[0005a] In one aspect, the present disclosure refers to the use of an amount of cells effective to treat a cardiovascular disorder in the manufacture of a medicament for the treatment of the cardiovascular disorder, where the medicament is to be administered to a subject identified as a hyper-responder to cell therapy.

[0006] In one example, described herein is a method of treating a cardiovascular disorder in a subject in need thereof comprising administering to a subject identified as a hyper-responder to cell therapy an amount of cells to treat the cardiovascular disorder in the subject. In some examples, the subject is suffering from a cardiovascular disorder such as, for example, heart failure, adriamycin-induced cardiomyopathy, idiopathic dilated cardiomyopathy, ischemic cardiomyopathy, myocarditis, ischemic heart disease, cardiomyopathy due to infiltrative myocardial disease, cardiomyopathy due to amyloidosis, cardiomyopathy due to sarcoidosis, cardiomyopathy due to hemochromatosis, peripartum cardiomyopathy, cardiomyopathy due to hypertension, cardiomyopathy due to infection with the human immunodeficiency virus, cardiomyopathy due to connective-tissue disease, cardiomyopathy due to scleroderma, cardiomyopathy due to systemic lupus erythematosus, cardiomyopathy due to Marfan's syndrome, cardiomyopathy due to polyarteritis nodosum, cardiomyopathy due to nonspecific connective-tissue disease, cardiomyopathy due to ankylosing spondylitis, cardiomyopathy due to rheumatoid arthritis, cardiomyopathy due to relapsing polychondritis, cardiomyopathy due to Wegener's granulomatosis, cardiomyopathy due to mixed connective-tissue disease, cardiomyopathy due to substance abuse, cardiomyopathy due to chronic alcohol abuse, cardiomyopathy due to cocaine abuse, cardiomyopathy due to doxorubicin therapy, restrictive cardiomyopathy, familial cardiomyopathy, cardiomyopathy due to valvular heart disease, cardiomyopathy due to endocrine dysfunction, cardiomyopathy due to thyroid disease, cardiomyopathy due to carcinoid, cardiomyopathy due to pheochromocytoma, cardiomyopathy due to acromegaly, cardiomyopathy due to neuromuscular disease, cardiomyopathy due to neoplastic heart disease, cardiomyopathy due to congenital heart disease, cardiomyopathy due to complication of coronary-artery bypass surgery, cardiomyopathy due to radiation, cardiomyopathy due to critical illness, cardiomyopathy due to endomyocardial fibroelastosis, cardiomyopathy due to thrombotic thrombocytopenic purpura, cardiomyopathy due to rheumatic carditis, cardiomyopathy due to leukotriene therapy, cardiomyopathy due to lithium therapy or

cardiomyopathy due to prednisone therapy. In various examples, the method improves vascular tone.

[0007] In some examples, the cells are mesenchymal stem cells, induced pluripotent stem cells, embryonic stem cells and/or cardiac stem cells. In some examples, the cells are mesenchymal stem cells (MSCs). In some examples, the cells (e.g., MSCs) are allogeneic cells (e.g., allogeneic MSCs). In some examples, the cells (e.g., MSCs) are autologous cells (e.g., autologous MSCs). In some examples, the cells (e.g., MSCs) are obtained from bone marrow, cord blood, adipose tissue, Wharton's Jelly or amniotic fluid.

[0008] In some examples, the method comprises determining the presence or absence of one or more pathologic variants in a gene associated with a cardiovascular disorder in a sample of the subject, wherein the absence of the pathologic genetic variant(s) identifies the subject as a hyper-responder to cell therapy. In some examples, the subject is screened for one or more pathologic genetic variants set forth in Figure 1 (i.e., it is determined whether the subject comprises a mutation in one or more of the genes of Figure 1). In some examples, the subject is screened for one or more pathologic genetic variants in one or more of the following genes: ACTC, NYH7, MYH6, MYBPC3, TNNT2, TNNC1, TNNI3, TPM1, TTN, DMD, DES, LDB3, SGCD, PDLIM3, VCL, RYAB, ILK, LAMA4, FLNC, TCAP, CSRP3, ACTN2, MYPN, ANKRD1, BAG3, LMNA, TMPO, PSEN1, PSEN2, PLN, EYA4, TAZ/G4.5, CPT2, ACADVL, RBM20, ABCC, SCN5A, GATAD1, PRDM16, GAA, FKRP, CTNNA3, DSP, PKP2, SOS2, and ALMS1 (i.e., any combination of the referenced genes are contemplated). Thus, in some examples, the subject (e.g., a subject presenting with a cardiovascular disorder), lacks a pathologic genetic mutation in one or more of the genes set forth in Figure 1 (e.g., ACTC, NYH7, MYH6, MYBPC3, TNNT2, TNNC1, TNNI3, TPM1, TTN, DMD, DES, LDB3, SGCD, PDLIM3, VCL, RYAB, ILK, LAMA4, FLNC, TCAP, CSRP3, ACTN2, MYPN, ANKRD1, BAG3, LMNA, TMPO, PSEN1, PSEN2, PLN, EYA4, TAZ/G4.5, CPT2, ACADVL, RBM20, ABCC, SCN5A, GATAD1, PRDM16, GAA, FKRP, CTNNA3, DSP, PKP2, SOS2, and/or ALMS1). In some examples, the subject lacks a pathologic mutation in one or more of the following genes: ANKRD, BAG3, DMD, GATAD1, LDB3, LMNA, MYBPC3, MYH6, RBM20, TNNT2, TTN and RBM20. Optionally, the subject lacks a pathologic mutation in all of ANKRD, BAG3, DMD, GATAD1, LDB3, LMNA, MYBPC3, MYH6, RBM20, TNNT2, TTN and RBM20.

[0009] The cells (e.g., mesenchymal stem cells, induced pluripotent stem cells, embryonic stem cells or cardiac stem cells) are administered according to any suitable method, including those known in the art. In some examples, the cells are administered locally. In some examples, the cells (e.g., mesenchymal stem cells, induced pluripotent stem cells, embryonic stem cells or cardiac stem cells) are administered by transendocardial injection.

[0010] The cells (e.g., mesenchymal stem cells, induced pluripotent stem cells, embryonic stem cells or cardiac stem cells) are optionally administered in an amount ranging from about 20 million to about 10 billion cells. In some examples, the cells (e.g., mesenchymal stem cells, induced pluripotent stem cells, embryonic stem cells or cardiac stem cells) are administered in an amount ranging from about 20 million to about 30 million cells, or about 20 millions to about 40 million cells, or about 20 million to about 50 million cells, or about 20 million to about 60 million cells, or about 20 million to about 70 million cells, or about 20 million to about 80 million cells, or about 20 million to about 90 million cells, or about 30 million to about 50 million cells, or about 30 million to about 70 million, or about 30 million to about 90 million cells, or about 50 million to about 100 million cells, or about 100 million to about 300 million cells, or about 200 million to about 400 million cells, or about 500 million to about 1 billion cells, or about 500 million to about 10 billion cells. In some examples, about 20 million, or about 25 million, or about 30 million, or about 35 million, or about 40 million, or about 45 million, or about 50 million, or about 55 million, or about 50 million, or about 55 million, or about 60 million, or about 65 million, or about 70 million, or about 75 million, or about 80 million, or about 85 million, or about 90 million, or about 95 million, or about 100 million, or about 200 million, or about 300 million, or about 400 million, or about 500 million, or about 600 million, or about 700 million, or about 800 million, or about 900 million, or about 1 billion, or about 2 billion, or about 3 billion, or about 4 billion, or about 5 billion, or about 6 billion, or about 7 billion, or about 8 billion, or about 9 billion, or about 10 billion cells are administered to the subject.

[0011] In some examples, administration of the cells (e.g., mesenchymal stem cells, induced pluripotent stem cells, embryonic stem cells or cardiac stem cells) to the subject results in an increase in flow-mediated vasodilation (FMD) in the subject of at least 3%.

[0012] In any of the methods described herein, the subject is a human subject.

BRIEF DESCRIPTION OF THE FIGURES

[0013] Figure 1 is a table providing the genetic profiles of individual patients. Colored cells represent PV- ((patients 6, 10, 18, 22, 28 and 34), VUS (patient 1 (TTN), patient 2 (GATAD1, GAA), patient 3 (LDB3), patient 4 (LMNA, PRDM16), patient 5 (FKRP), patient 7 (ACADVL), patient 9 (CTNNA3, DSP, SOS2, ALMS1), patient 11 (ANKRD1), patient 13

What is claimed is:

1. Use of an amount of cells effective to treat a cardiovascular disorder in the manufacture of a medicament for treating the cardiovascular disorder in a subject, where the subject is identified as a hyper-responder to cell therapy.

2. The use of claim 1, wherein the cell therapy is mesenchymal stem cell therapy, cardiac stem cell therapy, induced pluripotent stem cell therapy, or embryonic stem cell therapy.

3. The use of claim 2, wherein the cell therapy is mesenchymal stem cell therapy.

4. The use of claim 3, wherein the cell therapy is allogeneic mesenchymal stem cell therapy.

5. The use of claim 3, wherein the cell therapy is autologous mesenchymal stem cell therapy.

6. The use of claim 1, wherein the method comprises determining the presence or absence of a pathologic variant in one or more genes associated with a cardiovascular disorder in a sample of the subject, wherein the absence of the pathologic genetic variant(s) identifies the subject a hyper-responder to cell therapy.

7. The use of claim 6, wherein the one or more genes are selected from ACTC, NYH7, MYH6, MYBPC3, TNNT2, TNNC1, TNNI3, TPM1, TTN, DMD, DES, LDB3, SGCD, PDLIM3, VCL, RYAB, ILK, LAMA4, FLNC, TCAP, CSRP3, ACTN2, MYPN, ANKRD1, BAG3, LMNA, TMPO, PSEN1, PSEN2, PLN, EYA4, TAZ/G4.5, CPT2, ACADVL, RBM20, ABCC, SCN5A, GATAD1, PRDM16, GAA, FKRP, CTNNA3, DSP, PKP2, SOS2, and ALMS1 and combinations thereof.

8. The use of claim 6, wherein the one or more genes are selected from the group consisting of ANKRD, BAG3, DMD, GATAD1, LDB3, LMNA, MYBPC3, MYH6, RBM20, TNNT2, TTN and RBM20, and combinations thereof.

9. The use of claim 1, wherein the cardiovascular disorder is heart failure, adriamycin-induced cardiomyopathy, idiopathic dilated cardiomyopathy, ischemic cardiomyopathy, myocarditis, ischemic heart disease, cardiomyopathy due to infiltrative myocardial disease, cardiomyopathy due to amyloidosis, cardiomyopathy due to sarcoidosis, cardiomyopathy due to hemochromatosis, peripartum cardiomyopathy, cardiomyopathy due to

hypertension, cardiomyopathy due to infection with the human immunodeficiency virus, cardiomyopathy due to connective-tissue disease, cardiomyopathy due to scleroderma, cardiomyopathy due to systemic lupus erythematosus, cardiomyopathy due to Marfan's syndrome, cardiomyopathy due to polyarteritis nodosum, cardiomyopathy due to nonspecific connective-tissue disease, cardiomyopathy due to ankylosing spondylitis, cardiomyopathy due to rheumatoid arthritis, cardiomyopathy due to relapsing polychondritis, cardiomyopathy due to Wegener's granulomatosis, cardiomyopathy due to mixed connective-tissue disease, cardiomyopathy due to substance abuse, cardiomyopathy due to chronic alcohol abuse, cardiomyopathy due to cocaine abuse, cardiomyopathy due to doxorubicin therapy, restrictive cardiomyopathy, familial cardiomyopathy, cardiomyopathy due to valvular heart disease, cardiomyopathy due to endocrine dysfunction, cardiomyopathy due to thyroid disease, cardiomyopathy due to carcinoid, cardiomyopathy due to pheochromocytoma, cardiomyopathy due to acromegaly, cardiomyopathy due to neuromuscular disease, cardiomyopathy due to neoplastic heart disease, cardiomyopathy due to congenital heart disease, cardiomyopathy due to complication of coronary-artery bypass surgery, cardiomyopathy due to radiation, cardiomyopathy due to critical illness, cardiomyopathy due to endomyocardial fibroelastosis, cardiomyopathy due to thrombotic thrombocytopenic purpura, cardiomyopathy due to rheumatic carditis, cardiomyopathy due to leukotriene therapy, cardiomyopathy due to lithium therapy or cardiomyopathy due to prednisone therapy.

10. The use of claim 1, wherein the cells are to be administered locally.

11. The use of claim 10, wherein the cells are to be administered by transendocardial injection.

12. The use of claim 1, wherein the cells are to be administered in an amount ranging from 20 million to 10^9 cells.

13. The use of claim 11 or claim 12, wherein the cells are to be administered by one or more transendocardial injections into one or more sites on the ventricle of the subject.

14. The use of claim 11, wherein the cells are to be administered by ten transendocardial injections into ten sites on the left ventricle of the subject.

15. The use of claim 11, wherein the cells are to be administered by fifteen transendocardial injections into fifteen sites on the left ventricle of the subject.

16. The use of claim 11, wherein the cells are to be administered by twenty transendocardial injections into twenty sites on the left ventricle of the subject.

17. The use of claim 11 or claim 12, wherein the cells are to be administered in an amount of about 400 million cells.

18. The use of claim 1, wherein administration of the cells results in an increase in flow-mediated vasodilation (FMD) in the subject of at least 3%.

19. The use of claim 1, wherein administration of the cells results in an increase of ejection fraction in the subject compared to the ejection fraction of the subject prior to treatment with the cells.

20. The use of claim 1, wherein administration of the cells results in the subject having an increased six-minute walk distance compared to the six-minute walk distance prior to treatment with the cells.