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Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.
For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

Experimental design

1. Sample size

Describe how sample size was determined.

Initial sample size per experiment was determined based on preliminary studies, and were different for different types of assays, as necessary to achieve statistical significance of data. Statistical methods were not used to predetermine sample size. Instead, sample sizes were chosen to include a minimum of n=3 independent biological replicates per experiment, and multiple independent experiments were performed. To further verify the experimental results, the experiments were repeated using three iPS cell lines from three different donors.

2. Data exclusions

Describe any data exclusions.

No data were excluded from the analyses.

3. Replication

Describe the measures taken to verify the reproducibility of the experimental findings.

A total of 253 independently grown cardiac tissues were analyzed, with 12-94 tissues per experimental group, and excellent reproducibility of the experiments.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Engineered tissues were randomly allocated into the experimental groups

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

The investigators as well as the facilities providing specific analytical assessments were blinded to experimental group allocation.

Note: all in vivo studies must report how sample size was determined and whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒	A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	A statement indicating how many times each experiment was replicated
☐	☒	The statistical test(s) used and whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒	Test values indicating whether an effect is present *Provide confidence intervals or give results of significance tests (e.g. P values) as exact values whenever appropriate and with effect sizes noted.*
☐	☒	A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒	Clearly defined error bars in all relevant figure captions (with explicit mention of central tendency and variation)

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	All software packages used in the study (e.g., for the measurements of force, contractility, and calcium responses) is specified in the Methods. The commercial or open source software included LabChart 8, Matlab 2014b, and GraphPad Prism 5. The custom-developed software will be made available to other investigators if requested.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a third party.	There are no restrictions, all materials used in the study are available.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	All antibodies and their sources are specifically described in the table within the "Immunofluorescent staining" section of the Methods.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	Three lines of human induced pluripotent stem cells (iPS cells) were used in the experiments. These cell lines were obtained through Material Transfer Agreements from Stephen Duncan, University of Wisconsin (C2A line), Bruce Conklin, Gladstone Institute (WT11 line) and Masayuki Yazawa, Columbia University (IMR90 line).
b. Describe the method of cell line authentication used.	All iPS lines we have used are well characterized and published. The autheticity of these lines and their derivatives (iPS-cardiomyocytes) were further confirmed by monitoring marker expression and conducting functional assays. This was also the method for assuring reproducibility of the experiments over 4 years of duration of the study.
c. Report whether the cell lines were tested for mycoplasma contamination.	The cells were regularly tested for mycoplasma (by PCR) and karyotype.
d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	No commonly misidentified cells were used.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide all relevant details on animals and/or animal-derived materials used in the study.	No animals were used.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.	There were no human research participants in the study.