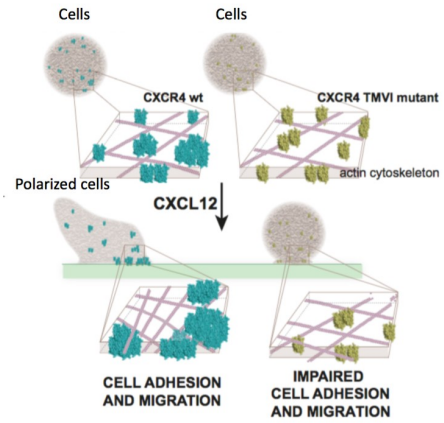
Therapeutic targets in chemokine receptors to select useful compounds for pathologies treatment that intervene in chemokine responses

CSIC has identified a molecular target into the transmembrane VI (TMVI) region of the chemokine receptors, specifically in CXCR4. This target is now being used to design and detect selective compounds that modulate/antagonize chemokine-mediated function by altering receptor oligomerization, in contrast to the classical strategies based on ligand binding blockade. As oligomerization is the active conformation of this receptor, its inhibition blocks cell movement towards chemoattractant gradients. In accordance, this target is very useful for altering immune cell infiltration in tissues during autoimmune and inflammatory diseases or in cancer metastasis. As CXCR4 is also the main coreceptor for T-tropic HIV-1 viruses, these antagonists would be very useful to block HIV-1 infection and to reduce the viral load of AIDS patients.
Industrial partners from the pharmaceutical industry are being sought to collaborate through a patent licence agreement.

The residues responsible for chemokine-mediated receptor oligomerization are a therapeutic target that can be exogenously modulated in order to treat cancer metastasis, inflammatory and autoimmune diseases or HIV-1 infection.

The specific sequence within the amino acid sequence of the CXCR4 is directly involved in receptor oligomerization, being thus a promising therapeutic target to intervene in chemokine-mediated responses within cells.

All the technology required for the screening of small compounds acting on this target, both *in vitro* and *in vivo,* is available at the CNB lab.



CXCR4 forms monomers, dimers, and nanoclusters at the cell membrane.

Main innovations and advantages

- The invention falls within the fields of medicine and pharmacology, particularly within the field of therapeutic targets for the screening of compounds useful in the treatment of diseases or clinical conditions which symptoms or pathology are a consequence of the events triggered by chemokine signaling, such as inflammatory and autoimmune diseases, as well as cancer or HIV-1 infection.
- The invention relates to the identification of molecular targets in chemokine receptors/chemokine complexes whose modulation is crucial to intervene in specific chemokine-mediated cell responses without altering others.
- The exogenous modulation of these therapeutic targets would allow to specifically block some of the events triggered by the ligand to its receptor without affect ligand binding.
- The invention have been tested in *in vivo* experiments using a murine model for neutrophils movement.
- The new target represents a completely new and effective approach to antagonize chemokine responses, opposed to the classical strategies based on ligand binding blockade that have always failed to obtain valuable drugs for clinical purposes.

Patent Status

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