Characterizing antibody-antigen/superantigen interactions

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Antibody structure





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<u>VH family</u> (heavy variable FWRs):

• VH1, VH2, ..., VH7

<u>VL family</u> (light variable FWRs):

- Vк1, ..., Vк6
- Vλ

<u>CL family</u> (light constant):

Cκ, Cλ



<u>Isotypes</u> (heavy constant):

- IgM
- IgA1, IgA2
- IgD
- IgG1, IgG2, IgG3, IgG4
- IgE

What we could:

Manipulate interactions of Ab to antigen and/or superantigens via mutagenesis

Observe allosteric communications between distal regions of Ab

I. Manipulate interactions: Ab – antigen/superantigen





Mutations disrupted superantigen protL binding on IgG1





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I. Manipulate interactions: Ab – antigen/superantigen

Mutations disrupt

Binding kinetics of Trastuzumab mutants against protein L





Figure S3: (A). Unfavorable binding mode of protein L to the deate mutants superimposed on that of WT highlighting diminishing binding effect accompared to WT in which the protein L flipped 180 degree outward from the protein sufficiency area (SASA) by KWR1 (residue 1-24) w



naged the FWR1 β -strands, which

 Protle (B2-strand, α-helix), righter strain (A). Unfavorable binding mode of protein L to the delTE r compared to WT, in which the protein L flipped 180 degree outward from binding mode (Craille et al. 2001) to the VkEWR1 of Trastuzumab. The β str delsh the interactions are highlighter in black (WT) blue (def), green (d (delTE). Protein L (deep teal color) contains 1 helix and four β-strands (β2 Vk-FWR1). Protein L binding energies of the WT and of the two single end to the superimposed on that of WT highlighting diminishing binding effect for mutants superimposed on that of WT highlighting diminishing binding effect for mutants superimposed on that of WT highlighting diminishing binding effect for mutants protein and α helix). (C) Exposures of the Vk-FWR1 (residue 1-24) we the superimposed on that of WT highlighting diminishing binding effect for mutants protein and α helix). (C) Exposures of the Vk-FWR1 (residue 1-24) we the superimposed on the super su

Mutations disrupted HER2 binding





- Several key contacts between CDRs and HER2 were lost due to FWR3 conformational changes
- Buried CDR3 loop in delTE might've diminished binding to HER2
- Allosteric effect on FWR1 conformation

Mutations disrupted superantigen spA binding on IgE





A single mutation on VH-CDR2 affected spA binding



The spA binds specifically only to VH3 family antibodies; while having <u>similar VH3 FWRs</u> and sharing the <u>same Ce</u>:

- Our pertuzumab VH3 IgE did not bind the spA,
- But trastuzumab VH3 IgE interacted strongly with spA

