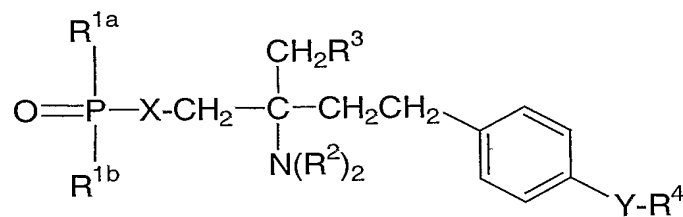


The invention also encompasses a method of reducing or preventing the activation of the S1P1/Edg1 receptor in a mammalian patient in need thereof comprising administering to said patient a compound which is an agonist of the S1P1/Edg1 receptor in an amount effective for reducing or preventing the activation of S1P1/EDG1 receptor, wherein said compound possesses a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor of at least 20 fold as measured by the ratio of EC50 for the S1P1/Edg1 receptor to the EC50 for the S1P3/Edg3 receptor as evaluated in the ³⁵S-GTPγS binding assay and wherein said compound possesses an EC50 for binding to the S1P1/Edg1 receptor of 100 nM or less as evaluated by the ³⁵S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR¹ or (CH₂)₁₋₂, optionally substituted with 1-4 halo groups;

R¹ is H, C₁₋₄alkyl or haloC₁₋₄ alkyl;

20

R^{1a} is H, OH, C₁₋₄alkyl, or OC₁₋₄ alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C₁₋₄ alkyl or haloC₁₋₄ alkyl;

each R² is independently selected from the group consisting of: H, C₁₋₄ alkyl and haloC₁₋₄ alkyl,

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R³ is H, OH, halo, C₁₋₄alkyl, OC₁₋₄alkyl, O-haloC₁₋₄alkyl or hydroxyC₁₋₄alkyl,

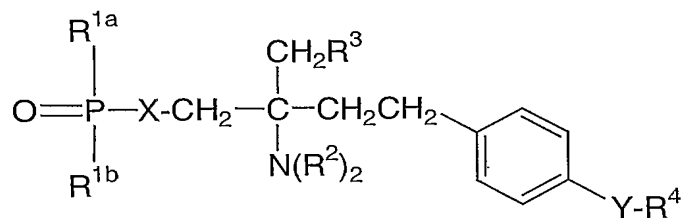
Y is selected from the group consisting of: -CH₂-, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

10

R⁴ is selected from the group consisting of: C₄₋₁₄alkyl and C₄₋₁₄alkenyl.

The invention also encompasses a method of inhibiting an infiltration of a lymphocyte into a respiratory tissue in a mammalian patient in need thereof by promoting a sequestration of the lymphocyte in a lymph node thereby preventing release of a pro-inflammatory mediator in the respiratory tissue comprising administering to said patient a compound which is an agonist of the S1P₁/Edg1 receptor in an amount effective for modulating airway function, wherein said compound possesses a selectivity for the S1P₁/Edg1 receptor over the S1P₃/Edg3 receptor of at least 20 fold as measured by the ratio of EC₅₀ for the S1P₁/Edg1 receptor to the EC₅₀ for the S1P₃/Edg3 receptor as evaluated in the ³⁵S-GTPγS binding assay and wherein said compound possesses an EC₅₀ for binding to the S1P₁/Edg1 receptor of 100 nM or less as evaluated by the ³⁵S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR¹ or (CH₂)₁₋₂, optionally substituted with 1-4 halo groups;

5

R¹ is H, C₁₋₄alkyl or haloC₁₋₄ alkyl;

R^{1a} is H, OH, C₁₋₄alkyl, or OC₁₋₄ alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

10

R^{1b} represents H, OH, C₁₋₄ alkyl or haloC₁₋₄ alkyl;

each R² is independently selected from the group consisting of: H, C₁₋₄ alkyl and haloC₁₋₄ alkyl,

15

R³ is H, OH, halo, C₁₋₄alkyl, OC₁₋₄alkyl, O-haloC₁₋₄alkyl or hydroxyC₁₋₄alkyl,

Y is selected from the group consisting of: -CH₂-, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

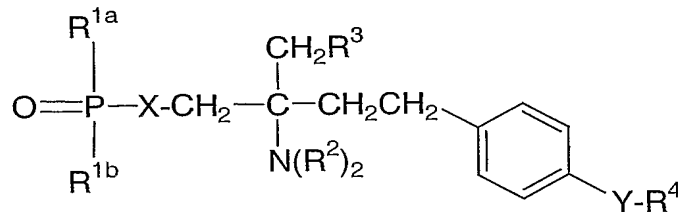
20

R⁴ is selected from the group consisting of: C₄₋₁₄alkyl and C₄₋₁₄alkenyl.

WHAT IS CLAIMED IS:

1. A method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound which is an agonist of the S1P₁/Edg1 receptor in an amount effective for treating said immunoregulatory abnormality, wherein said compound possesses a selectivity for the S1P₁/Edg1 receptor over the S1P₃/Edg3 receptor of at least 20 fold as measured by the ratio of EC₅₀ for the S1P₁/Edg1 receptor to the EC₅₀ for the S1P₃/Edg3 receptor as evaluated in the ³⁵S-GTPγS binding assay and wherein said compound possesses an EC₅₀ for binding to the S1P₁/Edg1 receptor of 100 nM or less as evaluated by the ³⁵S-GTPγS binding assay,

with the proviso that the compound does not fall within formula A:



A

15

or a pharmaceutically acceptable salt or hydrate thereof, wherein:

X is O, S, NR¹ or (CH₂)₁₋₂, optionally substituted with 1-4 halo groups;

20 R¹ is H, C₁₋₄alkyl or haloC₁₋₄ alkyl;

R^{1a} is H, OH, C₁₋₄alkyl, or OC₁₋₄ alkyl, the alkyl and alkyl portions being optionally substituted with 1-3 halo groups;

R^{1b} represents H, OH, C₁₋₄ alkyl or haloC₁₋₄ alkyl;

each R² is independently selected from the group consisting of: H, C₁₋₄ alkyl and haloC₁₋₄ alkyl,

5

R³ is H, OH, halo, C₁₋₄alkyl, OC₁₋₄alkyl, O-haloC₁₋₄alkyl or hydroxyC₁₋₄alkyl,

Y is selected from the group consisting of: -CH₂-, -C(O)-, -CH(OH)-, -C(=NOH)-, O and S, and

10

R⁴ is selected from the group consisting of: C₄₋₁₄alkyl and C₄₋₁₄alkenyl.

2. The method according to Claim 1 wherein the compound has a selectivity for the S1P₁/Edg1 receptor over the S1P₃/Edg3 receptor of at least 100 fold as measured by the ratio of EC₅₀ for the S1P₁/Edg1 receptor to the EC₅₀ for the S1P₃/Edg3 receptor as evaluated in the ³⁵S-GTPγS binding assay.

3. The method according to Claim 2 wherein the compound has a selectivity for the S1P₁/Edg1 receptor over the S1P₃/Edg3 receptor of at least 200 fold as measured by the ratio of EC₅₀ for the S1P₁/Edg1 receptor to the EC₅₀ for the S1P₃/Edg3 receptor as evaluated in the ³⁵S-GTPγS binding assay.

4. The method according to Claim 3 wherein the compound has a selectivity for the S1P₁/Edg1 receptor over the S1P₃/Edg3 receptor of at least 500 fold as measured by the ratio of EC₅₀ for the S1P₁/Edg1 receptor to the EC₅₀ for the S1P₃/Edg3 receptor as evaluated in the ³⁵S-GTPγS binding assay.

5. The method according to Claim 4 wherein the compound has a selectivity for the S1P₁/Edg1 receptor over the S1P₃/Edg3 receptor of at least 2000

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