**Translational Systems Biology: New Computational Technologies and Trial Designs for a Continuum of Personalized Therapy**

August 24-25, 2023
NCI Shady Grove, TE406/408/410
9609 Medical Center Drive, Rockville, MD 20850

**Goal of the Symposium:**
This symposium will focus on utilizing patient clinical and -omic data with systems biology models in clinical settings. Advances in translational oncology using systems biology approaches have been significant in recent years. To take full advantage of these advancements for the benefit of patients, we will explore building innovative and streamlined clinical trials for incorporating biomarkers and new drug treatment strategies into clinical practice. Attendees will examine the areas of medicine that have the greatest potential to implement systems biology methods in the near future. We will discuss plans for building the necessary clinical trial infrastructure across the nation to reduce barriers to entry of these methods and result in democratization of data and resources. Opportunities for collaboration between research institutes, pharmaceutical/biotech companies, the National Cancer Institute, ARPA-H and foundations will be explored. The outcome of this cross-disciplinary symposium will be the development of action items to facilitate the integration of systems biology into clinical trials in a manner that is efficient, accessible to research and clinical communities, and quickly benefits patients. One deliverable of the Symposium will be a manuscript outlining a call-to-action.

**Day 1 - Thursday, August 24, 2023**

8:00 - 8:30 am: Registration and coffee

**8:30 - 8:40 am: Introductory remarks (Dinah Singer, NCI)**

**8:40 – 9:00 am: Meeting overview (Andrea Bild, City of Hope)**

**9:00 - 10:15 am: Session 1 (12-minute talks, 3-minute questions)**

**Session 1 - Innovative technologies and methods for translational medicine**
**Moderator: Shannon Hughes (NCI)**

| Time | Presentation | Speaker |
|---|---|---|
| **9:00** | Multiscale modeling of clinical cancer progression | Sylvia Plevritis (Stanford University) |
| **9:15** | Forging the future of precision oncology with AI/ML and multimodal biomarkers | Aritro Nath (COH) |
| **9:30** | DNA Methylation: From Bench to Bedside | Beth Chang (GRAIL) |

| | | |
|---|---|---|
| **9:45** | Integrative genomic biomarkers for cancer clinical studies | Andrew Kung (Memorial Sloan Kettering) |
| **10:00** | Challenges for Selecting and Scheduling Combination Therapeutics | Matt Lazzara (University of Virginia) |

**10:15 am-10:45 am: Break**

**10:45 am- 12:00 pm: Session 2**

**Session 2 - Innovative clinical trial designs that implement systems biology models**
**Moderator: Mia Levy (Foundation Medicine) and Laura Heiser (OHSU)**

| Time | Presentation | Speaker |
|---|---|---|
| **10:45** | Innovative Clinical Trial Designs for Applying Thoracic Systems Biology | Wade Iams (Vanderbilt University) |
| **11:00** | Utilizing Systems Biology Models to Improve Outcomes of Metastatic Hormone Receptor Positive Breast Cancer | Rachel Layman (MD Anderson) |
| **11:15** | An algorithm-driven strategy for a novel targeted therapy in breast cancer | Jose Silva (Icahn School of Medicine) |
| **11:30** | Integrating evolutionary mathematical models into clinical trials | Robert Gatenby (Moffitt Cancer Center) |
| **11:45** | Challenges and Opportunities for Biomarker Intensive Studies in Oncology | Sunil Sharma (TGen) |

**Lunch and working group discussions:**

**12:00 pm– 12:15 pm: Break and Pick-up lunch**

**12:00 pm-12:40 pm: Discussion**

**12:40 pm- 1:05 pm: Report discussion results (~3 min per table)**

**Discussant Leaders: Sylvia Plevritis and Bob Gatenby**

WORKING GROUP discussion:

What are various trial frameworks that enable flexible incorporation of biomarkers and use of new drug combinations based on systems biology methods? What are challenges associated with obtaining/analyzing the tests/data and/or integration between data types and how do we overcome them?

What are innovative approaches to data analysis and integration that can inform patient response to therapy? What are challenges and potential solutions for these approaches?

How do we rapidly implement an adaptive trial design, where treatments can be adjusted in real-time based on emerging data and patient response? What measurements can be taken during the continuum of a patient's care?

**1:05 pm-1:15 pm: Break**

**1:15 pm- 2:30 pm: Session 3**

**Session 3 - Opportunities for technology advancement and collaboration across pharma, biotech, government, and academia (landscape analysis)**
**Moderator: Jill Barnholtz-Sloan (NCI) and Andrea Bild (COH)**

| Time | Presentation | Speaker |
|---|---|---|
| **1:15** | Transforming Cancer Care with Foundation Medicine | Mia Levy (Foundation Medicine) |
| **1:30** | Addressing problems in Drug Discovery and Early Development with molecular profiling: opportunities for new technology and collaboration | Paul Rejto (Pfizer) |
| **1:45** | Emerging uses of cfDNA analyses in clinical trials & oncology translational research | Shiva Malek (Novartis) |
| **2:00** | AI-Enabled Precision Medicine is Here: Multi-Modal Data Collaborations to Advance Cancer Care and Drug Development | Calvin Chao (Tempus) |
| **2:15** | Clinical Research Opportunities in collaboration with the Center for Cancer Research, NCI | James Gulley (NCI) |

**2:30 pm - 2:45 pm: Break**

**2:45 pm– 3:45 pm: Session 4**

**Session 4 - How to effectively match the speed of discovery and development with translation (implementation)**
**Moderator: Edison Liu (Jackson Labs)**

| Time | Presentation | Speaker |
|---|---|---|

| | | |
|---|---|---|
| **2:45** | Insights from ISPY 2: A transformative Bayesian-driven platform trial | Anna D. Barker (Ellison Institute) |
| **3:00** | Key technologies to accelerate Biomarker-to-Bedside translation | Joris Van Dam (Exact) |
| **3:15** | Reaching Escape Velocity<br>Climb out of the valley of death & accelerate your product to market | Debbie Lin (Caris) |
| **3:30** | Public-private partnerships can accelerate path of drug development and clinical testing | Stacey Adam (FNIH) |

**3:45 pm- 4:00 pm: Break**

**4:00 pm- 4:40: Working Group Discussion**

**4:40 pm- 5:00 pm: Report discussion results (~3 min per table)**

**Discussant Leaders: Andrea Bild and Shiva Malek**

WORKING GROUP discussion:

What are opportunities in collaborations of pharma with intramural NCI, cooperative groups, consortiums? How can these collaborations be maximized and deployed in a facile manner?

What are current opportunities and challenges to move discoveries to translation and then to commercialization?

What are the essential characteristics of a successful team that can work across academia, NCI and industry to carry out rapid clinical trials that have translational oncology biomarkers incorporated?

**Day 2- Friday, August 25, 2023**

8:30 - 8:45 am: Registration and coffee

**8:45 – 9:00 am: Day 1 recap and charge for the day (Sylvia Plevritis)**

**9:00 – 9:15 am: ARPA-H Overview (Tyler Best)**

**9:15 – 10:45 am Session 5**

**Session 5 - Challenges and solutions for forward and reverse translational oncology**

| Time | Presentation | Speaker |
|---|---|---|
| **9:15** | Integrating research insights into clinical trials | Laura Heiser (SMMART, OHSU) |
| **9:30** | Clinical Trial Designs: Looking Ahead | Sumithra Mandrekar (Mayo Clinic) |
| **9:45** | Technology and data foundations for accelerated therapeutic success, strong security and easy compliance | Kristy Cloyd-Warwick (DNAnexus) |
| **10:00** | Data Commons Lessons Learned and Future Directions | Jill Barnholtz-Sloan (NCI) |

**10:15 am- 10:30 am: Break**

**10:30 am-11:10 am: Discussion**

**11:10 am- 11:30 am: Report discussion results (~3 min per table)**

**Discussant Leaders: Shannon Hughes and Sandy Anderson**

WORKING GROUP discussion:

How do we learn from previous challenges and set up data and information sharing infrastructures in the most effective way?

What strategies can be utilized to ensure speed in acquiring, integrating and sharing data?

What flexible statistical designs are important for biomarker development and implementation? Are there critical benchmarks for evaluating new biomarkers?

**11:30 am-11:45 am: Break and Pick-up lunch**

**11:45 am-12:45 pm: White Paper working lunch:** We will draft a manuscript detailing the findings from our symposium. We will discuss: Innovation, landscape, and implementation sections, as well as key messages and examples.

**12:45 pm-1:00 pm: Wrap-up and next steps (Andrea Bild, Sylvia Plevritis, Shannon Hughes)**