

Antibody: Antigen

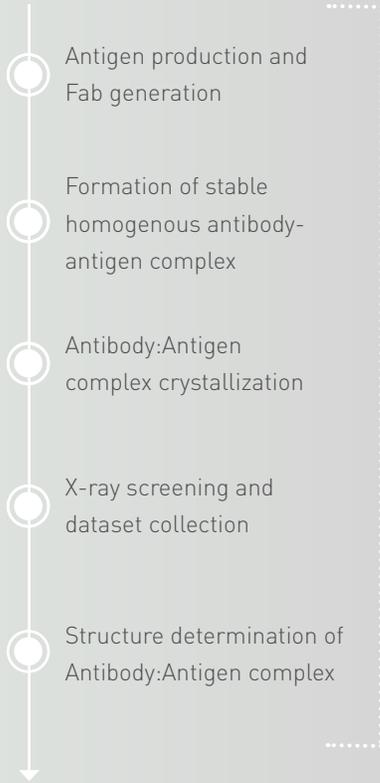
Unambiguously define your epitope-paratope interactions

- Improve binding interactions using structural data
- Obtain data imperative to strengthening patent applications

Accelerate the development of your
antibody therapeutic programs

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COLLABORATE@BE4.COM

Working with Beryllium



Antigen production and Fab generation

Formation of stable homogenous antibody-antigen complex

Antibody:Antigen complex crystallization

X-ray screening and dataset collection

Structure determination of Antibody:Antigen complex

2-4 MOS

DELIVERABLE

Fully annotated Protein Data Bank-coordinate and structure factor files

+ 70% SUCCESS
rate for antibody-antigen complex with a mean resolution of 3.0 Å

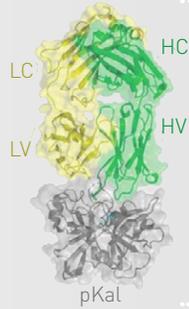
+ 90% SUCCESS
rate for humanized Fab structure with a mean resolution of 2.1 Å

SCIENTIFIC CASE STUDY

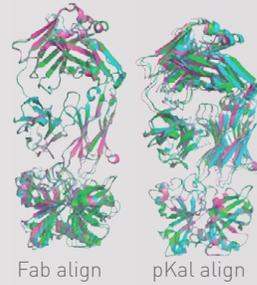
Collaboration with Dyax Corp.

Dyax Corp. wanted to understand how their antibody (DX-2930) was inhibiting a protease involved in hereditary angioedema (HAE).

X-ray crystallographic analysis of the pKal catalytic domain complexed with the DX-2930 Fab:



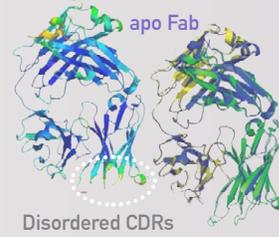
Ribbon structure of the pKal-DX-2930 Fab complex with transparent surface rendering.



All three resolved DX-2930-pKal complex structures from this study.



Overlay of pKal catalytic domain structure alone with the pKal catalytic domain crystallized in complex with DX-2930.



Left, crystal structure of the unbound DX-2930 Fab reveals disordered heavy chain CDR loops but an intact light chain CDR2.

Right, overlay of the apo-DX-2930 Fab.

EXPERIENCE / INSIGHT:

Beryllium generated recombinant human plasma kallikrein (pKal) for assays and crystallization using baculovirus infected insect cells with secreted expression and native refolding.

Complex formation with the Dyax provided Fab of DX-2930 was used to determine a proper stoichiometric ratio, essential for success in crystallography.

To understand the interaction between DX-2930 and pKal with atomic resolution, we crystallized the Fab portion of DX-2930 both alone and in a complex with a deglycosylated variant of the human pKal catalytic domain.

SOLUTION:

Results clearly showed the molecular details of the epitope/paratope interactions, thus providing a biological rationale to how the antibody is functioning.

In the Fab alone structure, the CDR loops are disordered, thus suggesting the antibody-antigen interaction is not pre-formed, thus the interaction between the two is an induced fit.

DX-2930 functions by specifically blocking the active site of pKal, thus acting similar to the Serpin C1 inhibitor that is deficient in individuals with hereditary angioedema.

These results have been published in the Journal of Biological Chemistry (Kenniston, J. A. et al. 2014, 289, 23596).