

Claims

1. A bispecific antibody (BsAB), wherein said BsAB comprises two binding domains, wherein the first binding domain is specific for ALK-1 and the second binding domain is specific for BMPR-2.
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2. A BsAB according to claim 1, wherein the ALK-1 is human ALK-1 or a fragment thereof, and wherein the BMPR-2 is human BMPR-2 or a fragment thereof.
3. A BsAB according to claim 1 or 2, wherein said BsAB has agonistic activity for ALK-1/BMPR-2 signaling in a target cell.
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4. A BsAB according to claim 3, wherein said target cell is an endothelial cell.
5. A BsAB according to any one of claims 1 to 4, wherein said BsAB promotes dimerization of ALK-1 and BMPR-2.
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6. A BsAB according to any one of claims 1 to 5, wherein said BsAB promotes dimerization of ALK-1 and BMPR-2, such that an EC50 of the BsAB can be determined in a suitable assay to detect dimerization of ALK-1 and BMPR-2.
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7. A BsAB according to any one of claims 1 to 6, wherein an effective dose of said BsAB promotes phosphorylation of SMAD1 and/or SMAD5.
8. A BsAB according to any one of claims 1 to 7, wherein an effective dose of said BsAB has an anti-apoptotic effect in endothelial cells.
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9. A BsAB according to any one of claims 1 to 8, wherein an effective dose of said BsAB reduces the apoptosis of endothelial cells observed upon starvation of the cells.
10. A BsAB according to any one of claims 1 to 9, wherein an effective dose of said BsAB reduces the apoptosis of endothelial cells treated with an effective dose of TNF α and/or cycloheximide (CHX).
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11. A BsAB according to any one of claims 1 to 10, wherein the BsAB binds ALK-2 or an antigen according to SEQ ID 117 with an affinity that is lower or equal to the binding affinity of the BsAB for bovine serum albumin.
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12. A BsAB according to any one of claims 1 to 11, wherein an EC50 of said BsAB has a lower osteogenic activity than an EC50 of rhBMP-9.
13. A BsAB according to any one of claims 1 to 12, wherein C2C12 cells treated with the EC50 of rhBMP-9 have a higher alkaline phosphatase (ALP) activity than C2C12 cells treated with the same concentration of BsAB.
14. A BsAB according to any one of claims 1 to 13, wherein said BsAB has no osteogenic activity in C2C12 cells.
15. A BsAB according to any one of claims 1 to 14 for use as a medicament.
16. A BsAB according to any one of claims 1 to 15 for use in the treatment of pulmonary hypertension.
17. A method to test the suitability of a BsAB for use in therapy comprising
(i) analyzing the ability of the BsAB to promote dimerization of ALK-1 and BMPR-2, and
(ii) optionally comparing the binding affinities of the BsAB for ALK-2 and BSA, and
(iii) selecting the BsAB as suitable, where the BsAB at least promotes dimerization of ALK-1 and BMPR-2 as determined according to step (i) and optionally binds ALK-2 with an affinity that is lower or equal to the BsABs affinity for BSA, as determined according to step (ii).
18. A method to test the suitability of a BsAB for use in therapy comprising
(i) analyzing the ability of the BsAB to promote dimerization of ALK-1 and BMPR-2, and
(ii) optionally analyzing the ability of the BsAB to promote dimerization of ALK-2 and BMPR-2, and
(iii) selecting the BsAB as suitable, where the BsAB at least promotes dimerization of ALK-1 and BMPR-2 as determined according to step (i) and optionally does not promote dimerization of ALK-2 and BMPR-2 as determined according to step (ii).