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(54) Title: FGF2-BINDING PEPTIDES AND USES THEREOF

(57) Abstract: FGF2-binding peptides are here described, which have been designed starting from the N-terminal region of PTX3, in particular spanning the PTX3(82-110) region. Synthetic peptides related to this sequence are able to bind FGF2 and to inhibit its pro-angiogenic activity in vitro and in vivo with no anticipated impact on innate immunity.

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AMENDED CLAIMS

[received by the International Bureau on 20 July 2007.]

1. A FGF2-binding peptide of formula I:

$$R_1\text{-AIa-}X_1\text{-PrO-}X_2\text{-AIa-}R_2$$

(D

wherein:

X-I is an amino acid selected between Arg and Lys;

X_2 is an amino acid selected between Cys and Thr;

R_1 is either absent or consists of the amino acid sequence selected from SEQ ID NO: 1 and SEQ ID NO: 3;

R_2 is either absent or consists of the amino acid sequence selected from SEQ ID NO: 2 and SEQ ID NO: 4, with the following provisions:

when R_1 is absent, also R_2 is absent; when R_1 is the amino acid sequence of SEQ ID NO: 1, R_2 is the amino acid sequence of SEQ ID NO: 2; when R_1 is the amino acid sequence of SEQ ID NO: 3, R_2 is an amino acid sequence selected between SEQ ID NO: 2 and SEQ ID NO: 4; a precursor or a pharmaceutically acceptable salt thereof.

2. The peptide according to claim 1, wherein X_1 is Arg.

3. The peptide according to claim 1 or 2, wherein X_2 is Cys.

4. The peptide according to any preceding claim, which consists of the amino acid sequence selected among SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 10.

5. A fused chimeric peptide comprising the peptide according to any of previous claims.

6. The fused chimeric peptide according to claim 5 wherein the fused amino acid sequence belongs to a protein sequence other than human PTX3 selected from the group of: membrane-bound proteins, extracellular regions of membrane-bound proteins, immunoglobulin constant regions, multimerization domains, extracellular proteins, signal peptide-containing proteins, export signal-containing proteins.

7. A conjugated chimeric peptide comprising the peptide according to any of previous claims.

8. A nucleic acid molecule encoding the peptide according to any of previous claims, or hydridizing with the above nucleic acid, or including a degenerated sequence thereof.

9. An expression vector comprising the nucleic acid molecule according to claim 8.

10. A host cell transformed with the expression vector according to claim 9.

11. The host cell according to claim 10 wherein the peptide is secreted or expressed on the membrane surface of the cell.

12. A peptide of claims 1 to 7 for use as a medicament.

13. A peptide of claims 1 to 7 for use as an anti-disease brought about by an altered angiogenesis.

14. The peptide of claim 13 in which the altered angiogenesis is provoked by an altered activation of the growth factor FGF2.

15. The peptide of claim 13 or 14 in which the disease is selected from the group consisting of arthritic disease, tumor metastasis, diabetic retinopathy, psoriasis, chronic inflammation, arteriosclerosis or tumor.

16. The peptide of claim 15 in which the tumor is selected from the group of: sarcoma, carcinoma, carcinoid, bone tumor or neuroendocrine tumor.

17. A peptide of claims 1 to 7 for use as anti-disease associated with uncontrolled FGF2-dependent proliferation of fibroblasts or smooth muscular cells, cicatrization linked to excessive fibroblastic response, and restenosis after angioplastic.

18. A pharmaceutical composition comprising a therapeutically effective amount of the peptide according to any of claims 1-7 and suitable diluents and/or excipients and/or adjuvants.