



Leiden University Research & Innovation Services

S1P₃ receptor specific ligand opens new therapeutic opportunities for cardiovascular disorders or respiratory failure

Market sector(s): Cardiovascular, Pulmonary pharmaceuticals

Commercial opportunity: Collaboration or licensing opportunity

Leiden University and the Academic Medical Center at the University of Amsterdam (both located in the Netherlands) have identified the first specific Sphingosine 1-Phosphate 3 (S1P₃) receptor agonist. The compound and the innovative technology that led to its design are now available for licensing purposes and/or for collaborative therapeutic development of lung or cardiovascular afflictions.

Description

Five members of the S1P receptor family have been identified so far named S1P₁ through S1P₅. The S1P₁, S1P₂ and S1P₃ receptors are ubiquitously expressed and are the most important receptors in the cardiovascular system whereas the S1P₄ and S1P₅ receptors show more restricted expression pattern (S1P₄; lung and lymphoid system, S1P₅; brain).

S1P receptors are involved in many biological processes and may have an important role in many pathophysiological disease states such as atherosclerosis, cancer and auto-immunity. Despite their importance the number of ligands that specifically interact with S1P receptors is very limited. In addition, subtype specific S1P ligands are as good as non-existing. The absence of subtype selective S1P ligands generally hampers pharmacological research of these receptors.

Chemists from Leiden University have synthesized the first compound that can be used as a specific S1P₃ receptor agonist. The S1P₃ receptor subtype plays a critical role in cardiovascular physiology and lung epithelial barrier function and therefore opens opportunities for new cardiovascular or pulmonary treatments.

In the vasculature, endothelial S1P₃ receptor stimulation mediates nitric oxide production that is thought to have many advantageous effects in different cardiovascular pathologies (e.g.

atherosclerosis). Recent studies indicate that High Density Lipoprotein (HDL)-induced vasodilatation is S1P₃ receptor-dependent. In addition it has been clearly shown that S1P has protective effects on the heart during for instance ischemia. And, as in the vasculature, the protective effects of HDL under these conditions are, at least partly, mediated via stimulation of cardiac S1P₃ receptors.

In the lung, S1P₃ is exclusively expressed in pulmonary epithelium and selective S1P₃ agonists and/or antagonists would be of help to elucidate the mechanisms involved in respiratory failure such as Adult Respiratory Distress Syndrome and could eventually also be of therapeutic importance in this disease.

Key benefits

- First selective agonist to subtype S1P₃ receptors.
- S1P₃ ligands may show protective effects in the cardiovascular system.
- New derivatives may be generated with higher selectivity of pharmaceutical response and less undesirable side effects.

Applications

- Determination of S1P₃ receptor role and functions.
- Cardiovascular treatments (i.e. Atherosclerosis).
- Pulmonary treatments (i.e. Adult Respiratory Distress Syndrome).

Luris

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