Antibody Humanization and De-immunization

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Summary
Antibody Humanization, irrespective of the specific strategy followed, can potentially introduce structural alteration in the antibody molecule that may affect its stability and often also results in a reduction of antigen binding affinity. When designing humanized antibodies it is imperative that key residues are present in the framework in order to retain antibody affinity.

Humanization Platform
We show here a number of case studies describing how the combined antibody humanization and de-immunization approach can be used to improve the developability of humanized antibodies, generating antibodies which are less immunogenic than those designed using a classical approach.

Antibody Humanization with Retained Affinity

De-immunization of VB6-845® Fab
- Viventia’s VB6-845® is a anti-EpCAM recombinant immunotoxin
- Humanized Fab fragment fused to a de-immunized toxin (bougainin)
- Observed immune response to Fab mostly
- Fab was de-immunized in silico using Epibase™
- De-immunized Fab showed reduced T cell activation potential in vitro

In silico De-immunization
- Screening for T cell epitopes using Epibase™
- Antibody structure modelling
- Substitutions to eliminate T-cell epitopes while retaining affinity for target
- 14/19 (74%) of proposed mutations retained expression and binding affinity for EpCAM

In Vitro verification of De-immunization
- Screening for T helper cell responses using PBMCs from healthy donors
- Detection methods covering immune responses to antigenic determinants

Viventia Biotechnologies

De-immunization provides a cost effective and rapid solution to further reducing or avoiding potential immunogenicity risk of therapeutic proteins

The results show Lonza’s how unique approach of humanization combined with de-immunization will result in a less immunogenic molecule than when performing classical humanization.