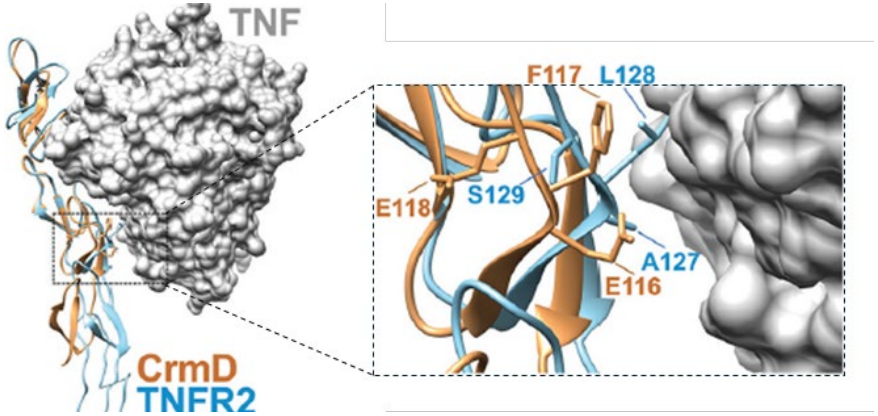
Technology Offer CSIC/SS/002

Novel Etanercept variants with improved therapeutical effect



Novel mutant variants of the fusion protein Etanercept with improved TNF neutralizing specificity and therapeutical effect, ameliorating the side effects associated to the clinical use of Etanercept.

Intellectual Property

Patent filed in EP, US, CN

Stage of development

Preclinical in vivo (mouse model)

Intended Collaboration

Licensing and/or co-development

Contact

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Market need

Etanercept (Enbrel®) is one of the leading biologics for chronic inflammatory diseases such as rheumatoid arthritis, ankylosing spondylitis or psoriasis. It works by blocking TNF via a soluble TNFR2–Fc fusion. presenting several limitations:

- Incomplete control of inflammatory cascades (e.g. chemokines), leaving a substantial part of the inflammatory axis intact.
- Dose limitations and safety constraints.
- Non specific activity against lymphotoxin (LTα), worsening susceptibility to infections
- Incomplete responses or loss of efficacy in high proportion of patients.

Proposed solution

Inspired by viral immunomodulators, a new etanercept-derived bifunctional inhibitor by fusing TNFR2–Fc with a viral chemokine binding domain (SECRET) was engineered. This novel variant maintains full binding affinity and inhibitory activity against TNF while adding high affinity chemokine neutralization.

In vivo studies using a an arthritis mouse model showed that the fusion protein performed equivalently to double dose etanercept, demonstrating increased potency per mg. Additionally, this variant displays a >60 fold reduction in anti LTα activity, essentially abolishing LTα inhibition, preserving immune competence. The invention represents a next-generation etanercept, specifically optimized to modulate broader inflammatory networks.

Competitive advantages

- Novel mechanism inspired by viral immunomodulators, ·offering a mechanism unattainable by monoclonal antibodies or current TNF inhibitors.
- Superior biological efficacy through dual inhibition of TNF and chemokines.
- Demonstrated in vivo potency equivalent to higher doses of Etanercept.
- Improved safety profile with preserved immune competence.