Discussion Topics

SESSION I: ONCOGENE ACTIVITIES AND THE ACQUISITION OF MALIGNANT PHENOTYPE
(10:00 AM – 12:15 PM)
Chairs: Dr. Dean Felsher (Stanford University) and Dr. Elizabeth Jaffee (Johns Hopkins University [JHU])

Suggested Discussion Topics

- A systematic understanding of oncogene functions – defining the molecular mechanisms responsible for gain of malignant phenotype. (We can discuss early- vs. late-onset cancers in this context.)
  - Oncogene allele-specific phenotypes and relationships with specific tissue landscapes in tumor formation.
  - Key oncogene categories, nature, cell of origin, timing, cellular hubs, and dynamics of cell intrinsic cooperating and antagonistic mechanisms.
  - Disparate disease outcomes, mechanisms of acquisition of resistance and treatment responses – gain insights to develop new therapeutic targets.

- Redundancies and exclusivities of commonly activated oncogenes (co-occurring or mutually exclusive).

- Differential germline risk predisposition in high-risk individuals.

- Consider the relative importance of temporal sequence vs. the number of driver mutations. Could the temporal sequences be important for stage- or tissue-specific fitness?

- How do normal tissues tolerate multiple driver mutations and yet maintain normal phenotypes (e.g. epidermal cells)? What events are required to break this resistance and lead to frank tumor progression?

- Why do pediatric cancers appear to have a low number of mutations?

SESSION II: ONCOGENIC EFFECTS AND DETERMINANTS OF CELL FATE
(1:15 – 3:30 PM)
Chairs: Dr. Trever Bivona (UCSF) and Dr. Anirban Maitra (MD Anderson Cancer Center)

Suggested Discussion Topics

- Cellular processes that are cooperative, compensatory, or antagonistic in nature during tumorigenesis. Specifically, how oncogenes contribute to:
  - Progression
  - Differentiation
  - Plasticity
  - Quiescence
  - Senescence
  - Any other important cell state

SESSION III: ONCOGENE ADDICTION: POSSIBLE MECHANISMS AND POTENTIAL VULNERABILITIES (3:45 – 5:30 PM)
Chairs: Dr. Robert Coffey (Vanderbilt University Medical Center [VUMC]) and Dr. Eileen White (Rutgers University)

Suggested Discussion Topics

- What defines a true addiction and what is its significance in tumor growth and sustainability?
- Emergence of treatment resistance in different tissue contexts.
- Potential targets for therapeutic vulnerabilities and synthetic lethality for “drugging the addict”.

SESSION IV: LEVERAGING RESOURCES, TOOLS, AND MODELS (8:35 – 11:00 AM)
Chairs: Dr. Kevin Haigis (DFCI) and Dr. Linghua Wang (MD Anderson)

Suggested Discussion Topics

- In silico approaches in developing atlases of oncogene alterations, co-regulatory cooperators, effectors responsible for oncogenic potential, and interrogating the mechanistic network across cancer types and subtypes.
- Interrogating the multi-omic state for an enhanced mechanistic understanding of oncogene-driven tumor initiation, progression, and/or maintenance.
- Identification of potential new players.
- Identifying high-fidelity models that recapitulate human disease and/or preserve clinical annotation.
- Key challenges and how to overcome them.
- Other topics -- polymorphisms, composite mutations etc.