

Maximizing VHH lead generation for therapeutic breakthroughs

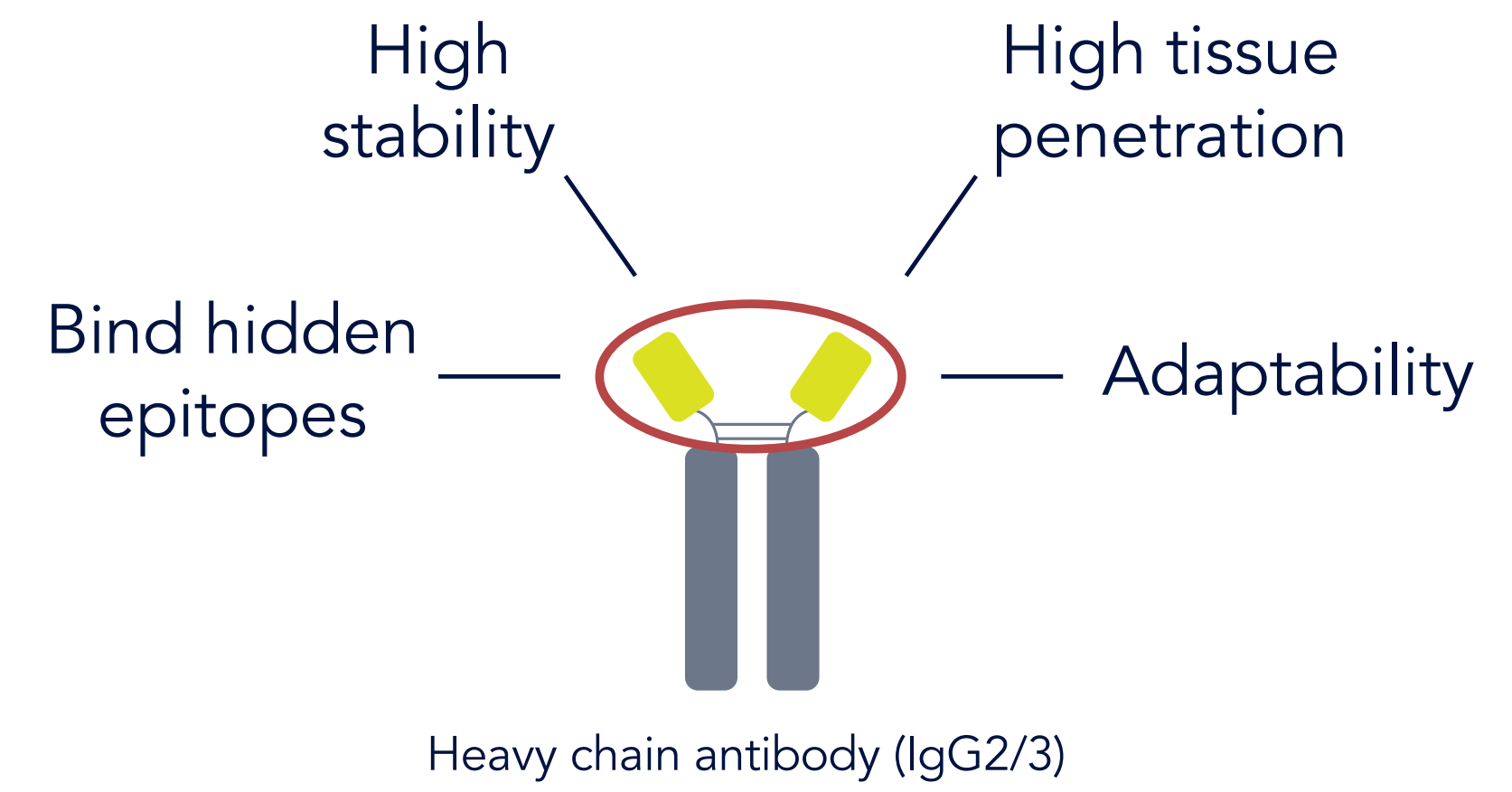


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Introduction:

VHHs, the variable domains of camelid heavy chain (IgG2/3) antibodies, also called single-domain antibodies, have gained a significant amount of interest over the last years due to distinct advantages, including the ability to bind hidden epitopes, high stability, high tissue penetration and adaptability for use in CAR-Ts and bi- and multispecifics. Although VHHs are now entering the clinic, ImmunoPrecise Antibodies (IPA) has over two decades of R&D experience with these powerful antigen binding fragments.

Leveraging its broad expertise in phage display and single B cell technologies, IPA is at the forefront of VHH discovery, delivering panels of sequence diverse VHHs against numerous challenging targets from phage libraries as well as via its rapid, high-throughput single B-cell technologies. IPA's comprehensive downstream VHH characterization, data-driven down-selection mediated by amongst others *in silico* immunogenicity analyses, and engineering including humanization, form a highly customizable and robust platform, accelerating therapeutic VHH development towards the clinic while minimizing risks.



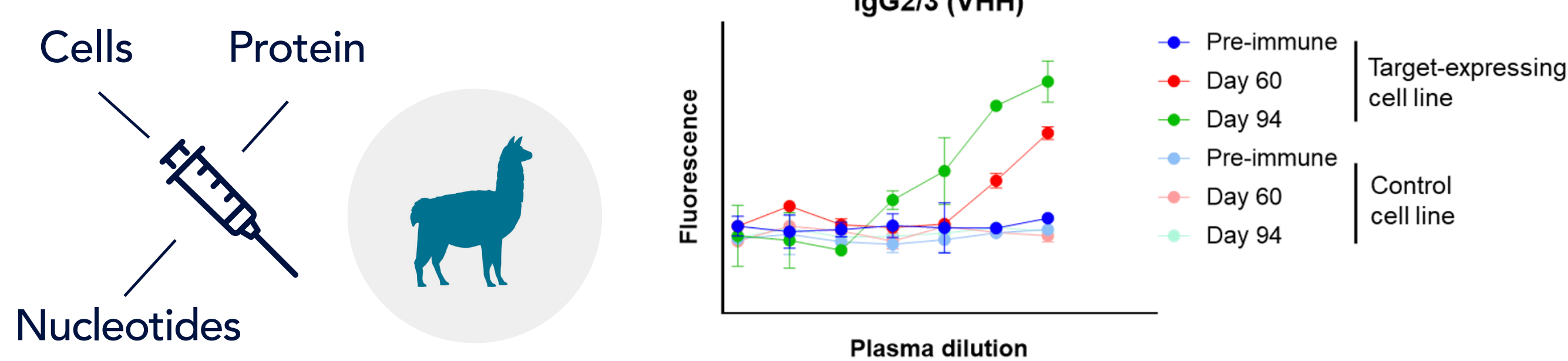
Highly customizable, robust lead generation technologies to accelerate therapeutic VHH development

Diversity-focused VHH discovery technologies built on extensive expertise

Immunization strategies and IgG2/3 plasma response

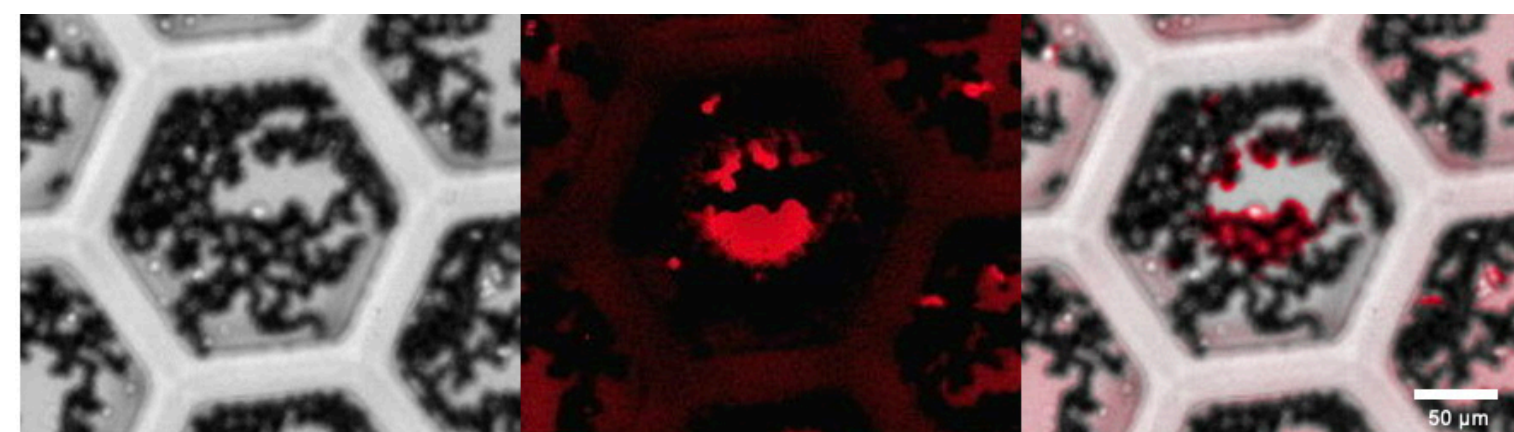
Flexible immunization strategies to induce heavy chain antibody responses

IgG2/3 target specific plasma reactivity of immunized camelids



Robust, rapid B cell discovery technologies

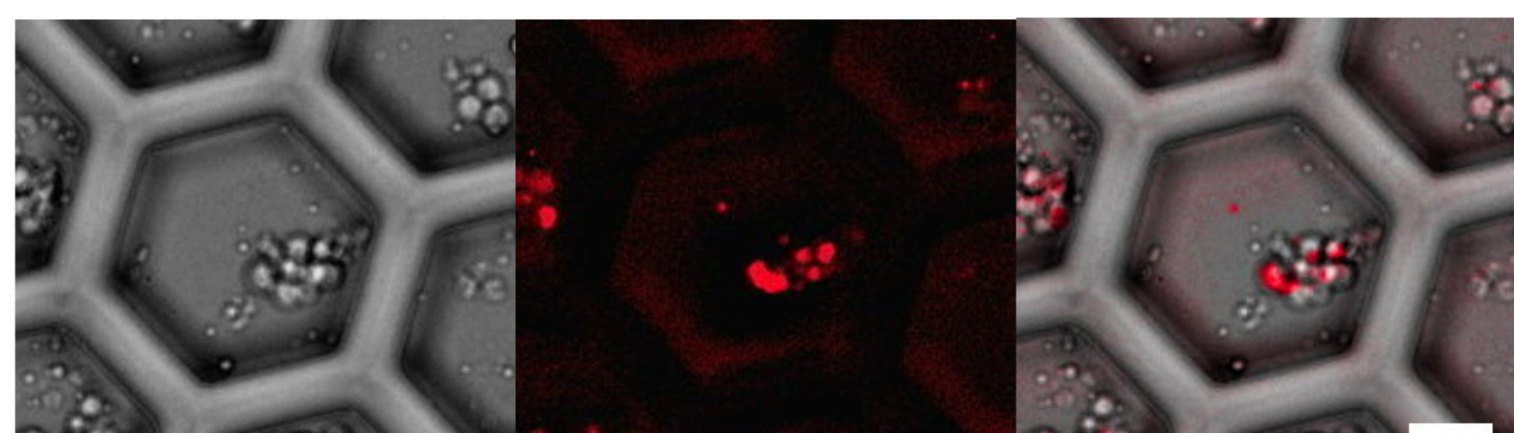
Antibody binding towards target-coated beads



Example workflow

- Joint seeding of B cells with target-coated beads or target-expressing cells into nanowells
- Automated scanning allows for target specific and/or functional camelid IgG2/3 detection
- High-throughput scanning of up to 1 million wells per day

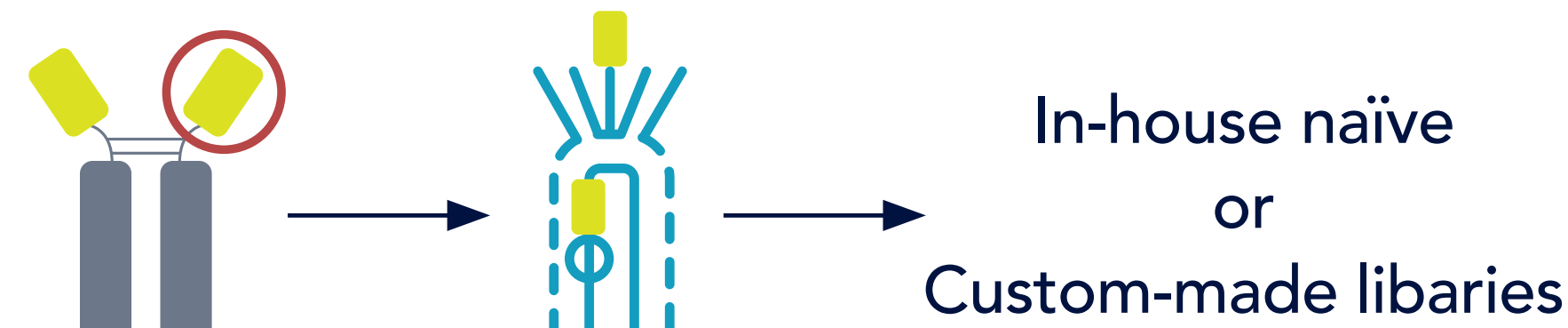
Antibody binding towards target-expressing cell



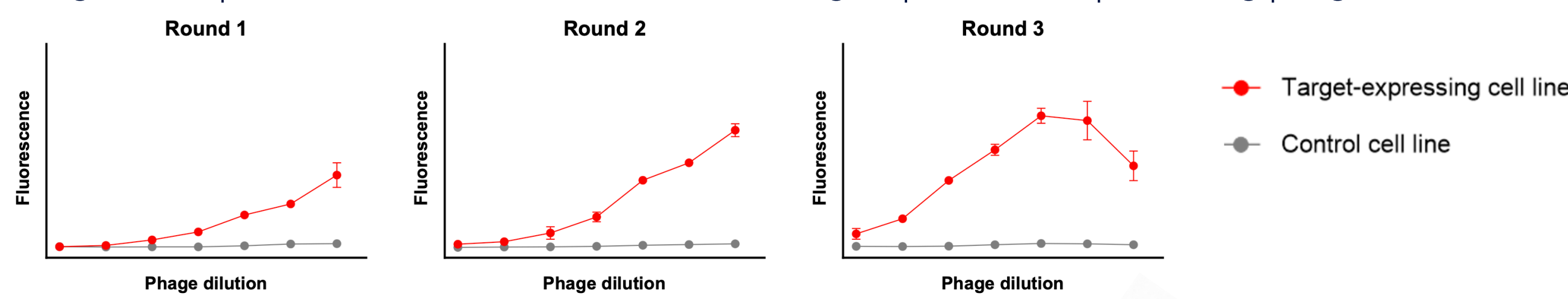
Bright-field Fluorescent channel Overlay images
Target binding

Flexible, established phage display platforms

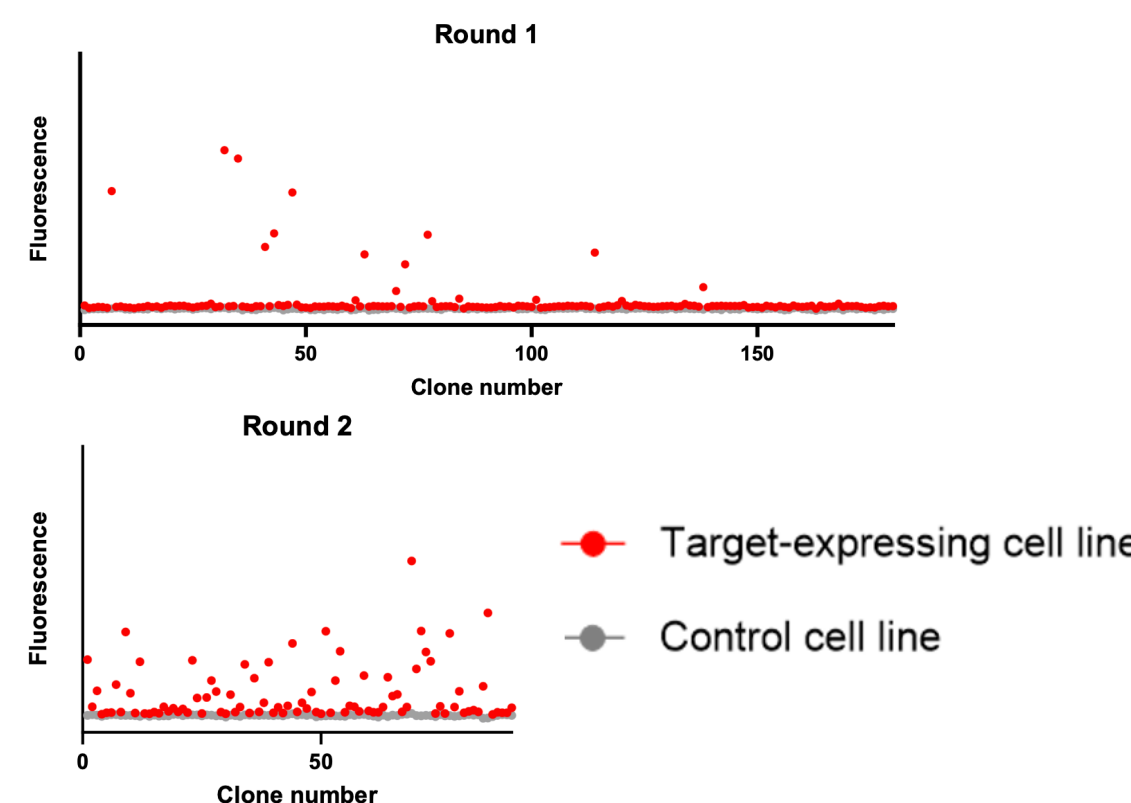
VHH phage libraries



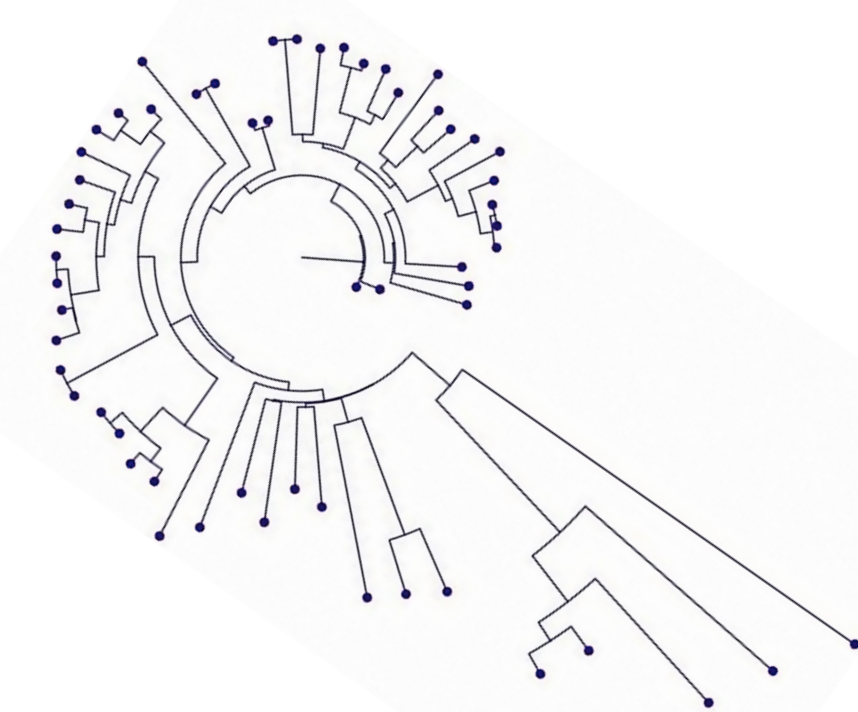
Program-adaptable selection rounds to enrich for target specific VHH-presenting phages



Monoclonal screening yields target-specific VHHs



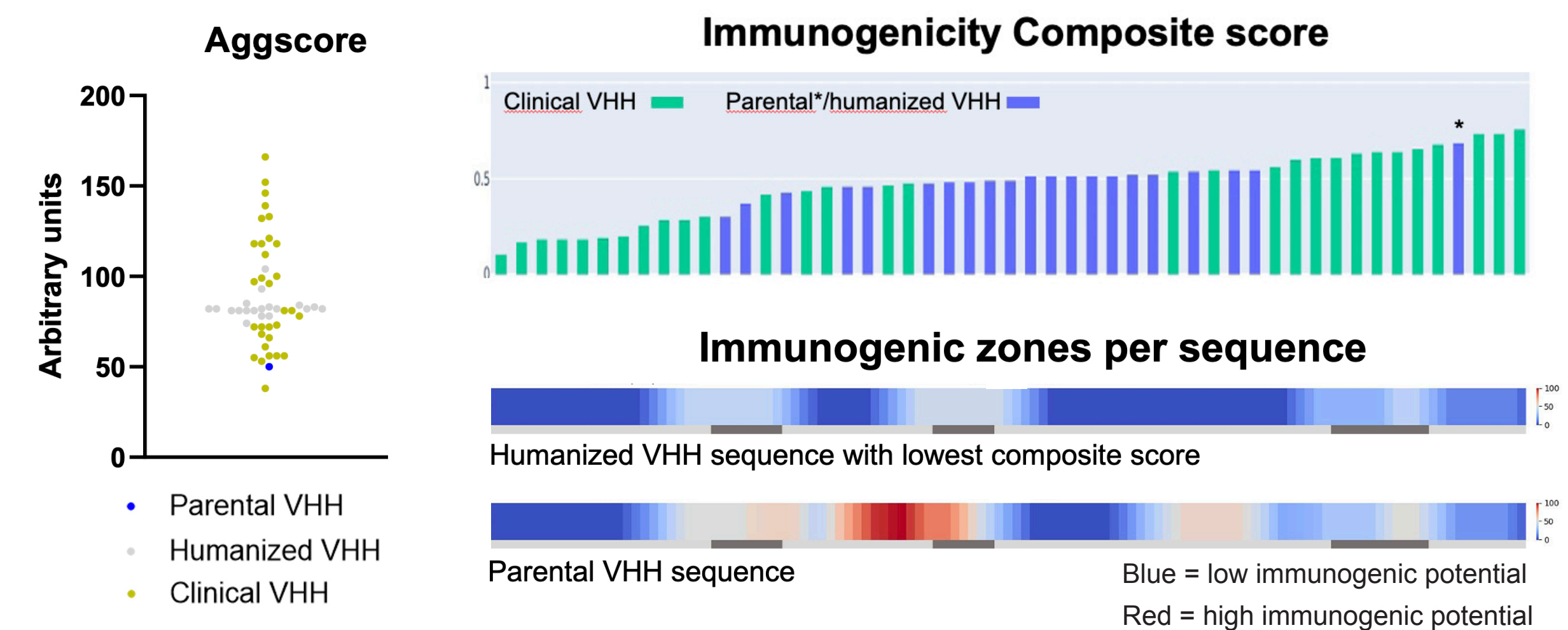
Phylogenetic tree displaying VHH sequence diversity



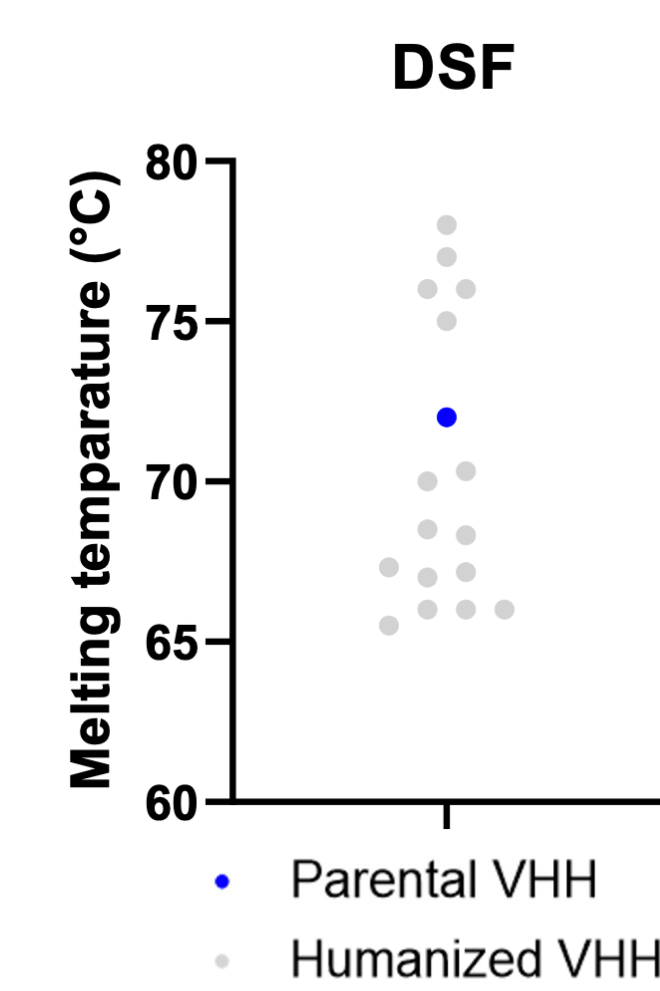
Data-driven de-risking, accelerating VHH development

Humanization with integrated immunogenicity and developability assessment

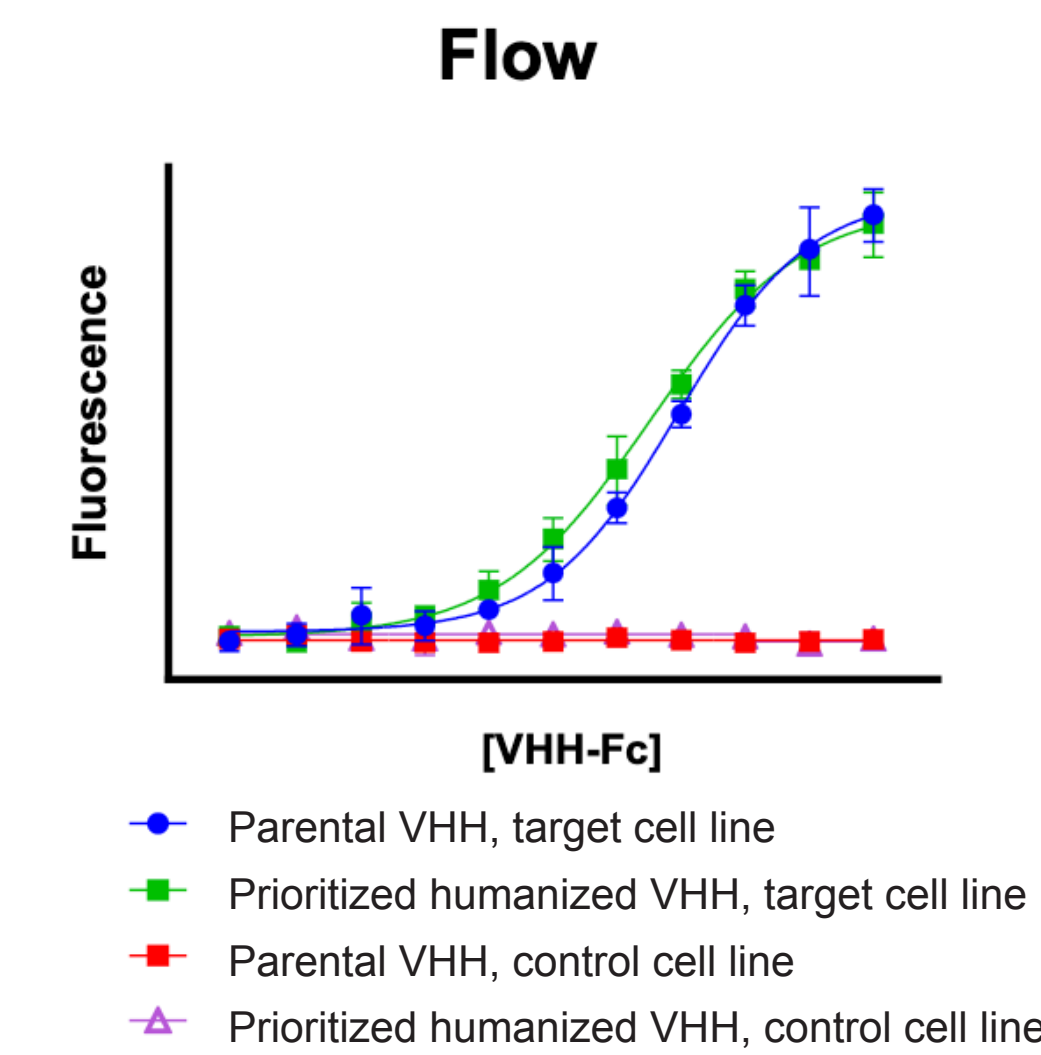
In silico assessments revealed that humanized VHH variants show developability characteristics comparable to clinical VHH and low immunogenic potential. Example outputs are shown.



Developability characteristics of parental and humanized VHH variants. Example output is shown.

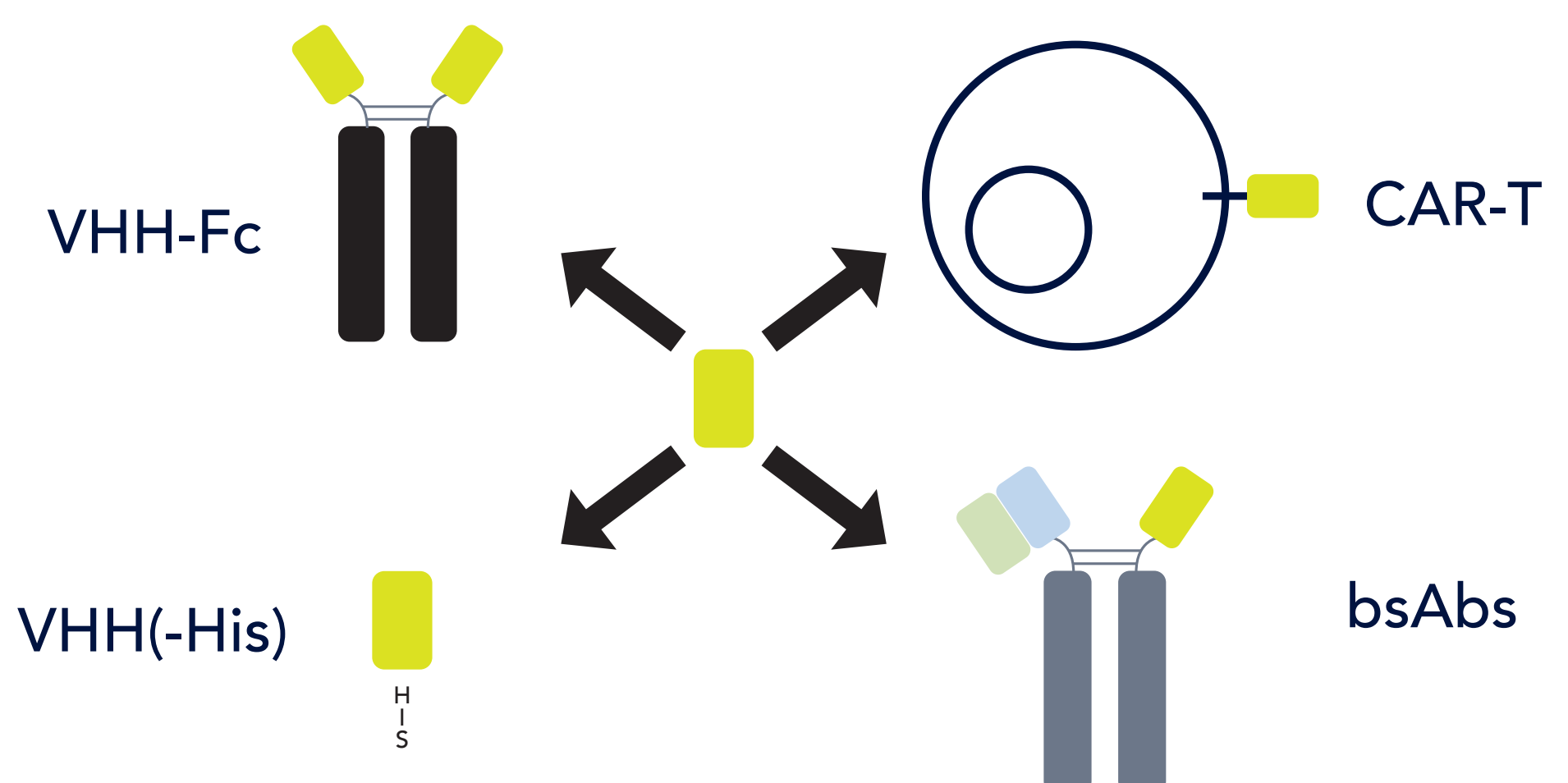


Prioritized humanized VHH shows similar binding properties as parental VHH.

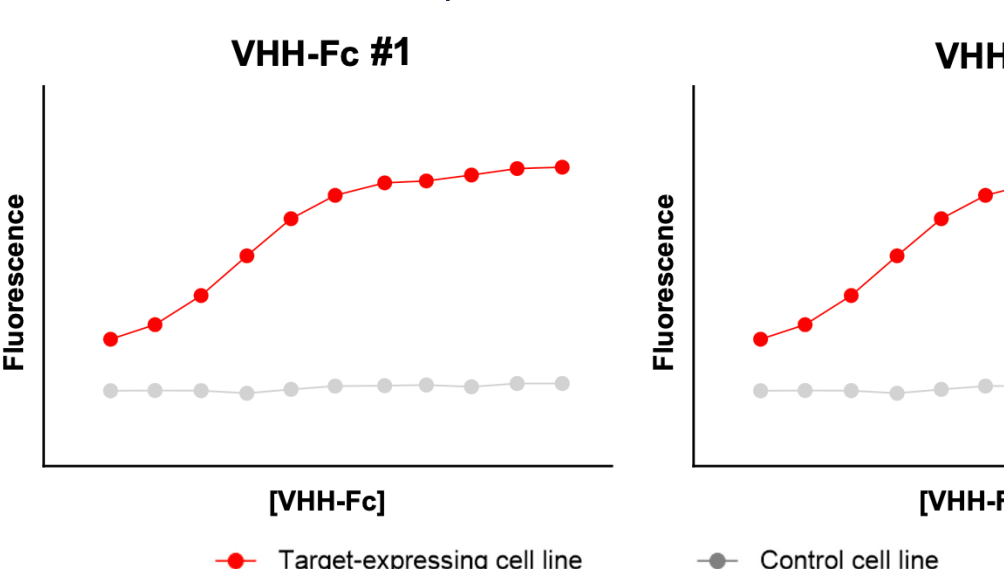


Customized re-formatting, production and validation

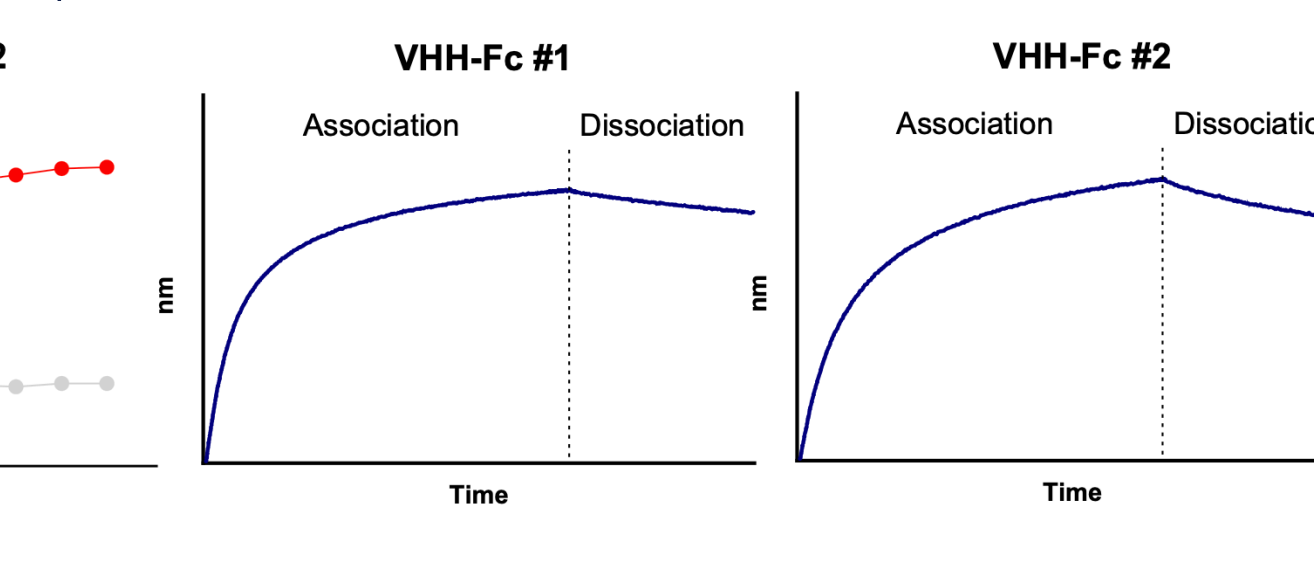
Multiple VHH re-formatting options available



Flow cytometry-based reactivity validation of recombinantly produced VHH-Fc



Octet-based kinetic measurements of recombinantly produced VHH-Fc



A single solution for single domain antibody-based therapeutics

Conclusion:

Leveraging its extensive experience with VHHs and highly customizable and robust technologies, IPA provides a single solution for accelerated therapeutic VHH lead generation while minimizing risks for further clinical development.