOR CANCER THERAPY

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The Signal Transducer and Activator of Transcription (STAT) family of proteins comprise transcription factors that mediate cytokine and growth factor responses. Persistent activation of one STAT family member, Stat3, is oncogenic and prevalent in a wide variety of human cancers, including solid and hematologic tumors. Stat3 activation promotes the growth and survival of human cancer cells by inducing constitutive expression of genes that encode anti-apoptotic proteins, cell cycle regulators and angiogenic factors. Moreover, Stat3 has an important role in autocrine and paracrine cytokine loops driving many human cancers. Stat3 activation by cytokines such as interleukin-6 (IL-6) is mediated through the Janus family kinases (JAK) including Jak2. These observations provide a molecular basis for persistent Stat3 activation in solid tumors, and highlights Jak2 kinase as a potential target for cancer therapy. Using novel small-molecule Jak2 inhibitors, we demonstrate a predominant role of Jak2 in mediating basal and cytokine-induced Stat3 activation in solid human tumor cell lines. Blockade of Stat3 activation with Jak2 inhibitors is associated with abrogation of Stat3 nuclear translocation and tumorigenesis. In IL-6 expressing tumor cells, Jak2 is a key regulator of IL-6 autocrine signaling, thereby promoting the growth and survival of these cells. Treatment of tumor-bearing mice with Jak2 inhibitor suppresses the growth of human prostate, ovarian, and breast cancer xenografts harboring Stat3 activity. Our data support a central role of Jak2 in Stat3 dependent oncogenesis, and provide a rationale for targeting Jak2 in human solid tumors with persistent Stat3 activity.

SMALL-MOLECULE INHIBITORS OF THE IDO PATHWAY AS IMMUNE MODULATORS

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Established tumors create a state of functional unresponsiveness (tolerance) toward their own antigens that acts as a fundamental impediment to cancer immunotherapy. Indoleamine 2,3-dioxygenase (IDO) is an endogenous molecular mechanism of acquired peripheral tolerance. IDO has been shown to contribute to acquired tolerance in pregnancy, mucosal tolerance, and induced tolerance to tissue transplants. In cancer, IDO can be expressed by tumor cells, but even more importantly it can also be expressed by immunoregulatory cells of the host immune system, such as plasmacytoid dendritic cells (pDCs). In preclinical models, IDO expression by DCs can suppress effector T cell activation, and can drive de novo differentiation of Foxp3+ Tregs from CD4+ T cells. IDO can also directly activate pre-existing mature Tregs for markedly increased suppressor activity. In addition to promoting Treg differentiation and activation, IDO and its downstream signaling pathway GCN2 kinase can act to block differentiation along the pro-inflammatory TH17 pathway. IDO may thus help stabilize the suppressive Treg phenotype and suppress proinflammatory T-helper cell differentiation. Orally-bioavailable small-molecule IDO-inhibitor drugs are in development, and the first of these (1-methyl-D-tryptophan, D-1MT) is in Phase I clinical trials. In preclinical models, 1MT shows synergy when combined with a number of conventional chemotherapeutic agents. 1MT also shows synergy with anti-tumor vaccines; and the combination of 1MT plus vaccine allows clonal expansion and effector maturation of tumor-specific T cells, even in mice with large established tumors. Vaccination plus 1MT can also drive reversal of Treg-mediated suppression, and promote re-programming of pre-existing Foxp3+ Tregs into polyfunctional T-helper cells in tumor-draining lymph nodes. Thus, IDO appears positioned at the intersection of several key regulatory pathways that contribute to tumor-induced immune suppression. Small-molecule IDO-inhibitor drugs may thus help overcome the state of functional immunologic tolerance toward tumors, particularly when combined with conventional cytotoxic chemotherapeutic agents and active anti-tumor immunization.

Presentation Abstracts – Friday

(primary authors listed in italics)

SOLUBLE, HIGH AFFINITY T CELL RECEPTORS AS CANCER THERAPEUTICS

Rebecca Ashfield[1], Katherine Adams[1], Giovanna Bossi[1], Daniel Williams[1], Rebecca Dennis[1], Samantha Paston[1], Jane Harper[1], Namir Hassan[1], Emmet McCormack[2], Bent Jakobsen[1]
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T cell Receptors (TCRs) are able to recognise cancer-associated peptide epitopes presented on the surface of tumour cells by Class I HLA molecules. Many cancer patients, however, are unable to mount an effective anti-tumour T cell response, either as a result of low T cell avidity or by the induction of tumour escape mechanisms resulting in T cell inhibition or anergy. In order to generate potent tumour targeting agents, we have engineered soluble T cell Receptors (sTCRs) which retain the native αβ structure, and used phage display technology to produce high affinity variants with pico-molar affinities. Specifically, high affinity sTCRs have been generated which recognise three cancer-associated epitopes: NY-ESO157-165, Melan-A/MART 126-35 and gp100 280-288, all presented by HLA-A2. The sTCRs specifically target to HLA-A2+, antigen+ melanoma cells in vitro and in vivo.

With the aim of generating therapeutic proteins for cancer, we fused high affinity sTCR molecules to a scFv antibody domain specific for CD3. These fusion proteins simultaneously target HLA-peptide complexes on the surface of tumour cells, and activate adjacent CD3+ T cells regardless of their antigen specificity. Such 're-directed' T cells kill tumour cells expressing low levels of target antigen (<100 molecules per cell). We have demonstrated that sTCR-antiCD3 fusions a) kill melanoma cells expressing physiological levels of epitope in vitro, b) are more potent than a T cell clone, and c) demonstrate anti-tumour activity in vivo. We are currently planning to carry out a clinical trial in cancer patients with a sTCR-antiCD3 fusion protein.

SMALL MOLECULE CURCUMIN ANALOGS INDUCE APOPTOSIS IN HUMAN MELANOMA CELLS VIA STAT3 INHIBITION BUT DO NOT ALTER THE CELLULAR RESPONSE TO IMMUNOTHERAPEUTIC CYTOKINES

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Curcumin has anti-tumor activity in numerous experimental cancer models and has been shown to inhibit a variety of cellular targets including STAT3. However, recent studies from our laboratory indicated that curcumin adversely affects the responsiveness of immune cells to cytokines with anti-tumor properties (IFNα, IFNγ, IL-2, IL-12). To overcome this lack of selectivity, we synthesized and evaluated curcumin analogs predicted to target STAT3 via molecular modeling and cell-based assays. It was hypothesized that these curcumin analogs could serve as potent, STAT3 specific inhibitors that induce melanoma cell apoptosis but do not antagonize the action of interferons or interleukins. FLLL32 is a small molecule inhibitor of STAT3 phosphorylation and dimerization that approximates curcumin when locked into its diketone tautomeric form. Time course and dose-response studies revealed that FLLL32 reduced phosphorylated STAT3 (pSTAT3), STAT3-DNA binding and induced apoptosis at micromolar amounts in multiple human metastatic, vertical and radial growth phase melanoma celll lines (IC50 range=1.3-2.1μM at 48hr). FLLL32 induced processing of caspase-3, -8 and -9 proteins, reduced cyclin D1 (a STAT3-regulated protein) and decreased mitochondrial membrane potential. Cell death induced by FLLL32 was caspase-dependent as the pan-caspase inhibitor (Z-VAD-FMK) abrogated the pro-apoptotic effects of this compound. FLLL32 was specific in that it did not interact with STAT1 protein. Pre-treatment of melanoma cells with FLLL32 did not inhibit IFN γ-induced pSTAT1 or downstream STAT1-mediated gene expression (interferon-regulatory factor-1) as determined by Real Time PCR. Since STAT3 function in immune cells can promote tolerance to tumors, we evaluated whether FLLL32 would affect the responsiveness of peripheral blood mononuclear cells (PBMCs) to stimulation with cytokines that play a role in tumor progression (IL-6) or immunosurveillance (IFNγ, IL-2). Pre-treatment with FLLL32 eliminated basal and IL 6-induced pSTAT3 in PBMCs from healthy donors. In contrast, FLLL32 pre-treatment did not adversely affect IFNγ-induced pSTAT1 or IRF1 transcription in PBMCs. Similarly, FLLL32 pre-treatment did not adversely affect IL-2 induced STAT5 phosphorylation. Importantly, treatment of PBMCs or NK cells with FLLL32 did not decrease viability or granzyme b and IFN-γ production when cultured with K562 targets. These data support further investigation of FLLL32 as a lead compound for STAT3 inhibition and therapy of melanoma and other malignancies.

Oral Presentation Abstracts

Presentation Abstracts – Saturday *(primary authors listed in italics)*

Adoptive Transfer

CELL TRANSFER THERAPY FOR PATIENTS WITH METASTATIC CANCER

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Adoptive cell transfer (ACT) therapy refers to a treatment approach in which lymphocytes with anti-tumor activity are transferred to the tumor bearing host with the aim of mediating tumor regression. ACT represents the best available treatment for patients with metastatic melanoma and can mediate objective responses (RECIST criteria) in up to 72% of patients.

We have conducted a series of three consecutive clinical protocols in patients with metastatic melanoma utilizing autologous tumor infiltrating lymphocytes (TIL) that are grown ex vivo from resected lesions and reinfused into the autologous patient along with interleukin-2 (IL-2). In the first of these trials, 43 patients were treated with autologous TIL transfer following a non-myeloablative chemotherapy consisting of cyclophosphamide (60mg/kg for two days) and fludarabine (25 mg/m2 for five days). In the second and third clinical trials this chemotherapy was given in conjunction with either 200cGy or 1200 cGy. The objective response rates (by RECIST criteria) in these three trials were 49%, 52% and 72%. In the latter trial, seven patients (28%) were complete responders. Durable responses have been seen at all sites including lung, liver, brain, bone, lymph nodes and subcutaneous tissues. Twelve of the 13 complete responses in the three trials are ongoing between 21 and 26 months. Forty-two of the 53 responding patients had received prior IL-2 and many had received prior chemotherapy as well. The actuarial three year survival for patients receiving the chemoradiation preparative regimen was 44%. Thus T cell based immunotherapy is capable of mediating the regression of large vascularized invasive metastatic melanoma in humans. The widely held belief that immunotherapy can only affect minimal disease in the adjuvant setting is certainly not the case.

There is a significant association between persistence of the transferred cells in the circulation at one month and the likelihood of achieving a clinical response ($p<0.001$). Cells with longer telomeres ($p<0.01$) and with higher percentage of cells expressing CD27 ($p<0.001$) are also associated with objective clinical responses.

Some patients do not have easily harvestable lesions to provide a source for the TIL. In addition, TIL with anti-tumor activity can only reproducibly be obtained from patients with melanoma and not from other cancers. We have thus developed new approaches to ACT that involve the transduction of anti-tumor T cell receptors into autologous circulating lymphocytes. This genetic engineering provides normal circulating peripheral lymphocytes with anti-tumor activity that is often as strong or stronger than TIL obtained by conventional methods. In current clinical trials of the adoptive transfer of these gene modified cells, objective response rates are approximately 30%. We have now generated retroviruses that encode either conventional or chimeric T cell receptors that can recognize antigens such as NY-ESO-1, CEA and CD19 that are present on common cancers. Clinical trials using the adoptive transfer of these genetically engineered cells are now underway.

In summary, adoptive cell therapy can mediate the complete regression of metastatic melanomas in heavily pretreated patients. The ability to genetically engineer normal circulating lymphocytes to acquire anti-tumor properties provides an opportunity to extend this approach to patients with common epithelial tumors.

Presentation Abstracts – Saturday

(primary authors listed in italics)

WHAT ARE THE FUNCTIONAL AND PHENOTYPIC QUALITIES OF THERAPEUTICALLY SUCCESSFUL ANTI-TUMOR T CELLS?

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We have previously described how vaccination and lymphodepletion can augment the therapeutic effectiveness of naturally occurring or genetically engineered tumor-specific T cells upon adoptive transfer. Immunoablation using chemotherapy or/and total body irradiation enhances adoptive immunotherapy by liberating Toll-like receptor agonists from commensal gut bacteria and by eliminating T regulatory cells, myeloid-derived suppressor cells and "sinks" for homeostatic cytokines.

Our current work is focused on elucidating the functional and phenotypic qualities of adoptively transferred T cells that are associated with tumor rejection. We have observed that the state of differentiation of anti-tumor T cells prior to their adoptive transfer is critically important for their effectiveness. Until recently, it was thought that the optimal anti-tumor CD8+ T cells would be those that were highly cytolytic and capable of releasing large amounts of IFN-gamma upon encounter with tumor cell targets when tested prior to adoptive transfer. However, it seems clear now that cytotoxic T cells represent a terminal, pro-apoptotic differentiation state of CD8+ T cells. Paradoxically, the acquisition of full effector function in vitro impairs the in vivo antitumor efficacy of adoptively transferred CD8+ T cells (Gattinoni, J Clin Invest, 2005). Central memory CD8+ T cells (eg those grown in IL-15) confer superior antitumor immunity compared with effector memory T cells expanded using IL-2 (Klebanoff, Proc Natl Acad Sci, 2004 & 2005). Furthermore, naïve cells or CD8+ T memory stem cells activated in the presence of IL-21 or Wnt, which are even less mature, are still more effective than central memory cells (Hinrichs, Blood, 2008; Gattinoni, Nat Med, 2009). Thus, the state of maturation of CD8+ T cells before adoptive transfer is inversely correlated with their effectiveness in vivo: "Younger" T cells are better. It is important to note that undifferentiated T cells must be capable of maturing into fully functional T cells after transfer. This in vivo activation and differentiation of early CD8+ T cell subsets can be enhanced by homeostatic cytokines and encounter with the cognate antigen (Gattinoni, Nat Rev Immunol, 2006).

T cell differentiation is also critically important for anti-tumor CD4+ T cells, which can be robustly polarized in vitro prior to transfer. This polarization can skew their expression of transcription factors, cytokines, chemokines and cell surface markers. CD4+ T cells that are polarized to produce IL-17 (Th17 cells) have increased effectiveness in anti-tumor models when compared with other T cell subsets tested (Muranski, Blood, 2008). Importantly, these Th17 cells evolve after transfer into an immunoablated host into cells that are capable of producing IFN-gamma. Thus, the differentiation states of anti-tumor CD8+ and CD4+ T cells are critical determinants of their effectiveness in vivo. These studies are consistent with data from human studies that indicate that "young"/undifferentiated T cells have increased effectiveness in the adoptive immunotherapy of melanoma and point the way towards the use of appropriately polarized CD4+ T cells in patients with cancer.

PROGRAMMING TUMOR-REACTIVE EFFECTOR MEMORY CD8+ T CELLS IN VITRO OBIVATES THE REQUIREMENT FOR IN VIVO VACCINATION

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CD8+ T cells can undergo programmed activation and expansion in response to a short TCR stimulus, but whether in vitro programming can substitute for an in vivo antigen (Ag) stimulation remains unknown. We show that self/tumor-reactive effector memory CD8+ T cells (TEM) programmed in vitro either with peptide-pulsed APCs or plate bound anti-CD3/anti-CD28 embark on a highly stereotyped response of in vivo clonal expansion and tumor destruction nearly identical to that of vaccine-stimulated TEM cells. The programmed response was associated with an interval of Ag-independent IFN-gamma release that facilitated the dynamic expression of the major histocompatibility complex (MHC) class I restriction element H-2Db on responding tumor cells, leading to recognition and subsequent tumor lysis. Further, the transfer of programmed cells genetically deficient in IFN-gamma or a delay in the transfer of programmed cells more than 24h after stimulation entirely abrogated the benefit of in vitro programming. These findings extend the phenomenon of a programmable effector response in CD8+ T cells to a therapeutic intervention relevant to current adoptive cell transfer protocols.

Oral Presentation Abstracts

Presentation Abstracts – Saturday

(primary authors listed in italics)

ENGINEERED T CELLS FOR CANCER THERAPY

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While there are exciting examples of successful clinical strategies to mobilize the immune system to attack cancer cells, overall the results have been disappointing in randomized clinical trials. We are exploring the use of engineered T cells bearing chimeric receptors and strategies to augment their antitumor efficacy in adoptive transfer settings. The surface membrane glycoprotein mesothelin is a promising target for the immunotherapy of mesothelioma, ovarian, and pancreatic tumors due to the uniform overexpression of mesothelin and the benign phenotype of mesothelin null mice. We hypothesize that previous trials of adoptive immunotherapy for cancer that have used CTL have failed due to poor trafficking to sites of tumor, and insufficient effector functions to self antigens. Our preclinical data indicates that use of lentiviral engineered T cells with chimeric receptors that incorporate a 'tumor resistance genotype' should have improved function for cancer immunotherapy. We have tested mesothelin redirected T cells in humanized mouse models bearing tumor xenografts. The T cells are able to eradicate large, well established tumors at an in vivo E:T ratio of at least 1:70. As a complementary strategy, we have engineered artificial antigen presenting cells (aAPC) to express ligands for either CD28 or ICOS. These aAPC appear to be useful to reprogram T cells, and increase the antitumor efficacy of adoptively transferred T cells. In ongoing clinical trials testing adoptive transfer of T cells after retroviral or lentiviral gene transfer we find that 1) the T cells engraft and persist at high levels for 10 years or more, indicating that central memory T cells with "stem cell like qualities" can be transduced, and 2) rectal mucosal biopsy studies taken from patients after adoptive transfer indicate that the T cells traffic with high efficiency to IEL. Finally, our preclinical studies with B. Jakobsen testing TCRs engineered for high affinity indicate the ability to "convert" polyclonal T cells to monoclonal T cells with potent redirected specificity for surrogate antigens, suggesting that tumor antigens for which substantial repertoire limitations in the natural pool of available T cells can be targeted with the adoptive transfer of engineered T cells.

References

1. Carpenito C, et al. 2009. Control of large established tumor xenografts with genetically retargeted human T cells containing CD28 and CD137 domains. Proc Natl Acad Sci U S A 106:3360.
2 Milone MC, et al 2009. Chimeric receptors containing CD137 signal transduction domains mediate enhanced survival of T cells and increased antileukemic efficacy in vivo. Mol Ther.
3 Wang GP, et al. 2009. Analysis of Lentiviral Vector Integration in HIV+ Study Subjects Receiving Autologous Infusions of Gene Modified CD4+ T Cells. Mol. Ther.
4 Perez EE, et al. 2008. Establishment of HIV Resistance in CD4(+) T cells by Genome Editing using Zinc Finger Nucleases. Nature Biotechnology 26:808.
5 Varela Rohena A, et al. 2008. Control of HIV immune escape by CD8 T cells expressing enhanced T cell receptor. Nature Med. 14:1390.
6 June,C.H. 2007. Principles of adoptive T cell cancer therapy. J Clin Invest 117:1204.

Presentation Abstracts – Saturday

(primary authors listed in italics)

ADOPTIVE TRANSFER OF T CELLS GENETICALLY MODIFIED USING THE SLEEPING BEAUTY SYSTEM

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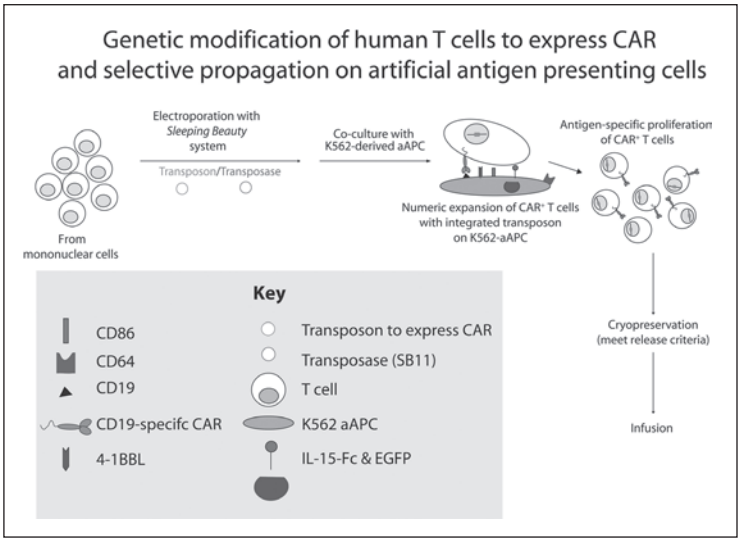
Clinical trials have demonstrated some therapeutic successes after infusing T cells genetically modified to be tumor-specific upon expression of a chimeric antigen receptor (CAR). The therapeutic potential of infused CAR+ T cells is tied to their in vivo persistence and ability to be fully activated upon binding tumor-associated cell-surface antigen, independent of MHC, within the malignant microenvironment. Thus, not only must gene transfer introduce a desired immunoreceptor, but T cells should be manipulated ex vivo to maintain their replicative potential and effector functions. To fulfill the promise of T cells as biologic therapies, iterative changes are needed to genetically modify and then re-modify T cells as we progress from the bench to the bedside and back again. We have used the Sleeping Beauty (SB) transposon/transposase system as a facile approach to genetically modifying T cells, derived from peripheral and neonatal blood, to introduce one or more CARs as well as other immunomodulatory and imaging transgenes. When SB transposition of T cells is combined with their selected propagation on artificial antigen presenting cells (aAPC), generated from K562 (in collaboration with Dr. Carl June), we can reliably produce CAR+ T cells that have desired specificity, demonstrate sustained proliferation, and can function as effector cells within tumor microenvironments. This technology can be translated into clinical practice using both off-the-shelf DNA plasmids and aAPC as defined by standard operating procedures, which makes this methodology straightforward and cost-effective. We have adapted the SB system for its first-in-human use, generated a master-cell bank of aAPC (by PACT under the auspices of NHLBI) and manufactured clinical grade SB DNA plasmids. These platform technologies should enable us to infuse clinical-grade CAR+ T cells, such as with specificity for CD19 on malignant B cells (Figure). It is hoped that this approach to gene transfer and propagation and will enable us and others to undertake a series of human clinical trials infusing genetically modified T cells, as well as other lymphocyte populations, to improve the efficacy of adoptive immunotherapy. The plasticity of our approach based on the non-viral gene transfer of SB plasmids may be important not only for gene therapy trial development in the USA, but can be considered an opportunity for other countries to genetically manipulate human cells in compliance with current good manufacturing practices.



Poster Listing

Poster #: *(primary authors listed in italics)*

Adoptive Transfer

1 ERADICATION OF ESTABLISHED CD19-POSITIVE LEUKEMIA USING A SINGLE INJECTION OF CHIMERIC IMMUNORECEPTOR MODIFIED LENTIVIRAL TRANSDUCED T CELLS IN A XENOGRAFT NOG MOUSE MODEL

David M. Barrett[1], Carmine Carpenito[2], Yang Bing Zhao[2], Michael Kalos[2], Carl June[2], Stephan Grupp[1]

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2 SYNERGISTIC KILLING OF TUMOR CELLS BY IL-2 ACTIVATED NK CELLS AND TUMOR-SPECIFIC CTLS

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3 TCR AGAINST CANCER TESTIS ANTIGEN MAGE-A3 FOR TARGETED ADOPTIVE IMMUNOTHERAPY OF CANCER

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4 ADOPTIVE CELL THERAPY (ACT) USING T CELLS EXPRESSING A CHIMERIC ANTIGEN RECEPTOR FOR VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR-2 (VEGFR-2) PROMOTES TUMOR DESTRUCTION AND ENHANCES IMMUNOTHERAPY IN MICE

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5 IMMUNE RESPONSES TO MURINE T CELL RECEPTORS IN PATIENTS ENROLLED IN TCR GENE THERAPY TRIALS

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6 ROLE OF COMPLEMENT IN T CELL TUMOR INFILTRATION AND REJECTION

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7 EVIDENCE FOR CD4 T CELL-MEDIATED TUMOR REGRESSION AND THE MECHANISM OF THE SUBSEQUENT TUMOR IMMUNE ESCAPE

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8 IMPROVING TUMOR INFILTRATING LYMPHOCYTE SURVIVAL AND FUNCTION FOR MELANOMA ADOPTIVE T CELL THERAPY THROUGH 4-1BB COSTIMULATION

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9 MECHANISMS OF CD8 MEMORY LOSS TO NEUROBLASTOMA AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Poster #: *(primary authors listed in italics)*

10 EPSTEIN-BARR VIRUS SPECIFIC T CELLS AS THERAPY FOR RELAPSED / REFRACTORY EBV-POSITIVE LYMPHOMAS

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11 GENETICALLY ENGINEERED CD56-SPECIFIC T CELLS FOR THE TREATMENT OF RECURRENT NEUROBLASTOMA

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12 THE IMPACT OF CLINICAL PARAMETERS, IN CANCER PATIENTS REFRACTORY TO STANDARD THERAPY, ON THE FEASIBILITY OF EXPANDING TUMOR ANTIGEN SPECIFIC T-CELLS EX VIVO

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13 T-CELL DELIVERY OF INTERLEUKIN-12 TO THE TUMOR MICROENVIRONMENT TRIGGERS POTENT ENDOGENOUS ANTI-TUMOR RESPONSES

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14 LABELING OF DENDRITIC CELLS AND LYMPHOCYTES WITH IRON OXIDE MR CONTRAST AGENTS FOR CELLULAR MRI

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16 ANTIGEN SPECIFIC T-CELLS CULTURED IN IL-21 DEMONSTRATE SUPERIOR ANTI-TUMOR EFFICACY SECONDARY TO THE SECRETION OF IL-17 AND TNF-ALPHA

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17 IL-15 IS SUPERIOR TO IL-2 IN SUPPORTING ANTIGEN-SPECIFIC EXPANSION AND MAINTENANCE OF T-CELL MEMORY IN MELANOMA CD8+ TUMOR-INFILTRATING LYMPHOCYTES

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18 USING 19F MRI FOR IN VIVO TRACKING OF THERAPEUTIC CELLS

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Poster Listing

Poster #: *(primary authors listed in italics)*

19 ADOPTIVE TRANSFER IMMUNOTHERAPY OF CANCER PATIENTS ACCORDING TO LYMPHOCYTES PHENOTYPING PLUS TUMOR MARKERS MONITORING

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21 HIGH QUALITY AND HIGH AVIDITY T CELL CLONES SPECIFIC FOR TUMOR-ASSOCIATED ANTIGENS AND HOW TO FIND THEM

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22 IMPACT OF BORTEZOMIB-INDUCED PROTEASOME INHIBITION ON ANTI-TUMOR T CELL RESPONSES IN VIVO

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23 COMBINATION THERAPY WITH ANTI-ANGIOGENIC AGENTS AND ADOPTIVE CELL THERAPY (ACT) IN A MURINE TUMOR MODEL

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Clinical Trials of New Agents

24 ANTITUMOR EFFECT OF CONCHOLEPAS CONCHOLEPAS HEMOCYANIN (CCH) USING B16-F10 MOUSE MELANOMA CELLS AS A MODEL

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25 INCREASED CD4 AND CD8 MEMORY T CELL PROLIFERATION FOLLOWING ANTI-OX40 ADMINISTRATION TO CANCER PATIENTS: IMMUNOLOGIC ASSESSMENT OF A PHASE I CLINICAL TRIAL

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26 ELEVATED ANGIOTENSIN II LEVELS IN PLASMA AND MALIGNANT EFFUSIONS OF CANCER PATIENTS: RECOMBINANT HUMAN ACE2 AS NOVEL BIOLOGICAL THERAPY OF CANCER

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Poster #: *(primary authors listed in italics)*

27 EVALUATION OF IMMUNE AND CLINICAL RESPONSES IN A PHASE 1 TRIAL OF INTRANODAL NAKED DNA PRIMING AND PEPTIDE BOOST WITH PRAME AND PSMA (MKC1106 PP), IN PATIENTS WITH ANTIGEN-POSITIVE SOLID TUMORS

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28 IMMUNE AND CLINICAL RESPONSES IN A PHASE I TRIAL OF INTRANODAL NAKED DNA PRIMING AND PEPTIDE BOOST WITH MART-1 AND TYROSINASE (MKC1106 MT) IN PATIENTS WITH ADVANCED MELANOMA

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29 IMP321 AND WEEKLY PACLITAXEL AS FIRST-LINE CHEMO-IMMUNOTHERAPY FOR METASTATIC BREAST CANCER (MBC)

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30 APOPTOSIS REGULATOR PROTEIN PBF IS AN IMMUNOLOGICAL TARGET FOR PATIENTS WITH OSTEOSARCOMA

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31 SYNERGISTIC EFFECT OF TEMOZOLAMIDE CHEMOTHERAPY AND γδ T CELL-BASED IMMUNOTHERAPY FOR GLIOBLASTOMA MULTIFORME

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32 A PILOT STUDY OF DENILEUKIN DIFTITOX (DD) IN COMBINATION W/ HIGH-DOSE INTERLEUKIN-2 (HD IL-2) FOR PATIENTS (PTS) W/ METASTATIC RENAL CELL CARCINOMA (RCC)

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33 GLOBAL GENE EXPRESSION IN ACTIVATED $CD56^{DIM}CD16^{+}$ HUMAN NK CELLS

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34 IGF-IR IS A TUMOR ANTIGEN IN PATIENTS WITH BREAST CANCER

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Poster Listing

Poster #: *(primary authors listed in italics)*

35 IGF-IR PEPTIDE-BASED VACCINES INHIBIT TUMOR GROWTH IN A MURINE MODEL OF BREAST CANCER

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36 DIFFERENTIAL MODULATION OF HEPATIC AND SPLENIC DENDRITIC CELL NUMBER AND FUNCTIONS WITH SYSTEMIC IL-12 THERAPY

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37 TUMOR ANTIGEN NY-ESO-1 DERIVED CD8+ T CELL EPITOPES ARE PRESENTED DIFFERENTLY BY DCS AND MELANOMA CELLS

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38 CIMAVAX EGF, VACCINE FOR NSCLC TREATMENT:INTERIM ANALYSIS OF A PHASE III CLINICAL TRIAL

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39 IDENTIFICATION AND CHARACTERIZATION OF INTERLEUKIN-4 RECEPTOR α (IL-4Rα) CHAIN IN HUMAN ANAPLASTIC THYROID CARCINOMA AND TARGETING OF IL-4 RECEPTOR FOR THERAPY

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40 ROLE OF INTERFERON-GAMMA-INDOLEAMINE 2,3 DIOXYGENASE AXIS IN REGULATION OF IL-12-MEDIATED ANTITUMOR IMMUNITY

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41 HIGH DOSE IL-2 FOLLOWED BY TEMOZOLOMIDE RESULTS IN RESPONSE RATES OF HIGH QUALITY IN METASTATIC MELANOMA

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42 IDENTIFICATION OF INTERLEUKIN-13 RECEPTOR ALPHA2 CHAIN AS A BIOMARKER FOR TUMOR INVASION AND METASTASIS USING A MOUSE MODEL OF HUMAN PANCREATIC CANCER

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43 *IN VIVO* OVEREXPRESSION OF INTERLEUKIN 4 RECEPTOR α(IL-4Rα) IN A MOUSE MODEL OF HUMAN BLADDER CARCINOMA SENSITIZES TUMORS TO RECOMBINANT CHIMERIC IMMUNOTOXIN CONSISTING OF INTERLEUKIN 4 AND PSEUDOMONAS EXOTOXIN

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Poster #: *(primary authors listed in italics)*

44 EXPRESSION OF THE INTERFERON-LAMBDAS GENE WITH ADENOVIRUSES INDUCED CYTOTOXIC EFFECTS TO ESOPHAGEAL CARCINOMA

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45 AN EFFECTIVE INTERLEUKIN-2 CANCER IMMUNOTHERAPY DELIVERED BY A NOVEL POLYMERIC NANOPARTICLE IN MELANOMA

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46 CLINICAL ACTIVITY FOLLOWING THE ADMINISTRATION OF THE MAGE-A3 ANTIGEN-SPECIFIC CANCER IMMUNOTHERAPEUTIC (ASCI) IN BOTH MELANOMA AND NSCLC IS ASSOCIATED WITH SIMILAR PREDICTIVE BIOMARKERS PRESENT PRIOR TREATMENT

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47 POLYSACCHARIDE KRESTIN STIMULATES IL-12 PRODUCTION IN DENDRITIC CELLS AND THE DEVELOPMENT OF ANTIGEN SPECIFIC T CELLS VIA TLR2 ACTIVATION

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48 IL-15 ADMINISTRATION TO RHESUS MACAQUES EXPANDS NK AND MEMORY T CELLS AND INDUCES LONG-LASTING CHANGES IN T CELL HOMEOSTASIS

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49 PI3K TARGETING BY THE BETA-GBP CYTOKINE IN THE BIOLOGICAL THERAPY OF CANCER

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50 BOTH INNATE AND ADAPTIVE EFFECTOR CELLS CONTRIBUTE TO THE ANTI-TUMOR ACTIVITY OF MVA-BN®-HER2, A VACCINE CANDIDATE IN DEVELOPMENT FOR THE TREATMENT OF HER-2-POSITIVE BREAST CANCER

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51 HIGH IMMUNOGENIC POTENTIAL OF P53 MRNA-TRANSFECTED DENDRITIC CELLS IN PATIENTS WITH PRIMARY BREAST CANCER

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Poster Listing

Poster #: *(primary authors listed in italics)*

52 EXPLORING THE IMMUNOGENICITY OF DCS PULSED WITH HLA-A2 RESTRICTED TUMOR ANTIGENS IN COLOMBIAN INDIVIDUALS

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53 IL-24 REGULATION OF HOMEOSTASIS IN THE SKIN MICROENVIRONMENT DURING INFLAMMATION

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54 RACE AFFECTS CLINICAL RESPONSIVENESS TO INTERFERON ALPHA IN A DISEASE-DEPENDENT FASHION

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55 MODULATION OF LYMPHOCYTE FUNCTION FOR CANCER THERAPY: A PHASE II TRIAL OF TREMELIMUMAB IN ADVANCED GASTRIC AND OESOPHAGEAL ADENOCARCINOMA

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56 EXPRESSION OF THE OX40 CO-STIMULATORY RECEPTOR IS REGULATED THROUGH A DUAL TCR/ COMMON GAMMA CHAIN CYTOKINE-DEPENDENT MECHANISM

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57 EFFECTS OF CONTINUOUS IMMUNIZATION WITH MVA-BN®-HER2: TOLERABILITY AND IMMUNE RESPONSES TOWARDS TRANSGENE AND VECTOR

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58 CANCER IMMUNOTHERAPY USING MONOCYTE-DERIVED DCS STIMULATED WITH OK-432 AND PROSTAGLANDIN E2 PULSED WITH GP100 EPITOPE PEPTIDE IN MALIGNANT MELANOMA

Marimo Sato, Akira Kanamoto, Masahisa Jinushi, Hisako Katano, Kimiyasu Yoneyama, Akihiko Itoh, Hideaki Tahara

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59 IDENTIFICATION AND CHARACTERIZATION OF NOVEL HLA CLASS I ASSOCIATED PEPTIDES PRESENTED NATURALLY ON LUNG CANCER CELLS

Gomathinayagam Sinnathamby, Vivekananda Shetty, Punit Shah, Zacharie Nickens, Julie Hafner, Lisa Mariello, Ramila Philip

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60 THE EFFECT OF NK CELLS ON LYMPHOCYTE SUBPOPULATION IN CANCER AND AUTOIMMUNE DISEASES

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Poster #: *(primary authors listed in italics)*

61 UPDATE ON THE PREDICTIVE NATURE OF A NOVEL MELANOCYTIC GENE EXPRESSION SIGNATURE FOR OUTCOME TO HIGH-DOSE IL-2 TREATMENT IN PATIENTS WITH ADVANCED MELANOMA
Ryan J. Sullivan[1], Yujin Hoshida[2], Jean-Philippe Brunet[2], Julie Aldridge[3], Steven Tahan[4], Daniel Cho[1], James W. Mier[1], David F. McDermott[1], Todd Golub[2], Michael B. Atkins[1]
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62 IN VITRO IMMUNIZATION OF HUMAN PBMC USING TARGETED ACTIVATED T CELLS TO INDUCE SPECIFIC PRIMARY HUMORAL ANTIBODY RESPONSES AGAINST BREAST CANCER
Archana Thakur, Oxana Norkina, Lawrence G. Lum
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63 EVALUATION OF A NOVEL HUMAN CD4+CD25DIMFOXP3- T CELL POPULATION IN CANCER PATIENTS UNDERGOING IL-2 TREATMENT
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64 IMMUNIZATION WITH LISTERIA MONOCYTOGENES BASED VACCINES CAUSES PLEOTROPIC EFFECTS ON TUMOR MICROENVIRONMENT
Anu Wallecha, Vafa Shahabi, John Rothman, Sandra Rivera, Paulo C. Maciag
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65 IMMUNIZATION AGAINST WEAK TUMOR ANTIGENS: THE ROLE OF PEPTIDE-MHC STABILITY
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66 SUCCESSFUL IMMUNOTHERAPY WITH IL-2/ANTI-CD40 DIRECTLY COINCIDES WITH SPECIFIC CHEMOKINE-MEDIATED MITIGATION OF AN IMMUNOSUPPRESSIVE TUMOR MICROENVIRONMENT
Jonathan M. Weiss[1], Timothy C. Back[1], Anthony Scarzello[1], Jeff J. Subleski[1], Veronica L. Hall[1], Jimmy K. Stauffer[1], Dejan Micic[1], Kory Alderson[2], William J. Murphy[2], Robert H. Wiltrout[1]
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67 ACTIVATION OF ANTI-TUMOR FUNCTIONS OF NATURAL KILLER CELLS AND SUPPRESSION OF PRO-TUMOR FUNCTIONS OF MONOCYTES BY LENALIDOMIDE
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68 INTRATUMORAL IMMUNOTHERAPY WITH CHITOSAN/IL-12 ERADICATES ESTABLISHED TUMORS AND ELICITS DURABLE, TUMOR-SPECIFIC IMMUNE RESPONSES
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69 INTERFERON-GAMMA (IFNγ) INHIBITS RENAL CELL CARCINOMA GROWTH BY LIMITING POLYAMINE PRODUCTION AND INCREASING NITRIC OXIDE (NO)
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Poster Listing

Poster #: *(primary authors listed in italics)*

Enhancing Cancer Vaccines / Combinations

70 NOVEL IMMUNOGENIC HLA-A*0201-RESTRICTED EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) SPECIFIC T CELL EPITOPE IN HEAD AND NECK CANCER PATIENTS

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71 ANDROGEN ABLATION AUGMENTS CELLULAR IMMUNE RESPONSES TO PSA IN A HUMANIZED PSA/HLA-A2.1 TRANSGENIC MOUSE MODEL

M Simo Arredouani[1], Stephanie Tseng-Rogenski[2], Brent Hollenbeck[2], Deborah Defeo-Jones[3], Clara Hwang[2], Martin G. Sanda[1]

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72 SAFETY DATA OF MONTANIDE ISA 51VG AND MONTANIDE ISA 720VG IN HUMAN THERAPEUTIC VACCINES

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73 DENDRITIC CELL REDIRECTION OF REGULATORY T CELL RESPONSES TO OVARIAN TUMOR ANTIGENS

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74 SPERM PROTEIN 17 VACCINATION INDUCES A LONG-TERM PROTECTIVE IMMUNE RESPONSE AGAINST OVARIAN CANCER

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75 E6020, A NOVEL IMMUNOADJUVANT, IS EFFECTIVE AT STIMULATING HER2/NEU CANCER IMMUNITY IN HEALTHY DONORS AND BREAST CANCER PATIENTS

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76 SELF-RENEWING, PROLIFERATING AUTOLOGOUS MELANOMA CELLS, ALONE OR COMBINED WITH DENDRITIC CELLS, AS VACCINE IMMUNOTHERAPY FOR PATIENTS WITH METASTATIC MELANOMA: RESULTS OF CONSECUTIVE PHASE II TRIALS

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Poster #: *(primary authors listed in italics)*

77 MAGE-A3 ANTIGEN-SPECIFIC CANCER IMMUNOTHERAPEUTIC IN METASTATIC MELANOMA: FINAL RESULTS OF A RANDOMIZED OPEN-LABEL PHASE II STUDY OF THE EORTC MELANOMA GROUP (16032-18031)

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78 TUMOR ENDOTHELIAL MARKER 1 AS A TARGET FOR GENETIC VACCINE

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79 SELF-ADJUVANTING MESSENGER RNA-BASED VACCINES INDUCE COMPLETE ADAPTIVE IMMUNE RESPONSES

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80 IDENTIFICATION OF IMMUNOGENIC MHC CLASS I AND CLASS II EPITOPES FROM THE TUMOR REJECTION ANTIGEN PAX2

Doreen Haase[1], Anne Marie Asemissen[2], Stefan Stevanovic[3], Anne Letsch[2], Antonia Busse[2], Eckhard Thiel[2], Hans-Georg Rammensee[3], Ulrich Keilholz[2], Carmen Scheibenbogen[1]
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81 A HIGH-THROUGHPUT SCREENING ASSAY TO IDENTIFY AGENTS THAT ENHANCE T CELL RECOGNITION OF HUMAN MELANOMAS

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82 ENHANCEMENT OF A P53-BASED CANCER VACCINE BY HETEROLOGOUS PRIME/BOOST IMMUNIZATION AND TOLL-LIKE RECEPTORS STIMULATION

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83 IMPACT OF RADIATION ON IMMUNOTHERAPY (IT) TARGETS

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84 CHARACTERIZATION OF TUMOR-INFILTRATING MYELOID CELLS IN HLA-DR2B TRANSGENIC MOUSE MODEL OF PROSTATE CANCER

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85 HELPER ACTIVITY OF NK CELLS DURING THE DENDRITIC CELL-MEDIATED INDUCTION OF MELANOMA-SPECIFIC CTL RESPONSES

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Poster Listing

Poster #: *(primary authors listed in italics)*

86 TOPICAL PEPTIDE IMMUNIZATION WITH NY-ESO-1B PEPTIDE (SLLMWITQC) USING RESIQUIMOD AS AN IMMUNE ADJUVANT

Aaron Mansfield, Lisa Kottschade, Rob McWilliams, Edward Creagan, Judith Kaur, Gary Croghan, Fernando Quevedo, Svetomir Markovic

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87 A NOVEL BREAST/OVARIAN CANCER PEPTIDE VACCINE PLATFORM THAT PROMOTES SPECIFIC TYPE-1 BUT NOT TREG/TR1-TYPE RESPONSE

Karkada Mohan[1,2], Genevieve M. Weir[1], Tara Quinton[1], Leeladhar Sammatur[1], Lisa D. MacDonald[1], Alecia Grant[1], Robert Liwski[3], Ridas Juskevicius[3], Gomathinayagam Sinnathamby[4], Ramila Phillip[4], Marc Mansour[1]

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88 DNA VACCINE TARGETING IL-13 RECEPTOR ALPHA2 INDUCES TUMOR IMMUNITY IN MURINE SOLID TUMOR MODELS*

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89 PEPTIDE/IFA EMULSION DEPOTS ARE A GRAVEYARD FOR TUMOR ANTIGEN-SPECIFIC CD8+ T CELLS

Willem Overwijk, *Yared Hailemichael*, Zhimin Dai, Nina Jaffarzad, Patrick Hwu

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90 AUTOLOGOUS VACCINE AHICE, ACTIVE IMMUNE THERAPY AGAINST BREAST CANCER

Ioulia Papapolychroniadou[4], Hannes Anthopoulos[2], Konstantinos Papapolychroniadis[1], Vasilis Papadopoulos[1], Panagiotis Ginopoulos[3], Epaminontas Fahantidis[1]

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91 SYNERGISTIC EFFECTS OF CHEMO-IMMUNOTHERAPY COMBINATION: MECHANISMS INVOLVED AND IMPLICATIONS FOR THE DESIGN OF THERAPEUTIC PROTOCOLS AGAINST CANCER

Antonella Sistigu[1], Mara Valentini[1], Iole Macchia[1], Laura Bracci[1], Federica Moschella[1], Eleonora Aricò[1], Giovanna Schiavoni[1], Francesca Urbani[1], Imerio Capone[1], Paola Nisticò[2], Virginia Ferraresi[2], *Enrico Proietti*[1]

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92 EXPLOITING THE HUMORAL IMMUNE RESPONSE TO IDENTIFY TUMOR/TUMOR-ASSOCIATED ANTIGENS RECOGNIZED FOLLOWING COMBINATION IMMUNOTHERAPY IN MEN WITH HORMONE-REFRACTORY PROSTATE CANCER

Sachin Puri[1], James A. Thompson[1], Janet C. Siebert[2], Tarsem Moudgil[1], Theresa Ratzow[1], Shawn Jensen[1], Michael Lacelle[1], Daniel Haley[1], Christian H. Poehlein[1], Edwin Walker[1], Nathalie Sacks[3], Kristen Hege[3], Hong-Ming Hu[1,4], Todd Coffey[1], Carlo Bifulco[1], Walter J. Urba[1], Brendan Curti[1], Bernard A. Fox[1,5]

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93 ONCOLYTIC HERPES SIMPLEX VIRUS ACTIVATION OF FLT3-LIGAND GENERATED DENDRITIC CELLS FOR CANCER IMMUNITY

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Poster #: *(primary authors listed in italics)*

94 THE MELANOMA VACCINE MICROENVIRONMENT: DO NEGATIVE CONTRIBUTORS OF IMMUNE FUNCTION COMPARTMENTALIZE THE VACCINE SITE?
Jochen Schaefer, Donna Deacon, Mark Smolkin, James Patterson, Gina Petroni, Craig Slingluff
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95 THE SYNTHETIC THIAZOLOQUINOLONE IMMUNOSTIMULATORY COMPOUND CL075 SERVES AS A TOLL-LIKE RECEPTOR 7/8 AGONIST AND SUBSTITUTES FOR R848 TO PRODUCE MATURE HUMAN MONOCYTE-DERIVED DENDRITIC CELLS WITH THE CAPACITY TO SECRETE HIGH AMOUNTS OF IL-12(P70) CYTOKINE
Stefani Spranger[1], Miran Javorovic[1], Maja Buerdek[1], Susanne Wilde[1], Stephanie Tippmer[2], Iris Bigalke[2], Christiane Geiger[1], Bernhard Frankenberger[1], Dolores J. Schendel[1]
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96 AUTOLOGOUS MELANOMA CELL VACCINE: ESTABLISHING STABLE CELL LINES WITH HETEROGENEOUS TUMOR-ASSOCIATED ANTIGENS WITHIN SHORTER DURATION AND PASSAGE
Senthamil R. Selvan[1], Denysha J. Carbonell[1], Abner W. Fowler[1], Andrea R. Beatty[1], Mepur H. Ravindranath[2], Robert O. Dillman[1]
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97 EFFECTS OF MELANOMA-DERIVED HELPER PEPTIDES AND CYCLOPHOSPHAMIDE ON THE IMMUNOGENICITY OF A MULTIPEPTIDE MELANOMA VACCINE
Craig Slingluff[1], Gina Petroni[1], Kimberly Chianese-Bullock[1], Mark Smolkin[1], Merrick Ross[2], Naomi Haas[3], Kelly Smith[1], Cheryl Murphy[1], Walter Olson[1], Nadedja Galeassi[1], William Grosh[1]
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98 AD-E2A PREVENTIVE AND THERAPEUTIC IMMUNIZATIONS CONFER TUMOR PROTECTION OR DELAY TUMOR GROWTH IN TRANSPLANTABLE HER-2+ MOUSE TUMOR MODELS
Chiara Triulzi[1], Simona Vertuani[1], Claudia Curcio[2], Josef Seibt[3], Federica Cavallo[2], Wei-Zen Wei[4], Rolf Kiessling[1]
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99 IMPACT OF LOW DOSE CYTOXAN ON CIRCULATING MELANOMA ANTIGEN-SPECIFIC TREGS IN VIVO
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100 ADENOVIRUS-INFECTED HUMAN DENDRITIC CELLS ACTIVATE NATURAL KILLER CELLS VIA PLASMA MEMBRANE-BOUND TNF AND IL-15
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101 ERADICATION OF ESTABLISHED TUMORS BY ADMINISTRATION OF A CELLULAR VACCINE SECRETING AN APC-SPECIFIC CTLA-4-ERBB2/HER2 FUSION PROTEIN
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Poster Listing

Poster #: *(primary authors listed in italics)*

102 ACTIVE SPECIFIC VACCINATION FOLLOWING IMMUNE DEPLETION WITH CYCLOPHOSPHAMIDE AND SUBSEQUENT IMMUNE RECONSTITUTION AUGMENTS INDUCTION OF TUMOR SPECIFIC T-CELLS IN A GASTRIC CANCER MOUSE MODEL

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103 POWERFUL INDUCTION OF NK CELL TUMORICIDAL FUNCTIONS BY TYPE-1-POLARIZED DC: POSITIVE FEEDBACK BETWEEN DC AND NK CELLS

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104 ABROGATION OF LOCAL CANCER RECURRENCE AFTER RADIOFREQUENCY ABLATION BY DENDRITIC CELL-BASED HYPERTHERMIC TUMOR VACCINE

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105 INDEPENDENT REGULATION OF THE EFFECTOR FUNCTION AND CHEMOKINE RESPONSIVENESS OF CD8+ T CELLS VERSUS T CELL EXPANSION BY DENDRITIC CELL-BASED VACCINES

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106 INCREASED LEVEL OF CD4+FOXP3+ REGULATORY T CELLS AND DECREASED LEVEL OF DENDRITIC CELLS IN MYLTIPLE MYELOMA PATIENTS

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107 DAMAGE [DAMP] AND PATHOGEN [PAMP] ASSOCIATED MOLECULAR PATTERN MOLECULES DECREASE CYTOPLASMIC ZINC IN HUMAN DENDRITIC CELLS [DC] AND PROMOTE HIGH MOBILITY GROUP B1 [HMGB1] CYTOSOLIC TRANSLOCATION

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108 MULTIPLE-PEPTIDE VACCINES IN CANCER PATIENTS WITH EARLY DISEASE OR LIMITED TUMOR BURDEN

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109 IMMUNE REGULATION IN ENDOMETRIOSIS AND ENDOMETRIOSIS-RELATED OVARIAN CANCER

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Poster #: *(primary authors listed in italics)*

110 APPLICATION OF REAL-TIME MRNA CYTOKINE ASSAY FOR IMMUNE MONITORING OF CELL-MEDIATED IMMUNE RESPONSES IN BREAST CANCER

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111 RELATIONSHIP BETWEEN PSYCHOLOGICAL STRESS AND IMMUNOSUPPRESSIVE CELL POPULATIONS IN BREAST CANCER PATIENTS

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112 AUTOLOGUS VACCINE AHICE© AN IMMUNOTHERAPY PATENT AGAINST PANCREATIC CANCER

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113 A RARE ADVANCED STAGE CASE OF MEDULARY THYROID CANCER. SIGNIFICANT OUTCOME BY AUTOLOGOUS HUMAN IMMUNE VACCINE-AHICE THERAPY

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114 A NOVEL SOFTWARE APPLICATION FOR ELISPOT DATA CALCULATION, CONVERSION, AND QUALITY ASSURANCE REPORTING

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115 VACCINATION OF LEUKAEMIA PATIENTS WITH A MHC CLASS I PEPTIDE OF WILMS TUMOR GENE 1 (WT1) PEPTIDE WITH UNSPECIFIC T HELPER STIMULATION IS ABLE TO INDUCE WT1-SPECIFIC IGM RESPONSES BUT FAILS TO INDUCE IGG RESPONSES

David Stather[1], Carmen Scheibenbogen[2], Olga A. Elisseeva[3], Sandra Bauer[2], Yoshihiro Oka[3], Haruo Sugiyama[3], Eckhard Thiel[1], Ulrich Keilholz[1], Anne Letsch[1]
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116 TUMOR-DERIVED MICROVESICLES (TMV) DELIVER IMMUNOSUPPRESSIVE TGF-β1 TO DISTINCT IMMUNE CELLS IN PATIENTS WITH HEAD AND NECK CANCER

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Poster Listing

Poster #: *(primary authors listed in italics)*

117 SIMILAR T CELL RECEPTOR BETA SEQUENCES IDENTIFIED IN MELANOMA-REACTIVE T CELLS AND IN VIVO 6-THIOGUANINE-RESISTANT T CELLS FROM MELANOMA PATIENTS
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Manipulation of the Tumor Microenvironment

118 THE ROLE OF INDOLEAMINE 2,3 DIOXYGENASE ENZYMES (IDO-1 AND -2) IN PROSTATE CANCER
Irina Banzola, Giovanni Sais, Cèdric Poyet, Tullio Sulser, Maurizio Provenzano
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119 MUC1 IMMUNOBIOLOGY IN TRANSGENIC PRECLINICAL MODELS FOR ENDOMETRIOSIS AND ENDOMETRIOID OVARIAN CANCER
Raluca A. Budiu, Gina M. Mantia-Smaldone, Joan Brozick, Robert P. Edwards, Anda M. Vlad
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120 ALPHA-TOCOPHERYLOXYACETIC ACID: A TUMOR APOPTOGEN THAT STIMULATES THE ANTI-TUMOR IMMUNE RESPONSE
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121 INDOLEAMINE 2,3-DIOXYGENASE EXPRESSION BY MURINE T CELLS FOLLOWING IN VITRO EXPOSURE TO TUMOR CULTURE SUPERNATANT
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122 CELLULAR AND MOLECULAR REQUIREMENTS FOR REJECTION OF B16 MELANOMA IN THE SETTING OF REGULATORY T CELL DEPLETION AND HOMEOSTATIC PROLIFERATION
Justin Kline, Long Zhang, Thomas Gajewski
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123 GENERATION OF ANTIGEN-PRESENTING CELLS FROM TUMOR-INFILTRATED CD11B MYELOID CELLS WITH DNA DEMETHYLATING AGENT 5-AZA-2'-DEOXYCYTIDINE
Sergei Kusmartsev, Irina Daurkin, Evgeniy Eruslanov, Johannes Vieweg
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124 THE ROLES OF COX-2 INHIBITOR IN REGULATORY T CELLS AND TH17 CELLS' TUMOR IMMUNE REGULATION
Sung Yong Lee, Hye Ok Kim, Hye Kyoung Choi, Kyoung Ju Lee, Gyu Young Hur, Jae Jeong Shim, Kwang Ho In, Kyoung Ho Kang, Se Hwa Yoo
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125 ETHYL PYRUVATE ADMINISTRATION INHIBITS HEPATIC METASTASES, ALTERS TUMOR CELL METABOLISM
Xiaoyan Liang[1,2], Antonio Romo-de Vivar[1,2], Tao Wang[2], Nicole E. Schapiro[1], Bennett Van Houten[1], Andrew A. Amoscato[1], Herbert J. Zeh[1], Michael T. Lotze[1], Michael E. de Vera[1,2]
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126 CYCLIC PIFITHRIN-α DECREASES HMGB1 EXPRESSION AND INCREASES CELL VIABILITY, ATP CONSERVATION, HMGB1 TRANSLOCATION AND AUTOPHAGY
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Poster #: *(primary authors listed in italics)*

127 ANTI-VIRAL STATE SEGREGATES TWO MOLECULAR PHENOTYPES OF PANCREATIC ADENOCARCINOMA: POTENTIAL RELEVANCE FOR ADENOVIRAL GENE THERAPY

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128 TUMOR-SELECTIVE INDUCTION OF CTL -ATTRACTING CHEMOKINES AND LOCAL SUPPRESSION OF TREG-ATTRACTING CHEMOKINES BY THE COMBINATION OF IFNα, POLY-I:C AND COX INHIBITORS

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129 DEPLETION OF MACROPHAGES IN TUMOR MICROENVIRONMENT USING LIPOSOMAL CLODRONATE AUGMENTS ADOPTIVE T CELL THERAPY IN A MELANOMA MOUSE MODEL

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130 OPPOSING ROLES FOR HIF-1α AND HIF-2α IN TUMOR-INFILTRATING MACROPHAGES

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131 RADIOPROTECTION IN NORMAL TISSUE AND DELAYED TUMOR GROWTH BY BLOCKADE OF CD47 SIGNALING

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Monoclonal Antibodies / Combinations

132 IMPAIRED HUMORAL RESPONSE TO INFLUENZA VACCINE AND PROLONGED B MEMORY CELLS DEPLETION AS CONSEQUENCE OF RITUXIMAB BASED IMMUNOCHEMOTHERAPY IN NON HODGKIN LYMPHOMA PATIENTS (NHL PTS)

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133 CAN B CELLS, THE SMALL IGNORED GUYS HIDDEN IN MELANOMA TISSUES, PUT US ON THE RIGHT TRACK FOR TUMOR SPECIFIC ANTIGENS?

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Poster Listing

Poster #: *(primary authors listed in italics)*

134 DEVELOPMENT OF STREPTOCOCCAL SUPERANTIGEN-DERIVED ANTI-CANCER IMMUNOTHERAPEUTICS
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135 NANOCELL DELIVERY OF PHA-665752 AND CEUTUXIMAB ENABLES HIGH EFFICACY PHOTODYNAMIC THERAPY COMBINATION TREATMENT FOR PANCREATIC CANCER IN PRECLINICAL MICE MODEL
Lei Z. Zheng, Prakash Rai, Conor Evans, Bryan Spring, Tayyaba Hasan
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Regulatory & Activated T Cell Subsets

136 CUTANEOUS T-REGULATORY CELL FREQUENCY PREDICTS THE MAGNITUDE OF TUMOR VACCINE-INDUCED MEMORY RESPONSES
Yushe Dang, Lupe G. Salazar, Doreen Higgins, Janice Morihara, Meredith Slota, Jennifer Childs, Nicole Bates, Emily Jackson, Mary L. Disis
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137 CYTOTOXIC T-CELLS STRIKE BACK: ACTIVATED CD8+ T-EFFECTOR/MEMORY CELLS ELIMINATE CD4+ CD25+ FOXP3+ T-SUPPRESSOR CELLS FROM TUMORS VIA FASL MEDIATED APOPTOSIS
Mehmet O. Kilinc, Rachael B. Turner, Tao Gu, Lauren P. Virtuoso, Nejat K. Egilmez
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138 EVALUATION OF TREGS IN MELANOMA PATIENTS TREATED WITH DENDRITIC CELL VACCINES AND IL-2 +/- METRONOMIC CYCLOPHOSPHAMIDE
Eva Ellebæk[1,2], *Lotte Engell-Nørregård*[1,2], Jon Bjørn[1], Marie Brimnes[1], Kirsten Nikolajsen[1], Mads Hald Andersen[1], Per thor Straten[1], Inge Marie Svane[1,2]
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139 CTREGS (CIRCULATING REGULATORY T CELLS) REDUCTION IN MELANOMA PATIENTS TREATED WITH INTRAVENOUS HIGH-DOSE IFNα2B
Giusy Gentilcore[1], Maria L. Ascierto[1,2], Maria Napolitano[1], Marilena Capone[1], Ester Simeone[1], Antonio Da Ponte[1], Corrado Caraco'[1], Ena Wang[2], Nicola Mozzillo[1], Francesco M. Marincola[2], Paolo A. Ascierto[1]
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140 HUMAN PERIPHERAL BLOOD AND BONE MARROW EBV-SPECIFIC T CELL REPERTOIRE IN LATENT INFECTION REVEALS DISTINCT MEMORY SUBSETS BASED ON CYTOKINE PROFILES
Manuel Guerreiro[1], Il-Kang Na[1,2], Anne Letsch[2], Doreen Haase[1], Christian Meisel[1], Sandra Bauer[1], Petra Reinke[3,4], Hans-Dieter Volk[1,4], Carmen Scheibenbogen[1]
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141 HELPLESS CD8+ T CELLS ARE NOT HOPELESS
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Poster #: *(primary authors listed in italics)*

142 HUMAN FOXP3+ T REGS: FACTS OR TECHNICAL ARTEFACTS?
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143 ANTI-TUMOR IMMUNITY INDUCED BY TLR-7 LIGATION IS LIMITED BY INFLAMMATION INDUCED IMMUNOSUPPRESSION BUT CAN BE RESTORED VIA IL-10 BLOCKADE
Hailing Lu, Ekram Gad, Yi Yang, Amy Chang, Mary L. Disis
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144 TUMOR DERIVED ADENOSINE ENHANCES GENERATION OF ADAPTIVE REGULATORY T CELLS (TR1)
Magis Mandapathil[1,2], Stephan Lang[2], Edwin K. Jackson[3], Elieser Gorelik[1], Theresa L. Whiteside[1]
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145 CHARACTERIZATION OF IMMUNE RESPONSE DURING OSTEOLYTIC PROGRESSION OF BREAST CANCER
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146 ACUTE INFLAMMATION WITH IL-18/IL-12 OR AGALCER TREATMENT INDUCES LIVER INKT CELL APOPTOSIS AND REPOPULATION FROM PERIPHERAL TISSUES, WHEREAS CHRONIC INFLAMMATION ABLATES SYSTEMIC INKT CELLS WITH THYMIC-DEPENDENT REPOPULATION
Jeff J. Subleski, Veronica L. Hall, Anthony J. Scarzello, Thomas B. Wolfe, John R. Ortaldo, Deborah L. Hodge, Jon M. Weiss, Tim Chan, Robert H. Wiltrout
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147 TUMOR-DERIVED MICROVESICLES INDUCE, EXPAND AND MODULATE BIOLOGICAL ACTIVITY OF HUMAN CD4+CD25+FOXP3+ T REGULATORY CELLS
Marta Szajnik, Malgorzata Czystowska, Miroslaw J. Szczepanski, Magis Mandapathil, Theresa L. Whiteside
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148 IDENTIFICATION OF HEME OXYGENASE-1 SPECIFIC REGULATORY CD8+ T CELLS IN CANCER PATIENTS
Mads H. Andersen[1], Rikke B. Sørensen[1], Marie K. Brimnes[1], Inge Marie Svane[1,2], Jürgen C. Becker[3], Per thor Straten[1]
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Targeted Therapeutics and Biological Therapy

149 IN VITRO ANTICANCER PROPERTY OF NBD PEPTIDE THROUGH INHIBITION OF NF-KB ACTIVATION
Maria L. Ascierto[1,2], Giusy Gentilcore[2], Carmela Gravina[2], Andrea Worschech[1], Zoltan Pos[1], Richard Y. Wang[1], Emiliana Natale[2,3], Marilena Capone[2], Anna De Maio[3], Giuseppe Pirozzi[2], Silvana De Martino[2], Ena Wang[1], Francesco M. Marincola[1], Paolo A. Ascierto[2]
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150 ELEVATED SOLUBLE MICA PREDICTS NON-RESPONSIVENESS TO CTLA-4 BLOCKADE
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Poster Listing

Poster #: *(primary authors listed in italics)*

151 STAT3-SPECIFIC SMALL MOLECULE CURCUMIN ANALOGS FLLL32 AND FLLL62 INDUCE APOPTOSIS AND ENHANCE THE DIRECT ANTI-TUMOR EFFECT OF INTERFERONS
Matthew A. Bill, Jim R. Fuchs, Chenglong Li, Eric B. Schwartz, Jiayuh Lin, Dale G. Hoyt, Benjamin Foor, Dan Otterson, Jennifer Yui, William E. Carson, Pui-Kai Li, *Gregory B. Lesinski*
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152 REENGINEERING CLINICAL-GRADE DENDRITIC CELLS BY GILZ SILENCING TO DEVELOP A HIGHLY POTENT CANCER VACCINE
Dominique Cathelin, Özcan Met, Inge Marie Svane
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153 MULTIFUNCTIONAL NANOPARTICLES: A NONVIRAL VECTOR FOR TUMOR-TARGETED DELIVERY OF THERAPEUTIC SIRNA AND PNA OLIGONUCLEOTIDES
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154 THE STUDY OF PRE-MIR-15A INDUCING APOPTOSIS ON LYMPHOMATIC CELLS
Dongmei He
Jinan University, Guangzhou, China

155 THE STUDY OF MIR-15A AND MIR-16-1 ENHANCING THE SENSITIVITY OF RAJI CELLS TO ARA-C
Dongmei He, Qin Chen, Feiyan Zou
Jinan University, Guangzhou, China

156 INVESTIGATION OF ANTI-CANCER EFFECTS OF BORIC ACID IN VITRO
Hakan Istanbulluoglu, Recai Ogur, Mahmut Ilker Yilmaz, Omer Faruk Tekbas
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157 TARGETED "HYBRID PEPTIDE" THAT BINDS TRANSFERRIN RECEPTOR AND DISINTEGRATES CANCER CELL MEMBRANE
Megumi Kawamoto, Tomohisa Horibe, Masayuki Kohno, Koji Kawakami
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158 POTENT, ORALLY ACTIVE HYDROXYLAMIDINE INHIBITORS OF INDOLEAMINE-2,3-DIOXYGENASE SUPPRESS GROWTH OF IDO-EXPRESSING TUMORS THROUGH SYSTEMIC INHIBITION OF TRYPTOPHAN CATABOLISM
Holly K. Koblish, Michael J. Hansbury, Kevin J. Bowman, Gengjie Yang, Richard B. Sparks, Eddy W. Yue, Andrew P. Combs, Peggy A. Scherle, Kris Vaddi, Jordan S. Fridman
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159 A NOVEL SMALL MOLECULE INHIBITS STAT3 PHOSPHORYLATION AND ACTIVITIES AND EXHIBITS POTENT GROWTH SUPPRESSIVE ACTIVITY IN HUMAN CANCER CELLS
Li Lin[1,4], Brian Hutzen[1,2], Sarah Ball[1,2], Mingxin Zuo[1], Stephanie DeAngelis[1], Elizabeth Foust[1], Pui-Kai Li[3], Chenglong Li[3], Jiayuh Lin[1,2]
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160 CHEMOIMMUNOTHERAPY USING POLYSACCHARIDE KRESTIN AND PACLITAXEL IS SUPERIOR TO STANDARD NEOADJUVANT THERAPY IN A MOUSE MODEL OF LOCALLY ADVANCED NEU MEDIATED BREAST CANCER
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Poster #: *(primary authors listed in italics)*

161 A CLINICAL STUDY COMBINING MULTIPLE IMMUNE MODULATORS AND AN APC-TARGETED HCGβ VACCINE (CDX-1307)

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162 IMMUNEPOTENT CRP ENHANCES THE ACTIVITY OF CISPLATIN AND PREVENTS ITS SIDE EFFECTS

Moisés A. Franco Molina, Edgar Mendoza-Gamboa, Clara Isaza Brando, Pablo Zapata Benavides, Paloma Castillo Tello, Diana Zamora Avila, Diana Miranda Hernández, Crystel Sierra Rivera, Magda Vera García, Reyes Tamez Guerra, Cristina Rodríguez Padilla
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163 ARSENIC TRIOXIDE INDUCES APOPTOSIS IN NB-4, AN ACUTE PROMYELOCYTIC LEUKEMIA CELL LINE, THROUGH SUPPRESSION OF NUCLEAR FACTOR KAPPA B-MEDIATED INDUCTION OF TELOMERASE AND SURVIVIN

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164 RIZ1 REGULATES PROLIFERATION OF MONOCYTIC LEUKEMIA CELLS IN RESPONSE TO TNF-α VIA ACTIVATION OF P53

Abu Shadat M. Noman, Naoki Koide, Imtiaz I.- E. Khuda, Jargalsaikhan Dagvadorj, Gantsetseg Tumurkhuu, Yoshikazu Naiki, Takayuki Komatsu, Tomoaki Yoshida, Takashi Yokochi
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165 THE ANTI-PROLIFERATIVE AND ANTIVIRAL EFFECT OF INTERFERON BETA ON BREAST CANCER CELL LINE AND ITS MUTANTS

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166 KI-67 AS A TARGET FOR NANOTECHNOLOGY MEDIATED LIGHT ACTIVATABLE CANCER THERAPY

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167 BORTEZOMIB SENSITIZES RENAL CANCER CELLS TO TRAIL-MEDIATED APOPTOSIS IN VITRO AND IN VIVO

Thomas J. Sayers[1], Kristen Jacobsen[2], Anil Shanker[1], Alan D. Brooks[1]
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168 CATUMAXOMAB (REMOVAB): THE ROAD FROM PRECLINICAL DEVELOPMENT TO APPROVAL

Diane Seimetz
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169 INHIBITION OF HUMAN CERVICAL CANCER CELL GROWTH BY A COX-2 INHIBITOR,ETORICOXIB

Shweta Tripathi[1], Sudhir Chandna[2], Bilikere Srinivasa Dwarkanath[2], Daman Saluja[1], Madhu Chopra[1]
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Poster Listing

Poster #: *(primary authors listed in italics)*

170 SUPERIOR SURVIVAL OF EWING SARCOMA FAMILY OF TUMOUR PATIENTS ASSOCIATES WITH HIGH EXPRESSION OF C5 AT TUMOR SITE

Suvi Savola[1], Arto Klami[3], Samuel Myllykangas[1], Katia Scotlandi[4], Piero Picci[4], Cristina Manara[4], Sakari Knuutila[1], *Jukka Vakkila*[2]

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171 TRANSCRIPTIONAL ALTERATION INDUCED BY TREATMENT OF TRADITIONAL CHINESE MEDICINE (PHY-906) IN COLON CANCER

Ena Wang[1], Scott Bussom[2], Jinguo Chen[1,2], Courtney Quinn[1,2], Lam Wing[2], Zaoli Jiang[2], Dan Xi[3], Libin Jia[3], Jeffrey White[3], Francesco M. Marincola[1], Yung-Chi Cheng[2]

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172 TYPE-1-POLARIZED DENDRITIC CELLS (αDC1S) LOADED WITH AUTOLOGOUS OR ALLOGENEIC TUMOR MATERIAL ARE EFFECTIVE INDUCERS OF TUMOR-SPECIFIC CTLS AGAINST CLL, PROSTATE, COLORECTAL, OVARIAN, AND ENDOMETRIAL CANCER

Eva U. Wieckowski[1,3], Je-Jung Lee[1,3], Robbie Mailliard[1,3], Ravikumar Muthuswamy[1,3], Gurkamal Chatta[2,3], Herbert Zeh[1,3], Kenneth Foon[2,3], George L. Maxwell[4], Ron Herberman[3], Robert Edwards[2,3], David Bartlett[1,3], Pawel Kalinski[1,3]

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173 CROSS TALK BETWEEN CONSTITUTIVE ANTI-VIRAL STATE IN CANCER CELL LINES AND THE HOST'S IMMUNE RESPONSE DURING ONCOLYTIC THERAPY

Andrea Worschech[1,2,3], Maria L. Ascierto[1], Nanhai Chen[2], Yong A. Yu[2], Qian Zhang[2], Giovanni DiPasquale[5], Zoltan Pos[1], Ena Wang[1], Aladar A. Szalay[2,4], Francesco M. Marincola[1]

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174 SIGNATURES ASSOCIATED WITH REJECTION OR RECURRENCE IN HER-2/NEU POSITIVE MAMMARY TUMORS

Andrea Worschech[1,2,3], Maciej Kmieciak[4], Keith L. Knutson[5], Harry D. Bear[4], Aladar A. Szalay[3], Ena Wang[1], Francesco M. Marincola[1], Masoud H. Manjili[4]

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Viral and Cellular Proteomic Targets

175 MECHANISMS UNDERLYING THE SELECTIVE IMPAIRMENT OF EBNA1-SPECIFIC EFFECTOR T-CELLS OBSERVED IN PTLD

K. Jones[1], J. Nourse[1], L. Morrison[2], F. Vari[1], D. Moss[2], M. K. Gandhi[1,3]

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Poster #: **Late-Breaking Abstracts** *(presenting authors listed in italics)*

176 A RARE ADVANCED STAGE CASE OF PERITONEAL CANCER. SIGNIFICANT OUTCOME BY AUTOLOGOUS HUMAN VACCINE AHICE, IMMUNE THERAPY

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177 PLURIPOTENT STEM CELLS FROM THE HAIR FOLLICLE (HFPSCs) AFTER SPECIFIC TRANSDIFFERENTIATION REGENERATE HEALTHY BREAST TISSUE AND BLOOD VESSELS AFTER MASTECTOMY IN TREATED WITH CHEMOTHERAPY, ABS, AND RADIATION HORMONE REFRACTORY BREAST CANCER ANIMAL MODELS CIRCUMVENTING CAPSULAR CONTRACTURE, CTD, HEMATOMA/ SEROMA, CALCIFICATION, ATROPHY, NECROSIS, FIBROMYALGIA SYNDROME, NEUROENDOCRINE IMMUNITY, DIFFUSE SYSTEMIC INFLAMMATORY DISEASE AND TERATOMAS

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178 OXALIPLATIN INCREASES THE ANTITUMOR EFFECT OF VECTOR-DELIVERED INTERLEUKIN-12 EXPRESSION IN A MURINE MODEL OF HEPATIC COLORECTAL CANCER METASTASES

Manuela Gonzalez-Aparicio[1], Itsaso Mauleon[1], Pilar Alzuguren[1], Sandra Hervas-Stubbs[1], Uxua Mancheno[1], Julien Crettaz[1], Gloria Gonzalez-Aseguinolaza[1], Jesus Prieto[1, 2], *Ruben Hernandez-Alcoceba*[1]
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179 PACLITAXEL AND TRAIL SYNERGIZE TO KILL PACLITAXEL-RESISTANT SMALL CELL LUNG CANCER CELLS THROUGH A CASPASE INDEPENDENT MECHANISM MEDIATED THROUGH AIF

Terri B. Hunter[1], Kimberly Luddy[1], Tracy Catlin[1], Scott J. Antonia[1]
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180 NOVEL APPROACH TO TN-THERAPEUTIC VACCINE

Hsiao-Ling Chiang[1, 2], *Jaulang Hwang*[1], Chi-Yu Lin[1, 2], Fan-Dan Jan[3], Chiao-En Chen[1], Chia-Tse Hsu[1], Shin Nieh[4], Chun-Cheng Lin[3]
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181 TARGET GENE THERAPY FOR MELANOMA USING ANTIBODY TO MELANOMA-ASSOCIATED CHONDROITIN SULFATE PROTEOGLYCAN

Kazunori Kato[1, 2], Naoya Sakuragi[1, 2], Kiminori Nakamura[2], Hirofumi Hamada[2]
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182 ADOPTIVE CO-TRANSFER OF TUMOR SPECIFIC CD4+ T CELLS AWAKENS HOST PROTECTIVE IMMUNITY TO MHC-II- OVARIAN CANCER THROUGH CD40-MEDIATED LICENSING OF DCS AND CCL5 SECRETION

Yolanda C. Nesbeth[1], Diana G. Martinez[1], Seiko Toraya[1], Uciane K. Scarlett[1], Juan R. Cubillos-Ruiz[1], Melanie R. Rutkowski[1], Jose R. Conejo-Garcia[1, 2]
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183 RETINOBLASTOMA PROTEIN-INTERACTING ZINC FINGER 1 (RIZ1) REGULATES INNATE IMMUNE RESPONSES AND PROLIFERATION OF LEUKEMIA CELL AS A TOLL LIKE RECEPTOR 4 (TLR4) RESPONSIVE GENE

Abu Shadat M. Noman[1], Naoki Koide[1], Imtiaz I.- E. Khuda[1], Jargalsaikhan Dagvadorj[1], Gantsetseg Tumurkhuu[1], Yoshikazu Naiki[1], Takayuki Komatsu[1], Tomoaki Yoshida [1], Takashi Yokochi[1]
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184 SPECIFIC SILENCING OF ENDOGENOUS TCR WITH SIRNAS IN HUMAN LYMPHOCYTES IMPROVED EXPRESSION AND ANTI-TUMOR REACTIVITY OF TRANSDUCED TUMOR-SPECIFIC TCRS

Sachiko Okamoto[1], Junichi Mineno[1], Hiroaki Ikeda[2], Hiroshi Fujiwara[3], Masaki Yasukawa[3], Hiroshi Shiku[2], Ikunoshin Kato[1]

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185 IMMUNOSENESCENCE IN CANCER PATIENTS: IMPACT OF CYTOMEGALOVIRUS INFECTION

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186 COMPARABLE IMMUNE RESPONSE OF P53 PEPTIDE VACCINE DELIVERED BY DIRECT SUBCUTANEOUS INJECTIONS OR BY INTRAVENOUS INFUSIONS OF PEPTIDE-PULSED DENDRITIC CELLS IN OVARIAN CANCER PATIENTS

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187 POLYVALENT TRAIL PARTICLES OVERCOME CHEMOTHERAPEUTIC PLATEAU

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188 THERAPEUTIC CELL ENGINEERING USING SURFACE-CONJUGATED SYNTHETIC NANOPARTICLES

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189 ADVERSE SKIN REACTIONS TO WILMS TUMOR-1 PEPTIDE VACCINATION COMBINED WITH GEMCITABINE THERAPY IN TWO PATIENTS WITH ADVANCED PANCREATIC AND BILIARY CANCER

Takako Wakeda[1], Miho Kaida[1], Atsuko Soeda[1], Yuriko Hoshi[1], Yuni Yamaki[1], Hideki Ueno[1], Chigusa Morizane[1], Shunsuke Kondo[1], Yasushi Kojima[1], Masafumi Ikeda[1], Takuji Okusaka[1], Yoichi Takaue[1], Yuji Heike[1]

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190 COMPARISON OF MONOCYTE-DERIVED DENDRITIC CELLS FROM COLORECTAL CANCER PATIENTS, NON-SMALL-CELL-LUNG-CANCER PATIENTS AND HEALTHY DONORS

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