CLAIMS

1. An isolated ELABELA polypeptide comprising a sequence CXXXRCXXXHSRVPFP (SEQ ID NO: 1), in which X represents an amino acid residue, or a fragment, homologue, variant or derivative thereof, which comprises an ELABELA activity selected from the group consisting of: maintaining self-renewal of a stem cell, maintaining pluripotency of a stem cell, maintaining growth of a stem cell, promoting growth of a stem cell, inhibiting apoptosis, binding to the cell surface of an embryonic stem cell, biasing differentiation of a stem cell toward an endodermal or mesodermal lineage, binding to apelin receptor (APLNR), binding to CXCR4 receptor, activating the P13K/AKT pathway, cardioprotection, for example restoration or maintenance of cardiac function during ischemia and/or reperfusion, reduction of oxidative stress, reduction of infarct size and inhibition of HIV infection.

2. An isolated ELABELA polypeptide according to Claim 1, selected from one or more of the following:

(a) a sequence SEQ ID NO: 162 (XXXXXXXCXXXRCXXXHSRVPFP), in which X represents an amino acid residue, and in which position 1 of SEQ ID NO: 162 comprises a basic amino acid residue, preferably K or R;

(b) a sequence SEQ ID NO: 163 (XXXXXXXXCXXXRCXXXHSRVPFP), in which X represents an amino acid residue, and in which position 1 of SEQ ID NO: 163 comprises a basic amino acid residue, preferably K or R.

(c) a sequence SEQ ID NO: 163 (XXXXXXXXCXXXRCXXXHSRVPFP), in which X represents an amino acid residue, in which positions 1 and 2 of SEQ ID NO: 163 comprise a pair of basic amino acid residues, preferably KK, KR, RK or RR.

3. An isolated ELABELA polypeptide according to any of Claims 1 or 2, which comprises a sequence selected from the group consisting of: SEQ ID NO: 2 to SEQ ID NO: 18, preferably a human ELABELA sequence shown as SEQ ID NO: 2.

4. An isolated ELABELA polypeptide according to any of Claims 1, 2 or 3, which further comprises a signal sequence such as a human ELABELA signal sequence shown in SEQ ID NO: 19.

5. An isolated ELABELA polypeptide according to any preceding claim, which comprises a sequence selected from the group consisting of: SEQ ID NO: 20 to SEQ ID NO: 36, preferably a human ELABELA sequence shown as SEQ ID NO: 20.

6. An isolated ELABELA polypeptide according to any preceding claim, which comprises an intramolecular covalent bond between cysteine residues at or about positions 1 and 6, with reference to the numbering in the sequence CXXXRCXXXHSRVPFP (SEQ ID NO: 1), or in which one or both cysteine residues comprise a reduced cysteine having a sulfhydryl group.

7. An isolated ELABELA polypeptide according to any preceding claim, which comprises any one or more of the following:

(a) a mutation of a basic residue at position 31, preferably in which a basic residue at position 31 is mutated to a neutral residue, more preferably in which K or R at position 31 is mutated to A or G;

(b) a mutation of a basic residue at position 32, preferably in which a basic residue at position 32 is mutated to a neutral residue, more preferably in which K or R at position 32 is mutated to A or G; or

(c) a R31G, R31A, K31G or K31A substitution, preferably an R32G, R32A, K32G or K32A substitution

with reference to the position numbering of a human ELABELA sequence shown as SEQ ID NO: 20.

8. A isolated nucleic acid comprising a sequence capable of encoding an ELABELA polypeptide according to any preceding claim.

9. A isolated nucleic acid according to Claim 8, which comprises a nucleic acid sequence shown in any of SEQ ID NO. 37 to SEQ ID NO: 46, preferably a human ELABELA nucleic acid sequence SEQ ID NO: 37 or SEQ ID NO: 42.

10. A vector such as an expression vector comprising a nucleic acid according to Claim 8 or 9, a host cell such as a bacterial, fungal or yeast cell comprising such a vector or a nucleic acid, or a transgenic non-human animal comprising such a host cell, such a vector or such a nucleic acid, preferably a mammal such as a mouse.

11. An isolated antibody or antigen-binding fragment thereof capable of specifically binding to any one or more of the following:

(a) a polypeptide comprising the sequence CMPLHSRVPFP (SEQ ID NO: 52);

(b) a polypeptide comprising the sequence QRPVNLTMRRKLRKHNC (SEQ ID NO: 53);

(c) a polypeptide comprising the sequence QRPVNLTMRRKLRKHNCLQRRCMPLHSRVPFP (SEQ ID NO: 2);

(d) an ELABELA polypeptide according to any of Claims 1 to 7;

(e) an ELABELA polypeptide encoded by a nucleic acid according to Claim 8 or 9; and

(f) an ELABELA polypeptide comprising the sequence of any of SEQ ID NOs: 1-36;

the antibody or antigen-binding fragment thereof further optionally comprising a label.

12. An isolated shRNA or siRNA molecule capable of modulating any combination of the expression, amount or activity of an ELABELA polypeptide according to any of Claims 1 to 7, preferably comprising a sequence selected from the group consisting of: SEQ ID NO: 47 to SEQ ID NO: 51.

13. A method of assaying a compound of interest, the method comprising:

(a) contacting an ELABELA polypeptide according to any of Claims 1 to 7 with a candidate compound and performing an assay to determine if the candidate compound binds to the ELABELA polypeptide;

(b) contacting an ELABELA polypeptide according to any of Claims 1 to 7 with a candidate compound and performing an assay to determine if the candidate compound modulates an activity of the ELABELA polypeptide; or

(c) contacting a cell expressing an ELABELA polypeptide according to any of Claims 1 to 7 with a candidate compound and performing an assay to determine if the candidate compound causes an elevated or reduced expression, amount or activity of the ELABELA polypeptide in or of the cell;

preferably further comprising isolating or synthesising the compound of interest so identified.

14. A method of down-regulating *in vitro* or *ex vivo* any combination of the expression, amount or activity of an ELABELA polypeptide according to any of Claims 1 to 7, the method comprising exposing the ELABELA polypeptide to an antibody or antigen-binding fragment thereof according to Claim 11 or an shRNA or siRNA according to Claim 12.

15. A isolated polypeptide according to any of Claims 1 to 7, a isolated nucleic acid according to Claim 8 or 9, a vector, host cell or transgenic non-human animal according to Claim 10, an isolated antibody or antigen-binding fragment thereof according to Claim 11 or an isolated shRNA or siRNA molecule according to Claim 12 for use in the treatment, prophylaxis or alleviation of an ELABELA associated condition selected from the group consisting of:

(a) cardiac dysfunction, hypertension, or a cardiovascular anomaly in blood pressure, cardiac contractility or fluid balance;

(b) a cardiovascular disease such as cardiac hypertrophy, coronary artery disease (CAD), atherosclerosis, post-infarct treatment, myocardial ischemia-reperfusion injury or atrial fibrillation, coronary heart disease, heart failure, pulmonary arterial hypertension (PAH);

(c) a condition associated with high blood pressure, such as hypertension, angina, congestive heart failure or erectile dysfunction; and

(d) a condition associated with HIV infection, such as AIDS in an individual.

16. An isolated ELABELA polypeptide according to any of Claims 1 to 7 for use as a vasodilator.

17. A method of manipulating a cell *in vitro* or *ex vivo*, the method comprising modulating, preferably up-regulating, any combination of the expression, amount or activity of an ELABELA polypeptide according to any of Claims 1 to 7 in or of the cell, such as by exposing the cell to an ELABELA polypeptide according to any of Claims 1 to 7 or introducing a nucleic acid according to Claim 8 or 9 or a vector according to Claim 10 into the cell.

18. A method according to Claim 17 for maintaining or enhancing self-renewal and/or pluripotency in or of a stem cell, in which up-regulation of the expression, amount or activity

of an ELABELA polypeptide results in maintenance or enhancement of self-renewal and/or pluripotency in or of the stem cell.

19. A method comprising detecting any combination of the expression, amount or activity of an ELABELA polypeptide according to any of Claims 1 to 7 in or of a cell, such as a stem cell, tissue, organ or organism.

20. A combination comprising a first part comprising a sequence MPLHSRVPFP or QRPVNLTMRRKLRKHN or both and a second part comprising a polypeptide of interest, preferably in which the first part and the second part are covalently joined, such as by chemical conjugation, or in which the combination comprises a fusion protein comprising the first part and the second part.

21. An expression construct capable of expressing a fusion protein according to Claim 20.

22. A method of detecting or quantifying a polypeptide of interest, the method comprising producing a combination according to Claim 20 and detecting the presence of or quantifying the first part of the combination.

23. A method of isolating a polypeptide of interest, the method comprising producing a combination according to Claim 20 and exposing the combination to a molecule capable of specifically binding to the first part, such as an antibody or antigen-binding fragment thereof according to Claim 11.

24. A method comprising conjugating or otherwise joining a polypeptide of interest to a sequence MPLHSRVPFP or QRPVNLTMRRKLRKHN or both.

25. A method of making an ELABELA polypeptide or fragment thereof, the method comprising: (a) expressing a nucleic acid encoding a sequence comprising CXXXRCXXXHSRVPFP (SEQ ID NO: 1) in a cell, in which X is an/any amino acid residue, and in which the polypeptide fragment maintains self-renewal, pluripotency, or both of a stem cell; or (b) using chemical synthesis to generate a synthetic polypeptide or fragment thereof comprising CXXXRCXXXHSRVPFP (SEQ ID NO: 1) or a fragment having the sequence of SEQ ID NO: 53.

26. An immunoassay kit for measuring or detecting ELABELA expression, the immunoassay kit comprising:

(a) a coating antigen comprising one or more isolated antibodies or antigen-binding fragments thereof that specifically binds to one or more of the following:

(i) a polypeptide comprising the sequence CMPLHSRVPFP (SEQ ID NO: 52);

(ii) a polypeptide comprising the sequence QRPVNLTMRRKLRKHNC (SEQ ID NO: 53);

(iii) a polypeptide comprising the sequence QRPVNLTMRRKLRKHNCLQRRCMPLHSRVPFP (SEQ ID NO: 2); or

(iv) an ELABELA polypeptide comprising the sequence of any of SEQ ID NOs: 1-36; and

(b) instructions for using said coating antigen.

27. An immunoassay kit according to Claim 26, in which the isolated antibodies or antigen-binding fragments thereof are labelled.

28. An immunoassay kit according to Claim 26 or 27, further comprising an enzyme labelled reagent, a secondary antibody or antigen-binding fragment thereof that specifically binds to the isolated antibodies or antigen-binding fragments, a solid substrate, or any combination thereof.