Presenter Disclosure Information

Lisa H. Butterfield, Ph.D.

The following relationships exist related to this presentation:

There are no relationships to disclose related to this presentation.

However, in the interests of full disclosure, the following relationships exist (2015):

Scientific Advisory Board member:
Caladrius (formerly NeoStem), 2014 – present

Advisory Board participation:
Oxford Immunotec, Affymetrix/eBioscience, Merck, Biodesix

Immunotherapy Biomarkers Task Force
2014-2015

Biomarkers Task Force Steering Committee:

Lisa Butterfield, PhD

Nora Disis, MD

Bernie Fox, PhD

Samir Khleif, MD

Francesco Marincola, MD

Biomarkers Task Force Working Group Leaders:

Magdalena Thurin, PhD and Guiseppe Massucci, MD, PhD

Jianda Yuan, MD

David Stroncek, MD

Sacha Gnjatic, PhD

Immunotherapy Biomarkers Task Force
History/Background

Previously:
Society Workshops: Immunologic Monitoring and Immune Biomarkers

2002 Workshop and Recommendations: Keilholz, et al. JIT

2005 Workshop Summary: Lotze, et al. JIT

2008: Assembled Immunotherapy Biomarkers Taskforce Steering Committee
Taskforce "Preamble" JTM 2008
SITC Workshop 2009 and Meeting Report JTM 2009
Taskforce meeting at the NIH 2010, "Recommendations" paper (CCR 2011), and "Resources" document (JTM 2011)

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Recommendations from the iSBTc-SITC/FDA/NCI Workshop on Immunotherapy Biomarkers

Source of Variability	Recommendation
Patient	Save DNA/RNA/cells/tumor to understand host variation include healthy donor control
Blood draw	Standardized tubes and procedures
Processing/cryopreservation/ thaw	Standardized procedures and reagents
Cellular product	Phenotypic and functional assays to characterize the individual product, development of potency assays
Assay choice	Standardized functional tests
Assay conduct	Standardized operating procedures (SOPs)
Assay analysis	Appropriate biostatistical methods
Data reporting	Full details, controls, quality control/assurance (QA/QC) MIATA guidelines
Newest, non-standardized technology	Sufficient blood/tissue to interrogate the samples *now*, as well as *later*, to generate new hypotheses

Butterfield, CCR 2011

What's new in Immune Biomarkers:

New classes of interventions
Small molecules and checkpoint inhibitors successfully tested and approved

New areas of biology impacting immune response
Metabolism, microbiome, signaling pathway modulation

New technologies and high-throughput approaches
Mass cytometry, exome sequencing, TCR diversity, epigenetics

New and old drugs impacting immunity:
Chemotherapy, radiation, ablation, also immune modulators

Bioinformatics, complex data analysis,
new biological samples—and not just from melanoma

Immunotherapy Biomarkers Task Force 2014-2016

Biomarkers Task Force: Working Groups:

GROUP 1: “Immune monitoring assay standardization and validation—update” *Leaders: Magdalena Thurin, PhD and Giuseppe Massucci, MD, PhD*

GROUP 2: “New developments in biomarker assays and technologies” *Leader: Jianda Yuan, MD*

GROUP 3: “Assessing immune regulation and modulation systematically (high-throughput approaches)” *Leader: David Stroncek, MD*

Group 4: “Baseline immunity, tumor immune environment and outcome prediction” *Leader: Sacha Gnjatic, PhD*

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Immunotherapy Biomarkers Task Force 2014-2015

Activities:

1. Ongoing calls/working group activities
2. Preamble/overview commentary (Steering Committee, JITC March 2015)
3. Immune Biomarkers SITC Guest Society Symposium at AAI 2015
4. Biomarker Technology short reports 1/month in JITC (starting June '15)
5. New State of the Art/Recommendations for the field manuscripts in JITC in 2015 from the Working Groups (WG2 submitted to JITC)
6. Clinical trial analysis project: standard cellular/cytokine assays and high-throughput molecular analyses (contracts…..)
7. Summary 1 day meeting at the NIH: April 1st, 2016

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SITC Biomarkers Task Force
JITC Technology Primers

Format:

Name(s) of the technology:

Description of the technology:

Type of data obtained/readout:

Limitations of the approach:

Types of samples needed and special issues pertaining to samples:

Level of evidence:

SITC Biomarkers Task Force
JITC Technology Primers

Status Update:

1. *Immunosequencing* by Ilan Lanny Kirsch (June – WG1)
2. *Enzyme-linked immunospot assay (ELISpot), Fluorospot* by Sylvia Janetzki (July – WG1)
3. *Single Cell Network Profiling (SCNP)* by Rachael E. Hawtin and Alessandra Cesano (August– WG1)
4. *Flow and Mass Cytometry* by Holden Maecker and Alexandre Harari (Sept.– WG2)
5. *Clinical Validation for Predictive Biomarkers* by Kevin Dobbin (October – WG1)
6. *Epigenetic regulation* by Thomas Kleen and Jianda Yuan (November – WG2)
7. *Nanostring Platform* by Alessandra Cesano (December 2015 – WG1)
8. *Protein microarray (seromics)* by Bernard Fox and Jianda Yuan (Jan. 2016 – WG2)

3-4 additional reports in queue and in development

SITC Biomarkers Task Force
ECOG 1608

E1608 PI: F. S. Hodi;

Hodi, F.S., Lee, S., McDermott, D.F., Rao, U.N., Butterfield, L.H., Tarhini, A.A., Leming, P., Puzanov, I., Shin, D.,Kirkwood, J.M. **Ipilimumab plus sargramostim vs Ipilimumab Alone for Treatment of Metastatic Melanoma: A Randomized Clinical Trial.** **JAMA** Nov 5, 2014.

Clinical trial analysis project:

1. Standard cellular/cytokine assays (Pittsburgh)
    - PBMC flow cytometry, serum analytes

2. High-throughput molecular analyses (Sidra)
    - PBMC DNA and RNA

Determine signals, tumor analysis next?

Immunotherapy Biomarkers Task Force 2014-2016 Participants

Magdalena Thurin, PhD	**David F. Stroncek, MD**
John Alvarez, MD, PhD	Michael Cannarile, PhD
Alessandra Cesano, MD, PhD	Madhav Dhodapkar, MD
Kevin K. Dobbin, PhD	Tim Greten, MD
Rachael Hawtin, PhD	Jean Charles Grivel, PhD
Sylvia Janetzki, MD	David Kaufman, MD, PhD
Ilan (Lanny) Kirsch, MD	Peter P. Lee, MD
Giuseppe V. Masucci, MD, PhD	**Francesco Marincola, MD**
Raj K. Puri, MD, PhD	Sergio Rutella, MD, PhD
Senthamil R. Selvan, PhD	Barbara Seliger, MD, PhD
Paul Robbins, PhD	Janet Siebert, MS
Howard Z. Streicher, MD	Giorgio Trinchieri, MD
Zhe (Jenny) Zhang, PhD	
	Sacha Gnjatic, PhD
Jianda Yuan, MD	Vincenzo Bronte, MD
Raphael Clynes, MD, PhD	Laura Rosa Brunet, DSc
Periklis Foukas, MD, PhD	Marcus Butler, MD
Bernard A. Fox, PhD	**Mary L. (Nora) Disis, MD**
Alexandre Harari, PhD	Jerome Galon, MD
Priti Hegde, PhD	Leif G. Hakansson, MD, PhD
Thomas O. Kleen, PhD	Brent A. Hanks, MD, PhD
Pia Kvistborg , PhD	Vaios Karanikas, PhD
Christina Maccalli, PhD	**Samir N. Khleif, MD**
Holden T. Maecker, PhD	John M. Kirkwood, MD
Harlan Robins, PhD	Lance Miller, PhD
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Edward C. Stack, PhD	Isabelle Tanneau, MSc
Ena Wang, MD	Jon M. Wigginton, MD
Theresa L. Whiteside, PhD	
Yingdong Zhao, PhD	
Heinz Zwierzina, MD	**Lisa H. Butterfield, PhD**

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Lessons and Take Home Messages

•*Key points*: The SITC Immune Biomarkers Task Force is working together, focused on four areas.

•*Potential impact on the field:*

•New state of the art and recommendations to the field are forthcoming.

•New technology reports monthly in JITC

•*Lessons learned*: lessons are being learned and disseminated

•See you April 1st, 2016 at the NCI