

## Major Resources Table

In order to allow validation and replication of experiments, all essential research materials listed in the Methods should be included in the Major Resources Table below. Authors are encouraged to use public repositories for protocols, data, code, and other materials and provide persistent identifiers and/or links to repositories when available. Authors may add or delete rows as needed.

### Animals (in vivo studies)

Species	Vendor or Source	Background Strain	Sex	Persistent ID / URL
Rattus norvegicus	In house breeding	WT	Male	13452
Rattus norvegicus	In house breeding	WT	Male	13453
Rattus norvegicus	In house breeding	WT	Male	13844
Rattus norvegicus	In house breeding	WT	Male	13845
Rattus norvegicus	In house breeding	WT	Male	13846
Rattus norvegicus	In house breeding	WT	Male	18246
Rattus norvegicus	In house breeding	WT	Male	18249
Rattus norvegicus	In house breeding	WT	Male	13454
Rattus norvegicus	In house breeding	WT	Male	13774
Rattus norvegicus	In house breeding	WT	Male	18240
Rattus norvegicus	In house breeding	WT	Male	18244
Rattus norvegicus	In house breeding	WT	Male	14315
Rattus norvegicus	In house breeding	KO	Male	14024
Rattus norvegicus	In house breeding	KO	Male	14242
Rattus norvegicus	In house breeding	KO	Male	18212
Rattus norvegicus	In house breeding	KO	Male	18238
Rattus norvegicus	In house breeding	KO	Male	16991
Rattus norvegicus	In house breeding	KO	Male	16999
Rattus norvegicus	In house breeding	KO	Male	14245
Rattus norvegicus	In house breeding	KO	Male	18204
Rattus norvegicus	In house breeding	KO	Male	18233
Rattus norvegicus	In house breeding	KO	Male	14244
Rattus norvegicus	In house breeding	KO	Male	14245
Rattus norvegicus	In house breeding	WT	Male	15392
Rattus norvegicus	In house breeding	WT	Male	18274
Rattus norvegicus	In house breeding	WT	Male	15403
Rattus norvegicus	In house breeding	WT	Male	22958
Rattus norvegicus	In house breeding	WT	Male	22654
Rattus norvegicus	In house breeding	WT	Male	22962
Rattus norvegicus	In house breeding	WT	Male	23017
Rattus norvegicus	In house breeding	KO	Male	19677
Rattus norvegicus	In house breeding	KO	Male	19672
Rattus norvegicus	In house breeding	KO	Male	19916
Rattus norvegicus	In house breeding	KO	Male	00350
Rattus norvegicus	In house breeding	KO	Male	00351
Rattus norvegicus	In house breeding	KO	Male	00352
Rattus norvegicus	In house breeding	KO	Male	00353

We are aware that physiological and pathophysiological processes in the bodies of humans and animals may be sex-dependent. Such sex-dependent differences in severity and symptomatology have also been observed in cardiovascular patients and in animal models. However, for this experiment we have chosen to initially select only male animals because

male animals usually react more sensitively with blood pressure increases than female animals, which can be protected from blood pressure increases by their sex hormones.

In future experiments, we will also use female animals to confirm that our findings are sex-independent.

Another reason for limiting the experiments to the use of males was German animal legislation, which is particularly restrictive in Berlin, and authorities enforce that scientists carry out animal experiments with as few animals as possible.

## Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Persistent ID / URL
PDE3A	Bethyl lab	A302-740A	1:1000	<a href="https://www.fortislife.com/search?query=pde3a&amp;pageSize=15">https://www.fortislife.com/search?query=pde3a&amp;pageSize=15</a>
PDE3A	Santacruz	SC 293446	1:20	<a href="https://www.scbt.com/p/pde3a-antibody-2d7">https://www.scbt.com/p/pde3a-antibody-2d7</a>
PDE3A	Novusbio	H00005139-M03	1:50	<a href="https://www.novusbio.com/products/pde3a-antibody-2d7_h00005139-m03">https://www.novusbio.com/products/pde3a-antibody-2d7_h00005139-m03</a>
Flag	Sigma	F7425	1:2000	<a href="https://www.sigmaaldrich.com/GB/en/product/sigma/f7425">https://www.sigmaaldrich.com/GB/en/product/sigma/f7425</a>
GAPDH	ProteinTech	60004-1-1g	1:5000	<a href="https://www.ptglab.com/products/GAPDH-Antibody-60004-1-1g.htm">https://www.ptglab.com/products/GAPDH-Antibody-60004-1-1g.htm</a>
phosphoPKA substrate antibody	Cell signaling	9621S	1:1000	<a href="https://www.cellsignal.com/products/primary-antibodies/phospho-ser-thr-pka-substrate-antibody/9621">https://www.cellsignal.com/products/primary-antibodies/phospho-ser-thr-pka-substrate-antibody/9621</a>
phosphoPKA substrate antibody	Cell Signalling	9624	1:1000	<a href="https://www.cellsignal.com/products/primary-antibodies/phospho-pka-substrate-rxrs-t-100g7e-rabbit-mab/9624">https://www.cellsignal.com/products/primary-antibodies/phospho-pka-substrate-rxrs-t-100g7e-rabbit-mab/9624</a>
SMAD4	Cell Signaling	46535	1:1000	<a href="https://www.cellsignal.com/products/primary-antibodies/smad4-d3r4n-xp-rabbit-mab/46535">https://www.cellsignal.com/products/primary-antibodies/smad4-d3r4n-xp-rabbit-mab/46535</a>
SMAD4	Genetex	GTX01674	1:100	<a href="https://www.genetex.com/Product/Detail/SMAD4-antibody-B-8/GTX01674">https://www.genetex.com/Product/Detail/SMAD4-antibody-B-8/GTX01674</a>
GATA4	Cell Signaling	36966	1:1000	<a href="https://www.cellsignal.com/products/primary-antibodies/gata-4-d3a3m-rabbit-mab/36966">https://www.cellsignal.com/products/primary-antibodies/gata-4-d3a3m-rabbit-mab/36966</a>
HDAC1	Cell Signaling	34589	1:1000	<a href="https://www.cellsignal.com/products/primary-antibodies/hdac1-d5c6u-xp-rabbit-mab/34589">https://www.cellsignal.com/products/primary-antibodies/hdac1-d5c6u-xp-rabbit-mab/34589</a>
Lamin B	Cell Signaling	12586	1:1000	<a href="https://www.cellsignal.com/products/primary-antibodies/lamin-b1-d4q4z-rabbit-mab/12586">https://www.cellsignal.com/products/primary-antibodies/lamin-b1-d4q4z-rabbit-mab/12586</a>
Lamin A/C	Cell Signaling	4777s	1:1000	<a href="https://www.cellsignal.com/products/primary-antibodies/lamin-a-c-4c11-mouse-mab/4777?site-search-type=Products&amp;N=4294956287&amp;Ntt=4777s&amp;fromPage=plp&amp;_requestid=599758">https://www.cellsignal.com/products/primary-antibodies/lamin-a-c-4c11-mouse-mab/4777?site-search-type=Products&amp;N=4294956287&amp;Ntt=4777s&amp;fromPage=plp&amp;_requestid=599758</a>
Actin1 alpha	Proteintech	17521-1-AP	1:1000	<a href="https://www.ptglab.com/products/ACTA1-skeletal-Muscle-Actin-Specific-Antibody-17521-1-AP.htm">https://www.ptglab.com/products/ACTA1-skeletal-Muscle-Actin-Specific-Antibody-17521-1-AP.htm</a>
RFP	Abcam	Ab62341	1:2000	<a href="https://www.abcam.com/rfp-antibody-ab62341.html">https://www.abcam.com/rfp-antibody-ab62341.html</a>
PKA $\alpha$ cat	Santacruz	Sc-28315	1:1000	<a href="https://www.scbt.com/p/pkaalpha-cat-antibody-a-2">https://www.scbt.com/p/pkaalpha-cat-antibody-a-2</a>

DOI [to be added]

PKARII $\alpha$	Santacruz	Sc-908	1:1000	<a href="https://www.scbt.com/p/pka-ii-alpha-reg-antibody-c-20">https://www.scbt.com/p/pka-ii-alpha-reg-antibody-c-20</a>
GFP	abcam	Ab6556	1:1000	<a href="https://www.abcam.com/gfp-antibody-ab6556.html">https://www.abcam.com/gfp-antibody-ab6556.html</a>
Anti mouse HRP	SCBT	Sc2005	1:5000	<a href="https://www.scbt.com/p/goat-anti-mouse-igg-hrp">https://www.scbt.com/p/goat-anti-mouse-igg-hrp</a>
Anti mouse HRP	Jackson immuno research lab	115-035-003	1:5000	<a href="https://www.jacksonimmuno.com/catalog/products/115-035-003">https://www.jacksonimmuno.com/catalog/products/115-035-003</a>
Anti Rabbit HRP	SCBT	Sc2030	1:5000	<a href="https://www.scbt.com/p/goat-anti-rabbit-igg-hrp-cruz-marker-compatible">https://www.scbt.com/p/goat-anti-rabbit-igg-hrp-cruz-marker-compatible</a>
Anti rabbit HRP	Jackson immuno research lab	11-035-003	1:5000	<a href="https://www.google.com/search?q=11-035-003&amp;rlz=1C1CHBF_enGB833GB833&amp;oq=11-035-003&amp;aqs=chrome..69i57.678j0j4&amp;sourceid=chrome&amp;ie=UTF-8">https://www.google.com/search?q=11-035-003&amp;rlz=1C1CHBF_enGB833GB833&amp;oq=11-035-003&amp;aqs=chrome..69i57.678j0j4&amp;sourceid=chrome&amp;ie=UTF-8</a>
Alexaflour 647	Thermo Fischer Scientific	A-21235	1:350	<a href="https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-21235">https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-21235</a>
Alexaflour 488	Thermo Fischer Scientific	A-11008	1:350	<a href="https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11008">https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11008</a>

## DNA/cDNA Clones

Clone Name	Sequence	Source / Repository	Persistent ID / URL
Flag SMAD4	Clone Id Ora42717	Genescript	<a href="https://www.genscript.com/gene/rattus-norvegicus/50554/smad4.html">https://www.genscript.com/gene/rattus-norvegicus/50554/smad4.html</a>
Flag HDAC1	Clone Id Ora13308	Genescript	<a href="https://www.genscript.com/gene/rattus-norvegicus/297893/hdac1.html">https://www.genscript.com/gene/rattus-norvegicus/297893/hdac1.html</a>
mCherry	Cat # 1767	Vector Biolabs	<a href="https://www.vectorbiolabs.com/product/1767-mcherry-adenovirus/">https://www.vectorbiolabs.com/product/1767-mcherry-adenovirus/</a>
Ad-HDAC1 virus	Cat # 1498	Vector Biolabs	<a href="https://www.vectorbiolabs.com/product/1498-histone-deacetylase-1-adenovirus/?azsid=5f965e30-8caa-4c14-99f2-30f63f1ddd14&amp;i=1">https://www.vectorbiolabs.com/product/1498-histone-deacetylase-1-adenovirus/?azsid=5f965e30-8caa-4c14-99f2-30f63f1ddd14&amp;i=1</a>
Ad-RFP PDE3A1		Vector Biolabs	Customised
Ad-RFP PDE3A2		Vector Biolabs	Customised
Ad-RFP DNPDE3A1		Vector Biolabs	Customised
Ad-RFP DNPDE3A2		Vector Biolabs	Customised

Name	Vendor or Source	Sex (F, M, or unknown)	Persistent ID / URL
hiPSC line LUMCi027-A-1	Leiden University Medical Center, LUMC	Female	<a href="https://hpscereg.eu/cell-line/LUMCi027-A-1">https://hpscereg.eu/cell-line/LUMCi027-A-1</a>
hiPSC line LUMC0099iCTRL04	Leiden University Medical Center, LUMC	Female	<a href="https://hpscereg.eu/cell-line/LUMCi004-A">https://hpscereg.eu/cell-line/LUMCi004-A</a>
AX5858	Censo biotechnologies Ltd, Edinburgh, UK	Female	<a href="https://axolbio.com/">https://axolbio.com/</a>

DOI [to be added]

hiPSC line M00398C08	A gift from Christian Pinset, Institute for Stem cell Therapy and Exploration of Monogenic diseases (I-Stem, France)	unknown	<a href="https://orcid.org/0000-0002-7840-2179">https://orcid.org/0000-0002-7840-2179</a>
hiPSC line M00180	A gift from Christian Pinset, Institute for Stem cell Therapy and Exploration of Monogenic diseases (I-Stem, France)	Female	<a href="https://orcid.org/0000-0002-7840-2179">https://orcid.org/0000-0002-7840-2179</a>
HEK 293T "293T (ATCC CRL-3216)"	American Type Culture Collection	female	<a href="https://www.atcc.org/products/crl-3216">https://www.atcc.org/products/crl-3216</a>

## Data & Code Availability

Description	Source / Repository	Persistent ID / URL
Project files generated from mass spectrometry analysis of PDE interactome and phosphoproteome experiments deposited under the project name "Integrated proteomics unveils regulation of cardiac myocytes hypertrophic growth by a nuclear cAMP nanodomain under the control of PDE3A"	PRIDE (PRoteomics IDentification Database)	<a href="http://www.ebi.ac.uk/pride">www.ebi.ac.uk/pride</a> Project accession: PXD033773

## Other

Description	Source / Repository	Persistent ID / URL
Fluorimetric histone deacetylase kit CS1010	Sigma- Aldrich	<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>
Raeasy kit ( Cat no 74104)	Qiagen	<a href="http://www.qiagen.com/">http://www.qiagen.com/</a>
QuantiTect® Reverse Transcription Kit (Cat no 205311)	Qiagen	<a href="http://www.qiagen.com/">http://www.qiagen.com/</a>
The NE-PER Nuclear and Cytoplasmic Extraction Reagent Kit ( Cat No 78333)	Thermo Fischer	<a href="https://www.thermofisher.com/uk/en/home.html">https://www.thermofisher.com/uk/en/home.html</a>
iScript™ cDNA Synthesis Kit	Biorad	<a href="https://www.bio-rad.com/">https://www.bio-rad.com/</a>
Norepinephrine	Sigma- Aldrich	<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>
Cilostamide, isoproterenol	Sigma- Aldrich	<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>
<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>	Sigma- Aldrich	<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>
3-isobutyl-1-methylxanthine (IBMX)	Sigma- Aldrich	<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>
Norepinephrine	Sigma- Aldrich	<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>
BAY 60-7550	Sigma- Aldrich	<a href="https://www.sigmaaldrich.com/">https://www.sigmaaldrich.com/</a>