A comprehensive developability panel for accelerating antibody development into the clinic with a selective and highly predictive set of assays

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ADIMAB

Adimab's advancements in developability lead to clinical success

140+ Pharma/Biotech Partners

650+ Therapeutic Programs

91 Clinical Advancements

6 Approved Products

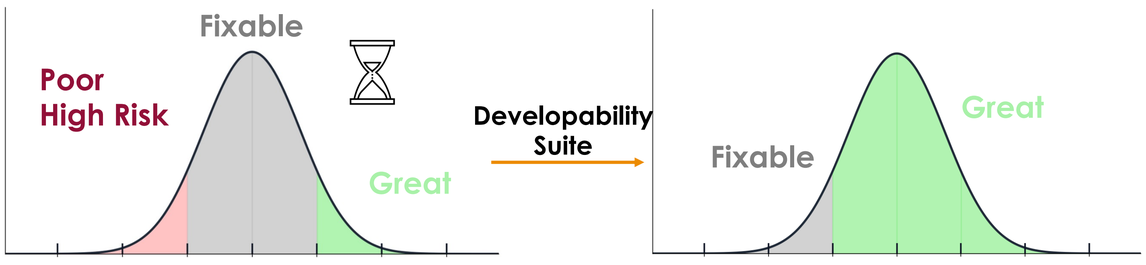
PNAS 2017
Biophysical properties of the clinical-stage antibody landscape.

mAbs 2019
Deamidation and isomerization liability analysis of 131 clinical-stage antibodies.

mAbs 2024
Assessment and incorporation of in vitro correlates to pharmacokinetic outcomes in antibody developability workflows.

Early de-risking reduces cost and accelerates development

A robust developability suite embedded in early screening increases the chances of rapidly progressing a successful molecule



Building a successful workflow that seamlessly incorporates developability during selection

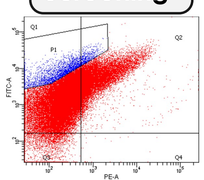
Library Design

Optimized library to minimize **biophysical** and **chemical liabilities**

Yeast strain engineering

Yeast **expression** filters out poor expressors

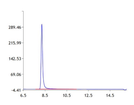
PSR Screening[2]



Removes highest **Polyreactive** binders

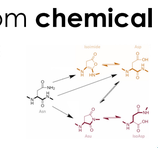
Experimental & ML HIC screening

Eliminate high **hydrophobicity** clones



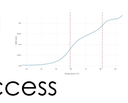
ML chemical liability de-risking

Optimize candidates away from **chemical liabilities**



Tm and Tagg analysis

Robust **thermal stability** for formulation success

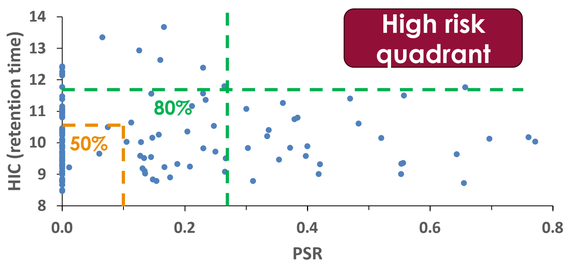


ML: machine learning, HIC: hydrophobic interaction chromatography, PSR: polyspecificity reagent, Tm/Tagg: melting temperature and aggregation temperature

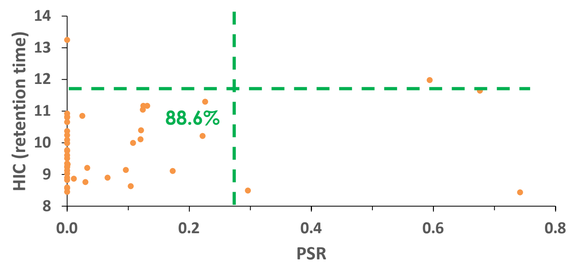
Polyreactivity and hydrophobicity in developability gating

- An evaluation of hydrophobic interaction chromatography (HIC) and polyspecificity reagent (PSR) across clinical phase antibodies suggest a 'high risk' zone.
- A combination of these two assays provides a powerful predictor of clinical risk

External Clinical Phase Molecules



Clinical Phase Molecules from Adimab



Data generated from 137 external Clinical Phase Ab[1]

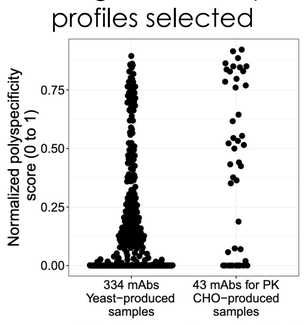
Adimab's developability strategy biases final candidates towards optimal profile region

Select developability attributes correlate to clearance

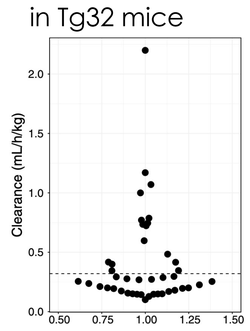
Challenge: There are limited recourses to mitigate rapid clearance. Therefore, assays that can predict risk early are of **high value**

- 43 IgGs with diverse biophysical properties assessed for clearance.
- Strong correlation between **clearance** and **PSR, BVP, and FcRn column binding[3]**

Antibodies with a broad range of developability profiles selected



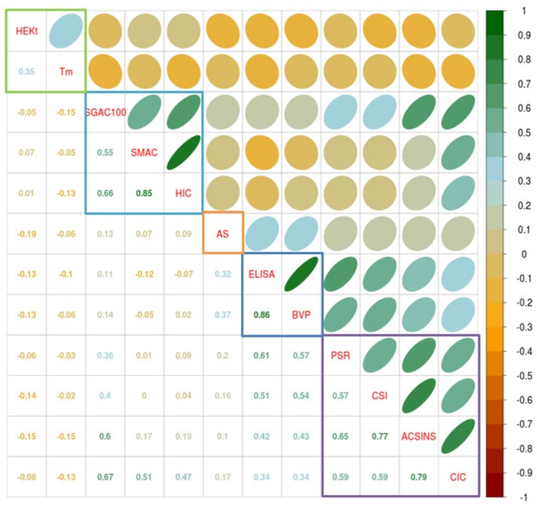
Range of antibody clearance measured in Tg32 mice



Assay	Category of measure	Rank correlation to CL: Coefficient, ρ
cIEF	General Developability/ Manufacturability	0.26
CS-SINS		−0.01
Fab Tm		−0.06
HIC		0.39
SEC		0.11
Fab pI		0.23
AC-SINS	Self-Association/ Interaction	0.55
CIC Column		0.59
FcRn Cellular	FcRn Binding	0.56
FcRn Column		0.63
BVP Binding	Non-specificity/Charge-based Interactions	0.67
Heparin Column		0.3
PSR		0.69

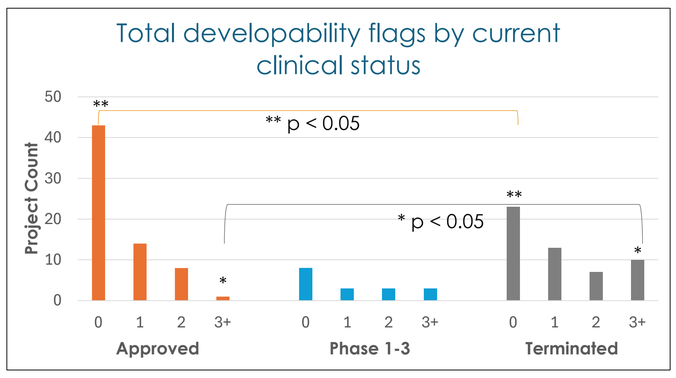
Biophysical properties of the clinical-stage landscape

An in-house analysis of 137 antibodies enabled the determination of developability ranges across 5 clusters of biophysical properties[1].



Legend: HEKt (expression), Tm (melting temp), SGAC (salt-gradient affinity-capture), SMAC (standup monolayer absorption chromatography), HIC (hydrophobic interaction chromatography), AS (accelerated stability), BVP (baculovirus particle), PSR (polyspecificity reagent), CSI (clone self-interaction) AC-SINS(affinity-capture self-interaction nanoparticle spectroscopy), CIC (cross-interaction chromatography).

Total developability flags by current clinical status



A strong statistical correlation is evident in the number of developability flags between the approved and terminated projects. Although project termination can have many causes, **developability is a critical factor in project success**.

Chemical Liability Prediction

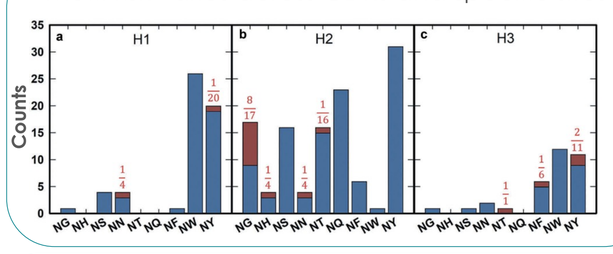
Challenge: Analysis of chemical liabilities is time and material intensive

The Adimab Advantage

Database: > 700 antibodies with 11,000 site specific accelerated stress data points (deamidation, isomerization, oxidation)[4]

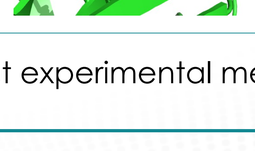
Combine site-specific sequence motifs with structural model information

Motif risk varies across CDRs and specific sites

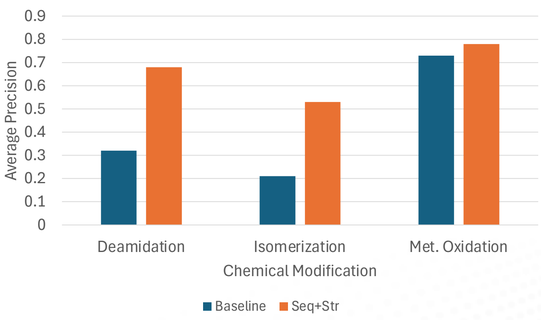


Motif in broader sequence and structure context

QDV**NT**AVA +



Sequence and Structure Improve Prediction Score



Result: Low throughput experimental method replaced with a **rapid ML approach**

References

1. Jain T et al. Biophysical properties of the clinical-stage antibody landscape. PNAS 2017; 114(5):944-949
2. Xu Y et al. Addressing polyspecificity of antibodies selected from an in vitro yeast presentation system: a FACS-based, high-throughput selection and analytical tool. Protein Eng. Des. Sel. 2013; 26(10):663-70
3. Jain T et al. Assessment and incorporation of in vitro correlates to pharmacokinetic outcomes in antibody developability workflows. mAbs 2024; 16(1):2384104
4. Lu X et al. Deamidation and isomerization liability analysis of 131 clinical-stage antibodies. mAbs 2019; 11(1):45-57

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