PrecisionBio
Accelerating Antibody Discovery

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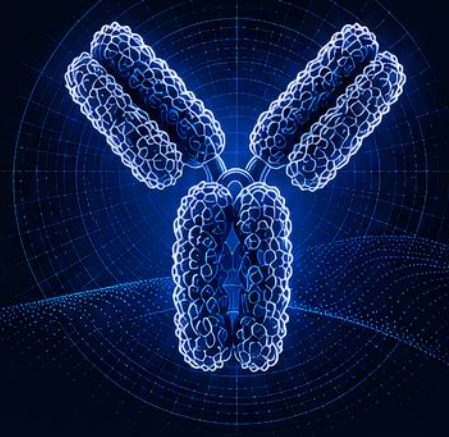
TECHNICAL NOTE

Computational Approaches to Antibody Humanization:

An Overview of *In Silico* Frameworks for CDR Grafting and Sequence Optimization



POPULAR HUMANIZATION STRATEGIES

1. CHIMERIC ANTIBODIES

Fuse non-human variable domains with human constant regions to reduce immunogenicity.

2. CDR GRAFTING (MOST WIDELY USED)

Graft non-human CDR loops onto human germline frameworks to retain affinity and stability.

3. TRANSGENIC MOUSE PLATFORMS

Mice engineered with human immunoglobulin loci produce fully human antibodies in vivo.

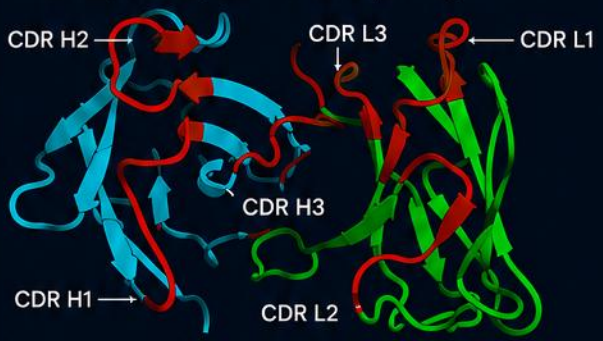
KEY STRUCTURAL CONSIDERATIONS IN CDR GRAFTING

CANONICAL STRUCTURAL RESIDUES (CSRs)
Stabilize CDR conformation. Mutating CSRs can reduce stability and affinity.

VERNIER ZONE RESIDUES
Modulate CDR loop geometry and antigen binding. Must be evaluated carefully.

CDR STEM RESIDUES
Located next to CDR loops. Their compatibility strongly influences graft success.

Two Fab regions of an antibody. The CDRs of the heavy chain and light chains are CDR H1, CDR H2, CDR H3 and CDR L1, CDR L2, and CDR L3 respectively.



RANKING HUMAN FRAMEWORKS

SEQUENCE SIMILARITY
Heavy and light chain sequence similarity.

STRUCTURAL FITNESS
Evaluate CDR stem residue compatibility.

GEOMETRY SCORES
RMSD-based scores for loop attachment points.

HUMAN GERMLINE FRAMEWORK LIBRARY (PDB / GERMLINE DATABASES)

In Silico Scoring & Ranking

HIGHER SCORE (LESS COMPATIBLE) ★★★

★★★★ LOWER SCORE (BETTER COMPATIBLE)

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Smarter Design. Better Therapeutics. Faster Impact.

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