Monoclonal Antibodies

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Biochemistry 118Q

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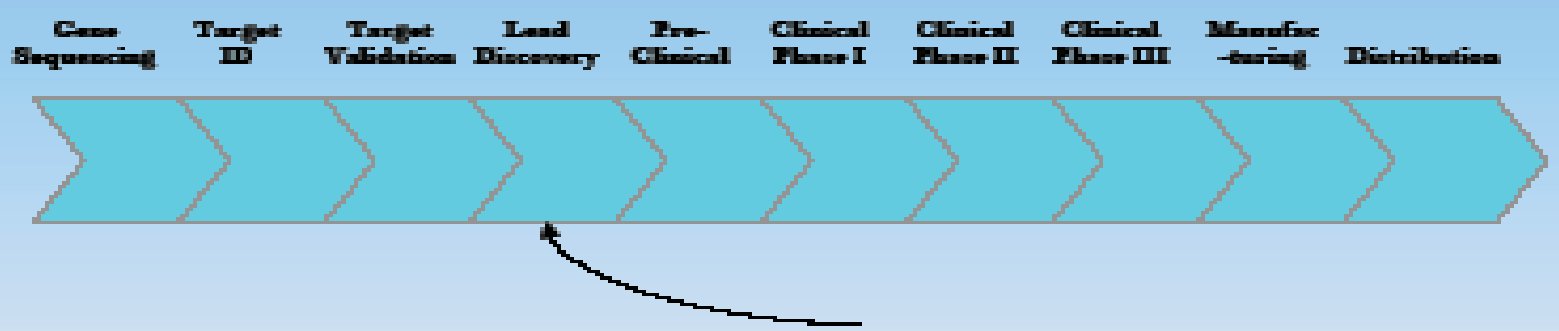
Overview

- Monoclonal Antibodies
- Applications
- Genomics

Drug Development

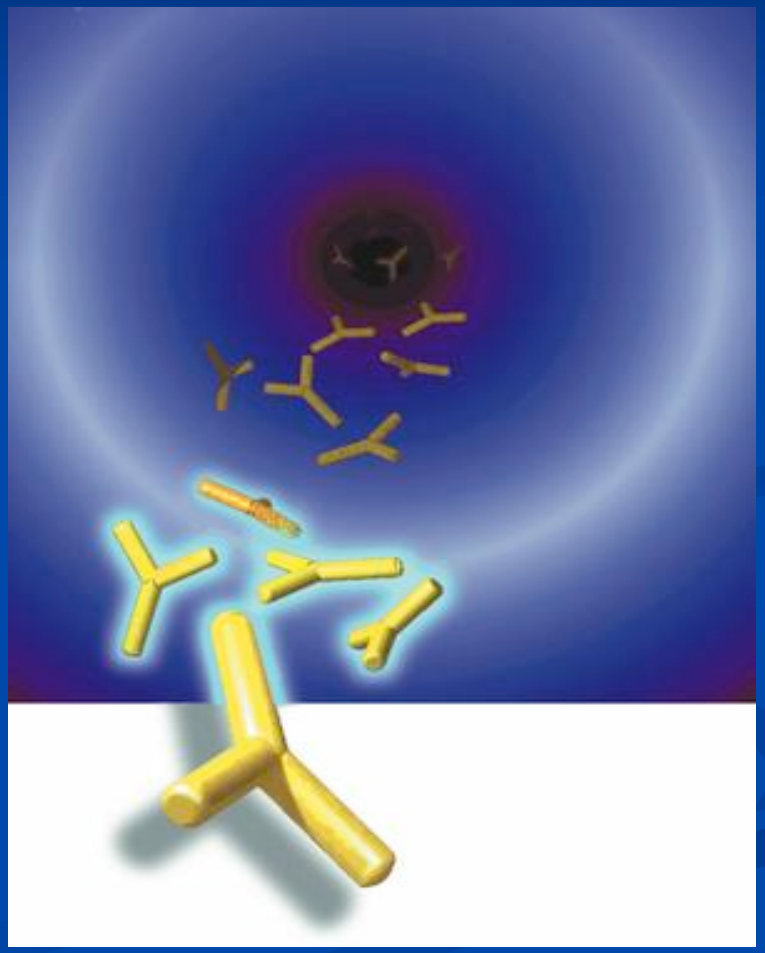


Evaluate leads to 'cure' the problem, e.g.:

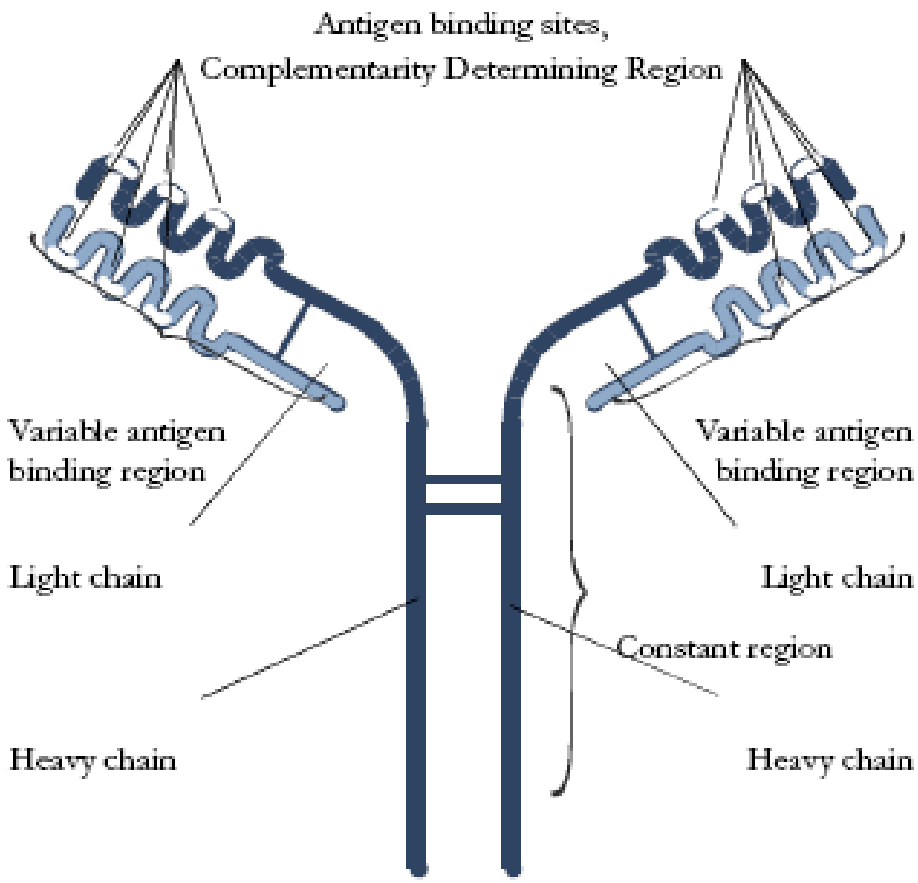
- Replace missing or defective protein with gene therapy
- Anti-sense RNA to prevent protein expression
- Antibody to remove protein
- Stimulation of synthesis to replace protein

Smart Bombs

- Specificity
- Targeting
- Variety



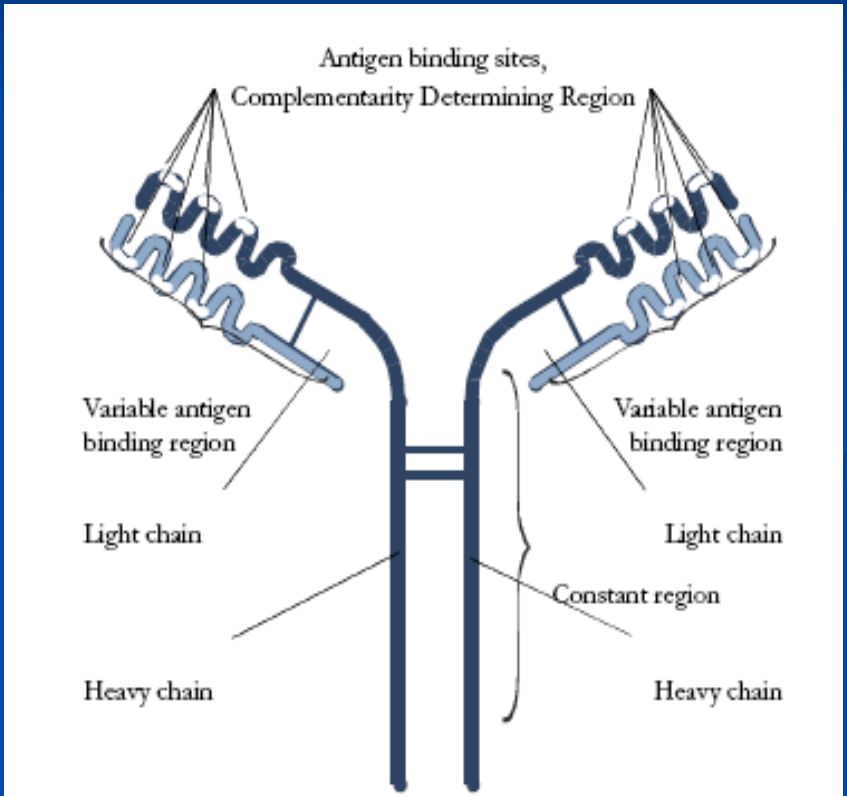
Antibodies and the Immune System



The antibody molecule

Antibodies and the Immune System

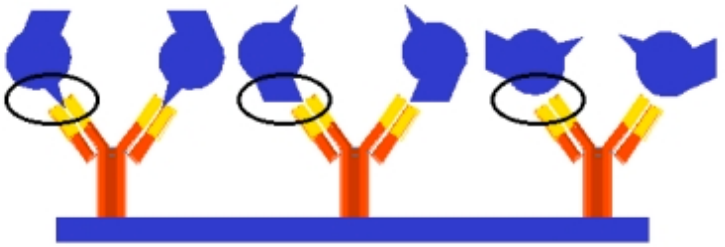
- B-cells
- Splicing
- Limitless



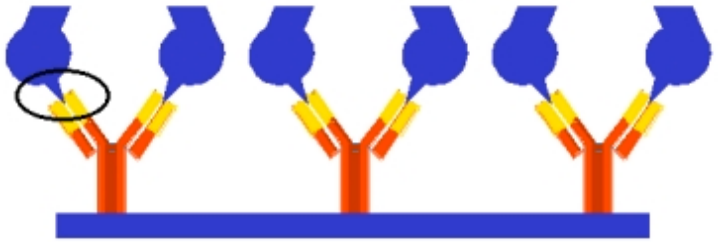
The antibody molecule

Antibodies and the Immune System

Polyclonal Ab recognises different antigen epitopes



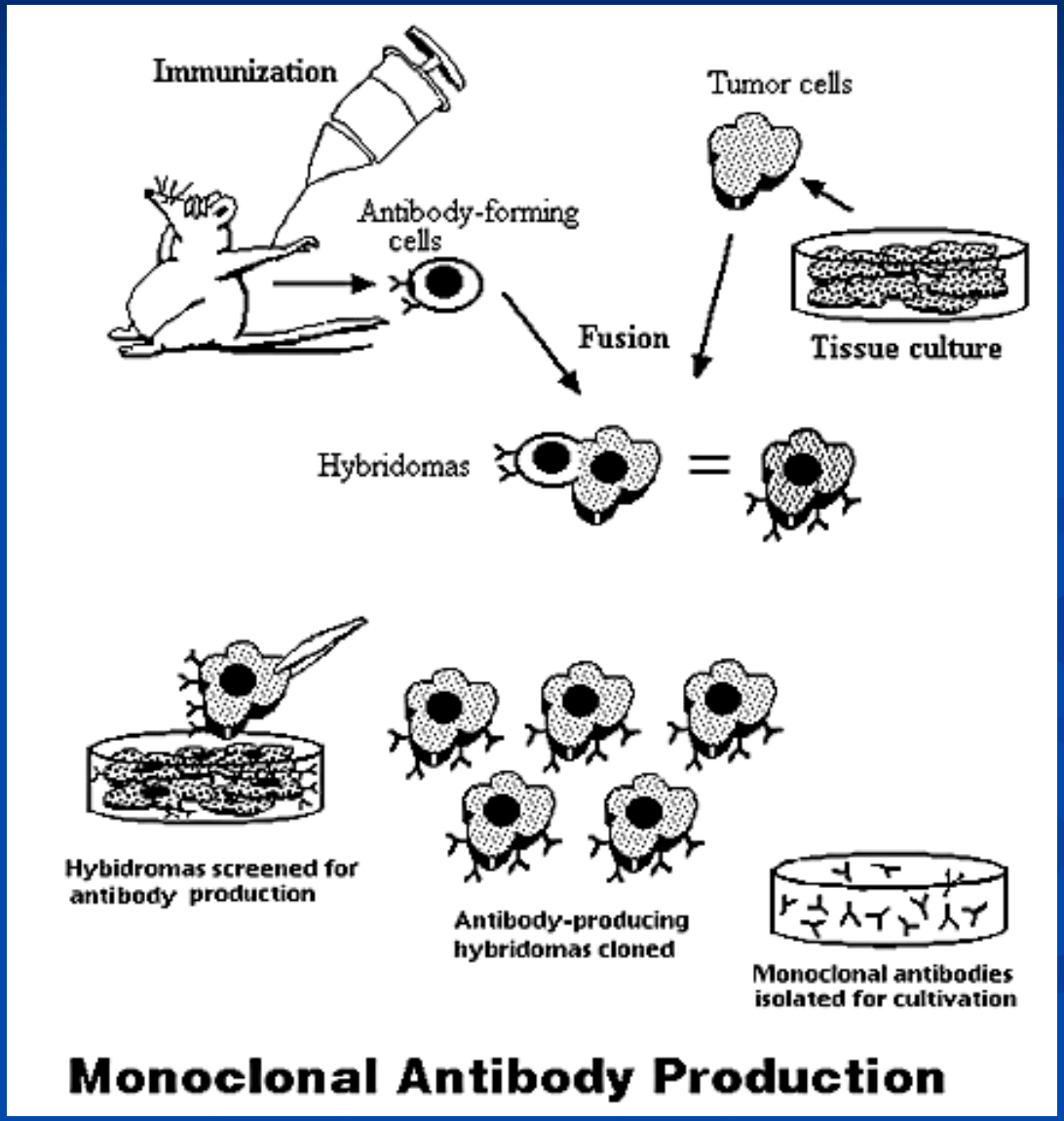
Monoclonal Ab recognises a single antigen epitope



Monoclonal Antibodies

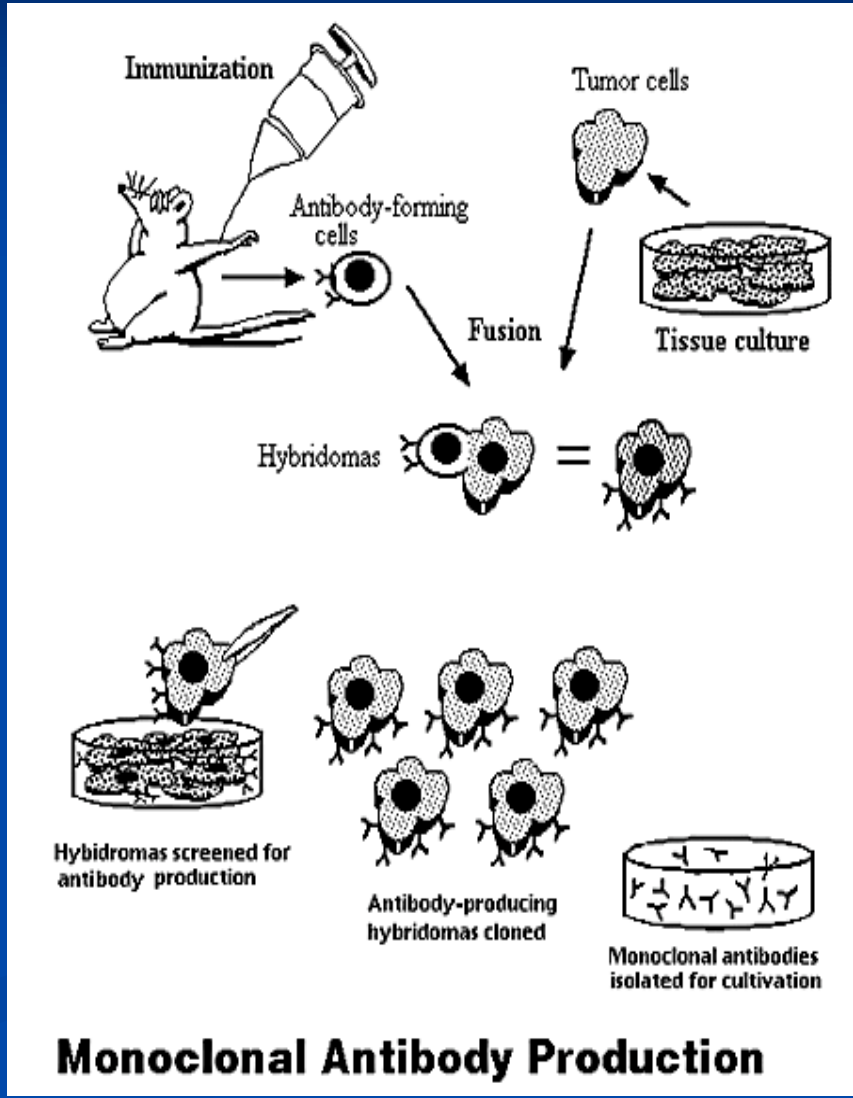
- Single Specificity
- Unlimited Production

Monoclonal Antibodies



Monoclonal Antibodies

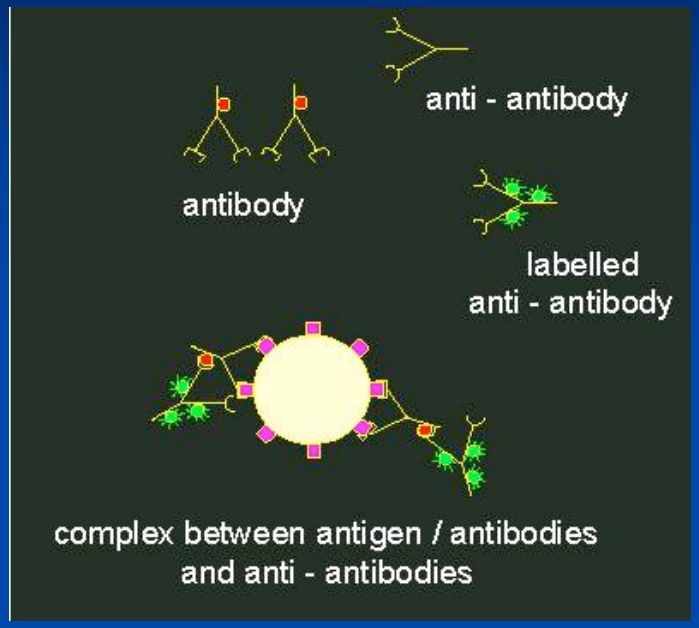
- 1975- Köhler and Milstein
- Immunized mice
- Fused B cells with myeloma cells
- Hybridomas
- Nobel Prize

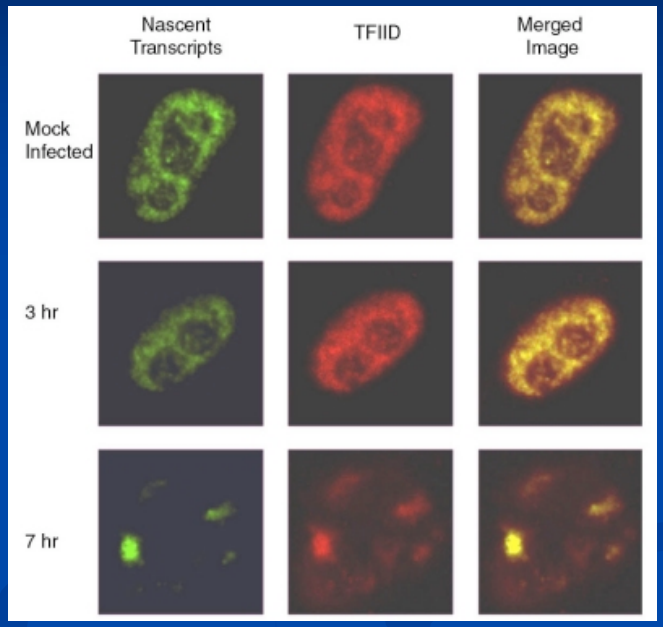


Applications

- Grouping blood types and identifying viruses
- Labeling in tests for pregnancy, cancers, blood clots, and heart disease.
- Purification of proteins and drugs
- Counteract transplant rejection

Applications

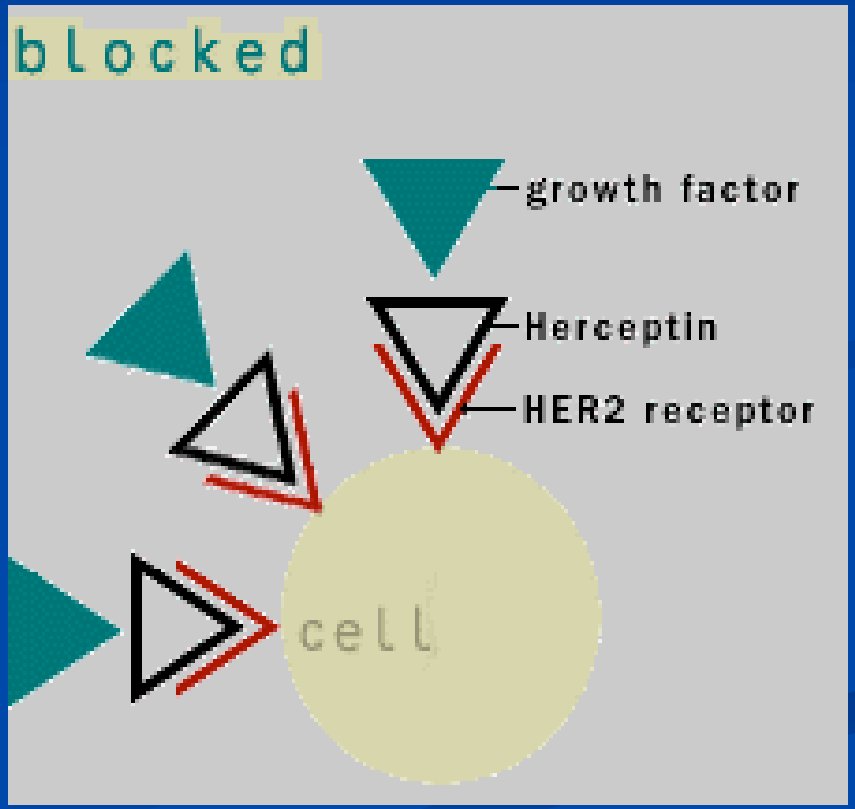




- Fluorescence Imaging
- Carrier molecule – radioactive cargo, cytotoxins, etc.
- Binds receptors

Applications

- Rituxan – CD20 on B cells (Ron Levy)
- Herceptin – HER2, EGF receptor
- Vitaxin – vascular integrin, antiangiogenesis



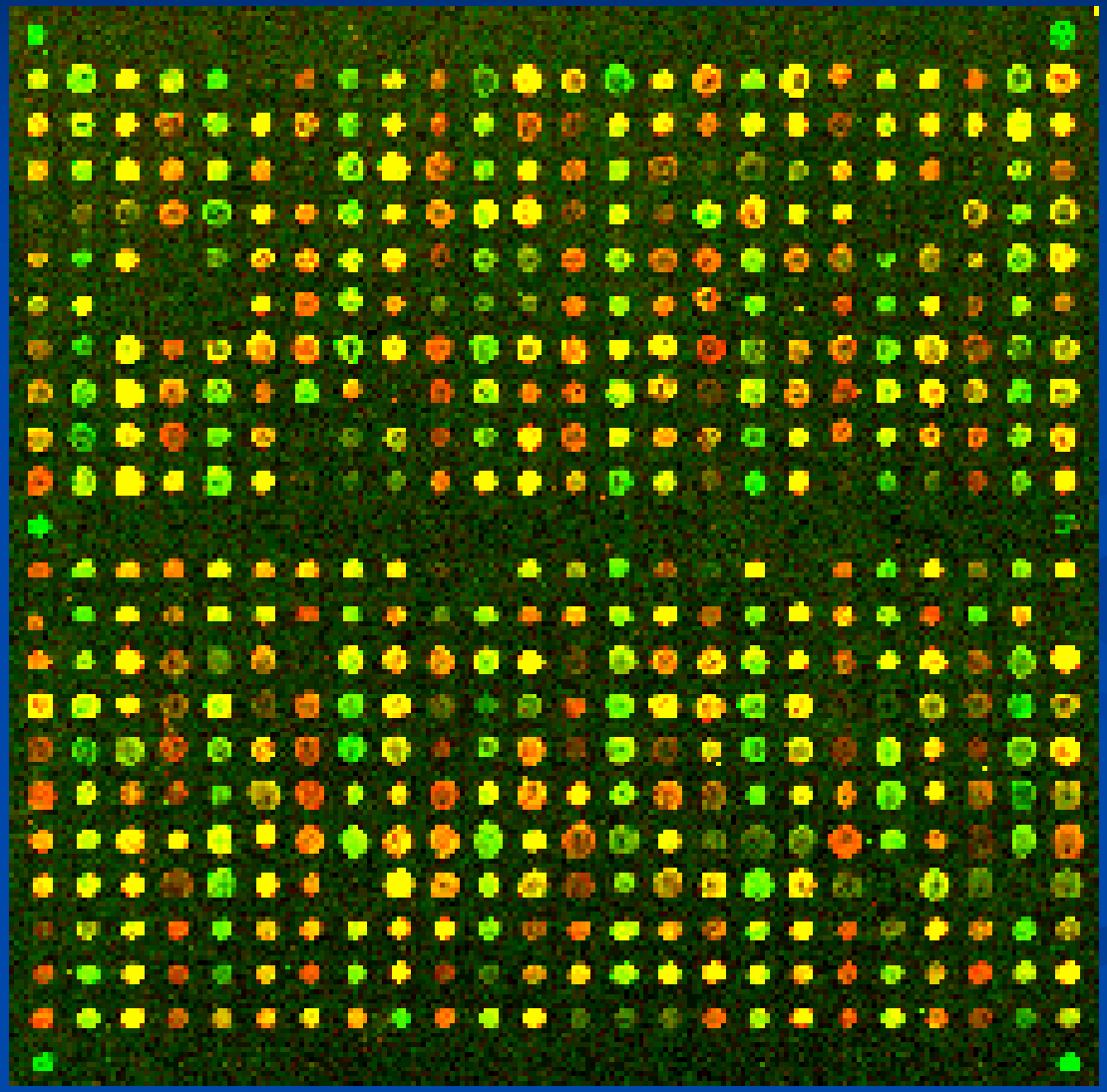
Problems

- Mouse antibodies foreign
- Production of human anti-mouse antibodies (HAMA)
- Rapid inactivation

Solutions

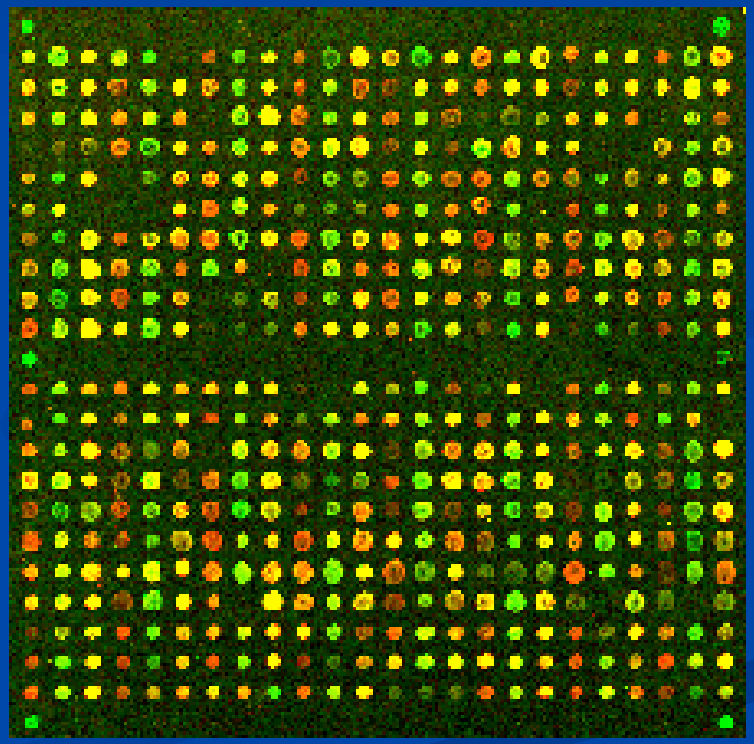
- Chimeric antibodies – human-mouse hybrid antibodies with mouse CDR fused with human constant regions
- Splicing mouse CDR into human antibody gene regions
- Transgenic mice

Genomics



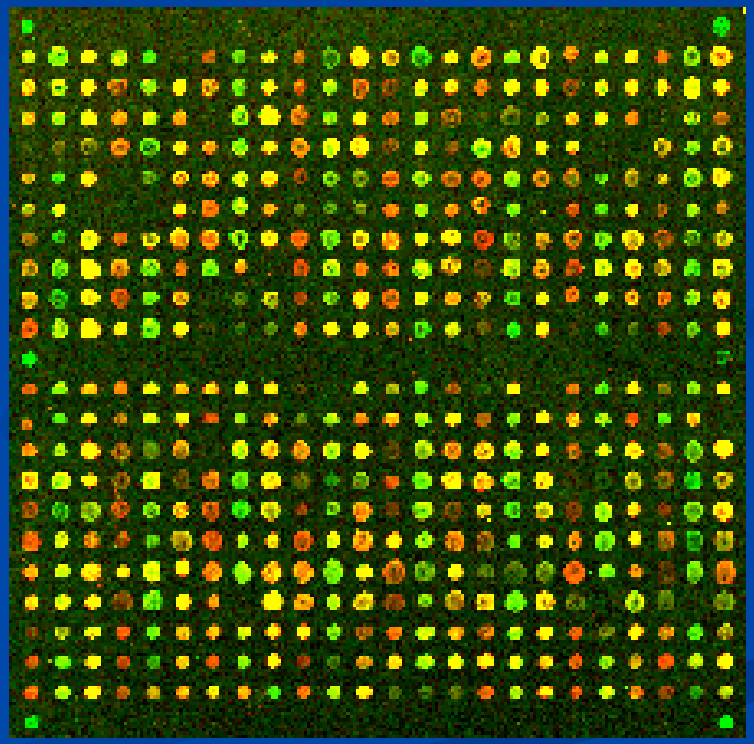
Genomics

- Genomic databases
- Microarrays
- Additional Screenings
- Antibody production



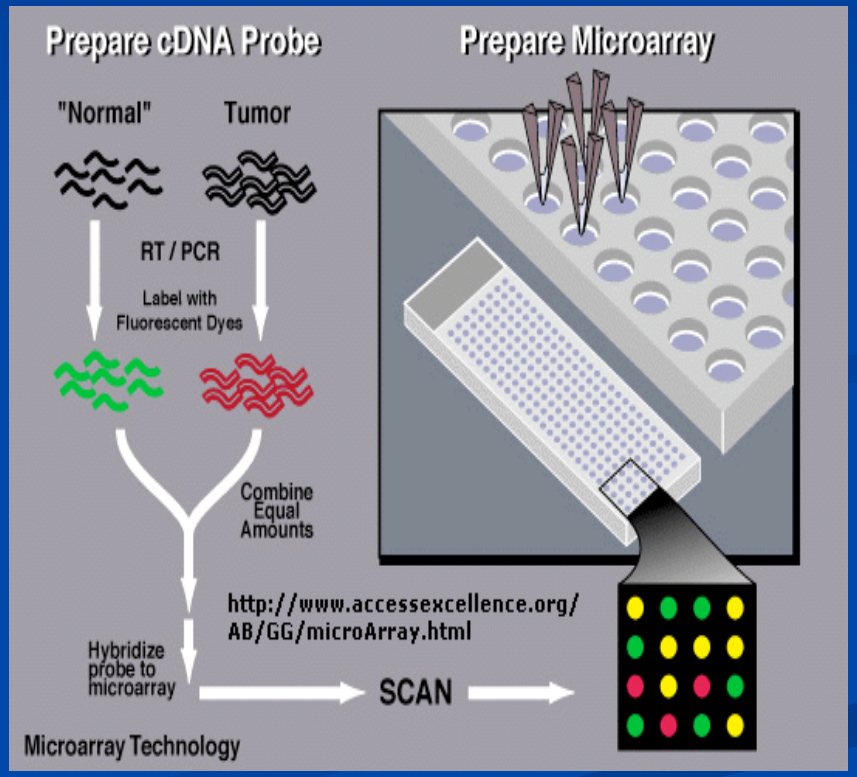
Genomics

- Identify surface receptors associated with major cancers
- Search genome databases for genes regulating receptors



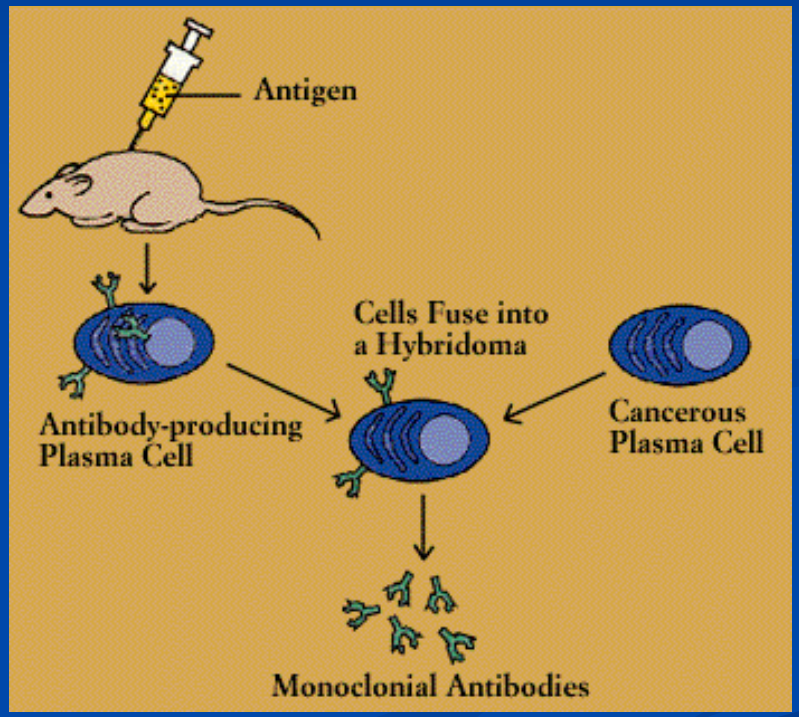
Genomics

- Compare gene sequences to that of living cancer cells
- Use microarrays to find genes active in cancer but not in normal cells
- Identify target receptor proteins



Genomics

- Inject mouse with protein
- Extract antibodies
- Test against cancer cells
- Continue drug development process



Outlook

- Transplant rejection, Cancer, Autoimmune diseases, infectious diseases
- Creation of libraries with antibodies against different antigens

Monoclonal Antibodies