

Coinhibition & Costimulation Session: SITC 2015

Co-Chairs:

Andrew D. Weinberg, PhD –Providence Cancer Center, Portland, OR

Jedd D. Wolchok, MD, PhD – Memorial Sloan Kettering Cancer Center

8:35 a.m. – 8:40 a.m. **Introduction**

Andrew Weinberg, PhD

8:40 a.m. – 9:05 a.m. **Combined Coinhibition in the Clinic**

Jedd D. Wolchok, MD, PhD – Memorial Sloan Kettering Cancer Center

9:05 a.m. – 9:30 a.m. **The Negative Checkpoint Regulator VISTA in Cancer and Tolerance**

Isabelle Le Mercier, PhD – Geisel School of Medicine at Dartmouth

9:30 a.m. – 9:50 a.m. **OX40 Agonist Agents in Pre-clinical Models**

Daniel Hirschhorn-Cymerman, PhD – Memorial Sloan Kettering Cancer Center

9:50 a.m. – 10:05 a.m. **Agonist Anti-4-1BB Plus Neutralizing Anti-CTLA-4 or –PD-L1 Synergize to Promote Tumor Regression by Rescuing Dying Dysfunctional CD8+ T Cells Within the Tumor Microenvironment**

Brendan Horton, MD, PhD – University of Chicago

10:05 a.m. – 10:20 a.m. **PD-1 Blockade Upregulate Tim-3 Expression as a Compensatory Regulation of Immune Check Point Receptors in HNSCC TIL**

Gulidana Shayan – University of Pittsburgh

The Genesis of T Cell Costimulation



Pillars Article: Antigen Presentation by Chemically Modified Splenocytes Induces Antigen-Specific T Cell Unresponsiveness In Vitro and In Vivo. *J. Exp. Med.* 1987. 165: 302–319

Marc K. Jenkins and Ronald H. Schwartz

Signal 1 (TCR) without Signal 2(?) Leads to Unresponsive T Cells

**CD28-mediated signalling
co-stimulates murine T cells
and prevents induction
of anergy in T-cell clones**

**Fiona A. Harding*†, James G. McArthur*†,
Jane A. Gross‡, David H. Raulet* & James P. Allison*§**

NATURE · VOL 356 · 16 APRIL 1992

**CD28 stimulation acts as “Signal 2” and prevents
T cell unresponsiveness.**

Hence at least 2 signals are needed to activate T cells

Enhancement of Antitumor Immunity by CTLA-4 Blockade

Dana R. Leach, Matthew F. Krummel, James P. Allison*

SCIENCE • VOL. 271 • 22 MARCH 1996

**CTLA-4 (homology to CD28) is a coinhibitory protein that
when blocked can enhance T cell immunity to tumors**

Agonists to TNF-Receptors Enhance anti-Tumor Immunity

Monoclonal antibodies against the 4-1BB T-cell activation molecule eradicate established tumors.

Melero I1, Shuford WW, Newby SA, Aruffo A, Ledbetter JA, Hellström KE, Mittler RS, Chen L.

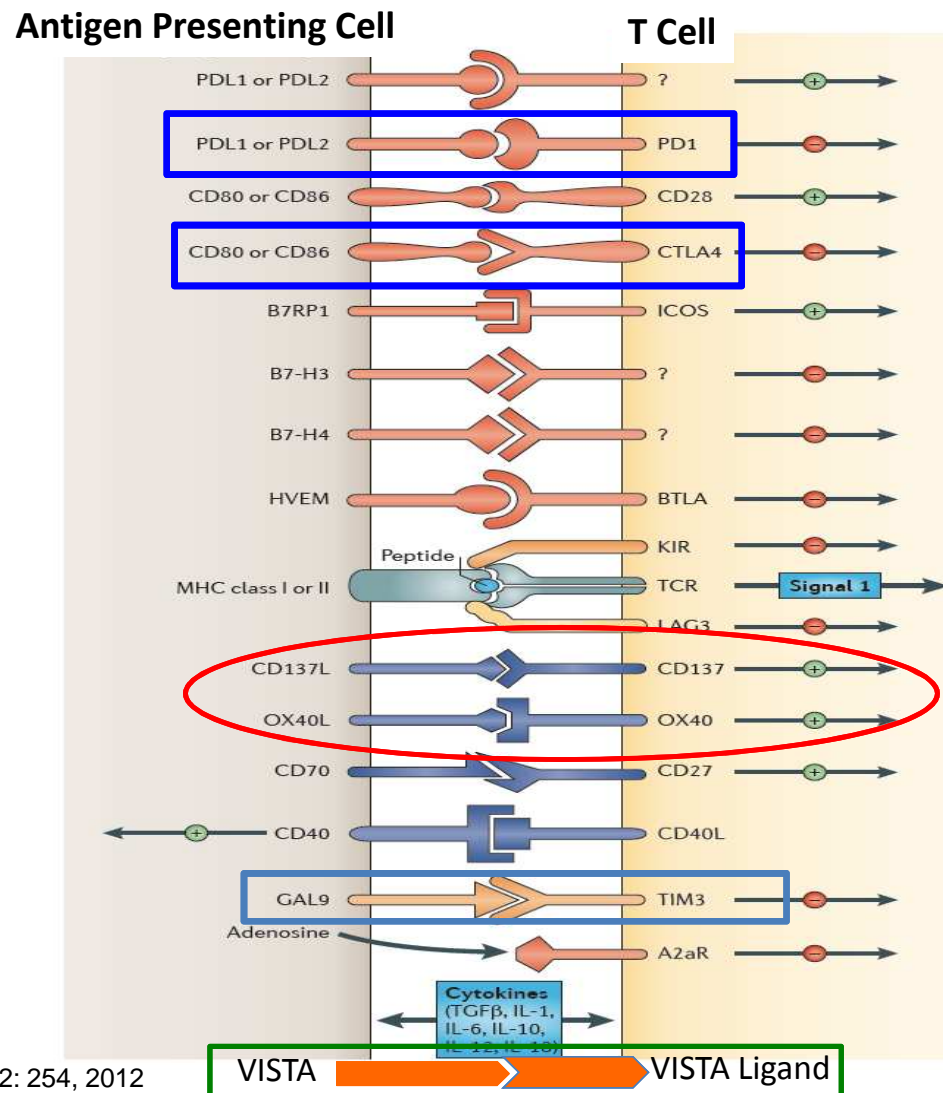
Nat Med. 1997 Jun;3(6):682-5.

Engagement of the OX-40 receptor in vivo enhances antitumor immunity.

Weinberg AD, Rivera MM, Prell R, Morris A, Ramstad T, Vetto JT, Urba WJ, Alvord G, Bunce C, Shields J.

J Immunol. 2000 Feb 15;164(4):2160-9

Multiple co-stimulatory and inhibitory interactions regulate T cell responses



Pardoll: Nature Rev Cancer 12: 254, 2012

T Cell Based Immunotherapy: A Deeper Dive

Marriott Resort Wailea Beach, Maui, HI • June 10 - 12, 2016



"Think Tank" Approach



Maui Meeting Speakers:

Basic T Cell Biology and Function:

- Steve Hedrick, UCSD
- Carl Ware, Burnham Institute, San Diego
- Doug Green, St Jude's, Memphis
- Pam Ohashi, U of Toronto
- Charlie Surh, Institute for Basic Science, Korea
- Steve Ziegler, Benaroya Institute, Seattle
- David Masopust, U of Minnesota
- Richard Flavell, Yale

Preclinical Cancer Immunotherapy:

- Jim Allison, MD Anderson
- Bob Schreiber, Washington University, St Louis
- Lieping Chen, Yale
- Andy Weinberg, Providence Cancer Center, Oregon
- Bernie Fox, Providence Cancer Center, Oregon
- Samir Khleif, Georgia Regents University
- Brad Nelson, U of British Columbia, Victoria
- Phil Greenberg, U of Washington

Clinical Immunotherapy:

- Tom Gajewski, U of Chicago
- Brendan Curti, Providence Cancer Center, Oregon
- Pam Sharma, MD Anderson
- Carl June, U of Penn, Philadelphia
- Paul Tumeh, UCLA
- Lisa Butterfield, University of Pittsburgh



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