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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main

Statistical parameters

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text, or Metrious section).					
n/a	Cor	nfirmed			
	\boxtimes	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement			
	\boxtimes	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly			
		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.			
	\boxtimes	A description of all covariates tested			
		A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons			
		A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)			
		For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>			
\boxtimes		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings			

Our web collection on <u>statistics for biologists</u> may be useful.

For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes

Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated

Software and code

Policy information about availability of computer code

State explicitly what error bars represent (e.g. SD, SE, CI)

Clearly defined error bars

Data collection

- $1.\ FibPredictor\ was\ utilized\ as\ a\ commercially\ available\ software\ for\ generating\ native-like\ amyloid\ fibril\ structures,\ as\ previously\ published\ (DOI:\ 10.1007/s00894-016-3066-1).\ This\ software\ is\ available\ online\ at:\ http://nanohub.org/resources/fibpredictor$
- 2. DichroCalc was used to calculate theoretical CD spectra using predicted PDB files from FibPredictor. This web interface, which predicts secondary structure type using a variety of matrix method parameters, is described as previously published (DOI: 10.1093/bioinformatics/btp016). This commercially available software is available at: http://comp.chem.nottingham.ac.uk/dichrocalc/
- 3. Disconnect open-source software was used to predict Tandem-MS peptide fragmentation patterns for peptides containing disulfide bonds. This software is described as previously published (DOI: 10.1039/C3MB25534D and DOI: 10.1371/journal.pone.0044913). This software is available at http://www.mmass.org.

Data analysis

GraphPad Prism 6 was used to plot all spectra and perform statistical analysis, as described in the methods section.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about <u>availability of data</u>

All manuscripts must include a <u>data availability statement</u>. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The authors declare that all data supporting the findings of this study are available within the article and its supplementary information files.

Field-specific reporting						
Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.						
Life sciences Behavioural & social sciences						
For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf						
Tot a reference copy of th	ne document w	itii ali sectioris, see <u>nature.com autriorsy politicisy reporting summary-mat.pur</u>				
Life sciences						
Study design	l					
All studies must disclose on these points even when the disclosure is negative.						
Sample size	Sample size for test animals with peptide injection was n=5 for this proof-of-concept study.					
Data exclusions	No data points were excluded.					
Replication	All attempts at replication were successful.					
Randomization	Animals were randomly selected to recieve the various treatments. There was no predetermination of treatment.					
Blinding	n/a					
Materials & 6	exnerim	vental systems				
Materials & experimental systems Policy information about availability of materials						
Policy information about <u>availability of materials</u> n/a Involved in the study						
n/a Involved in the study Unique materials						
Antibodies						
Eukaryotic cell lines						
Research animals						
Human research participants						
Unique materials						
Obtaining unique	materials	Synthesis of the unique, functionalized cyclic peptides are described in the text. Characterization of these materials is also included.				
Antibodies						
Antibodies used		Primary Antibodies: Mouse-anti-rat-α-actinin (sarcomeric) antibody (A7811) from Sigma Mouse-anti-rat CD68 (MCA341R) from Biorad Rat-anti-rabbit cleaved caspase-3 (9664) from Cell Signaling				
		Secondary Antibodies: Goat-anti-mouse Alexa Fluor 488 (A-11001) from Thermo Fisher Goat-anti-rabbit 647 (A-31573) from Thermo Fisher				
Validation		The validation results for all commercial antibodies used are available on the manufacturers website.				

Eukaryotic cell lines

Policy information about <u>cell lines</u>

Cell line source(s)

Unspun whole human blood (citrated, non-heparinized) from Biological Specialty Corporation (LS23 95099) were used within

Cell line source(s)	20 days of receipt.				
	Human fetal cardiomyocyte progenitor cells (hCMPCs) were isolated from human fetal hearts as described in the methods section.				
Authentication	Whole human blood was tested in accordance with AABB guidelines and FDA requirements for infectious disease state tests. Tests were negative for Hepatitis B surface antigen, HVB NAT, HIV 1&2 antibody, HIV NAT, HCV antibody, HCV NAT, syphilis, west nile virus NAT, HTLV I/II (leukocyte products only), and T.cruzi antibodies.				
Mycoplasma contamination	Stem cells were confirmed mycoplasma negative before undertaking any experiments.				
Commonly misidentified lines (See <u>ICLAC</u> register)	n/a				
Research animals					
Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research					
Animals/animal-derived materia	S Female Sprague-Dawley rats				
Method-specific reporting					
n/a Involved in the study					
ChIP-seq					

Flow cytometry

Magnetic resonance imaging