

# Designed Chemokine-Selective Peptides in the Fight Against Atherosclerosis and Inflammation

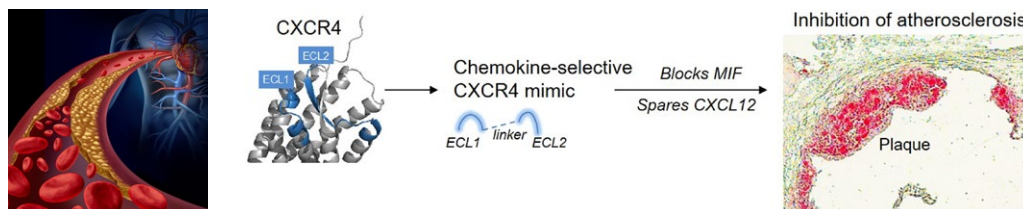
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## CHALLENGE

In coronary heart diseases, a progressive narrowing of blood vessels results in a life-threatening interruption of the blood flow to the heart. **Atherosclerosis** is considered the main underlying pathology. Here, **accumulating lipids** result in the thickening and hardening of blood vessels as **plaques**. In recent years, atherosclerosis has also been linked to **inflammatory processes** orchestrated by **cytokines and chemokines**. By acting on their target cells via specific surface receptors, these small signal proteins drive **the migration of immune cells** in tissue and bloodstream to sites of infection or sterile inflammatory foci. Due to their strong involvement in different inflammatory processes, they represent promising therapeutic targets. One key signaling hub in atherosclerotic pathogenesis is the chemokine receptor CXCR4. CXCR4 is ubiquitously expressed, but has particularly critical roles in atherosclerosis when expressed on leukocytes and aortic endothelial cells. It also exerts **context-dependent functions** depending on the engaged ligand. Binding the classical chemokine ligand CXCL12 leads to important **atheroprotective** effects, whereas activation by the atypical chemokine ligand MIF, also known as a **potent pro-inflammatory cytokine**, promotes atherosclerosis. Despite the unmet need for effective anti-inflammatory therapeutic approaches directed against cytokine- and chemokine-mediated pathways, **selectively targeting** a specific chemokine-receptor axis has proven to be challenging.

## INNOVATION

Our novel approach involves soluble peptide-based mimics of the CXCR4 receptor. These mimics show potent chemokine-selectivity and differentiate between MIF and CXCL12. By localizing to atherosclerotic plaques, they inhibit MIF-mediated leukocyte recruitment and arterial adhesion<sup>1</sup>. Importantly, they do not affect the atheroprotective function of CXCL12.



## COMMERCIAL OPPORTUNITIES

Our selective CXCR4 mimics represent a novel class of therapeutics for the treatment of **atherosclerotic plaques** and **related inflammatory diseases**:

- **cost-effective production** by routine solid phase peptide synthesis methodology
- **small-medium-sized peptides (<30 residues)**
- **high potency and target specificity** and **good proteolytic stability**
- **Structural template** for small molecule design with anti-atherosclerotic function
- IP covers **extension of approach** to other chemokine receptors and/or different selectivity

## DEVELOPMENT STATUS

Proof-of-concept in in vivo Apoe<sup>-/-</sup> mouse model, human plasma, and patients' biopsy samples.

## REFERENCES:

- 1 doi: 10.1038/s41467-020-19764-z

### IP rights:

\*EP filed in 2020

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