fusionantibodies

A novel approach to Affinity Maturation

Proving the results with anti-Cathepsin S mAb

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Welcome to Fusion Antibodies

- Fusion Antibodies offers services supporting all aspects of early therapeutic antibody development from discovery to clinical supply
- > 20 years experience engineering mAbs
- Clinically validated platforms (up to Phase II)
- Rational Affinity Maturation Platform (RAMP™) developed through successful experience with humanization (CDRx™) platform

A Novel Approach to Affinity Maturation

- Natural approach to library design

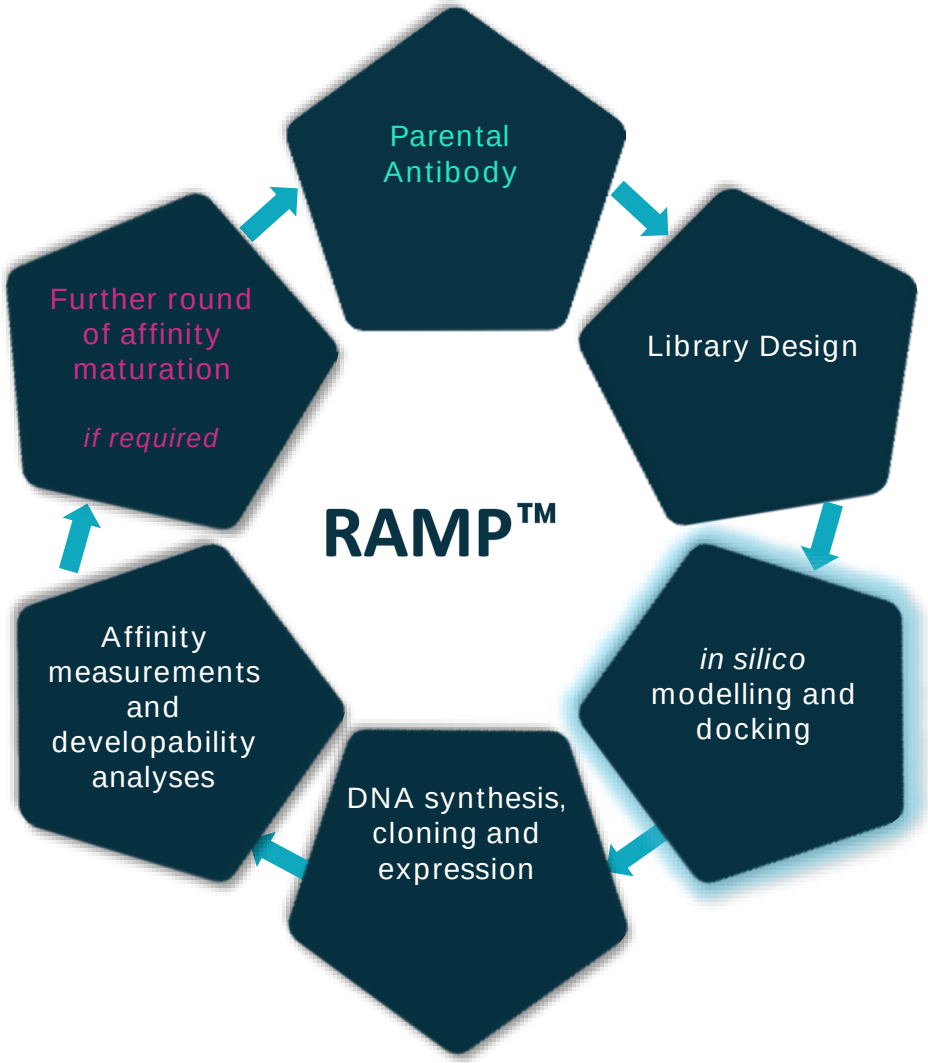
Naturally occurring mutations are introduced in combination in both CDRs and frameworks and sequence liabilities are not allowed.

- *In Silico* selection

In silico modelling and docking for selection for improved affinity and stability.

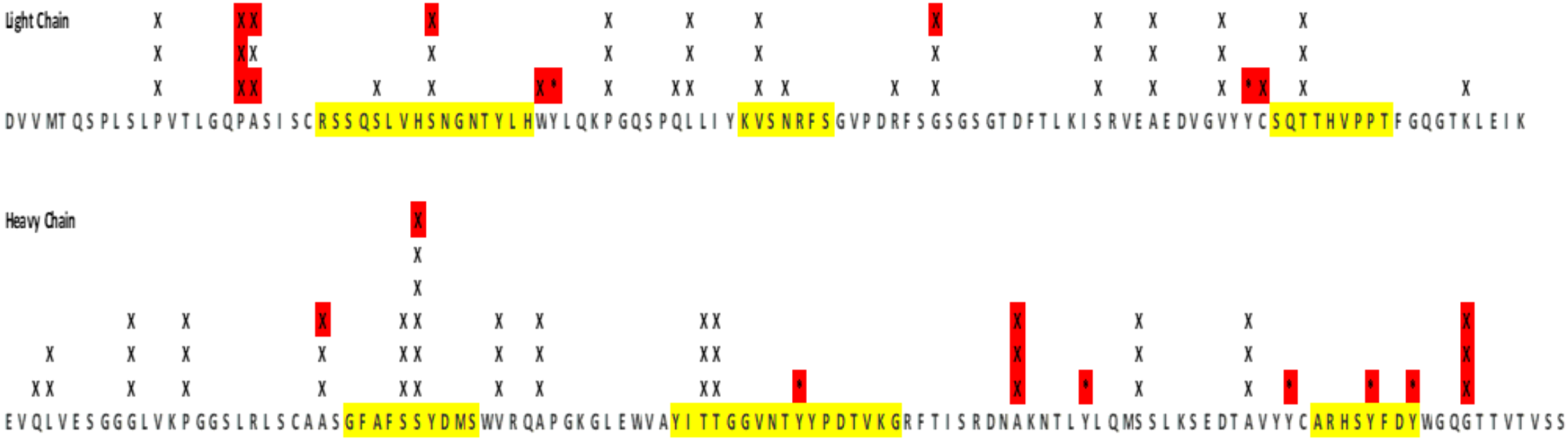
- Micro Library Expression

Expression of micro library of variants (<100), in IgG format in CHO. Binding kinetics and biophysical attributes of all variants are characterized *in vitro*.



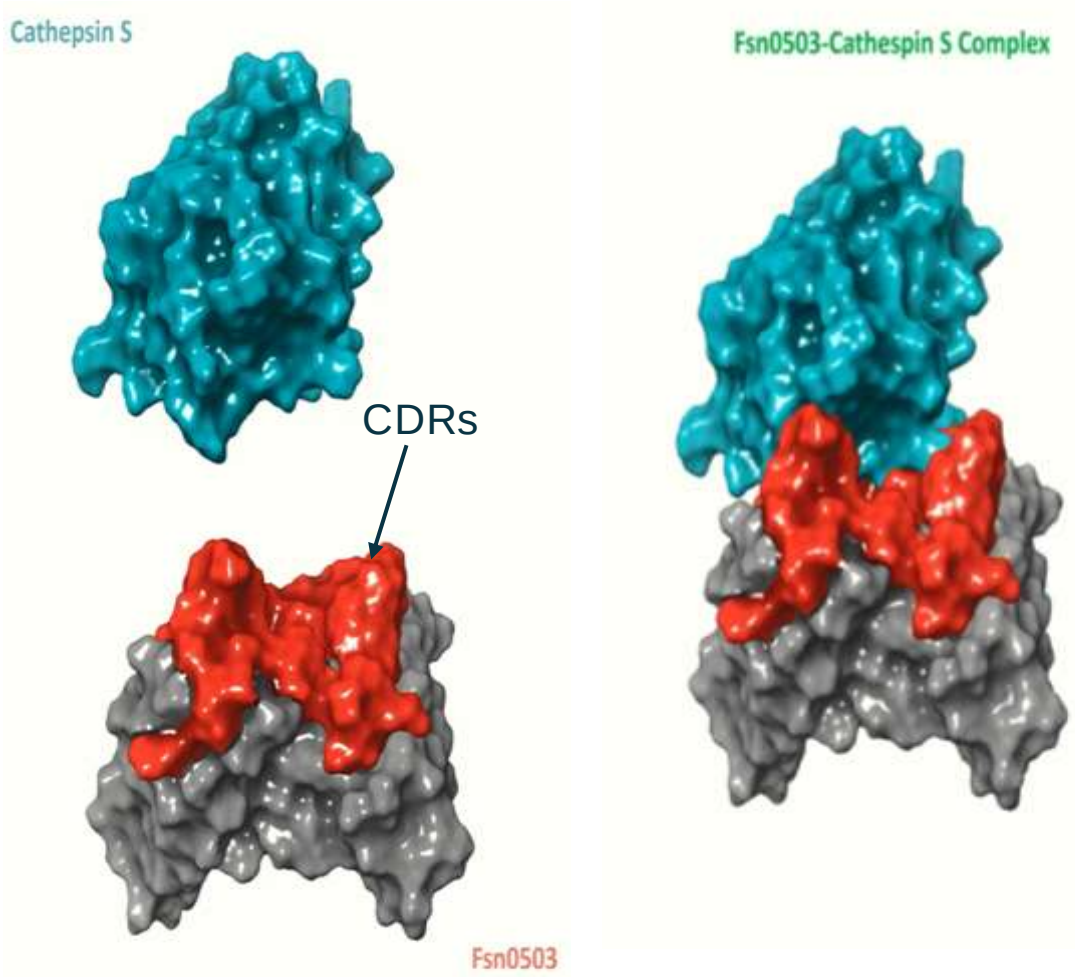
Anti-Cathepsin S mAb: Library Design

- Variable domain sequences analysed for motifs susceptible to mutation
- Corresponding amino acids plotted above the parental sequence
- Undesirable amino acids or STOP codons highlighted in red and not incorporated into library
- Observed that CDR-H3 had no functional mutations



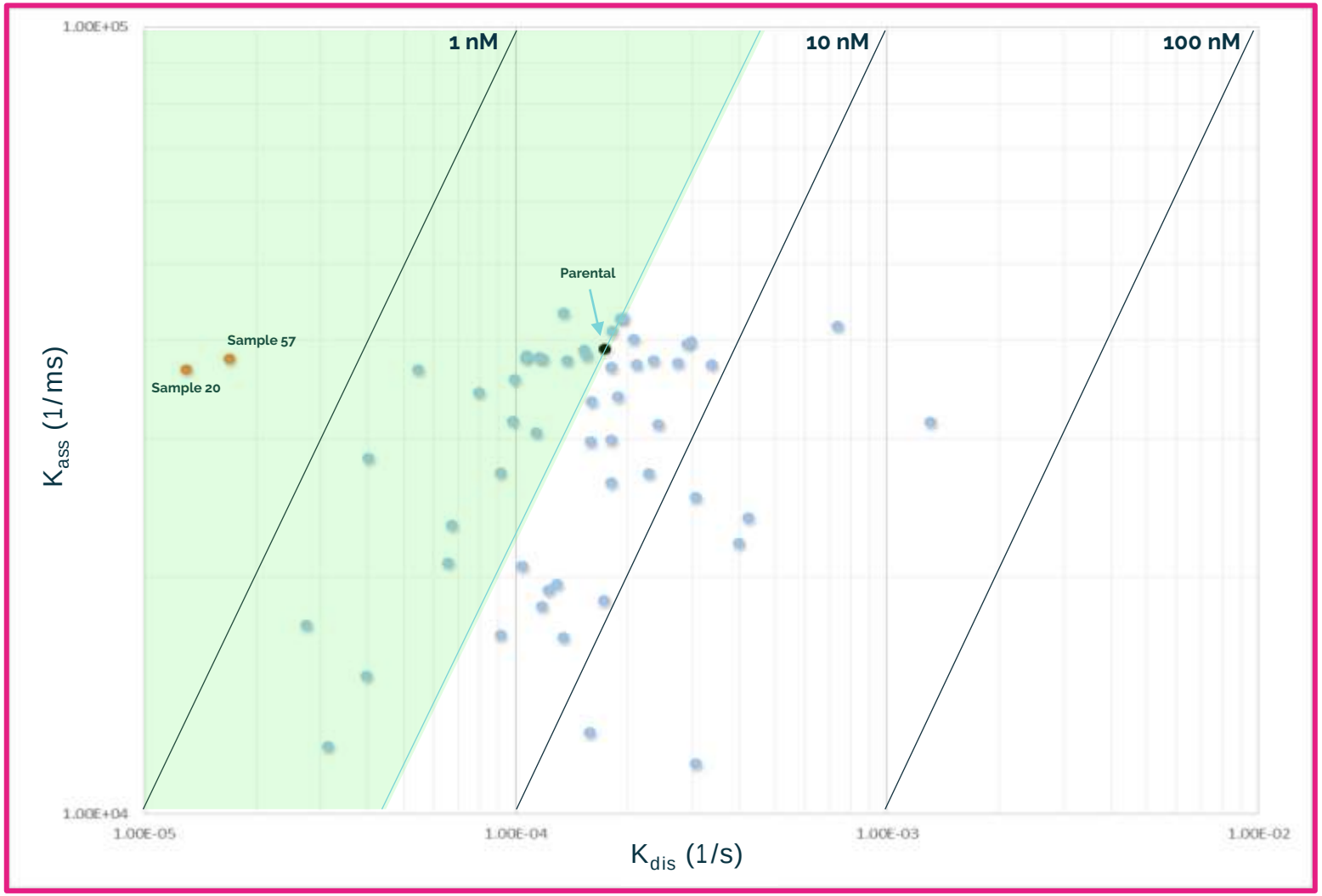
Anti-Cathepsin S mAb: Rapid *in silico* Selection

- Parental mAb variable domains docked to target Cathepsin S - mutations incrementally introduced and changes to affinity and stability predicted
- Only variants with predicted improvements in both affinity and stability were selected
- More mutations were made within the framework regions than the CDRs



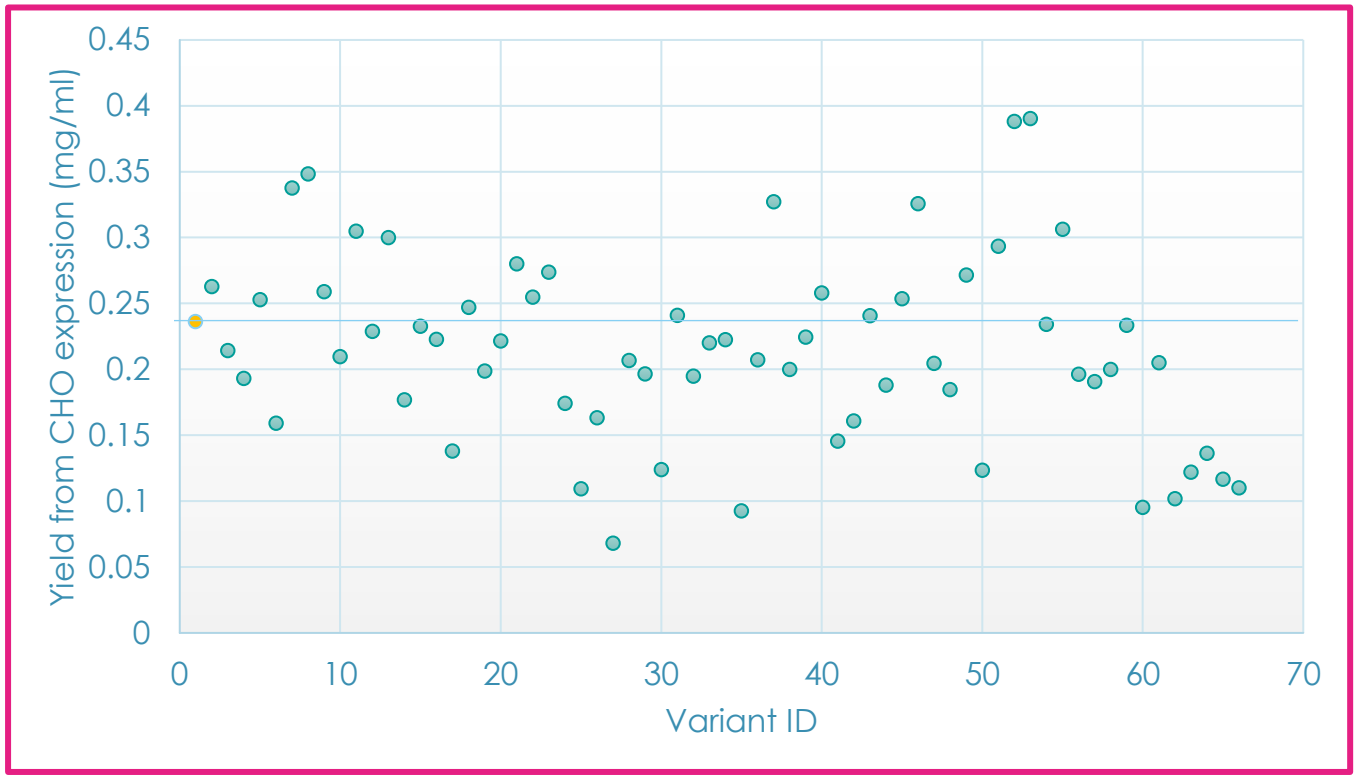
Anti-Cathepsin S mAb: Affinity Analysis

- Binding to recombinant Cathepsin S was measured by BLI (Octet)
- Approx. 40% of variants demonstrated improved affinity
- Two variants showed >10-fold increase in affinity with one round of RAMP™
- All variants expressed maintained good developability attributes



Anti-Cathepsin S mAb: Expression Analysis

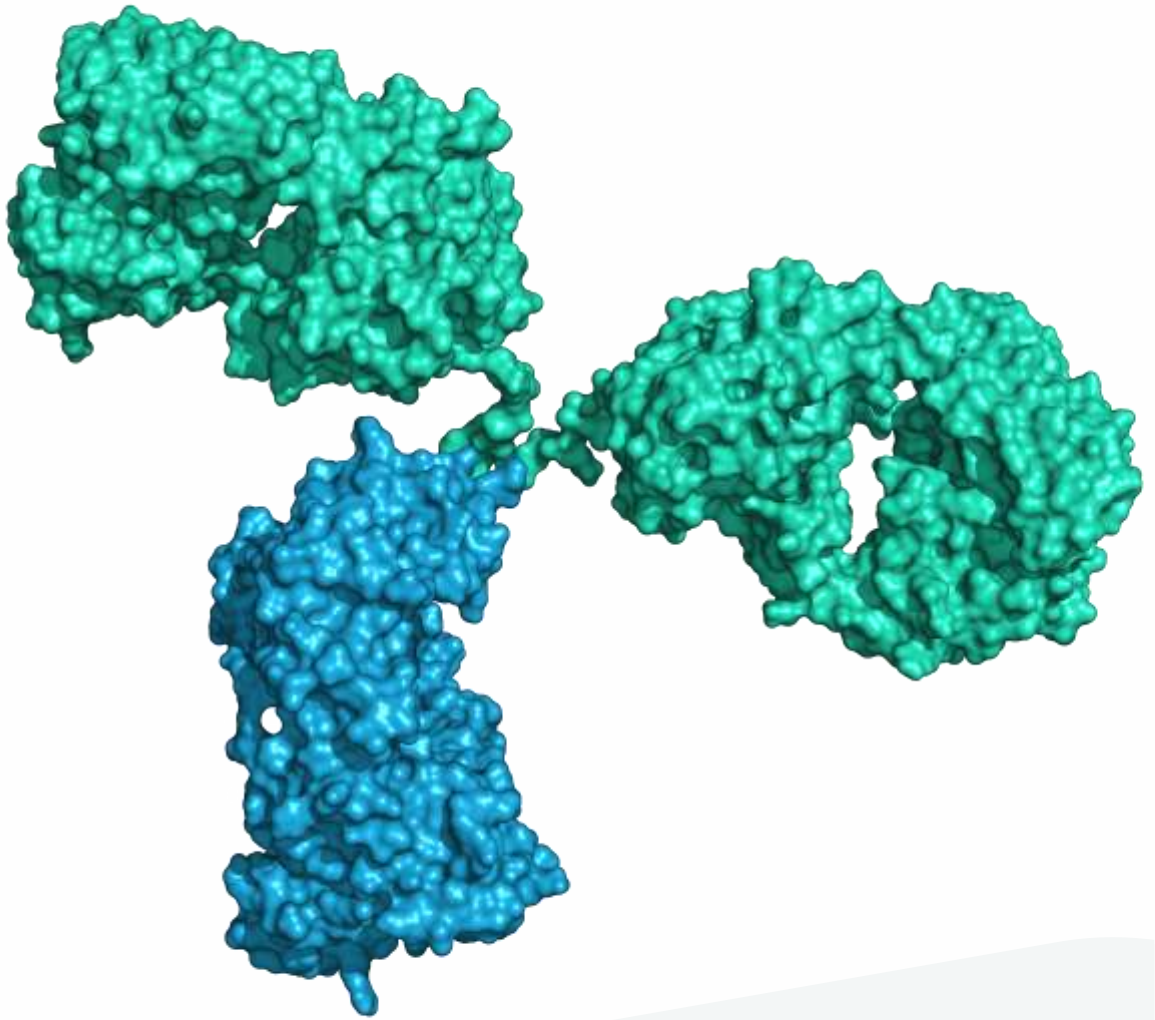
- Micro-library (66 variants) selected for small-scale expression in CHO cells
- Robust yields for all variants (an average yield of 214.8mg/L observed)
- High expression supports developability potential



A final word....

RAMP™ enables drug discovery scientists to not only increase the affinity for their molecule, but can also improve the developability profile.

Our library design approach explores the natural hypermutation space, introducing diversity in both the frameworks and the CDRs.



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