Zimmermann et al. Biotechnol. Bioeng. (2000), 68(1), 106 to 14. It was possible that the mammalian engineered heart tissues has coordinated beating with directed force development and heart muscle like physiology and pharmacological responses. The pouch-like structure described in WO 2008/058917 is based on said mammalian engineered heart tissue accordingly. This mammalian engineered heart tissue includes cardiomyocytes. The engineered heart tissue may also be obtained from heart tissue other than cardiomyocytes. For example, fibroblasts, smooth muscle cells etc. may be used.

However, despite the recent increased focus on developing advanced models of engineered tissues, several clinical challenges remain to be addressed: Engineered cardiac structures should be of a clinical relevant size and thickness and consists of immunologically tolerable cell populations in a matrix similar to the host heart. In addition, these structures must also be able to connect to the host blood supply, propagate electrical pulses which must be synchronised with the host myocardium and subsequently generate sufficient contactile force to aid in blood circulation.

Aim of the present invention is to provide new pouch-like structures for applications in heart failure treatment, disease modelling, drug development, and target identification as well as validation.

Brief description of the present invention

In a first aspect, the present invention relates to pouch-like structure suitable for enclosing at least a part of a heart of a mammal, comprising: an engineered tissue comprising genetically engineered cells that contain a transgene encoding a paracrine factor operably linked to an inducible promoter or a heterologous promoter, wherein the genetically engineered cells are cells other than cardiac myocytes and are selected from the group consisting of fibroblasts, smooth muscle cells, endothelial cells, mesenchymal stem cells, cardiac stem cells, pericytes, leucocytes, precursor cells, and pluripotent stem cells. Also described herein is a pouch-like structure suitable for enclosing at least a part of the heart of a mammal, said pouch-like structure comprises an engineered tissue wherein at least a part of the engineered tissue comprised genetically engineered cells, like, genetically engineered cells other than cardiomyocytes, whereby said genetically engineered cells, like, other than cardiomyocytes contain a gene encoding a paracrine factor, said gene encoding the paracrine factor being under control of an inducible promoter system or heterologous promoter system.

For example, the paracrine factor may be protein factors including different types of growth factors like IGF-1 but also other types of compounds having cardio protective or regeneration inducing properties on cardiac tissue, like nucleic acid molecules including miRNA.

The inducible promoter system or the heterologous promoter system may be a chemically inducible promoter system known in the art.

In one example the engineered tissue present in the pouch-like structure contains additionally cardiomyocytes.

In a further example, the present disclosure relates to a method for the preparation of a pouch-like structure suitable for enclosing at least a part of the heart of a mammal and comprising engineered tissue, said engineered tissue comprising genetically engineered cells, like, genetically engineered cells other than cardiac myocytes, which contain a gene encoding a paracrine factor and said gene being under control of an inducible promoter system or an heterologous promoter system, said method comprises the step of

a) providing a matrix having a recess in one surface of the matrix, which recess has appropriate dimensions to hold a defined reconstitution volume for the formation of the pouch-like structure,
b) providing a body having dimensions corresponding to the desired dimensions of the interior of the pouch-like structure to be formed, and positioning the body in the recess of the matrix such that the body is spaced from the walls of the recess to form a space between the body and the walls of the recess corresponding to the reconstitution volume needed for formation of a pouch-like structure,
c) depositioning a reconstitution mixture in the recess, which reconstitution mixture comprises mammalian cells, like allogenic cells, or autologous cells, and suitable scaffold material which can be incubated to form an engineered tissue structure comprising said cells,
d) incubating the reconstitution mixture until the tissue construct forms within the matrix recess between the body and the matrix,
e) exchanging the culture medium once the pouch-like construct has formed around the central body,
f) removing the body with the tissue construct adherent thereto from the matrix recess, and
g) separating the tissue construct form the body,

wherein at least a part of the mammalian cells present in the engineered tissue structure are genetically engineered cells, like, genetically engineered cells other than cardiac myocytes whereby said genetically engi-

Claims:

1. A pouch-like structure suitable for enclosing at least a part of a heart of a mammal, comprising: an engineered tissue comprising genetically engineered cells that contain a transgene encoding a paracrine factor operably linked to an inducible promoter or a heterologous promoter, wherein the genetically engineered cells are cells other than cardiac myocytes and are selected from the group consisting of fibroblasts, smooth muscle cells, endothelial cells, mesenchymal stem cells, cardiac stem cells, pericytes, leucocytes, precursor cells, and pluripotent stem cells.

2. The pouch-like structure according to claim 1 wherein said engineered tissue further comprises at least one of myocytes and cells of heart tissue other than cardiac myocytes.

3. The pouch-like structure according to claim 1 wherein said paracrine factor has cardioprotective and/or cardio regeneration inducing activity.

4. The pouch-like structure according to claim 1 wherein said inducible promoter is chemically inducible.

5. The pouch-like structure according to claim 4 wherein said inducible promoter is selected from a tetracycline based promoter, a rapamycin based promoter, a progesterone based promoter, or an ecdysone based promoter.

6. The pouch-like structure according to claim 1 wherein said engineered tissue further comprises contractile cardiomyocytes, wherein said cardiomyocytes are not genetically engineered.

7. The pouch-like structure according to claim 3 wherein the paracrine factor is selected from the group consisting of IGF-1, VEGF, HGF, PDGF, SDF-1, and miRNA.

8. The pouch-like structure according to claim 3 wherein the paracrine factor is miRNA selected from the group consisting of miR133, miR1, miR15 family, miR-199a-3p, miR-590-3p, miR1825, and miR33b.