integral molecular

Case Study:
How does a biparatopic CXCR2 nanobody inhibit with high potency and efficacy?

NOVARTIS

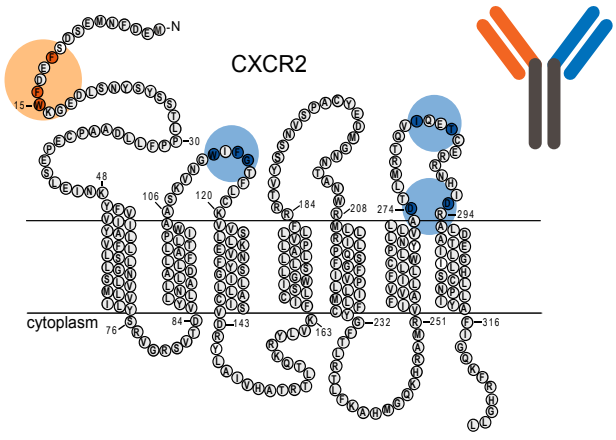
THE NEED

Novartis together with Ablynx developed a biparatopic CXCR2 nanobody for inflammation. The potency and efficacy of this biparatopic nanobody was greater than its component monovalent counterparts. Novartis required detailed epitope information to characterize mechanism-of-action, and to file intellectual property.

THE SOLUTION

Shotgun Mutagenesis

Integral Molecular developed a comprehensive mutagenesis library of CXCR2. Two monovalent nanobodies (127D1 and 163E3) were mapped using the CXCR2 library. 127D1 was shown to bind a linear epitope at the N-terminus of CXCR2 and 16E3 was shown to bind a complex conformational epitope formed by extracelluar loops 1 and 3.



THE IMPACT

Mechanism of Action

Epitope mapping using Shotgun Mutagenesis revealed that component nanobodies bound to distinct, non-overlapping sites on the CXCR2 receptor. The biparatopic nanobody is able to bind epitopes across two different CXCR2 receptors, leading to efficient inhibition.

Clinical implication

An Investigational New Drug (IND) application was filed for this nanobody and approved by the FDA.

Intellectual Property

Novartis was able to use amino acid resolution epitope maps of nanobodies 127D1 and 163E3 in a patent in order to protect its biparatopic nanobody.

Publication

Data featured in Molecular Pharmacology, Bradley et al. 2015.

Looking for more information? Contact us below:

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