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Society for Immunotherapy of Cancer

27th Annual Meeting Final Program

October 26-28, 2012 • North Bethesda, MD

2012 SITC

www.sitcancer.org

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TABLE OF CONTENTS

MESSAGE FROM THE PRESIDENT

Dear Colleagues,

Welcome to SITC 2012! Since 1986, the SITC Annual Meeting & Associated Programs has united participants from academia, industry, and government organizations worldwide to share their knowledge and expertise in the field of tumor immunology and cancer immunotherapy. Highlights this year include expanded activities for early career scientists including the first ever Professional Development Session, an educational primer on tumor immunology and cancer immunotherapy, a workshop focused on the tumor microenvironment and a hot topic symposium exploring the recent advances in anti-PD-1 and anti-PD-L1.

SITC has seen incredible changes and made great strides in the advancement of cancer immunotherapy over the past year. With the implementation of our new Strategic Plan, SITC's goals of increasing engagement, fostering collaborations and providing top-notch educational opportunities are reflected in each of our endeavors and achievements. As my tenure as SITC President comes to an end, I am proud to report on key major accomplishments from the past two extraordinary years of change:

- Transitioned the Society name to better reflect our shared mission, to the Society for Immunotherapy of Cancer (SITC)
- Started a new journal – *Journal for Immunotherapy of Cancer* (JITC) – an open-access, online journal dedicated exclusively to our field, featuring free paper submissions for SITC members for the first year
- Launched a newly redesigned website – featuring easier navigation and expanded resources for professionals
- Established the *Forward Fund* – a dedicated effort aiming to financially support grants for junior investigators in cancer immunology and immunotherapy
- Developed the first ever Cancer Immunotherapy Guidelines – under the leadership of Dr. Howard Kaufman
- Supported the Immunoscore Project – an initiative to validate an intratumoral T cell infiltrate as a prognostic biomarker for patients with colon cancer
- Expanded collaborative efforts – presented the first ever Cancer Immunotherapy Primer at ASCO; founded the World Immunotherapy Council, an organization created to liaise with international cancer immunology organizations; staged the Joint Symposium on Cancer Immunotherapy with the Chinese Society for Clinical Oncology (CSCO) and the Chinese American Hematologist and Oncologist Network (CAHON); and organized the first ever SITC guest society session at AAI (slated for 2013)

A special thanks to all of the leadership, volunteers, and colleagues who have worked tirelessly on these initiatives; the success of SITC is possible because of your dedication.

With the continued engagement and support of its members and volunteers, SITC continues to lead the science, progress and innovation in this field. I encourage you to take advantage of all that the Society and the SITC 27th Annual Meeting & Associated Programs have to offer. This should prove to be a stimulating meeting filled with innovative science and a catalyst for collaboration in the field. Engage, collaborate and advance the field!

Sincerely,

Thomas F. Gajewski, MD, PhD
SITC President

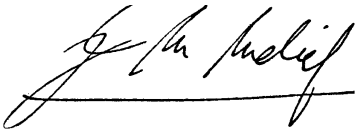
Dear Attendees,

We are pleased to welcome you to the SITC 27th Annual Meeting! Through its expansive programs, the Annual Meeting gathers clinicians and scientists from around the globe to interact and discuss the most important issues in cancer immunotherapy, promoting productive collaboration to accomplish better cancer patient outcomes. We hope that you take this opportunity to learn the latest advances in cancer immunotherapy during the poster viewing sessions, discover the multi-faceted world of cancer immunotherapy research and application at the plenary and concurrent sessions and connect with the other dynamic attendees during the networking and poster receptions as well as *The Checkpoints* performance on Saturday night. Here are some more of this year's Annual Meeting highlights:

- Keynote Speakers – Listen to two leading immunotherapists, Drs. Theresa Whiteside and Robert Schreiber share their expertise in the keynote addresses
- Networking Opportunities – Connect with colleagues at the networking receptions and extended meal times
- Poster Presentations – Check out the record-breaking number of poster presentations on the latest cutting-edge immunotherapy research
- Timely Educational Sessions – Sessions such as T Cell Modulating Strategies and Immunity of Oncolytic Viruses will keep you up-to-date and informed of the latest developments in the hot topics of our field. Other sessions will feature updates of partner organizations, including the Food and Drug Administration, the Cancer Immunotherapy Trials Network and the National Cancer Institute
- Hot Topic Symposium – Leaders in the field will deliver dynamic presentations and engage attendees in interactive Q & A on the topic "PD-1/PD-L1: Right on Target"
- Exhibits – Explore the most innovative biotechnology and pharmaceutical companies' offerings in the Exhibit Hall.

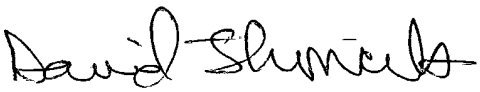
Thank you to the entire faculty of the program who lent their time and talents to an exceptional group of sessions. We hope you will take every opportunity to broaden your horizons on the most recent and pressing topics in cancer immunotherapy. Welcome to SITC 2012!

Sincerely,



Cornelis J.M. Melief, MD, PhD
Annual Meeting Organizer

Antoni Ribas, MD
Annual Meeting Organizer



David F. Stroncek, MD
Annual Meeting Organizer

WEDNESDAY, OCTOBER 24

7:00 am - 8:00 am	Continental Breakfast for Workshop Attendees
8:00 am - 5:00 pm	SITC Workshop - Focus on the Target: The Tumor Microenvironment (Day 1)
1:30 pm - 5:30 pm	Early Career Scientists Professional Development Session

THURSDAY, OCTOBER 25

7:00 am - 8:00 am	Continental Breakfast for Workshop and Primer Attendees
8:00 am - 5:00 pm	SITC Workshop - Focus on the Target: The Tumor Microenvironment (Day 2)
8:00 am - 5:00 pm	SITC Primer on Tumor Immunology and Cancer Immunotherapy™

FRIDAY, OCTOBER 26

7:00 am - 7:45 am	New Member Breakfast Gathering
7:00 am - 7:45 am	Continental Breakfast for Annual Meeting Attendees
7:50 am - 8:00 am	SITC 27th Annual Meeting Begins/President's Welcome
8:00 am - 8:45 am	Richard V. Smalley, MD Memorial Lectureship: Theresa L. Whiteside, PhD
8:45 am - 11:30 am	Plenary Session 301: T Cell Modulating Strategies
11:30 am - 12:00 pm	Plenary Session 302: Late-Breaking Oral Abstracts
12:00 pm - 1:30 pm	Lunch with Exhibits, Poster Viewing and Presentations
1:30 pm - 3:00 pm	Concurrent Session 304: DC Subsets/Cancer Vaccines
1:30 pm - 3:00 pm	Concurrent Session 305: Targeting Immune Suppression
3:15 pm - 5:15 pm	Plenary Session 306: Immunity of Oncolytic Viruses
5:15 pm - 5:30 pm	General Session 307: Cancer Immunotherapy Guidelines (CIG) Update
5:30 pm - 5:45 pm	General Session 308: US Food and Drug Administration (FDA) Update
5:45 pm - 6:00 pm	General Session 309: National Cancer Institute (NCI) Update
6:00 pm - 6:30 pm	SITC Membership Business Meeting
Immediately Following the Business Meeting - 8:00 pm	Poster and Networking Reception
8:00 pm - 10:00 pm	Early Career Scientists Networking Event

SATURDAY, OCTOBER 27

7:00 am - 7:45 am	Early Career Scientists "Meet the Expert" Breakfast (ticket required)
7:00 am - 7:45 am	Continental Breakfast for Annual Meeting Attendees
8:00 am - 8:45 am	Keynote Address: Robert D. Schreiber, PhD
8:45 am - 11:30 am	Plenary Session 401: Combining Immunotherapy and Other Therapies
11:30 am - 12:30 pm	Plenary Session 402: Critical Issues in Immunotherapy Clinical Trials
12:30 pm - 12:45 pm	Plenary Session 403: Late-Breaking Abstract
12:45 pm - 2:00 pm	Lunch with Exhibits, Poster Viewing and Presentations
2:00 pm - 3:30 pm	Concurrent Session 404: T Cell Manufacture and Potency Testing
2:00 pm - 3:30 pm	Concurrent Session 405: Single Cell High Throughput Technologies Immune Monitoring
4:00 pm - 5:20 pm	Plenary Session 406: Presidential Abstract Session
5:20 pm - 5:50 pm	General Session 408: Cancer Immunotherapy Trials Network (CITN) Update
5:50 pm - 6:15 pm	Awards Ceremony
Immediately Following the Awards Ceremony - 8:00 pm	Presidential Reception with Poster Viewing
8:00 pm	*The Checkpoints* Performance

SUNDAY, OCTOBER 28

7:00 am - 7:45 am	Continental Breakfast for Annual Meeting Attendees
8:00 am - 10:15 am	Plenary Session 500: Adoptive T Cell Transfer and Cell Therapy as Cancer Immunotherapy (CARS)
10:15 am	SITC Annual Meeting Adjourns
10:30 am - 12:00 pm	Hot Topic Symposium - PD-1/PD-L1: Right on Target

Forward Fund
Advancing Cancer Immunotherapy

WHY THE SITC *FORWARD* FUND WAS ESTABLISHED

- Provide grants to promising young post-doctoral researchers to help them complete cancer immunotherapy research projects and bridge the gap between their doctoral studies and faculty appointments
- Encourage more young scientists to enter the field of cancer immunotherapy research at academic, governmental and industry institutions
- Interact with patients and advocacy networks to address their specific needs for education and resources on cancer immunotherapy as a viable treatment option
- Develop policies on best practices in cancer immunotherapy clinical trials, assessment of relevant immunologic biomarkers and clinical management
- Educate clinical oncologists and laboratory scientists on the complex state of the art principles underlying cancer immunology and their application to the clinic
- Expand international collaborations among cancer immunotherapy researchers to identify and overcome major barriers in the field worldwide

WHAT THE SITC *FORWARD* FUND WILL DO

The *Forward* Fund will provide grants that will help attract the brightest young minds in cancer and/or immunology research to the cancer immunotherapy domain. It will inform those outside of the cancer immunotherapy field about the huge promise of this modality, which offers the potential of creating long-term remissions and/or prolongation of survival for people suffering from an expanding array of advanced cancer types. The Fund will also educate established clinical oncologists regarding the application and potential benefits of this treatment modality.

In this inaugural year of the *Forward* Fund, we are proud to announce that the Fund financially supports the Richard V. Smalley, MD Memorial Award, the Presidential Award and the Young Investigator Travel Awards. Information about these awards can be found in the following pages.

HOW YOU CAN HELP

The SITC leadership team is striving to raise **$1 million** in **four years** to support research and educational opportunities for basic and translational scientists and clinical investigators who are focusing on cancer immunotherapy. It is an ambitious goal, but a crucial one to continue to enhance the advances in this important area of cancer research. The SITC *Forward* Fund respectfully asks for your support in the following ways.

General Charitable Gifts*

Contributions in any amount are welcomed to support the mission and efforts of the Fund. Donations may be made online using the SITC Donation Form, the SITC Pledge Support Form, or by contacting info@sitcancer.org.

- General Contributions
- Honoraria Transfer
- Estate Gifts
- Memorials
- Named Honor Funds
- "Friend of the Society" Ribbons

All *Forward* Fund donors will be recognized in the Society e-newsletter, on SITC 2012 badge ribbons, The SITC Immune Monitor, during the Membership Business Meeting, on signs prominently displayed at SITC 2012, as well as on the Society website for the year following the donation.

For more information about the many ways to contribute to the *Forward* Fund, please visit the SITC Registration Desk or visit www.sitcancer.org/support/forwardfund.

**As a 501(c)(3) organization, donations made to SITC are tax deductible as charitable contributions to the extent allowed by law.*

FORWARD FUND STEERING COMMITTEE

Co-Chairs

Michael B. Atkins, MD
Georgetown-Lombardi Comprehensive Care Center

Ronald B. Herberman, MD
Intrexon Corporation

Members

Ernest C. Borden, MD
Cleveland Clinic Foundation

Charlese T. Garnett Benson, PhD
Georgia State University

Mehmet O. Kilinc, PhD
University at Buffalo / SUNY

Larry W. Kwak, MD, PhD
MD Anderson Cancer Center

Michael T. Lotze, MD
University of Pittsburgh Cancer Institute

Kimberly A. Shafer-Weaver, PhD
National Institutes of Health

Theresa L. Whiteside, PhD
University of Pittsburgh Cancer Institute

Supported by the SITC Forward Fund

In memory of his many achievements, both professionally and personally, the Society for Immunotherapy of Cancer (SITC) established the *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 recipient also provides a keynote scientific lecture at the Annual Meeting as part of his/her acceptance.

2012 RICHARD V. SMALLEY, MD MEMORIAL AWARD RECIPIENT

In recognition of her outstanding research, work, and achievements in cancer immunotherapy, the Society for Immunotherapy of Cancer (SITC) proudly presents the 2012 ***Richard V. Smalley, MD Memorial Award*** to Theresa L. Whiteside, PhD, of the University of Pittsburgh Cancer Institute.

Dr. Whiteside received both her MA and PhD degrees in Microbiology from Columbia University, New York, NY. She became a Diplomate of the American Board of Medical Laboratory Immunology in 1979. She spent a year (1984-85) working at the Ludwig Institute for Cancer Research in Lausanne, Switzerland as a Fogarty Senior International Fellow. At the University of Pittsburgh, Dr. Whiteside rose through the faculty ranks to become Associate Professor (1979) and Professor of Pathology (1989-present). In 1986, she became a member of the University of Pittsburgh Cancer Institute and was appointed Director of the Immunologic Monitoring and Diagnostic Laboratory, a position she held until stepping down in July 2010. In recognition of her research achievements in the biology of head and neck cancer, Dr. Whiteside was granted secondary appointments as Professor of Otolaryngology and Professor of Immunology at the University of Pittsburgh School of Medicine.

Dr. Whiteside's research interests are in tumor immunology and immunotherapy with special focus on mechanisms of tumor-induced immunosuppression, cytokine networks, development of anticancer vaccines, immunology of human head and neck cancer and the role of natural immunity in the control of cancer progression. Her research is in mechanisms of tumor escape from the host immune system and the development of therapies designed to eliminate tumor escape. Currently, she is investigating the role of regulatory T cells in cancer progression as well as contributions of tumor-derived microvesicles (MV) to apoptosis of CD8+ effector cells in the peripheral circulation of patients with cancer and in the tumor microenvironment. Dr. Whiteside is also interested in dendritic cells (DC) as vehicles for delivering tumor antigens to T cells. She is investigating components of antigen processing machinery (APM) in human DC with an objective of defining and optimizing conditions for optimal antigen processing and crosspresentation.

Dr. Whiteside is a recognized expert in immune monitoring of patients with cancer. She has authored 505 peer-reviewed publications in scientific journals and 118 chapters and review articles. She is the author of a book on human tumor-infiltrating lymphocytes and co-editor of several scientific books. She has trained over 80 postdoctoral fellows from the United States and abroad.

Since 2002, Dr. Whiteside has served on numerous NIH and DOD study sections and is a past member of the Board of Scientific Counselors for NIDCR. She is a member of numerous journal editorial boards and a scientific reviewer for many other scientific journals. Dr. Whiteside has been a member of SITC since 1994 and has contributed much to the Society since then. She served on the Board of Directors from 2004 to 2007, participated in the Strategic Planning Task Force, aided the Biomarkers Development Task Force, and is currently a member of the *Forward* Fund Steering Committee.

Dr. Whiteside will give the keynote address on Friday, October 26 at 8:00 am and she will be presented the Richard V. Smalley, MD Memorial Award during the Awards Ceremony on Saturday, October 27.

Forward Fund
Advancing Cancer Immunotherapy

RICHARD V. SMALLEY, MD (1932 – 2004)

As one of the Society's charter members, Dr. Richard V. Smalley was an integral part of the SITC 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. While Dr. Smalley was serving as SITC Treasurer from 1994-1998, the Society faced many challenges as the environment for biological therapy changed. Dr. Smalley met these challenges with inspirational devotion to the Society and field and administered the Society from his own home. SITC's success is due in large part to the consummate dedication and leadership of Dr. Richard Smalley.

PREVIOUS RICHARD V. SMALLEY, MD MEMORIAL AWARD RECIPIENTS

2011
Ralph M. Steinman, MD
The Rockefeller University

2010
James P. Allison, PhD
Memorial Sloan-Kettering Cancer Center

2009
Isaiah J. Fidler, DVM, PhD
MD Anderson Cancer Center

2008
Giorgio Parmiani, MD
San Raffaele Foundation

2007
Ernest C. Borden, MD
Cleveland Clinic Foundation

2006
Ronald Levy, MD
Stanford University School of Medicine

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

Attention Early Career Scientists, Young Investigators and Students!

SITC 2012 features more opportunities than ever before for early career professionals and students. Join the Early Career Scientists (ECS) Committee for the following educational and networking events at SITC 2012.

- ECS Professional Development Session – Wednesday, October 24 from 1:30 pm-5:30 pm
- ECS Networking Event – Friday, October 26 at 8:00 pm
- ECS "Meet-the-Expert" Breakfast – Saturday, October 27 from 7:00 am-7:45 am

Supported by the Forward Fund

SITC supports growth and achievement among young investigators in the field of cancer immunotherapy. To fulfill this goal, SITC offers several special opportunities for young investigators and early career scientists at the SITC 27th Annual Meeting.

PRESIDENTIAL TRAVEL AWARDS

Four qualified abstracts submitted in any category and authored by young investigators have been awarded the Presidential Travel Award. These authors will provide 20-minute oral presentations during the Presidential Abstract Session at the Annual Meeting.

SITC Presidential Travel Award recipients receive:
- Up to $750 in Travel Reimbursement
- 1-Year Membership with SITC
- Presidential Travel Award Certificate
- Presidential Travel Award Winner Poster Ribbon

The winners of the 2012 SITC Presidential Travel Awards are:

Cesar Evaristo, PhD
University of Chicago
Chicago, IL

Madhusudhanan Sukumar, PhD
National Cancer Institute
Bethesda, MD

Nathan Singh
University of Pennsylvania
Philadelphia, PA

Claire Vanpouille-Box, PhD
New York University
New York, NY

PRESIDENTIAL AWARD

Of the four Presidential Travel Award winners, one will be selected as the Presidential Award recipient by SITC leadership. The recipient will be determined based on his/her presentation during the Presidential Abstract Session on Saturday, October 27 at 4:00 pm. The recipient will be announced during the Awards Ceremony on Saturday evening.

SITC Presidential Award recipient receives:
- $1,000 Honorarium
- Up to $1,000 in Travel Reimbursement
- 1-Year Membership with SITC
- Commemorative Presidential Award Plaque
- Presidential Award Winner Poster Ribbon

Forward Fund
Advancing Cancer Immunotherapy

Supported by the Forward Fund

ABSTRACT TRAVEL AWARDS

SITC awarded six Abstract Travel Awards to selected young investigators presenting a poster at the Annual Meeting. Selection of award recipients was done by a committee of SITC leadership. Recipients will be recognized during the Awards Ceremony at the Annual Meeting on Saturday evening.

SITC Travel Award recipients receive:
- Up to $750 in Travel Reimbursement
- SITC Travel Award Winner Certificate
- SITC Travel Award Winner PosterRibbon

Forward Fund
Advancing Cancer Immunotherapy

The winners of the 2012 SITC Abstract Travel Awards are:

Maria Libera Ascierto, PhD
National Institutes of Health
Bethesda, MD

Michael Postow, MD
Memorial Sloan-Kettering Cancer Center
New York, NY

David Rushworth
MD Anderson Cancer Center
Houston, TX

Huimin Tao
University of Michigan
Ann Arbor, MI

Seng-Ryong Woo, PhD
University of Chicago
Chicago, IL

Yan Yang
MD Anderson Cancer Center
Houston, TX

PAST PRESIDENTIAL AWARD RECIPIENTS

The Society is dedicated to the promotion and dissemination of cancer immunotherapy education, especially for young investigators. For more than 20 years, SITC has awarded dozens of early career scientists with tens of thousands of dollars in travel awards. Many of these recipients have gone on to serve on the SITC Board of Directors, lead SITC committees and become leading cancer immunotherapy experts. The past Presidential Award recipients are listed below.

2011
Joshua Brody, MD
Stanford University Medical Center
Palo Alto, CA

2010
Michael A. Curran, PhD
Memorial Sloan-Kettering Cancer Center
New York, NY

2009
Weiyi Peng, MD, PhD
MD Anderson Cancer Center
Houston, TX

2008
Andrea Facciabene, PhD
University of Pennsylvania
Philadelphia, PA

2007
Amy K. Wesa, PhD
University of Pittsburgh
Pittsburgh, PA

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

2006
Ulf Petrausch
Earle A. Chiles Research Institute
Portland, OR

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

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

2004
Luca Gattinoni, MD
National Cancer Institute
Bethesda, MD

Jiali Li, PhD
Stanford University
Palo Alto, CA

2003
Steven E. Finkelstein, MD
National Cancer Institute
Rockville, MD

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

2002
Erin B. Dickerson, PhD
University of Wisconsin, Madison
Madison, WI

2001
Julia A. Coronella, PhD
University of Arizona
Tucson, AZ

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

Robbie B. Mailliard
University of Pittsburgh
Pittsburgh, PA

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

1998
Clemens Esche, MD
University of Pittsburgh
Pittsburgh, PA

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

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

1996
Carmen Scheibenbogen, MD
University Hospital Benjamin Franklin
Berlin, Germany

1995
Jon M. Wigginton, MD
National Cancer Institute
Frederick, MD

1994
Laurence Zitvogel, MD, PhD
University of Pittsburgh
Pittsburgh, PA

1993
David G. Maloney, MD, PhD
Stanford University
Stanford, CA

1992
Carol A. Nieroda, MD
National Cancer Institute
Bethesda, MD

1991
Judith Kantor, PhD
National Cancer Institute
Bethesda MD

ABOUT SITC

The Society for Immunotherapy of Cancer (SITC) was established in 1984 to facilitate the exchange and promotion of scientific information about the use of biological cancer therapies. SITC 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, SITC provides intimate channels for the discussion of current clinical trial results and methodologies, as well as means to collaborate on new initiatives in tumor immunology and biological therapy. It is these key interactions and innovations that help advance the progress of cancer research and therapies and lead to better patient outcomes.

MISSION STATEMENT

It is the mission of the Society for Immunotherapy of Cancer to improve cancer patient outcomes by advancing the science, development and application of cancer immunology and immunotherapy through our core values of interaction/integration, innovation, translation and leadership in the field.

CORE VALUES

- Interaction/Integration: Facilitate the exchange of information and education among basic and translational researchers, clinicians, young investigators, societies and groups sharing the mission of SITC
- Innovation: Challenge the thinking and seek the best research in the development of cancer immunotherapy
- Translation: Facilitate the transfer of cancer immunology and immunotherapy research from the bench to the clinic and back
- Leadership: Define what is new and important and effectively communicate it to all relevant stakeholders

NEW SITC JOURNAL - *JOURNAL FOR IMMUNOTHERAPY OF CANCER*

The *Journal for ImmunoTherapy of Cancer* (JITC) is the official journal of the Society for Immunotherapy of Cancer (SITC). JITC is comprised of four sections: Reviews/Editorials, Basic Tumor Immunology, Clinical/Translational Cancer Immunotherapy and Immunotherapy Biomarkers. JITC is a peer-reviewed, online, open access journal that aims to advance effective cancer immunotherapy by acting as a platform for the most important findings in the field. It encompasses all aspects of cancer immunology and immunotherapy, from basic research to clinical applications, and offers authors thorough peer review with immediate publication of accepted manuscripts.

MEMBERS AND MEETING ATTENDEES

Society membership continues to grow and now includes more than 550 influential leaders and scientists engaged in immunotherapy/biological therapy of cancer, including academicians, senior researchers, clinicians, students, government representatives, and industry leaders from around the world. SITC's members represent 17 medical specialties and are engaged in research and treatment of at least a dozen types of cancer. With major developments and recent FDA approvals in the field of cancer immunotherapy, the SITC Annual Meeting & Associated Programs attendance is growing as well, attracting over 800 of the brightest minds in the field. Both scientists and clinicians alike from around the globe convene at SITC to share data, hear the most recent advances in the field and find collaboration opportunities.

Disease States Represented by SITC Constituents

SITC 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 Represented by SITC Constituents

- 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

SITC MEMBERSHIP INFORMATION

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

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

MEMBERSHIP TYPES

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

Affiliate Membership ($220 annual dues) Available to individuals active or otherwise interested in the biological therapy of cancer. Affiliate membership does not include the right to vote. Business/educational resumé or Curriculum Vitae required for application.

Scientist-in-Training (Student) Membership ($50 annual dues) Available to individuals enrolled in MD or PhD academic programs or those participating in postdoctoral fellowships and residency programs who show a demonstrated interest in biological therapy of cancer. Student membership does not include the right to vote. Proof of enrollment and letter of recommendation or Curriculum Vitae required for application.

SITC MEMBERSHIP BENEFITS

- FREE submission to the Journal for ImmunoTherapy of Cancer (JITC), SITC's NEW official open access and peer review journal comprised of four sections:
  - Reviews/Editorials
  - Basic Tumor Immunology
  - Clinical/Translational Cancer Immunotherapy
  - Immunotherapy Biomarkers.

  JITC encompasses all aspects of cancer immunology and immunotherapy, from basic research to clinical applications and it offers authors fast, fair and thorough peer review with immediate publication of accepted manuscripts.
- Reduction in submission fees and opportunity for rapid publication in SITC's subsection of the open-access *Journal of Translational Medicine*
- Reduction in registration fees for SITC Annual Meeting & Associated Programs
- Free access to speaker presentations and slide sets from past SITC live events
- Access to "Members Only" section of SITC website, including an online directory of SITC members, free access to resource documents and webinars and much more!
- Eligibility to serve on SITC committees
- Eligibility to serve on SITC Board of Directors (Regular members)
- Eligibilty for Young Investigator Awards
- Discount on SITC enduring materials
- Access to the best science in the field
- Early access to timely information on what is new and relevant to biological approaches for the treatment of cancer
- Opportunities to participate in and shape discussions that guide progress in the field
- Opportunities to network with colleagues to develop new ideas, establish new collaborations to advance your work, and participate in active scientific exchange
- Access to luminaries in the field, including leading scientists and clinical researchers
- Guidance on relevant and timely issues
- The opportunity to advance your career

SITC MEMBERSHIP APPLICATION

Please check the membership category you are applying for:
☐ Regular ☐ Affiliate ☐ Scientist-in-Training (Student)

Name: _____

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

Institution/Company: _____

Title: _____ Dept: _____

Mailing Address: _____

City: _____ State: _____ Postal Code: _____

Country: _____ Email: _____

Phone: _____ Fax: _____

Work Sector (check one):
☐ Academia ☐ Government ☐ Industry/Corporate ☐ Not-for-Profit Organization

Practice or Work Setting (check one):
☐ Clinic ☐ Government ☐ Hospital ☐ Lab ☐ Lab & Clinic (translational) ☐ Medical School/University
☐ Pharmaceutical/Biotech ☐ None

Field(s) of specialty (check all that apply):

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

Disease state(s) (check those most affiliated with your research or practice):

☐ Breast	☐ Hepatocellular	☐ Lung	☐ Neuroblastoma	☐ Renal Cell
☐ Colorectal	☐ Kidney	☐ Lymphoma	☐ Ovarian	☐ Others _____

Application Requirements

Regular applicants:
☐ I will email my CV or educational resumé to info@sitcancer.org.
☐ My CV or educational resumé is enclosed.

Affiliate applicants:
☐ I will email my business or educational resumé to info@sitcancer.org.
☐ My business or educational resumé is enclosed.

Scientist-in-Training (Student) applicants:
☐ I will email my letter of recommendation or CV and proof of enrollment to info@sitcancer.org.
☐ My letter of recommendation or CV and proof of enrollment are enclosed.

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

Membership Fee:
☐ Regular/Affiliate ($220) ☐ Scientist-in-Training (Student) ($50)
☐ Check (enclosed) Make checks payable to SITC in U.S. dollars drawn from a U.S. bank.
☐ VISA ☐ MasterCard ☐ American Express ☐ Discover

Card Holder: _____

Card Number: _____ Exp.: _____

Signature: _____ Date: _____

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

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Forward Fund

www.sitcancer.org/support/forwardfund

Show your support for the field and help move cancer immunotherapy *Forward*! Purchase your "Friend of the Society" Ribbon at the SITC Registration Desk for a minimum donation of $50, or make a general *Forward* Fund contribution. All contributions to the SITC *Forward* Fund support research, training, education, faculty development grants and all SITC awards, including the Richard V. Smalley, MD Award and the Young Investigator Travel Awards.

The SITC 27th Annual Meeting provides a multidisciplinary educational environment composed of cutting-edge research, informative oral presentations, poster presentations and valuable networking opportunities unique to SITC.

ORGANIZERS

Cornelis J.M. Melief, MD, PhD
Leiden University Medical Center

Antoni Ribas, MD
University of California, Los Angeles Medical Center

David F. Stroncek, MD
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INTENDED AUDIENCE

The audience for the SITC 27th Annual Meeting is basic and clinical investigators from academic institutions, industry and regulatory agencies, including clinicians, basic and translational researchers, graduate students, postdoctoral fellows and allied health professionals involved in cancer research.

POSTER AND SESSION TOPICS

The SITC 27th Annual Meeting consists of lectures, oral abstracts, and poster presentations, which will address the latest developments in the following areas:

- Adoptive T Cell Transfer and Cell Therapy as Cancer Immunotherapy (CARS)
- Combining Immunotherapy and Other Therapies
- DC Subsets/Cancer Vaccines
- Immunity of Oncolytic Viruses
- Immunotherapy Combinations *
- Innate Immunity in Cancer *
- Single Cell High Throughput Technologies Immune Monitoring
- T Cell Manufacture and Potency Testing
- T Cell Modulating Strategies
- Targeted Therapies and Anti-Tumor Immunity *
- Targeting Immune Suppression
- Therapeutic Monoclonal Antibodies in Cancer *
- Tumor Microenvironment *
- Tumor Vasculature, Chemokines and Lymphocyte Trafficking to the Tumor *

** Denotes poster only category.*

PROGRAM GOALS

- Exchange information on the most recent advances in tumor immunology and cancer immunotherapy
- Convey recent advances in biology and immunotherapy as they relate to specific cancers and various immunotherapy modalities, cell subsets, animal models and aspects of negative regulation in the tumor microenvironment
- Identify promising research opportunities, new techniques and clinical applications incorporating these advances
- Establish dialogue between academia, industry and government on these advances

EXPECTED LEARNER OUTCOMES

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

- Summarize the most recent advances in tumor immunology and cancer immunotherapy
- Integrate recent advances in cancer immunology and immunotherapy into basic, clinical and translational research
- Incorporate new research and techniques into clinical applications for cancer immunotherapy
- Establish and solidify collaborations among the various members of academia, industry, government and clinical practices to promote clinical evaluation of these advances in more efficient trials

The SITC 27th Annual Meeting is a non-accredited continuing education event. No credits are offered for physician participation in this educational program.

SPECIAL UPDATE SESSIONS

The SITC 27th Annual Meeting offers a unique forum for special updates, major national and international initiatives and important society projects including:

- Cancer Immunotherapy Guidelines (CIG) Update
- Cancer Immunotherapy Trials Network (CITN) Update
- National Cancer Institute (NCI) Update
- U.S. Food and Drug Administration (FDA) Update

EVALUATIONS

Please take time to complete the evaluation form provided for each session you attend. Your input and comments are essential in planning future educational events. Completed evaluations may be returned to the SITC Registration Desk.

EXHIBITS

The SITC 27th 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 Main Level, Salons A-D of the North Bethesda Marriott. The hall is open Friday and Saturday with booths staffed throughout the day, during all lunches and evening receptions. For a complete exhibit hall floor plan and exhibit company listings, refer to pages 36-39.

EXHIBIT HALL LOCATION & HOURS

Main Level, Salons A-D

Friday, October 26:	10:00 am – 8:00 pm
Saturday, October 27:	10:00 am – 8:00 pm

"FRIEND OF THE SOCIETY" RIBBONS

SITC is committed to furthering the field of cancer immunotherapy/biologic therapy through the establishment of the *Forward* Fund to support research, training, and education. SITC members can show their support for this Fund and their commitment to their field by purchasing a "Friend of the Society" ribbon at the SITC Registration Desk. "Friend of the Society" ribbons are designed to be worn on the name badges of delegates attending SITC 2012. Ribbons may be acquired for a minimum donation of $50 and can be purchased personally or for distribution to other recipients. In addition to wearing ribbons, all donors will be recognized on signs at SITC 2012 and on the Society's website.

**As a 501(c)(3) organization, donations made to SITC are tax deductible as charitable contributions to the extent allowed by law.*

MEMBERSHIP

Members of SITC are designated by a red "Member" ribbon on their name badge. For information on how to become a member, membership classifications and a complete list of member benefits, please see page 14. All non-members are invited to complete the membership application form on page 15. For any membership questions or to apply for membership, please stop by the SITC Registration Desk.

MESSAGES

A self-service message board is available in the registration area for attendees to post notes or leave messages for other attendees. Please check for any message that my be left for you.

PHOTO/VIDEO POLICY

Photography and videography are prohibited in all SITC general sessions, poster and exhibit locations unless prior written approval is received from the SITC office. SITC often employs the services of a professional photographer/videographer at SITC events to capture images and audiovisual (AV) recordings for use in society archival and promotional material. Your attendance at SITC events implies your permission for images and AV recordings captured during these events to be used for purposes of SITC archival and promotional materials and publications and waives your rights for compensation or ownership of these images.

REGISTRATION

Registration packets are ready for pick up at the SITC Registration Desk located in the Ballroom Foyer on the Main Level for those pre-registered for the Annual Meeting. On-site registration for the SITC Annual Meeting & Associated Programs is accepted, space permitting. Separate registrations and fees are required for the Professional Development Session, Primer and Workshop. The Hot Topic Symposium on Sunday, October 28 is complimentary for meeting delegates, but does require advance registration. Hot Topic Symposium-only registration is $200 on-site.

Guest Registration

Guest registration is available to people accompanying registered delegates and grants admission to evening receptions, but does not permit attendance to scientific sessions. Guests may register at the SITC Registration Desk for a fee of $125. Badges for pre-registered guests are provided in the delegate's registration packet. Society members or authors/co-authors of abstracts may not utilize the guest rate.

Registration Desk Location & Hours

Main Level, Ballroom Foyer

Tuesday, October 23	5:00 pm – 8:00 pm
Wednesday, October 24	7:00 am – 5:00 pm
Thursday, October 25	7:00 am – 6:00 pm
Friday, October 26	7:00 am – 6:00 pm
Saturday, October 27	7:00 am – 5:00 pm
Sunday, October 28	7:30 am – 12:00 pm

YOUNG INVESTIGATOR MEETING FEATURES

SITC supports growth and achievement among young investigators and early career scientists in the field of cancer immunotherapy. To fulfill this mission, SITC offers several specialized opportunities for early career scientists in association with the 27th Annual Meeting & Associated Programs: the Professional Development Session, Evening Networking Event, "Meet-the-Expert" Breakfast, and Presidential and Travel Awards. See page 23 for more information on the Early Career Scientist Committee and the 2012 planned activities.

SPEAKER CHECK-IN DESK

Faculty are required to check in and upload their presentations no later than four hours before the session starts.

Speaker Check-In Desk Location & Hours

Main Level, Ballroom Foyer

Tuesday, October 23	5:00 pm – 8:00 pm
Wednesday, October 24	7:00 am – 5:00 pm
Thursday, October 25	7:00 am – 6:00 pm
Friday, October 26	7:00 am – 6:00 pm
Saturday, October 27	7:00 am – 5:00 pm
Sunday, October 28	7:30 am – 12:00 pm

SPEAKER PRESENTATION SLIDES

Following the SITC Annual Meeting, all registered attendees will receive FREE access to faculty presentations as permitted. Presentations will be posted on the SITC website (www.sitcancer.org) by the end of November. Watch for an e-mail with viewing instructions.

HOTEL AND VENUE INFORMATION

Business Services

A full-service business center is located within the hotel to assist guests with their fax, copy, internet and parcel/post needs.

Hotel Location

The Bethesda North Marriott Hotel & Conference Center serves as the headquarters for the SITC 27th Annual Meeting. It is located at 5701 Marinelli Road, Bethesda, Maryland 20852 USA. Phone: 1-800-859-8003

Hotel Dining

Meritage

Meritage offers a casual, yet upscale environment where classic regional American cuisine is served with a Mediterranean flair and an extensive wine list. Open for breakfast, lunch and dinner.

On The Rocks

On The Rocks, open daily at 2:00 pm, is the perfect spot to enjoy conversation and a cocktail. Casual dining, six LCD TVs, comfortable seating and a seasonal outdoor veranda is open for both lunch and dinner.

Internet

Wireless internet is available in the hotel lobby for free. There is no internet access in the conference center meeting space.

Recreation & Entertainment

A health club and pool are available for use 24 hours a day with your guest room key. The Bethesda North Marriott Hotel is just blocks away from area attractions. For complete information on local activities visit the Montgomery County Maryland Convention & Visitors Bureau at www.visitmontgomery.com.

Bethesda, Maryland is located within 20 miles of Washington, D.C. For more information on things to do within Washington, D.C., contact the Washington D.C. Convention & Visitors Bureau at (202) 789-7000 or visit their website at www.washington.org.

Transportation Options

It's easy to get around Bethesda with its easy-to-use public transportation system. The Bethesda North Marriott Hotel is located within 20 miles of Washington, D.C. and access to the city is easy with taxis or the Metro. Taxis are readily available within the city and the Metro train operates Monday through Sunday at varying hours.

The Bethesda North Marriott Hotel is located across the street from the White Flint Metro Station (Red Line). Base fares start at $1.70* per trip (including trips between all downtown points). One-day tickets can be purchased for $14.00,* which allows unlimited travel after 9:30 am on weekdays and all day on weekends. For complete information on the Metro, visit www.wmata.com.

MAIN LEVEL

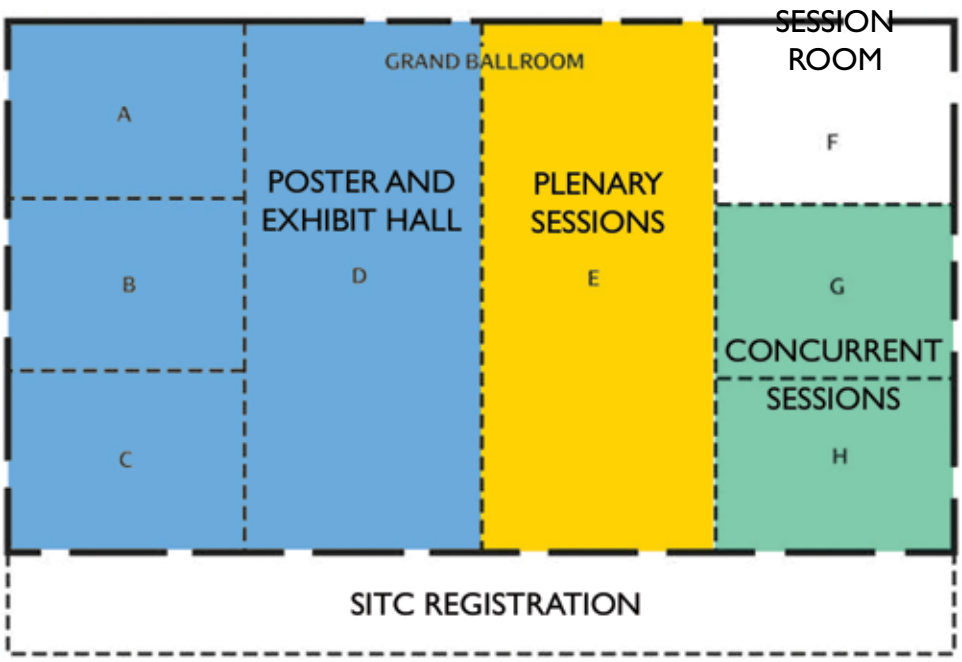

Exhibit and Poster Hall	Grand Ballroom A-D
Primer	Grand Ballroom G-H
Professional Development Session	Grand Ballroom Salon F
Workshop	Grand Ballroom E
Plenary Sessions	Grand Ballroom E
Concurrent Session	Grand Ballroom G-H
"Meet-the-Expert" Breakfast	Brookside A-B
New Member Breakfast	Brookside A-B

LOWER LEVEL

In conjunction with the 27th Annual Meeting, SITC also offers four Associated Programs: the Early Career Scientists Professional Development Session, the SITC Workshop - Focus on the Target: The Tumor Microenvironment, the SITC Primer on Tumor Immunology and Cancer Immunotherapy™ and the Hot Topic Symposium. These programs require separate registration. For more information about these Associated Programs, please visit the SITC Registration Desk located in the Ballroom Foyer on the Main Level.

EARLY CAREER SCIENTISTS PROFESSIONAL DEVELOPMENT SESSION

Supported by the Forward Fund

Wednesday, October 24, 2012
1:30 pm – 5:30 pm
Presenter slides will be available on the SITC website following SITC 2012.

The Professional Development Session is a half-day event intended to educate early career attendees in a large group didactic setting about relevant career development topics that lead to successful scientific careers in cancer immunotherapy and provide an opportunity to network with leaders in the field.

Organizers
Christian Capitini, MD – *University of Wisconsin*
William Redmond, PhD – *Earle A. Chiles Research Institute*

SITC WORKSHOP – FOCUS ON THE TARGET: THE TUMOR MICROENVIRONMENT

Wednesday – Thursday, October 24-25, 2012
8:00 am – 5:00 pm
Presenter slides will be available on the SITC website following SITC 2012.

The development of cancer has historically been attributed to genomic alterations of normal host cells, with cancer treatments historically targeting the malignant cell itself. It is now clear that tumor growth and development is a complex process that involves both malignant transformation and the influence of normal host cells, including fibroblasts, endothelial cells, lymphocytes, monocytes and macrophages. The tumor microenvironment has emerged as a critical target for cancer diagnosis, prognosis and therapy.

This two-day workshop on the tumor microenvironment will include presentations from thought leaders in the field and cover topics from basic tumor immunobiology to clinical immunotherapy trials that incorporate agents that modulate the tumor microenvironment. It will end with a presentation of progress on the development of the immunoscore - an ongoing initiative to promote the incorporation of an analysis of immune infiltrates within primary tumors as part of their standard pathologic evaluation for cancer diagnosis, prognosis and therapy.

Organizers
Leisha Emens, MD, PhD - *Johns Hopkins University*
Jerome Galon, PhD - *INSERM-Cordeliers Research Center*
Samir Khleif, MD - *Georgia Health Sciences*
Samuel Silverstein, MD - *Columbia University*

SITC PRIMER ON TUMOR IMMUNOLOGY AND CANCER IMMUNOTHERAPY™

Thursday, October 25, 2012
8:00 am – 5:00 pm
Presenter slides will be available on the SITC website following SITC 2012.

The understanding of tumor immunobiology has increased dramatically in recent years, leading to the successful development of new immune-based treatment options to improve cancer patient outcomes. The SITC Primer on Tumor Immunology and Cancer Immunotherapy™ is designed to provide a foundation for understanding core immunology principles as they relate to basic and clinical research in immunotherapy of cancer.

Prominent investigators will summarize central themes and recent research in tumor immunology and cancer immunotherapy including innate immunity, dendritic cells, T cell differentiation, antibody therapy and the tumor microenvironment as well as recent advances in the clinical application of cancer vaccines, coinhibition and costimulation of immune cells for immunotherapy, adoptive immunotherapy and immune monitoring in clinical trials of cancer immunotherapies. These topics will be addressed in a series of lectures by thought leaders in the field and through interactive question and answer discussions.

Organizers
Charles Drake, MD, PhD - *Johns Hopkins University*
Mario Sznol, MD - *Yale University School of Medicine*

HOT TOPIC SYMPOSIUM

Sunday, October 28, 2012
10:30 am – 12:00 pm
Presenter slides will be available on the SITC website following SITC 2012.

Each year immediately following the conclusion of the Annual Meeting, the Society hosts a 1½ hour Hot Topic Symposium to address a rapidly developing key issue in the field of cancer immunotherapy. In this final program, leaders in the field deliver dynamic presentations on cutting-edge research and participate in interactive question and answer sessions with the audience. This year, the Symposium will explore the latest scientific and clinical data on drugs and drug combinations targeting the PD-1/PD-L1 checkpoint pathway.

Immune checkpoints in the tumor microenvironment are potent mediators of local immunosuppression, and blockade of these pathways can rejuvenate antitumor immunity leading to tumor elimination. Clinical translation based on the prototypical checkpoint receptor, CTLA-4, has opened the door to a rich pipeline of related but nevertheless unique compounds. The PD-1/PD-L1 checkpoint pathway has recently emerged as a valid target for cancer immunotherapy, extending the reach of immunotherapy into common epithelial malignancies.

Organizers
Suzanne Topalian, MD - *Johns Hopkins University School of Medicine*
Ira Mellman, PhD - *Genentech, Inc.*

SITC 2012 is comprised of non-accredited continuing education events. No credits are offered for physician participation in these educational programs.

The Early Career Scientists (ECS) Committee was established to partner with SITC leadership to address the needs of early career scientists in the fields of immunology and biological therapy.

Members of the committee include students, postdoctoral fellows, and early career professionals in academia, industry and regulatory agencies. ECS Committee members participate in many activities and continually seek opportunities for early career scientists to advance SITC's mission and programming. The main goal of the committee is to leverage society relationships and resources to enhance the career development of outstanding young investigators in the field.

For SITC 2012, the ECS Committee has organized several events to connect early career scientists with leaders in the field of cancer immunotherapy on a variety of career development topics. The events are intended for graduate, medical and postbaccalaureate students; clinical fellows; postdoctoral fellows; assistant professors; and other early career professionals. Space for these events is limited and priority will be given to early career scientists.

EVENING NETWORKING EVENT

Friday, October 26, 2012
8:00 pm - 10:00 pm

All students and early career scientists are invited to attend this informal networking event. Located at the meeting venue, this event is a great way to meet with peers in the field. Pizza and salad will be provided and a cash bar will be available. Pre-registration is required for this event. For more information or to register for the Evening Networking Event, please visit the SITC Registration Desk.

"MEET-THE-EXPERT" BREAKFAST

Saturday, October 27, 2012
7:00 am - 7:45 am

The "Meet-the-Expert" Breakfast will focus on unique issues related to the career development of early career scientists. Key leaders in the field will facilitate roundtable discussions on particular areas of interest. Experts will answer questions and lead informal dialogues to help provide guidance and direction. Separate registration is required for this event. Tickets for the "Meet-the-Expert" Breakfast have been included in the registration materials for those attendees who have pre-registered. Tickets may still be available; inquire at the SITC Registration Desk.

Organizers

Christian Capitini, MD - *University of Wisconsin*
William Redmond, PhD - *Earle A. Chiles Research Institute*

Topics (ticketed event)

- **Developing Successful Collaborations**
  Leader: Pamela S. Ohashi, PhD – *Ontario Cancer Institute*
- **Finding Your Niche**
  Leader: Edward Nelson, MD – *University of California Irvine*
- **Grant Writing**
  Leader: Paul Sondel, MD, PhD – *University of Wisconsin*
- **Publishing Papers**
  Leader: Francesco Marincola, MD – *National Institutes of Health*
- **Translational Research**
  Leader: Padmanee Sharma, MD, PhD – *MD Anderson Cancer Center*
- **Managing a Research Lab**
  Leader: James W. Hodge, PhD, MBA – *National Cancer Institute*
- **Work-Life Balance**
  Leader: Charles G. Drake, MD, PhD – *Johns Hopkins University*

Program Goals

- Produce scientifically significant discussions and provide guidance relevant to the career development of early career scientists
- Provide early career scientists with an opportunity to meet key experts in the field and facilitate interactions in an informal small-group setting
- Mentor early career scientists on the state of research in today's environment through expert guidance on timely and relevant topics in cancer immunotherapy

Expected Learner Outcomes

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

- Locate resources available that will facilitate career development related to grant writing, finding one's niche, publishing papers, collaborations, translational research, and/or laboratory management
- Develop a framework for action, with an understanding of the complexities and potential pitfalls related to the key issue under discussion
- Summarize answers provided by experts in the field to specific questions related to the career development topic.
- Implement improved processes of communication between early career scientists and established researchers and experts

Abstracts submitted in conjunction with the SITC 27th Annual Meeting are published in the November/December 2012 issue of the *Journal of Immunotherapy*, one of the Society's journals. Members of SITC receive this issue as well as online access to the Journal with their yearly subscription as a benefit of membership. For those not subscribing, abstracts are available on the SITC website, in the Poster Abstract Book and beginning on page 40 of this program.

ORAL ABSTRACTS

Many of the session co-chairs have selected oral presenters from submitted abstracts that were deemed appropriate to the session topic and included timely information. Each oral abstract presentation is followed by a five minute question and answer period. For a complete listing of the selected oral abstracts, please see page 40.

LATE-BREAKING ABSTRACTS

To fulfill SITC's commitment to the most cutting-edge science, late-breaking abstract submission was offered from August 8 – August 22, 2012. The highest scoring submissions were selected for oral presentation during Plenary Session 302: Late-Breaking Oral Abstracts on Friday, October 26.

POSTER ABSTRACTS

Accepted posters for the SITC 27th Annual Meeting are on display in the Exhibit Hall, Salons A-D on the Main Level of the hotel. Posters are available for viewing Friday and Saturday of the Annual Meeting. Please see page 54 or the Poster Abstract Book for a listing of the posters on display. During the presentation times listed on this page, designated posters are staffed by their respective authors, allowing for information exchange and interaction between researchers and attendees.

POSTER LOCATION AND HALL HOURS

Main Level, Salons A-D
Friday, October 26: 10:00 am – 8:00 pm
Saturday, October 27: 10:00 am – 8:00 pm

POSTER NUMBERS

- Adoptive T Cell Transfer and Cell Therapy as Cancer Immunotherapy (CARS) 1-23
- Combining Immunotherapy and Other Therapies 24-50
- DC Subsets/Cancer Vaccines 51-81
- Immunity of Oncolytic Viruses 82-83
- Immunotherapy Combinations * 84-100
- Innate Immunity in Cancer * 101-113
- Single Cell High Throughput Technologies Immune Monitoring 114-121
- T Cell Manufacture and Potency Testing 122-124
- T Cell Modulating Strategies 125-129
- Targeted Therapies and Anti-Tumor Immunity * 130-157
- Targeting Immune Suppression 158-175
- Therapeutic Monoclonal Antibodies in Cancer * 176-182
- Tumor Microenvironment * 183-202
- Tumor Vasculature, Chemokines and Lymphocyte Trafficking to the Tumor * 203-206

** Denotes poster only category.*

POSTER PRESENTATIONS/STAFFING HOURS

Odd Number Posters (authors are present)
Friday, October 26 12:30 pm – 1:30 pm
6:30 pm – 7:15 pm

Even Number Posters (authors are present)
Friday, October 26 7:15 pm – 8:00 pm
Saturday, October 27 1:00 pm – 2:00 pm

The following descriptions provide a brief overview of the context for the plenary and concurrent sessions.

T CELL MODULATING STRATEGIES

Plenary Session
Friday, October 26
8:45 am - 11:30 am

Multiple T cell subsets may be involved in responses to cancer. Pharmacological and genetic strategies allow specific selection or activation of certain subsets with higher potency to fight cancer. The functional activity of immune modulating agents and adoptive cell transfer therapy can vary depending on which lymphocyte subset is being activated. The phenotype and function of lymphocytes with greater ability to become memory cells and progenitors to memory cells are being defined, opening the door to their specific use in immunotherapy strategies.

DC SUBSETS/CANCER VACCINES

Concurrent Session
Friday, October 26
1:30 pm - 3:00 pm

Dendritic cells (DC) continue to arouse interest because of their central role in initiation and regulation of cell-mediated immune responses. This year, the specialization in function of different subsets of human DC will be highlighted, particularly with respect to their use in immunotherapeutic strategies. Recent advances in the use of different DC subsets in clinical trials will be discussed as well as a comparison of immunotherapy with ex vivo prepared DC versus direct in vivo targeting of DC with cancer vaccines or other immuno-therapeutics.

Cancer vaccines come in different modalities. The specifications for cancer vaccines will be discussed as well as the immuno-monitoring assays required to establish their mode of action and potency. In addition, the synergy of cancer vaccines with other cancer treatment modalities will be highlighted, including synergy with chemotherapy, irradiation and checkpoint control monoclonal antibodies.

TARGETING IMMUNE SUPPRESSION

Concurrent Session
Friday, October 26
1:30 pm - 3:00 pm

Regulatory mechanisms counteract effective eradication of cancers by immune effector cells. The identification of these pathways has allowed the identification of novel strategies to potentiate immunotherapy of cancers. In this session, the nature of the most frequent inhibitory pathways will be discussed, followed by their elimination in preclinical models and clinical trials. The session will address targeting of Tregs, MDSC, CTLA-4, PD-1, IDO and NO in the tumor microenvironment and elsewhere.

IMMUNITY OF ONCOLYTIC VIRUSES

Plenary Session
Friday, October 26
3:15 pm - 5:15 pm

Oncolytic viruses selectively kill cancer cells while sparing normal cells. The mechanisms by which this has been achieved as well as further improvements in cancer cell selectivity will be discussed. Preclinical models and clinical trials with oncolytic viruses will be highlighted. Finally, oncolytic virus exploitation of immune mechanisms and the prospect of further enhancement of these by additional highly specific immunotherapy will be discussed.

COMBINING IMMUNOTHERAPY AND OTHER THERAPIES

Plenary Session
Saturday, October 27
8:45 am - 11:30 am

As new generations of highly targeted therapies are being developed for the treatment of cancer, it is important to understand how they impact the immune system and how to combine them with immunotherapies. Many of these targeted therapies have high initial antitumor activities but are limited by the development of acquired resistance. Their combination with immune modulating agents may allow inducing more durable tumor responses. Since the targeted therapies are usually systemic therapies, then they may have additional effects on the immune system, which may potentiate or counteract the antitumor activity of immunotherapies. Therefore, it is of great importance to gain a detailed molecular understanding of how they differentially impact on lymphocytes and cancer cells.

T CELL MANUFACTURE AND POTENCY TESTING

Concurrent Session
Saturday, October 27
2:00 pm - 3:30 pm

The clinical effectiveness of tumor infiltrating lymphocyte (TIL) therapy for the treatment of metastatic melanoma has improved as have the methods used to produce TIL. As a result, TIL treatment is becoming more widespread and multicenter clinical trials with centralized TIL processing are being considered. Progress in the development of centralized GMP methods for TIL production and the identification of possible TIL potency markers will be discussed.

SINGLE CELL HIGH THROUGHPUT TECHNOLOGIES IMMUNE MONITORING

Concurrent Session
Saturday, October 27
2:00 pm - 3:30 pm

New technologies for immune monitoring are increasing our understanding of how the immune system can be turned on to fight cancer. Advances in immune monitoring allow multiparametric analyses in immune cells, which can more readily define the effects of immunotherapies compared to older platforms based on single readouts of effector functions or quantiation of lymphocytes with a particular tumor specificity. This includes the use of technologies that allow combined surface phenotype and intracellular signaling analyses of multiple proteins as well as multiplexed assays for time-course evaluation of immune responses.

ADOPTIVE T CELL TRANSFER AND CELL THERAPY AS CANCER IMMUNOTHERAPY (CARS)

Plenary Session
Sunday, October 28
8:00 am - 10:15 am

Adoptive T cell transfer and cell therapy are evolving cancer immunotherapy approaches with promising clinical activity. These therapies are being used for a greater number of cancer patients and their efficacy is being improved by using selected T cell populations, reprogramming T cells, and genetically engineering T cells. The most recent scientific approaches and clinical trials will be reviewed.

Did you miss SITC 2012? Or do you want to share the experience with your colleagues?

Slides from SITC 2012 will soon be available online. Check the SITC website at **www.sitcancer.org** in early December.

FRIDAY, OCTOBER 26, 2012

7:00 am - 6:00 pm	**Registration Open**	Grand Ballroom Foyer
7:00 am - 7:45 am	**New Member Breakfast Gathering**	Lower Level, Brookside Room
7:00 am - 7:45 am	**Continental Breakfast**	Grand Ballroom Foyer
10:00 am - 8:00 pm	**Exhibit and Poster Hall Open**	Grand Ballroom Salons A-D
7:50 am - 8:00 am	**SITC 27th Annual Meeting Begins - President's Welcome** Thomas F. Gajewski, MD, PhD - *University of Chicago*	Grand Ballroom Salon E
8:00 am - 8:45 am	**Richard V. Smalley, MD Memorial Lectureship** Theresa L. Whiteside, PhD - *University of Pittsburgh Cancer Institute*	Grand Ballroom Salon E
8:45 am - 11:30 am	**Plenary Session 301: T Cell Modulating Strategies** Co-Chair: Nicholas P. Restifo, MD - *National Cancer Institute* Co-Chair: Cassian Yee, MD - *Fred Hutchinson Cancer Research Center*	Grand Ballroom Salon E
8:45 am - 9:15 am	Curative Cancer Immunotherapy Using Stem Cell-like T Cells Nicholas P. Restifo, MD - *National Cancer Institute*	
9:15 am - 9:45 am	Adoptive T Cell Therapy: Faster, Higher, Stronger Cassian Yee, MD - *Fred Hutchinson Cancer Research Center*	
9:45 am - 10:15 am	**Refreshments and Networking**	Grand Ballroom Salons A-D
10:15 am - 10:45 am	Profound Negative Regulation of T Cell Immunity by Nk Cells Pamela S. Ohashi, PhD - *Ontario Cancer Institute/University Health Network*	
10:45 am - 11:00 am	Memory CD8+ T Cells Induce Precocious Effector Differentiation of Naïve CD8+ T Cells in a FasL-Fas Dependent Manner: a New Mode of T-T Lymphocyte Interaction and Cross Talk Christopher A. Klebanoff, MD - *National Institutes of Health*	
11:00 am - 11:15 am	Optimizing the Therapeutic Potential of PD-L1 Blockade as a Single Agent and Through Combination Therapy Bryan A. Irving, PhD - *Genentech, Inc.*	
11:15 am - 11:30 am	Blockade of PD-L1 Mediated Immunosupression for Cancer Therapy - MEDI4736, Monoclonal Antibody Discovery and Preclinical Development Ross A. Stewart, PhD - *MedImmune*	
11:30 am - 12:00 pm	**Plenary Session 302: Late-Breaking Oral Abstracts** Chair: Francesco Marincola, MD - *National Institutes of Health*	Grand Ballroom Salon E
11:30 am - 11:45 am	A Phase II Study with the Anti-CTLA-4 mAb Tremelimumab in Advanced Malignant Mesothelioma: MESOTTREM-2008 Luana Calabró, MD - *University Hospital of Siena*	
11:45 am - 12:00 pm	Treatment of Non-Hodgkin Lymphoma with CAR-Transduced CD19-Specific Central Memory Derived T Cells Stephen J. Forman, MD - *City of Hope*	
12:00 pm - 1:30 pm	**Lunch with Exhibits, Poster Viewing and Presentations** (Lunch provided to registered attendees)	Grand Ballroom Salons A-D
12:30 pm - 1:30 pm	**Odd Numbered Poster Presentations by Authors**	Grand Ballroom Salons A-D

FRIDAY, OCTOBER 26, 2012

1:30 pm - 3:00 pm	**Concurrent Session 304: DC Subsets/Cancer Vaccines** Co-Chair: Pawel Kalinski, MD, PhD - *University of Pittsburgh Cancer Institute* Co-Chair: Cornelis J.M. Melief, MD, PhD - *Leiden University Medical Center*	Grand Ballroom Salons G-H
1:30 pm - 1:55 pm	Promoting the Effectiveness of Synthetic Cancer Vaccines Cornelis J.M. Melief, MD, PhD - *Leiden University Medical Center*	
1:55 pm - 2:08 pm	Preoperative Sipuleucel-T Results in Tumor Lymphocyte Infiltration in Prostate Cancer Specimens: Evidence of Immune Activation and Response Within the Prostate Tumor Microenvironment Lawrence Fong, MD - *University of California, San Francisco*	
2:08 pm - 2:21 pm	A Novel Dendritic Cell-based Vaccine for HER-2-Positive Early Breast Cancer Brian Czerniecki, MD, PhD - *University of Pennsylvania*	
2:21 pm - 2:34 pm	Randomized Trial of Two Active-Specific Immunotherapy Products Derived From Autologous, Proliferating, Self-renewing Tumor Cells in Patients with Metastatic Melanoma Robert O. Dillman, MD, FACP - *Hoag Cancer Center*	
2:34 pm - 3:00 pm	Optimization of DC-based Cancer Therapies Pawel Kalinski, MD, PhD - *University of Pittsburgh Cancer Institute*	
1:30 pm - 3:00 pm	**Concurrent Session 305: Targeting Immune Suppression** Co-Chair: Michael H. Kershaw, PhD - *Peter MacCallum Cancer Centre* Co-Chair: David H. Munn, MD - *Georgia Health Sciences University*	Grand Ballroom Salon E
1:30 pm - 2:00 pm	IDO and Immune Suppression David H. Munn, MD - *Georgia Health Sciences University*	
2:00 pm - 2:15 pm	Enrichment of CTLA4+CD39+CD25+FOXP3+ Regulatory T Cells in Head and Neck Cancer Patients is Promoted by Therapy with Cetuximab and Correlated with Clinical Outcome Hyun-Bae Jie, PhD - *University of Pittsburgh*	
2:15 pm - 2:30 pm	miR-124 as a Novel Immunotherapeutic Molecule to Reverse Glioma-mediated Immune Suppression and Enhance Anti-Tumor Clearance Amy B. Heimberger, MD - *University of Texas MD Anderson Cancer Center*	
2:30 pm - 3:00 pm	The Tumor Microenvironment Can Vary with Anatomical Site to Affect Responses to Therapy Michael H. Kershaw, PhD - *Peter MacCallum Cancer Centre*	
3:00 pm - 3:15 pm	**Refreshments and Networking**	Grand Ballroom Salons A-D
3:15 pm - 5:15 pm	**Plenary Session 306: Immunity of Oncolytic Viruses** Co-Chair: Howard L. Kaufman, MD, FACS - *Rush University Medical Center* Co-Chair: Aladar A. Szalay, PhD - *Genelux Corporation*	Grand Ballroom Salon E
3:15 pm - 3:45 pm	Tropism of Oncolytic Vaccinia Virus Constructs for Human Mononuclear Cell Subsets Boris Minev, MD - *Genelux Corporation*	
3:45 pm - 4:15 pm	Oncolytic Virotherapy as Cancer Immunotherapy Richard Vile, PhD - *Mayo Clinic*	

FRIDAY, OCTOBER 26, 2012

4:15 pm - 4:45 pm	Modulating the Tumor Microenvironment to Enhance Antitumor Immunity in Preclinical and Clinical Settings: Antigen Encoding Poxvirus Vectors Overcome Immune Escape Edmund C. Lattime, PhD - *The Cancer Institute of New Jersey*	
4:45 pm - 5:00 pm	Effect of HCV Viraemia on NK Cells Maria Libera Ascierto, PhD - *National Institutes of Health*	
5:00 pm - 5:15 pm	Combination Therapy of Intratumoral CRT/E7 Vaccinia Virus and Cisplatin Treatment Enhance the Antigen-Specific T Cell Immune Responses and Therapeutic Antitumor Effects Sung Yong Lee, MD, PhD - *Johns Hopkins Medical Institutions*	
5:15 pm - 5:30 pm	**General Session 307: Cancer Immunotherapy Guidelines (CIG) Update** Howard L. Kaufman, MD, FACS - *Rush University Medical Center*	Grand Ballroom Salon E
5:30 pm - 5:45 pm	**General Session 308: US Food and Drug Administration (FDA) Update** Raj K. Puri, PhD - *US Food and Drug Administration, CBER*	Grand Ballroom Salon E
5:45 pm - 6:00 pm	**General Session 309: National Cancer Institute (NCI) Update** William Merritt, PhD - *National Cancer Institute*	Grand Ballroom Salon E
6:00 pm - 6:30 pm	**SITC Membership Business Meeting** **(SITC members and potential members are invited to attend)**	Grand Ballroom Salon E
Immediately Following the Business Meeting - 8:00 pm	**Poster and Networking Reception**	Grand Ballroom Salons A-D
6:30 pm - 7:15 pm	**Odd Numbered Poster Presentations by Authors**	Grand Ballroom Salons A-D
7:15 pm - 8:00 pm	**Even Numbered Poster Presentations by Authors**	Grand Ballroom Salons A-D
8:00 pm - 10:00 pm	**Early Career Scientists Evening Networking Event**	Lower Level, Brookside A-B

SATURDAY, OCTOBER 27, 2012

7:00 am - 5:00 pm	**Registration Open**	Grand Ballroom Foyer
7:00 am - 7:45 am	**"Meet-the Expert" Breakfast** (Separate Registration Required)	Lower Level, Brookside A-B
7:00 am - 7:45 am	**Continental Breakfast**	Grand Ballroom Foyer
10:00 am - 8:00 pm	**Exhibit and Poster Hall Open**	Grand Ballroom Salons A-D
8:00 am - 8:45 am	**Keynote Address: Using Genomics to Understand Cancer Immunoediting and Guide Immunotherapy** Robert D. Schreiber, PhD - *Washington University School of Medicine*	Grand Ballroom Salon E
8:45 am - 11:30 am	**Plenary Session 401: Combining Immunotherapy and Other Therapies** Co-Chair: Laurence Zitvogel, MD, PhD - *Institute Gustave Roussy* Co-Chair: Antoni Ribas, MD - *UCLA Medical Center*	Grand Ballroom Salon E
8:45 am - 9:15 am	Combining Immunotherapy and Targeted Therapy for Melanoma Antoni Ribas, MD - *UCLA Medical Center*	
9:15 am - 9:30 am	PD-1/PD-L1 Blockade after Transient Lymphodepletion to Treat Myeloma Bryon D. Johnson, PhD - *Medical College of Wisconsin*	

SATURDAY, OCTOBER 27, 2012

9:30 am - 9:45 am	Pharmacokinetics and Immunological Effects of Human Il-15/Il-15Ra Heterodimeric Complexes in Mice and Macaques Cristina Bergamaschi, Ph.D. - *Frederick National Laboratory for Cancer Research*	
9:45 am - 10:00 am	ADXS11-001 Lm-LLO Immunotherapy Targeting HPV-E7: Preliminary Safety and Survival Data From A Phase 2 Study in Indian Women With Recurrent/Refractory Cervical Cancer Robert Petit, PhD - *Advaxis*	
10:00 am - 10:30 am	**Refreshments and Networking**	Grand Ballroom Salons A-D
10:30 am - 11:00 am	Immunomodulation and Tyrosine Kinase Inhibition Ronald DeMatteo, MD, FACS - *Memorial Sloan-Kettering Cancer Center*	
11:00 am - 11:30 am	Imatinib Mesylate: An Efficient Cancer Immunotherapy Laurence Zitvogel, MD, PhD - *Institute Gustave Roussy*	
11:30 am - 12:30 pm	**Plenary Session 402: Critical Issues in Immunotherapy Clinical Trials** Co-Chair: Samir N. Khleif, MD - *Georgia Health Sciences* Co-Chair: Howard Streicher, MD - *National Institutes of Health*	Grand Ballroom Salon E
11:30 am - 11:45 am	The Projection of Immunotherapy Clinical Design of the 21st Century Howard Streicher, MD - *National Institutes of Health*	
11:45 am - 12:00 pm	Critical Issues for Early Trial Design in Immunotherapy Samir N. Khleif, MD - *Georgia Health Sciences*	
12:00 pm - 12:15 pm	Design Issues in the Immunotherapy Combinatorial Trials Antoni Ribas, MD - *UCLA Medical Center*	
12:15 pm - 12:30 pm	Discussion	
12:30 pm - 12:45 pm	**Plenary Session 403: Late-Breaking Oral Abstract** Chair: Francesco Marincola, MD – *National Institutes of Health* 12-Chemokine Gene Signature Identifies Lymph Node-Like Structures In Melanoma: Potential For Patient Selection For Immunotherapy? Jim Mulè, PhD - *H. Lee Moffitt Cancer Center & Research Institute*	Grand Ballroom Salon E
12:45 pm - 2:00 pm	**Lunch with Exhibits, Poster Viewing and Presentations** (Lunch provided to registered attendees)	Grand Ballroom Salons A-D
1:00 pm - 2:00 pm	**Even Numbered Poster Presentations by Authors**	Grand Ballroom Salons A-D
2:00 pm - 3:30 pm	**Concurrent Session 404: T Cell Manufacture and Potency Testing** Co-Chair: David F. Stroncek, MD - *National Institutes of Health* Co-Chair: Daniel J. Powell, Jr., PhD - *University of Pennsylvania*	Grand Ballroom Salons G-H
2:00 pm - 2:30 pm	TIL Adoptive Cell Therapy for Melanoma: Trials and Tribulations in the Quest for FDA Approval Laszlo G. Radvanyi, PhD - *MD Anderson Cancer Center*	
2:30 pm - 3:00 pm	Developing Commercially Relevant T Cell Therapy Manufacturing Processes Jon Rowley, PhD - *Lonza Walkersville, Inc.*	
3:00 pm - 3:30 pm	Artificial Antigen Presenting Cells as a Standardized Platform for TIL Expansion Daniel J. Powell, Jr., PhD - *University of Pennsylvania*	

SATURDAY, OCTOBER 27, 2012

2:00 pm - 3:30 pm	**Concurrent Session 405: Single Cell High Throughput Technologies Immune Monitoring** Co-Chair: Begonya Comin-Anduix, PhD - *UCLA School of Medicine* Co-Chair: Alessandra Cesano, MD, PhD - *Nodality, Inc*	Grand Ballroom Salon E
2:00 pm - 2:30 pm	A Single Cell Network Profiling (SCNP) View of the Immune System Alessandra Cesano, MD, PhD - *Nodality, Inc.*	
2:30 pm - 2:45 pm	Dissection of Anti-CTLA4-induced Cytotoxic T Cell Responses in Melanoma Pia Kvistborg, MD - *Netherlands Cancer Institute*	
2:45 pm - 3:00 pm	High-Throughput Identification of Biomarkers of Longevity in Ipilimumab-Treated Melanoma Patients Using Polychromatic Flow Cytometry Janet C. Siebert, MS - *CytoAnalytics*	
3:00 pm - 3:30 pm	A Shape for Cancer and Immunity at the Single Cell Level Garry P. Nolan, PhD - *Stanford School of Medicine*	
3:30 pm - 4:00 pm	**Refreshments and Networking**	Grand Ballroom Salons A-D
4:00 pm - 5:20 pm	**Plenary Session 406: Presidential Abstract Session** Chair: Thomas F. Gajewski, MD, PhD - *University of Chicago*	Grand Ballroom Salon E
4:00 pm - 4:20 pm	Forcing NF-sB in T Cells Promotes Tumor Rejection Cesar Evaristo, PhD - *University of Chicago*	
4:20 pm - 4:40 pm	CARs For Childhood Cancer: Development and Comparison of Permanently and Transiently-Modified T-cells Targeting ALL and Neuroblastoma Nathan Singh - *University of Pennsylvania*	
4:40 pm - 5:00 pm	Inhibition of Glycolytic Flux Enhances CD8+ T Cell Memory, Stemness and Anti-Tumor Function Madhusudhanan Sukumar, PhD - *National Cancer Institute*	
5:00 pm - 5:20 pm	TGFß is a Master Regulator of the Pro-immunogenic Effects of Radiotherapy Claire Vanpouille-Box, PhD - *NYU School of Medicine*	
5:20 pm - 5:50 pm	**General Session 408: Cancer Immunotherapy Trials Network (CITN) Update** CITN Progress Overview Martin A. Cheever, MD - *CITN Principal Investigator, Fred Hutchinson Cancer Research Center* IL15 Trial Jeffrey S. Miller, MD - *University of Minnesota Cancer Center* IL7 Trial Lawrence Fong, MD - *University of California, San Francisco* IDO Inhibitor Trial (Melanoma) Craig L. Slingluff, Jr., MD - *University of Virginia* IDO Inhibitor Trial (Ovarian Cancer) Kunle Odunsi, MD, PhD - *Roswell Park Cancer Institute*	Grand Ballroom Salon E
5:50 pm - 6:15 pm	**Award Presentations**	Grand Ballroom Salon E
Immediately Following the Awards Ceremony - 8:00 pm	**Presidential Reception with Poster Viewing**	Grand Ballroom Salons A-D
8:00 pm	***The Checkpoints* Performance**	Grand Ballroom Salon E

SUNDAY, OCTOBER 28, 2012

7:30 am - 12:00 pm	**Registration Open**	Grand Ballroom Foyer
7:00 am - 7:45 am	**Continental Breakfast**	Grand Ballroom Foyer
8:00 am - 10:15 am	**Plenary Session 500: Adoptive T Cell Transfer and Cell Therapy as Cancer Immunotherapy (CARS)** Co-Chair: Steven A. Rosenberg, MD, PhD - *National Cancer Institute* Co-Chair: Philip D. Greenberg, MD - *University of Washington*	Grand Ballroom Salon E
8:00 am - 8:30 am	Adoptive Immunotherapy of Cancer Steven A. Rosenberg, MD, PhD - *National Cancer Institute*	
8:30 am - 9:00 am	Building a Better T Cell for Targeting Tumors Philip D. Greenberg, MD - *University of Washington*	
9:00 am - 9:30 am	Targeting CD19 in Adult and Pediatric Leukemia Michel Sadelain, MD, PhD - *Memorial Sloan-Kettering Cancer Center*	
9:30 am - 9:45 am	Adoptive T Cell Therapy with a TCR Engineered for Nanomolar Affinity Shows Improved Anti-Tumor Efficacy Compared to the Micromolar Wildtype TCR Carolina M. Soto - *University of Illinois*	
9:45 am - 10:00 am	Selection of PD-1, LAG-3, TIM-3 and 41BB positive CD8 T Cells in the Fresh Tumor Digest Enriches forMelanoma-reactive Cells Alena Gros, PhD - *National Cancer Institute*	
10:00 am - 10:15 am	Role of the PD-1/PD-L1 Pathway on Regulatory T Cell Development, Induction and Iunction in Vivo Justin P. Kline, MD - *University of Chicago*	
10:15 am	**Annual Meeting Adjourns**	

Hot Topic Symposium
PD-1/PD-L1: Right on Target

10:30 am - 12:00 pm

Free for Annual Meeting Attendees!

Inquire at the Registration Desk for more details.

Maria Libera Ascierto, PhD
National Institutes of Health
Oral Abstract Presenter

Cristina Bergamaschi, PhD
Frederick National Laboratory for Cancer Research
Oral Abstract Presenter

Luana Calabrò, MD
University Hospital of Siena
Oral Abstract Presenter

Alessandra Cesano, PhD
Nodality, Inc.
Co-Chair, Invited Faculty

Begonya Comin-Anduix, PhD
UCLA School of Medicine
Co-Chair

Brian Czerniecki, PhD
University of Pennsylvania
Oral Abstract Presenter

Ronald DeMatteo, MD, FACS
Memorial Sloan-Kettering Cancer Center
Invited Faculty

Robert O. Dillman, MD, FACP
Hoag Cancer Center
Oral Abstract Presenter

Charles G. Drake, MD, PhD
Johns Hopkins University
Invited Faculty

Cesar Evaristo, PhD
University of Chicago
Oral Abstract Presenter

Lawrence Fong, MD
University of California, San Francisco
Oral Abstract Presenter

Stephen J. Forman, MD
City of Hope
Oral Abstract Presenter

Dmitry I. Gabrilovich, MD, PhD
H. Lee Moffitt Cancer Center and Research Institute
Invited Faculty

Thomas F. Gajewski, MD, PhD
University of Chicago
Chair, Invited Faculty

Philip D. Greenberg, MD
University of Washington
Co-Chair, Invited Faculty

Alena Gros, PhD
National Cancer Institute
Oral Abstract Presenter

Amy B. Heimberger, MD
MD Anderson Cancer Center
Oral Abstract Presenter

James W. Hodge, PhD, MBA
National Cancer Institute
Invited Faculty

Bryan A. Irving, PhD
Genentech, Inc
Oral Abstract Presenter

Hyun-Bae Jie, PhD
University of Pittsburgh
Oral Abstract Presenter

Bryon D. Johnson, PhD
Medical College of Wisconsin
Oral Abstract Presenter

Pawel Kalinski, MD, PhD
University of Pittsburgh Cancer Institute
Co-Chair, Invited Faculty

Howard L. Kaufman, MD, FACS
Rush University Medical Center
Co-Chair

Michael H. Kershaw, PhD
Peter MacCallum Cancer Centre
Co-Chair, Invited Faculty

Samir N. Khleif, MD
Georgia Health Sciences
Co-chair, Invited Faculty

Christopher A. Klebanoff, MD
National Institutes of Health
Oral Abstract Presenter

Justin P. Kline, MD
University of Chicago
Oral Abstract Presenter

Pia Kvistborg, MD
Netherlands Cancer Institute
Oral Abstract Presenter

Edmund C. Lattime, PhD
The Cancer Institute of New Jersey
Invited Faculty

Sung Yong Lee, MD, PhD
Johns Hopkins Medical Institutions
Oral Abstract Presenter

Francesco Marincola, MD
Chair, National Institutes of Health
Invited Faculty

Cornelis J.M. Melief, MD, PhD
Leiden University Medical Center
Organizer, Co-Chair, Invited Faculty

Boris Minev, MD
Genelux Corporation
Oral Abstract Presenter

David H. Munn, MD
Georgia Health Sciences University
Co-Chair, Invited Faculty

Edward L. Nelson, MD
University of California, Irvine
Invited Faculty

Garry P. Nolan, PhD
Stanford School of Medicine
Invited Faculty

Pamela S. Ohashi, PhD
Ontario Cancer Institute/University Health Network
Invited Faculty

Robert Petit, PhD
Bristol-Myers Squibb Company
Oral Abstract Presenter

Daniel J. Powell, Jr., PhD
University of Pennsylvania
Co-Chair, Invited Faculty

Laszlo G. Radvanyi, PhD
MD Anderson Cancer Center
Invited Faculty

Nicholas P. Restifo, MD
National Cancer Institute
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Antoni Ribas, MD
UCLA Medical Center
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Steven A. Rosenberg, MD, PhD
National Cancer Institute
Co-Chair, Invited Faculty

Jon Rowley, PhD
Lonza Walkersville, Inc.
Invited Faculty

Michel Sadelain, MD, PhD
Memorial Sloan-Kettering Cancer Center
Invited Faculty

Robert D. Schreiber, PhD
Washington University School of Medicine
Keynote

Padmanee Sharma, MD, PhD
MD Anderson Cancer Center
Invited Faculty

Janet C. Siebert, MS
CytoAnalytics
Oral Abstract Presenter

Nathan Singh
University of Pennsylvania
Oral Abstract Presenter

Paul M. Sondel, MD, PhD
University of Wisconsin
Invited Faculty

Carolina M. Soto
University of Illinois
Oral Abstract Presenter

Ross A. Stewart, PhD
MedImmune
Oral Abstract Presenter

Howard Streicher, MD
National Institute of Health
Invited Faculty

David F. Stroncek, MD
National Institutes of Health
Organizer, Co-Chair

Madhusudhanan Sukumar, PhD
National Cancer Institute
Oral Abstract Presenter

Aladar A. Szalay, PhD
Genelux Corporation
Co-Chair

Claire Vanpouille-Box, PhD
NYU School of Medicine
Oral Abstract Presenter

Richard Vile, PhD
Mayo Clinic
Invited Faculty

Theresa L. Whiteside, PhD
University of Pittsburgh Cancer Institute
Smalley Lectureship Keynote

Cassian Yee, MD
Fred Hutchinson Cancer Research Center
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Laurence Zitvogel, MD, PhD
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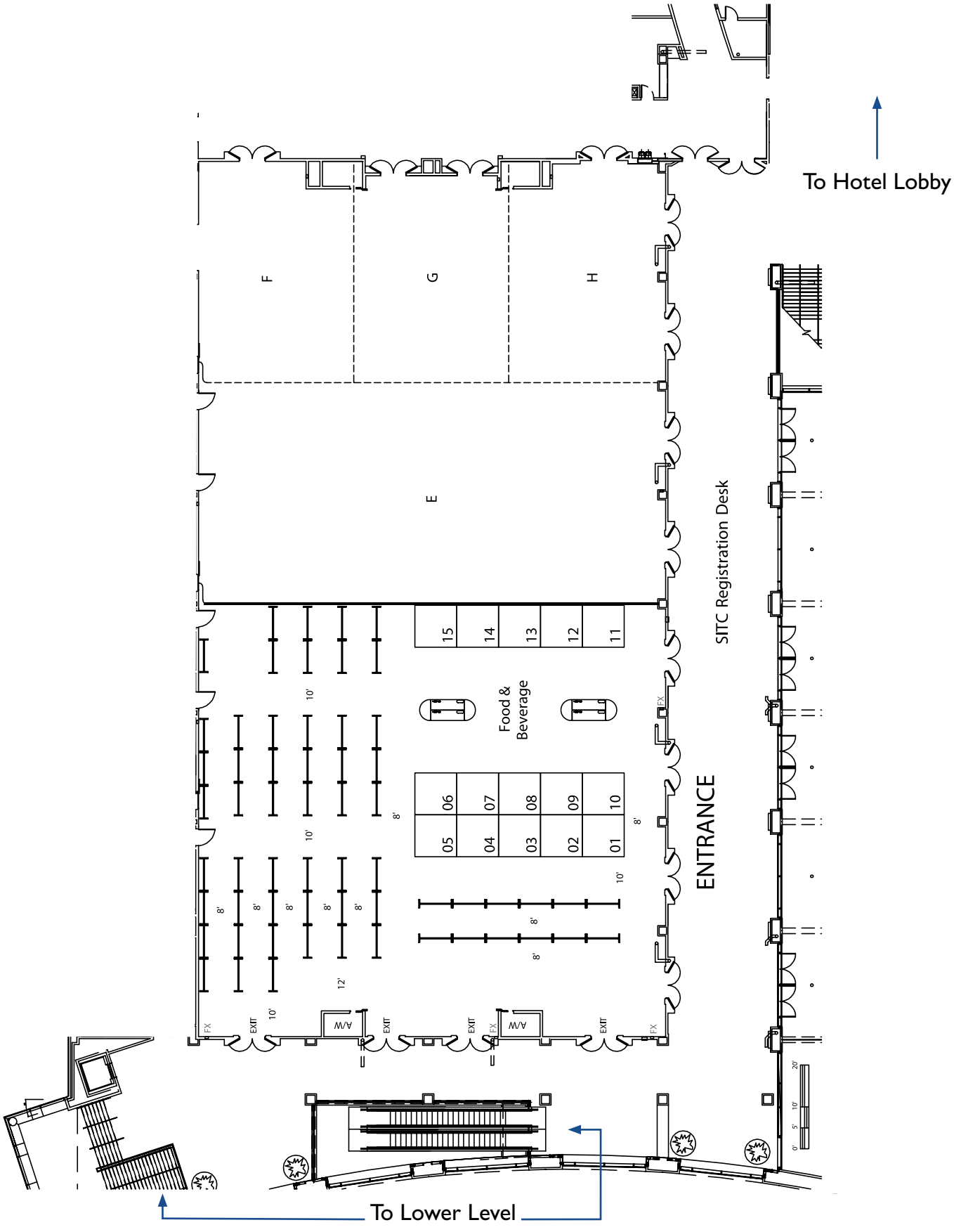
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FRIDAY, OCTOBER 26, 2012

T CELL MODULATING STRATEGIES

MEMORY CD8+ T CELLS INDUCE PRECOCIOUS EFFECTOR DIFFERENTIATION OF NAÏVE CD8+ T CELLS IN A FASL-FAS DEPENDENT MANNER: A NEW MODE OF T-T LYMPHOCYTE INTERACTION AND CROSS TALK

Christopher A. Klebanoff[1], Christopher D. Scott[1], Anthony J. Leonardi[1], Yun Ji[1], Rahul Roychoudhuri[1], Ena Wang[2], Zhiya Yu[1], Francesco M. Marincola[2], Luca Gattinoni[1], Nicholas P. Restifo[1]

[1]*CCR, NCI, Bethesda, MD*
[2]*CC, NCI, Bethesda, MD*

Naïve (T_N), stem cell memory (T_{SCM}) and central memory (T_{CM}) $CD8^+$ T cell subsets have been shown to confer superior engraftment and anti-tumor efficacy relative to more differentiated effector memory (T_{EM}) and effector (T_{EFF}) $CD8^+$ T cells. However, whether the presence of more differentiated T_{EM} and T_{EFF} negatively influence the potential of their less differentiated counterparts remains unknown. Herein, we describe a previously unrecognized interaction between T_N and memory $CD8^+$ T cells (T_{MEM}) that directly enhanced the effector differentiation of T_N via non-apoptotic Fas signaling resulting in downstream activation of the pro-differentiation Akt pathway. Using congenic markers to indelibly fate-track $CD8^+$ T cell subsets, we found that the presence of T_{MEM} during priming caused T_N to differentiate more rapidly than T_N activated alone, a process we have termed precocious differentiation. In addition to an accelerated loss of the lymphoid homing markers CD62L and CCR7 and the naïve-associated transcription factors (TFs) Tcf7, Lef1, and Klf2, T_N primed with T_{MEM} acquired higher levels of IFNγ, granzyme B, and the effector-associated TFs T-bet and Blimp-1. Investigations using microarray analysis of re-isolated T_N and T_{MEM} demonstrated the pervasiveness of this phenomenon as T_N transcriptionally associated with T_{MEM} by hierarchical clustering within 18 hours of activation. This process was TCR-ligation dependent, cell-dose dependent, and required cell-cell contact as it was entirely abrogated by physical separation of T_{MEM} from T_N using a semipermeable membrane. Mechanistically, disruption of FasL-Fas signaling either by antibody blockade of FasL or use of T_N deficient in the Fas receptor prevented precocious differentiation while provision of exogenous FasL trimer in the absence of T_{MEM} recapitulated this phenomenon. To interrogate the biologic significance of precocious differentiation, we adoptively transferred T_N activated alone or in the presence of T_{MEM} to treat hosts bearing B16 melanoma tumors. Naïve cells primed either in vitro or in vivo with T_{MEM} acquired a terminally differentiated phenotype upon transfer, as evidenced by low levels of CD27 and high KLRG1 expression, and exhibited significantly impaired persistence and antitumor activity compared with T_N primed alone. These findings provide evidence that more differentiated T_{EM} and T_{EFF} actively corrupt the full therapeutic potential of less differentiated anti-tumor T cells and demonstrate that their physical separation is required for optimal efficacy of adoptive T cell-based immunotherapies.

Key Word: Melanoma immunotherapy, Adoptive immunotherapy, Memory CD8+ T cells.

OPTIMIZING THE THERAPEUTIC POTENTIAL OF PD-L1 BLOCKADE AS A SINGLE AGENT AND THROUGH COMBINATION THERAPY

Bryan A. Irving, Heather Maecker, Yagai Yang, Marina Moskalenko, Jeanne Cheung, Daniel S. Chen, Ira Mellman

Oncology, Genentech, South San Francisco, CA

PD-L1, through engagement of the inhibitory receptor PD-1, impairs the capacity of chronically activated T cells to proliferate, produce cytokines, or effectively kill target cells in response to their cognate antigen. Expression of PD-L1 is prevalent among human tumors and can impede anti-tumor immunity resulting in immune evasion by tumor cells. Recent clinical data demonstrate the ability of antibody blockade of the PD-1/PD-L1 pathway to induce tumor regression in multiple tumor types. Here we describe the activity of a monoclonal antibody that targets PD-L1 and inhibits its interaction with both known receptors, PD-1 and B7.1. The IgG1 antibody was engineered with an Fc modification that abolishes FcγR binding in order to reduce antibody-mediated killing of Ag-experienced T cells that express elevated levels of PD-L1 or susceptible tissues that harbor higher levels of PD-L1 expression. In vitro, the Fc-modification in IgG1 prevents antibody-dependent cell-mediated cytotoxicity (ADCC) by NK cells at concentrations of 20 ug/ml; in contrast, an IgG4 isotype antibody, often considered to be ineffective in mediating efficient ADCC provides significant killing at concentrations as low as 0.2-2 ug/ml. Targeting PD-L1 with an Fc-effectorless antibody is expected to optimize both efficacy by protecting PD-L1hi tumor-infiltrating lymphocytes from depletion and safety by reducing tissue damage and potential presentation of auto-antigens from PD-L1-expressing tissues targeted by the antibody. In syngeneic tumor studies conducted with a human/mouse chimeric Fc-modified antibody, anti-tumor activity occurs rapidly and can translate into durable tumor-specific immunity. Significant synergy is observed combining PD-L1 blockade with selected chemotherapeutics, small molecule inhibitors of oncogenic pathways or blockade of VEGF. Some treatments that enhance anti-tumor efficacy of anti-PD-L1 can impede responses of alternative T cell-enhancing therapies, highlighting the need to understand mechanism for predicting effective combination regimens. Finally, immune-enhancing activity of BRAF V600 mutation inhibitors provides support for combining anti-PD-L1 with

vemurafenib in patients with BRAF V600-mutant melanoma. The broad development potential of the engineered IgG1 anti-PD-L1 antibody, both as a single agent and in combination with tumor-targeted therapies will be discussed.

Key Word: Cancer immunotherapy, PD-1.

BLOCKADE OF PD-L1 MEDIATED IMMUNOSUPRESSION FOR CANCER THERAPY - MEDI4736, MONOCLONAL ANTIBODY DISCOVERY AND PRECLINICAL DEVELOPMENT

Ross Stewart[1], Kathy Mulgrew[2], Suping Wang[3], Matthieu Chodorge[1], Danielle Marcus[1], Amanda Watkins[1], Marat Alimzhanov[3], Michelle Morrow[1], Scott Hammond[2], Vahe Bedian[3], Matthew McCourt[1]

[1]*MedImmune, Cambridge, United Kingdom*
[2]*MedImmune, Gaithersburg, MD*
[3]*AstraZeneca, Waltham, MA*

PD-L1 (B7-H1) is part of a complex system of signalling checkpoints that are involved in controlling T cell activation and helps to regulate normal immune responses, through its interaction with the PD-1 and CD80 receptors. A high proportion of tumor infiltrating T cells over express PD-1, as a result of chronic antigenic stimulation. Many tumors take advantage of this by up-regulating PD-L1, allowing them to hijack the PD-1/PD-L1 signalling axis to inhibit the anti-tumor T cell response and evade detection and elimination by the host immune system. Anti-PD-L1 antibodies, which block the interaction of PD-L1 with its receptors, have the potential to overcome this inhibitory signalling and re-instate anti-tumor immunity.

Using hybridoma technology and high throughput screening MedImmune has identified a series of fully human antibodies specific for human PD-L1. Further characterisation of these antibodies led to the identification of a single high affinity antibody, MEDI4736, with the ability to relieve PD-L1 mediated suppression of T-cell activation in vitro and to enhance sub-optimal T-cell activation in a mixed lymphocyte reaction. In vitro testing shows that MEDI4736 does not trigger non-specific cytokine release in whole blood, and is only able to activate T cells in the context of an active T-cell receptor signal.A surrogate anti-mouse PD-L1 antibody shows significant anti-tumour activity in a syngeneic model when dosed in combination with chemotherapy. Similarly MEDI4736 is able to inhibit tumour growth in a novel in vivo xenograft model, via a mechanism that is dependent on the presence of tumour specific human T cells.

These results demonstrate MEDI4736 is a selective antagonist of PD-L1 and may be a promising approach to targeting immune escape mechanisms observed in tumours.

Key Word: PD-1.

LATE-BREAKING ABSTRACTS SESSION I

A PHASE II STUDY WITH THE ANTI-CTLA-4 MAB TREMELIMUMAB IN ADVANCED MALIGNANT MESOTHELIOMA: MESOT-TREM-2008. (CLINICALTRIALS.GOV ID: NCT01649024)

Luana Calabrò[1], Ester Fonsatti[1], Aldo Morra[2], Ornella Cutaia[1], Ramy Ibrahim[3], Alessandra di Pietro[3], Diana Giannarelli[5], Anna Maria Di Giacomo[1], Riccardo Danielli[1], Maresa Altomonte[1], Luciano Mutti[4], Michele Maio[1]

[1]*Medical Oncology and Immunotherapy, University Hospital of Siena, Siena, Italy*
[2]*Euganea Medica Radiology Center, Padua, Italy*
[3]*Clinical Development Oncology-MedImmune, Gaithersburg,, MD*
[4]*Laboratory of Medical Oncology, Vercelli, Italy*
[5]*Istituto Tumori Regina Elena, Roma, Italy*

Background: Anti-CTLA-4 monoclonal antibodies (mAb) are showing significant activity in different tumor types; however, no data are available in MM patients (pts). We report results from the phase II, study MESOT-TREM-2008 that investigated safety, clinical and immunologic efficacy of tremelimumab in MM pts.

Methods: Advanced MM pts, who progressed on a first-line platinum-based regimen, were enrolled in the study and received tremelimumab at 15 mg/kg i.v. on day (d) 1 and 90 for 4 cycles or until progressive disease (PD). Primary endpoint was objective response (OR); secondary endpoints were safety, disease control rate (DCR), overall survival (OS), and immunologic activity. Tumor assessment per modified RECIST Criteria was performed at screening and at d 80 of each cycle. Adverse events (AE) were collected according to the CTC v3.0. Peripheral blood mononuclear cells collected at baseline, d 14, 30, 60, and 90 of each cycle were analyzed for an extensive panel of phenotypic and T-cell activation markers.

Results: 29 MM pts, 11 stage III and 18 stage IV, 22 males, 7 females, median age 61 (47-77) years, ECOG performance status 0-2, were enrolled. As of Aug 2012 all pts received at least 1 dose of tremelimumab (median 2; range 1-7), 11 pts are alive of whom 6 are still on treatment. Two pts had partial response (PR) (+180 d) and 4 prolonged stable disease (SD) (+270 d). DCR was 33.0% (9/29). The median OS was 10.7 months (95% CI: 0-22.1); the 1 year OS rate was 46.3%. Grade 1-2 AE occurred in 86% of pts; three pts had gastrointestinal grade 3 or hepatic and pancreatic grade 4 AE that resolved after steroids. Among investigated markers, a significant increase in the percentage and absolute number of CD4+HLA-DR+, CD4+CD45RO+, CD4+ICOS+, CD8+HLA-DR+, and CD8+ICOS+ T cells was detected at d 14, and d 30 after the first dose of tremelimumab, it slowly declined thereafter, and resumed upon re-dosing.

Conclusion: Tremelimumab shows clinical activity in MM pts, with AEs observed consistent with Tremelimumab safety profile in other indications. Treatment associates with major changes in activated and memory T cells, and ICOS+CD4+ T cells may represent a predictive marker of response as their levels correlate with the clinical course. Based on these results the ongoing phase II study MESOTREM-2012 is exploring a different schedule of treatment with tremelimumab in refractory MM pts.

Key Word: Tremelimumab, Mesothelioma, anti-CTLA-4 monoclonal antibody.

TREATMENT OF NON-HODGKIN LYMPHOMA WITH CAR-TRANSDUCED CD19-SPECIFIC CENTRAL MEMORY DERIVED T CELLS

Leslie Popplewell[1], Christine E. Brown[1], Xiuli Wang[1], Araceli Naranjo[1], Jamie Wagner[1], Wen-Chung Chang[1], William Bretzlaff[1], Brenda Chang[1], Desiree Daniels[1], Julie R. Ostberg[1], Renate Starr[1], ChingLam W. Wong[1], Suzette Blanchard[2], Michelle Mott[3], Bernadette Pulone[3], Michael C. Jensen[4], Stanley R. Riddell[4], *Stephen J. Forman*[1]

[1]*Hematology and Hematopoietic Cell Transplantation, BRI, COHNMC, Duarte, CA*
[2]*Information Sciences, COHNMC, Duarte, CA*
[3]*Nursing Department, COHNMC, Duarte, CA*
[4]*Program in Immunology, Fred Hutchinson Cancer Research Center, Seattle, WA*

We have initiated a first-in-human clinical trial to evaluate the safety and immunologic endpoints of central memory T cell (Tcm) immunotherapy for treatment of Non-Hodgkin Lymphoma (NHL). Because Tcm have a unique capacity for self renewal, proliferation, persistence, and an ability to differentiate into effector T cells that can immediately target tumor cells, we hypothesized that adoptive transfer of such cells is a promising strategy for treating high risk CD19+ disease such as NHL. Thus, we developed a clinical-scale immunomagnetic purification method to isolate CD8+CD45RO+CD62L+ Tcm, genetically modify them to express a CD19-specific chimeric antigen receptor (CAR), and expand them in vitro with IL-2/IL-15. This process results in the procurement of cells for clinical use within 3-6 weeks (i.e., 1-3x10e9 final product derived from 7-15x10e6 Tcm). These Tcm-derived effector cells (Te(cm)) exhibit CD19-specific cytolytic activity and Tc1 cytokine production, consist of a broad repertoire based on TCR Vβ usage, retain expression of central memory markers (e.g., CD62L/CD28), and, upon transfer into NSG mice, exhibit IL-15 dependent engraftment. We also consistently obtain cell products with > 45% CAR expression and an average integrated vector copy number of < 5/cell. Under a phase I/II trial (BB-IND14645, NCT01318317), autologous CD19-specific CD8+ Te(cm) are administered on day+2 following autologous hematopoietic stem cell transplant of NHL patients as a strategy to eradicate minimal residual disease and to establish a reservoir of memory T cells that will incorporate into the recipient's long-lived immune cell repertoire. To date, 2 patients have been treated on this protocol with 5x10e7 Te(cm). After 7 and 2 months, respectively, the HSCT-associated engraftment in these patients is normal, and no dose limiting toxicities or serious adverse events related to T cell infusion have been observed. The patients continue to be tested at scheduled intervals for persistence of gene-modified T cells, and presence of CD19+ B cells as a surrogate for anti-CD19 activity. Other patients continue to be accrued as part of the dose escalation strategy.

Key Word: Adoptive immunotherapy, Chimeric receptors, CD19.

DC SUBSETS/CANCER VACCINES

PREOPERATIVE SIPULEUCEL-T RESULTS IN TUMOR LYMPHOCYTE INFILTRATION IN PROSTATE CANCER SPECIMENS: EVIDENCE OF IMMUNE ACTIVATION AND RESPONSE WITHIN THE PROSTATE TUMOR MICROENVIRONMENT

Lawrence Fong[1], Vivian Weinberg[1], Stephen Chan[1], Jeff Simko[1], Robert B. Sims[2], Nadeem A. Sheikh[2], Peter Carroll[1], Eric J. Small[1]

[1]*Helen Diller Family Comprehensive Cancer Center, UCSF, San Francisco, CA*
[2]*Dendreon Corp., Seattle, WA*

Background: Sipuleucel-T is an FDA-approved autologous cellular immunotherapy for patients with asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer (mCRPC). To date, studies of sipuleucel-T have investigated the immune response in the autologous product and in peripheral blood. The immune effects of sipuleucel-T in prostatic cancer tissue are unknown.

Methods: NeoACT (P07-1; NCT00715104) is an open-label, Phase 2 study of patients with localized prostate cancer who received sipuleucel-T (3 infusions at approximately 2-week intervals), beginning 6-7 weeks prior to radical prostatectomy (RP). The primary endpoint was the change in the frequency of infiltrating lymphocytes from pre-treatment (prostatic biopsy material) to post-treatment with sipuleucel-T (RP specimens), as assessed by immunohistochemistry (IHC).

Results: Of 42 enrolled patients, 37 received all 3 pre-RP sipuleucel-T infusions and were evaluable by IHC. Significant increases (>3 fold) in infiltrating CD3+, CD4+, and CD8+ T cells were observed at the tumor rim (where benign and malignant tissues interface), compared with the pre-treatment biopsy (all pairwise p=0.0001). The majority of CD3+ T cells at the tumor rim were PD-1 and Ki-67 positive. CD4+/FoxP3+ T cells were increased at the tumor rim (~2 fold; P=0.004), but represented a small proportion

of the observed T cells. The frequency of CD20+ B cells was also increased at the tumor rim. This type of lymphocyte infiltration was not seen in a cohort of 12 concurrent cases that did not receive neoadjuvant treatment. Systemic B cell and T cell activation was observed following treatment. Increased expression of activation markers CD134, CD137, CD278, and CD279 were observed in circulating T cells following the first infusion. Activated mature B cells increased during dose preparation in all 3 doses ($P<0.01$); memory B cells were progressively increased ($P<0.05$ third vs. first product). In patients with available peripheral blood samples to assess antibody response (n=13), significant increases in prostatic acid phosphatase (PAP)-specific IgG and IgM antibodies were observed at the time of RP compared with baseline ($P<0.05$; Wilcoxon signed rank test).

Conclusions: Systemic administration of sipuleucel-T was associated with an antigen-specific immune response, and resulted in localized T and B cell infiltrates in resected prostate cancers at the interface of the benign and malignant tissue. This is the first report of immune effects of sipuleucel-T in the prostate tumor micro-environment.

Key Word: Cancer immunotherapy, Prostate cancer, Tumor microenvironment.

A NOVEL DENDRITIC CELL-BASED VACCINE FOR HER-2-POSITIVE EARLY BREAST CANCER

Brian J. Czerniecki[1], Shuwen Xu[2], Ursula Koldovsky[2], Gary K. Koski[3]

[1]*Surgery, University of Pennsylvania, Philadelphia, PA*
[2]*Harrison Department of Surgery Research, University of Pennsylvania, Philadelphia, PA*
[3]*Department of Biological Sciences, Kent State University, Kent, OH*

Twenty-seven patients with HER-2/neu over-expressing ductal carcinoma in situ (DCIS) of the breast were enrolled in a neoadjuvant vaccine trial for safety and immunogenicity of IL-12-secreting dendritic cells pulsed with 6 promiscuous MHC class II-binding peptides plus an additional two HLA-A2.1 class I-binding peptides. The DCs were activated with a combination of interferon-gamma plus a special clinical grade bacterial lipopolysaccharide and injected directly into groin lymph nodes at 4 weekly intervals prior to scheduled surgical resection of DCIS. Post-immunization we observed Th sensitization via ELISPOT against at least one of the 6 promiscuous class II peptides in 22 of 25 (88%) evaluable subjects, while 11 of 13 (84.6%) HLA-A2.1-positive subjects had responses to at least one of the class I peptides. For many of the immunized subjects, these anti-peptide responses proved to be quite durable, with enhanced ELISPOT activity extending beyond 50 months post-vaccination. Interestingly, at the time of surgery, 5 of 27 subjects (18.5%) displayed no evidence of residual DCIS, and among the 22 subjects with remaining DCIS, HER-2 expression fell to virtually undetectable levels in 11 (50%). Immunohistochemical analysis and comparison of pre-immunization biopsy with post-vaccine surgical specimens also showed elaborate infiltrations of CD4+ (Th), CD8+ (CTL) and CD20+ (B cell) lymphocytes into the area of DCIS as an apparent consequence of vaccination. Also of note was a pronounced difference in responsiveness between subjects with estrogen receptor (ER)-expressing disease and those without estrogen receptor. For example, after vaccination no residual DCIS was found in 40% of the ER- subjects, compared to only 5.9% of the ER+ subjects. In addition, continued high HER-2 expression was found in only 10% of the ER- subjects, while it remained elevated in 47.1% of the ER+ subjects ($p<.04$). Finally, within the ER- subject population, we have not observed any in-breast recurrence events, with the earliest patients of this trial now out beyond 88 months post-vaccination. These results indicate that this approach may hold promise for the secondary prevention of early breast cancer, particularly in the ER- patient population.

Key Word: Breast cancer, Cancer vaccine, Dendritic cell.

RANDOMIZED TRIAL OF TWO ACTIVE-SPECIFIC IMMUNOTHERAPY PRODUCTS DERIVED FROM AUTOLOGOUS, PROLIFERATING, SELF-RENEWING TUMOR CELLS IN PATIENTS WITH METASTATIC MELANOMA

Robert O. Dillman[1,2], Andrew N. Cornforth[3], Carol DePriest[4], Edward F. McClay[5], Thomas T. Amatruda[6], Denysha Carbonell[3], Cristina de Leon[1], Robin Ellis[1], Cheryl Mayorga[1], James M. Cubellis[7]

[1]*Hoag Institute for Research and Education, Hoag Hospital, Newport Beach, CA*
[2]*Hoag Family Cancer Institute, Hoag Hospital, Newport Beach, CA*
[3]*California Stem Cell, Inc, Irvine, CA*
[4]*Celerion, Inc, Lincoln, NE*
[5]*Melanoma Research Center of San Diego, Encinitas, CA*
[6]*Hubert H. Humphrey Cancer Center, Robbinsdale, MN*
[7]*CalOptima, Orange, CA*

Only 10% of metastatic melanoma patients survive five years, even though many can achieve substantial tumor reduction by surgical resection and/or radiation therapy and/or systemic therapy. An effective, non-toxic, consolidation immunotherapy may benefit such patients. Self-renewing autologous tumor cells may be an ideal source of tumor immunogen for patient-specific active specific immunotherapy because of expression of antigens associated with tumor stem cells and/or progenitor tumor cells, and unique patient-specific neo-antiogens. We initiated a randomized trial to compare two promising patient-specific immunotherapy cell products that were associated with 5-year survival rates of 28% and 50% in successive single arm trials involving 74 and 54 patients respectively.

Patients had to have a diagnosis of metastatic melanoma and availability of an autologous melanoma cell line. Patients were stratified by whether their most advanced stage had been regional or distant metastases, and by whether they had measurable disease at the time of treatment, then they were randomized to receive irradiated autologous proliferating tumor cells (TC) or autologous dendritic cells (DC) loaded with antigens from such cells. Both products were injected subcutaneously in 500 microgram of granulocyte-macrophage colony stimulating factor, weekly for three weeks and then monthly for five months. Accrual closed prematurely when the cell biology laboratory was closed by the funding institution for budgetary reasons. An analysis was performed in September 2011, when 21/42 patients were deceased, no patients were lost to follow up, and all surviving patients had been followed for at least 6 months after randomization. Patients in the two arms did not differ in baseline characteristics, and all patients received prescribed therapy. Treatment was well tolerated. Survival was superior in the DC arm (HR 0.27, 95% CI 0.098-0.729) with median survival not reached versus 15.9 months, and 2-year survival rates of 72% versus 31% (p=0.007). An updated survival analysis will be performed at the end of September 2012 by which time additional deaths will have occurred, and all surviving patients will have a minimum of 18 months of follow up.

(Supported by the Hoag Hospital Foundation, NCT00436930).

Key Word: Melanoma immunotherapy, DC-based vaccine, Autologous Vaccine AHICE.

TARGETING IMMUNE SUPPRESSION

ENRICHMENT OF CTLA4+CD39+CD25+FOXP3+ REGULATORY T CELLS IN HEAD AND NECK CANCER PATIENTS IS PROMOTED BY THERAPY WITH CETUXIMAB AND CORRELATED WITH CLINICAL OUTCOME

Hyun-Bae Jie[1], Patrick J. Schuler[2,1], Fernando Concha-Benavente[1], Raghvendra Srivastava[1], Steve Lee[1], Robert L. Ferris[1]

[1]*Pathology, Immunology and Otolaryngology, University of Pittsburgh Cancer Institute and University of Pittsburgh School of Medicine, Pittsburgh, PA*
[2]*Otorhinolaryngology, University Duisburg-Essen, Essen, Germany*

The EGFR-targeted antibody, cetuximab, is clinically effective against head and neck cancer (HNC) in conjunction with chemo/radiotherapy (CRT), but only in 15 - 20% of patients. A better understanding of the influence of cetuximab on the host immune system and the tumor microenvironment, including regulatory T cells (Treg) and NK cell function, may help to increase clinical response rates. Here we report that the frequency of peripheral blood Treg in HNC patients with active disease is significantly increased after cetuximab-based therapy. A significant enrichment of circulating and intratumoral $CD4^+CD25^+FOXP3^+$ Treg were detected, which were increased in tumor-infiltrating lymphocytes (TIL) compared with peripheral blood lymphocytes (PBL). We also observed that immune checkpoint inhibitory receptors (IRs, CTLA-4, TIM-3, PD-1 but not LAG-3) were significantly upregulated on $FOXP3^+CD25^{hi}$ intratumoral Treg when compared to those in peripheral blood lymphocytes (PBL). Moreover, ectonucleotidase CD39 that contributes to generating adenosine, a pivotal immune suppressive metabolite in the tumor microenvironment, was highly upregulated and tightly correlated with phenotype of Treg cells, defined by CD25, FOXP3 and CTLA-4 expression in intratumoral Treg cells. Although patients treated with cetuximab exhibited variable FOXP3, CTLA-4, and CD39 expression on intratumoral Treg cells, their expression levels at baseline were highly upregulated on these suppressive TIL. In addition, cetuximab/NK cells-mediated ADCC was strongly suppressed by autologous $CD4^+CD39^+CD25^+$ Treg cells, which is mediated by Treg-derived TGF-β. Furthermore, lower Treg frequency bfore treatment was associated with better clinical response to cetuximab treatment. Together, our findings reveal that in both tumor and peripheral blood of HNC patients, $FOXP3^+$ Treg cells are highly enriched in the tumor microenvironment by cetuximab treatment and associated with clinical outcome. These results suggest that functional inhibition of T cells using blockade of CTLA-4 or CD39 enzymatic activity may enhance cetuximab immunotherapy by inhibiting immune suppressive activities of Treg cells in the tumor microenvironment.

Key Word: Regulatory T cells, NK cells, Tumor microenvironment.

MIR-124 AS A NOVEL IMMUNOTHERAPEUTIC MOLECULE TO REVERSE GLIOMA-MEDIATED IMMUNE SUPPRESSION AND ENHANCE ANTI-TUMOR CLEARANCE

Amy B. Heimberger[1], Jun Wei[1], Ling-Yuan Kong[1], Fei Wang[1], Shuo Xu[1,5], Tiffany Doucette[1], Sherise D. Ferguson[1], Yuhui Yang[1], Kayla McEnery[1], Krishan Jethwa[1], Olsi Gjyshi[1], Wei Qiao[2], Frederick Lang[1], Ganesh Rao[1], Greg Fuller[3], George A. Calin[4]

[1]*Neurosurgery, The University of Texas MD Anderson Cancer Center, Houston, TX*
[2]*Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX*
[3]*Neuropathy, The University of Texas MD Anderson Cancer Center, Houston, TX*
[4]*Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX*
[5]*Neurosurgery, Qilu Hospital of Sandong University, Jinan, China*

MicroRNAs (miRs) have been shown to modulate critical gene transcripts involved in tumorigenesis, but their role in tumor-mediated immune suppression is unknown. In this study, we evaluated miRNAs that are preferentially down-regulated in malignancy and that interact with immune suppressive pathways as potential new therapeutics. On the basis of miRNA-gene expression of gliomas using tissue microarrays, in situ hybridization, and molecular modeling, we selected miR-124 as the lead candidate for modulating signal transducer and activator of transcription 3 (STAT3), a key molecular hub of tumor-mediated immune suppression. In a glioma tissue microarray, miR-124 expression was significantly down modulated in all grades and types of gliomas relative to normal brain. Upon up regulating miR-124 in glioma cancer stem cells (gCSCs), STAT3 was inhibited; this inhibition reversed tumor-mediated immune suppression, as reflected by an increase in T cell proliferation, Foxp3+ regulatory T cell (Treg) inhibition, and pro-inflammatory immune response up regulation. Treatment of immune-suppressed glioblastoma patient T cells with miR-124 induced a marked effector response. Furthermore, the in vivo local or systemic administration of miR-124 in multiple murine models of glioma, including genetically engineered heterogeneous high-grade gliomas, exerted potent anti-glioma therapeutic effects secondary to STAT3 inhibition in the immune cell population and secondarily enhanced effector responses in the local tumor microenvironment. In summary, miR-124 may be a novel immune-activating agent for glioma treatment (including all grades and types); by exploiting the immune system to mediate direct tumor cytotoxicity, the vexing problem of miR delivery to tumors has been overcome.

Key Word: Immunosuppression, Tumor immunity, Immunotherapy.

IMMUNITY OF ONCOLYTIC VIRUSES

TROPISM OF ONCOLYTIC VACCINIA VIRUS CONSTRUCTS FOR HUMAN MONONUCLEAR CELL SUBSETS

Nanhai G. Chen[1,2], Mehmet O. Kilinc[1], Qian Zhang[1,2], Jason Aguilar[1], Desislava Tsoneva[3], Uma Patel[1], Boris Markosian[4], Maysam Pessian[4], Boris Minev[1,4,5], Aladar A. Szalay[1,2,3]

[1]*Genelux Corporation, San Diego, CA*
[2]*Radiation Oncology, University of California San Diego, La Jolla, CA*
[3]*University of Wurzburg, Wurzburg, Germany*
[4]*University of California San Diego, La Jolla, CA*
[5]*Division of Neurosurgery, University of California San Diego, La Jolla, CA*

Background: Recent clinical trials with oncolytic viruses demonstrated their safety, and in some cases tumor selectivity. However, very little is known about the intricate interaction of the oncolytic viruses with the host immune system. Understanding this process is a key element in revealing the mechanisms of viruses' antitumor activity, and an essential prerequisite in designing more effective oncolytic viral constructs.

Methods: We analyzed the tropism of clinically relevant oncolytic vaccinia virus constructs for human mononuclear cell subsets. We used four constructs: GLV-1h68 - derived from the LIVP strain; GLV-1h254 - a derivative of GLV-1h68; GLV-2b372 - derived from the LIVP 1.1.1. strain (plaque purified isolate of the nonattenuated LIVP strain), and GLV-0b347 - derived from the WR strain (Figure 1).

The ability of these constructs to infect and amplify in the human mononuclear cell subsets was studied with fluorescent microscopy, flow cytometry, and plaque assays for viral replication.

Results: We found that our oncolytic virus constructs preferentially infect monocytes and activated T cells, followed by B-lymphocytes, NK cells and the resting T lymphocytes. The LIVP 1.1.1.-based construct was the most efficient in infecting the mononuclear cell subsets, followed by the WR-based construct and both LIVP-based constructs. Cytotoxicity of all virus constructs for the infected mononuclear cells was similar at each tested time point. The results of the plaque assays for viral replication suggested an abortive infection in all tested subsets. In all experiments, the viral amplification and cytotoxicity were significantly higher in the control cancer cells than in any of the mononuclear cell subsets.

Conclusions: Our findings corroborate the initial clinical trial findings that these constructs are safe as they infect but do not kill most of the healthy human mononuclear cells, in contrast to most cancer cell lines tested to date. These findings are very relevant to the development of optimized clinical grade oncolytic vaccinia viruses and understanding the mechanisms of oncolytic virus-host interactions.

Key Word: Immunotherapy, Oncolytic viruses, Immunology.

Figure 1

EFFECT OF HCV VIRAEMIA ON NK CELLS

Maria Libera Ascierto[1,2], Cathy Schechterly[1], Davide Bedognetti[1], Valeria De Giorgi[1], Jenny Reinboth[1], Sara Tomei[1], Lorenzo Uccelini[1], Quizhen Liu[1], Ena Wang[1], Harvey Alter[1], Andrea De Maria[2], Francesco Marincola[1]

[1]*National Institutes of Health, Bethesda, MD*
[2]*University of Genoa, Genoa, Italy*

Besides the central role of NK cells in the pathogenesis of many viral infections, there is surprisingly little known about NK cells in HCV persistent viraemia. Imbalance of activating and inhibitory NK cell receptors contributes to the outcome of chronic HCV infection, although it has not been so well described. In the current study, we evaluated molecular profile of peripheral NK cells from healthy donors, chronically viraemic HCV-treatment-naïve patients and patients who spontaneously achieved virus eradication by whole-genome gene expression analysis (Affymetrix Human Gene ST.1.0 Arrays). FACS analysis of target activating cytoxicity receptors (NCR1, NCR2 and NCR3) was also assessed. Class comparison showed an up regulation of genes involved in the activation of effector functions of NK cells, such as GNLY, NKG2E, NKG2F and NKG2C in patients with spontaneous eradication of virus infection. On the contrary, an enhanced expression of genes involved in IFN signaling and IL-15 production, such as CXCL11, HLA-DOB, PTK, IFNβ and IFNα ,was found to occur in chronically viraemic HCV patients. As previously described, FACS analysis shows an overexpression of NCRs in patients bearing chronic viraemia. Counter intuitively, neither a statically significant difference nor a trend between the group in comparisons were detected when NCRs were evaluated at the transcriptional level. Taken all together, our findings indicate that NK cells from chronic infected patients display an (reactive?) overexpression of the IFN pathways already at the transcriptional level with an activation of NCRs only gained at the protein level suggesting the interference of post-transcriptional mechanisms (eg. microRNA). Interestingly, other markers of immunoactivation, (i.e., immuno-effector function genes; GNLY) and other activating receptors are upregulated at the transcriptional level by the NK cells of patients who successfully eradicated viral infections. The evaluation of the corrisponding proteins expression on cell surface is currently ongoing. In conclusion we showed NK molecular signatures associated with HCV viraemia persistence. The functional interpretation of these data will need the integrated analysis of gene and protein expression as well as a detailed assessment of post-translational mechanisms.

Key Word: HAV/HBV/HCV infections, Immune escape, Innate immunity.

COMBINATION THERAPY OF INTRATUMORAL CRT/E7 VACCINIA VIRUS AND CISPLATIN TREATMENT ENHANCE THE ANTIGEN-SPECIFIC T CELL IMMUNE RESPONSES AND THERAPEUTIC ANTITUMOR EFFECTS

Sung Yong Lee[1,5], Tae Heung Kang[1], Jayne Knoff[1], Chien-Fu Hung[1,4], Tzyy Choou Wu[1,2,3]

[1]*Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, MD*
[2]*Obstetrics and Gynecology, Johns Hopkins Medical Institutions, Baltimore, MD*
[3]*Molecular Microbiology and Immunology, Johns Hopkins Medical Institutions, Baltimore, MD*
[4]*Oncology, Johns Hopkins Medical Institutions, Baltimore, MD*
[5]*Department of Internal Medicine, Korea University Medical Center, Seoul, Republic of Korea*

Cervical cancer is the third most common female cancer in the world. Despite current treatment regimens, including radiation therapy and chemotherapy, stages 3 and 4 cervical cancers have a low five-year survival rate. Cancer immunotherapy has emerged as an alternative innovative therapy that may improve survival rates. Here we utilize a cervical cancer model and employ the chemotherapeutic agent cisplatin to generate an accumulation of CD11c+ dendritic cells (DCs) in tumor loci along with a vaccinia virus vector expressing the chimeric protein calreticulin linked to HPV-16 E7 (CRT/E7-VV) to generate an E7-specific CD8+ T cell response. In this study, we explored the treatment of E7-expressing tumor-bearing mice with cisplatin in combination with intratumoral or intraperitoneal injection of CRT/E7-VV. We found that the combination of cisplatin and intratumoral injection of CRT/E7-VV significantly inhibited tumor growth and increased E7-specific CD8+ T cells in blood compared to cisplatin treated mice receiving intraperitoneal injection of CRT/E7-VV or mice treated with cisplatin alone. Furthermore, combination treatment with cisplatin and intratumoral CRT/E7-VV generated a systemic antitumoral and therapeutic response and reduces immunosuppressive myeloid-derived suppressor cells. The general methodology employed in this study may potentially be utilized as a platform to improve cancer immunotherapy. It will be important to continue examining possibilities for utilizing the treatment discussed here in combination with current treatment regimens for to improve survival of advanced stage cervical cancer.

Key Word: Cancer vaccine, Calreticulin, Chemotherapy.

SATURDAY, OCTOBER 27, 2012

COMBINING IMMUNOTHERAPY AND OTHER THERAPIES

PD-1/PD-L1 BLOCKADE AFTER TRANSIENT LYMPHODEPLETION TO TREAT MYELOMA

Tyce Kearl, Weiqing Jing, Bryon D. Johnson

Medical College of Wisconsin, Milwaukee, WI

Early phase clinical trials targeting the programmed death receptor-1/ligand-1 (PD-1/PD-L1) pathway to overcome tumor-mediated immunosuppression have reported promising results for a variety of cancers. This pathway appears to play an important role in the failure of immune reactivity to malignant plasma cells in multiple myeloma patients, as the tumor cells express relatively high levels of PD-L1 and T cells show increased PD-1 expression. We have found that T cells in the tissues where myeloma cells reside upregulate PD-1 and are suppressed when this receptor is engaged by PD-L1. In the current study, we demonstrate that PD-1/PD-L1 blockade with a PD-L1-specific antibody elicits rejection of a murine myeloma when combined with lymphodepleting irradiation. This particular combined approach has not previously been shown to be efficacious in other tumor models, and efficacy has only been observed when other immune therapies have been added to this combination. The anti-tumor effect of lymphodepletion/anti-PD-L1 therapy was most robust when tumor antigen-experienced T cells were present either through cell transfer or survival after non-myeloablative irradiation. In vivo depletion of CD4 or CD8 T cells, but not NK cells, completely eliminated anti-tumor efficacy of the lymphodepletion plus anti-PD-L1 therapy, indicating that both T cell subsets are necessary for tumor cell rejection. Elimination of myeloma by T cells occurs relatively quickly as tumor cells in the bone marrow were nearly non-detectable by five days after the first anti-PD-L1 treatment, suggesting that anti-myeloma reactivity is primarily mediated by pre-activated T cells and not newly generated myeloma-reactive T cells. The CD4 T cell requirement is interesting since we speculate that pre-activated CD8 CTL are primarily responsible for the elimination of tumor cells; thus, an ongoing interaction between CD4 and CD8 T cells may be necessary to facilitate tumor cell killing. Anti-PD-L1 plus lymphodepletion did not improve survival in two solid tumor models, suggesting that the effect may be limited to hematologic malignancies. In summary, our results support the clinical testing of lymphodepletion and PD-1/PD-L1 blockade as a novel therapeutic approach for improving the survival of patients with multiple myeloma.

Key Word: Immune-mediated tumor rejection, Multiple myeloma, PD-1.

PHARMACOKINETICS AND IMMUNOLOGICAL EFFECTS OF HUMAN IL-15/IL-15RA HETERODIMERIC COMPLEXES IN MICE AND MACAQUES

Cristina Bergamaschi[1], Antonio Valentin[1], Viraj Kulkarni[1], Jenifer Bear[1], Margherita Rosati[1], Candido Alicea[1], Raymond Sowder[2], Elena Chertova[2], Barbara K. Felber[1], George N. Pavlakis[1]

[1]*Vaccine Branch, Center for Cancer Research, Frederick National Laboratory for Cancer Research, Frederick, MD*
[2]*Retroviral Protein Chemistry Core, AIDS and Cancer Virus Program, SAIC-Frederick, Inc., Frederick National Laboratory for Cancer Research, Frederick, MD*

IL-15 is a member of the γ-chain family of cytokines with non-redundant effects on the immune system, including stimulation of the proliferation, survival and function of NK and T cells. Due to its properties, IL-15 has potential for use in different clinical settings such as cancer and infectious disease immunotherapy. We have previously showed that co-expression of IL-15 and the IL-15 Receptor alpha (IL-15Rα) in the same cell allows for efficient production and secretion of bioactive IL-15 heterodimer in vivo, whereas the single-chain IL-15 is unstable and poorly secreted. In addition, analysis of sera from lymphoablated melanoma patients revealed that circulating IL-15 exists exclusively in association with soluble IL-15Rα (sIL-15Rα), suggesting that the IL-15 heterodimer is the natural biologically relevant form of the cytokine in vivo.

We developed IL-15/sIL-15Rα expression vectors producing high levels of bioactive cytokine. We have also developed stable cell lines overproducing IL-15/sIL-15Rα heterodimers. Delivery in mice and macaques of IL-15/sIL-15Rα purified protein complexes and injection of IL-15/sIL-15Rα-expressing DNA gave similar results, resulting in a great expansion of NK and T cells. We compared pharmacokinetics and biological effects of purified IL-15 heterodimers with E.Coli produced single-chain IL-15. Upon intraperitoneal injection in mice, IL-15 heterodimers showed a favorable pharmacokinetics and induced a greater proliferation of NK and CD8 T cells in spleen and lung, in comparison to single-chain IL-15. Upon intravenous injection in macaques, the plasma half-life of IL-15 heterodimers was 6x longer than single-chain IL-15. Interestingly, subcutaneous injection (s.c.) of IL-15 heterodimers in macaques resulted in persistent bioactive level of plasma IL-15 for up to 72 hours. Five repeated administrations of IL-15 heterodimers in macaques by s.c. route every 3 days resulted in a massive expansion of NK, γδ and CD8 T cells in the peripheral blood.

In conclusion, in comparison to single-chain IL-15, heterodimeric IL-15 cytokine is more stable in vitro and in vivo, has longer plasma half-life and is more bioactive in mice and macaques. The favorable pharmacokinetics/pharmacodynamics profile of the heterodimers allow lower dose, simple s.c. delivery and lower the possibility of toxicity due to cytokine spike, therefore it is the most favorable form for clinical applications of IL-15.

Key Word: Cancer immunotherapy, Interleukin-15, CD8+ T cells.

ADXS11-001 LM-LLO IMMUNOTHERAPY TARGETING HPV-E7: PRELIMINARY SAFETY AND SURVIVAL DATA FROM A PHASE 2 STUDY IN INDIAN WOMEN WITH RECURRENT/REFRACTORY CERVICAL CANCER

Robert Petit[1], Partha Basu[2]

[1]*Advaxis, Inc., Princeton, NJ*
[2]*Chittaranjan National Cancer Institute, Kolkata, India*

ADXS11-001 (ADXS-HPV) Lm-LLO immunotherapy is a live attenuated Listeria monocytogenes (Lm) bioengineered to secrete a HPV-16-E7 fusion protein targeting HPV transformed cells. The Lm vector serves as its own adjuvant and infects APC where it cross presents, stimulating both MHC class I and II pathways resulting in specific T-cell immunity to tumors. Here we describe preliminary safety and survival data associated with ADXS-HPV treatment in Lm-LLO-E7-015, an ongoing randomized Phase 2 study being conducted in India in 110 patients with recurrent/refractory cervical cancer who have been treated previously with chemotherapy, radiotherapy or both.

Patients are randomized to either 3 doses of ADXS11-001 at $1x10^9$ cfu or 4 doses of ADXS11-01 at $1x10^9$ cfu with cisplatin chemotherapy. Naprosyn and oral promethazine are given as premedication and a course of ampicillin is given 3 days after infusion thereby clearing any residual vector. Patients receive CT scans at baseline and 3, 6, 9, 12 and 18 months. The primary endpoint is 12 month survival.

As of May 18, 2012, 109 patients have received 255 doses of ADXS11-001The percentage of patients alive at 6 months is 65% (47/72); at 9 months 40% (22/55) and at 12 months 31% (13/42). Although not always observed in immunotherapy that improves survival, tumor responses have been observed in both treatment arms with 4 complete responses (elimination of tumor burden), 5 partial responses (≥30% reduction in tumor burden) by RECIST and 33/76 (43%) patients with stable disease (≤20% increase in tumor burden or ≤ 30% reduction) in tumor burden. Clinical benefit is not HPV strain specific as tumor responses have been observed in patients infected with several different high risk HPV strains including HPV16, 18, 31, 33, and 45.

ADXS11-001 Treatment has been well tolerated with 95 mild-moderate (Gr 1-2), and 1 Gr3 (dyspnea) adverse events possibly related to the immunotherapy reported in 36% (39/109) of patients. These non-serious adverse events were predominately transient, non-cumulative cytokine release syndrome symptoms that develop within hours of infusion. These symptoms typically responded to symptomatic treatment, or resolved without treatment and were not cumulative or delayed in onset.

ADXS11-001 (ADXS-HPV) immunotherapy can be safely administered to patients with advanced cancer alone and in combination with chemotherapy. ADXS11-001 is well tolerated and presents a predictable and manageable safety profile. Early signs of clinical benefit including CRs and PRs in a refractory disease setting merit further investigation. Updated findings will be presented at the meeting.

Key Word: Cancer immunotherapy, Advanced cancer, Active immunotherapy.

HOT TOPIC SESSION II

12-CHEMOKINE GENE SIGNATURE IDENTIFIES LYMPH NODE-LIKE STRUCTURES IN MELANOMA: POTENTIAL FOR PATIENT SELECTION FOR IMMUNOTHERAPY?

J. L. Messina, D. A. Fenstermacher, S. Eschrich, X. Qu, A. E. Berglund, M. C. Lloyd, M. J. Schell, V. K. Sondak, J. S. Weber, and J. J. Mulé

Moffitt Cancer Center, Tampa, FL, USA

We have interrogated a 12-chemokine gene expression signature (GES; derived from an immune-related, metagene grouping analysis) on genomic arrays of 14,492 distinct solid tumors and show broad distribution across different histologies (24 tissue types). We hypothesized that this 12-chemokine GES might accurately predict a unique intratumoral immune reaction in stage IV (non-locoregional) melanoma metastases. Melanomas with a high chemokine signature showed increased expression values in all 12 chemokine genes when compared to melanomas with a low chemokine signature. Statistical tests of differences among the 12 genes confirmed principal component analysis results, indicating up-regulation of gene expression (p value ranges, 3.25e-05 to 2.22e-16). The 12-chemokine GES predicted the presence of unique, lymph node-like structures. These structures have the general appearance of "typical" peripheral lymph nodes, albeit much smaller in size, and are constructed of the necessary immune components, including lymphatics, CD86+ antigen presenting cells, and B cell follicles with adjacent T cell (CD4+ and CD8+) zones. Of interest, FoxP3+ cells (putative T regulatory cells) were found to be very few in numbers. The direct correlation between the 12-chemokine GES score and the presence of unique, lymph nodal structures was also associated with better overall survival of the subset of melanoma patients. There was a highly significant (p=0.008) association between increased survival and the value of the mean score of the 12-chemokine GES. One patient with long survival duration had received immunotherapy with an anti-CTLA4 antibody (ipilimumab) and has had a partial response of over 30 months duration. The use of this novel 12-chemokine GES may reveal basic information on in situ mechanisms of the anti-tumor immune response, potentially leading to improvements in the identification and selection of melanoma patients most suitable for immunotherapy.

This work was supported in part by the NCI-NIH (1 R01 CA148995-01 to JJM), the V Foundation, and the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation.

SINGLE CELL HIGH THROUGHPUT TECHNOLOGIES IMMUNE MONITORING

DISSECTION OF ANTI-CTLA4-INDUCED CYTOTOXIC T CELL RESPONSES IN MELANOMA

Pia Kvistborg[1], Daisy Philips[1], Sander Kelderman[1], Bianca Hemskerk[1], Christian Ottensmeier[2], Antoni Ribas[3], Daniel Speiser[4], Christian Blank[1], John Haanen[1], Ton Schumacher[1]

[1]*Department of Immunology, Netherlands Cancer Institute, Amsterdam, Netherlands*
[2]*Southampton University Hospitals, Southampton, United Kingdom*
[3]*UCLA Jonsson Comprehensive Cancer Center, LA, CA*
[4]*Ludwig Center, Lausanne, Switzerland*

There is strong evidence that melanoma-reactive T cell responses induced by immunotherapeutic interventions such as anti-CTLA4 (Ipilimumab) treatment can exert clinically meaningful effects. However, at present we have very little information on how these therapies influence tumor-specific T cell responses. Furthermore, as the number of potential melanoma-associated antigens to which these responses can be directed is very high, classical strategies to map cytotoxic T cell reactivity do not suffice. Knowledge of such reactivities would be useful to design targeted strategies, selectively aiming to induce immune reactivity against these antigens.

We have aimed to address this issue by designing MHC class I molecules occupied with UV-sensitive 'conditional' peptide ligands, thereby allowing the production of very large collections of pMHC complexes for T cell detection. Secondly, we have developed a 'combinatorial coding' strategy that allows the parallel detection of dozens of different T cell populations within a single sample. The combined use of MHC ligand exchange and combinatorial coding allows the high-throughput dissection of disease- and therapy-induced CTL immunity. We have now used this platform to monitor immune reactivity against a panel of 145 melanoma-associated epitopes in patients receiving Ipilimumab treatment.

Comparison of PBMC samples from 26 melanoma patients pre- and post-therapy demonstrates a significant increase in the number of detectable melanoma-associated CD8 T cell responses (p=0.006). Furthermore, kinetic data on T cell responses during Ipilimumab therapy suggest that this broadening generally occurs within weeks after start of therapy. The pattern of reactivities detected is highly patient specific, and this is most pronounced for reactivities directed against cancer/testis antigens.

Interestingly, the magnitude of melanoma-specific T cell responses that was already detected prior to start of therapy was not significantly altered (p=0.8).

These results establish the pattern of melanoma-specific T-cell reactivity induced by anti-CTLA4 treatment and form a benchmark for evaluation of other immunotherapeutic interventions, like anti-PD1 treatment, that are currently undergoing clinical evaluation. Furthermore, the data suggest that the clinical activity of Ipilimumab may be mostly due to epitope spreading, rather than through enhancement of pre-existing immune activity.

Key Word: CD8+ T cells, CTLA-4, Immunotherapy.

HIGH-THROUGHPUT IDENTIFICATION OF BIOMARKERS OF LONGEVITY IN IPILIMUMAB-TREATED MELANOMA PATIENTS USING POLYCHROMATIC FLOW CYTOMETRY

Janet Siebert[1], Edwin B. Walker[2], Brendan D. Curti[2], Walter J. Urba[2]

[1]*CytoAnalytics, Denver, CO*
[2]*Earle A. Chiles Research Institute, Robert W. Franz Cancer Research Center, Providence Cancer Center, Portland, OR*

PBMCs from 12 patients with advanced stage IV melanoma treated with 4 cycles of ipilimumab (Expanded Access Program) were interrogated using a 12-parameter flow cytometry staining panel to delineate discrete memory and effector T cell subsets, and a 10-parameter panel to delineate T regulatory (Treg) cell subsets. Patients received 4 doses of ipilimumab administered at weeks 1, 4, 7, and 10. Analysis was performed on PBMCs collected at week 1 prior to the first dose, at week 7 after two doses, and at week 12. The 12-color memory/effector panel consisted of CD3, CD4, CD8, CCR7, CD45RA, CD27, CD28, ICOS, Ki67, PD-1, NKG2D, and CTLA-4. The 10-color Treg panel consisted of CD3, CD4, CD25, FoxP3, CD45RA, Helios, ICOS, Ki67, NKG2D, and PD-1. Application of Exhaustive Expansion (Siebert et al. JTM 2010) generated nearly 20,000 subphenotypes for each parent population (CD4+ and CD8+) in the memory/effector panel and 6,561 subphenotypes in the Treg panel. To identify putative biomarkers of longevity, we analyzed these phenotypes for correlations with survival. As we were particularly interested in predicting patients likely to show a durable response to therapy, we searched for phenotypes for which the baseline readouts or the week 7 fold-change readouts (week 7/baseline) could predict survival >400 days (7 patients) with 100% sensitivity and at least 60% specificity. We further limited our search to phenotypes that were a credible percentage of the overall parent population (>= 0.5% of CD4+ or CD8+), and, in the case of week 7 fold-change readouts, showed a fold change >= 2 for each of the "long-lived" patients; and to phenotypes in which the readouts for the "long-lived" patients were well separated from the majority of the "short-lived" patients (at least 3 of 5 short-lived patients having readouts <= 80% of the minimum readout of the long-lived patients). In the memory/effector panel, we identified 32 phenotypes in which the week 7 fold change matched these criteria. All of these phenotypes were CD4+ and none were CD8+. The probability of this

occurring by random is approximately 1 in 4 billion (0.5^{32}). Additionally, all phenotypes were ICOS+. The probability of this occurring by random is approximately 1 in 2.5 quadrillion (0.33^{32}). Further analysis of the 32 phenotypes suggests that "long-lived" patients rather than "short-lived" patients are more likely to show large fold increases in early activated memory CD4+ T cells. The ability to predict clinical response early in the course of therapy would have important impact on patient care. Thus, we are planning to validate these findings in a larger group of patients.

Key Word: Flow cytometry, Biomarker, Ipilimumab.

PRESIDENTIAL ABSTRACT SESSION

INHIBITION OF GLYCOLYTIC FLUX ENHANCES CD8+ T CELL MEMORY, STEMNESS AND ANTI-TUMOR FUNCTION

Madhusudhanan Sukumar[1], Jie Liu[2], Yun Ji[1], Rahul Roychoudhuri[1], Zhiya Yu[1], Christopher Klebanoff[1], Toren Finkel[2], Nicholas Restifo[1], Luca Gattinoni[1]

[1]*Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD*
[2]*Center for Molecular Medicine, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD*

The ability of tumor-reactive T cells to eradicate tumors following adoptive transfer correlates with their capacity to robustly proliferate and persist for a long period of time. These qualities are predominantly found in naïve and less differentiated memory cells such as memory stem cells (TSCM) and central memory cells (TCM) but the determinants of these attributes are poorly understood. While numerous transcriptional and epigenetic changes have been implicated in the generation and maintenance of various T cell subsets, it remains unclear whether changes in cellular metabolism have an influence on T cell fate and function. We found that naïve T cells, which rely on fatty acid oxidation as a primary source for ATP generation, dramatically shifted to a glucose metabolism following antigen stimulation and effector differentiation. Sorting effector cells based on their glucose uptake revealed that cells incorporating less glucose had an enhanced ability to engraft and establish long-term memory following adoptive transfer suggesting that glucose metabolism might determine T cell fate decisions. Specific blockade of glycolysis during T cell priming by the hexokinase inhibitor, 2-deoxyglucose (2-DG) prevented effector differentiation resulting in the generation of memory CD8+ T cells. Furthermore, we found that genes that transduce Wnt β-catenin signaling that are related to T cell stemness such as T cell factor 7 (Tcf7) and lymphoid enhancer binding-factor 1 (Lef1) were dramatically increased in CD8+ T cells sorted for low glucose and also in 2DG treated CD8+ T cells compared to untreated controls. Most importantly, we observed a 100-fold increase in the frequency of secondary memory CD8+ T cells detected in lymphoid and non-lymphoid organs and an enrichment of TCM over senescent KLRG1+ T cells upon adoptive transfer of 2DG-treated cells compared to controls. In tumor-bearing mice, 2-DG treated cells exhibited increased tumor-infiltration, cytokine functionality, and resulted in the regression of large-vascularized tumors. 2-DG treatment led to sustained activation of Foxo1, a transcription factor that promotes T cell memory, through inhibition of the mTOR pathway. These findings identify glycolysis as a key metabolic pathway that limits T cells from entering into the memory pool and provide a basis for the rational design of new adoptive immunotherapies through the specific modulation of glucose metabolism.

Key Word: Adoptive immunotherapy, Memory CD8+ T cells, Immune-mediated tumor rejection.

FORCING NF-κB IN T CELLS PROMOTES TUMOR REJECTION

Cesar Evaristo, Luciana Molinero, Thomas Gajewski, Maria-Luisa Alegre

University of Chicago, Chicago, IL

T cells play an important role in the elimination of tumors. Tumor-specific T cells can be found in cancer patients despite tumor growth. However, in tumor-bearing hosts, tumor-specific T cells can have reduced viability, be intrinsically anergized, extrinsically suppressed, or lack sufficient effector function to successfully reject tumors. Therapeutic strategies aimed at promoting T cell survival and amplifying T cell differentiation/effector function would be extremely desirable as novel cancer therapies.

NF-κB activity has been reported to be reduced in T cells from tumor-bearing hosts. Our previous results indicate that reduced NF-κB activation results in impaired survival of T cells, decreased Th1 and Th17 differentiation and increased iTreg differentiation. Mice with reduced T cell-NF-κB activity fail to reject cardiac and pancreatic islet allografts in the absence of any pharmacological treatment. We hypothesize that forced activation of NF-κB in T cells should have the opposite effect and promote T cell survival, facilitate Th1/Th17 differentiation and prevent iTreg differentiation, which would be beneficial to reject tumors.

We generated mice expressing a constitutively active form of IKKβ (CA-IKKβ) in T cells. Ectopic expression of CA-IKKβ resulted in phosphorylation of NF-κB. Transgene expression was limited to CD4+, CD8+ and NKT cells and T cells showed increased NF-κB activation and nuclear translocation. T cell numbers were comparable to littermate controls, but CA-IKKβ mice had fewer Tregs and increased frequency of activated T cells that produced IFNγ upon re-stimulation. When B16-SIY melanoma cells were injected subcutaneously, tumors grew progressively in control littermates, whereas

they were rejected by mice expressing CA-IKKβ in T cells. CA-IKKβ expressing T cells were necessary for tumor control, as shown by antibody-mediated depletion of CD4+ and CD8+ T cells. Furthermore, adoptive transfer of CA-IKKβ-expressing, but not wild-type, T cells into immune-compromised (RAG-deficient) hosts prior to inoculation of tumor cells was sufficient for tumor control. Tumor control was associated with a massive increase in the number of tumor-specific IFNγ-producing CD8+ T cells and IKKβ-CA+ CD8+ T cells were able to control tumor growth in the absence of CD4+ T cell help. Interestingly, on the other hand, IKKβ-CA+ CD4+ T cell help was sufficient to induce tumor control by WT CD8+ T cells. Finally, enhanced tumor control was observed in immune-competent mice when fewer than 5% of T cells expressed CA-IKKβ.

Our results demonstrate NF-κB to be at the cross-roads of major T cell fate decisions that uniquely synergize for control of tumor growth and may be translatable to the clinic.

Key Word: T cells, Melanoma.

TGFβ IS A MASTER REGULATOR OF THE PRO-IMMUNOGENIC EFFECTS OF RADIOTHERAPY

Claire Vanpouille-Box[1], Karsten A. Pilones[1], Sophie Bouquet[2], Jiri Zavadil[3], Silvia Formenti[2], Mary-Helen Barcellos-Hoff[2], Sandra Demaria[1]

[1]*Pathology, NYU School of Medicine, New York, NY*
[2]*Radiation Oncology, NYU School of edicine, New York, NY*
[3]*Pathology, NYU Cancer Institute and NYU Center for Health Informatics and Bioinformatics, New York, NY*

Radiation therapy has the potential to convert the tumor into an in situ individualized vaccine by inducing immunogenic cancer cell death and pro-inflammatory cytokines and chemokines; however this potential is rarely realized by irradiation alone. We hypothesized that radiation-induced immunosuppressive factors may hinder its pro-immunogenic effects. Transforming growth factor β (TGFβ) has immunosuppressive function for dendritic cells and T cells and is activated by radiation. Here we tested the hypothesis that inhibiting TGFβ during radiation treatment would induce an immunogenic response.

Poorly immunogenic, highly metastatic 4T1 carcinoma cells were injected s.c. in syngeneic BALB/c mice (day 0). TGFβ neutralizing 1D11 or isotype control 13C4 monoclonal antibodies were given i.p. (200μg/mouse) every other day from day 12 to 28. Tumors were irradiated with 6 Gy on five consecutive days beginning on day 13. Tumor growth was measured consecutively. Mice were euthanized at day 21 for analysis, at day 28 for enumeration of lung metastases, or followed for survival. Gene expression profiles were obtained using Affymetrix mouse genome 430 2.0 array.

Tumor growth rates and the frequency of lung metastases were similar in mice receiving control antibody or 1D11 alone. Radiation treatment caused significant ($p=0.0065$) tumor growth delay but did not inhibit lung metastases. In contrast, mice treated with both 1D11 and radiation exhibited significantly greater tumor growth control and reduced lung metastases ($p<0.0001$), and significantly prolonged survival ($p<0.005$). As expected, TGFβ signalling was inhibited with 1D11 as measured in CD4+ and CD8+ T cells from tumor-draining lymph nodes at day 21. CD8+ T cells producing IFNγ in response to a tumor-specific antigen were detected only in mice treated with 1D11 and radiation. Expression profiles showed that genes associated with immune response and T cell activation were upregulated in irradiated tumors of mice treated with 1D11 compared to other treatment groups. In vivo depletion experiments demonstrated that T cells were essential for the improved tumor control and inhibition of lung metastases of mice treated with 1D11 and radiation.

These data support a critical role for TGFβ as a regulator of the pro-immunogenic effects of local tumor radiotherapy. Inhibition of TGFβ during radiotherapy may promote self-immunization and achieve systemic control of metastatic disease.

Supported by DOD BCRP grant BC100481P2.

Key Word: Breast cancer, Radiotherapy, Immunotherapy.

CARS FOR CHILDHOOD CANCER: DEVELOPMENT AND COMPARISON OF PERMANENTLY AND TRANSIENTLY-MODIFIED T-CELLS TARGETING ALL AND NEUROBLASTOMA

Nathan Singh[1], David Barrett[2], Xiaojun Liu[3], Shuguang Jiang[3], Yangbing Zhao[3], Carl June[1,3], Stephan Grupp[1,2]

[1]*Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA*
[2]*Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, PA*
[3]*Abramson Family Cancer Research Institute, University of Pennsylvania, Philadelphia, PA*

Acute lymphocytic leukemia (ALL) and neuroblastoma (NB) account for ~40% of pediatric cancer deaths. While there have been remarkable advances in treatment, the last decade has seen a plateau in survival, suggesting that novel approaches are needed. We have previously demonstrated great clinical success using CD19-directed CAR T-cells (CART19) in adults with CLL. In this study we compare permanently (lenti) and transiently-modified (RNA) CART19 cells in a xenograft model of ALL, as well as the development and comparison of CAR T-cells directed against the NB antigen GD2.

To follow disease progression in vivo, we made the CD19+ ALL cell line Nalm-6 and the GD2+ NB cell line SY5Y bioluminescent. We used our established xenograft model of ALL, and developed xenograft models of NB. All cell lines and T-cells were human in origin.

Mice with established Nalm-6 were given either 1 dose of lenti or 3 doses of RNA CART19 cells, with lymphodepleting Cytoxan (CTX) between doses. Mice treated with lenti T-cells quickly cleared their ALL and remained disease-free. Mice given RNA T-cells showed disease reduction/control and a significant survival benefit, including long-term disease control in some animals.

To test GD2-directed CAR T-cells, NB cells were injected s.c. and given 15d to establish disease, followed by 3 doses of RNA GD2 CAR T-cells with intervening CTX. Intratumoral injection of cells resulted extensive tumor necrosis within 5d of the first treatment, and significant reduction in tumor volume. We then developed a disseminated model of NB, modeling the clinical circumstances in which adoptive therapy would be used. NB cells were injected IV, reproducibly resulting in liver and bone marrow disease, both relevant metastatic sites. Lenti GD2 CAR T-cells eradicated disease and prevented recurrence long-term. RNA GD2 CAR T-cells significantly slowed the progression of disease, and demonstrated massive expansion within tumor sites.

These data demonstrate the development of transiently-modified CAR T-cells to treat pediatric cancers, highlighting the importance of lymphodepletion and optimized dosing schedules. Our pilot NB data suggest that CAR therapy can mediate successful anti-tumor responses in both flank and disseminated models of NB. For antigens such as GD2, use of these transiently-modified T-cells may provide a greater degree of safety than permanently-modified cells, given the very high degree of clinical activity we have observed using CAR-modified cells.

Key Word: Humanized mouse model, Adoptive therapy, Chimeric receptors.

ADOPTIVE T CELL TRANSFER AND CELL THERAPY AS CANCER IMMUNOTHERAPY (CARS)

ADOPTIVE T CELL THERAPY WITH A TCR ENGINEERED FOR NANOMOLAR AFFINITY SHOWS IMPROVED ANTI-TUMOR EFFICACY COMPARED TO THE MICROMOLAR WILDTYPE TCR

Carolina M. Soto[1], Adam S. Chervin[2], David H. Aggen[2], Jennifer D. Stone[2], Hans Schreiber[3], Boris Engels[3], Edward J. Roy[1], David M. Kranz[2]

[1]*Neuroscience Program, University of Illinois, Urbana-Champaign, IL*
[2]*Department of Biochemistry, University of Illinois, Urbana-Champaign, IL*
[3]*Department of Pathology, University of Chicago, Chicago, IL*

Adoptive transfer of T cell receptor-transduced T cells has shown promise in clinical trials for cancer treatment. Recruitment of CD4+ helper T cells to the tumor could be beneficial, as CD4+ cells play a pivotal role in cytokine secretion as well as promoting the survival, proliferation and effector functions of tumor-specific CD8+ cytotoxic T lymphocytes. However, the TCR affinity that is optimal for redirection of CD4+ T cell activity is not known. Here we show that CD4+ T cells expressing a high-affinity TCR (nanomolar Kd value) against a class I-restricted tumor antigen mediated more effective tumor treatment against an established melanoma tumor model than the wild-type affinity TCR (micromolar Kd value). CD8+ T cells transduced to express nanomolar affinity TCRs were deleted in vivo, but CD4+ T cells with the same TCR resulted in enhanced survival and long-term persistence of effector memory T cells in a subcutaneous melanoma tumor model. The same approach is being examined for efficacy in the treatment of pulmonary metastatic melanoma. Using the same receptor, we have explored strategies to overcome the deletion of CD8+ T cells and mispairing with endogenous TCR chains. Toward these goals, we investigated a chimeric antigen receptor (CAR) that contained, by analogy with scFv-containing CARs, a Vα/Vβ single-chain TCR (scTv) of the high-affinity TCR linked to signaling domains. Unlike nanomolar affinity full length TCRs, nanomolar affinity scTv-CARs introduced into CD8+ T cells were not deleted in vivo, and there was no evidence of pairing with endogenous chains. Furthermore, both the CD8+ and CD4+ T cell subsets transduced with the scTv-CAR were capable of mediating tumor growth control. Overall, our results suggest that TCRs with nanomolar affinity could be advantageous in an adoptive T cell setting.

Key Word: TCR, T cells, Adoptive immunotherapy.

SELECTION OF PD-1, LAG-3, TIM-3 AND 41BB POSITIVE CD8 T CELLS IN THE FRESH TUMOR DIGEST ENRICHES FOR MELANOMA-REACTIVE CELLS

Alena Gros, Simon Turcotte, Eric Tran, Ken-ichi Hanada, John R. Wunderlich, Steven Rosenberg

Surgery Branch, National Cancer Institute, Bethesda, MD

Tumor reactive T cells can be found infiltrating melanoma lesions. However, the isolation of T cells specific for tumor antigens infiltrating these lesions has remained a challenge since there are no phenotypic parameters that can be used to consistently identify them. PD-1, LAG-3 and TIM-3 are some of the negative co-stimulatory molecules that have been proposed to be expressed on tumor-reactive T cells as a result of chronic antigen stimulation. 41BB, in the other hand, is a positive co-stimulatory molecule which is up-regulated on CD8 T cells upon TCR engagement. The main objective of our work was to characterize the phenotype of TIL in fresh melanoma tumor digests and to test whether any of the markers studied could be used to enrich for tumor-specific cells. We first studied the expression of PD-1, LAG-3, TIM-3 and 41BB on CD8 T cells in fresh melanoma tumor digests, as well as their stage of differentiation (CD62L, CCR7, CD45RO, CD27, CD28 and CD57). We found that CD8+ cells in melanoma tumors were enriched in effector memory-like cells (CD62L- CD45RO+) compared to peripheral blood. CD8+ tumor infiltrating lymphocytes showed higher frequencies of TIM-3 (15%), PD-1 (13%),LAG-3 (8%) and 41BB (2%) expression compared to peripheral blood. By using a Mart-1 peptide-MHC tetramer to analyze the phenotype of cells with specificity for a known melanoma antigen, we observed that these cells displayed an effector memory-like phenotype (CD62L-, CCR7-, CD45RO+) and higher levels of PD-1, LAG-3 and TIM-3 than the tetramer negative population. Furthermore, a subset of TIL co-expressed TIM-3, PD-1 and LAG-3 consistent with the presence of an exhausted phenotype in a subpopulation of CD8 TIL and suggesting some of these markers might be useful for enriching melanoma-reactive cells. Most importantly, we performed functional experiments in which we separated distinct T cell populations present in the fresh tumor digest according to expression of the phenotypic markers studied, expanded them in vitro and tested the reactivity of these populations against their autologous tumor cell lines. Tumor-reactivity was found preferentially in effector cells derived from the cells expressing PD-1, LAG-3, TIM-3 and 41BB in the fresh tumor digest but not in the cells lacking the expression of these markers. Positive selection of cells expressing PD-1, LAG-3, TIM-3 and 41BB resulted in a considerable enrichment of tumor reactive cells compared to the bulk CD8 T cells expanded from the fresh tumor digest. Our results suggest that tumor-reactive T cells in fresh melanoma digests express PD-1, LAG-3, Tim-3 and 41BB and thus, these markers can be used to enrich for melanoma-reactive cells.

Key Word: Melanoma immunotherapy, Adoptive immunotherapy, Tumor infiltration lymphocytes.

ROLE OF THE PD-1/PD-L1 PATHWAY ON REGULATORY T CELL DEVELOPMENT, INDUCTION AND FUNCTION IN VIVO

Xiufen Chen, Justin Kline

Medicine, University of Chicago, Chicago, IL

Regulatory T cells (Tregs) and the PD-1/PD-L1 pathway are important for the maintenance of peripheral tolerance. A subset of Tregs express PD-1 constitutively, suggesting a possible role for PD-1 in Treg biology. It has also been reported that PD-L1 promotes the induction of Treg in vitro. Based on these notions, we hypothesized that the PD-1/PD-L1 pathway may be important for Treg development, function and/or induction, and carried out a series of in vivo experiments to investigate this question. PD-1-/- mice harbored normal numbers of Tregs in the thymus and peripheral organs, and PD-1-/- Tregs developed normally in both polyclonal and Treg specific TCR transgenic bone marrow chimeras. PD-1-/- Tregs incorporated BrdU similarly to wildtype (WT) Tregs, suggesting that their in vivo Treg proliferation was normal. Compared to WT Treg, PD1-/- Treg expressed similar levels of Foxp3, CTLA-4, GITR and Helios and slightly lower levels of IL-2Rα (CD25). To assess the effect of PD-1 on Treg induction in vivo, naïve, polyclonal WT or PD-1-/- CD4+FoxP3- T cells were adoptively-transferred into RAG2-/- mice, and were subsequently analyzed for FoxP3 expression. A significantly lower frequency of transferred PD-1-/- CD4+ T cells expressed FoxP3 compared to WT CD4+ T cells. Further, in an OVA oral tolerance model, induction of FoxP3 expression was markedly decreased among PD-1-/- OT-II versus WT OT-II CD4+ T cells. WT or PD-1-/- OT-II T cells were also CFSE-labeled prior to adoptive transfer and OVA challenge. In this setting, PD-1-/- OT-II T cells proliferated more vigorously in vivo, and the highest percentage of Treg conversion among WT OT-II T cells occurred in after 3-4 cell divisions, consistent with published in vitro data. These data suggest that decreased Treg induction of PD-1-/- OT-II T cells may be related to their enhanced proliferative capability. Lastly, the function of PD-1-/- Tregs was analyzed in a B16 melanoma model, where total or Treg-depleted splenic T cells from WT or PD-1-/- mice were transferred into tumor-bearing RAG2-/- mice. Depletion of PD1-/- Tregs from the total PD-1-/- T cell population did not further augment tumor rejection as was seen when WT Treg were depleted from WT Total T cells, suggesting that PD-1-/- Tregs may have a defect in suppressive capability. In conclusion, our results strongly suggest that the PD-1/PD-L1 pathway is important for the in vivo induction of Tregs, while PD-1 appears to be dispensable for natural Treg development. Whether PD-1 plays a role in Treg-mediated suppression is currently under investigation. These data raise the possibility that PD-1 blockade in cancer patients may function not only to re-activate effector T cells, but also to prevent the induction of Tregs.

Key Word: PD-1, Treg cells.

ADOPTIVE T CELL TRANSFER AND CELL THERAPY AS CANCER IMMUNOTHERAPY (CARS)

1

ADOPTIVE CELL THERAPY USING EXPANDED AUTOLOGOUS TUMOR-INFILTRATING LYMPHOCYTES IN METASTATIC MELANOMA PATIENTS: ROLE OF SPECIFIC LYMPHOCYTE SUBSETS

Chantale Bernatchez[1], Minying Zhang[1], Patricia S. Fox[3], Jessica Ann Chacon[1], Cheng-Han Wu[1], Gregory Lizee[1], Sandy L. Mahoney[1], Gladys Alvarado[1], Rahmatu Mansaray[1,2], Orenthial J. Fulbright[1,2], Christopher L. Toth[1,2], Renjith Ramachandran[1,2], Seth Wardell[1,2], Audrey M. Gonzalez[1,2], Patrick Hwu[1], Laszlo Radvanyi[1]

[1]*Melanoma Medical Oncology, MD Anderson Cancer Center, Houston, TX*
[2]*Stem Cell Transplantation & Cellular Therapy, MD Anderson Cancer Center, Houston, TX*
[3]*Biostatistics, MD Anderson Cancer Center, Houston, TX2*

2

GAMMA DELTA T CELLS: NATURAL TUMOR KILLERS AMPLIFIED BY CHIMERIC ANTIGEN RECEPTORS

Drew C. Deniger, Sourindra Maiti, Kirsten Switzer, Tiejuan Mi, Simon Olivares, Harjeet Singh, Sonny Ang, Helen Huls, Dean A. Lee, Laurence J. Cooper

Division of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, TX

3

CLINICAL RESPONSE IN MELANOMA PATIENTS TREATED WITH ADOPTIVE CELL THERAPY USING LOW OR INTERMEDIATE DOSES OF INTERLEUKIN-2

Eva Ellebaek[1,2], Trine Z. Iversen[1,2], Niels Junker[1,2], Marco Donia[1], Lotte Engell-Noerregaard[1,2], Mads H. Andersen[1], *Per thor Straten*[1], Inge Marie Svane[1,2]

[1]*Center for Cancer ImmuneTherapy (CCIT), Copenhagen University Hospital, Herlev, Herlev, Denmark*
[2]*Department of Oncology, Copenhagen University Hospital, Herlev, Herlev, Denmark*

4

LOCAL COMPLEMENT ACTIVATION ABROGATES THE TUMOR-ENDOTHELIAL BARRIER AND MEDIATES T CELL HOMING AND TUMOR IMMUNE ATTACK

Andrea Facciabene[1], Francesco De Sanctis[1], Klara Balint[1], Paola Magotti[2], John Facciponte[1], Robert A. De Angelis[2], Wenchao C. Song[3], John D. Lambris[2], George Coukos[1]

[1]*Ovarian Cancer Research Center and Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA*
[2]*Department of Pathology & Laboratory Medicine, University of Pennsylvania, Philadelphia, PA*
[3]*Institute for Translational Medicine and Therapeutics and Department of Pharmacology, University of Pennsylvania, Philadelphia, PA*

5

CD123-SPECIFIC CAR REDIRECTED T CELLS EXHIBIT POTENT EFFECTOR ACTIVITY AGAINST ACUTE MYELOID LEUKEMIA WITHOUT ALTERING NORMAL HEMATOPOIETIC COLONY FORMATION IN VITRO

Armen Mardiros[1], Cedric Dos Santos[1], Tinisha McDonald[1], Christine E. Brown[1], Xiuli Wang[1], Wen-Chung Chang[1], Julie R. Ostberg[1], Ravi Bhatia[1], Michael C. Jensen[2], *Stephen J. Forman*[1]

[1]*Hematology and Hematopoietic Cell Transplantation, BRI, COHNMC, Duarte, CA*
[2]*Program in Immunology, Fred Hutchinson Cancer Research Center, Seattle, WA*

6

γ9- AND δ2-CDR3 DOMAINS REGULATE FUNCTIONAL AVIDITY OF T CELLS HARBORING γ9δ2T CELL RECEPTORS

Cordula Gründer[1], Suzanne van Dorp[1], Samantha Hol[1], Esther Drent[1], Kirsten Scholten[1], Sabine Heijhuurs[1], Wouter Scheper[1], Zsolt Sebestyen[1], Anton Martens[1,2], Roland Strong[3], Jürgen Kuball[1]

[1]*Hematology and Immunology, UMC Utrecht, Utrecht, Netherlands*
[2]*Cell Biology, UMC Utrecht, Utrecht, Netherlands*
[3]*Basic Sciences, FHCRC, Seattle, WA*

7

TARGETING CD22 EXPRESSING B CELL LEUKEMIA WITH CHIMERIC ANTIGEN RECEPTORS (CAR): ENGINEERING MEMBRANE PROXIMITY AND SECOND SIGNALING MOTIFS FOR OPTIMAL ACTIVITY

Waleed Haso[1], Daniel W. Lee[1], Ira H. Pastan[2], Dimiter S. Dimitrov[3], David Fitzgerald[2], Crystal L. Mackall[1], Rimas J. Orentas[1]

[1]*Pediatric Oncology Branch, NCI, CCR, NIH, Bethesda, MD*
[2]*Laboratory of Molecular Biology, NCI, CCR, NIH, Frederick, MD*
[3]*Protein Interactions Group; CCRNP; 2BRP; SAIC-Frederick, Inc.; NCI-Frederick, NIH, Frederick, MD*

8

BTLA: NEW BIOMARKER FOR A HIGHLY PROLIFERATIVE CD8+ TIL SUBSET ASSOCIATED WITH MELANOMA REGRESSION DURING ADOPTIVE CELL THERAPY

Cara Haymaker, Richard Wu, Chantale Bernatchez, Patrick Hwu, Laszlo Radvanyi

Melanoma Medical Oncology, MD Anderson Cancer Center, Houston, TX

9

HEMATOPOIETIC STEM CELL CHARACTERIZATION WITH A 19F TRACER AGENT; THE ABILITY TO EVALUATE CELLULAR PERSISTENCE

Brooke Helfer[1], Anthony Balducci[1], Zhina Sadeghi[2], Adonis Hijaz[2], Chris Flask[2], Amy Wesa[1]

[1]*Celsense, Inc, Pittsburgh, PA*
[2]*Case Western Reserve University, Cleveland, OH*

10

TARGETING MICROSATELLITE INSTABLE COLON CANCER WITH ADOPTIVELY TRANSFERRED REDIRECTED T CELLS

Else M. Inderberg-Suso[1], Sébastien Wälchli[1], Marit R. Myhre[1], Weiwen Yang[1], Sissel Trachsel[1], Johanna Olweus[1], Meng Yu Wang[2], Gunnar Kvalheim[2], Gustav Gaudernack[1]

[1]*Section for Immunology, Oslo University Hospital-Norwegian Radium Hospital, Oslo, Norway*
[2]*Section for Cell Therapy, Oslo University Hospital-Norwegian Radium Hospital, Oslo, Norway*

11

MIR155 AUGMENTS THE ANTI-TUMOR ACTIVITY OF CD8+ T CELLS BY ENHANCING RESPONSIVENESS TO HOMEOSTATIC CYTOKINES IN THE ABSENCE OF LYMPHODEPLETION

Yun Ji[1], Thelma Escobar[2], Christopher Klebanoff[1], Zhiya Yu[1], Madhusudhanan Sukumar[1], Zulmarie Franco[1], Douglas Palmer[1], Rahul Roychoudhuri[1], Anthony Leonardi[1], Stefan Muljo[2], Nicholas Restifo[1], Luca Gattinoni[1]

[1]*Surgery Branch, NCI, Bethesda, MD*
[2]*Laboratory of Immunology, NIAID, Bethesda, MD*

12

CYTOKINES IN THE IL-12 FAMILY DISTINCTLY IMPACT THE FUNCTIONAL FATE AND ANTI-TUMOR ACTIVITY OF TC17 CELLS

Sreenath Kundimi, Michelle H. Nelson, Logan W. Huff, Carolyn E. Rogers, Chrystal M. Paulos

Microbiology and Immunology, Medical University of South Carolina, Charleston, SC

13

GROWTH AND ACTIVATION OF NATURAL KILLER CELLS EX VIVO FROM CHILDREN WITH NEUROBLASTOMA FOR ADOPTIVE CELL THERAPY

Yin Liu[1,2], Hong-wei Wu[1], Michael A. Sheard[1], Richard Sposto[1,3], Srinivas S. Somanchi[4], Laurence J. Cooper[4], Dean A. Lee[4], Robert C. Seeger[1]

[1]*Hematology/Oncology, Children's Hospital Los Angeles, Los Angeles, CA*
[2]*Hematology/Oncology, Shanghai Children's Medical Center, Shanghai, China*
[3]*Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA*
[4]*Pediatrics, MD Anderson Cancer Center, University of Texas, Houston, TX*

14

EVALUATING THE SUSCEPTIBILITY OF SOLID TUMORS TO CHIMERIC ANTIGEN RECEPTOR MODIFIED T CELL THERAPIES

Adrienne H. Long[1,2], Waleed Haso[1], Daniel Lee[1], Steven Highfill[1], Rimas Orentas[1], Crystal Mackall[1]

[1]*Pediatric Oncology Branch, National Institutes of Health, Bethesda, MD*
[2]*Department of Microbiology-Immunology, Northwestern University, Feinberg School of Medicine, Chicago, IL*

15

CYTOTOXIC T CELLS EXPRESSING GUCY2C-SPECIFIC CHIMERIC ANTIGEN RECEPTOR AS TARGETED THERAPY FOR METASTATIC COLORECTAL CANCER

Michael S. Magee[1], Adam E. Snook[1], Adam R. Hersperger[2], Glen Marszalowicz[3], Scott A. Waldman[1]

[1]*Pharmacology and Experimental Therapeutics, Thomas Jefferson University, Philadelphia, PA*
[2]*Microbiology and Immunology, Thomas Jefferson University, Philadelphia, PA*
[3]*School of Biomedical Engineering, Drexel University, Philadelphia, PA*

16

INDUCIBLE COSTIMULATOR (ICOS) AUGMENTS THE ANTITUMOR ACTIVITY OF TC17 CELLS

Michelle Nelson, Sreenath Kundimi, Carolyn Rogers, Logan Huff, David Cole, Mark Rubinstein, Chrystal Paulos

Medical University of South Carolina, Charleston, SC

17

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18

IMMUNOTHERAPY OF CANCER: REPROGRAMMING TUMOR-IMMUNE CROSSTALK

Kyle K. Payne[1], Charles E. Hall[1], Amir A. Toor[2], Harry D. Bear[3], Xiang-Yang Wang[4], Masoud H. Manjili[1]

[4]*Human & Molecular Genetics, Virginia Commonwealth University - Massey Cancer Center, Richmond, VA*

19

MRNA MEDIATED T CELL REPROGRAMMING FOR ADOPTIVE IMMUNOTHERAPY

Peter M. Rabinovich, Sherman M. Weissman

Genetics, Yale School of Medicine, New Haven, CT

20

CARS FOR CHILDHOOD CANCER: DEVELOPMENT AND COMPARISON OF PERMANENTLY AND TRANSIENTLY-MODIFIED T-CELLS TARGETING ALL AND NEUROBLASTOMA

Nathan Singh[1], David Barrett[2], Xiaojun Liu[3], Shuguang Jiang[3], Yangbing Zhao[3], Carl June[1,3], Stephan Grupp[1,2]

[1]*Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA*
[2]*Division of Oncology, Children's Hospital of Philadelphia, Philadelphia, PA*
[3]*Abramson Family Cancer Research Institute, University of Pennsylvania, Philadelphia, PA*

21

PHASE I STUDY OF INTRAPERITONEAL ADOPTIVE CELL THERAPY WITH MHC NON-RESTRICTED TALL-104 CELLS IN PATIENTS WITH PERITONEAL CARCINOMATOSIS

Carmelo Bengala[1], Valeria Rasini[1], Rita Sternieri[1], Massimo Dominici[1], Alessia Andreotti[2], Roberta Gelmini[2], Luigi Cafarelli[1], Sara Caldrer[1], Cristina Masini[1], Fabrizio Nannipieri[3], *Silvia Trasciatti*[3], Pierfranco Conte[1]

[1]*Division of Medical Oncology, Department of Oncology, Hematology and Respiratory Diseases, University Hospital, Modena, Italy*
[2]*Division of Surgery 1, Department of Surgery, University Hospital, Modena, Italy*
[3]*R&D, Galileo Research, Pisa, Italy*

22

DUAL-SPECIFIC T CELLS: COMBINING CAR-ENGINEERED T CELLS WITH ONCOLYTIC VIROTHERAPY

Heather VanSeggelen[1], Joanne A. Hammill[1], Jennifer D. Bassett[1], Carole Evelegh[1], Galina F. Denisova[1], Brian Rabinovich[2], Jonathan L. Bramson[1]

[1]*Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada*
[2]*MD Anderson Cancer Center, Houston, TX*

23

VACCINATION TO ENHANCE THE IN VIVO PROLIFERATION OF VZV-SPECIFIC T CELLS REDIRECTED TO GD2+ TUMORS

Miyuki Tanaka-Yanagisawa[1], Minhtran Ngo[1,2], Jun Ando[1], Jiali Sun[1], Ann Leen[1,3], Cliona Rooney[1,3,4]

[1]*Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX*
[2]*Translational Biology and Molecular Medicine, Baylor College of Medicine, Houston, TX*
[3]*Department of Pediatrics, Baylor College of Medicine, Houston, TX*
[4]*Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX*

COMBINING IMMUNOTHERAPY AND OTHER THERAPIES

24

OUTCOMES OF PATIENTS WITH MALIGNANT MELANOMA TREATED WITH IMMUNOTHERAPY PRIOR TO OR AFTER BRAF TARGETED INHIBITORS

Allison Ackerman[1], Oliver Klein[2], David F. McDermott[1], Donald P. Lawrence[3], Anasuya Gunturi[1], Keith T. Flaherty[3], F. Stephen Hodi[4], Nageatte Ibrahim[4], Richard Kefford[3,6,5], Alexander M. Menzies[6], Michael B. Atkins[1,7], Daniel C. Cho[1], Georgina V. Long[3,6,5], Ryan J. Sullivan[3]

[1]*Beth Israel Deaconess Medical Center, Boston, MA*
[2]*Westmead Hospital, Sydney, NSW, Australia*
[3]*Massachusetts General Hospital, Boston, MA*
[4]*Dana Farber Cancer Institute, Boston, MA*
[5]*University of Sydney, Sydney, NSW, Australia*
[6]*Melanoma Institute Australia, North Sydney, NSW, Australia*
[7]*Georgetown Lombardi Comprehensive Cancer Center, Washington, DC*

25

LOCAL LOW DOSE IRRADIATION PROMOTES NORMALIZATION OF ABERRANT TUMOR VASCULATURE AND TUMOR IMMUNE REJECTION THROUGH INDUCTION OF INOS+ INTRAEPITHELIAL MACROPHAGES

Felix Klug[1], Hriyadesh Prakash[1], Tobias Seibel[1], Christina Pfischke[1], Ralf H. Voss[4], Karin Timke[2], Hubertus Schmitz-Winnenthal[3], Jürgen Weitz[3], Günther Hämmerling[5], Peter Huber[3], *Philipp Beckhove*[1]

[5]*Division of Molecular Immunology, German Cancer Research Center, Heidelberg, Germany*

26

SUB-LETHAL IRRADIATION OF HUMAN COLORECTAL CARCINOMA CELLS IMPARTS ENHANCED AND SUSTAINED EXPRESSION OF IMPORTANT MODULATORS OF EFFECTOR CTL ACTIVITY

Anita Kumari, *Charlie Garnett-Benson*

Cellular Molecular Biology and Physiology, Georgia State University, Atlanta, GA

27

IN VIVO ADMINISTRATION OF INTERLEUKIN 15 (IL15) DOES NOT AUGMENT TRANSFER OF CD8+ T EFFECTOR CELLS IN NON-HUMAN PRIMATES (NHP)

Carolina Berger, Michael Berger, Brian Beard, Hans-Peter Kiem, Stanley R. Riddell

Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, WA

28

SELECTIVE BRAF INHIBITION IMPAIRS REVERSIBLE TIL INFILTRATION IN BRAFV600E/PTEN-/- MOUSE MODEL OF HUMAN MELANOMA

Anna Hooijkaas, Jules Gadiot, *Christian U. Blank*

Dept Medical Oncology & Div Immunology, The Netherlands Cancer Institute (NKI-AVL), Amsterdam, Netherlands

29

REPETITIVE IMMUNOTHERAPY IMPROVES COMPLETE RESPONSE RATES AND SURVIVAL FOR ADVANCED MELANOMA PATIENTS

Brendon J. Coventry[1], Peter Hersey[2], Martin L. Ashdown[3]

[1]*Surgery, University of Adelaide, Adelaide, SA, Australia*
[2]*Medical Oncology, University of Sydney, Sydney, NSW, Australia*
[3]*Medicine, University of Melbourne, Melbourne, VIC, Australia*

30

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31

COMBINING THE RECOMBINANT IMMUNOTOXIN SS1P WITH THE BH3-MIMETIC ABT-737 INDUCES CELL DEATH IN PANCREATIC CANCER CELLS

Kevin Hollevoet[1], Antonella Antignani[2], David Fitzgerald[2], Ira Pastan[1]

[1]*Moleculary Biology Section at Laboratory of Molecular Biology, NCI, Bethesda, MD*
[2]*Biotherapy Section at Laboratory of Molecular Biology, NCI, Bethesda, MD*

32

EX-VIVO DETECTABLE MAGE-SPECIFIC T CELLS CORRELATE WITH COMPLETE REMISSION IN METASTATIC BREAST CANCER PATIENTS

Maxwell Janosky, Rachel Sabado, Cruz Crystal, Isabelita Vengco, Farah Hasan, Sylvia Adams

New York University, New York, NY

33

HMGB1, A POTENTIAL NEW TARGET FOR MESOTHELIOMA THERAPY

Sandro Jube[1], Zeyana Rivera[1], Marco Bianchi[2], Amy Powers[1], Ena Wang[3], Ian Pagano[1], Harvey Pass[4], Giovanni Gaudino[1], Michele Carbone[1], Haining Yang[1]

[1]*Cancer Biology, University of Hawaii Cancer Center, Honolulu, HI*
[2]*San Rafaelle University and Research Institute, Milan, Italy*
[3]*Department of Transfusion Medicine, NIH, Bethesda, MD*
[4]*Department of Cardiothoracic Surgery, NYU School of Medicine, New York, NY*

34
COMBINATION THERAPY WITH HSP90 INHIBITORS AND INTERFERONS SYNERGISTICALLY INCREASES MHC EXPRESSION LEADING TO ENHANCED TUMOR CELL RECOGNITION; IMPLICATIONS FOR IMMUNOTHERAPY

James T. Kurnick[3,1], Timothy J. Haggerty[1], Lenora B. Rose[1], Ian S. Dunn[1], Estelle E. Newton[1], Franco Pandolfi[2]

[1]*CytoCure LLC, Beverly, MA*
[2]*Medicine, Catholic University Col. of Med., Rome, Italy*
[3]*Pathology, Massachusetts Gen. Hosp., Boston, MA*

35
EFFECTIVE ACTIVATION OF HIGHLY PURIFIED NK CELLS EXPANDED EX VIVO FOR THE ERADICATION OF EPITHELIAL OVARIAN CANCER CELLS

In-Kyung Lee[1], Shin-Wha Lee[2]

[1]*Department of Obstetrics and Gynecology, Asan Institute for Life Science, Seoul, Republic of Korea*
[2]*Department of Obstetrics and Gynecology, Asan Medical Center, Seoul, Republic of Korea*

36
THE COMBINATION OF CHEMOTHERAPY AND MYCOBACTERIUM ENHANCES THE ANTIGENICITY OF TUMOURS AND STIMULATE ALLOGENEIC T-CELL RESPONSES

Wai Liu, Daniel Fowler, Angus Dalgleish

Division of Clinical Sciences (Oncology), St George's University of London, London, United Kingdom

37
COMBINED RADIOTHERAPY AND IMMUNOTHERAPY USING CPG OLIGODEOXYNUCLEOTIDES AND INDOLAMINE 2,3 DIOXYGENASE (IDO) BLOCKADE IN MURINE 4T-1 MAMMARY CARCINOMA RESULTS IN GREATER ANTI-TUMOR EFFECTS

Arta M. Monjazeb[1], Gail Sckisel[2], Annie Mirsoian[2], Steven Pai[3], Anthony Zamora[2], William J. Murphy[4]

[1]*Radiation Oncology, UC Davis, Sacramento, CA*
[2]*Immunology, UC Davis, Sacramento, CA*
[3]*Comparative Pathology, UC Davis, Sacramento, CA*
[4]*Dermatology, UC Davis, Sacramento, CA*

38
IMMUNO-SENSITIZATION OF MALIGNANT GLIOMAS BY NATURAL POLYPHENOLS

Chandramouli Mandalaparty[1], Andrew Huang[1], Sandeep Mittal[1], Ping Q. Dou[2], *Prahlad Parajuli*[1]

[1]*Neurosurgery, Wayne State University & Karmanos Cancer Institute, Detroit, MI*
[2]*Oncology, Wayne State University & Karmanos Cancer Institute, Detroit, MI*

39
EVALUATING THE SAFETY OF COMBINED IPILIMUMAB AND RADIOTHERAPY FOR THE TREATMENT OF METASTATIC MELANOMA

Michael A. Postow, Christopher A. Barker, Shaheer A. Khan, Jedd D. Wolchok

Memorial Sloan-Kettering Cancer Center, New York, NY

40
CSPG4 AS A COMBINATORIAL TARGET OF ANTIBODY-BASED IMMUNOTHERAPY FOR MALIGNANT MESOTHELIOMA

Zeyana S. Rivera[1], Soldano Ferrone[2], Xinhui Wang[2], Sandro Jube[1], Maria Prat[3], Haining Yang[1], Giovanni Gaudino[1], Michele Carbone[1]

[1]*Cancer Biology, University of Hawaii Cancer Center, Honolulu, HI*
[2]*Immunology, Hillmann Cancer Center, Honolulu, PA*
[3]*Biomedical Sciences, University of Piemonte Orientale, Novara, Italy*

41
INHIBITION OF PROTEASOME DEUBIQUITINATING ACTIVITY RENDERS TUMOR CELLS SENSITIVE TO TRAIL-MEDIATED APOPTOSIS BY NATURAL KILLER CELLS AND T CELLS

Dhifaf Sarhan, Erik Wennerberg, Padraig D'Arcy, Deepthy Gurajada, Stig Linder, Andreas Lundqvist

Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden

42
PERSONALIZED PEPTIDE VACCINE IN COMBINATION WITH CHEMOTHERAPY FOR PATIENTS WITH ADVANCED COLORECTAL CANCER

Tetsuro Sasada, Shigeru Yutani, Satoko Matsueda, Nobukazu Komatsu, Kyogo Itoh

Department of Immunology and Immunotherapy, Kurume University School of Medicine, Kurume, Japan

43
TUMOR-DIRECTED MYELOID EXPANSION IS REVERSED BY RADIATION THERAPY

Talicia Savage[1], Michael J. Gough[1], Benjamin Cottam[1], Pippa Newell[1,2], William L. Redmond[1], Keith S. Bahjat[1], Marka R. Crittenden[1,2]

[1]*Earle A Chiles Research Institute, Providence Cancer Center, Portland, OR*
[2]*The Oregon Clinic, Portland, OR*

44
INTRAVESICAL TREATMENT OF ORTHOTOPIC BLADDER CANCER WITH CHITOSAN/IL-12 INDUCES SYSTEMIC TUMOR-SPECIFIC IMMUNITY
Sean G. Smith, Lirong Yang, David Zaharoff

Biomedical Engineering, University of Arkansas, Fayetteville, AR

45
SYNERGISTIC THERAPEUTIC EFFECT OF BLOCKING TWO IMMUNE INHIBITORY PATHWAYS CONCURRENTLY IN THE CONTEXT OF A TOLEROGENIC TUMOR MICROENVIRONMENT IN VIVO
Stefani Spranger[1], Michael Leung[1], Thomas F. Gajewski[1,2]

[1]Pathology, University of Chicago, Chicago, IL
[2]Medicine, University of Chicago, Chicago, IL

46
TGFβ IS A MASTER REGULATOR OF THE PRO-IMMUNOGENIC EFFECTS OF RADIOTHERAPY
Claire Vanpouille-Box[1], Karsten A. Pilones[1], Sophie Bouquet[2], Jiri Zavadil[3], Silvia Formenti[2], Mary-Helen Barcellos-Hoff[2], Sandra Demaria[1]

[1]Pathology, NYU School of Medicine, New York, NY
[2]Radiation Oncology, NYU School of Medicine, New York, NY
[3]Pathology, NYU Cancer Institute and NYU Center for Health Informatics and Bioinformatics, New York, NY

47
INTRATUMORAL CHITOSAN/IL-12 NEOADJUVANT TO TUMOR RESECTION REDUCES BREAST CANCER METASTASIS
Jimmy Vo, Lirong Yang, David Zaharoff

Department of Biomedical Engineering, University of Arkansas, Fayetteville, AR

48
PHASE II TRIAL DAILY PULSE INTERLEUKIN-2 THERAPY DURING MARROW/LYMPHOCYTE RECOVERY IN ACUTE MYELOID LEUKEMIA NCT#01289678
Paul R. Walker, Manali K. Kamdar, Adam S. Asch

Oncology, Leo Jenkins Cancer Center, Brody School of Medicine at East Carolina University, Greenville, NC

49
DASATINIB PRIMES HUMAN CELLS OF MYELOID ORIGIN TO TLR-INDUCED IL12 SYNTHESIS
Matthias Wölfl[1], Stefanie Schwinn[1], Young-Eun Yoo[1], Marie L. Ress[1], Martin Chopra[2], Susanne C. Schreiber[1], Victor I. Ayala[3], Claes Ohlen[3], Matthias Eyrich[1], Andreas Beilhack[2], Paul G. Schlegel[1]

[1]Children's Hospital, University of Würzburg, Würzburg, Germany
[2]Department of Medicine II, University of Würzburg, Würzburg, Germany
[3]AIDS and Cancer Virus Program, Frederick National Laboratory for Cancer Research, Frederick, MD

50
INHIBITING MONOCYTE/MACROPHAGE-NEUROBLASTOMA CELL INTERACTIONS WITH LENALIDOMIDE INCREASES TUMOR CELL RESPONSE TO CYCLOPHOSPHAMIDE AND TOPOTECAN
Yibing Xu[1], Jianping Sun[1], Zesheng Wan[1], Robert Seeger[1,2]

[1]Center for Cancer and Blood Diseases and Saban Research Institute, Childrens Hospital Los Angeles, Los Angeles, CA
[2]Keck School of Medicine, University of Southern California, Los Angeles, CA

DC SUBSETS/CANCER VACCINES

51
SELECTION OF A CONTROL INFECTIOUS DISEASE VACCINE FOR CANCER IMMUNOTHERAPY TRIALS
Katherine Arns[1], Janet A. Englund[3], Mary L. Disis[1], Chihiro Morishima[1,2]

[1]Tumor Vaccine Group, University of Washington, Seattle, WA
[2]Department of Laboratory Medicine, University of Washington, Seattle, WA
[3]Department of Pediatrics, University of Washington, Seattle, WA

52
MONTANIDE™ ISA 51VG AND MONTANIDE™ ISA 720VG, ADJUVANTS DEDICATED TO HUMAN THERAPEUTIC VACCINES
Stephane Ascarateil[1], Heloise Imbault[2]

[2]SEPPIC, Inc, Fairfield, NJ

53
EFFECT OF AGE ON IMMUNITY AND RESPONSES TO BREAST CANCER VACCINATION
Dominick Auci, Meredith Slota, Doreen Higgins, Jennifer Childs, Lupe Salazar, Andrew Coveler, Mary (Nora) L. Disis

University of Washington, Seattle, WA

54

MEMORY CD8+ T CELLS, SECONDARY EXPANSION AND SELF-HELP: HOW HETEROLOGOUS PRIME-BOOST VACCINATION CIRCUMVENTS THE NEED FOR CD4+ T CELL HELP AND CD40-CD40L-SIGNALING

Jessica A. Shugart, Shelly Bambina, Ryan Montler, *Keith S. Bahjat*

Earle A. Chiles Research Institute, Providence Cancer Center, Portland, OR

55

3-DAY DENDRITIC CELLS FOR POSTREMISSION VACCINATION IN AML: CHARACTERIZATION OF TLR-AGONIST MATURED DCS EXPRESSING THE LEUKEMIA-ASSOCIATED ANTIGENS WT1 AND PRAME

Barbara Beck[1], Christiane Geiger[2], Iris Bigalke[3], Felix S. Lichtenegger[1], Mirjam H. Heemskerk[4], Stein Saboe-Larssen[5], Marion Subklewe[1], Dolores J. Schendel[2,3]

[1]*Department of Internal Medicine III, University of Munich, Campus Grosshadern, Munich, Germany*
[2]*Institute of Molecular Immunology, Helmholtz Zentrum München, Munich, Germany*
[3]*GMP Unit, Helmholtz Zentrum München, Munich, Germany*
[4]*Department of Hematology, Leiden University Medical Center, Leiden, Netherlands*
[5]*Department of Cellular Therapy, Oslo University Hospital, Oslo, Norway*

56

CHARACTERIZATION OF TWO-DAY DERIVED ALPHA DENDRITIC CELLS SUITABLE FOR CANCER IMMUNOTHERAPY

David A. Bernal-Estévez[2,1], Carlos A. Parra-López[1,2]

[1]*Department of Microbiology and Immunology, Universidad Nacional de Colombia, Bogotá, Colombia*
[2]*Immunology and Clinical Oncology Research Group (GIIOC), Fundación Salud de los Andes, Bogotá, Colombia*

57

LARGE SCALE (GMP) PRODUCTION AND FIRST CLINICAL EXPERIENCE WITH A NEW GENERATION OF FAST DCS TRANSFECTED WITH MRNA HTERT AND SURVIVIN

Iris Bigalke[1], Marianne Lundby[1], Julitta Kasten[2], Stein Sæbøe-Larssen[1], Hege Haakenstad[1], Dolores J. Schendel[2], Gunnar Kvalheim[1]

[1]*Dept. of Cellular Therapy, Oslo University Hospital, Oslo, Norway*
[2]*Institute of Molecular Immunology, Helmholtz Zentrum Muenchen, Muenchen, Germany*

58

TRANSCRIPTIONAL SIGNATURES IN DENDRITIC CELLS: CORRELATION OF PATIENT VARIABILITY WITH CLINICAL OUTCOME

Luciano Castiello[1], David F. Stroncek[1], Masaki Terabe[2], Hanh Khuu[1], Lauren V. Wood[2], Jay A. Berzofsky[2], Marianna Sabatino[1]

[1]*Department of Transfusion Medicine, Clinical Center, National Institutes of Health, Bethesda, MD*
[2]*Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD*

59

MELANOMA CANCER STEM CELLS OF MESENCHYMAL AND NEURAL CREST ORIGIN USED IN AUTOLOGOUS DENDRITIC CELL-BASED IMMUNOTHERAPY RESULT IN 50% 5-YEAR SURVIVAL RATES

Andrew N. Cornforth[1], Denysha Carbonell[1], Michael McGary[1], Jackie McLoughlin[1], Robert O. Dillman[2]

[1]*California Stem Cell, Irvine, CA*
[2]*Hoag Memorial Hospital, Newport Beach, CA*

60

A PHASE 1 TRIAL OF A NOVEL VACCINE TARGETING NY-ESO-1 TO THE DENDRITIC CELL RECEPTOR DEC-205 IN COMBINATION WITH TOLL-LIKE RECEPTOR AGONISTS

Madhav Dhodapkar[1], Biwei Zhao[2], Ding Wang[3], Richard D. Carvajal[4], Mary Keohan[4], Ellen Chuang[5], Rachel Sanborn[6], Jose Lutzky[7], John Powderly[8], Harriet Kluger[1], Mario Sznol[1], Sheela Tejwani[3], Andrea Crocker[2], Laura Vitale[2], Venky Ramakrishna[2], Michael Yellin[2], Thomas Davis[2], Tibor Keler[2]

[1]*Yale University, New Haven, CT*
[2]*Celldex Therapeutics, Inc., Needham, MA, MA*
[3]*Henry Ford Health System, Detroit, MI*
[4]*Memorial Sloan Kettering Cancer Center, New York, NY*
[5]*Cornell University, New York, NY*
[6]*Providence Portland Medical Center, Portland, OR*
[7]*Mt. Sinai Medical Center, Miami Beach, FL*
[8]*Carolina BioOncology Institute, Huntersville, NC*

61
PHASE I PEPTIDE VACCINE WITH MONTANIDE ISA-51 VG IN CHILDREN WITH REFRACTORY CENTRAL NERVOUS SYSTEM (CNS) TUMORS

Sharon Gardner[1], Rachel Sabado[1], Genevieve Legault[1], David Zagzag[2], Krysten Brown[1], Crystal Cruz[1], Farah Hasan[1], Martin Jadus[3], Isabelita Vengco[1], Nina Bhardwaj[1]

[1]*NYU Cancer Institute, New York University Langone Medical Center, New York, NY*
[2]*Pathology, New York University Langone Medical Center, New York, NY*
[3]*Pathology and Laboratory Medicine Service, VA Long Beach Healthcare System, Long Beach, CA*

62
SEMI-ALLOGENEIC CANCER VACCINES

Sebastiano Gattoni-Celli

[1]*Radiation Oncology, Medical University of South Carolina, Charleston, SC*
[2]*Ralph H. Johnson VA Medical Center, Charleston, SC*

63
ASSESSMENT OF CELLULAR IMMUNE RESPONSES FOLLOWING POXVIRUS BASED CANCER IMMUNOTHERAPIES

Fatema Legrand, Rachel Owen, Amanda Enstrom, Olivia Hwang, Gayatri Paranjpe, Jinsoo Joo, Joy Su, Bernadette Callejo, Alex Cheung, Jess Nolin, Olga Bandman, Wayne Godfrey, Reiner Laus, Alain Delcayre

BN ImmunoTherapeutics, Mountain View, CA

64
EVALUATION OF HER-2 SPECIFIC HUMORAL IMMUNE RESPONSES IN BREAST CANCER PATIENTS TREATED WITH MVA-BN®-HER2

Fatema A. Legrand[1], Rachel Owen[1], Amanda Enstrom[1], Olivia Hwang[1], Gayatri Paranjpe[1], Joy Su[1], Bernadette Callejo[1], Alex Cheung[1], Jess Nolin[1], Olga Bandman[1], Ulf Reimer[2], Holger Wenschuh[2], Reiner Laus[1], Wayne Godfrey[1], Alain Delcayre[1]

[1]*BN ImmunoTherapeutics, Mountain View, CA*
[2]*JPT Peptide Technologies GmbH, Berlin, Germany*

65
THERAPEUTIC EFFECT OF CANCER STEM CELL-BASED VACCINE

Lin Lu, Huimin Tao, Martin Egenti, Max S. Wicha, Alfred E. Chang, Qiao Li

University of Michigan, Ann Arbor, MI

66
DISCOVERY OF UNIQUE BIOMARKERS WHICH PREDICT CLINICAL RESPONSES TO DENDRITIC CELL VACCINE

Masato Mitsuhashi[1], Yoichi Kato[2]

[1]*Hitachi Chemical Research Center, Inc., Irvine, CA*
[2]*Shin-Yokohama Kato Clinic, Yokohama, Japan*

67
NOVEL CLINICAL RESEARCH IMMUNE MONITORING MODEL OF EX VIVO INDUCTION OF MRNA

Masato Mitsuhashi[1], Mieko Ogura[1], Vivian Tovar[1], Marc Mansour[2], Mohan Karkada[2]

[1]*Hitachi Chemical Research Center, Inc., Irvine, CA*
[2]*Immunovaccine Inc., Halifax, NS, Canada*

68
A BI-INSTITUTIONAL PILOT STUDY OF PEPTIDE-BASED VACCINES IN COMBINATION WITH POLY ICLC IN PATIENTS WITH WHO GRADE 2 LOW-GRADE GLIOMA

Hideho Okada[1], Lisa H. Butterfield[1], Ronald L. Hamilton[1], Mark O. Lively[2], Michael D. Chan[2], Andres M. Salazar[3], Douglas M. Potter[1], Edward G. Shaw[2], Frank S. Lieberman[1]

[1]*University of Pittsburgh Cancer Institute, Pittsburgh, PA*
[2]*Wake Forest University School of Medicine, Winston-Salem, NC*
[3]*Oncovir, Inc, Washington, DC*

69
TUMOR-DERIVED ALPHA-FETOPROTEIN IMPAIRS THE DIFFERENTIATION OF HUMAN DENDRITIC CELLS

Angela D. Pardee[1], Lisa H. Butterfield[1,2,3]

[1]*Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA*
[2]*Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA*
[3]*Department of Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA*

70
PEPTIDE VACCINE THERAPY FOR CHILDHOOD GLIOMAS: INTERIM RESULTS OF A PILOT STUDY

Ian Pollack[1], Regina Jakacki[1], Lisa Butterfield[2], Hideho Okada[2]

[1]*Children's Hospital of Pittsburgh, Pittsburgh, PA*
[2]*University of Pittsburgh Cancer Institute, Pittsburgh, PA*

71
IDENTIFICATION OF A NOVEL AGE-RELATED DENDRITIC CELL DEFICIENCY AND ITS IMPACT ON TUMOR IMMUNITY

Josef Goldufsky[2,3], Michelle Farazi[2], Zachary Cohn[3], Keven J. Stonewall[3], Stephanie Linnane[3], Justine Nguyen[3], Howard Kaufman[1,2,3], Andrew D. Weinberg[4], *Carl E. Ruby*[1,2,3]

[1]General Surgery, Rush University Medical Center, Chicago, IL
[2]Immunology/Microbiology, Rush University Medical Center, Chicago, IL
[3]Rush University Cancer Center, Rush University Medical Center, Chicago, IL
[4]Earle A Chiles Research Center, Providence Portland Medical Center, Portland, OR

72
IMA910, A NOVEL MULTI-PEPTIDE CANCER VACCINE FOR ADVANCED COLORECTAL CANCER, INDUCES MULTIPLE CD8+ AND CD4+ T-CELL RESPONSES ASSOCIATED WITH IMPROVED SURVIVAL

Sabrina Kuttruff[1], Sarah Kutscher[1], Andrea Mayer[1], Oliver Schoor[1], Jörg Ludwig[1], Frank Mayer[2], Erika Hitre[3], Elzbieta Nowara[4], László Torday[5], Thomas Höhler[6], Vincenzo Bronte[7], Tim Maughan[8], Richard Adams[9], Bernhard Rössler[1], Dominik Maurer[1], Verona Vass[1], Juha Lindner[1], Nina Pawlowski[1], Claudia Trautwein[1], Jörn Dengjel[1], Norbert Hilf[1], Toni Weinschenk[1], Carsten Reinhardt[1], *Harpreet Singh*[1], Steffen Walter[1]

[1]immatics biotechnologies, Tübingen, Germany
[2]University of Tübingen, Tübingen, Germany
[3]National Institute of Oncology, Budapest, Hungary
[4]Centrum Onkologii Instytut im. Marii Sklodowskiej-Curie, Gliwice, Poland
[5]University of Szeged, Szeged, Hungary
[6]Prosper Hospital Recklinghausen, Recklinghausen, Germany
[7]University of Verona, Verona, Italy
[8]University of Oxford, Oxford, United Kingdom
[9]Velindre Hospital, Cardiff, United Kingdom

73
AUGMENTING ANTITUMOR T CELL RESPONSES TO MIMOTOPE VACCINATION BY BOOSTING WITH NATIVE TUMOR ANTIGENS

Jonathan D. Buhrman, Kimberly R. Jordan, Lance U'Ren, Jonathan Sprague, Charles B. Kemmler, *Jill E. Slansky*

Immunology, University of Colorado School of Medicine, Denver, CO

74
THERAPEUTIC SYSTEMIC VACCINATION IN SUBJECTS WITH PREINVASIVE HPV DISEASE IS ASSOCIATED WITH CHANGES IN THE IMMUNE CELLS INFILTRATING THE TARGET TISSUE

C. L. Trimble[1], J. Teague[2], T. C. Wu[1], N. C. Barat[1], R. A. Clark[2]

[1]Johns Hopkins Medical Institutions, Baltimore, MD
[2]Harvard Medical School, Boston, MA

75
TUMOR AUTOPHAGOSOME-BASED CANCER VACCINE COMBINED IMMUNOTHERAPY WITH ANTI-OX40 PROVIDES THERAPEUTIC IMMUNITY AGAINST ESTABLISHED BREAST CANCER

Christopher G. Twitty[1], Hong-Ming Hu[1], Bernard A. Fox[1,2]

[1]Earle A Chiles Research Institute, Portland, OR [2] Molecular Microbiology & Immunology, Oregon Health & Science University, Portland, OR

76
DRIBBLES, AN AUTOPHAGOSOME-ENRICHED VACCINE, INDUCE PRO-INFLAMMATORY BDCA3 EXPRESSING MONOCYTES IN HUMAN PBMC

Rieneke van de Ven[1,2], Traci L. Hilton[3], Mari F. van den Hout[4], Berbel J. Sluijter[4], Tanja D. de Gruijl[4], Bernard A. Fox[1], Hong Ming Hu[2], Sandra Aung[3]

[1]Laboratory of Molecular and Tumor Immunology, Earle A. Chiles Research Institute at Providence Cancer Center, Portland, OR
[2]Laboratory of Cancer Immunobiology, Earle A. Chiles Research Institute at Providence Cancer Center, Portland, OR
[3]UbiVac, Earle A. Chiles Research Institute at Providence Cancer Center, Portland, OR
[4]Immunotherapy Laboratory, VU University Medical Center/ Cancer Center Amsterdam, Amsterdam, Netherlands

77
INDUCTION OF MAGE-A6-SPECIFIC CD8+ T-CELL RESPONSES USING MAGE-A6 AND MYCOPLASMA PENETRANS HF-2 PERMEASE-DERIVED PEPTIDES

Lazar Vujanovic[1,2], John M. Kirkwood[1,2], Walter J. Storkus[1,3,4], Lisa H. Butterfield[1,2,3]

[1]University of Pittsburgh Cancer Institute, Pittsburgh, PA
[2]Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA
[3]Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA
[4]Dermatology, University of Pittsburgh School of Medicine, Pittsburgh, PA

78
ALARMIN HMGN1 PROMOTES ANTITUMOR IMMUNITY
Feng Wei[1], De Yang[1,2], Poonam Tewary[1], O. M. Zack Howard[1], Joost J. Oppenheim[1]

[1]*Laboratory of Molecular Immunoregulation, Frederick National Laboratory for Cancer Research (FNLCR), Frederick, MD*
[2]*Basic Research Program, SAIC-Frederick, Inc., Frederick, MD*

79
AUTOPHAGY IN TUMOR CELLS IS CRITICAL FOR INNATE IMMUNE SENSING OF A GROWING TUMOR AND BRIDGING TO AN ADAPTIVE IMMUNE RESPONSE
Seng-Ryong Woo[1], Mercedes Fuertes[1], Michael Leung[1], Michael Furdyna[1], Thomas F. Gajewski[1,2]

[1]*Pathology, University of Chicago, Chicago, IL*
[2]*Medicine, University of Chicago, Chicago, IL*

80
PHASE I TRIAL OF A MULTI-EPITOPE PULSED DENDRITIC CELL VACCINE TARGETING CANCER STEM CELLS IN PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA
John S. Yu[1,2], Surasak Phuphanich[1], Christopher Wheeler[1], Jeremy Rudnick[1], Mia Mazer[1], Hong Q. Wang[1], Miriam Nuno[1], Jaime E. Richardson[1], Xuemo Fan[1], Jianfei Ji[1], Ray Chu[1], James G. Bender[2], Elma S. Hawkins[2], Chirag G. Patil[1], Keith Black[1]

[1]*Neuro-Oncology Program, Cedars-Sinai Medical Center, Los Angeles, CA*
[2]*Immunocellular Therapeutics Ltd, Woodland Hills, CA*

81
ENHANCING WHOLE TUMOR CELL VACCINATION BY TARGETING DENDRITIC CELLS THROUGH NY-ESO-1/CRT/TLR4 INTERACTIONS
Gang Zeng[1], Le Xu[1], David H. Nguyen[1], Quang T. Luong[2]

[1]*Urology, UCLA, Los Angeles, CA*
[2]*Medicine, UCLA, Los Angeles, CA*

IMMUNITY OF ONCOLYTIC VIRUSES

82
CORRELATION BETWEEN HUMAN AND ONCOLYTIC VACCINIA VIRUS TRANSCRIPTIONAL PROFILE
Jennifer Reinboth[1,2,3], Maria L. Ascierto[2,4], Nanhai G. Chen[1,5], Qian Zhang[1,5], Yong A. Yu[1,5], Richard J. Aguilar[1], Andrea Worschech[6], Yingdong Zhao[7], Ena Wang[2], Francesco M. Marincola[2], Aladar A. Szalay[1,3,5]

[1]*Genelux Corporation, San Diego Science Center, San Diego, CA*
[2]*Infectious Disease and Immunogenetics Section, Department of Transfusion Medicine, CC, and trans-NIH Center for Human Immunology, National Institutes of Health, Bethesda, MD*
[3]*Department of Biochemistry, University of Wuerzburg, Wuerzburg, Germany*
[4]*Department of Health Sciences and Center of Excellence for Biomedical Research, University of Genoa, Genoa, Italy*
[5]*Department of Radiation Oncology, Rebecca and John Moores Comprehensive Cancer Center, University of California, San Diego, CA*
[6]*Department of Internal Medicine II, University of Wuerzburg, Wuerzburg, Germany*
[7]*Biometric Research Branch, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, MD*

83
ONCOLYIC MYXOMA VIRUS DELIVERY OF IMMUNOTHERAPEUTIC GENES TO BRAIN TUMORS
Vesna Tosic[1], Diana L. Thomas[2], David M. Kranz[3], Jia Liu[5], Grant McFadden[5], Amy L. MacNeill[4], Edward J. Roy[1,2]

[1]*Molecular and Integrative Physiology, University of Illinois at Urbana-Champaign, Urbana, IL*
[2]*Neuroscience Program, University of Illinois at Urbana-Champaign, Urbana, IL*
[3]*Biochemistry, University of Illinois at Urbana-Champaign, Urbana, IL*
[4]*Pathobiology at College of Veterinary Medicine, University of Illinois at Urbana-Champaign, Urbana, IL*
[5]*Molecular Genetics and Microbiology, University of Florida, Gainesville, FL*

IMMUNOTHERAPY COMBINATIONS

84
ATTENUATED HUMORAL RESPONSE TO SEASONAL AND PANDEMIC (A/H1N1 2009) VIROSOMAL AND MF-59 ADJUVATED INFLUENZA VACCINES IN COMPLETE REMISSION NON-HODGKIN LYMPHOMA PATIENTS PREVIOUSLY TREATED WITH RITUXIMAB CONTAINING REGIMENS

Davide Bedognetti[1], Gabriele Zoppoli[2], Mario Roberto Sertoli[2], Maria Libera Ascierto[1], Francesco Marincola[1], Filippo Ansaldi[2], Andrea De Maria[2]

[1]*Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD*
[2]*IRCCS San Martino-IST, Genova, Italy*

85
MTERT GENETIC VACCINE COMBINED WITH CHEMOTHERAPY AUGMENTS ANTIGEN-SPECIFIC IMMUNE RESPONSE AND CONFERS TUMOR PROTECTION IN TIME DEPENDED FASHION

Stefano Ugel[1], Jens Rueter[1], Francesco De Sanctis[1], Elisa Scarselli[2], Carmela Mennuni[2], Nicola La Monica[2], George Coukos[1], *Andrea Facciabene*[1]

[1]*Ovarian Cancer Research Center and Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA*
[2]*Cancer Therapy, Istituto Ricerche Biologia Molecolare (IRBM), Roma, Italy*

86
A NOVEL AUTOPHAGOSOME CANCER VACCINE DERIVED FROM NON-SMALL CELL LUNG CANCER (NSCLC) CONTAINS AT LEAST SIX NCI PRIORITIZED CANCER ANTIGENS AND LIGANDS FOR TLR 2, 3, 4, 7 AND 9

Traci L. Hilton[1], Christopher Dubay[2], Chris G. Twitty[2], Bernard A. Fox[2], Hong-Ming Hu[3], Sandra Aung[1]

[1]*UbiVac, Portland, OR*
[2]*Laboratory of Molecular and Tumor Immunology, Earle A. Chiles Research Institute at Providence Cancer Center, Portland, OR*
[3]*Laboratory of Cancer Immunobiology, Earle A. Chiles Research Institute at Providence Cancer Center, Portland, OR*

87
THE PROCLAIMSM (PROLEUKIN® OBSERVATIONAL STUDY TO EVALUATE TREATMENT PATTERNS AND CLINICAL RESPONSE IN MALIGNANCY) STUDY: THE RESPONSE RATES FOR HIGH DOSE INTERLEUKIN-2 (HD IL-2) THERAPY

Howard Kaufman[1], David McDermott[2], Michael Morse[3], James Lowder[4], Michael Wong[5]

[1]*Rush University, Chicago, IL*
[2]*Harvard University, Boston, MA*
[3]*Duke University, Durham, NC*
[4]*Prometheus Laboratories Inc, San Diego, CA*
[5]*University of Southern California, Los Angeles, CA*

88
PD-L1 BLOCKADE IMPROVES THE EFFICACY OF ADOPTIVELY TRANSFERRED TUMOR INFILTRATING LYMPHOCYTES IN A COLON CARCINOMA MODEL

Krithika N. Kodumudi, Amy Mackay, Jessica Seigel, John Robinson, Shari Pilon-Thomas

Immunology, H. Lee Moffitt Cancer Centre, Tampa, FL

89
AGING RESULTS IN ACUTE TNF-α-DEPENDENT LETHALITY FOLLOWING SYSTEMIC IMMUNOTHERAPY: IMPACT OF BODY FAT CONTENT

Myriam N. Bouchlaka[1], Gail D. Sckisel[2], Mingyi Chen[4], *Annie Mirsoian*[2], Anthony E. Zamora[2], Emanual Maverakis[6], Hui-Hua Hsiao[2], Arta M. Monjazeb[3], William J. Murphy[5], Dennis Taub[7]

[1]*Microbiology and Immunology, University of Nevada School of Medicine, Reno, CA*
[2]*Dermatology, UC Davis, Sacramento, CA*
[3]*Oncology, UC Davis, Sacramento, CA*
[4]*Pathology and Laboratory Medicine, UC Davis, Sacramento, CA*
[5]*Dermatology and Internal Medicine, UC Davis, Sacramento, CA*
[6]*VA, Northern CA Health Care System, Sacramento, CA*
[7]*NIA-IRP, NIH Biomedical Research Center, Baltimore, MD*

90
WITHDRAWN BY AUTHOR

91
PHARMACOLOGICAL CHARACTERISTICS OF PEPEROMIA PELLUCIDA (L.) KUNTH AS WELL AS FICUS PUMILA L. AND ITS APPLICATION IN IMMUNOLOGICAL CELLS OF WISTAR RATS

Md. Ariful Haque Mollik

[1]Biological Sciences, Biotech Concern, Mirpur, Bangladesh
[2]Biological Sciences, Peoples Integrated Alliance, Mirpur, Bangladesh
[3]Research and Development, Prescience Trust Funds, Phoenixville, PA

92
HER-2 PEPTIDE VACCINATION SUPPRESSES SPONTANEOUS TUMORIGENESIS AND TUMOR STEM CELL EXPANSION IN MMTV-PYVT TRANSGENIC MOUSE MODEL

Yong Park[1], Eun-Young Gil[1], In Sun Kim[2], Mary L. Disis[3], Uk Hyun Jo[1], *Kyong Hwa Park*[1]

[1]Internal Medicine, Korea University College of Medicine, Seoul, Republic of Korea
[2]Pathology, Korea University College of Medicine, Seoul, Republic of Korea
[3]Medicine, University of Washington, Seattle, WA

93
TOPICAL IMIQUIMOD INDUCES IMMUNE ACTIVATION AND REGRESSIONS OF CUTANEOUS MELANOMA METASTASES

Elise P. Salerno[1], Ena Wang[2], Franco Marincola[2], Craig L. Slingluff[1]

[1]Division of Surgical Oncology, Department of Surgery, University of Virginia, Charlottesville, VA
[2]Infectious Disease and Immunogenetics Section, Department of Transfusion Medicine, Clinical Center and Center for Human Immunology, NIH, Bethesda, MD

94
BLOCKING IL-18 DURING IL-12+IL-15 THERAPY AMELIORATES TOXICITY AND ERADICATES MALIGNANCY

Jeff Subleski, Tim Back, Anthony Scarzello, Jonathan Weiss, Wiltrout H. Robert

Frederick National Laboratory for Cancer Research, National Cancer Institute, Frederick, MD

95
UTILIZING EFFECTOR B CELLS IN CANCER ADOPTIVE IMMUNOTHERAPY

Huimin Tao, Lin Lu, Martin Egenti, Alfred E. Chang, Qiao Li

University of Michigan, Ann Arbor, MI

96
REGULATORY T CELLS AND MYELOID-DERIVED SUPPRESSOR CELLS IN THE TUMOR MICROENVIRONMENT UNDERGO FAS-DEPENDENT CELL DEATH DURING IL-2/ACD40 THERAPY

Jonathan M. Weiss[1], Jeff J. Subleski[1], Tim Back[1], Xin Chen[2], Stephanie K. Watkins[1], Hideo Yagita[3], Thomas J. Sayers[2], William J. Murphy[4], Robert H. Wiltrout[1]

[1]Cancer and Inflammation Program, Frederick National Laboratory for Cancer Research, Frederick, MD
[2]Basic Science Program, SAIC Frederick, Frederick, MD
[3]Immunology, Juntendo University School of Medicine, Tokyo, Japan
[4]Dermatology, University of California, Davis, CA

97
IMMUNOGENICITY OF P53 SYNTHETIC LONG PEPTIDE VACCINATION WITH INTERFERON-α RESULTS IN INCREASED P53-SPECIFIC POLYFUNCTIONAL T-CELL FREQUENCIES

Marij J. Welters[1], Frank Speetjens[2], Eliane Zeestraten[2], Sepideh Saadatmand[2], Linda F. Stynenbosch[1], Rob Valentijn[3], Jaap Oostendorp[3], Lorraine Fathers[3], Cornelis van de Velde[2], Peter Kuppen[2], Sjoerd H. van der Burg[1], Cornelis J. Melief[4]

[1]Clinical Oncology, Leiden University Medical Center, Leiden, Netherlands
[2]Surgery, Leiden University Medical Center, Leiden, Netherlands
[3]Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, Netherlands
[4]ISA Pharmaceuticals, Bilthoven, Netherlands

98
THE TRANSIENT NATURE OF SIGNIFICANT TOXICITIES ASSOCIATED WITH HIGH DOSE INTERLEUKIN (HD IL-2): PRELIMINARY DATA FROM THE PROCLAIMSM STUDY

Michael K. Wong[1], Howard L. Kaufman[2], Michael Morse[3], David F. McDermott[4], James N. Lowder[5]

[1]Medicine, University of Southern California, Los Angeles, CA
[2]Surgery, Rush University, Chicago, IL
[3]Medicine, Duke University, Durham, NC
[4]Medicine, Harvard University, Boston, MA
[5]Clinical, Prometheus Laboratories Inc, San Diego, CA

99
FORCED LIGHT EXPRESSION IN TRAMP TUMORS INDUCES PROSTATE CANCER SPECIFIC IMMUNITY AND REDUCES TUMOR VOLUME

Lisa Yan[1], Diane Da Silva[1], Shreya Kanodia[2], Bhavna Verma[1], W. Martin Kast[1]

[1]*Molecular Microbiology and Immunology, University of Southern California, Los Angeles, CA*
[2]*Cancer Center, University of Hawaii, Honolulu, HI*

100
PHENOTYPIC AND FUNCTIONAL PARALLELS BETWEEN ANTIGEN-NONSPECIFIC CD8+ MEMORY T CELLS FOLLOWING CANCER IMMUNOTHERAPY AND INFLUENZA INFECTION

Anthony E. Zamora[1,2], Gail D. Sckisel[1,2], Julia K. Tietze[1], Nicole Baumgarth[3], William J. Murphy[1,4]

[1]*Department of Dermatology, School of Medicine, University of California, Davis, Sacramento, CA*
[2]*Graduate Group in Immunology, University of California, Davis, Davis, CA*
[3]*Center for Comparative Medicine, University of California, Davis, Davis, CA*
[4]*Department of Internal Medicine, School of Medicine, University of California, Davis, Sacramento, CA*

INNATE IMMUNITY IN CANCER

101
NK CELL MOLECULAR SIGNATURES ARE PREDICTIVE OF RELAPSE FREE SURVIVAL OF FAVORABLE PROGNOSIS OF BREAST CANCER PATIENTS

Maria Libera Ascierto[1,3], Michael O. Idowu[2], Yingdong Zhao[1], Davide Bedognetti[1], Sara Tomei[1], Paolo A. Ascierto[4], Ena Wang[1], Francesco Marincola[1], Andrea De Maria[3], Masoud Manjili[2]

[1]*National Institute of Health, Bethesda, MD*
[2]*Virginia Commowealth University, Richmond, VA*
[3]*University of Genoa, Genoa, Italy*
[4]*Istituto Tumori Fondazione" G. Pascale", Naples, Italy*

102
THE AIM2 INFLAMMASOME INHIBITS IFN-β PRODUCTION TRIGGERED BY TUMOR-DERIVED DNA

Leticia Corrales[1], Seng-Ryong Woo[1], Thomas F. Gajewski[1,2]

[1]*Pathology, University of Chicago, Chicago, IL*
[2]*Medicine, University of Chicago, Chicago, IL*

103
GENOMIC CHARACTERIZATION OF MELANOMA CELL LINES

Valeria De Giorgi[1], Sara Tomei[1], Qiuzhen Liu[1], John Wunderlich[2], Lorenzo Uccellini[1], Maria L. Ascierto[1], Davide Bedognetti[1], Ena Wang[1], Franco M. Marincola[1]

[1]*Infectious Disease and Immunogenetics Section (IDIS), Department of Transfusion Medicine, National Institutes of Health, Bethesda, MD*
[2]*Surgery Branch, NCI, National Institutes of Health, Bethesda, MD*

104
TUMOR IMMUNE SUBTYPES DISTINGUISH TUMOR SUBCLASSES WITH CLINICAL IMPLICATIONS IN BREAST CANCER PATIENTS

Esther de Kruijf[1], *Charla Engels*[1], Willemien van de Water[1,2], Esther Bastiaannet[1,2], Vincent Smit[3], Cornelis van de Velde[1], Gerrit-Jan Liefers[1], Peter Kuppen[1]

[1]*Surgery, Leiden University Medical Center, Leiden, Netherlands*
[2]*Gerontology & Geriatrics, Leiden University Medical Center, Leiden, Netherlands*
[3]*Pathology, Leiden University Medical Center, Leiden, Netherlands*

105
INTRADERMAL TOLL LIKE RECEPTOR-2 (TLR2) AGONIST MYCOBACTERIUM W (CADI-05) IN THE TREATMENT OF BCG REFRACTORY NON MUSCLE INVASIVE TRANSITIONAL CELL CARCINOMA OF BLADDER

Bakulesh M. Khamar[1], Michael O'Donnell[2], Chandra P. Belani[3]

[1]*Research & Development, Cadila Pharmaceuticals Limited, Ahmedabad, India*
[2]*Urology, University of Iowa Hospitals & Clinics, Iowa, IA*
[3]*Penn State Hershey Cancer Institute, Hershey, PA106*

106
OPEN-LABEL, RANDOMIZED MULTICENTER PHASE II CLINICAL TRIAL OF AN INTRADERMAL TOLL-LIKE RECEPTOR-2 (TLR2) AGONIST MYCOBACTERIUM W (CADI-05) VERSUS INTRAVESICAL BCG IN NEWLY DIAGNOSED NON MUSCLE INVASIVE TRANSITIONAL CELL CARCINOMA OF BLADDER

Bakulesh M. Khamar[1], Michael O'Donnell[2], Bhaswat Chakraborty[1]

[1]*Research & Development, Cadila Pharmaceuticals Limited, Ahmedabad, India*
[2]*Urology, University of Iowa Hospitals & Clinics, Iowa*

107
TLR8 AGONIST VTX-2337 ENHANCES HUMAN NK CELL FUNCTION VIA INFLAMMASOME ACTIVATION AND IL-18 INDUCTION
Hailing Lu[1], Gregory N. Dietsch[2], Maura A. Matthews[2], Yi Yang[1], Mary L. Disis[1], Robert M. Hershberg[2]

[1]*University of Washington, Seattle, WA*
[2]*VentiRx Pharmaceuticals, Seattle, WA*

108
IFN-GAMMA-INDUCIBLE PROTEIN-10 STIMULATES MIGRATION OF ACTIVATED NATURAL KILLER CELLS TOWARD MELANOMA TUMORS
Erik Wennerberg[1], Veronika Kremer[1], Richard Childs[2], *Andreas Lundqvist*[1,2]

[1]*Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden*
[2]*Hematology Branch, National Heart Lung and Blood Institute, National Institutes of Health, Bethesda, MD*

109
CLINICAL EVIDENCE FOR THE EFFECTIVENESS OF TRADITIONAL NATUROPATHIC MEDICINES TREATMENT FOR DIFFERENT TYPES OF CANCER IN THE SAN FRANCISCO OF CALIFORNIA UNITED STATES OF AMERICA
Md. Ariful Haque Mollik

[1]*Research and Development, Prescience Trust Funds, Phoenixville, PA*
[2]*Biological Sciences, Peoples Integrated Alliance, Mirpur, Bangladesh*
[3]*Health and Nutrition, Biogene Life Care, Paltan, Bangladesh*

110
MYELOID CELL POPULATIONS IN PATIENTS WITH HEPATOCELLULAR CARCINOMA: CORRELATION WITH LIVER-DIRECTED THERAPY
Pippa Newell[1], Talicia Savage[1], Ben Cottam[1], Ron Wolf[2], Chet Hammill[2], Kevin Sasadeusz[3], Tyler Thiesing[3], Marka Crittenden[2], Paul Hansen[2], Michael Gough[1]

[1]*Earle A. Chiles Research Institute, Providence Cancer Center, Portland, OR*
[2]*The Oregon Clinic, Portland, OR*
[3]*Interventional Radiology, Providence Cancer Center, Portland, OR*

111
TYPE I INTERFERON SIGNALING IN A MOUSE DE NOVO GLIOMA MODEL
Takayuki Ohkuri, Arundhati Ghosh, Akemi Kosaka, Jianzhong Zhu, Maki Ikeura, Simon C. Watkins, Hideho Okada, Saumendra N. Sarkar

University of Pittsburgh, Cancer Institute, Pittsburgh, PA

112
PROGNOSTIC AND PREDICTIVE RELEVANCE OF IMMUNOLOGICAL BIOMARKERS IN COLORECTAL CANCER
Marlies Reimers, Eliane Zeestraten, Gerrit-Jan Liefers, Cornelis van de Velde, Peter Kuppen

Surgery, Leiden University Medical Center, Leiden, Netherlands

113
T CELL-DEPENDENT ANTI-TUMOR ACTIVITY OF NK CELLS
Anil Shanker[1,2], Roman V. Uzhachenko[1]

[1]*Biochemistry and Cancer Biology, Meharry Medical College School of Medicine, Nashville, TN*
[2]*Cancer Biology, Vanderbilt University, Vanderbilt-Ingram Comprehensive Cancer Center, Nashville, TN*

SINGLE CELL HIGH THROUGHPUT TECHNOLOGIES IMMUNE MONITORING

114
USE OF IMMUNE MONITORING ASSAYS IN THE CLINICAL DEVELOPMENT OF IMMUNOTHERAPIES
Dr. Henry Hepburne-Scott

Serametrix Corporation, Carlsbad, CA

115
CTLA-4 DEFINES DISTINCT T CELL SIGNALING POPULATIONS IN HEALTHY DONORS AND METASTATIC MELANOMA PATIENTS
Drew Hotson[1], Andy Conroy[1], Erik Evensen[1], Giusy Gentilcore[2], Ester Simeone[2], Assunta Esposito[2], Marcello Curvietto[2], Alessandra Cesano[1], Rachael Hawtin[1], Paolo Ascierto[2]

[1]*Nodality, Inc, South San Francisco, CA*
[2]*G. Pascale National Tumor Foundation Institute, Naples, Italy*

116
ALTERED MONOCYTE PHENOTYPE DISTRIBUTION PREDICTS SURVIVAL IN MULTIPLE MYELOMA PATIENTS
Yi Lin, Peggy Bulur, Michael Gustafson, Dennis Gastineau, Allan Dietz, Vincent Rajkumar

Mayo Clinic, Rochester, MN

117

GLOBAL AND INTRATUMORAL DIVERSITY OF THE TCR REPERTOIRE IN GLIOBLASTOMA MULTIFORME AND LOW-GRADE GLIOMA

Jennifer S. Sims[1], Zahra Bhaiwala[1], Yaping Feng[3], Peter A. Sims[3], Yufeng Shen[3], Peter D. Canoll[2], Jeffrey N. Bruce[1]

[1]*Neurological Surgery, Columbia University, New York, NY*
[2]*Pathology and Cell Biology, Columbia University, New York, NJ*
[3]*Columbia Initiative for Systems Biology, Columbia University, New York, NY*

118

ELISA TOOL: AN OPEN-SOURCE RELATIONAL DATABASE MODULE FOR ELISA EXPERIMENTAL DATA

Elizabeth O'Donoghue, Meredith Slota, Dominick Auci, Mary (Nora) L. Disis

University of Washington, Seattle, WA

119

HARMONIZATION OF CELLULAR IMMUNOLOGICAL BIOMARKERS BY AN INTERNATIONAL NETWORK: THE CANCER IMMUNOTHERAPY IMMUNOGUIDING PROGRAM (CIP)

Marij J. Welters[1], Cecile Gouttefangeas[2], Christian H. Ottensmeier[3], Steffen Walter[4], Cedrik M. Britten[5], Sjoerd H. van der Burg[1]

[1]*Clinical Oncology, Leiden University Medical Center, Leiden, Netherlands*
[2]*Immunology, Eberhard-Karls University, Tuebingen, Germany*
[3]*Cancer Sciences, Southampton University Hospitals, Southampton, United Kingdom*
[4]*immatics biotechnologies GmbH, Tuebingen, Germany*
[5]*TRON GmbH, Mainz, Germany*

120

ANALYSIS OF HOST IMMUNE CELL INFILTRATION OF IMMUNOSTAINED HUMAN TUMORS USING A COMPUTER-ASSISTED PATTERN RECOGNITION IMAGE ANALYSIS (PRIA) APPROACH

Marie Cumberbatch[1], Helen K. Angell[1,2], Xiu Huan Yap[1,3], Neil Gray[1], Christopher Womack[1], *Robert W. Wilkinson*[1]

[1]*Innovative Medicines Oncology, AstraZeneca, Macclesfield, United Kingdom*
[2]*Immune Modulation Research Group, University of Nottingham, Nottingham, United Kingdom*
[3]*Department of Pharmacy and Pharmacology, University of Bath, Bath, United Kingdom*

121

PREDOMINANT USE OF A SINGLE TCR BY CEA-SPECIFIC T CELLS IN INDEPENDENT PANCREATIC CANCER PATIENTS TREATED WITH CEA PEPTIDE (CAP1-6D)/MONTANIDE/GM-CSF VACCINATION

Yuanyuan Zha[1], Hedy Kindler[2], Thomas Gajewski[1,2]

[1]*Human Immunologic Monitoring Facility, University of Chicago, Chicago, IL*
[2]*Department of Medicine, Section of Hematology/Oncology, University of Chicago, Chicago, IL*

T CELL MANUFACTURE AND POTENCY TESTING

122

DC VACCINE POTENCY CORRELATES WITH EFFICIENT INDUCTION OF TUMOR-SPECIFIC IMMUNE RESPONSES AFTER VACCINATION OF ADVANCED MELANOMA PATIENTS: PRELIMINARY DATA WITH AN IN VITRO FUNCTIONAL ASSAY

Angela Riccobon[1], Valentina Ancarani[1], Elena Pancisi[1], Massimiliano Petrini[1], Laura Fiammenghi[1], Anna Maria Granato[1], Valentina Soldati[1], Laura Ridolfi[1], Francesco de Rosa[1], Linda Valmorri[2], Giorgia Gentili[2], Oriana Nanni[2], Giuseppe Migliori[4], Dino Amadori[3], Francesco M. Marincola[5], Ruggero Ridolfi[1], *Massimo Guidoboni*[1,5]

[1]*Immunotherapy and Somatic Cell Therapy, IRCCS-IRST, Meldola (FC), Italy*
[2]*Biostatistics and Clinical Trial Unit, IRCCS-IRST, Meldola (FC), Italy*
[3]*Medical Oncology, IRCCS-IRST, Meldola (FC), Italy*
[4]*Blood Transfusion Unit, Morgagni-Pierantoni Hospital, Forli' (FC), Italy*
[5]*IDIS/DTM, NIH, Bethesda, MD*

123

A NOVEL HUMAN TCR EFFICIENT CLONING SYSTEM CONFERS CANDIDATE FOR TCR GENE THERAPY WITHIN 10 DAYS

Eiji Kobayashi[1], Eishiro Mizukoshi[2], Hiroyuki Kishi[1], Hiroshi Hamana[1], Terumi Nagai[1], Tatsuhiko Ozawa[1], Hidetoshi Nakagawa[2], Aishun Jin[1], Shuichi Kaneko[2], Atsushi Muraguchi[1]

[1]*Department of Immunology, University of Toyama, Toyama, Japan*
[2]*Department of Gastroenterology, Kanazawa University, Kanazawa, Japan*

124

A HLA-NULL CELL-BASED SYSTEM FOR THE RAPID AND SPECIFIC EXPANSION OF ANY CAR+ T CELL INDEPENDENT OF ANTIGEN-SPECIFIC STIMULATION

David Rushworth, Bipulendu Jena, Simon Olivares, Hiroki Torikai, Dean Lee, Laurence Cooper

Pediatrics, MD Anderson Cancer Center, Houston, TX

T CELL MODULATING STRATEGIES

125

FORCING NF-κB IN T CELLS PROMOTES TUMOR REJECTION

Cesar Evaristo, Luciana Molinero, Thomas Gajewski, Maria-Luisa Alegre

University of Chicago, Chicago, IL

126

RAPAMYCIN TREATMENT ENDOWS CAR-ENGINEERED CD8+ EFFECTOR T CELLS WITH MEMORY-LIKE PROPERTIES RESULTING IN ENHANCED IN VIVO ENGRAFTMENT

Joanne A. Hammill[1], Heather VanSeggelen[1], Jennifer D. Bassett[1], Sara Nolte[1], Galina F. Denisova[1], Carole Evelegh[1], Brian Rabinovich[2], Jonathan L. Bramson[1]

[1]*Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada*
[2]*M.D. Anderson Cancer Center, Houston, TX*

127

IDENTIFICATION OF IMMUNOGENIC EPITOPES FROM CANCER STEM CELL ANTIGENS FOR THE DESIGN OF MULTI-EPITOPE TH1 CD4+ T CELL VACCINES AGAINST BREAST CANCER

Meredith Slota, Ling-Yu Kuan, Dominick Auci, Mary (Nora) L. Disis

University of Washington, Seattle, WA

128

INHIBITION OF GLYCOLYTIC FLUX ENHANCES CD8+ T CELL MEMORY, STEMNESS AND ANTI-TUMOR FUNCTION

Madhusudhanan Sukumar[1], Jie Liu[2], Yun Ji[1], Rahul Roychoudhuri[1], Zhiya Yu[1], Christopher Klebanoff[1], Toren Finkel[2], Nicholas Restifo[1], Luca Gattinoni[1]

[1]*Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD*
[2]*Center for Molecular Medicine, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD*

129

SAFETY AND CLINICAL ACTIVITY OF THE ANTI-PD-L1 ANTIBODY BMS-936559 IN PATIENTS WITH SOLID TUMORS

Scott S. Tykodi[1], Julie R. Brahmer[2], Wen-Jen Hwu[3], Laura Q. Chow[1], Suzanne Topalian[2], Patrick Hwu[3], Kunle Odunsi[4], Luis H. Camacho[5], John Kauh[6], Henry C. Pitot[7], Omid Hamid[8], Drew M. Pardoll[2], William Feely[9], Payal Divanji[9], Susan M. Parker[9], Changyu Wang[9], Kent Thudium[9], Mohan Srinivasan[9], Mark Selby[9], Alan Korman[9], Stacie M. Goldberg[9]

[1]*University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA*
[2]*Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD*
[3]*MD Anderson Cancer Center, Houston, TX*
[4]*Roswell Park Cancer Institute, Buffalo, NY*
[5]*St. Luke's Episcopal Hospital, Houston, TX*
[6]*The Winship Cancer Institute of Emory University, Atlanta, GA*
[7]*Mayo Clinic College of Medicine, Rochester, MN*
[8]*The Angeles Clinic, Santa Monica, CA*
[9]*Bristol-Myers Squibb, Princeton, NJ*

TARGETED THERAPIES AND ANTI-TUMOR IMMUNITY

130

Withdrawn by Author

131

EN2: A CANDIDATE ANTIGEN FOR THE DEVELOPMENT OF TARGETED THERAPIES IN BREAST CANCER

Nicola E. Annels, Giulia Falgari, Shadi Bokaee, Catherine Riley, Mick Denyer, Guy Simpson, Hardev Pandha

Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom

132

TRENDS IN CIRCULATING TUMOR CELLS (CTCS) IN MULTIPLE ADJUVANT (ADJ) TRIALS OF HER2-SPECIFIC PEPTIDE VACCINES (PV) IN BREAST CANCER (BRCA) PTS

J. S. Berry[1], T. J. Vreeland[1], A. F. Trappey[1], D. F. Hale[1], G. T. Clifton[1], A. K. Sears[1], R. Patil[2], N. M. Shumway[1], J. P. Holmes[3], S. McCall[1], G. A. Merrill[1], S. Ponniah[4], E. A. Mittendorf[5], G. E. Peoples[1]

[1]*SAMMC, San Antonio, TX*
[2]*RPCI, Buffalo, NY*
[3]*RRMG, Santa Rosa, CA*
[4]*USUHS, Bethesda, MD*
[5]*MDACC, Houston, TX*

133
IMCGP100: A NOVEL BI-SPECIFIC BIOLOGIC IMMUNOTHERAPY FOR THE TREATMENT OF MALIGNANT MELANOMA

Giovanna Bossi[1], Namir Hassan[1], Katherine Adams[2], Jane Harper[1], Sandrine Buisson[1], Samantha Paston[1], Nathaniel Liddy[1], Rebecca Ashfield[1], Frayne Bianchi[1], Emma Baston[1], Andrew K. Sewell[3], Yi Li[1], Brian Cameron[1], Andrew Johnson[1], Annelise Vuidepot[1], Penio Todorov[1], Michael Kalos[4], Carl June[4], Giorgos Karakousis[4], Gerry Linette[5], David A. Price[5], Daniel Williams[2], Yvonne McGrath[1], Bent K. Jakobsen[1]

[1]*Immunocore Ltd, Abingdon, United Kingdom*
[2]*Adaptimmune Ltd, Abingdon, United Kingdom*
[3]*Cardiff University, Cardiff, United Kingdom*
[4]*University of Pennsylvania, Philadelphia, PA*
[5]*Washington University School of Medicine, St. Louis, MO*

134
THE CANCER/TESTIS ANTIGENS ROPPORIN AND AKAP-4 ARE NOVEL TARGETS FOR MULTIPLE MYELOMA IMMUNOTHERAPY

Leonardo Mirandola[1,2], Raffaella Chiaramonte[1,2], Yuefei Yu[2], Fred Hardwicke[2], Nicholas D'Cunha[2], Tijani Luckman[2], Diane D. Nguyen[2], Everardo Cobos[2], *Maurizio Chiriva-Internati*[2]

[1]*Heatlh Sciences, Università degli Studi di Milano, Milano, Italy*
[2]*Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX*

135
GENERATION OF AN ANTITUMOR RESPONSE AND IMMUNITY USING A SMALL MOLECULE DRUG (PV-10)

Craig Dees, S. Blair, J. Harkins, T. Scott, E. Wachter

Provectus Pharmaceuticals, Knoxville, TN

136
ACTIVE IMMUNOTHERAPY WITH PROSTVAC® DEMONSTRATES POTENT ANTI-TUMOR EFFICACY IN A MOUSE MODEL OF PROSTATE CANCER

Ryan B. Rountree, Stefanie J. Mandl, Joseph Cote, Tracy dela Cruz, Thierry Giffon, Evan Gordon, Susan P. Foy, John R. Lombardo, Erica Trent, Reiner Laus, Alain Delcayre

BN ImmunoTherapeutics, Mountain View, CA

137
INCREASED CD4 T CELL AND ANTIBODY RESPONSES BY ADDITION OF RECOMBINANT HER2 PROTEIN TO MVA-BN®-HER2

Stefanie J. Mandl, Ryan B. Rountree, Joseph Cote, Tracy dela Cruz, Thierry Giffon, John R. Lombardo, Erica Trent, Reiner Laus, Alain Delcayre

BN ImmunoTherapeutics, Mountain View, CA

138
A NOVEL ASSAY TO MEASURE THE IMMUNOGENICITY OF DIFFERENT IONIZING RADIATION (IR) REGIMENS

Encouse B. Golden, Silvia C. Formenti

Radiation Oncology, New York University, New York, NY

139
RAPID ASSESSMENT OF TIME, DOSE, AND FRACTION DEPENDENT RELEASE OF EXTRACELLULAR HMGB1 AFTER IONIZING RADIATION (IR)

Encouse B. Golden[1], Leonard Liebes[3], Sandra Demaria[2], Mary Helen Barcellos-Hoff[1], Silvia C. Formenti[1]

[1]*Radiation Oncology, New York University, New York, NY*
[2]*Pathology, New York University, New York, NY*
[3]*Medicine, New York University, New York, NY*

140
THE UTILIZATION OF PSEUDOMONAS AERUGINOSA EXOTOXIN T AS A POTENTIAL CHEMOTHERAPEUTIC AGENT FOR SOLID TUMORS

Joe Goldufsky[1,2], Stephen Wood[1], Howard L. Kaufman[1,2,3], Sasha Shafikhani[1,2], Carl Ruby[1,2,3]

[1]*Immmunology/Microbiology, Rush University Medical Center, Chicago, IL*
[2]*Cancer Center, Rush University Medical Center, Chicago, IL*
[3]*General Surgery, Rush University Medical Center, Chicago, IL*

141
PRALATREXATE (FOLOTYN TM) MAY EXERT AN ANTI-MARGINAL ZONE LYMPHOMA (MZL) EFFECT THROUGH AN IMMUNE MEDIATED MECHANISM

Kevin M. Gallagher[1], Philip A. Haddad[1,2]

[1]*LSUHSC, Feist-Weiller Cancer Center, Shreveport, LA*
[2]*Overton Brooks VAMC, Shreveport, LA*

142
RNADJUVANT® COMBINED WITH ANTIGEN INDUCES SUPERIOR ANTI-TUMOR ACTIVITY COMPARED TO POLY I:C AND HAS A VERY FAVOURABLE SAFETY PROFILE

Regina Heidenreich, Mariola Fotin-Mleczek, Patrick Baumhof, Birgit Scheel, Söhnke Voss, Thomas Kramps, Karl Josef Kallen

CureVac GmbH, Tübingen, Germany

143

IMCMAGE1: A NOVEL BI-SPECIFIC BIOLOGIC RE-DIRECTING T CELLS TO KILL MAGE-A3/A6 PRESENTING CANCERS

Linda Hibbert[1], N. Hassan[1], D. Baker[1], J. Harper[1], K. Adams[1], G. Bossi[1], N. Liddy[1], S. Paston[1], R. Ashfield[1], Y. McGrath[1], D. Williams[1], B. Cameron[1], A. Johnson[1], A. Vuidepot[1], P. Roberts[2], C. Hatton[2], M. Kalos[3], C. June[3], B. K. Jakobsen[1]

[1]*Immunocore Ltd., Abingdon, United Kingdom*
[2]*Clinical Haematology, Churchill Hospital, Oxford, United Kingdom*
[3]*University of Pennsylvania, Philadelphia, PA*

144

IMMUNE-MODULATION BY EPIDERMAL GROWTH FACTOR RECEPTOR SIGNALING PATHWAY IN THE PATHOGENESIS OF SKIN RASH AND ANTI-TUMOR IMMUNITY

Im Jin S.[1,3], Shaad Abdullah[1], Steven A. Porcelli[2], Roman Perez-soler[1]

[1]*Medicine, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY*
[2]*Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY*
[3]*Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX*

145

ANTIBODY-DIRECTED CPG TARGETS TUMOR MICROENVIRONMENT AND PROVIDES ACTIVE IMMUNOTHERAPY

Julie K. Jang-Wu[1], Peisheng Hu[1], Zhongjun Li[1], Leslie A. Khawli[2], Alan L. Epstein[1]

[1]*Pathology, Keck School of Medicine of USC, Los Angeles, CA*
[2]*Genentech Inc., South San Francisco, CA*

146

ANALYSIS OF PSA-SPECIFIC T CELL RESPONSE IN PSA-TRANSGENIC MOUSE: A USEFUL MODEL TO STUDY PROSTATE CANCER IMMUNOTHERAPY

Seema Dubey, Dev Karan

Department of Urology, The University of Kansas Medical Center, Kansas City, KS

147

PRE-EXISTING IMMUNITY TO CANCER OVER-EXPRESSED ANTIGENS INVERSELY CORRELATE WITH THE LEVEL OF MYELOID SUPPRESSOR CELLS IN CIRCULATION

Mohan Karkada[1,2], Nadia Al-Banna[1], Tara Quinton[1], Lori Wood[3], Arik Drucker[3], James Bentley[3], Marc Mansour[1], Daniel Rayson[3]

[1]*Immunovaccine Inc, Halifax, NS, Canada*
[2]*Microbiology/Immunology, Dalhousie University, Halifax, NS, Canada*
[3]*Medicine/Oncology, Dalhousie University, Halifax, NS, Canada*

148

TWO-PRONGED APPROACH TO IMMUNOTHERAPY OF ACUTE MYELOID LEUKEMIA USING CPG-STAT3 SIRNA

Sakib D M. Hossain[1], Qifang Zhang[1], Sergey Nechaev[1], Anna Kozlowska[1], Hongjun Liu[4], Piotr Swiderski[2], Claudia Kowolik[2], John J. Rossi[3], Ravi Bhatia[4], Ya-Huei Kuo[4], Marcin Kortylewski[1]

[1]*Cancer Immunotherapeutics and Tumor Immunology, Beckman Research Institute at City of Hope, Duarte, CA*
[2]*Molecular Medicine, Beckman Research Institute at City of Hope, Duarte, CA*
[3]*Molecular Biology, Beckman Research Institute at City of Hope, Duarte, CA*
[4]*Hematopoietic Stem Cell and Leukemia Research, Beckman Research Institute at City of Hope, Duarte, CA*

149

IMPROVING THE IMMUNOGENICITY OF IMMUNOTHERAPEUTIC MINOR HISTOCOMPATIBILITY ANTIGEN UTA2-1

Rimke Oostvogels[1,2], Rieuwert Hoppes[3], Monique C. Minnema[1], Maarten E. Emmelot[2], Maureen van Elk[2], Robbert M. Spaapen[2,3], Henk M. Lokhorst[1], Huib Ovaa[3], Tuna Mutis[2]

[1]*Hematology, University Medical Center Utrecht, Utrecht, Netherlands*
[2]*Clinical Chemistry and Hematology, University Medical Center Utrecht, Utrecht, Netherlands*
[3]*Cell Biology, Dutch Cancer Institute, Amsterdam, Netherlands*

150
SEARCH FOR COMMON NON-SMALL CELL LUNG CANCER (NSCLC) TUMOR ANTIGEN IDENTIFIES A GLYCOLIC PATHWAY ENZYME, PKM2, AS A POTENTIAL DRUG TARGET, COMMON TO 8 NSCLC CELL LINES TESTED
Sachin Puri[1], Bharat H. Joshi[2], Akiko Suzuki[2], Bhaskar Bhattacharya[2], Tarsem Moudgil[1], Jing Han[2], Raj K. Puri[2], Bernard Fox[1,3]

[1]*Molecular & Tumor Immunology, Earle A Chiles Research Institute, Portland, OR*
[2]*Center for Biologics Evaluation & Research, Food Drug Adminsitration, Bethesda, MD*
[3]*Molecular Microbiology and Immunology, Oregon Health and Science University, Portland, OR*

151
INDUCTION OF MULTIPOTENT Vδ2-NEGATIVE γδT-CELLS AFTER CMV-REACTIVATION IN ALLOGENEIC STEM CELL TRANSPLANTATION
Wouter Scheper[1], Suzanne van Dorp[1], Sabina Kersting[1], Floor Pietersma[1], Samantha Hol[1], Zsolt Sebestyen[1], Sabine Heijhuurs[1], Victoria Macu-Malina[1], Cordula Grunder[1], Sabine Becke[3], Bodo Plachter[3], Debbie van Baarle[1,2], Jurgen Kuball[1]

[1]*Hematology & Immunology, UMC Utrecht, Utrecht, Netherlands*
[2]*Internal Medicine & Infectious Diseases, UMC Utrecht, Utrecht, Netherlands*
[3]*Institute for Virology, UMC of the Johannes Gutenberg-University, Mainz, Germany*

152
DIFFERENTIAL EFFECTS OF THE TYROSINE KINASE INHIBITORS ON T CELL GROWTH PROPERTIES AND ACTIVITY
Franziska Stehle, Corinna Fahldieck, Jana Kalich, Kristin Schulz, Dagmar Riemann, *Barbara Seliger*

Institute of Medical Immunology, Martin Luther University Halle-Wittenberg, Halle, Germany

153
IMMUNE SUPPRESSIVE ACTIVITY MEDIATED BY ONCOGENES AND LOSS OF TUMOR SUPPRESSOR GENE ACTIVITY
Juergen Bukur[1], Sandra Leisz[1], André Steven[1], Christian V. Recktenwald[1], Bernhard Hiebl[2], *Barbara Seliger*[1]

[1]*Institute of Medical Immunology, Martin Luther University Halle-Wittenberg, Halle, Germany*
[2]*Center of Basic Medical Science, Martin Luther University Halle-Wittenberg, Halle, Germany*

154
SUCCESSFUL TREATMENT OF ESTABLISHED MOUSE MELANOMA WITH IL-12 ELECTROTRANSFER IS DEPENDENT ON THE DELIVERY PARAMETERS USED
Shawna Shirley, Cathryn Lundberg, Fanying Li, Niculina Burcus, Richard Heller

Old Dominion University, Norfolk, VA

155
DEVELOPMENT OF BIVALENT LISTERIA MONOCYTOGENES -LLO IMMUNOTHERAPY THAT CONCOMITANTLY TARGETS TUMOR CELLS AND ANGIOGENESIS
Anu Wallecha, Kimberly Ramos, Inga Malinina, Reshma Singh

Research and Development, Advaxis Inc., Princeton, NJ

156
PSEUDOMONAS AERUGINOSA EXOTOXIN T INDUCES CYTOTOXICITY AND BLOCKS APOPTOTIC COMPENSATORY PROLIFERATION SIGNALING
Stephen Wood, Sasha Shafikhani, Gayathri Sivaramakrishnan

Microbiology/Immunology, Rush University Medical Center, Chicago, IL

157
THE ANTI-TUMOR T CELL RESPONSE PLAYS A CRITICAL ROLE IN THE THERAPEUTIC EFFECT OF DASATINIB ON C-KIT MUTANT MASTOCYTOMA AND CAN BE POTENTIATED BY ANTI-OX40 ANTIBODY
Yan Yang, Chengwen Liu, Weiyi Peng, Rina M. Mbofung, Gregory Lizee, Willem W. Overwijk, Scott E. Woodman, Patrick Hwu

Melanoma Medical Oncology, MD Anderson Cancer Center, Houston, TX

TARGETING IMMUNE SUPPRESSION

158
MODULATION OF REGULATORY T CELLS BY TARGETING THE NFAT-FOXP3 PROTEIN:PROTEIN INTERACTION
Nicola E. Annels, Guy R. Simpson, Shadi Bokaee, Catherine Riley, Mick Denyer, Hardev Pandha, Richard Morgan

Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom

159
DRIVING ANTI-CANCER IMMUNE RESPONSES IN THE CORRECT DIRECTION: IMPORTANT CLINICAL FACTS LOST IN TRANSLATION

Brendon J. Coventry[1], Martin L. Ashdown[2]

[1]*Surgery & Immunotherapy, University of Adelaide, Adelaide, SA, Australia*
[2]*Medicine, University of Melbourne, Melbourne, VIC, Australia*

160
OVARIAN TUMOR-INFILTRATING T CELLS AND MYELOID CELLS MEDIATE IMMUNE SUPPRESSION THROUGH PD-1/PD-L1 PATHWAY

Jaikumar Duraiswamy[1], Gordon J. Freeman[2], George Coukos[1]

[1]*Ovarian Cancer Research Center and Dept of Obstetrics & Gynecology, University of Pennsylvania, Philadelphia, PA*
[2]*Dana Farber Cancer Institute, Harvard Medical School, Boston, MA*

161
OVERCOMING TUMOR-INDUCED NEGATIVE REGULATORY PATHWAYS IN MURINE MODELS OF RHABDOMYOSARCOMA

Steven L. Highfill, Crystal L. Mackall

Pediatric Oncology Branch, NCI, Bethesda, MD

162
NOS1 OVEREXPRESSION BY MELANOMA CELLS CONTRIBUTES TO TYPE I IFNα SIGNAL DYSFUNCTION IN IMMUNE CELLS

Qiuzhen Liu[1,2], Sara Tomei[1], Maria L. Ascierto[1], Valeria D. Giorgi[1], Cuilian Dai[3], Lorenzo Uccellini[1], Tara Spivey[1], Zoltan Pos[1], Jaime Thomas[1], Jennifer Reinboth[1], Daniela Murtas[1], Davide Bedognetti[1], Ena Wang[1], Francesco M. Marincola[1]

[1]*Infectious Disease and Immunogenetics Section (IDIS), Department of Transfusion Medicine, Clinical Center and trans-NIH Center for Human Immunology (CHI), National Institutes of Health, Bethesda, MD*
[2]*Cancer Research Institute, Southern Medical University, Guangzhou, China*
[3]*Department of Cardiology, The Affiliated Hospital of Zunyi Medical College, Zunyi, China*

163
ANTI-GR-1 ANTIBODY DEPLETION FAILS TO ELIMINATE HEPATIC MYELOID DERIVED SUPPRESSOR CELLS IN TUMOR BEARING MICE

Chi Ma[1], Tamar Kapanadze[1,2], Jaba Gamrekelashvili[1,2], Michael P. Manns[2], Firouzeh Korangy[1], Tim F. Greten[1]

[1]*Medical Oncology Branch, National Cancer Institute/NIH, Bethesda, MD*
[2]*Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany*

164
CANCER STEM CELLS ISOLATED FROM SOLID TUMORS CAN DISPLAY IMMUNOMODULATORY ACTIVITY FOR T CELL RESPONSES

Cristina Maccalli[1], Andrea Volontè[1], Ena Wang[2], Francesca Sanvito[3], Luca Albarello[3], Claudio Doglioni[3], Francesco M. Marincola[2], Giorgio Parmiani[1]

[1]*Molecular Oncology, San Raffaele Scientific Institute, Milan, Italy*
[2]*Transfusion Medicine, Clinical Center, and Center for Human Immunology, National Institutes of Health, Bethesda, MD*
[3]*Unit of Pathology, San Raffaele Scientific Institute, Milan, Italy*

165
TUMOR-DERIVED ADENOSINE ENHANCES GENERATION AND SUPPRESSIVE FUNCTIONS OF HUMAN ADAPTIVE REGULATORY T CELLS

Magis Mandapathil[1], Malgorzata Harasymczuk[4], Miroslaw J. Szczepanski[4], Edwin K. Jackson[3], Stephan Lang[2], Theresa L. Whiteside[3]

[1]*Otorhinolaryngology, University of Marburg, Marburg, Germany*
[2]*Otorhinolaryngology, University of Duisburg-Essen, Essen, Germany*
[3]*Pathology, University of Pittsburgh, Pittsburgh, PA Whiteside*[3]
[4]*Otorhinolaryngology, University of Poznan, Poznan, Poland*

166
THERAPEUTIC EXOSOME REMOVAL TO TARGET TUMOR-MEDIATED IMMUNE SUPPRESSION

Annette M. Marleau[1], Paul Duffin[1], Douglas D. Taylor[2], James A. Joyce[1], Richard H. Tullis[1]

[1]*Aethlon Medical, San Diego, CA*
[2]*University of Louisville, Louisville, KY*

167
GM-CSF-INDUCED IL-4Rα EXPRESSION ON GLIOMA-INFILTRATING MONOCYTES PROMOTES IMMUNOSUPPRESSION AND GLIOMA GROWTH

Gary Kohanbash[1,2], Kayla McKaveney[1], Masashi Sakaki[1], Mitsugu Fujita[3], *Hideho Okada*[1]

[1]*Brain Tumor Program, University of Pittsburgh Cancer Institute, Pittsburgh, PA*
[2]*Infectious Diseases and Microbiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA*
[3]*Kinki University, Osaka, Japan*

168

INVARIANT NATURAL KILLER T (INKT) CELLS REGULATE THE RESPONSE TO RADIOTHERAPY AND ANTI-CTLA-4 BY TARGETING DENDRITIC CELLS

Karsten A. Pilones[1], Joseph Aryankalayil[1], Silvia Formenti[2], Sandra Demaria[1]

[1]*Pathology, NYU School of Medicine, New York, NY*
[2]*Radiation Oncology, NYU School of Medicine, New York, NY*

169

CYCLOOXYGENASE-2 INHIBITION CONSTRAINS INDOLEAMINE 2,3-DIOXYGENASE-1 EXPRESSION BY ACUTE MYELOID LEUKEMIA CELLS

Giuseppina Bonanno[1], Annabella Procoli[1], Andrea Mariotti[1], Valentina Folgiero[2], Daniela Natale[2], Raimondo De Cristofaro[3], Franco Locatelli[2], *Sergio Rutella*[2]

[1]*Gynecology, Catholic Univ. Med. School, Rome, Italy*
[2]*Pediatric Hematology and Oncology, IRCCS Bambino Gesù Children's Hospital, Rome, Italy*
[3]*Medicine and Geriatrics, Catholic Univ. Med. School, Rome, Italy*

170

INDOLEAMINE 2,3-DIOXYGENASE-1 (IDO1) IS EXPRESSED IN A SUBGROUP OF CHILDHOOD ACUTE MYELOID LEUKEMIAS

Valentina Folgiero[1], Daniela Natale[1], Alessandra Del Bufalo[2], Roberta Caruso[1], Luciana Vinti[1], Valentina Coletti[1], Raimondo De Cristofaro[3], Franco Locatelli[1], *Sergio Rutella*[1]

[1]*Hematology and Oncology, IRCCS Bambino Gesù Children's Hospital, Rome, Italy*
[2]*Hygiene and Preventive Medicine, Catholic Univ. Med. School, Rome, Italy*
[3]*Medicine and Geriatrics, Catholic Univ. Med. School, Rome, Italy*

171

HUMAN REGULATORY B CELLS AND T EFFECTOR CELLS UTILIZE EXOGENOUS ADENOSINE TO ATTENUATE THEIR FUNCTIONAL RESPONSES

Zenichiro Saze[1], Patrick J. Schuler[1], Chang-Sook Hong[1], Dongmei Cheng[2], Edwin K. Jackson[2], Theresa L. Whiteside[1]

[1]*Pathology, University of Pittsburgh, Pittsburgh, PA*
[2]*Pharmacology Chemical Biology, University of Pittsburgh, Pittsburgh, PA*

172

GITR LIGATION IMMUNOTHERAPY CAUSES TUMOR DEPENDENT LOSS OF REGULATORY T CELL LINAGE STABILITY

David Schaer[1], Sadna Budhu[1], Cailan Liu[1], Campbell Bryson[3], Nicole Malandro[1,3], Alan Houghton[1,2,3], Taha Merghoub[1,2], Jedd Wolchok[1,2,3]

[1]*Immunology Program, Sloan-Kettering Inst, New York, NY*
[2]*Dept Medicine, MSKCC, New York, NY*
[3]*Weill Medical College, Cornell University, New York, NY*

173

IMMUNOSTIMULATORY CANCER IMMUNOTHERAPY REGIMENS INDUCE SUBSEQUENT POTENT IMMUNOSUPPRESSIVE RESPONSES

Gail D. Sckisel[1], Myriam N. Bouchlaka[4], Annie Mirsoian[1], Hui-Hua Hsiao[1], Arta M. Monjazeb[2], William J. Murphy[1,3]

[1]*Dermatology, University of California, Davis Medical Center, Sacramento, CA*
[2]*Radiation/Oncology, University of California, Davis Medical Center, Sacramento, CA*
[3]*Internal Medicine, University of California, Davis Medical Center, Sacramento, CA*
[4]*School of Medicine, University of Nevada, Reno, Reno, NV*

174

COMPREHENSIVE FLOW CYTOMETRY TRACKING OF LYMPHOCYTE SUBSETS DURING HD IL-2 THERAPY FOR MELANOMA REVEALS A POSSIBLE ROLE FOR ICOS+CD4+T-REGULATORY CELLS IN LIMITING CLINICAL RESPONSE

Geok Choo Sim, Natalia Martin-Orozco, Lei Jin, Yan Yang, Sheng Wu, Edwina W. Washington, Deborah L. Sanders, Carol L. Lacey, Yijun Wang, Luis M. Vence, Patrick Hwu, Laszlo Radvanyi

Melanoma Medical Oncology, UT MD Anderson Cancer Center, Houston, TX

175

GALECTIN-1 KNOCKDOWN ENHANCES THE EFFICACY OF IMMUNOTHERAPY FOR MURINE MALIGNANT GLIOMA

Tina Verschuere[1], Jaan Toelen[2], Françoise Poirier[3], Louis Boon[4], Florence Lefranc[5], Robert Kiss[5], Stefaan Van Gool[1], Steven De Vleeschouwer[6,1]

[1]*Experimental Immunology, Catholic University Leuven, Leuven, Belgium*
[2]*Molecular Virology and Gene Therapy, Catholic University Leuven, Leuven, Belgium*
[3]*Institut Jacques Monod, Université Paris Diderot, Paris, France*
[4]*Bioceros BV, Utrecht, Netherlands*
[5]*Lab of Toxicology, University of Brussels, Brussels, Belgium*
[6]*Neurosurgery, University Hospital Gasthuisberg, Leuven, Belgium*

THERAPEUTIC MONOCLONAL ANTIBODIES IN CANCER

176

TARGETING OF PHOSPHATIDYLSERINE BY MONOCLONAL ANTIBODIES INDUCES INNATE AND SPECIFIC ANTI-TUMOR RESPONSES

Bruce Freimark[1], Jian Gong[1], Rich Archer[1], Van Nguyen[1], Christopher Hughes[3], Xianming Huang[2], Yi Yin[2], Philip Thorpe[2]

[1]*Preclinical Development, Peregrine Pharmaceuticals, Inc, Tustin, CA*
[2]*Pharmacology, University of Texas, Southwestern Medical Center, Dallas, TX*
[3]*Molecular Biology and Biochemistry, University California, Irvine, Irvine, CA*

177

ACTIVITY OF BRENTUXIMAB VEDOTIN (ADCETRIS TM) IN REPLACED PROGRESSIVE CD30+ TRANSFORMED MYCOSIS FUNGOIDES (TMF)

Srinivas S. Devarakonda[1], Philip A. Haddad[1,2]

[1]*LSUHSC, Feist-Weiller Cancer Treatment Center, Shreveport, LA*
[2]*Overton Brooks VAMC, Shreveport, LA*

178

ACTIVITY OF RITUXIMAB-BENDAMUSTINE (RB) IN SEQUENCE WITH BRENTUXIMAB VEDOTIN (ADCETRIS TM, BV) IN GRAY ZONE LYMPHOMA (GZL) BETWEEN HODGKINS LYMPHOMA (HL) AND DIFFUSE LARGE B CELL LYMPHOMA (DLBCL)

John P. Ponugupati[1], Philip A. Haddad[1,2]

[1]*Feist-Weiller Cancer Treatment Center, LSUHSC, Shreveport, LA*
[2]*Overton Brooks VAMC, Shreveport, LA*

179

DEVELOPMENT OF A NEW ADCC-LIKE ASSAY AND ITS CLINICAL VALUES OF THE PREDICTION OF TRASTUZUMAB RESPONSES

Yasuo Kodera[1], Mayu Yunokawa[1], Kazuhiro Obara[2], Fumiko Taguchi[1], Kenji Tamura[3], Yasuhiro Fujiwara[3], Masato Mitsuhashi[4], Fumiaki Koizumi[1]

[1]*Shien-Lab and Support Facility of Project Ward, National Cancer Center Hospital, Chuo-ku, Japan*
[2]*Hitachi Chemical Co., Ltd., Hitachi, Japan*
[3]*Department of Breast and Medical Oncology, National Cancer Center Hospital, Chuo-ku, Japan*
[4]*Hitachi Chemical Research Center, Inc., Irvine, CA*

180

A STUDY OF IMMUNE MECHANISMS OF ACTION OF ANTI-EPIDERMAL GROWTH FACTOR RECEPTOR ANTIBODIES CETUXIMAB AND PANITUMUMAB AND ITS IMPLICATION IN HEAD AND NECK CANCER THERAPY

Raghvendra M. Srivastava[1], Sandra P. Gibson[1], Andres Lopez-Albaitero[1], Jie Hyun-bae[1], Soldao Ferrone[2,3,4], Robert L. Ferris[1,4,3]

[1]*Otolaryngology, University of Pittsburgh, Pittsburgh, PA*
[2]*Surgery, University of Pittsburgh, Pittsburgh, PA*
[3]*Pathology, University of Pittsburgh, Pittsburgh, PA*
[4]*Immunology, University of Pittsburgh, Pittsburgh, PA*

181

EPIDERMAL GROWTH FACTOR RECEPTOR SIGNALING FACILITATES IMMUNE ESCAPE FUNCTION IN HEAD AND NECK CANCER

Raghvendra M. Srivastava[1], Jie Hyun-bae[1], Soldano Ferrone[1,2,3], Robert L. Ferris[1,3]

[3]*Surgery, Pathology, Immunology, University of Pittsburgh, Pittsburgh, PA, Pittsburgh, PA*

182

TARGETING REGULATORY T CELLS BY INTRACRANIAL CONVECTION-ENHANCED DELIVERY OF ANTI-CD25 PROMOTES TUMOR CLEARANCE IN MURINE GLIOMA

Vadim Tsvankin[1], Richard Leung[2], Benjamin Amendolara[1], Jennifer S. Sims[1], Allen Waziri[3], Peter Canoll[2], Jeffrey Bruce[1]

[1]*Neurosurgery, Columbia University, New York, NY*
[2]*Pathology and Cell Biology, Columbia University, New York, NY*
[3]*Neurosurgery, University of Colorado, Aurora, CO*

TUMOR MICROENVIRONMENT

183
INTRATUMORAL DELIVERY OF INTERLEUKIN-12 DNA WITH IN VIVO ELECTROPORATION CAN LEAD TO REGRESSION OF INJECTED AND NON-INJECTED TUMORS IN MERKEL CELL CARCINOMA: RESULTS OF A PHASE 2 STUDY

Shailender Bhatia[1], A. Blom[1], J. Iyer[1], D. Ibrani[1], O. Afanasiev[1], A. Daud[2], S. Yu[2], D. Byrd[1], U. Parvathaneni[1], R. Heller[3], T. Diep[4], E. Kitt[4], P. Nghiem[1]

[1]*UW, Seattle, WA*
[2]*UCSF, San Francisco, CA*
[3]*ODU, Norfolk, VA*
[4]*Oncosec, San Diego, CA*

184
ACCESSORY CELLS OF THE BONE MARROW MICROENVIRONMENT PROTECT MULTIPLE MYELOMA CELLS FROM T CELL CYTOTOXICITY THROUGH CELL ADHESION MEDIATED IMMUNE RESISTANCE (CAM-IR)

Sanne J. de Haart[1], Niels W. van de Donk[2,4], Monique C. Minnema[2], Tineke Aarts-Riemens[1], Rimke Oostvogels[1], Niels Bovenschen[3], Henk M. Lokhorst[2], Constantine S. Mitsiades[4], Tuna Mutis[1]

[1]*Clinical Chemistry and Hematology, University Medical Center Utrecht, Utrecht, Netherlands*
[2]*Hematology, University Medical Center Utrecht, Utrecht, Netherlands*
[3]*Pathology, University Medical Center Utrecht, Utrecht, Netherlands*
[4]*Medical Oncology, Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Boston, MA*

185
VACCINATION INTO THE TUMOR MICROENVIRONMENT USING RECOMBINANT VACCINIA EXPRESSING HER2/NEU LEADS TO TUMOR REGRESSION AND THE GENERATION OF A TUMOR-SPECIFIC SYSTEMIC T CELL RESPONSE IN A MOUSE MODEL OF HER2/NEU-OVEREXPRESSING MAMMARY CARCINOMA

Christiaan R. de Vries[1,3], Claude E. Monken[2,3], Edmund C. Lattime[1,2,3]

[1]*Department of Microbiology and Molecular Genetics, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ*
[2]*Department of Surgery, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ*
[3]*The Cancer Institute of New Jersey, New Brunswick, NJ*

186
IMMUNOPHENOTYPIC ANALYSIS OF TUMOR INFILTRATING T LYMPHOCYTES AND MODULATION OF ANTITUMOR IMMUNITY IN PATIENTS WITH BREAST CANCER: CORRELATION WITH CLINICOPATHOLOGICAL FEATURES

Soheir R. Demian[1], Ezzat M. Hassan[1], Seham AbouShousha[1], Abeer Al-Hadidi[2], Hend Kadry[1]

[1]*Immunology, Medical Research Institute, Alexandria, Egypt*
[2]*Clinical Pathology, Faculty of Medicine, Alexandria, Egypt*

187
CYSTEAMINE INHIBITS INVASION, METASTASIS AND EXTENDS SURVIVAL BY DOWN-REGULATING MATRIX METALLOPROTEINASES IN VIVO MOUSE MODEL OF HUMAN PANCREATIC CANCER

Toshio Fujisawa[1,4], Benjamin Rubin[2], Akiko Suzuki[1], Prabhudas S. Patel[1], Wiiliam A. Gahl[3], Bharat H. Joshi[1], Raj K. Puri[1]

[1]*Tumor Vaccines and Biotechnology Branch, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD*
[2]*Department of Ophthalmology, Suburban Hospital, Johns Hopkins School of Medicine, Bethesda, MD*
[3]*Section on Human Biochemical Genetics, Medical Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD*
[4]*Department of Gastroenterology, NTT Medical Center Tokyo, Tokyo, Japan*

188
THE EFFECT OF TUMOR-DERIVED ARGINASE ON T CELL SUPPRESSION AND TUMOR PROGRESSION

Katie A. Palen, Aaron A. Phillips, Bryon D. Johnson, *Jill A. Gershan*

Pediatrics, Medical College of Wisconsin, Milwaukee, WI

189
CHARACTERIZATION OF INTRA-TUMORAL IMMUNITY IN COMMON CANCERS: CD146 EXPRESSION IN CD4 T LYMPHOCYTES

Cécile Grange[1,2,3], Jean-François Cailhier[1,2,3], Réjean Lapointe[1,2,3]

[1]*Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM), Université de Montréal, Montreal, QC, Canada*
[2]*Institut du cancer de Montréal, Université de Montréal, Montreal, QC, Canada*
[3]*Department of Medecine, Université de Montréal, Montreal, QC, Canada*

190

NOVEL DUAL MODE FLUORINE MRI, NIR FLUORESCENT PROBE FOR NON-INVASIVE DETECTION OF TUMOR-ASSOCIATED INFLAMMATION

Anthony Balducci[1], Yi Wen[3], Yang Zhang[3], *Brooke Helfer*[1], Kevin Hitchens[2], Wilson Meng[3], Jelena Janjic[3], Amy Wesa[1]

[1]*Celsense Inc, Pittsburgh, PA*
[2]*Carnegie Mellon University, Pittsburgh, PA*
[3]*Duquesne University, Pittsburgh, PA*

191

DELICATE BALANCE AMONG THREE TYPES OF T CELLS IN CONCURRENT REGULATION OF TUMOR IMMUNITY

Liat Izhak[1], Elena Ambrosino[1], Jessica J. O'Konek[1], Stanley T. Parish[1], Zheng Xia[1], David Venzon[2], Jay A. Berzofsky[1], Masaki Terabe[1]

[1]*Vaccine Branch, NCI, NIH, Bethesda, MD*
[2]*Biostatistics and Data Management Section, NCI, NIH, Bethesda, MD*

192

INHIBITORY RECEPTORS ON TUMOR INFILTRATING LYMPHOCYTES REFLECT ABERRANT TCR TRIGGERING IN THE TUMOR MICROENVIRONMENT

Hyun-Bae Jie, Raghvendra Srivastava, Sandra Gibson, Robert L. Ferris

Pathology, Immunology and Otolaryngology, University of Pittsburgh Cancer Institute and University of Pittsburgh School of Medicine, Pittsburgh, PA

193

BONE MARROW-DERIVED STROMAL CELLS (BMSC) SHOW BOTH PRO-INFLAMMATORY AND IMMUNOSUPPRESSIVE CHARACTERISTICS IN MELANOMA MICROENVIRONMENT: AN IN VITRO STUDY BY CO-CULTURE OF BMSC, TIL AND MELANOMA

Ping Jin, Sara Civini, Heidi Wang, Jiaqiang Ren, Marianna Sabatino, Ena Wang, Francesco Marincola, David Stroncek

Department of Transfusion Medicine, Clinical Center, National Institutes of Health, Bethesda, MD

194

TRACKING TUMOR INFILTRATING B CELLS REVEALED CANCER INITIATING CELLS THAT COEXPRESS UNIQUE GD3 SIALILATED GLYCOSPHINGOLIPIDES AND CD20 IN METASTATIC MALIGNANT MELANOMAS

Beatrix Kotlan[1], Gabriella Liszkay[2], Gyorgy Naszados[3], Maria Godeny[3], Laszlo Toth[4], Laszlo Gobor[4], Andras Szollar[4], Vanda Plotar[5], Erika Toth[5], Miklos Kasler[6], Francesco M. Marincola[7]

[1]*Molecular Immunology and Toxicology, National Institute of Oncology, Budapest, Hungary*
[2]*Oncodermatology, National Institute of Oncology, Budapest, Hungary*
[3]*Diagnostic Radiology, National Institute of Oncology, Budapest, Hungary*
[4]*Oncosurgery, National Institute of Oncology, Budapest, Hungary*
[5]*Center of Surgical and Molecular Tumorpathology, National Institute of Oncology, Budapest, Hungary*
[6]*Board of Directors, National Institute of Oncology, Budapest, Hungary*
[7]*IDIS, Deapartment of Transfusion Medicine, Clinical Center, National Institutes of Health, Bethesda, MD*

195

PANCREATIC CANCER ASSOCIATED STELLATE CELLS DIFFERENTIATE IMMUNE CELLS INTO AN IMMUNOSUPPRESSIVE PHENOTYPE

Thomas A. Mace, Zeenath Ameen, Amy Collins, Sylwia Wojcik, Markus Mair, Tanios Bekaii-Saab, Mark Bloomston, Gregory B. Lesinski

The Ohio State University, Columbus, OH

196

THE IMMUNE CONTEXTURE IN HUMAN RENAL CELL CARCINOMA: TUMOR-TYPE SPECIFIC FEATURES WITH POTENTIAL RELEVANCE FOR PROGNOSIS AND THERAPY

Elfriede Noessner, Dorothee Brech, Judith Eckl, Anna N. Mendler, Petra U. Prinz

Institute of Molecular Immunology, Helmholtz Zentrum München, Munich, Germany

197

NATURAL HISTORY OF TUMOR GROWTH AND METASTASIS IN COMMON SPONTANEOUS MURINE BREAST CANCER MODELS

Ekram Gad[1], *Lauren R. Rastetter*[1], Meredith Slota[1], Marlese Koehnlein[1], Yushe Dang[1], Piper M. Treuting[2], Mary L. Disis[1]

[1]*Tumor Vaccine Group, Center for Translational Medicine in Women's Health, University of Washington, Seattle, WA*
[2]*Department of Comparative Medicine, University of Washington, Seattle, WA*

198
AKT+β-CAT LIVER TUMOR DEVELOPMENT IS DEPENDENT ON B CELLS
Anthony Scarzello, Jim Stauffer, Jeff Subleski, Jon Weiss, John Ortaldo, Robert Wiltrout

Cancer and Inflammation Program, LEI, National Cancer Institute, Frederick, MD

199
NEW TECHNOLOGIES FOR MEASUREMENTS OF TUMOR INFILTRATING LYMPHOCYTES
Anna Sherwood[1], Cindy Desmarais[1], Muneesh Tewari[2], Jamie Guenthoer[2], Charles Drescher[2], Jason Bielas[2], Harlan Robins[2]

[1]*Adaptive Biotechnologies, Seattle, WA*
[2]*Fred Hutchinson Cancer Research Center, Seattle, WA*

200
THE IMMUNE-RELATED ROLE OF BRAF MUTATION IN MELANOMA
Sara Tomei[1], Sara Civini[2], Davide Bedognetti[1], Valeria De Giorgi[1], Jennifer Reinboth[1], Maria Libera Ascierto[1], Qiuzhen Liu[1], Lorenzo Uccellini[1], Ena Wang[1], Francesco M. Marincola[1]

[1]*Infectious Disease and Immunogenetics Section (IDIS), Department of Transfusion Medicine, Clinical Center and trans-NIH Center for Human Immunology (CHI), NIH, Bethesda, MD*
[2]*Cell Processing Section (CPS), Department of Transfusion Medicine, Clinical Center, NIH, Bethesda, MD*

201
THE RATIO OF CO-CULTURED CD14+ MONOCYTES AND TUMOR CELLS INFLUENCES LOSS OF HLA-DR ON MONOCYTES
Deepti Warad[1], Michael P. Gustafson[2], Allan B. Dietz[2]

[1]*Division of Pediatric Hematology Oncology, Mayo Clinic, Rochester, MN*
[2]*Division of Transfusion Medicine Department of Lab Medicine and Pathology, Mayo Clinic, Rochester, MN*

202
S-NITROSYLATION OF ARGINASE-2 AS AN ALTERNATIVE MECHANISM USED BY NOS3 TO PROMOTE HUMAN RCC PROLIFERATION
Emily A. Songer[1], David J. Tate[1], John R. Patterson[1], *Arnold H. Zea*[1,2]

[1]*Stanley S. Scott Cancer Center, LSUHSC, New Orleans, LA*
[2]*Microbiology, LSUHSC, New Orleans, LA*

TUMOR VASCULATURE, CHEMOKINES AND LYMPHOCYTE TRAFFICKING TO THE TUMOR

203
IMMUNOLOGICAL PHENOTYPING OF COLORECTAL CARCINOMA LIVER METASTASES AND PRIMARY OVARIAN CANCER
Magdalena Kovacsovics-Bankowski, Lana Chisholm, Jonna Vercellini, Philippa Newell, Jun Ma, Paul Tseng, Ronald Wolf, Chet Hammill, Paul Hansen, Andrew Weinberg

Earle A. Chiles Research Institute, Providence Medical Center, Portland, OR

204
TREATMENT OF MELANOMA AND ENDOTHELIAL CELL LINES WITH TLR AGONISTS ALTERS IMMUNE ACTIVATING CYTOKINE PRODUCTION
Ileana S. Mauldin, Craig L. Slingluff

Surgery, University of Virginia, Charlottesville, VA

205
CROSS-REGULATION OF NF-κB-DRIVEN CHEMOKINE PRODUCTION BY STAT-1/IRF1 VERSUS PKA/PCREB PATHWAYS DETERMINES THE ABILITY OF TUMOR MICROENVIRONMENT TO PREFERENTIALLY ATTRACT EFFECTOR VERSUS REGULATORY CELLS
Ravikumar Muthuswamy[1], Erik Berk[1], Beth Fallert Junecko[2], Saumendra Sarkar[6], Herbert J. Zeh[1,5], Amer H. Zureikat[1,5], Daniel Normolle[4], Todd A. Reinhart[2,3], David L. Bartlett[1,5], Pawel Kalinski[1,3,5]

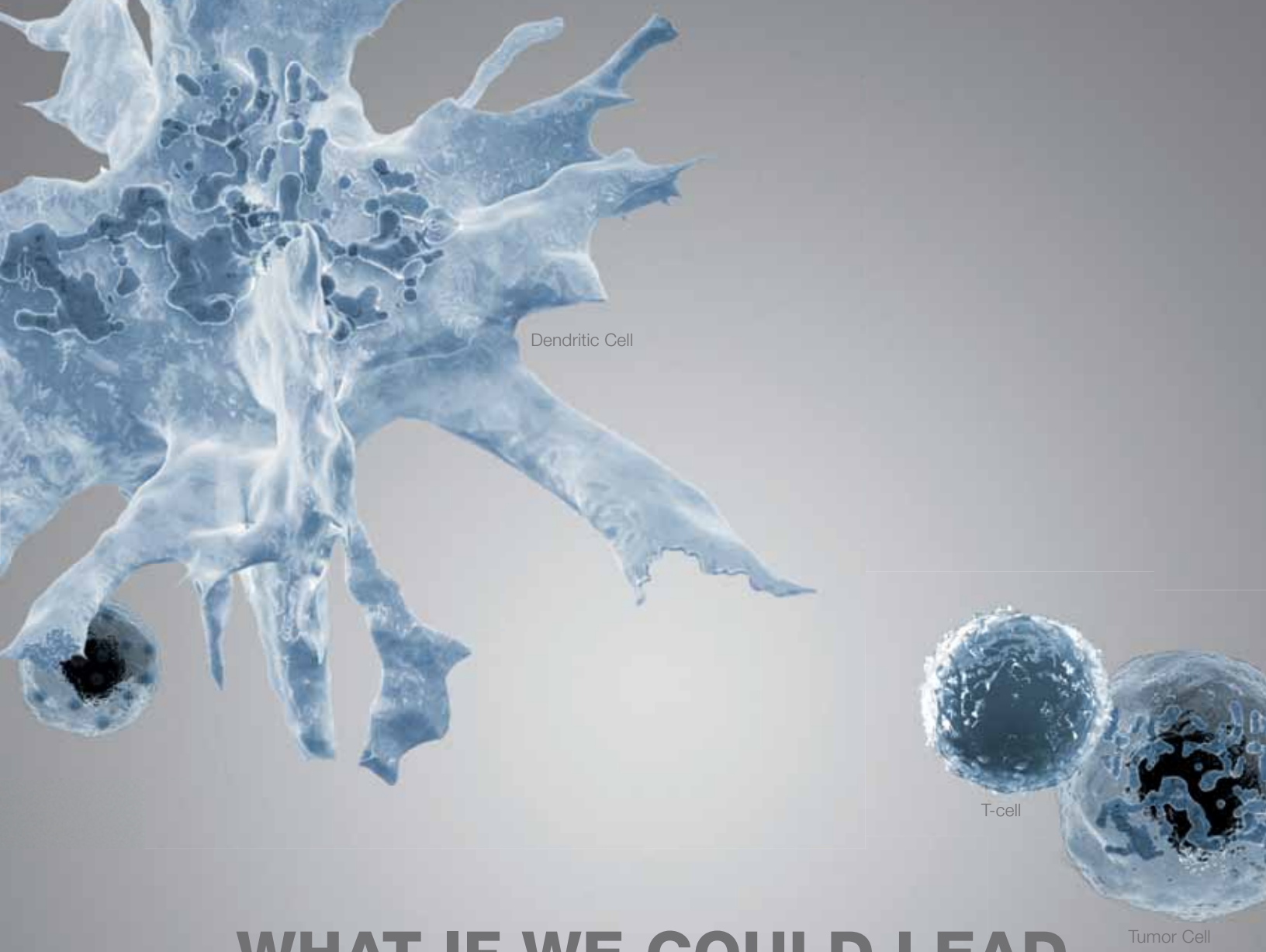
[1]*Surgery, UPMC, Pittsburgh, PA*
[2]*Infectious Diseases and Microbiology, University of Pittsburgh, Pittsburgh, PA*
[3]*Immunology, University of Pittsburgh, Pittsburgh, PA*
[4]*Statistics, University of Pittsburgh, Pittsburgh, PA*
[5]*UPCI, UPMC, Pittsburgh, PA*
[6]*Microbiology and molecular genetics, UPCI, Pittsbrugh, PA*

206

IL-18-PRIMED 'HELPER' NK CELLS MEDIATE THE ATTRACTION AND ACTIVATION OF DCS, PROMOTING THE ACCUMULATION OF TYPE-1-EFFECTOR T CELLS AT TUMOR SITES

Jeffrey L. Wong[1], Ravikumar Muthuswamy[1], Erik Berk[1], Robert P. Edwards[2,3,4], Pawel Kalinski[1,4,5]

[1]*Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA*
[2]*Ovarian Cancer Center of Excellence, Magee-Womens Research Institute, Pittsburgh, PA*
[3]*Peritoneal/Ovarian Cancer Specialty Care Center, University of Pittsburgh Cancer Institute, Pittsburgh, PA*
[4]*University of Pittsburgh Cancer Institute, Pittsburgh, PA*
[5]*Department of Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA*



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Reference: 1. Melcher A, Parato K, Rooney CM, Bell JC. Thunder and lightning: immunotherapy and oncolytic viruses collide. *Mol Ther*. 2011;19:1008-1016.

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The Society for Immunotherapy of Cancer (SITC) is proud to announce the launch of the Society's new official journal

Journal for ImmunoTherapy of Cancer

ABOUT THE JOURNAL

The Journal for Immunotherapy of Cancer (JITC) is the official journal of the Society for Immunotherapy of Cancer (SITC). It is an open access, online journal created by the Society for the many stakeholders in the tumor immunology and cancer immunotherapy community.

Through the development of our 2012-2015 Strategic Plan, it was clear that there was a need for an outlet and targeted publication platform dedicated to advancing the science of tumor immunology and cancer immunotherapy. The Society is thus responding to the tremendous excitement in the field and the increased momentum brought about by the latest approvals of immunotherapy-based treatments in various cancer types.

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