

CLAIMS

1. An inhibitor of a *Sghrt* transcript or *Sghrt* gene transcription to produce a *Sghrt* transcript, in which the inhibitor comprises a polynucleotide comprising a sequence that is complementary to any of SEQ ID NOs: 51 to 54, or a part thereof, or a sequence that has at least 75% sequence identity with such a polynucleotide.
2. An inhibitor according to Claim 1, in which the polynucleotide comprises:
 - (a) an inhibitor of a *Sghrt* transcript comprising a sequence complementary to any of SEQ ID NOs: 51 to 53; or
 - (b) an inhibitor of *Sghrt* gene transcription to produce a *Sghrt* transcript comprising a sequence complementary to SEQ ID NO: 54; or a part thereof, or a sequence that has at least 75% sequence identity with such a polynucleotide.
3. An inhibitor according to Claim 1 or 2, in which the polynucleotide is selected from the group consisting of: an antisense oligonucleotide; a gapmer; a short interfering RNA; a short hairpin RNA; a peptide and a CRISPR-Cas, optionally a CRISPR-Cas9.
4. An inhibitor according to Claim 1, 2 or 3, in which the inhibitor has a sequence that has at least 90% sequence identity, such as at least about 95% sequence identity with the polynucleotide.
5. An inhibitor according to any preceding claim, in which the polynucleotide comprises a sequence selected from the group consisting of:

Sghrt miR RNAi GGGTCTTTGCCTGGGTTTGTT (SEQ ID NO: 57);

Sghrt miR RNAi TGGAATGTATCTGGCTCAGAA (SEQ ID NO: 58);

Sghrt sgRNA1 TTTCGTCTGAGAGTCGGCTG (SEQ ID NO: 61);

Sghrt sgRNA2 ACCAGGTAGCCACTGACCGT (SEQ ID NO: 62); and

Sghrt KD TTCGGAACCTGAAGGA (SEQ ID NO: 64).

6. An inhibitor according to any preceding claim for use as a medicament or a cardiac regenerative agent or a cardiac proliferative agent.
7. Use of an inhibitor according to any preceding claim in the manufacture of a medicament for the prevention or treatment of cardiac disease, optionally in which the prevention or treatment of cardiac disease comprises rescuing or improving heart function or at least partially rescuing or improving one or more of the following: ejection fraction; left ventricle wall thickness; right ventricle wall thickness; left ventricular wall stress; right ventricular wall stress; ventricular mass; contractile function; cardiac hypertrophy; end diastolic volume; end systolic volume; cardiac output; cardiac index; pulmonary capillary wedge pressure; and pulmonary artery pressure.
8. Use according to Claim 7, in which the cardiac disease is selected from the group consisting of: myocardial infarction; heart failure; coronary artery disease; narrowing of the arteries; heart attack; abnormal heart rhythms; arrhythmias; heart failure; heart valve disease; congenital heart disease; heart muscle disease; cardiomyopathy; pericardial disease; aorta disease; marfan syndrome; genetic cardiomyopathy; non-genetic cardiomyopathy; cardiac hypertrophy; pressure overload-induced cardiac dysfunction; and damaged heart tissue.
9. A pharmaceutical composition comprising an inhibitor according to any of Claims 1 to 5, together with a suitable carrier, adjuvant, diluent and/or excipient.
10. A vector comprising or encoding a polynucleotide according to any of Claims 1 to 5, optionally in which the vector is selected from the group consisting of: a plasmid; a viral particle; a phage; a baculovirus; a yeast plasmid; a lipid based vehicle; a polymer microsphere, a liposome, and a cell based vehicle; a colloidal gold particle; lipopolysaccharide; polypeptide; polysaccharide; a viral vehicle; an adenovirus; a retrovirus; a lentivirus; an adeno-associated viruses; a herpesvirus; a vaccinia virus; a foamy virus; a cytomegalovirus; a Semliki forest virus; a poxvirus; a pseudorabies virus; an RNA virus vector; a DNA virus vector and a vector derived from a combination of a plasmid and a phage DNA, optionally in which the polynucleotide is operatively linked to an expression control sequence(s) to direct RNA synthesis,

optionally in which the vector comprises one or more selectable marker genes to provide a phenotypic trait for selection of transformed host cells.

11. An *in vitro* method for the proliferation, regeneration or dedifferentiation of a heart cell, the method comprising contacting the heart cell, optionally a cardiomyocyte, further
5 optionally an adult cardiomyocyte, with an inhibitor according to any of Claims 1 to 5, a pharmaceutical composition according to Claim 9 or a vector according to Claim 10.

12. A prognostic or diagnostic method to assess the regenerative or proliferative capacity of heart tissue before, after or during a cardiac treatment regimen comprising:

determining the presence or amount of a Sghrt transcript in a cardiac sample of the heart
10 tissue; and

where Sghrt transcript is present concluding the proliferative capacity of the heart tissue is poor; and

where Sghrt transcript is absent concluding the proliferative capacity of the heart tissue is good,

15 in which the Sghrt transcript is selected from the group consisting of SEQ ID NO: 51 to 53.

13. A method according to Claim 12, in which the determining step involves extracting RNA and performing single nuclear RNA-sequencing then comparing the RNA sequences obtained with any of SEQ ID NOs: 51 to 54 or a part thereof to determine whether a transcript
20 of Sghrt is present, optionally in which an amplification is undertaken before RNA-sequencing.

14. A method according to Claim 12 or 13, in which the determining step involves assaying for the functional activity of the transcript, including use of a competitive binding assay for the transcript target.

25 15. A kit comprising PCR primers for amplifying a Sghrt transcript according to Claim 1, and/or probes for hybridizing to the transcript, optionally in which the transcript is selected from the group consisting of SEQ ID NOs: 51 to 53.

16. A method for screening for a therapeutic agent that may be used to treat or to prevent a heart disorder in an individual, the method comprising:

- 5 analyzing a functional expression and/or an expression level of a Sghrt transcript, in which the Sghrt transcript is selected from the group consisting of SEQ ID NO: 51 to 53, in the presence and in the absence of a candidate therapeutic agent; and
- determining if the candidate therapeutic agent is a useful therapeutic agent for treating or preventing a heart disorder based on the differences in the functional expression and/or expression level of the Sghrt transcript in the presence of the candidate therapeutic agent and in the absence of the candidate therapeutic agent.