

ENGINEERING OF RARE, NATURALLY OCCURRING NON-DEVELOPABLE ANTIBODIES INTO POWERFUL THERAPEUTICS



THE NEED

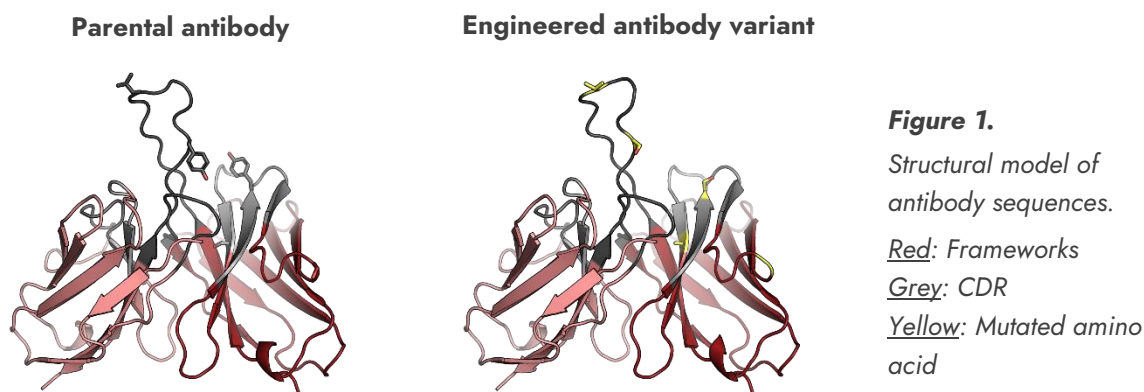
Improving developability of rare antibodies

YUMAB's proprietary naïve and fully human antibody library contains the complete human antibody repertoire without germline or CDR restrictions and spans $>10^{11}$ sequences. This includes rare antibodies with unusual structures and ultra-long CDRs. Such antibodies have the potential to bind to difficult-to-access epitopes (e.g., GPCRs, ion channels), and thus offer a unique mode of action. But as these are considered non-developable, they are often excluded from rationally designed antibody libraries or neglected in developability-driven AI selections.

THE SOLUTION

Boosting developability by tailored antibody engineering

Taking advantage of our engineering expertise, we preserved the unique structure and binding mechanism of one of YUMAB's human, ultra-long CDR3 antibodies by introducing only five amino acid exchanges on average (Figure 1).



These marginal modifications were sufficient to boost the developability characteristics significantly, making them even comparable to other, approved therapeutic antibodies (Figure 2).

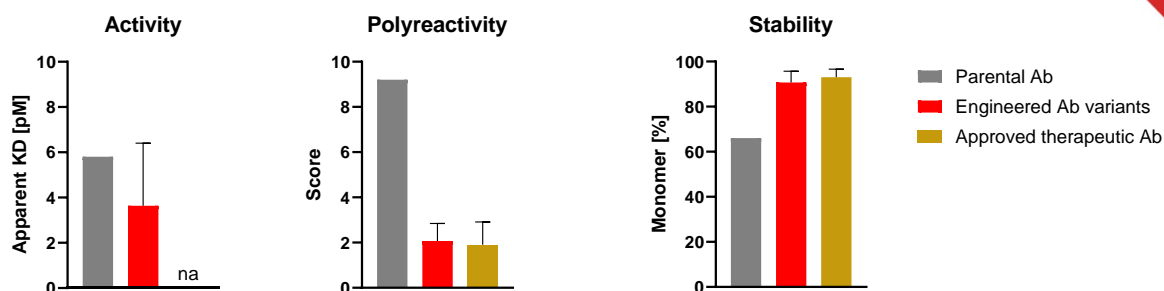


Figure 2.

The engineered antibody variants exhibit an identical activity as the parental antibody. But their developability features, such as polyreactivity and stability are significantly improved, comparable to other, approved therapeutic antibodies.

THE IMPACT

Transforming non-ideal antibodies into therapeutic leads

Focusing too early on developability features can restrict antibody panels, limit epitope coverage, and unnecessarily reduce functionality. However, engineering provides a straightforward solution for transforming non-ideal antibodies into therapeutic lead candidates. Our tailored approach achieves the desired developability characteristics without compromising on potential efficiency.

Contact us to learn more about our non-biased antibody library, our discovery or engineering services.

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