PRE-CONFERENCE WORKSHOP DAY TUESDAY DECEMBER 10, 2019

Workshop A

Exploring Solid Tumor Assay Development & Flow Cytometry

9:00am – 12:00pm

Many of the assays developed for use with cell therapies work well in liquid tumors. However, they do not address the inherent challenges associated with solid tumors. The need for more relevant technologies and methods in solid tumors is paramount. Flow cytometry is an essential tool for analysis of cell therapies, and mass cytometry is garnering significant interest as it promises to vastly expand the power of cytometry.

Challenges with both of these technologies arise when complex experiments require extensive analysis of multiple cell types and various functions within each of these groups in order to uncover relevant biology. The analysis panels become significantly large, leading to difficulties with spectral compensation (in flow cytometry), and multi-dimensional data interpretation (in CyTOF). Moreover, sample size is often a limiting factor, thus requiring appropriate preparation for each specific application. This workshop will address the challenges associated with the mentioned technologies and highlight approaches for mitigating these challenges.

Attendees will:

- Learn the requirements for design and development of cytometry-based assays
- Discuss how to improve flow cytometry validation methods
- Discuss important considerations when designing cytometry-based assays for solid tumors

Workshop Leader

Tamara Laskowski
Senior Research Scientist, Immunotherapy
MD Anderson Center

In her role as Senior Research Scientist, Dr. Laskowski's work involves immune-monitoring for solid tumor Immunotherapy clinical trials, and application of flow cytometry and CyTOF in the development of novel immunoassays for solid malignancy studies. Dr. Laskowski also shares an interest in technology innovation, and has developed multi-plex assays for testing therapies against solid tumors.

Workshop B

CAR-T Cell Manufacturing – Current Methods & Trends

1:00pm – 4:00pm

This workshop will provide an overview of current methods, used in manufacturing of CAR-T cells. As response to market demand, the number of competing technologies and platforms for manufacturing therapeutic T-cells continues to grow. What is changing in manufacturing since the first generation of CAR-T products were approved and what is coming? How do manufacturing processes dictate analytical testing of CAR-T cell products? Limitations and bottlenecks of the current manufacturing platforms will be discussed. Limitations and bottlenecks of the current manufacturing platforms will be discussed.

The overview of CAR-T manufacturing methods is based on analysis of clinical trials databases and results of CAR-T cell therapy trials, published in peer-reviewed medical literature.

Attendees will:

- Discover current manufacturing limitations and potential solutions
- Hear analytical techniques used during manufacturing whilst discussing their respective limitations and advantages

Workshop Leader

Alexey Bersenev
Director, Advanced Cell Therapy Lab
Yale University

Alexey Bersenev has expertise in clinical manufacturing of cellular products for clinical trials, including product and process development, cell processing and culture, operations of academic GMP facility and compliance with regulations. In addition to his position as Director of the Advanced Cell Therapy Lab at Yale-New Haven Hospital, he is an Assistant Professor of Clinical Laboratory Medicine at the Department of Laboratory Medicine at the Yale University.

CONFERENCE DAY ONE
WEDNESDAY DECEMBER 11, 2019

7.30 **Coffee & Registration**

Eric Alonzo
Senior Scientist, Cell Analytics
Bluebird Bio

8.25 **Chair's Opening Remarks**

Exploring Analytical Developments in Allogeneic Cell Therapies

Stacey Cranert
Senior Scientist
Poseida Therapeutics

8.30 **Development of Allogeneic Stem Cell Memory CAR-T Cells Using Poseida Nonviral Technology**

- Understanding the role of starting material in allogeneic CAR-T production
- Exploring challenges in cell counting

Jennifer Dashnau
Senior Director, Head of Analytical Development & Quality Control
Century Therapeutics

9.00 **Exploring Century Therapeutics' Approach to Analytical Development**

- Developing a comprehensive quality control and characterization strategy for allogeneic, engineered iPSC-based products
- Discussing considerations associated with cell banking

Michael Leek
CEO
TCBiopharm

9.30 **Use of Allogeneic Gamma-delta T Cells to Treat Acute Myeloid Leukemia**

- Manufacture of allogeneic cells
- Managing graft-versus-host and host-v-graft disease
- Update on clinical program

Tatjana Holzer
Team Coordinator, Concomitant Research of Cellular Immunotherapies
Miltenyi Biotec

10.00 **CAR T Cell Characterization During Manufacturing Using the CliniMACS® Prodigy**

- Automated CAR T cell manufacturing using the CliniMACS® Prodigy
- Characterization of CAR T cells during manufacturing
- Automated flow cytometric IPC/QC measurement and analysis
- Monitoring cell expansion and CAR transduction
- Phenotypic characterization of CAR T cells
- Next generation characterization of the CAR T cell phenotype

10.30 **Speed Networking**
This session is the ideal opportunity to get face-to-face time with many of the brightest minds working to advance cell therapies. Benchmark against the industry leaders and establish meaningful business relationships to pursue for the rest of the conference and beyond.

11.00 **Morning Refreshments**

Lawrence Lamb
CSO
Incysus

11.30 **Immune Monitoring of Product & Patient as Potential Predictors of Efficacy for Innate Lymphocyte Therapies**

- Recovery of normal immune cell number, diversity, and function is a strong predictor for patients achieving continuing remission
- This presentation will examine models of endogenous immune response to tumor, quality of cell therapy graft material pre and post manufacturing, and the process of immune recovery and function following treatment

Jean-Pierre Cabaniols
Head of the Analytical Department
Cellectis

12.00 **Functional Bio-assays Development for Allogeneic CAR T-Cell Therapies**

- New generation of cancer therapies based on gene-edited CAR T-cells (UCART) brings new challenges for functional assay development
- In addition to assess UCART batch functionality, the goal is to evaluate batch-to-batch variability. To this end, the assay itself must be as less variable as possible.
- Here we will discuss our approaches in which sources of variability (materials and techniques) are limited.

Examining Cell Therapy Product Release Testing

Stephanie Mgebroff
Director, Research Quality Control
Seattle Children's Institute

12.30 **Addressing Sample-Introduced Variability in Cell Product Release Testing**

- Sampling method suitability – ensuring the sample is representative of the product
- The effect of final formulation constituents on analytical testing
- Sample handling practice - to ensure stability and reproducible results

1.00 Lunch & Networking

Sarah Snykers
Quality Control Manager
Celyad

2.00 Rapid Microbial Methods for Final Release of Cell & Gene Therapy Products

- Classical versus fast track μbial alternatives
- Mycoplasma & endotoxin testing
- Method validation
- Regulatory guidance

Exploring Methods to Define Mechanism of Action of Cell Therapies

Franco Marincola
CSO
Refuge Biotech

2.30 Product Potency in the Era of "Synthetic Biology"

- Conditional cell behavior is a dynamic entity – how to pin down its motion?
- How to define mechanism of action (MOA) and mechanism of efficacy (MOE)?
- What are off-target effects?
- How specific needs specificity to be?
- From MOA/MOE to proof of concept: the big divide

Tania (Tali) Konry
Assistant Professor
Northeastern University

3.00 An Integrated Microfluidic Platform for Multi-dimensional Analysis and Multi-omic Classifications of Effector Immune Cell Functions

- The outcome of many pathological diseases such as infection and cancer is determined by the interaction of diseased cells with various immune cell subsets, both of which are phenotypically and functionally diverse. Induced resistance to chemo- and immuno-therapeutic drugs remain one of the main challenges in modern medicine.
- There exists significant inter-patient and even intra-patient variability in response to well-established drug regimens, making it difficult to predict a patient's response to applied treatments. Single-cell analysis techniques have great potential in revealing, and ultimately utilizing, patient-specific cellular information to devise a more personalized approach to therapeutic regimens.
- Towards this goal we have developed a platform technology for characterizing single cell response, cell-cell communication and novel drug/immunotherapy targets in various diseases and overall could be beneficial in improving the efficacy of antibody drug therapy and develop effective drug combinations.

3.30 Afternoon Refreshments & Scientific Poster Session

The learning and networking continues at the Poster Session, an informal part of the conference agenda, allowing you to connect with your peers in a relaxed atmosphere and continue to forge new, beneficial relationships. You will have the opportunity to present and review presentations displaying new data from analytical techniques for cell therapies.

4.30 Interactive Roundtable Discussions: Deep Dives into Key Existing & Emerging Technologies

Participate in a focused roundtable discussion to discuss key analytical technologies in an intimate environment. Each table will be led by an industry leader with experience in using the relevant methodology, so this is your opportunity to have your burning questions answered and benchmark your approach with your colleagues in the field. Roundtables will discuss the use of the following approaches

1. Novel Assay Development

Moderator:

Ajit Kamath
Analytical Development Scientist
Mustang Bio

2. Discussing New & Novel Analytical Techniques

Moderator:

Barrett Nehilla
Analytical Development
Torque Therapeutics

3. Next Generation Sequencing

Eric Alonzo
Senior Scientist, Cell Analytics
Bluebird Bio

5.15 Chair's Closing Remarks

CONFERENCE DAY TWO
THURSDAY DECEMBER 12, 2019

8.00 **Coffee & Registration**

Eric Alonzo
Senior Scientist, Cell Analytics
Bluebird Bio

8.55 **Chair's Opening Remarks**

Discussing Novel Cell Concentration Determination Techniques

Branly Orban
Senior Manager, CAR-T Quality Control Molecular Bioanalysis
Celgene

9.00 **General Overview of Cell Concentration Determination of CAR-T Drug Products**

- Cell concentration is a critical attribute for cellular products. Cell concentration guides cell culture maintenance through the manufacturing process and is essential for determining product dose. Throughout our process, we utilize three different automated cell counting methodologies
- Regardless of the methodology, each cell concentration determination method must be specific, accurate, precise and linear. The validated performance of the method must be maintained through appropriate procedural controls
- Equally important for the accuracy of the measurement is the quality of the sample being analyzed. There are multiple steps in the sample handling and preparation processes of cell suspension samples that need to be evaluated to ensure a representative sample is collected and analyzed

Laura Pierce
Biomedical Engineer
NIST

9.30 **Making Counting Count: Techniques & Standards to Improve Confidence in Cell Count & Viability Measurements**

- Analytical and statistical techniques to evaluate measurement performance and improve comparability for cell count and viability measurements.
- In-process measurement tools for greater confidence in measurements utilizing brightfield image-based cell counting methods
- DOE (design of experiment) and robustness strategies for establishing image analysis parameter settings in image-based cell counting methods

Advancing Flow Cytometry Techniques for Cell Therapies

Mahwish Natalia
Senior Scientist
Takeda

10.00 **Flow Cytometry Based CAR-T Analytical Strategies**

- Improving flow cytometry validation
- Outlining methods to increase resolution through conventional flow cytometry

Amber Giles
Associate Director, Process Development, Neo-Antigen
Kite Pharma

10.30 **Successful Alignment in Flow Cytometry-Based Assays**

- Method optimization: critical focus on panel development, the foundation of flow cytometry assays
- Gating and controls
- Data collection and reporting: MFI, % positive, absolute cell numbers, marker co-expression
- Strategies and considerations when data do not align

11.00 **Morning Refreshments & Networking**

Examining Strategies of Cell Therapy Leaders

Therese Choquette
Analytical Project Lead, Senior Fellow
Novartis

11.30 **Interpretation of Analytical Data from Autologous CAR-T Product & Considerations for Cohort Size**

- Variability and heterogeneity
- Impact on statistical testing for CQA
- Impact on specification settings

Tam Soden
Senior Director & Head of Analytical Development
Kite Pharma

12.00 Roadmap to Defining the Analytical Control Strategy for Cell Therapy Products

- Given the significant heterogeneity of incoming patient material, robust Analytical strategies are of paramount importance for process and product control of new cell therapy programs
- This presentation will speak to Analytical strategies for comprehensive product characterization and understanding of Kite's programs
- A roadmap to the evaluation of the critical quality attributes of these innovative therapeutics will be socialized with the audience, together with an in depth understanding to identify, and to develop the appropriate quality control strategy for overall safety, efficacy and toxicity and at various phases of clinical development through commercial
- Aspects of more progressive analytical technologies, traditionally applied in the realm of product characterization and understanding, but not as part of the routine product release in the regulated environments of manufacturing and QC organizations, and that are now being integrated into lifecycle planning for those methods as they evolve into attribute monitoring and validated release assays for a commercial product, will also be shared

Franco Marincola
CSO
Refuge Biotech

Rozanna Yaing
SVP, Quality & Regulatory Affairs
Incysus

Michael Leek
CEO
TCBiopharm

Tam Soden
Senior Director & Head of Analytical Development
Kite Pharma

12.30 Panel Discussion: Evaluating the Analytical Strategies of the Leading Companies in the Field

This interactive panel discussion will bring together the leading companies in the field to discuss key takeaways from pioneering cell therapy programs. Topics to be covered include:

- Investigating common analytical challenges encountered across various programs in different indications and with different specifications
- Balancing the complexities of analytical requirements with the drive to progress therapies to market
- Establishing collaborative relationships with other departments within the organization
- Lessons learned from the recent approvals of cell therapy products – how has feedback from agencies changed and shaped analytical strategies moving forward?

1.15 Lunch & Networking

Focusing on Cell Therapy Product Characterization

Steven Feldman
Director, Manufacturing & Process Development
Stanford School of Medicine

2.15 In-depth Analysis of CD19/22-bispecific CAR-T Cells Manufactured Using an Automated Cell Production Platform

- Process overview
- Product characterization from apheresis to cell infusion product
  - Expansion profile
  - Phenotype
  - Function
  - Biomarker analysis
- Analytical challenges for in-process and cell infusion products

Eric Alonzo
Senior Scientist, Cell Analytics
Bluebird Bio

2.45 Leveraging High-Dimensional '-omics' Technologies for Comprehensive Profiling of CAR-T Cells to Resolve Drug Product Complexity

- Challenges faced in identifying the active ingredient/characterizing the cell therapy drug product
- Move from more traditional assays to single-cell omics to uncover cellular drug product structure
- Challenges/learnings from single-cell approaches

Eric Alonzo
Senior Scientist, Cell Analytics
Bluebird Bio

3.15 Chair's Closing Remarks