Workshop

Monoclonal Antibodies in Cancer

Glenn Dranoff
Dana-Farber Cancer Institute

Ira Mellman
Genentech

George Weiner
University of Iowa

Quotes from Esteemed Oncologist

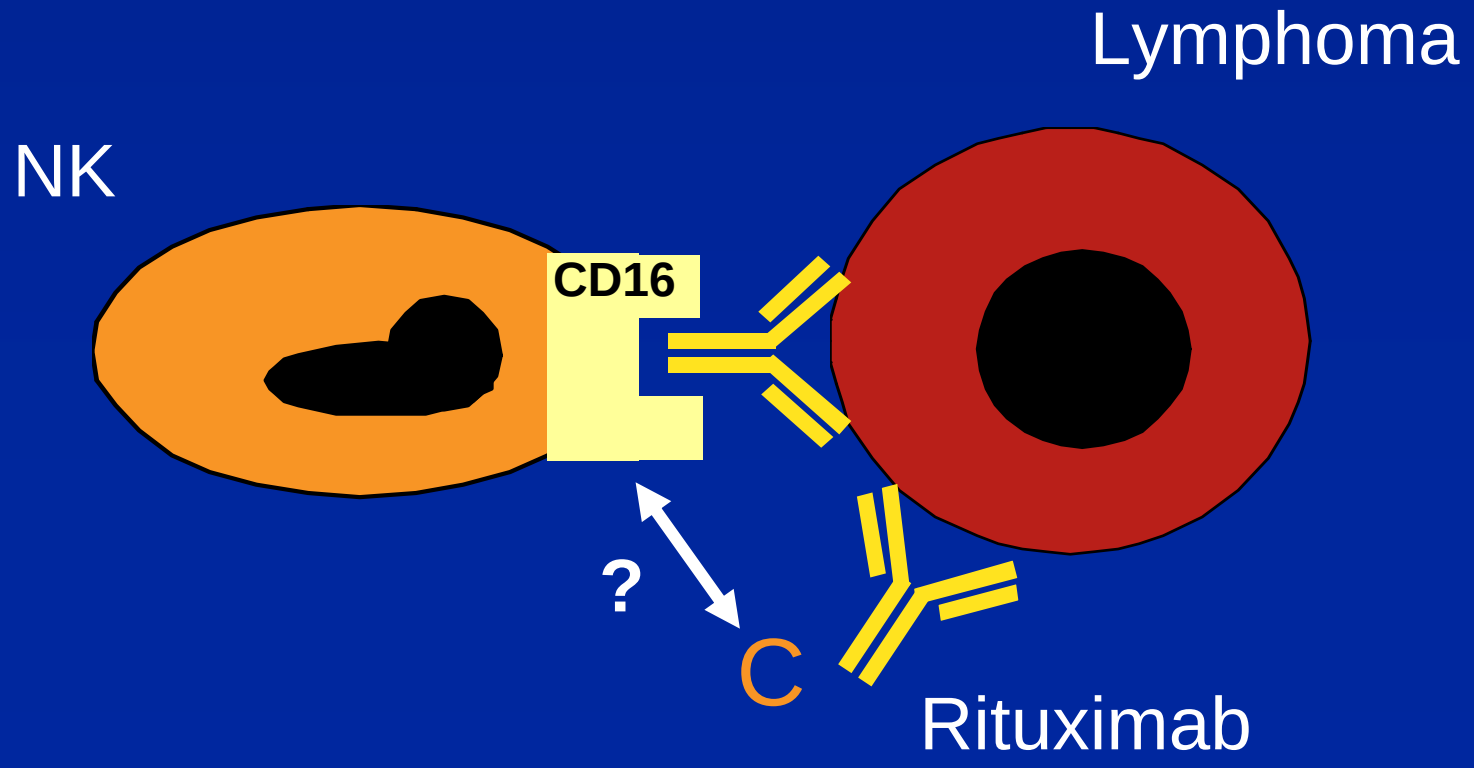
1989 to me – “I don’t know why you are so interested in anti-cancer monoclonal antibodies. You are throwing your career away on a failed hypothesis.”

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

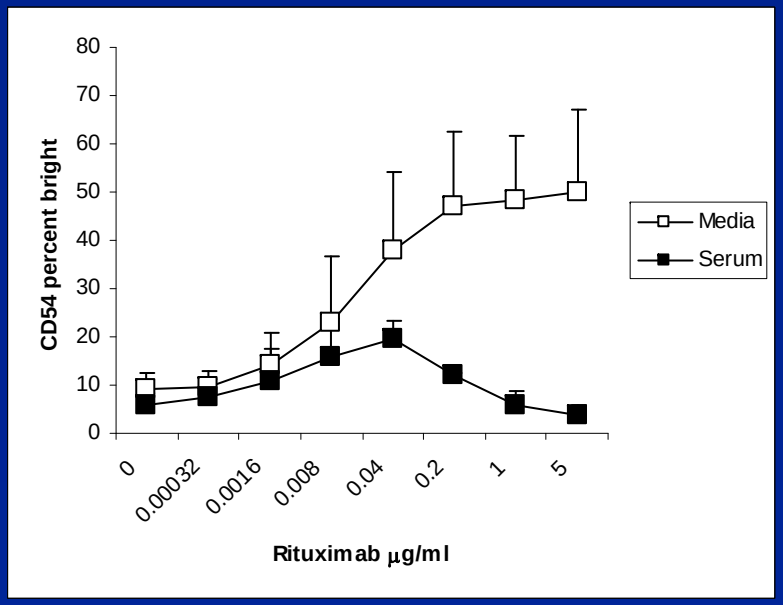
2010 to my post-doc – “I don’t know why you are so interested in anti-cancer antibodies. Further advances will be only incremental.”

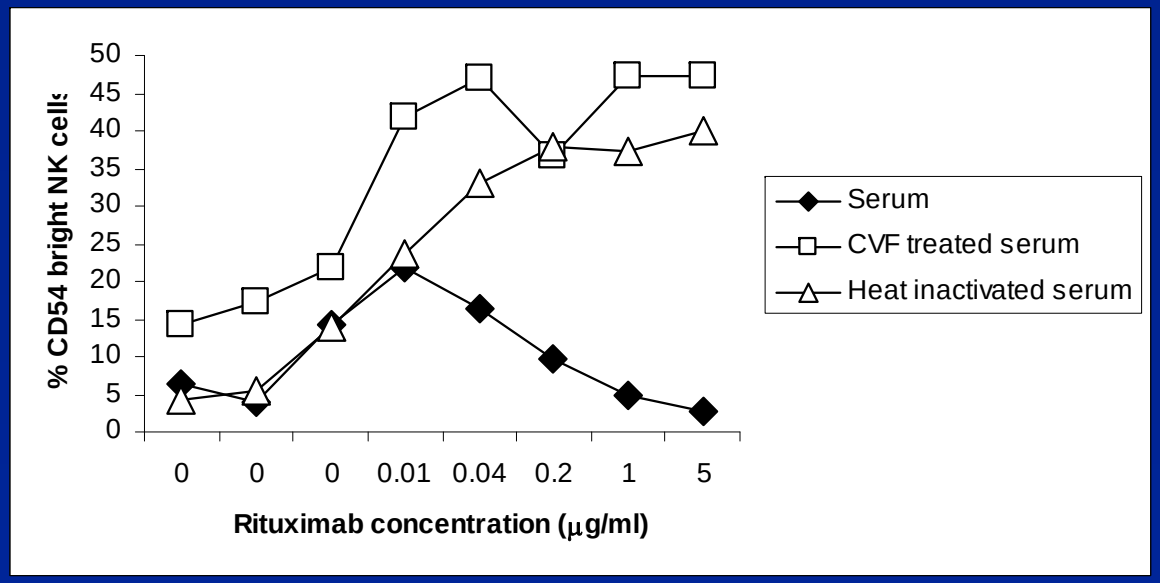
Still Much to Learn!

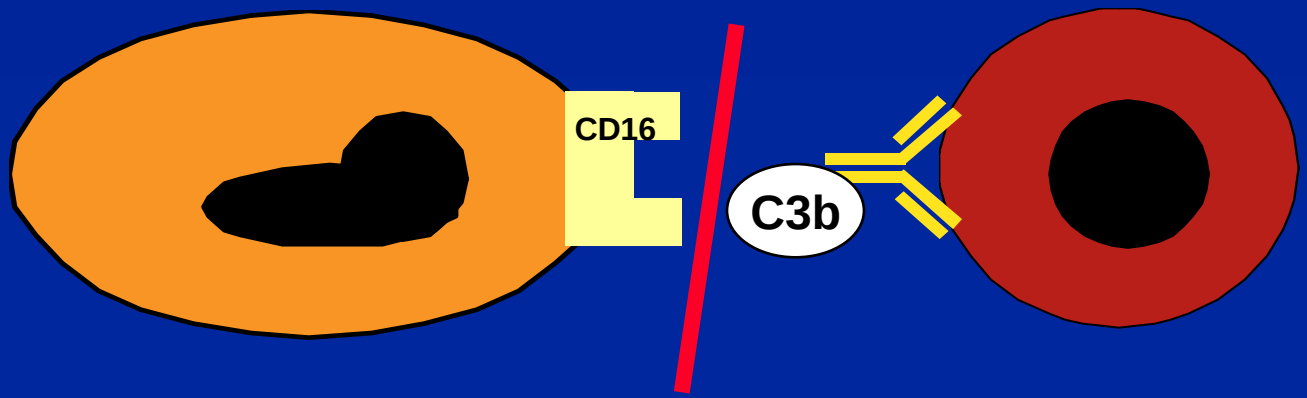
Example from my own laboratory
How do NK cell-mediated ADCC and Complement Interact?



Complement and NK activation

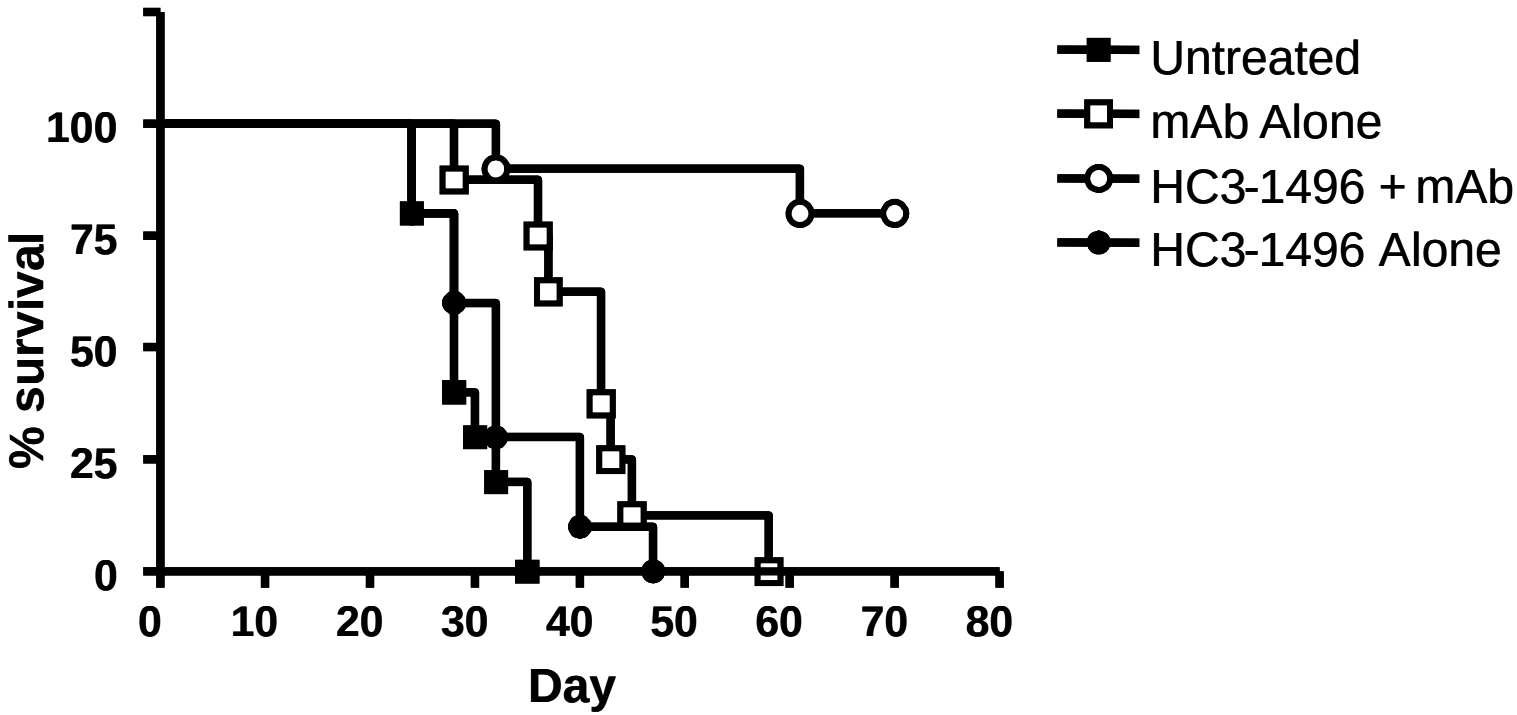






C3b inhibits monoclonal antibody-induced NK activation and ADCC

Depleting complement with HC3-1496 enhances efficacy of anti-cancer antibody therapy in a murine model

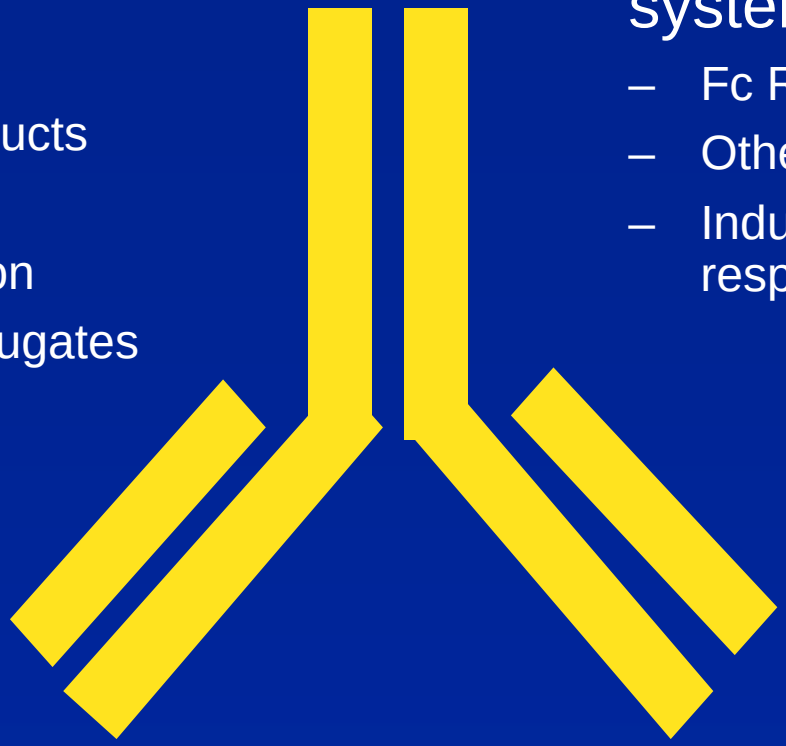


Ab structure

- 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 Moduation 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 Theraeputic 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

	Parameter	Research	Clinical Reality
In Vitro	Time		
	Target		
	Environment		
Animal	Time		
	Target		
	Environment		

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