NCI Immuno-Oncology Models Workshop

July 9 - 10, 2020

OVERARCHING QUESTIONS AND OPPORTUNITIES PROVIDED BY THE SPEAKERS

• To pursue models that reflect more precisely the biology of distinct molecular subsets of human tumors

• To integrate elements of host heterogeneity into mouse models, including germline variants and environmental factors

• In particular, to have robust models of the “cold tumor” phenotype, for preclinical studies of how to overcome this barrier to efficacy

Session 1: Mouse Models and Tumor Immune-Cell Interactions

- Identification of the best approaches to animal modeling that reduce powerful and often artificial inflammatory component associated with many current tumor models (including some transgenic one).
- To better characterize very few existing and develop new sporadic (stochastic) tumor models, which produce variable responses to immune intervention and allow for better understanding of the contribution of microenvironment to regulation of antitumor response in mice.
- To better characterize or improve spontaneous metastatic potential enabling studies that investigate the immunological implications of regional and distal metastasis. How do different metastatic sites affect immunotherapeutic response? Also, vice versa, what does immune control look like in metastases (dormant cells vs. micromets vs. macro?)
- How do we even assess what models represent what human cancers? What are the metrics?
- What are the sources of similarity in human tumors?
- What are some of the common immune-immune and immune-tumor cell relationships?

Session 2: Genetic Mouse Models for Immuno-Oncology

- Develop and utilize pre-clinical models so that they more accurately predict responses in human patients.
- Develop models that are “fully” human and allow for testing of human-specific biological agents.

Session 3: Human in Mouse Models

- Can/should we develop immuno-oncology models for clinical use (e.g., to directly select treatments) or keep them as research tools?
- Can we incorporate immuno-oncology (I-O) models in clinical trials to make them more personalized?
- How can we integrate systemic immune responses in human I-O models (i.e., organoids, explants, etc.)?
- Developing models that can elucidate mechanisms of inherent and acquired resistance.

Session 4: Models for Therapeutics

- What are the major limitations of the current humanized mouse models for immuno-oncology?
- What improvements in these models are required for increased translation to the clinic?
- To what extent can we recapitulate genetically complex patient leukemic status in humanized mice?

- Are we able to assess therapeutic efficacy against leukemia as well as adverse effect against normal human blood/immune system?

- Do we have any ways to target human malignancies and to activate human immunity in vivo? we integrate systemic immune responses in human I-O models (i.e., organoids, explants, etc.)?

Session 5: Tumor Organoids as Individualized Models for Cancer Treatment

- How much should patient-derived tumor organoid models recapitulate the heterogeneity and key features of specific tumors to offer the potential for timely testing of personalized treatment responses?

Session 6: Immune Toxicity and Comparative Models

- How can naturally occurring cancers in pet dogs complement studies of other animal models to enhance clinical translation of new therapies to humans?

- Which canine cancers have the most translational relevance to humans for development of immunotherapeutic strategies?

- What additional information/reagents/tools are needed to fully integrate canine cancers in the immuno-oncology drug development paradigm?

- Improved models that recapitulate immune-related adverse events with cancer immunotherapies are needed.

Session 7: Genomics of Response to Therapy and Computational Models

- To what extent do we need to understand spatial variation in tumors to improve treatment, and how should this guide our development of experimental models?

- Why is it so difficult to transfer drug responses from cell lines to patients, and what are the right strategies for developing predictive models that can be transferred?