

FORM 2

THE PATENTS ACT, 1970
(39 of 1970)
AND
THE PATENTS RULES, 2003

**COMPLETE
SPECIFICATION**

(See Section 10; rule 13)

TITLE OF THE INVENTION

“REGULATION OF RECEPTOR EXPRESSION THROUGH DELIVERY OF
ARTIFICIAL TRANSCRIPTION FACTORS”

APPLICANT

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The following specification particularly describes
the invention and the manner in which
it is to be performed

Claims

1. An artificial transcription factor comprising a polydactyl zinc finger protein targeting specifically a receptor gene promoter fused to an inhibitory or activatory protein domain, a nuclear localization sequence, and a protein transduction domain.
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2. An artificial transcription factor wherein the receptor gene promoter is the endothelin receptor A promoter.
- 10 3. An artificial transcription factor wherein the receptor gene promoter is the endothelin receptor B promoter.
4. An artificial transcription factor wherein the receptor gene promoter is the Toll-like receptor 4 promoter.
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5. An artificial transcription factor wherein the receptor gene promoter is the FCER1A promoter.
6. The artificial transcription factor according to claim 1, 2, 3, 4 or 5 comprising a
20 hexameric zinc finger protein.
7. The artificial transcription factor according to claim 2, 3, 4 or 5 comprising a zinc finger protein of a protein sequence selected from the group consisting of SEQ ID NO: 31 to
25 SEQ ID NO: 37, SEQ ID NO: 39 to SEQ ID NO: 43, SEQ ID NO: 45 to SEQ ID NO: 50, SEQ ID NO: 52, SEQ ID NO: 54 to SEQ ID NO: 57, SEQ ID NO: 59 to SEQ ID NO: 64, SEQ ID NO: 66 to SEQ ID NO: 80, SEQ ID NO: 82 to SEQ ID NO: 95, SEQ ID NO: 97 to SEQ ID NO: 118, SEQ ID NO: 120 to SEQ ID NO: 136, SEQ ID NO: 138 to SEQ ID NO: 143, SEQ ID NO: 145 to SEQ ID NO: 153, SEQ ID NO: 155 to SEQ ID NO: 164, SEQ ID NO: 166 to SEQ ID NO: 173, SEQ ID NO: 175 to SEQ ID NO: 181, and SEQ ID NO: 183
30 to SEQ ID NO: 191.
8. The artificial transcription factor according to claim 2, 3, 4 or 5 comprising a zinc finger protein of a protein sequence selected from the group consisting of SEQ ID NO 56, 83, 85, 101, 114, 118, 127, 133, 140, 142, 146, 147, 156, 159, 175, and 181.
- 35 9. The artificial transcription factor according to claim 2, 3, 4 or 5 comprising a zinc finger protein of SEQ ID NO 118, 133, 156, or 175.

10. The artificial transcription factor according to any one of claims 1 to 9 wherein the zinc finger protein is fused to an inhibitory protein domain.
- 5 11. The artificial transcription factor according to claim 10 wherein the inhibitory protein domain is N-terminal KRAB of SEQ ID NO: 1, C-terminal KRAB of SEQ ID NO: 2, SID of SEQ ID NO: 3, or ERD of SEQ ID NO: 4.
- 10 12. The artificial transcription factor according to any one of claims 1 to 9 wherein the zinc finger protein is fused to an activatory protein domain.
13. The artificial transcription factor according to claim 12 wherein the activatory protein domain is VP16 of SEQ ID NO: 5 or VP64 of SEQ ID NO: 6.
- 15 14. The artificial transcription factor according to any one of claims 1 to 13 wherein the nuclear localization sequences is a cluster of basic amino acids containing the K-K/R-X-K/R consensus sequence or the SV40 NLS of SEQ ID NO: 196.
- 20 15. The artificial transcription factor according to any one of claims 1 to 14 wherein the protein transduction domain is the HIV derived TAT peptide of SEQ ID NO: 7, the HSV-1 VP22 peptide, the synthetic peptide mT02 of SEQ ID NO: 192, the synthetic peptide mT03 of SEQ ID NO: 193, the R9 peptide of SEQ ID NO: 194, the ANTP domain, or the protective antigen/lethal factor N terminus PTD.
- 25 16. An artificial transcription factor comprising a polydactyl zinc finger protein targeting specifically the endothelin receptor A promoter fused to an inhibitory or activatory protein domain and a nuclear localization sequence.
- 30 17. An artificial transcription factor comprising a polydactyl zinc finger protein targeting specifically the endothelin receptor B promoter fused to an inhibitory or activatory protein domain and a nuclear localization sequence.
- 35 18. An artificial transcription factor comprising a polydactyl zinc finger protein targeting specifically the Toll-like receptor 4 promoter fused to an inhibitory or activatory protein domain and a nuclear localization sequence.

19. An artificial transcription factor comprising a polydactyl zinc finger protein targeting specifically the FCER1A promoter fused to an inhibitory or activatory protein domain and a nuclear localization sequence.

5 20. A pharmaceutical composition comprising an artificial transcription factor according to claims 1 to 19.

21. The artificial transcription factor according to claims 1 to 19 for use in modulating the reaction of cells to external stimuli and to other soluble signaling molecules.

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22. The artificial transcription factor according to claims 1 to 19 for use in treating diseases modulated by the binding of specific effectors to receptors, for which the polydactyl zinc finger protein is specifically targeting the receptor gene promoter.

15 23. The artificial transcription factor according to claims 2 or 6 to 16 for use in influencing the cellular response to endothelin, for lowering or increasing endothelin receptor A levels, and for use in the treatment of diseases modulated by endothelin.

20 24. The artificial transcription factor according to claims 3, 6 to 15 or 17 for use in influencing the cellular response to endothelin, for lowering or increasing endothelin receptor B levels, and for use in the treatment of diseases modulated by endothelin.

25 25. The artificial transcription factor according to claims 4, 6 to 15 or 18 for use in influencing the cellular response to lipopolysaccharide, for lowering or increasing Toll-like receptor 4 levels, and for use in the treatment of diseases modulated by lipopolysaccharide.

30 26. The artificial transcription factor according to claims 5 to 15 or 19 for use in influencing the cellular response to IgE, for lowering or increasing IgE receptor levels, and for use in the treatment of diseases modulated by IgE.

35 27. A method of treating diseases comprising administering a therapeutically effective amount of an artificial transcription factor according to claims 1 to 26 to a patient in need thereof, wherein the disease to be treated is modulated by the binding of specific effectors to receptors, for which the polydactyl zinc finger protein is specifically targeting the receptor gene promoter.

28. A method of treating a disease modulated by endothelin comprising administering a therapeutically effective amount of an artificial transcription factor according to claims 2, 3, or 6 to 17 to a patient in need thereof.

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