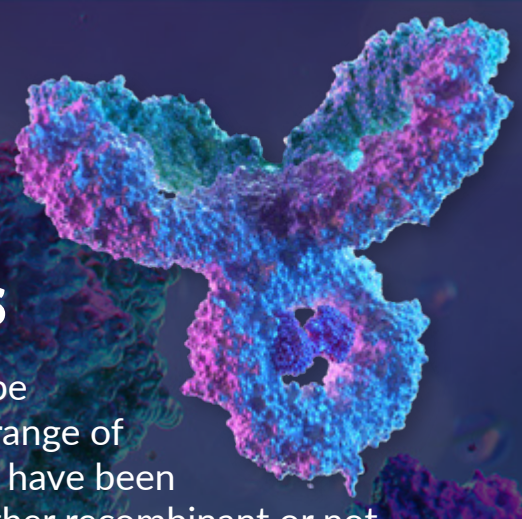
Recombinant Antibody Overview: Description, Production, and Applications



Monoclonal antibodies (mAbs) strongly bind to one epitope of a particular antigen, and are commonly used in a wide range of applications. For example, over 100 mAb-based therapies have been approved by the U.S. FDA.[1] Furthermore, mAbs can be either recombinant or not. Knowledge of how recombinant mAbs compare against conventional mAbs can help optimize workflows and speed discovery. This infographic presents such a comparison (description, production, similarities, and contrasts),[2–5] and modern applications.

Description

Conventional mAbs

- Produced by cloning a white blood cell
- At least some *in vivo* steps

Recombinant mAbs

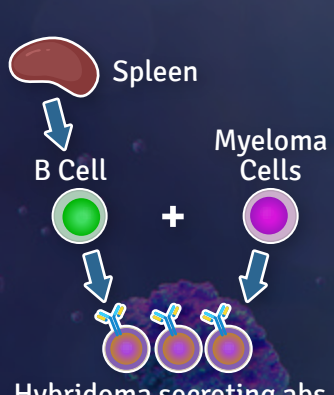
- Produced by introducing a gene into a cell line
- Solely *in vitro* steps

Production

Hybridoma technology

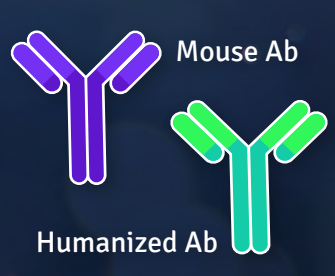
- Conventional mAb production
- Immunize an animal with a target antigen over the course of several weeks
- Extract mAb-producing B cells, and fuse with myeloma cells by centrifugation or electrofusion
- Screen resulting hybridoma cells for mAb production by using an animal or a cell culture

Mice immunized with antigen



B cells harvested and fused with myeloma cells

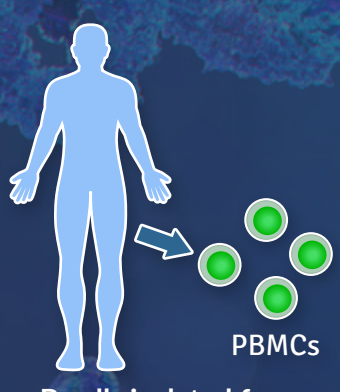
Hybridoma clones selected and screened



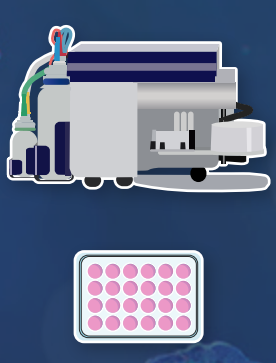
Chimeric/Humanized versions developed

Single B cell technology

- Conventional or recombinant mAb production
- Isolates and clones individual B cells for producing mAbs with retained post-translational modifications
- Retains variable heavy–light chain pairing for homogenizing the mAb binding site



B cells isolated from bone marrow/blood



Fluorescence-single antigen specific B cells sorted

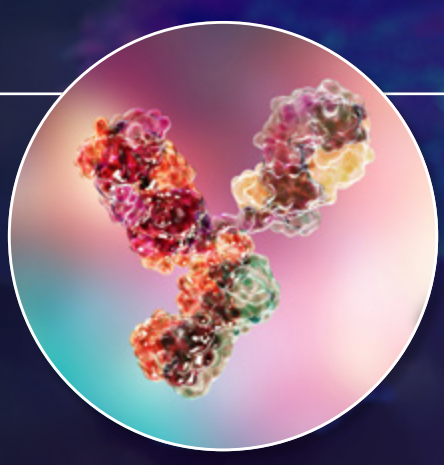
V_H & V_L segments cloned from monoclonals

Expression in cells, validation & production

Display technology

- Recombinant mAb production
- Includes phage, yeast, and other display technologies
- Mutations induced by DNA shuffling or PCR, and subsequent mAb production by cell culture
- Mammalian cells necessary to generate full-length mAbs with complex post-translational modifications

Similarities



- Highly specific compared with polyclonal antibodies
- Commonly administered therapeutically by intravenous infusion or injection
- Can be modified post-production:
  - Radiolabeled for radioimmunotherapy, such as to yttrium-90
  - Drug–antibody conjugate, such as to a chemotherapy agent
  - Antibody–antibody conjugate: bispecific mAb
- Expensive, averaging at least 6× the cost of a polyclonal antibody;[6] but production cost can perhaps be lowered by replacing use of protein A with polyethylene glycol precipitation[7]

Contrasts

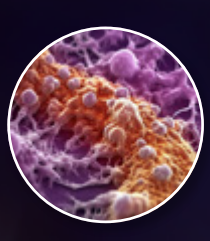
Conventional mAbs

- Use host animals
- Limited scalability
- Slower production: 6–9 mo
- More cell-line drift: inferior reproducibility
- Work only for immunogenic targets

Recombinant mAbs

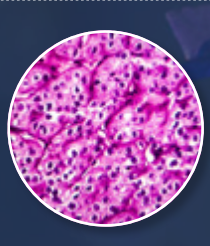
- Do not use host animals
- Highly scalable
- Faster production: 6–8 wk
- Less cell-line drift: superior reproducibility (but as with other mAbs, a comprehensive check for purity is necessary[8])
- Can be engineered against non-immunogenic targets

Some Applications of Recombinant mAbs



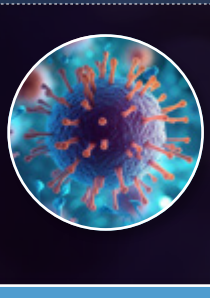
Translational research: Rheumatoid arthritis[9]

- **WHAT:** Evaluated the mechanism of action of pathogenic autoantibodies
- **FINDINGS:** One recombinant mAb eliminated arthritis in a mouse model within three days by disrupting neutrophil recruitment



Diagnostics: Kidney and thyroid cancer[10]

- **WHAT:** Developed a diagnostic tool for cadherin-16
- **FINDINGS:** Cadherin-16 positivity depended on the cancer: e.g., 100% for nephrogenic adenomas and 98% for oncocytomas



Therapeutics: SARS-CoV-2[11]

- **WHAT:** Obtained variant-neutral mAbs from recovered patients
- **FINDINGS:** Two human antibodies exceed the potency of the mAb sotrovimab against viral variants of concern, sometimes by >60×

Recombinant mAbs are used for many analysis, diagnostic, and clinical applications. The safety and efficacy depend on the recombinant mAb construct and the application. Understanding the basic science of conventional and recombinant mAbs—encompassing the production, similarities, and contrast—is essential to optimizing their use.

References

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