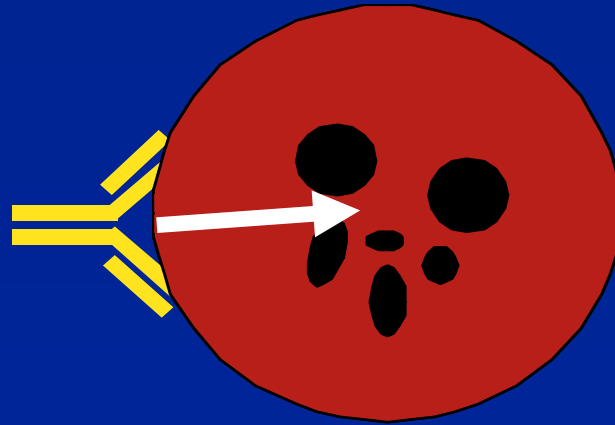


# Anti-Cancer Monoclonal Antibodies

Diverse Mechanisms of Action?

# Signaling Induced Apoptosis

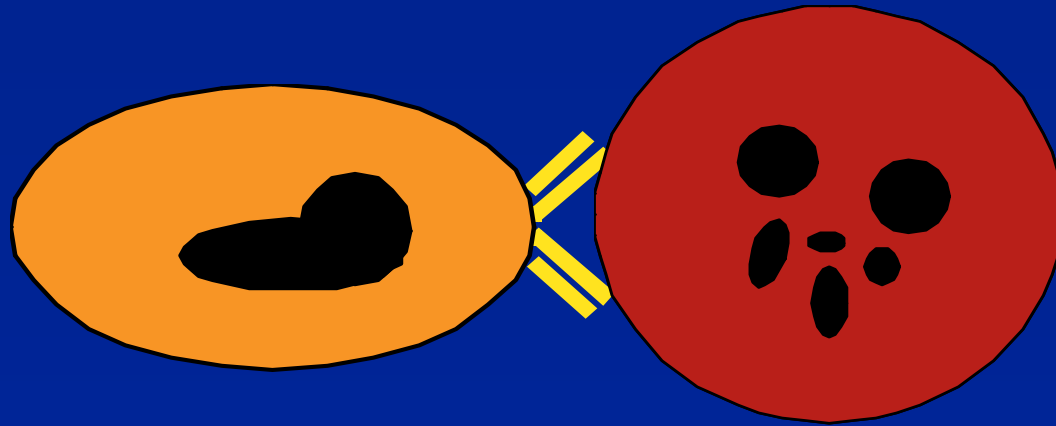


# Signaling Induced Apoptosis

Generation of Rituximab Polymer and Evaluation of CD20 Hyper-Crosslinking-Induced Apoptosis in Non-Hodgkin's Lymphomas.

*Nan Zhang, Leslie A Khawli, Peisheng Hu, Alan L Epstein.* Pathology, Keck School of Medicine, University of Southern California, Los Angeles, CA.

# Antibody Dependent Cellular Cytotoxicity



## Antibody Dependent Cellular Cytotoxicity

Enhanced Tumor Inhibition of MDA-MB-231 Breast Carcinoma by the Anti-Tissue Factor Antibody, CNTO 860, Is Mediated by Antibody Dependent Cellular Cytotoxicity.

*Cam Ngo, Bernie Scallon, Richard Tawadros, Frank McCabe, Hillary Millar, Marian T Nakada, G Mark Anderson.*

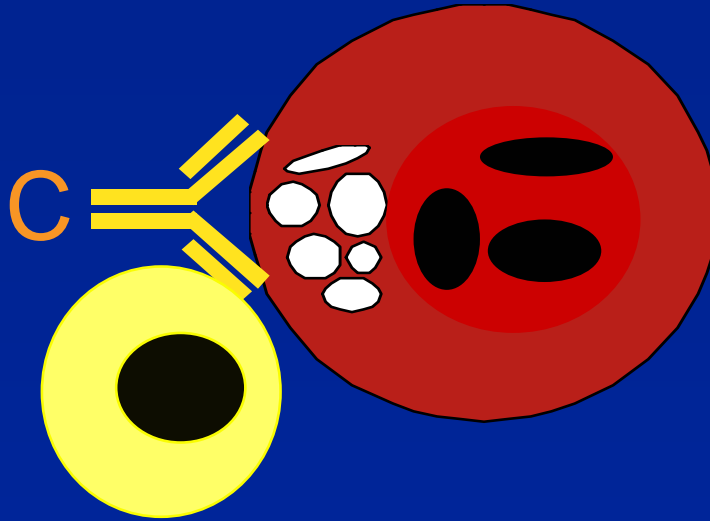
Oncology Research, Centocor, Inc, Radnor, PA; Molecular Biology, Centocor, Inc, Radnor, PA; Toxicology and Investigational Pharmacology, Centocor, Inc, Radnor, PA.

Improved Lytic Potential of a Therapeutic Monoclonal Antibody by Glycoform Engineering.

*Manfred Schuster, Pablo Umana, Geert C Mudde, Gottfried Himmeler, Hans Loibner.*

IGN312, igeneon AG, Vienna, Austria; CSO, Glycart Biotechnology AG, Zuerich, Switzerland.

# Complement Mediated Cytotoxicity

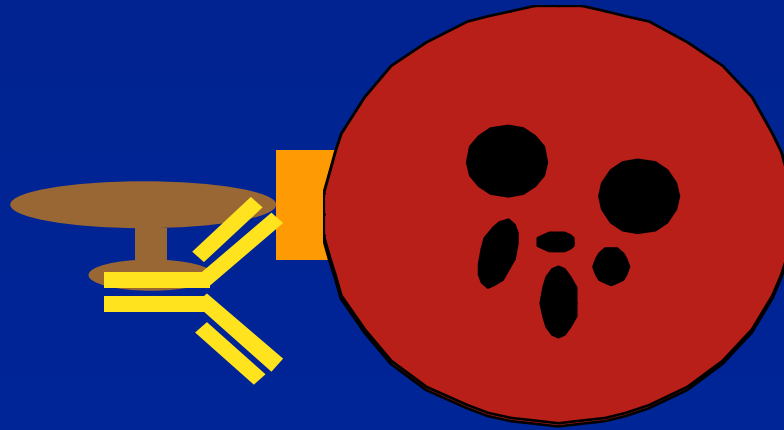


# Complement Medicated Cytotoxicity

A Phase I Trial of a Monoclonal Antibody Directed to Lewis Y.

*D Oruzio, G Schlimok, N Eller, C Aulmann, S Stranner, G Waxenecker, A Obwaller, H Loibner, G Mudde, G Himmeler.* Medizinische Klinik, Zentralklinikum, Augsburg, Germany; igeneon AG, Wien, Austria.

# Blocking an Activation Signal



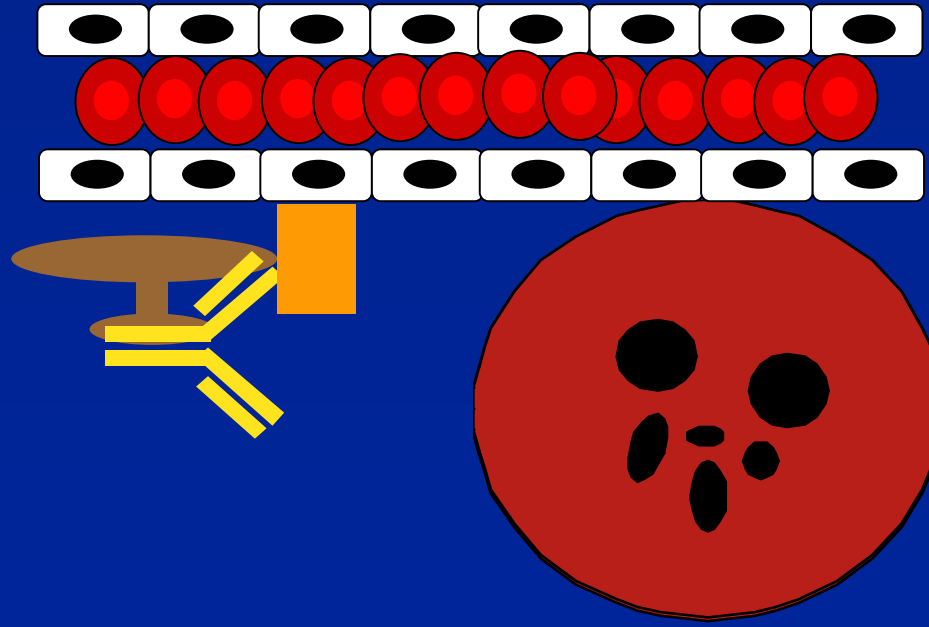


# Blocking an Activation Signal

M200, a Chimeric Antibody Against Integrin  $\alpha 5 \beta 1$ ,  
Inhibits Cancer Cell Growth In Vitro.

*Vinay Bhaskar, Pauline Wales, Danna Breinberg, Melvin  
Fox, Sun Ho.* Protein Design Labs, Inc., Fremont, CA.

# Blocking Angiogenesis or Other Vital Factors in Stroma



## Blocking Angiogenesis or Other Vital Factors in Stroma

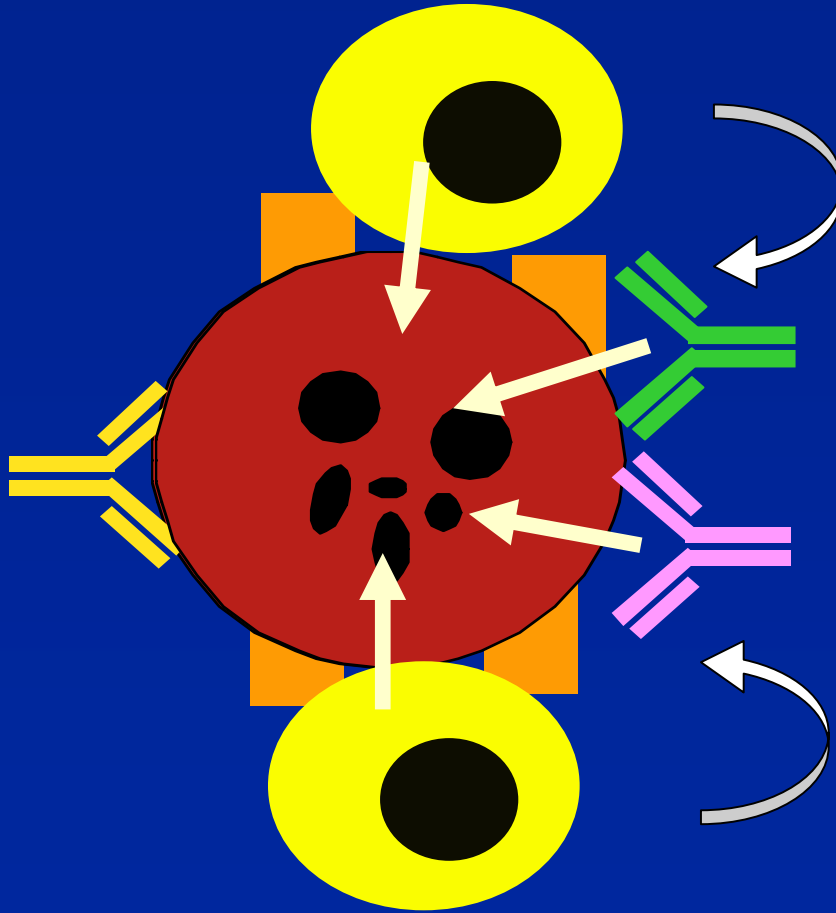
CNTO859, a Humanized Monoclonal Anti-Tissue Factor Antibody, Inhibits Experimental Tumor Growth in a BxPC-3 Human Pancreatic Adenocarcinoma Xenograft Tumor Model. *Richard Tawadros, Cam Ngo, Francis McCabe, Marian Nakada, G Mark Anderson.* Oncology Research, Centocor, Inc., Radnor, PA.

Anti-Angiogenic and Anti-Cancer Activity of Monoclonal Antibodies to CCL-2/MCP-1 (Monocyte Chemoattractant Protein-1).

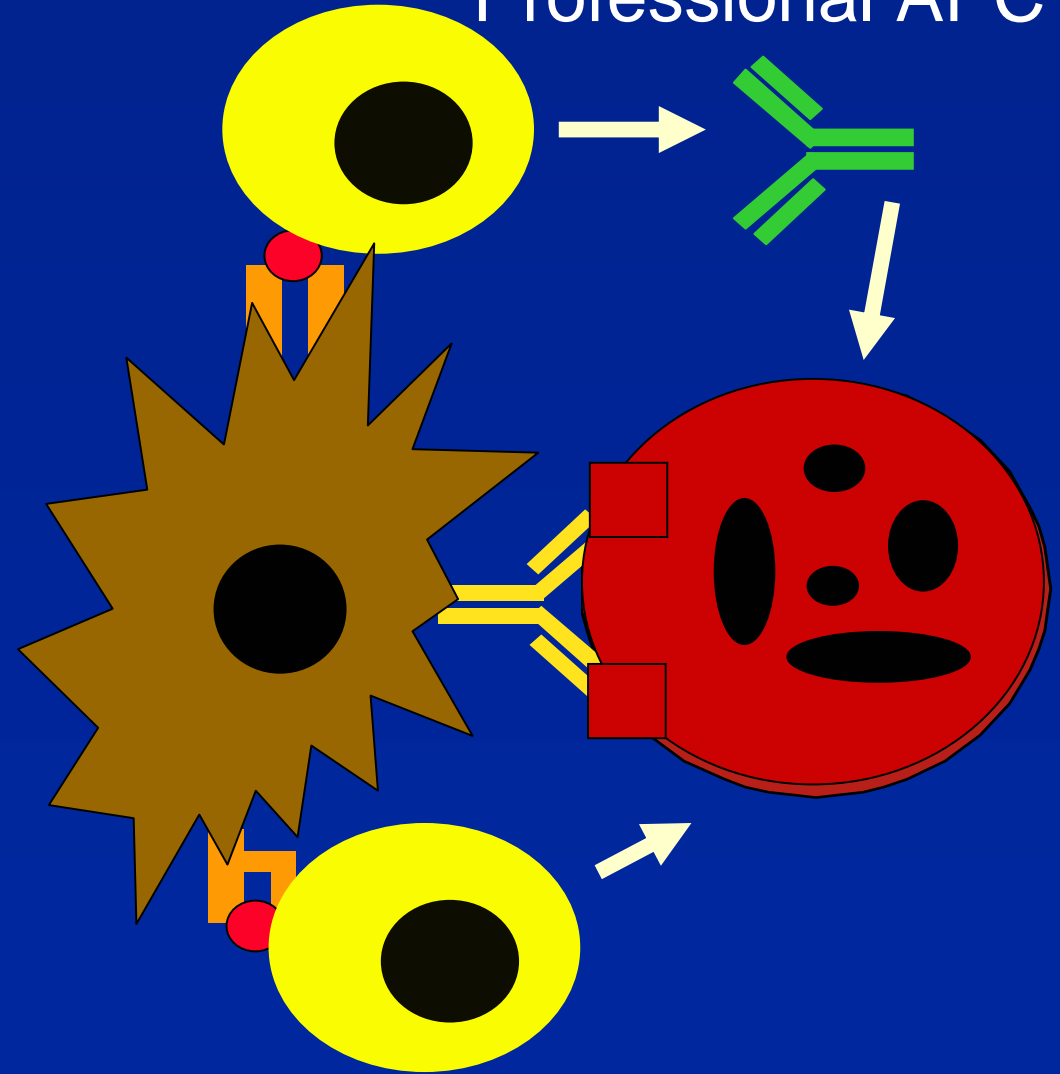
*Prabakaran Kesavan, Francis McCabe, Hillary Millar, Nicole Stowell, Patricia Rafferty, Peter Bugelski, Don Griswold, Anuk Das, Marian Nakada, Li Yan.* Oncology Research, Centocor; Immune-Mediated Inflammatory Disorders, Centocor, Malvern, PA.

# Enhanced Development of an Active Immune Response

Malignant cell as APC



Professional APC



# Enhanced Development of an Active Immune Response

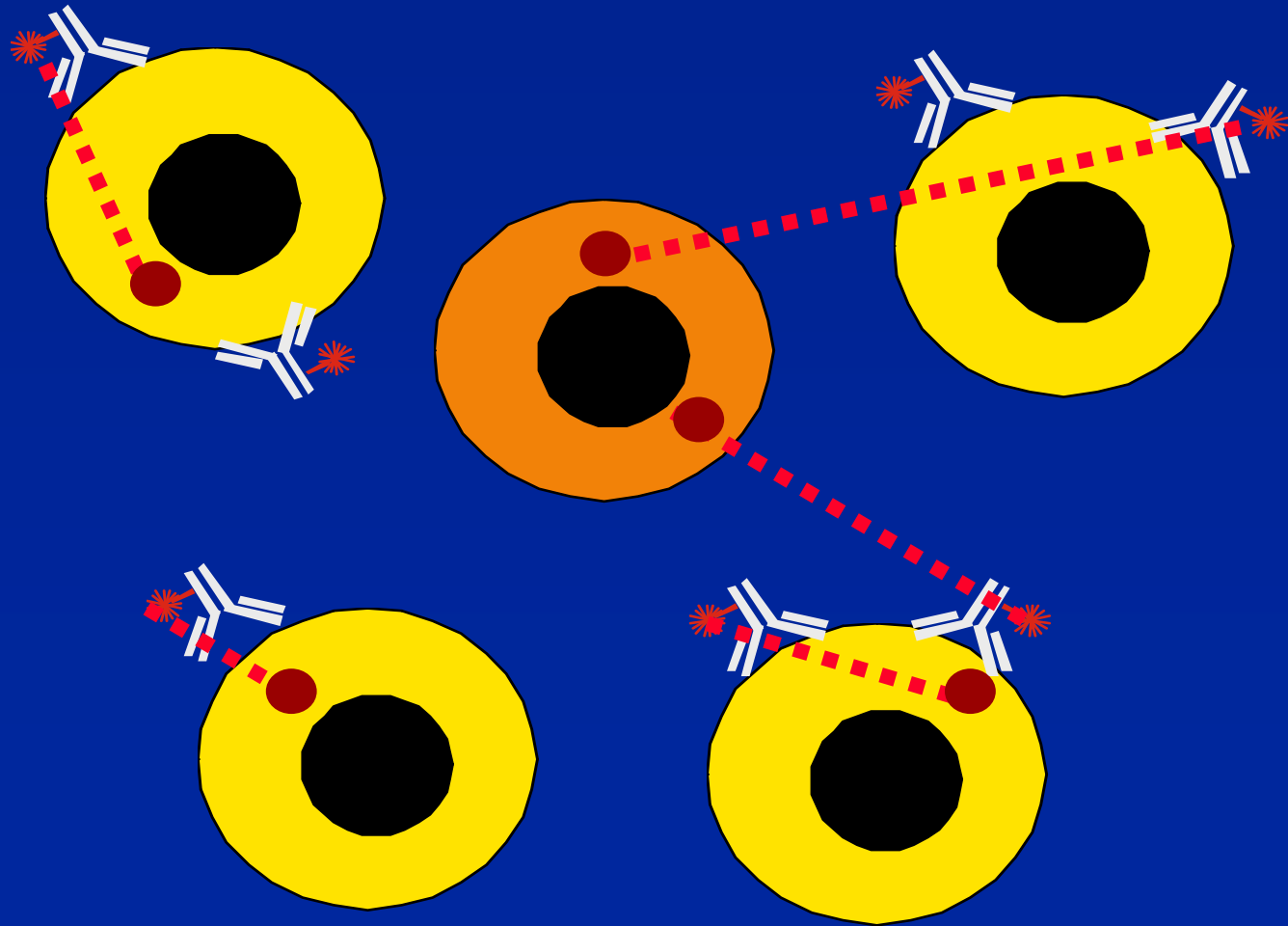
T-Regulatory Cell Based Immunotherapy Using Yeast Display Constructed Antibodies for the Treatment of Cancer in Humans. *Robyn Arias, Meg Flanagan, Keith Miller, Peisheng Hu, Alan Epstein.* Pathology, University of Southern California & Keck School of Medicine, Los Angeles, CA; Biomolecular Systems and Science, Pacific Northwest National Laboratories, Richland, WA.

Herceptin Enhances Class I-Restricted Antigen Presentation Recognized by HER 2/neu-Specific CTLs. *Koji Kono, Kousaku Mimura, Akihiro Takahashi, Hideki Fujii.* First Department of Surgery, University of Yamanashi, Tamaho, Yamanashi, Japan.

Combination Human B7.1/NHS76 and B7.1/Fc Fusion Protein Immunotherapy and CD25+ T-Regulatory Cell Depletion Produces Complete Remission of Transplanted Solid Tumors. *Aihong Liu, Peisheng Hu, Leslie A Khawli, Alan L Epstein.* Department of Pathology, University of California, Keck School of Medicine, Los Angeles, CA.

Monoclonal Antibodies Against 4-1BB Enhance the Antitumor Effects of Radiation. *Dietmar Siemann, Wenyin Shi.* Radiation Oncology, University of Florida, Gainesville, FL.

# Radioimmunotherapy



# Radioimmunotherapy

Generation, and Characterization of Two Tetravalent  
CH2 Domain-Deleted CC49 Mabs.

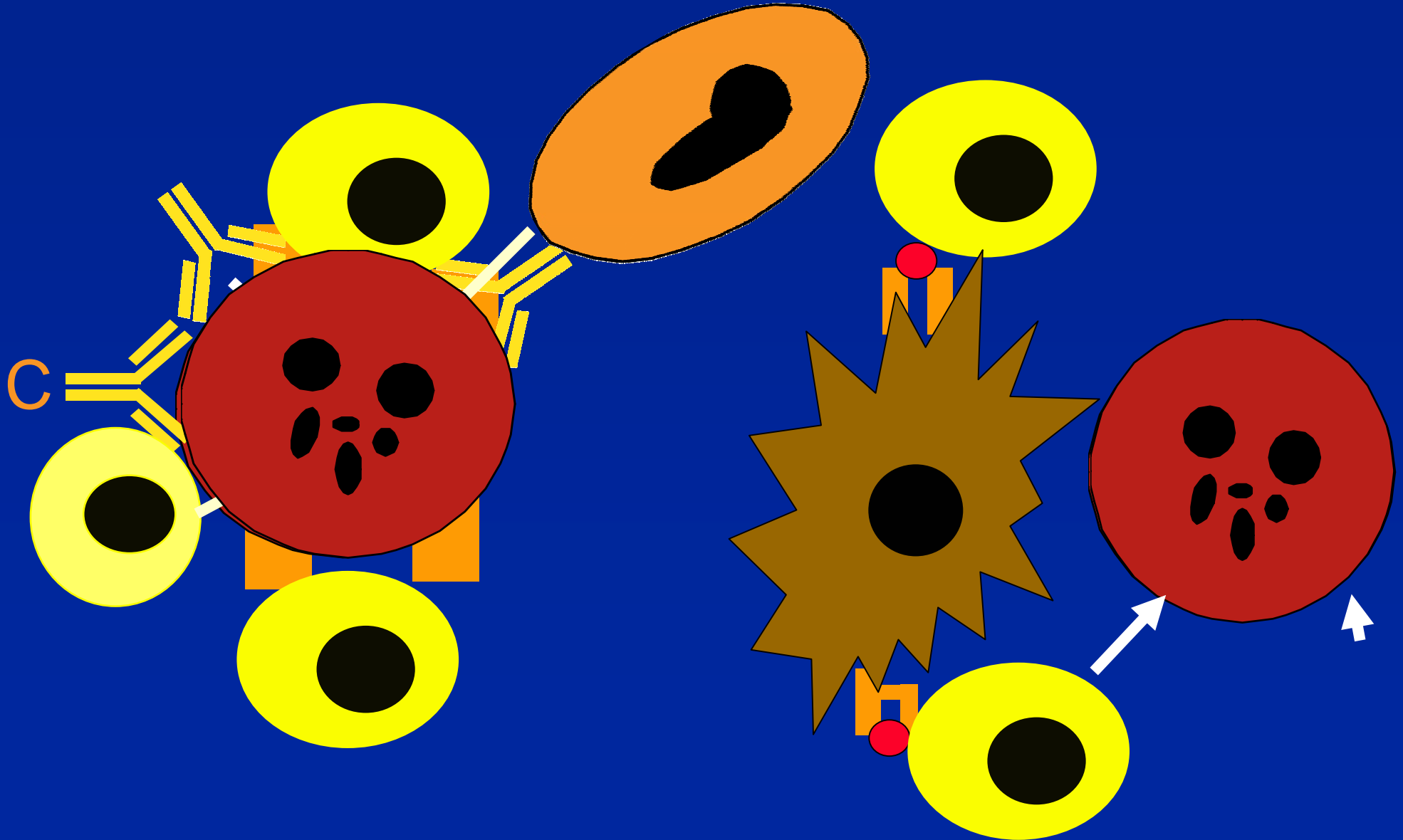
*Xiufeng Wu, Jennifer Hopp, Daniel Perret, Julie  
Chung, Mitchell E Reff, Scott M Glaser.* Discovery  
Research, Biogen Idec, San Diego, CA.



In Vivo Validation of Antibodies Against  
Ov1, a Novel Ovarian Cancer Target  
*Vinay Bhaskar, Debbie Law, Eric Ibsen,*  
*Gao Liu, Pui Seto.* Research, Protein Design Labs,  
Inc., Fremont, CA.



# Conclusion on mechanism of action



# How do we determine which mechanisms are really important?

Are in vitro studies informative?

Are xenograft therapy studies informative?

Are clinical correlative studies informative?

Does it really matter?