## SUMMARY

[0004] In one aspect, the present disclosure refers to a use of a Tjp1 inhibitor in the manufacture of a medicament for treating a heart disease in a subject, wherein the heart disease is a heart disease where heart cells regeneration is beneficial for the subject. In another aspect, the present disclosure refers to a cardiac patch, wherein the patch comprises the Tjp1 inhibitor as disclosed herein. In one example, there is provided a method for treating a heart disease in a subject comprising the step of administering to the subject a therapeutically effective amount of Tjp1 inhibitor. In one example, the Tjp1 inhibitor is a nucleic acid. In one example, the nucleic acid is selected from the group consisting of an siRNA, an shRNA, an antisense oligonucleotide, a gapmers, and a short hairpin Antisense Oligonucleotide (shAON). In one example, the nucleic acid binds to mRNA which encodes Tjp1 and forms a nucleic acid-mRNA complex. In one example, the mRNA in the nucleic acid-mRNA complex is cleaved and/or is not translated. In one example, the nucleic acid encoding the inhibitor has at least 90% identity to a sequence selected from the group consisting of SEQ ID NO:1 (CCGGGCCTGCATACAATAAAGCAAACTCGAGTTTGCTTTATTGTATGCAGGCTTTTTG), SEQ ID NO:2 (CCGGGGAACCACTCTATCAAGTATTCTCGAGAATACTTGATAGAGTGGTTCCTTTTTG), SEQ ID NO: 3 (CCGGCGTGGATTGAACTTACTAAATCTCGAGATTTAGTAAGTTCAATCCACGTTTTTG), and SEQ ID NO: 4 (CCGGCCGCGAAGTTATGAGCAAGTTCTCGAGAACTTGCTCATAACTTCGCGGTTTTTG).

[0005] In one example, the method further comprises administering an additional factor selected from the group consisting of a polypeptide and a nucleic acid together or separately with the Tjp1 inhibitor. In one example, the nucleic acid is encoding Cyclin A2. In one example, the polypeptide binds to ErbB4 receptors. In one example, the polypeptide binding ErbB4 receptors is selected from the group consisting of Neuregulin-1, Neuregulin-2 (NRG2), Neuregulin-3 (NRG3), Betacellulin (BTC), Epiregulin (EPR), Heparin Binding EGF-like Growth Factor (HB-EGF), Epidermal Growth Factor (EGF), β-Cellulin, Transforming Growth Factor Alpha (TGFα), and Amphiregulin (AR). In one example, the polypeptide binding ErbB4 receptors is Neuregulin-1 (NRG1). In one example, the

polypeptide activates Wnt signaling. In one example, the polypeptide activating Wnt signaling is selected from the group consisting of Wnts, Norrin, and R-spondin. In one example, the polypeptide is a growth factor or a secreted factor. In one example, the growth factor is Fibroblast Growth Factor (FGF) or Vascular Endothelial Growth Factor (VEGF). In one example, the secreted factor is Follistatin-like 1 (Fstl1).

[0006] In one example, wherein when the inhibitor is a nucleic acid inhibitor, the method comprises a virus-mediated delivery system. In one example, the virus is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, and a herpes simplex virus. In one example, the virus is an adeno-associated virus. In one example, the adeno-associated virus is AAV serotype 9.

[0007] In another example, there is provided use of a Tjp1 inhibitor in the manufacture of a medicament for treating a heart disease. In one example, the heart disease is selected from the group consisting of myocardial infarct, acute myocardial infarction (AMI), heart failure, cardiomyopathy, congenital heart disease, acquired cardiovascular disease, cardiomyocytes deficiency, cardiac ischemic reperfusion injury, cardiac trauma, and other cardiac injury in a patient where heart cells regeneration is beneficial.

[0008] In yet another example, there is provided a patch, wherein the patch comprises the Tjp1 inhibitor as defined herein.

[0009] In yet another example, there is provided a nucleic acid encoding a Tjp1 inhibitor, wherein the nucleic acid has at least 90% identity to a sequence selected from the group consisting of SEQ ID NO:1 (CCGGGCCTGCATACAATAAAGCAAACTCGAGTTTGCTTTATTGTATGCAGGCTTTTTG), SEQ ID NO:2 (CCGGGGAACCACTCTATCAAGTATTCTCGAGAATACTTGATAGAGTGGTTCCTTTTTG), SEQ ID NO: 3 (CCGGCGTGGATTGAACTTACTAAATCTCGAGATTTAGTAAGTTCAATCCACGTTTTTG), and SEQ ID NO: 4 (CCGGCCGCGAAGTTATGAGCAAGTTCTCGAGAACTTGCTCATAACTTCGCGGTTTTTG).

## BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The invention will be better understood with reference to the detailed description when considered in conjunction with the non-limiting examples and the accompanying drawings, in which:

[0011] **Figure 1** shows a set of experimental results that illustrate efficient inducible deletion of Tjp1 in cardiomyocytes (CMs). **Figure 1A** shows a Western blot analysis for expression of Tjp1 on lysates of control (Ctrl; $Tjp1^{F/F}$ Myh6-$Cre^{ERT2}$) and two independent

**Claims**

1. Use of a Tjp1 inhibitor in the manufacture of a medicament for treating a heart disease in a subject, wherein the heart disease is a heart disease where heart cells regeneration is beneficial for the subject.
2. The use of claim 1, wherein the Tjp1 inhibitor is a nucleic acid.
3. The use of claim 1 or 2, wherein the nucleic acid is selected from the group consisting of an siRNA, an shRNA, an antisense oligonucleotide, a gapmers, and a short hairpin Antisense Oligonucleotide (shAON).
4. The use of any one of the preceding claims, wherein the nucleic acid binds to mRNA which encodes Tjp1 and forms a nucleic acid-mRNA complex.
5. The use of any one of the preceding claims, wherein the mRNA in the nucleic acid-mRNA complex is cleaved and/or is not translated.
6. The use of any one of the preceding claims, wherein the nucleic acid encoding the inhibitor has at least 90% identity to a sequence selected from the group consisting of SEQ ID NO: 1 (CCGGGCCTGCATACAATAAAGCAAACTCGAGTTTGCTTTATTGTATGCAGGCTTTTTG), SEQ ID NO: 2 (CCGGGGAACCACTCTATCAAGTATTCTCGAGAATACTTGATAGAGTGGTTCCTTTTTG), SEQ ID NO: 3 (CCGGCGTGGATTGAACTTACTAAATCTCGAGATTTAGTAAGTTCAATCCACGTTTTTG), and SEQ ID NO: 4 (CCGGCCGCGAAGTTATGAGCAAGTTCTCGAGAACTTGCTCATAACTTCGCGGTTTTTG).
7. The use of any one of the preceding claims, wherein the use further comprises administering an additional factor selected from the group consisting of a polypeptide and a nucleic acid to be administered together or separately with the Tjp1 inhibitor.
8. The use of claim 7, wherein the nucleic acid is encoding Cyclin A2.
9. The use of claim 7, wherein the polypeptide binds to ErbB4 receptors.

10. The use of claim 9, wherein the polypeptide binding ErbB4 receptors is selected from the group consisting of Neuregulin-1, Neuregulin-2 (NRG2), Neuregulin-3 (NRG3), Betacellulin (BTC), Epiregulin (EPR), Heparin Binding EGF-like Growth Factor (HB-EGF), Epidermal Growth Factor (EGF), β-Cellulin, Transforming Growth Factor Alpha (TGFα), and Amphiregulin (AR).

11. The use of claim 10, wherein the polypeptide binding ErbB4 receptors is Neuregulin-1 (NRG1).

12. The use of claim 7, wherein the polypeptide activates Wnt signaling.

13. The use of claim 12, wherein the polypeptide activating Wnt signaling is selected from the group consisting of Wnts, Norrin, and R-spondin.

14. The use of claim 7, wherein the polypeptide is a growth factor or a secreted factor.

15. The use of claim 14, wherein the growth factor is Fibroblast Growth Factor (FGF) or Vascular Endothelial Growth Factor (VEGF).

16. The use of claim 14, wherein the secreted factor is Follistatin-like 1 (Fstl1).

17. The use of any one of the preceding claims, wherein when the inhibitor is a nucleic acid inhibitor, the use comprises a virus-mediated delivery system.

18. The use of claim 17, wherein the virus is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, and a herpes simplex virus.

19. The use of claim 18, wherein the virus is an adeno-associated virus.

20. The use of claim 19, wherein the adeno-associated virus is AAV serotype 9.

21. The use of any one of claims 1 to 20, wherein the heart disease is selected from the group consisting of myocardial infarct, acute myocardial infarction (AMI), heart failure, cardiomyopathy, congenital heart disease, acquired cardiovascular disease, cardiomyocytes deficiency, cardiac ischemic reperfusion injury, cardiac trauma, and other cardiac injury in a patient where heart cells regeneration is beneficial.

22. A cardiac patch, wherein the patch comprises the Tjp1 inhibitor as defined in any one of claims 1 to 20.