

Claims

1. At least one inhibitor for inhibiting any one or more of the following:
 - a) a *Sghrt* transcript;
 - b) *Sghrt* gene transcription to produce a *Sghrt* transcript;
comprising an isolated polynucleotide comprising or consisting of a sequence:
 - i) that is complementary to a *Sghrt* transcript or its coding sequences i.e. SEQ ID NO:51-54 or a part thereof; or
 - ii) that is complementary to gDNA *Sghrt* non-coding sequence provided in SEQ ID NO:67, or a part thereof;
 - iii) a sequence that shares at least 75% identity with the polynucleotide of i) and/or ii),optionally wherein said isolated polynucleotide interacts with its complementary sequence to block the function of same.
2. The inhibitor according to claim 1, wherein said isolated polynucleotide interacts with said transcript of *Sghrt* and so is complementary to any one of SEQ ID NOs:51-53, or a part thereof and/or interacts with said coding region for said transcript of *Sghrt* and so is complementary to SEQ ID NO:54, or a part thereof.
3. The inhibitor according to claim 1, wherein said isolated polynucleotide interacts with said *Sghrt* gene and so is complementary to the non-coding sequences provided in SEQ ID NO: 67, or a part thereof.
4. The inhibitor according to any one of the preceding claims, wherein said isolated polynucleotide is selected from the group comprising or 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.

5. The inhibitor according to any one of the preceding claims, wherein said isolated polynucleotide shares at least about 90% percentage sequence identity with the polynucleotide of i) or ii).
6. The inhibitor according to any one of the preceding claims, wherein said isolated polynucleotide shares at least about 95% percentage sequence identity with the polynucleotide of i) or ii).
7. The inhibitor according to any one of the preceding claims wherein said isolated polynucleotide comprises a sequence selected from the group comprising or 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: TTCGGAAGTTGAAGGA (SEQ ID NO. 64).
8. An inhibitor for inhibiting:

Sghrt gene transcription to produce a Sghrt transcript, said transcript is optionally a mRNA or a lincRNA;

the inhibitor comprising an isolated polynucleotide comprising or consisting of a sequence:

 - i) that is complementary to gDNA Sghrt SEQ ID NO:67, or a part thereof; or
 - ii) a sequence that shares at least 75% identity with the polynucleotide of i).
9. The inhibitor according to any one of the preceding claims for use as a medicament or a cardiac regenerative agent or a cardiac proliferative agent.
10. Use of an inhibitor according to any one of the preceding claims in the manufacture of a medicament for the prevention or treatment of cardiac disease, optionally wherein said preventing or treating 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.

11. The use according to claim 10, wherein said cardiac disease is selected from the group comprising or 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.

12. A pharmaceutical composition comprising the inhibitor according to any one of claims 1-11 and a suitable carrier, adjuvant, diluent and/or excipient.

13. A vector comprising or encoding said isolated polynucleotide according to any one of claims 1-12,

optionally wherein said vector is selected from the group comprising or 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 wherein said polynucleotide is operatively linked to an expression control sequence(s) to direct RNA synthesis,

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

14. 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 optionally an adult cardiomyocyte, with the inhibitor according to any one of claims 1-11, or the pharmaceutical composition according to claim 12, or the vector according to claim 13.
15. 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 said heart tissue; and
 - where Sghrt transcript is present concluding the proliferative capacity of said heart tissue is poor; and
 - where Sghrt transcript is absent concluding the proliferative capacity of said heart tissue is good.
16. The method according to claim 15, wherein said determining step involves extracting RNA and performing single nuclear RNA-sequencing then comparing the RNA sequences obtained with any one or more of SEQ ID Nos:51-54 and 67 or a part thereof to determine whether a transcript of Sghrt is present,
 - optionally wherein an amplification is undertaken before said RNA-sequencing.
17. The method according to claim 15 or claim 16, wherein said determining step involves assaying for the functional activity of said transcript, including use of a competitive binding assay for the transcript target.

18. A kit comprising PCR primers for amplifying the Sghrt transcript of claim 1, and/or probes for hybridizing to said transcript, optionally wherein the transcript is selected from the group consisting of SEQ ID Nos: 51-53.
19. A method for screening for a therapeutic agent that can be used to treat or to prevent a heart disorder in an individual, the method comprising:
- analyzing a functional expression and/or an expression level of a Sghrt transcript 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.