Accelerating single-domain antibody discovery against S.aureus ClfA to combat Antimicrobial Resistance (AMR): A high-efficiency yeast surface display platform

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This study presents a high-efficiency yeast display platform designed to rapidly discover and optimize conformationally selective single-domain antibodies (VHHs), demonstrated through the selection of anti-ClfA VHHs targeting a critical virulence factor in antimicrobial resistance. By leveraging continuous in vivo mutagenesis and affinity maturation, our EVOBodies™ platform achieves rapid enrichment cycles through straightforward yeast culturing and selection, delivering high-affinity clones in as little as two weeks.

The process begins with a decomplexification step to remove low-affinity binders, generating a focused, antigen-specific library. This is followed by a streamlined, iterative enrichment phase that progressively enhances binding affinity using yeast's robust mutation and display capabilities. This workflow enables the rapid production of VHHs with improved biophysical properties while minimizing time and manual intervention.

To validate the platform's performance, we successfully selected anti-ClfA VHHs.

ClfA, a key virulence factor in Staphylococcus aureus, facilitates immune evasion, making it a critical target in AMR research. The resulting high-affinity VHHs highlight the platform's potential for generating therapeutic candidates against resistant pathogens.

This case study illustrates the power of our yeast display system to accelerate antibody discovery workflows, providing a scalable and efficient solution for addressing global AMR challenges. The platform represents a valuable tool for next-generation therapeutic development and positions biologics at the forefront of innovative AMR solutions.