

CLAIMS

1. A Flt-1 decoy comprising:
 - (a) a VEGF binding domain of Flt-1; and
 - (b) a membrane anchoring domain;
- 5 in which the Flt-1 decoy does not substantially comprise an intracellular domain.
2. A Flt-1 decoy according to Claim 1 which is not soluble.
3. A Flt-1 decoy according to Claim 1 or 2, in which the Flt-1 decoy is not capable of signal transduction, such as through an SHC-GRB2, PI3K or PLC pathway.
4. A Flt-1 decoy according to Claim 1, 2 or 3, in which the Flt-1 decoy lacks an
- 10 intracellular domain, such as an intracellular signalling domain of Flt-1, preferably amino acids 819 to 1338 of GenBank Accession Number: NP_002010.2.
5. A Flt-1 decoy according to any preceding claim, in which the VEGF binding domain of Flt-1 comprises a sequence comprising amino acids 27 to 250 of GenBank Accession Number: NP_002010.2 or a fragment, homologue, variant or derivative thereof capable of
- 15 binding VEGF, preferably VEGF-A (NP_001020537.2) or VEGF-B (NP_001230662.1).
6. A Flt-1 decoy according to any preceding claim, in which the membrane anchoring domain comprises a transmembrane domain of Flt1 comprising amino acids 759 to 780 of GenBank Accession Number: NP_002010.2 or a fragment, homologue, variant or derivative thereof capable of anchoring the Flt-1 decoy to a cell membrane.
- 20 7. A Flt-1 decoy according to any preceding claim which comprises the sequence of Flt-1 (GenBank Accession Number: NP_002010.2) but without the intracellular domain (amino acids 819 to 1338 of GenBank Accession Number: NP_002010.2) or a fragment, homologue, variant or derivative thereof which is capable of binding VEGF and which is not soluble.
8. A combination of a Flt-1 decoy according to any preceding claim together with a
- 25 mirtron capable of inhibiting VEGF.
9. A combination according to Claim 8, in which the mirtron comprises:
 - (a) GTAAATGTATGTATGTGGGTGTTCAAGAGACACCCACACACATACATC
TCAGTTTTTTCTCTTTCTTTTCAG; or

(b) GTAGATTATGCGGATTAAATTTCAAGAGAGTTTGATCCGCATAATCTGT
CAGTTTTTTCTCTTTCTTTTCAG.

10. Use of a Flt-1 decoy according to any of Claims 1 to 7 or a combination according to Claim 8 or 9 in the preparation of a medicament for use as a VEGF inhibitor.
- 5 11. A Flt-1 decoy according to any of Claims 1 to 7 or a combination according to Claim 8 or 9 for use in a method of treatment or prevention of a disease.
12. A Flt-1 decoy or a combination for use according to Claim 11 in which the disease comprises macular degeneration, such as age related macular degeneration (AMD) or wet AMD, corneal neovascularization, diabetic retinopathy, retinal vein occlusions, retinopathy of
10 prematurity, any other ocular disease presenting with neovascularization, a cancer such as colon cancer, lung cancer, breast cancer, gastrointestinal stromal cancer, liver cancer, ovarian cancer, fallopian tube cancer, cervical cancer, primary peritoneal cancer, thyroid cancer, pancreatic neuroendocrine tumour, soft tissue sarcoma, glioblastoma or renal-cell carcinoma.
13. A nucleic acid capable of encoding a Flt-1 decoy according to any of Claims 1 to 7 or
15 a combination according to Claim 8 or 9.
14. An expression vector capable of encoding a Flt-1 decoy according to any of Claims 1 to 7 and a mirtron as defined in Claim 8 or 9.
15. An expression vector according to Claim 14 which is a viral expression vector such as an adenoviral expression vector, adeno-associated expression vector, plasmid construct naked
20 or complexed with liposomes or polymersomes or a dumbbell DNA construct.

CLAIMS

1. A combination of:
 - (i) Flt-1 decoy comprising:
 - (a) a VEGF binding domain of Flt-1; and
 - 5 (b) a membrane anchoring domain;

in which the Flt-1 decoy does not substantially comprise an intracellular domain; together with:
 - (ii) a mirtron capable of inhibiting VEGF.
2. A combination according to Claim 1, in which the Flt-1 decoy is not soluble.
- 10 3. A combination according to Claim 1 or 2, in which the Flt-1 decoy is not capable of signal transduction, such as through an SHC-GRB2, PI3K or PLC pathway.
4. A combination according to Claim 1, 2 or 3, in which the Flt-1 decoy lacks an intracellular domain, such as an intracellular signalling domain of Flt-1, preferably amino acids 819 to 1338 of GenBank Accession Number: NP_002010.2.
- 15 5. A combination according to any preceding claim, in which the VEGF binding domain of Flt-1 comprises a sequence comprising amino acids 27 to 250 of GenBank Accession Number: NP_002010.2 or a fragment, homologue, variant or derivative thereof capable of binding VEGF, preferably VEGF-A (NP_001020537.2) or VEGF-B (NP_001230662.1).
6. A combination according to any preceding claim, in which the membrane anchoring
 - 20 domain comprises a transmembrane domain of Flt1 comprising amino acids 759 to 780 of GenBank Accession Number: NP_002010.2 or a fragment, homologue, variant or derivative thereof capable of anchoring the Flt-1 decoy to a cell membrane.
7. A combination according to any preceding claim which comprises the sequence of Flt-1 (GenBank Accession Number: NP_002010.2) but without the intracellular domain (amino
 - 25 acids 819 to 1338 of GenBank Accession Number: NP_002010.2) or a fragment, homologue, variant or derivative thereof which is capable of binding VEGF and which is not soluble.
8. A combination according to any preceding claim, in which the mirtron comprises:

(a) GTAAATGTATGTATGTGGGTGTTCAAGAGACACCCACACACATACATC
TCAGTTTTTTCTCTTTCTTTTCAG; or

(b) GTAGATTATGCGGATTAAATTTCAAGAGAGTTTGATCCGCATAATCTGT
CAGTTTTTTCTCTTTCTTTTCAG.

- 5 9. A VEGF inhibitor comprising a combination according to any preceding claim.
10. A combination according to any preceding claim for use in the treatment or prevention of macular degeneration, such as age related macular degeneration (AMD) or wet AMD, corneal neovascularization, diabetic retinopathy, retinal vein occlusions, retinopathy of prematurity, any other ocular disease presenting with neovascularization, a cancer such as
- 10 colon cancer, lung cancer, breast cancer, gastrointestinal stromal cancer, liver cancer, ovarian cancer, fallopian tube cancer, cervical cancer, primary peritoneal cancer, thyroid cancer, pancreatic neuroendocrine tumour, soft tissue sarcoma, glioblastoma or renal-cell carcinoma.
11. A nucleic acid capable of encoding a combination according to any preceding claim.
12. An expression vector capable of encoding a Flt-1 decoy and a mirtron according to any
- 15 preceding claim.
13. An expression vector according to Claim 12 which is a viral expression vector such as an adenoviral expression vector, adeno-associated expression vector, plasmid construct naked or complexed with liposomes or polymersomes or a dumbbell DNA construct.