Workshop

Monoclonal Antibodies in Cancer

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University of Iowa
Quotes from Esteemed Oncologist

1989 to me – “I don’t know why you are so interested in anti-cancer monoclonal antibodies. You are throwing your career away on a failed hypothesis.”

2007 to ASCO – “Anti-cancer monoclonal antibodies represent a great advance in cancer therapy.”

2010 to my post-doc – “I don’t know why you are so interested in anti-cancer antibodies. Further advances will be only incremental.”
Still Much to Learn!

Example from my own laboratory
How do NK cell-mediated ADCC and Complement Interact?
C3b inhibits monoclonal antibody-induced NK activation and ADCC
Depleting complement with HC3-1496 enhances efficacy of anti-cancer antibody therapy in a murine model
Ab structure
- Novel constructs
- Kinetics
- Biodistribution
- Immunoconjugates

Interaction with immune system
- Fc Receptors
- Other receptors
- Induction of active immune response

Specificity
- Tumor antigen
- Signaling
- Immune response

Clinical Development
- Indications
- Combinations
- Assessing efficacy
Agenda

- **Tumor Targeted Antibodies** (Ira Mellman)
  - Targeting Activated HER2 I Solid Tumors (Mark Sliwkowski)
  - Antibody-Based Cancer Immunotherapy (Louis Weiner)
  - Combining Tumor Reactive mAbs with Cytokines to Induce ADCC in Patients (Paul Sondel)

- **Immunomodulatory Antibodies** (Glenn Dranoff)
  - Immune Modulation by Antibody (Leiping Chen)
  - Immunomodulation with Antibodies Blocking the B7-H1/PD-1 Axis (Susanne Topalian)

- **Antibodies as Vaccines** (Ira Mellman)
  - Antibody Therapeutics in Cancer: Converting Passive to Active Immunity (Raphael Clynes)
  - Antibody-Targeted Vaccines (Tibor Keler)

- **Antibody Engineering** (George Weiner)
  - Two in One Antibody: From Proof-of-Concept to Therapeutic Candidate (Germaine Fuh)
  - Engineered Anti-Cancer Antibodies with Enhanced Effector Functions (Pablo Umana)
  - T Cell Engaging BiTE Antibodies for Cancer Therapy (Patrick Baeuerle)
# Developing a Better Antibody Challenges

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**Clinical Trials**
- Most lack correlative studies
- Correlation is not causation
Monoclonal Antibodies in Cancer

“You are throwing your career away on a failed hypothesis.”

False

“Anti-cancer monoclonal antibodies represent a great advance in cancer therapy.”

True

“Further advances will be only incremental.”

False