3DM Antibodies

Antibody analysis

- sequence & structure
- literature
- patents

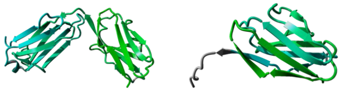
inhouse Ab annotations

bio-prodict
protein predictions

Antibody 3DM systems

3DM systems for different Ab-regions to facilitate specific use cases

Variable domain / Fab



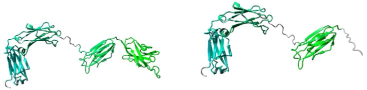
Antibodies, heavy chain Fab

137k sequences, 19.3k mutations

Antibodies, light chain

78k sequences, 10k mutations

Intact heavy chain / C-region



Antibodies, heavy chain

11.5k sequences, 6.9k mutations

CDR-specific alignments

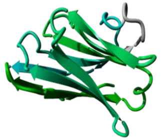
Antibodies heavy chain CDRs

112k sequences in 41 alignments

Antibodies light chain CDRs

55k sequences in 76 alignments

Nanobodies (VHH)



Nanobodies

3.9k sequences, 1.6k structures

3DM Antibodies and its toolset provide **insight in your antibody** sequence of interest

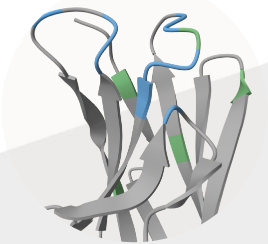
With 3DMs experience in protein engineering: ideal for literature analysis, **engineering**, and optimization of **target sequences**

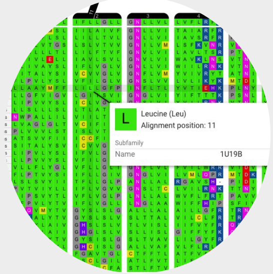
3DM systems

The power of 3DM

Structure-based MSA

1. Structural and sequence alignment to connect sequentially diverse subfamilies
2. Transfer data between all proteins in the alignment





L Leucine (Leu)
Alignment position: 11

Subfamily
Name 1U19B

Protein Data Transfer

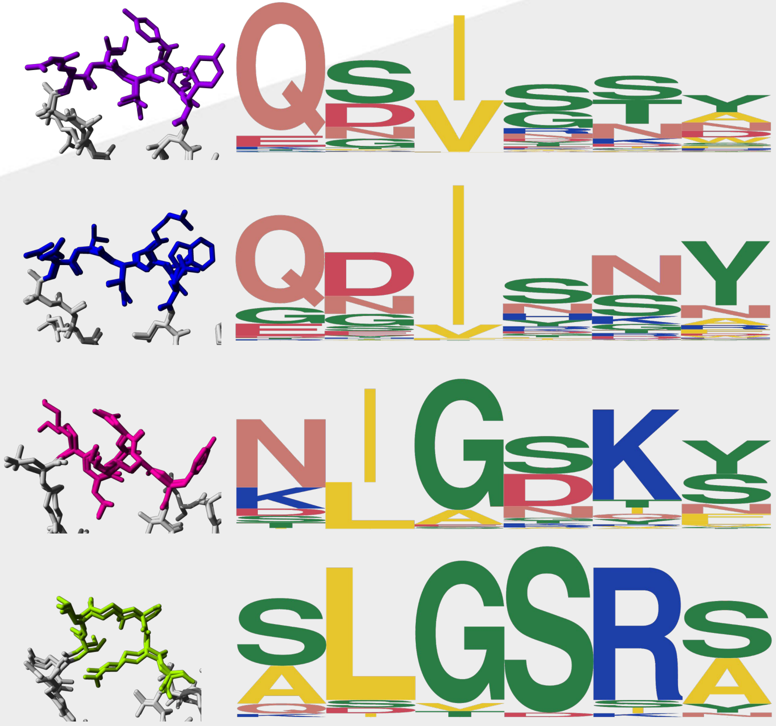
- Literature
- Patents
- Structural data
    - Protein contacts
    - Interdomain contact patterns
- Alignment data
    - Coevolution patterns (in CDRs)

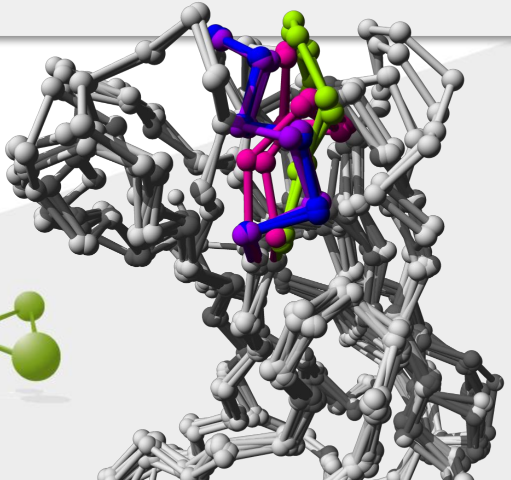
Powerful information system that **enhances antibody development**

CDR Conformation clusters

Enables sequence-based comparisons within and between structural conformations

- Structure-based clustering
  based on torsion angles and coordinates, specifically fine-tuned for each CDR-length
- Sequence-based identification of structural CDR conformation class
- over 300 CDR class-specific alignments in 3DM

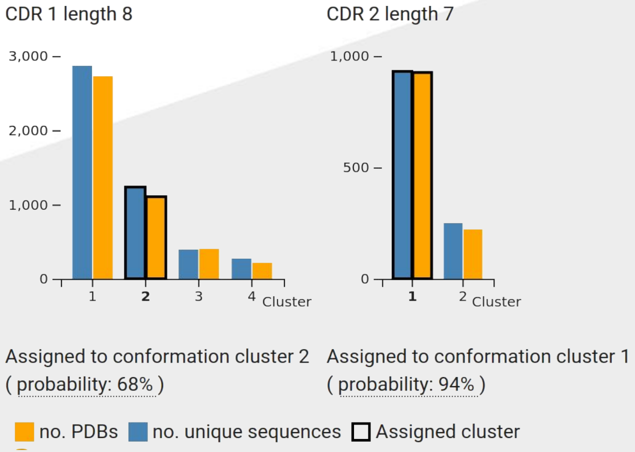




CDR classification in antibody analysis

annotate CDRs in your protein of interest

QVKLLEQSGGGVVQPGRSLRLSCAASGIFTLTYGIHWVRQAPGKGLEWVA 50
GLWYGTNKNYAESVKGRFTISRDNSKDTLYLMNSLRADDTAVYYCARALQ 100
GLIHEMDDWGKGTAVTVSSASTK



Assigned to conformation cluster 2 (probability: 68%)

Assigned to conformation cluster 1 (probability: 94%)

Visualize CDR location in sequence and structure

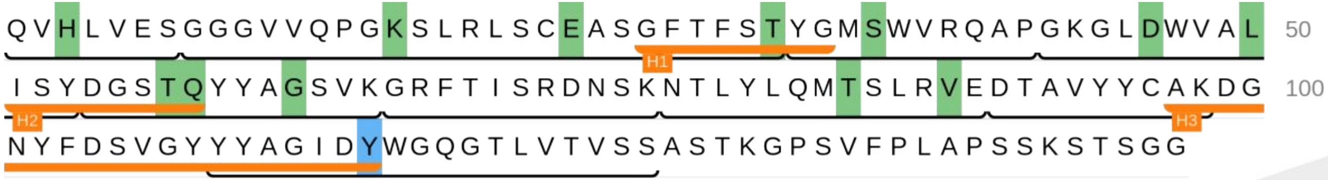
uses AlphaFold model when no PDB available

Assign CDRs to conformational cluster

Show distribution and statistics of the CDR clusters

with same CDR length as the assigned cluster

Germline annotation in antibody analysis



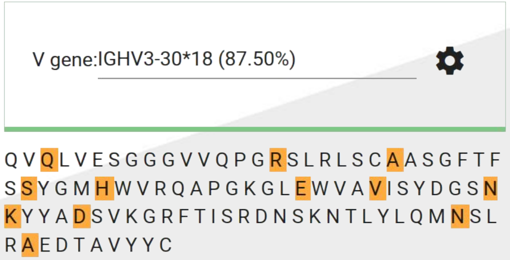
QVHLVESGGGVVQPGKSLRLSCEASGFTFSTYGMSWVRQAPGKGLDWVAL 50
ISYDGSTQYYAGSVKGRFTISRDNSKNTLYLQMTSLRVEDTAVYYCAKDG 100
NYFDSVGYYYYAGIDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGG

Identify the closest germline genes
supports IMGT germlines for 16 species

Visualize differences with protein of interest and germline hit

Investigate affinity maturation

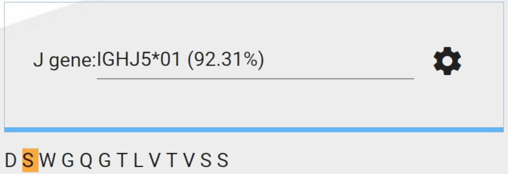
Humanness: compare residues with human germline (family) residue distribution



V gene:IGHV3-30*18 (87.50%)

QVQLVESGGGVVQPGRSLRLSCAASGFTF
SSYGMHWVRQAPGKGLEWVAVISYDGSN
KYYADSVKGRFTISRDNSKNTLYLQMNSL
RAEDTAVYYC

Gene segment	X92214_IGHV3-3018
Identity	88%
Similarity	89%
Hamming distance	12
Length	96
E-value	5e-62
Full gene segment sequence in IMGT	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC



J gene:IGHJ5*01 (92.31%)

DSWGQGTLVTVSS

Gene segment	J00256_IGHJ501
Identity	92%
Similarity	87%
Hamming distance	1
Length	13
E-value	0.00000753
Full gene segment sequence in IMGT	NWFDSWGQGTLVTVSS

3DM Antibody Developability

Developable Antibodies: Liability Insights and Large-scale Analysis

Use 3DM data to:

- Prioritize Ab Sequences
- De-risk developability issues

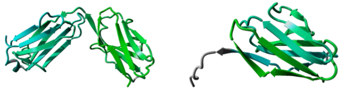
In-house antibody annotations: sequence insights based on alignment and structural features from 3DM

Applications:

- Aid candidate/lead selection by:
  - flagging sequence liabilities
  - insight in CDR and germline diversity
  - *add custom annotations*

in-house Ab sequences

3DM data
Fab targeted



3DM-based annotation modules

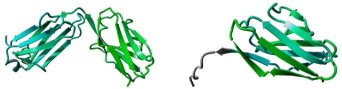
Derisked antibody sequences

Large scale Ab annotations

annotate your in-house sequences with 3DM Antibody Developability

in-house Ab sequences

3DM data
Fab targeted



Antibodies, heavy chain
137k sequences, 19.3k mutations

Antibodies, light chain
78k sequences, 10k mutations

- **CDR cluster assignment**
- **Closest germline annotation**
- **CDR covariance violations**
- **Post-translational modifications**
- **Conservation and unusual residues** New!
- **Framework accessibility and ligand contacts** New!

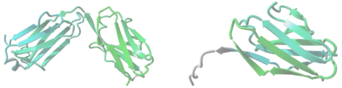
Correlate with in-house features

Large scale Ab annotations

example: CDR covariance violations

in-house Ab sequences

3DM data
Fab targeted



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CDR cluster assignment

Closest germline annotation

CDR covariance violations

Post-translational modifications

Conservation and unusual residues — New!

Framework accessibility and ligand contacts — New!

Correlate with in-house features

Module: CDR covariance violations

CDR cluster

closest germline

covariance violations

alignment data

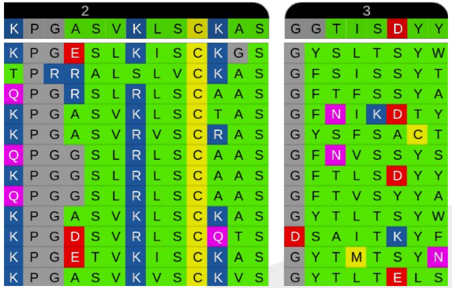
contacts

target residues

CDR

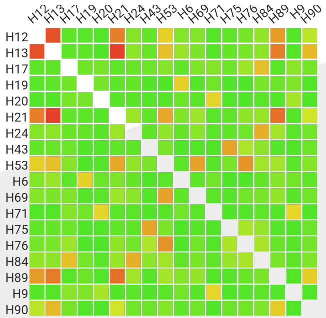
Antibodies heavy chain CDRs

Antibodies light chain CDRs

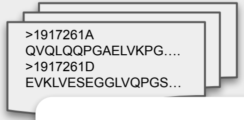


2												
K	P	G	A	S	V	K	L	S	C	K	A	S
K	P	G	E	S	L	K	I	S	C	K	G	S
T	P	R	R	A	L	S	L	V	C	K	A	S
Q	P	G	R	S	L	R	L	S	C	A	A	S
K	P	G	A	S	V	K	L	S	C	T	A	S
K	P	G	A	S	V	R	V	S	C	R	A	S
Q	P	G	G	S	L	R	L	S	C	A	A	S
K	P	G	G	S	L	R	L	S	C	A	A	S
Q	P	G	G	S	L	R	L	S	C	A	A	S
K	P	G	A	S	V	K	L	S	C	K	A	S
K	P	G	D	S	V	R	L	S	C	Q	T	S
K	P	G	E	T	V	K	I	S	C	K	A	S
K	P	G	A	S	V	K	V	S	C	K	V	S

3							
G	G	T	I	S	D	Y	Y
G	Y	S	L	T	S	Y	W
G	F	S	I	S	S	Y	T
G	F	T	F	S	S	Y	A
G	F	N	I	K	D	T	Y
G	Y	S	F	S	A	C	T
G	F	N	V	S	S	Y	S
G	F	T	L	S	D	Y	Y
G	F	T	V	S	Y	Y	A
G	Y	T	L	T	S	Y	W
D	S	A	I	T	K	Y	F
G	Y	T	M	T	S	Y	N
G	Y	T	L	T	E	L	S

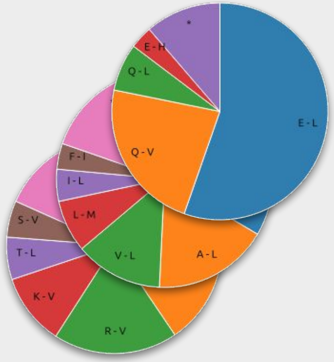


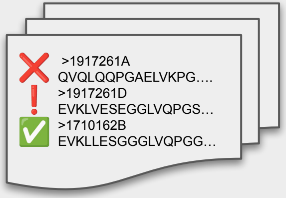
1. Extract 3DM positions from VH or VL CDR alignment that show strong co-evolution
2. Obtain residue distributions from alignment for these co-evolving pairs
3. Flag sequences that differ from most-occurring residue pairs on given positions



>1917261A
QVQLQQPGAELVKPG....
>1917261D
EVKLVESEGGLVQPGS...

in-house Ab sequences

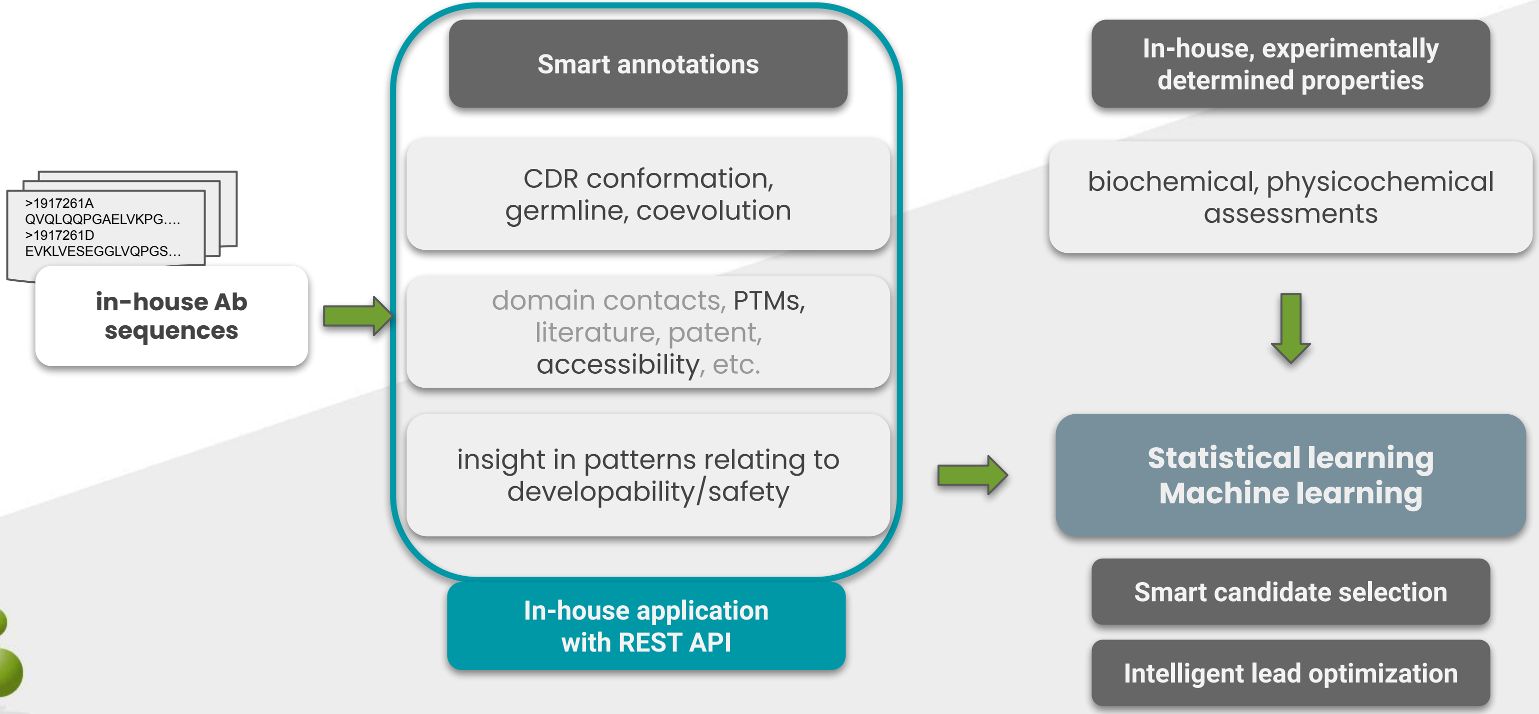




❌ >1917261A
QVQLQQPGAELVKPG....
❗ >1917261D
EVKLVESEGGLVQPGS...
✅ >1710162B
EVKLLESGGGLVQPGG...

DALILA: Large scale Ab annotations

on-premise deployment



```
>1917261A
QVQLQQPGAELVKPG….
>1917261D
EVKLVESEGGLVQPGS…
```

in-house Ab sequences

Smart annotations

CDR conformation, germline, coevolution

domain contacts, PTMs, literature, patent, accessibility, etc.

insight in patterns relating to developability/safety

In-house application with REST API

In-house, experimentally determined properties

biochemical, physicochemical assessments

Statistical learning
Machine learning

Smart candidate selection

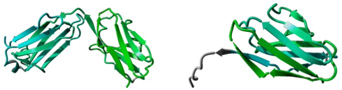
Intelligent lead optimization

Large scale Ab annotations

future capabilities

in-house Ab sequences

3DM data
Fab targeted



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CDR cluster assignment

Closest germline annotation

CDR covariance violations

Post-translational modifications

Conservation and unusual residues

Framework accessibility and ligand contacts

Correlate with in-house features

Patented sequences
IP & FTO

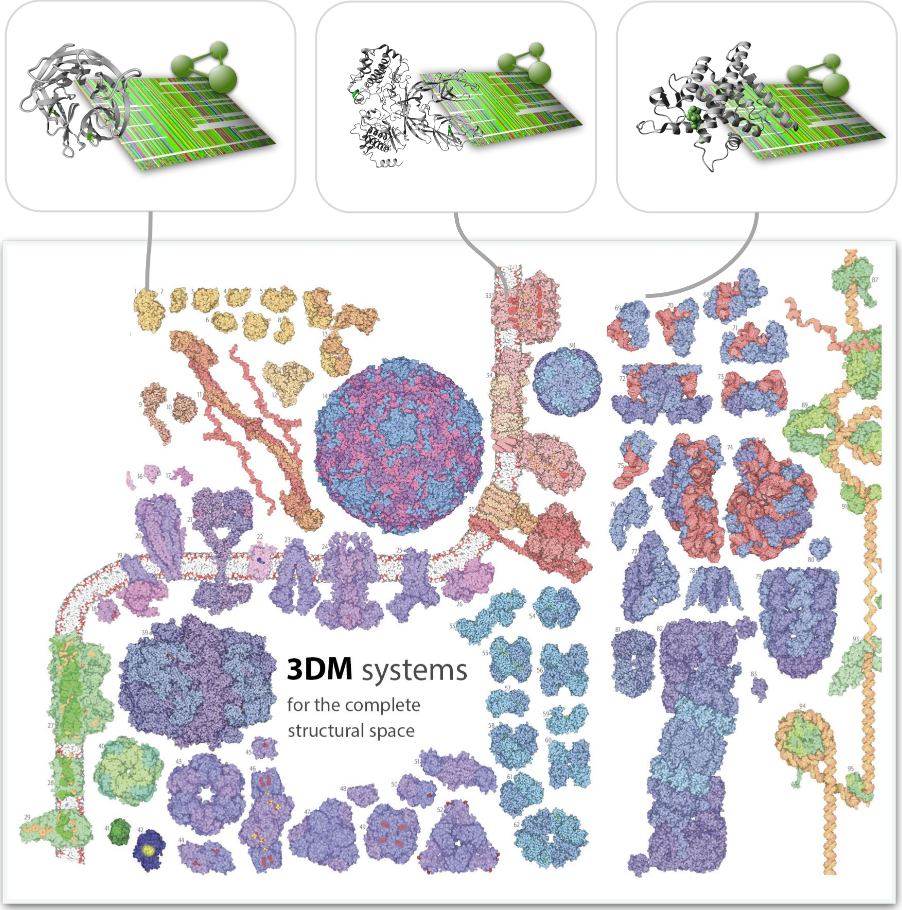
H3 analysis

Interdomain contacts

Humanness, humanization target residues

...
(custom annotations)

3DM for any target



With over 50,000 families available, 3DM covers the complete structural space, providing access to the full power of 3DM instantly.

50,000 3DM systems at the ready

Explore any protein target (antigen)

- Literature
- Conservation & variation
- protein-protein contacts

IP & FTO analysis

- Explore patent landscape
- Identify patents with similar sequences

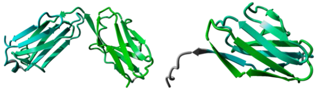
Epitope investigation

- Human variation
- Unique within Human?

What we offer

Existing Ab systems

Fab annotations
CDR clust, germline, etc.



Custom 3DM systems

private structures
multi-specific targets

Smart annotations

custom research and development

sequence insights,
no black box approach

focus on properties of interest

Custom development

catered to your needs

Optional annotations

related patented sequences

domain contacts

literature mutations

In-house deployment

keep data at your site

portable solution

integrate with existing pipelines

bio-prodict

protein predictions

amc Human Genetics
RWTH AACHEN UNIVERSITY
AJINOMOTO
ALMAC
ArcticZymes
acib
Aviagen
BASF
BAYER
ingenza
INVISTA
IPSEN
Johnson & Johnson
Johnson Matthey
KeyGene
LEAD PHARMA
LUND UNIVERSITY
B·R·A·I·N
Celgene
uniQure
CMBi
CHR HANSEN
Crucell
DSM
DTU Technical University of Denmark
MANCHESTER 1824 The University of Manchester
MERCK
METGEN
nbic
NOVARTIS
novo nordisk
novozymes
rijksuniversiteit groningen
DANISCO
Direvo
DUPONT
ew nutrition
evocatal
EVONIK
Firmenich
roal
Roche
sabic
SANDOZ
SANOFI PASTEUR
上海大学
StartLife
STRATOS
UNIVERSIDAD COMPLUTENSE MADRID
UNIVERSITEIT GENT
UNM
UFS UV
Universität Stuttgart
verdezyne
WAGENINGEN UR
YASARA
JÜLICH
Genmab
genomatica
gsk GlaxoSmithKline
TU Graz
HARVARD UNIVERSITY
Henkel
Human Genetics Nijmegen
iVENTION