A STREAMLINED DRUG DISCOVERY PLATFORM FOR THE PRODUCTION AND CHARACTERIZATION OF PROTEIN BIOLOGICS AND THEIR ANTIGENS

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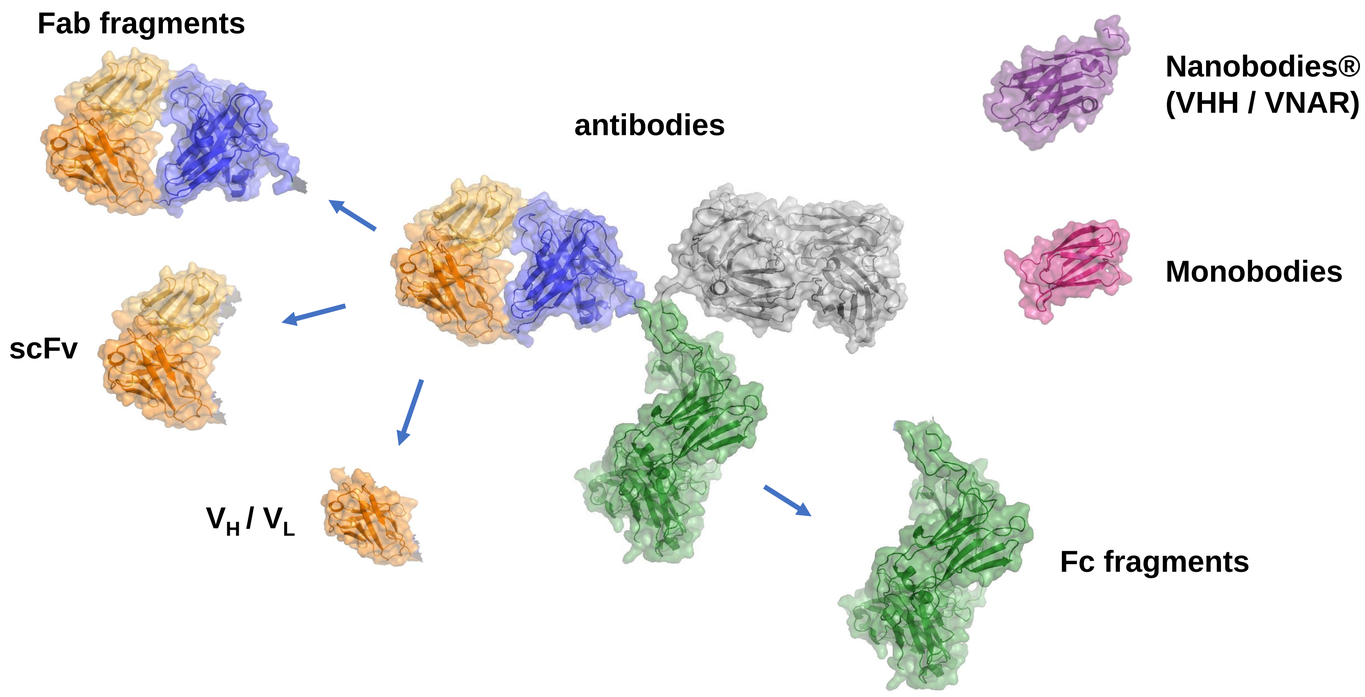
The rapid advancement of biologics has significantly impacted therapeutic approaches in modern medicine. To facilitate access to these therapeutics, we have developed a drug discovery platform designed for the efficient production and characterization of all classes of biologics and antigens.

This platform integrates key processes, beginning with the optimization of expression constructs. This is followed by customized high-throughput protein production, enabling swift progression to downstream applications. Biophysical characterization techniques are employed to assess affinity and kinetics, allowing for the identification of candidates with optimal therapeutic potential. Finally, X-ray crystallography and cryo-EM provide critical insights into the epitope-paratope interaction, informing further development. Our platform is tailored for maximal flexibility, offering entry and exit points at every step.

By combining these technologies and robust methodologies, our platform not only streamlines the drug discovery process but also enhances the characterization of biologics and antigens, paving the way for the development of novel therapeutic agents.



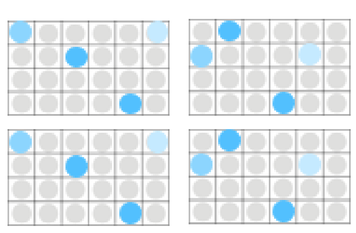
- **Turnaround times: Gene-to-protein: 3 weeks | Gene-to-assay: 4 weeks | Gene-to-structure: 5 weeks**
- **Consistent batch-to-batch quality achieved through cost-effective automation**
- **Streamlined processes through coordinated, one-stop services**

CONSTRUCT AND EXPRESSION SCOUTING

construct design

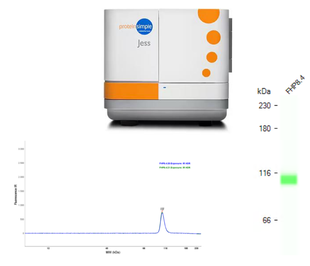
- Construct design based on published literature an *in silico* analysis
  → Prediction of secondary / tertiary structure and trans-membrane helices, disordered regions, etc.
- Individual domains vs. FL protein
- Screening of tag type and position
- Disease-relevant mutations
- Deletions and insertions
- Stabilizing mutations facilitating structural analysis
- Solubility tags for enhanced expression level

small-scale expression



- Full suite of expression hosts: *E. coli*, insect cells, mammalian cells
- High throughput by screening in 96-well format
- Proprietary vector system allows expression in *E. coli* and insect cells from same cDNA
- Comparison of vector systems and expression strategies
  → Time, temperature, etc.
- Optimization of expression of multi-subunit complexes
  → Expression of Single subunits, co-expression
- Assessment of expression level and solubility of constructs

test purification



- Parallelized purification by magnetic bead-based affinity capture
- Accurate expression level quantification by capillary electrophoresis
- Purity and yield assessment by SDS-PAGE

CUSTOMIZED HIGH-THROUGHPUT PROTEIN PURIFICATION

expression

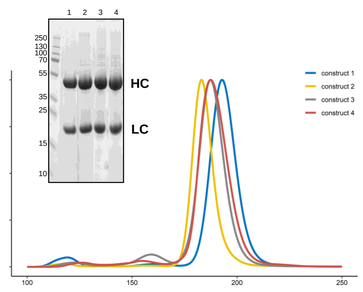
- Tailored high-throughput expression and purification of all protein classes
- Compatible with all common expression hosts:
  - *E. coli*
    → ^{15}N / ^{13}C labelling
  - Insect cells
    → Cell lines: Sf21 / Tni
  - Mammalian cells
    → Cell lines: HEK293F / CHO
    → Transient transfection, BacMam, stable cell lines
- Applicable to secreted proteins and monoclonal antibodies

applications

multi-upscale | multi-target | multi-parameter

purification

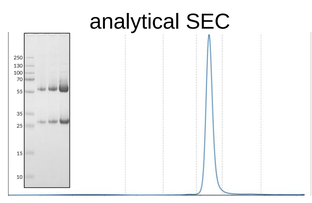
Parallelized ProteinA chromatography and preparative size exclusion



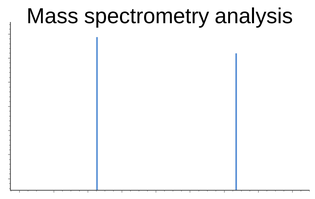
- Up to 24 parallelized purifications per week
- Tailored multi-step purification process
- Endotoxin-free setup
- Typical scale: up to100 mg

QC and formulation

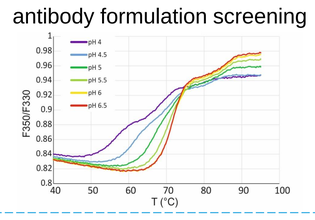
analytical SEC



Mass spectrometry analysis

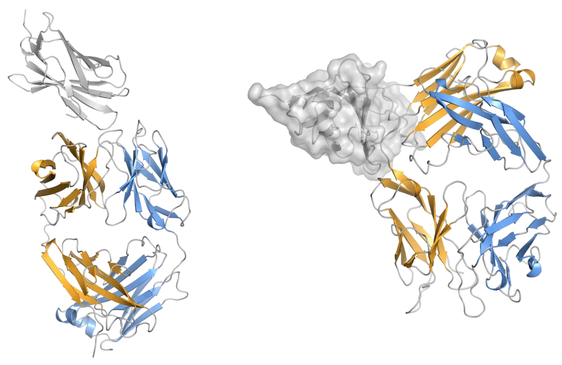


antibody formulation screening



PARATOPE AND EPITOPE MAPPING

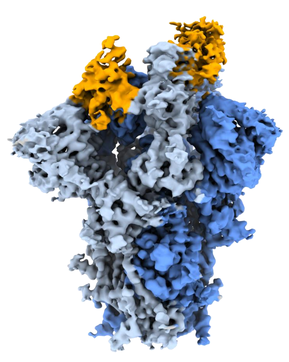
X-ray crystallography



Fab fragment with inhibitory receptor | Fab fragment in complex with VHH

- Structure determination of antibodies alone and in complex with antigen(s)
- Particularly suitable for smaller antibody formats (for example Fab fragments, VHH, scFv) and antigens
- High resolution structures provide detailed understanding of paratope and epitope-paratope interactions
- State-of-the-art infrastructure for crystallization screening, data collection and structure determination

cryo-EM



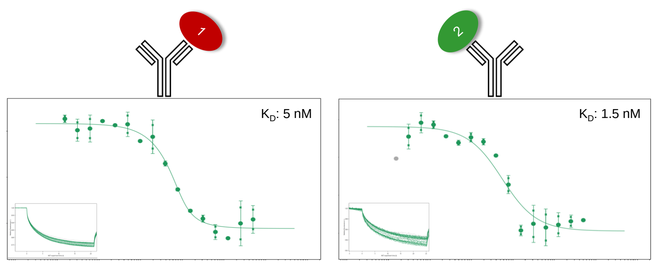
SARS-CoV-2 spike protein in complex with bispecific VHH

- Structure determination of antibodies in complex with antigens
- Suitable for challenging to crystallize antibody formats (for example IgGs) and antigens (for example membrane proteins)
- Medium resolution structures allow confirmation of epitope
- Reduced turnaround time enables epitope mapping
- State-of-the-art infrastructure for grid preparation, data collection and data processing

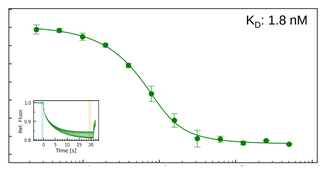
AFFINITY AND KINETICS

microscale thermophoresis

Interaction of bispecific antibody with antigen 1 and antigen 2



Binding of IL4 to IL4R alpha



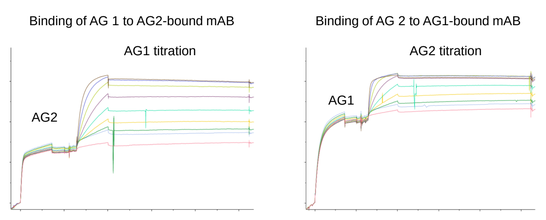
Established assays for interleukins

IL1	SPR
IL2	SPR
IL4 / IL4R	MST and SPR
IL7	SPR
IL13	MST and SPR
IL17A	MST and SPR
IL18	SPR
IL23R	MST and nanoDSF

- State-of equipment:
  - Biacore 8 K SPR systems
  - NanoTemper-certified MST and nanoDSF provider
- Label and label-free measurements
- Integrated platform from compound / fragment screening to hit validation
  - Up to 20000 compound measurements per day
  - Orthogonal techniques for hit validation

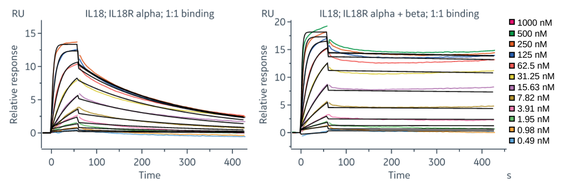
surface plasmon resonance

Binding of bispecific mAB to both antigens



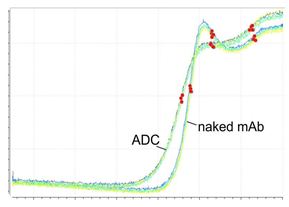
Determined parameters: k_a [1/s], k_d [1/d], k_D [mol/L], stoichiometry, Chi^2

Binding of IL18 to different IL18 receptor surfaces

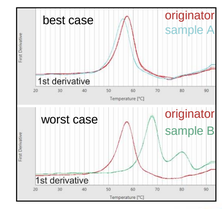


nanoDSF

Stability assessment of ADC



Biosimilar profiling



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