



CROSSTARGET: Anti-ICAM-1 antibodies with broad recognition for site-specific drug delivery

CHALLENGE

Effective drug delivery remains one of the key challenges in biomedicine. Most therapies cannot efficiently and selectively reach diseased tissues and cells, particularly across biological barriers such as the blood-brain barrier or into intracellular compartments, such as lysosomes.

ICAM-1 mediated drug delivery holds high potential, as ICAM-1 is overexpressed in most diseases and offers efficient transport to these destinations. Yet, its translation is hindered as current anti-ICAM-1 antibodies (Abs) do not recognize both human and species used in preclinical assays, nor can they discriminate between ICAM-1 variants expressed in different tissues or induce preferential transport to particular destinations. As an example, popular anti-ICAM-1 Ab Enlimomab, has failed several clinical trials since it does not recognize ICAM-1 variants lacking domain D2.

MARKET

ICAM-1 targeted delivery is useful for many pharmaceuticals since **ICAM-1 is overexpressed under inflammation, which underlies most diseases**.

First targeted market is the lysosomal storage disorders (LSDs), a set of rare genetic conditions affecting 1 in 2,000 live births and comprising 60 distinct diseases. LSDs treatment market is expected to reach USD 13 Billion by 2030.

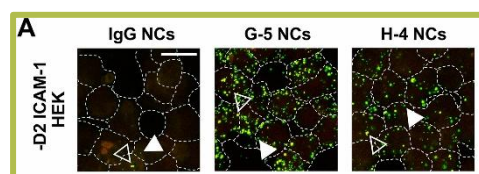
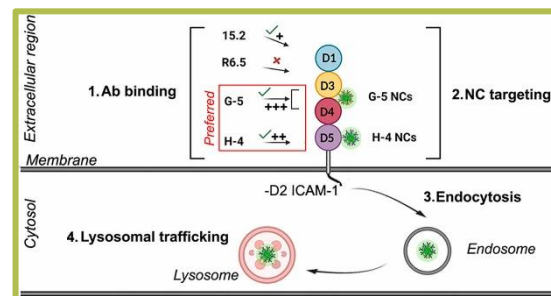
Enzyme replacement therapies (ERT) is the main therapeutic approach; yet it is effective for only 12 out of the 60 LSDs due to lack of transport to the central nervous system (CNS), which ICAM-1 targeting offers. There is a large and growing market for ERT and other CNS conditions.

ASSET

Prof. Silvia Muro and her team have developed **novel ICAM-targeting Abs that recognize several ICAM-1 variants** with **differential targeting** of organs and subcellular compartments across **preclinical and clinical species**. Therapeutic delivery is achieved via a unique, non-competing transcytosis route. By conjugating these Abs to therapeutic agents or nanoparticles, precise targeting with CNS or intracellular delivery is achieved.

ASSET VALUE

- ❖ Enabling highly specific non-competitive targeting, without receptors' sequestration, avoiding off target effects and preserving physiological transport
- ❖ Cross species recognition, binding to ICAM of multiple species, ensuring translatability from preclinical to clinical delivery
- ❖ Recognition of multiple ICAM-1 isoforms, including those lacking domain D2 missed by Enlimomab
- ❖ Transport across cellular barriers, such as the blood-brain barrier and the blood-lung barrier
- ❖ Enabling trafficking to intracellular compartments of large and various macromolecules
- ❖ Broad application possible as inflammatory factors and signals are involved in most known pathologies



Figures : Innovative Abs for NC targeting and intracellular transport mediated by ICAM-1, even in the case of isoforms lacking domain D2

Team

Silvia Muro - Scientific Leader
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Stage of Development

- Prior *in vivo* studies with less specific anti-ICAM-1 Abs showed good biodistribution (notably in brain and lungs) and therapeutic outcomes (sphingomyelinase).
- PoC with these new Abs has now showed improved performance achieved in cellular models

Exploitation Plan

Licensing.
Open to technical co-development or investment for preclinical phase completion.

Intellectual Property Status

- Priority patent filed in November 2023.
- Currently in PCT phase.
- Patent Owners : IBEC and ICREA

USES

- Hard-to-reach site specific drug delivery
- ICAM-1 biology research activities
- Lysosomal Storage Disorders Treatment combined with Enzyme Therapy