integral molecular

Case Study:
Is the HER2 epitope of Fynomer C12 distinct from trastuzumab and pertuzumab?

COVAGEN
Advanced Biopharmaceuticals

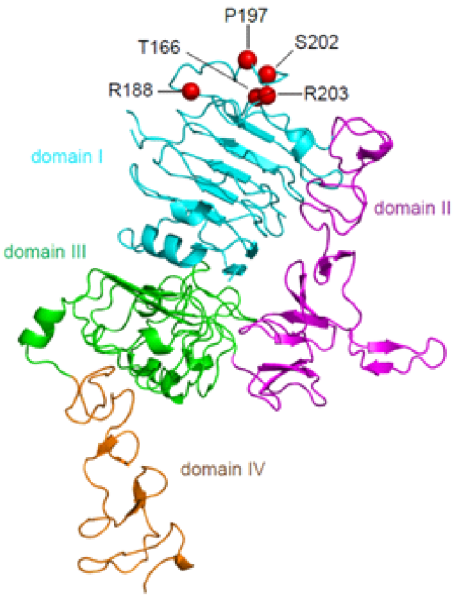
THE NEED

Covagen developed COVA208, a bispecific FynomAb which targets two epitopes on HER2. This included a novel moiety, Fynomer C12, which was combined with a region of pertuzumab to create a bispecific that demonstrated superior activity to trastuzumab and pertuzumab in tumor models. Covagen required detailed epitope information for the novel moiety (Fynomer C12). This allowed them to better understand the molecule's mechanism-of-action and to demonstrate its novelty.

THE SOLUTION

Shotgun Mutagenesis

Shotgun Mutagenesis epitope mapping by Integral Molecular clearly delineated the binding site of Fynomer C12 on HER2. The epitope was comprised of five amino acids on the surface of domain I, which is distinct from pertuzumab (domain II) and trastuzumab (domain IV).

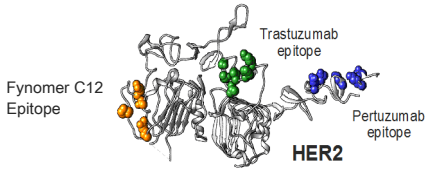


THE IMPACT

Mechanism of Action

Epitope mapping using Shotgun Mutagenesis revealed that the Fynomer C12 component of Covagen's bispecific molecule bound to an epitope distinct from approved therapeutics trastuzumab and pertuzumab. The bispecific was able to inhibit ligand-dependent and ligand-independent signaling.

COVA208 led to extensive HER2 receptor cross-linking, clustering and degradation. This was likely a result of targeting multiple epitopes on different receptors.



Clinical implication

Combining an existing therapeutic antibody into a bispecific with a novel binding epitope can create therapeutics with superior efficacy.

Publication

Data featured in Molecular Cancer Therapeutics, Brack et al. 2014.

Looking for more information? Contact us below:

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