

SUPPLEMENTAL MATERIAL

Supplemental Figures

Figure S1. PDE5 is Expressed in Pediatric RV Cardiomyocytes

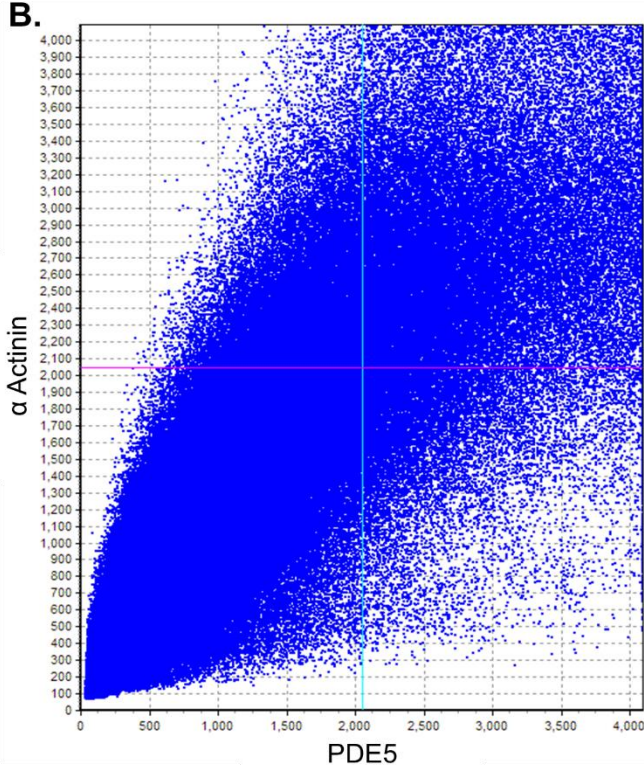
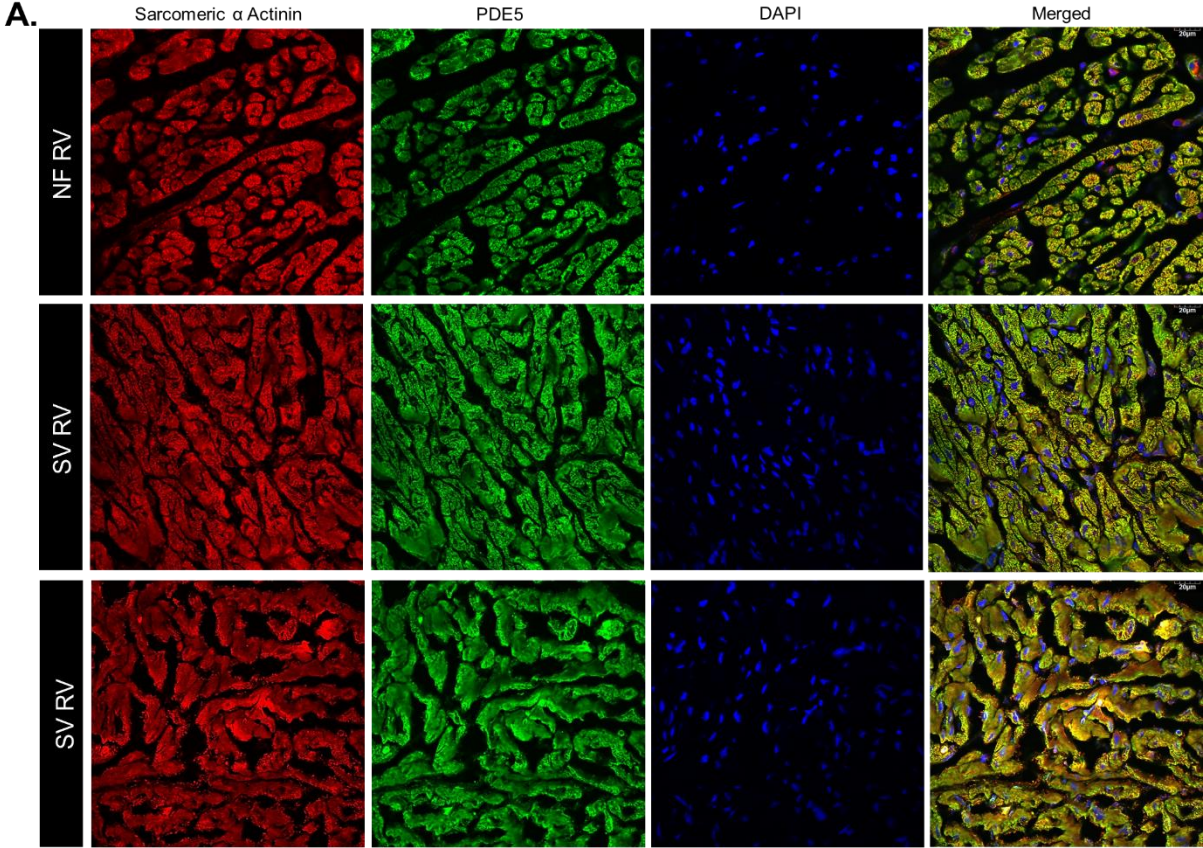


Figure S2. Top Canonical Pathways Activated by SV Serum Treatment *in vitro*

Top Canonical Pathways		
Name	NF vs SV Activation z-score	NF+PDE5i vs SV+PDE5i Activation z-score
Ceramide Signaling	1.7	1.4
p38 MAPK Signaling	1.6	0.82
Phospholipase C Signaling	2.5	0.38
Cardiac Hypertrophy Signaling	0.5	-1
Actin Cytoskeleton Signaling	1.8	-0.33

Supplemental Tables

Table S1. Subject Characteristics

ID	Age at Tissue Collection (yrs)	Sex	PDE3i	PDE5i	Non-PDEi Inotrope	Digoxin	ACEi	β -Blocker	Diuretic	Last Surgical Palliation	Indication for Transplant	RV PDE5 Activity	RV PDE5 Protein	RV PDE5 IHC	NRVM Serum Treatment RT-PCR	NRVM Serum Treatment RNAseq	RV RT-PCR
Single Right Ventricle (n=18)																	
1	3.85	F	Y	Y	N	Y	N	N	Y	Glenn	Systolic HF	X			X	X (pooled)	X
2	3.81	M	Y	N	N	NA	NA	N	NA	Fontan	Systolic HF	X	X				X
3	0.87	F	Y	N	N	Y	Y	N	N	Norwood	Systolic HF	X			X	X	X
4	0.83	F	Y	N	N	N	N	N	Y	Norwood	Systolic HF				X	X (pooled)	X
5	4.96	M	Y	N	Y	Y	Y	N	Y	Fontan	Systolic HF	X					
6	2.84	F	Y	N	N	Y	Y	N	Y	Glenn	Systolic HF	X	X				X
7	10.06	M	Y	Y	N	N	Y	N	Y	Fontan	Systolic HF, PLE	X			X		X
8	0.44	M	Y	N	N	N	Y	N	Y	Norwood	Systolic HF	X	X				X
9	2.27	M	Y	N	N	Y	Y	N	Y	Glenn	Systolic HF	X	X				X
10	0.99	F	N	N	N	Y	Y	N	Y	Norwood	Systolic HF	X	X		X		X
11	1.27	M	N	N	N	N	Y	N	Y	Hybrid Stage 1 (PA banding)	Systolic HF		X				X
12	2.92	M	Y	Y	N	Y	Y	N	Y	Glenn	Systolic HF		X	X	X	X	X
13	12.26	M	N	N	N	Y	Y	N	N	Glenn	Systolic HF			X	X		X
14	0.23	M	Y	N	N	Y	N	N	Y	Norwood	Systolic HF			X	X		X
15	4.75	M	N	N	N	N	N	N	N	Glenn	Systolic HF, PLE				X		
16	0.73	F	N	N	N	Y	N	N	Y	Hybrid Stage 1 (PDA stent, bilateral PA banding)	Systolic HF				X		X
17	0.92	M	N	N	N	N	N	N	Y	Norwood	Systolic HF				X		
18	5.08	M	N	Y	N	Y	Y	N	Y	Glenn	Systolic HF				X		
Non-Failing (n=17)																	
1	13.58	F	N	N	N	N	N	N	N	--	--				X	X	
2	11.48	M	N	N	N	N	N	N	N	--	--				X	X	
3	15.45	F	N	N	N	N	N	N	N	--	--				X	X	
4	0.42	F	N	N	N	Y	N	N	N	--	--				X		
5	7	M	N	N	N	N	N	N	N	--	--				X		
6	14	M	N	N	N	N	N	N	N	--	--	X					
7	1.3	F	N	N	Y	N	N	N	N	--	--	X	X				X
8	3.24	F	N	N	Y	N	N	N	N	--	--	X	X				X
9	9.51	M	N	N	Y	N	N	Y	N	--	--	X					X
10	7.4	M	N	N	Y	N	N	N	N	--	--	X	X				X
11	1.4	M	N	N	N	N	N	N	N	--	--	X	X				X
12	7	M	N	N	N	N	N	N	N	--	--		X				X
13	8	F	N	N	N	N	N	N	N	--	--	X	X				X
14	17	M	N	N	N	N	N	N	N	--	--		X				
15	13.65	M	N	N	N	N	N	N	N	--	--		X				
16	8.69	M	N	N	N	N	N	N	N	--	--		X				
17	2.87	M	N	N	Y	N	N	N	N	--	--			X			

Table S2. RT-qPCR Primer Sequences

Target	Sequence
r/h 18S F r/h 18S R	GCC GCT AGA GGT GAA ATT CTT G CTT TCG CTC TGG TCC GTC TT
r BNP F r BNP R	GGT GCT GCC CCA GAT GAT T CTG GAG ACT GGC TAG GAC TTC
r ANF F r ANF R	GCG AAG GTC AAG CTG CTT CTG GGC TCC AAT CCT GTC AAT
r β -MHC F r β -MHC R	CGC TCA GTC ATG GCG GAT GCC CCA AAT GCA GCC AT
r α -MHC F r α -MHC R	CCT GTC CAG CAG AAA GAG C CAG GCA AAG TCA AGC ATT CAT ATT TAT TGT G
h CERK F h CERK R	GCGGATGCCTGCTCTGTG ACT GCC TTG ATG TTT CCC GT
h CREB5 F h CREB5 r	AGA GAG CAA GTG AGC GAG AG CCA GGC CAA GCG ATG ATG TA
h FYN F h FYN R	GTA GTC ATG GCA ACC CGC TA ACA ACC CCC ACC CTC ATT TC
h ANKRD1 F h ANKRD1 R	GCC AAA GAC AGA GAA GGA GAT AC GAG ATC CGC GCC ATA CAT AAT
h ACTN2 F h ACTN2 R	GGA GAA CCG GAC TCC CGA GAA CTC CAG CTT CTT CTG CAT GGC TT
h MAFK F h MAFK R	CTG GGA TGC AGA CTC TCG AC CCC ACT CTT CAC CCT GCA AT

Table S3. Differentially Expressed Transcripts

Gene	Mean SV Fold vs NF
NF vs SV p<0.05	
5S_RRNA	-1.646180342
6720489N17RIK	-0.655669082
A930018M24RIK	-2.217353613
AABR06000382.1	1.001453421
AABR06007342.1	1.024314418
AABR06010214.2	1.650833181
AABR06010472.1	0.523964523
AABR06011545.1	-1.912229994
AABR06023589.1	0.58087928
AABR06024097.1	0.658273107
AABR06024251.1	0.413693705
AABR06026863.1	0.464373705
AABR06027280.1	1.050008555
AABR06029472.1	1.587547191
AABR06033179.1	0.673896244
AABR06036827.1	0.914353521
AABR06037778.1	2.045651522
AABR06038971.1	1.392086118
AABR06040258.1	-0.991919217
AABR06040815.1	-2.138605286
AABR06041819.1	-1.63444874
AABR06044860.1	-1.941822365
AABR06045205.1	-0.634564267
AABR06046241.1	1.712642835
AABR06048498.1	1.186323031
AABR06048982.1	1.972023405
AABR06053456.1	-1.202504971
AABR06053812.1	0.557585172
AABR06057556.1	0.323986256
AABR06058265.2	0.389768665
AABR06058815.1	1.050008555
AABR06060087.2	-0.873848025
AABR06060231.1	0.864326125
AABR06061565.1	1.215329037
AABR06064750.1	1.591720725
AABR06064824.1	0.974062854
AABR06065588.2	0.569561596
AABR06065806.1	-0.654542605

AABR06066473.1	0.897136763
AABR06069280.1	1.058057794
AABR06070504.1	-0.601679977
AABR06078259.1	2.345180871
AABR06080116.1	0.487362668
AABR06082055.1	-1.072294105
AABR06082339.1	-0.773580795
AABR06083207.1	1.64863059
AABR06085043.1	0.281667994
AABR06086840.1	0.569278487
AABR06087659.1	0.516177111
AABR06091093.1	0.53696711
AABR06098247.1	0.421485963
AABR06098740.1	0.302591378
AABR06100487.1	0.591194544
AABR06100487.2	0.644269592
AABR06100965.1	0.914576446
AABR06101044.1	1.591544099
AABR06107093.1	0.232294946
ABCB9	1.178008288
ABCC8	-0.893969086
ABHD8	-0.640625552
ABI3BP	0.792680895
ABLIM2	-1.471768608
ACE3	1.187308649
ACKR2	2.729050206
ACSL4	0.901234329
ACSS2	0.862136359
ACTC1	0.976344019
ACTN2	0.473984096
ACTR1A	0.356218257
ADAL	-0.857306886
ADAM10	-0.711785474
ADAM11	-0.818450795
ADAM15	0.843256277
ADAMTS19	1.993868118
ADAMTS3	-1.1835838
ADAMTS7	-0.627998946
ADAMTS8	-0.241177845
ADAMTSL3	-1.314154432
ADAMTSL5	0.507752592
ADAR	-0.399737376
ADCK3	-0.921416405

ADCY4	0.693384254
ADCY5	-0.429999298
ADCY8	-1.956614667
ADH1	2.525669885
ADI1	-0.37742382
ADM2	2.015688008
ADRA1D	-0.579228857
ADSSL1	-0.79703688
AGBL5	-0.568035088
AGFG1	0.464358617
AGK	0.4968621
AGPAT2	0.621798062
AK4	1.603186509
AKIP1	1.553030816
ALAS1	0.607059175
ALDH2	0.618122182
ALDH3A2	0.505519938
ALG3	0.351616428
ALOX12	-1.392308656
ALS2	-0.399081953
AMER1	-1.233632942
AMIGO1	-0.494631255
AMPD3	-0.731816225
ANGPTL2	0.862887553
ANKMY2	-0.366413575
ANKRD1	1.000858681
ANKRD10	-0.604316756
ANXA2	0.473586919
ANXA5	0.818955004
APOH	-1.511927729
APOLD1	0.868765479
ARAP3	1.218460535
ARHGAP27	0.842137506
ARHGAP29	-0.499353888
ARHGAP39	-0.572715807
ARHGEF10	-0.386789816
ARHGEF17	-0.580804818
ARHGEF5	-0.511437877
ARHGEF6	0.647089047
ARL16	0.449278229
ARL3	0.359324982
ARL4A	0.721526501
ARMC7	-0.557236111

ARNTL	0.571319797
ARRDC3	-1.270772383
ARVCF	-0.931398398
ASB14	-2.184012537
ASIC1	1.487656662
ASPM	-0.556329023
ATF3	2.074117271
ATF4	0.752754774
ATG14	-0.358460863
ATP11A	-0.492866863
ATP4A	1.403276052
ATP6AP1L	-1.198703469
ATP6V0E1	0.559518166
ATP8A1	1.134513847
ATXN10	0.548552037
ATXN7	-0.844295955
AVPI1	0.937307024
AXIN2	-0.698391243
AXL	0.518357854
B3GAT1	-2.567315433
B3GNT2	0.543064798
B3GNT5	1.83761358
B4GALNT2	-1.253235627
B4GALT1	0.569204579
BAHCC1	-0.74666213
BAK1	0.403997893
BC024978	-0.672785971
BCAT1	0.796309556
BCHE	-1.063980079
BCL11B	-1.142491371
BCL7A	-0.498557339
BCL9	-0.437607897
BDH1	1.020674305
BEAN1	1.870429754
BHLHE40	0.63220649
BHLHE41	-0.892122441
BIN2A	1.834335747
BMP2	1.00488817
BMP5	-1.367015495
BMP6	0.726489712
BNIP3	0.858950915
BOC	-0.651613607
BOD1	-0.545457139

BOK	0.891366501
BPIFA1	2.691508718
BRCA2	-0.569140911
BRD3	-0.484219438
BRINP2	-0.371621574
BTBD8	-0.953656804
BTG2	1.009718514
C1QTNF9	-1.187169215
C2CD4B	2.93241104
C2CD5	-0.82138836
C3AR1	1.418762964
CABLES1	0.930626676
CACNA1H	0.498424511
CAD	-0.388716222
CAMK1D	-0.960728214
CAMK2A	-0.600729884
CAMTA1	1.128395021
CAP1	0.376498046
CAPG	1.091327704
CAPN12	-1.436916241
CAR12	1.501524156
CAR4	2.847949081
CAR5B	1.25980516
CAR6	-0.439933583
CARD11	-0.848865617
CARNS1	-0.374214689
CARS2	-0.720018409
CASKIN1	-0.656284725
CASP7	-0.431343539
CASQ1	1.202216494
CATSPERG1	1.572822315
CBX2	-0.563298371
CC2D2A	-0.749337121
CCDC57	-0.603020492
CCDC68	0.941074138
CCDC69	-0.61884185
CCDC88C	-0.429617676
CCL20	1.595076825
CCL27	0.820903518
CCL3	1.80940481
CCL6	1.863063049
CCRL2	0.489995057
CCRN4L	1.258905519

CD14	1.012707794
CD163	2.483288826
CD209F	2.040668627
CD48	0.637964098
CD55	0.755469978
CD68	1.533628321
CDC25B	0.936615134
CECR5	0.458703377
CELSR1	-1.307257297
CELSR2	-0.644726883
CEP135	-0.552157662
CEP19	0.57443761
CEP41	-0.782752902
CEP70	-1.643398493
CEP78	-0.803495564
CERK	0.596368014
CERS5	0.395516777
CH25H	1.682644147
CHAC1	1.686483917
CHM	-0.347182963
CHRDL1	-1.021006539
CIART	1.242011466
CIRBP	-0.741622212
CISH	0.976447623
CKAP2L	-0.906547413
CLEC10A	2.504647627
CLEC2G	0.680231927
CLEC4E	2.329626079
CLIC5	1.272703198
CLN8	0.583371383
CMBL	-1.177577068
CMC2	0.441165143
CNIH4	0.372592599
CNKSR1	1.134149722
CNN3	0.791348191
CNST	-0.624057144
COG1	-0.373380429
COG5	-0.576986489
COL16A1	0.833148335
COL20A1	-0.621363276
COL4A1	0.897328345
COL7A1	2.03553376
COL8A1	0.552814626

COMMD7	-0.373449274
COX4I2	2.306721179
COX6A2	0.399834778
CP	1.461604819
CPA5	1.521265842
CPA6	1.959263673
CREB5	1.681945318
CRELD2	-0.865151283
CRISPLD2	1.458901688
CRLF1	3.222833299
CRYAB	0.75849718
CSDC2	1.561457456
CSF2RB	1.518450326
CSPG5	-1.110564292
CSRNP1	1.063936311
CSRP2	1.428900682
CSRP3	1.60105627
CTC1	-0.34194113
CTCF	-0.450757353
CTSS	2.501153207
CUL9	-0.442527427
CUX1	0.431857642
CUZD1	-1.510307757
CXXC4	-0.862522174
CXXC5	-0.394359254
CYBA	0.711377588
CYCS	0.387686479
CYP2D1	2.317435833
CYP3A18	-1.675609153
CYP4F17	-0.606518243
CYP4F6	-0.483476409
CYP51	1.125192064
DAAM2	1.212135674
DACT2	1.618053491
DAPP1	-0.545335948
DCAF4	-0.90309107
DCK	-0.530320166
DCLK1	0.854032065
DDIT4L2	-1.05613764
DDN	-1.78268379
DDT	0.510650151
DDX51	-0.545208802
DERL3	-1.843116568

DES	0.668723637
DESI1	0.436312798
DFFA	0.783492633
DHX37	-0.505303841
DIABLO	0.466802379
DIAPH1	0.499813113
DISP1	-0.581284839
DLK1	3.406254678
DMTN	-1.822787198
DNAH11	-1.495010964
DNAH17	0.682500843
DNAJB5	0.965922357
DNAJC15	0.384304513
DOCK7	-0.726597992
DOPEY1	-0.451034368
DOT1L	0.549078275
DPEP1	1.925691948
DRAXIN	2.2719842
DSE	0.641411019
DSTYK	-0.442941508
DTNA	0.587999645
DTWD1	-0.625871858
DUPD1	2.282007692
DUSP1	1.530446693
DUSP2	2.139316522
DUSP8	1.73360109
DYRK1B	-0.365057875
EBF1	0.960743094
EBP	0.790425006
ECHDC1	0.58774444
ECSCR	-1.115789665
EDA	-1.406385571
EDAR	1.793519803
EFCAB3	1.393841703
EFCAB6	1.970949463
EFHD1	-1.868263305
EFHD2	0.880960557
EFNB1	-0.45929298
EFNB3	-0.544563874
EGLN3	1.670807833
EHBP1L1	0.576776669
EIF4EBP1	0.742708748
ELL2	0.461369487

ELOF1	0.345665726
ELOVL2	-1.585085542
EMC9	-0.929668033
EMP3	0.576471398
ENAH	0.915218242
ENKUR	1.477806956
ENO1	0.652400547
ENPP3	1.867682641
EPHA3	-1.823959992
EPHX2	-0.508365619
EPPIN	0.727561998
EPS8	0.717475655
ERBB2	-0.617581977
ERMAP	2.191968584
ERO1L	0.873162703
ERRFI1	1.868350556
ESPNL	-0.884677397
ESRRB	1.184264221
ETL4	-0.814978224
EZH2	-0.502723117
F13A1	3.481630739
F3	0.800444756
FABP5	0.827882852
FADS3	0.82464374
FAM163A	-0.59051331
FAM167B	2.195118245
FAM168B	-0.485739252
FAM174B	-1.609417878
FAM175A	-0.474324141
FAM180A	1.980742222
FAM212B	0.540556946
FAM213A	1.413952667
FAM220A	-0.478750433
FAM46B	1.708124823
FAM78A	-0.670824545
FAM96A	0.481064058
FAXC	0.77634182
FBP2	-1.189706605
FBXL4	-0.396770857
FBXO21	-0.55985468
FCGBP	1.553074346
FCGR2A	2.296598166
FEN1	-0.350174952

FERMT3	1.523953867
FGD1	-1.076894887
FGF12	-0.924000416
FGG	-2.200948693
FGR	0.802932248
FHAD1	3.979124805
FHL1	1.497672313
FIGN	-1.015443529
FKBP10	0.555127838
FKBP1A	0.483427832
FKBP4	-0.578807197
FLRT3	-0.469312449
FLT1	1.553257762
FLT4	1.259633846
FNDC7	-1.821896529
FOSB	2.483675391
FOXO6	-0.607552528
FOXP2	-1.119218096
FRAS1	-1.26281888
FREM2	-1.499536133
FRRS1	0.786388371
FRS3	-0.638518496
FRZB	1.239555012
FSTL3	1.632902401
FXYD1	0.492222905
FXYD2	1.914514286
FYN	0.775763479
FZD1	-0.534849679
GABARAPL1	0.546947693
GABRE	1.9767419
GADD45G	1.421624727
GAL3ST3	-0.612368936
GARS	0.811071664
GCA	0.406042111
GDF5	2.94171532
GDPD1	-0.553517555
GEM	1.05547622
GFPT2	0.984027886
GGTA1	1.258736556
GHR	-0.755927371
GIPC3	1.303812691
GIPR	2.411461295
GLB1L2	-0.818851314

GLT8D2	0.662039704
GNB1L	-0.932957266
GNE	-0.466509936
GNG3	0.889066434
GOLM1	-0.345434275
GOT1	0.379544219
GPR125	-0.638479698
GPR155	0.765478095
GPR157	-0.535248243
GPR64	1.251070851
GPRASP2	-0.814422987
GPX4	0.262042127
GRAMD4	-0.620258826
GRB14	-0.409572793
GREM1	1.003698355
GRIN3B	-0.600803849
GRP	0.972838946
GRTP1	0.733812585
GSTA1	0.992718027
GSTA4	-0.974288409
GSTK1	0.481248537
GSTM1	0.750869547
GTF3C1	-0.470964572
GTPBP3	-0.459004886
GYG1	0.587367963
GYPC	-0.596658569
HADH	-1.008457234
HAMP	1.455015832
HCN1	2.653947167
HCN2	-0.705040269
HCN4	-0.730079213
HDAC9	-1.094687215
HEYL	-0.673805323
HFE2	-0.853250433
HIGD1B	3.225636784
HIST1H2BL	-1.552062578
HIVEP1	0.967971043
HMGA2	1.011625767
HMGCL	0.56531381
HMHA1	1.276143536
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WDR11	-0.5353588
WDR54	0.519311754
WDR93	1.790414689
WDSUB1	-0.702625262
WHAMM	0.366624388
WNT10B	1.185007788
XDH	1.619921499
XIRP2	1.537572238
YARS	0.75310832
YIPF7	1.993360045
YPEL2	-0.713871564
YWHAH	0.569478982
ZBTB8A	-0.533107548
ZDHHC9	0.836019047
ZFP1	-0.486454126
ZFP161	-0.568237295
ZFP192	-0.789658137

ZFP212	-0.431698119
ZFP213	-0.543945607
ZFP263	-0.597139666
ZFP266	-0.65221377
ZFP316	-0.986160388
ZFP354B	-1.127717412
ZFP385D	-1.096266605
ZFP445	-0.429929497
ZFP46	-0.627996193
ZFP512B	-0.594029337
ZFP532	-0.375245237
ZFP593	0.379785094
ZFP786	-1.097581975
ZFP799	-0.573286367
ZFP827	-0.615114638
ZHX3	-0.480083123
ZMAT1	-0.853497832
ZMYM3	-0.471329694
ZNRF2	0.574515279
ZSCAN2	-0.747083206
ZSCAN20	-0.420730198
ZSCAN29	-0.429269074

Table S4. Differentially Expressed Transcripts Normalized by PDE5i

Gene	Mean SV Fold vs NF	Mean SV+PDE5i Fold vs NF	Mean SV+PDE5i Fold vs NF+PDE5i
Up in SV & Normalized by PDE5i			
5S_RRNA	3.481630739	-1.664973829	0.937494426
6720489N17RIK	1.504925074	-0.193098424	-0.143313923
AABR06011545.1	1.311820517	-1.788831042	-1.487619989
AABR06040258.1	1.518450326	-0.585386635	-0.471364391
AABR06041819.1	3.510454328	-0.173357516	1.286348408
AABR06044860.1	3.677258249	0.202580584	1.66507312
AABR06045205.1	0.508382406	-0.634767316	-0.522009426
AABR06048498.1	0.630700329	0.864241807	1.372979088
AABR06053456.1	1.572822315	-0.702003564	-0.651231046
AABR06057556.1	0.376498046	0.440567851	0.339587489
AABR06058265.2	0.389276986	0.422925051	0.412805208
AABR06060087.2	1.393841703	-0.317386627	-0.427594354
AABR06065806.1	0.555223051	-0.484098766	-0.507920175
AABR06082055.1	2.195265811	-0.492993796	-0.152306877
AABR06082339.1	1.925691948	-0.242964303	0.000477384
ADAL	2.596319571	-0.295726422	0.563413079
ADAM11	1.553074346	-0.525541888	-0.270100073
ADAMTS8	0.607299276	-0.443140881	-0.061556389
ADCY5	0.569478982	-0.334567491	-0.277896589
ADSSL1	1.185007788	-0.56956097	-0.394054793
AGBL5	0.637964098	-0.648695743	-0.369115729
ALOX12	2.653947167	-0.384601397	0.100250131
ALS2	0.591802923	-0.377332867	-0.224139887
AMER1	2.483288826	-0.737208028	0.004974268
AMIGO1	0.573747075	-0.521749906	-0.341034753
ANKMY2	0.708971724	-0.12016992	-0.136520233
ANKRD10	0.519311754	-0.539028656	-0.484334576
APOH	1.914514286	-1.363221061	-0.754555005
ARHGAP29	0.359324982	-0.632721331	-0.504150938
ARHGAP39	0.372592599	-0.294912974	-0.558732781
ARHGEF10	0.576471398	-0.25010116	-0.224514802
ARHGEF5	0.334119808	-0.694308313	-0.536522932
ARRDC3	1.718219235	-1.139287837	-0.615454982
ATG14	0.421485963	-0.233370581	-0.296387406
ATP11A	0.509535115	-0.485288142	-0.379530943
ATXN7	2.045651522	-0.712171914	0.002740738
B3GAT1	1.894374158	-1.917176286	-1.810707272
B4GALNT2	2.702142491	-0.254708361	0.270996894

BAHCC1	1.334599684	-0.493149098	-0.313848359
BC024978	1.670807833	-0.308597238	-0.045615982
BCHE	1.457680313	-1.085302479	-0.586577869
BCL7A	0.632333694	-0.306970684	-0.306202384
BCL9	0.482363739	-0.200834111	-0.337011979
BHLHE41	0.232294946	-0.887931197	-0.93647711
BMP5	1.591720725	-0.768093077	-0.805161723
BOD1	0.672462628	-0.426474371	-0.335747883
BPIFA1	0.332649791	2.70083638	2.662564889
BRCA2	1.456152299	-0.168186934	-0.092913472
BRINP2	1.708124823	0.009671917	0.272708708
BTBD8	1.251070851	-0.401144329	-0.54095378
C1QTNF9	2.284211619	-1.048090679	-0.217393367
CAD	0.84072137	-0.225019343	-0.109889561
CAMK1D	0.941923694	-0.814899996	-0.64038037
CAR6	0.858950915	-0.475606333	-0.158785384
CCDC57	0.302591378	-0.752610621	-0.643045285
CCDC69	0.876609851	-0.307088042	-0.319824696
CCDC88C	0.552814626	-0.529809387	-0.284629376
CELSR1	1.682644147	-1.003765968	-0.679443388
CEP135	1.112401035	-0.374719764	-0.182291304
CEP78	1.463225918	-0.264687215	-0.316373967
CHM	0.737343232	-0.472927564	-0.10597625
CKAP2L	0.646150112	-0.925514553	-0.69956562
CLEC2G	1.332101002	0.685465496	1.109843645
CLN8	0.399374637	0.664820622	0.619185939
CMBL	2.072667715	-0.578290035	-0.327235909
CNIH4	0.351616428	0.216013713	0.351495313
COG1	0.611707324	-0.180441334	-0.193039723
COG5	1.458901688	-0.302867768	-0.098907197
COL20A1	1.587547191	-0.063906444	-0.060054493
COL8A1	0.433076134	0.395601574	0.617725139
COMMD7	0.733812585	-0.063759205	-0.135533004
COX6A2	0.395516777	0.498254473	0.428360969
CREB5	1.075131157	1.219645416	2.049346719
CRELD2	1.533628321	-0.660186635	-0.322672905
CRISPLD2	0.984026933	1.251610552	1.790256947
CTC1	0.449278229	-0.19402148	-0.26548223
CTCF	0.601527121	-0.388861808	-0.271856143
CYCS	0.345665726	0.264106238	0.365083108
CYP3A18	2.195118245	-0.948936673	-0.772192389
CYP4F17	1.050008555	-0.322480676	-0.251882665
CYP4F6	0.862887553	-0.301032338	-0.201130578

DCAF4	1.461604819	-0.448181511	-0.422013149
DCK	1.024314418	-0.168164444	-0.183844661
DDIT4L2	0.800038422	-1.03773375	-0.795678242
DDX51	0.901234329	-0.380008148	-0.240971046
DERL3	2.329626079	-1.321090734	-0.797793808
DMTN	2.574491134	-0.36177002	-0.427915468
DNAH11	1.64863059	-0.953757257	-0.882941052
DTNA	0.665999384	0.659331942	0.796924433
DTWD1	1.266555295	-0.209773082	-0.210022256
EDA	0.586807655	-1.395005658	-1.237817923
ELL2	0.383618991	0.342376125	0.478968026
ELOVL2	2.847949081	-0.590853908	-0.010878769
EPHX2	1.521265842	-0.230512602	0.030414321
ERBB2	1.011625767	-0.509681403	-0.277935484
ESPNL	1.863063049	-1.000977356	-0.189708336
ETL4	1.487656662	-0.541976911	-0.303562478
EZH2	0.750869547	-0.263370462	-0.257853938
FAM174B	1.592025395	-1.358103633	-1.03210068
FAM220A	1.154145267	-0.119099414	-0.088062074
FAM46B	1.29608542	1.336350284	2.132322846
FBP2	2.040070599	-0.64993448	-0.356758567
FBXL4	0.848768351	-0.059690297	-0.116352194
FBXO21	1.384623609	-0.153310184	-0.116955063
FEN1	0.533948917	-0.437112238	-0.217945862
FGD1	1.587292442	-0.807826138	-0.524562755
FGF12	1.125192064	-0.498932937	-0.542556314
FGG	3.238815978	-1.236320535	-0.035517217
FIGN	1.867682641	-0.608870035	-0.314944316
FLRT3	1.194739787	-0.172559273	-0.061666372
FNDC7	3.006693732	-1.212469598	-0.14380521
FOXP2	2.380982793	-0.61348372	0.058675919
FRS3	0.750307399	-0.486774507	-0.39571231
GAL3ST3	0.842137506	-0.107578123	-0.333414172
GCA	0.499813113	0.372778953	0.511639881
GDPD1	0.971187131	-0.114153017	-0.22561115
GNB1L	1.205390293	-0.776152756	-0.525014342
GOLM1	0.864326125	-0.231139008	-0.062441166
GPR157	0.992718027	-0.11488164	-0.201429986
GRAMD4	1.025397134	-0.424959006	-0.273015447
GRB14	0.448372954	-0.427653078	-0.333438369
GRTP1	0.473586919	0.385231303	0.832818486
GTPBP3	0.854032065	-0.108840816	-0.178425866
HADH	1.603186509	-0.46364702	-0.414137011

HCN4	0.955944665	-0.354662909	-0.408904742
HDAC9	1.038102165	-1.426823152	-0.743310258
HEYL	0.510590717	-0.518059224	-0.55728504
HFE2	1.295942797	-0.573563407	-0.433044833
HIST1H2BL	2.143409748	0.218276769	-0.656514042
HPN	1.980742222	-0.919580957	-0.729923052
HS3ST1	0.711377588	-1.332582404	-0.932093557
HSP90B1	0.721526501	-0.401443609	-0.192039429
HSPB6	0.296375234	0.569654592	0.550621222
HYOU1	1.25980516	-0.732746981	-0.387097414
INIP	0.546947693	-0.772063035	-0.577483248
IPP	1.650833181	-0.256597054	-0.024431005
IRX4	0.569278487	-0.342629448	-0.482378262
KCNJ12	1.789145696	-0.368015891	-0.318260436
KDM1B	0.917306227	-0.285089102	-0.159583249
KLHL34	2.483675391	-0.897372125	-0.01138461
KY	3.225636784	-1.735316324	-1.002462497
LARS2	0.726489712	-0.213081513	-0.135264729
LOC100174910	0.82237529	-0.046031359	-0.087681577
LOC100302465	3.069633506	-0.131495566	0.254925282
LOC100360260	0.641411019	-0.302866262	-0.192984542
LOC100362344	1.258736556	-1.082616493	-0.980074983
LOC100362658	0.656106121	-0.744447721	-0.656671462
LOC100365915	1.853556581	-0.615169372	-0.529441643
LOC100911267	1.687557545	-0.405587564	-0.500614427
LOC100911951	2.501153207	-0.916488799	-0.496195525
LOC102552284	0.43039593	-0.745669349	-0.446804172
LOC303140	2.327557269	-0.423765255	-0.210736435
LOC680663	2.179341817	-1.770233297	-1.539034084
LOC680964	0.573362082	-0.307334287	-0.335345198
LOC684841	2.296598166	0.319918695	-0.016029378
LOC685707	0.451289489	-0.584504338	-0.519773291
LOC687532	2.504647627	-1.366535143	-1.007728821
LOC688286	1.037789957	-0.310095534	-0.264025448
LOC689574	0.57443761	0.440497612	0.48818174
LOC691485	1.062956024	-0.444999582	-0.414587985
LOC691909	0.323986256	0.543267381	0.358510837
LPGAT1	1.050008555	-0.408934882	-0.163956765
LRFN5	3.244276742	-0.197602537	0.819805145
LRIG1	0.921639439	-0.460905861	-0.254280244
LRRK2	0.836019047	-0.39641578	-0.220265838
LSMEM1	1.878532953	-1.193288006	-0.802080945
LYPD3	1.793519803	-0.249749953	-0.176918104

MAP2	2.857216845	-0.846042587	0.368073039
MAP3K5	0.597041589	-0.555719909	-0.269373841
MED31	0.387686479	-0.057234219	-0.327777663
MEIS1	1.110049245	-0.319970243	-0.265919982
MELK	1.449705739	-0.06666294	-0.185932787
MGLL	1.29230487	-0.453111164	-0.442442151
MGME1	1.404963051	-0.296495709	-0.142454764
MIR143	2.280537245	0.091755883	0.500008871
MLH3	1.244169523	-0.165220747	-0.091874844
MLLT3	0.555145335	-0.691782158	-0.628579075
MLST8	0.843256277	-0.26010796	-0.148089488
MPV17	0.763013616	-0.146217234	-0.239842791
MTHFSD	1.05547622	-0.373546109	-0.290302816
MUTYH	1.161468964	-0.136897783	-0.103663092
MVB12B	0.903647871	-0.374911315	-0.33833462
MYH14	0.447945516	-0.731152165	-0.626473186
MYOZ2	0.507660833	0.397895851	0.684672365
MYZAP	0.873162703	-0.271176649	-0.137829836
NCAPD2	0.678536016	-0.216341412	-0.221177613
NCAPG2	1.478462699	-0.275368433	-0.126972984
NCKAP5	0.795594098	-0.862865933	-0.502239143
NCS1	0.735002552	-0.431210782	-0.451060172
NEDD4L	0.833148335	-0.283178275	-0.192161641
NEDD9	0.401560816	-0.392818486	-0.335014781
NEURL1B	3.226302448	-0.408868519	-0.19136973
NEURL2	1.124527937	-0.394539429	-0.072869532
NFIA	0.77634182	-0.475047901	-0.255463393
NGFR	0.319074373	-0.804298565	-1.009738678
NPRL3	0.4968621	-0.017000402	-0.264946334
NR0B2	1.358837082	-0.129619984	-0.048778609
NUDT8	0.782426697	-0.192550131	-0.239623354
OVOL2	3.015005338	-1.737645723	-0.183308547
PADI1	2.411461295	-2.686074842	-1.097369346
PAN2	0.587999645	-0.389294854	-0.298516064
PAQR8	0.436028678	-0.83974385	-0.728083885
PDIA4	1.050008555	-0.659156113	-0.4264617
PGAP2	0.802932248	-0.033733021	-0.096895353
PHACTR1	1.868350556	-1.050139437	-0.550647179
PIAS3	0.865728329	-0.230207001	-0.304504455
PIK3C2B	0.694064555	-0.463144659	-0.422747039
PIK3R2	0.406042111	-0.302996578	-0.440409071
PIWIL2	2.537708119	-0.594324581	-0.296163737
PKNOX1	1.07387682	-0.226931413	-0.048437646

PLAGL1	0.411782693	-0.605806283	-0.586792903
PLCL2	1.619921499	-0.304264833	-0.081834248
PLEKHA8	1.059469551	-0.420524234	-0.285765198
PLXNA3	0.31521587	-0.923756674	-0.861458899
PM20D2	2.306721179	-1.825617468	-0.991060556
POLD1	0.36042984	-0.304596952	-0.52723825
POMK	0.907297478	-0.119983951	-0.160853566
POT1	1.276143536	0.086005231	0.074592496
POT1B	1.794345023	-0.217208117	-0.08892054
PPAP2B	1.523953867	-0.618700588	-0.408586288
PPFIBP2	0.685491812	-1.315797801	-1.244026762
PREX1	0.870146536	-0.464687718	-0.365397942
PTER	0.442311757	0.321475699	0.537594301
PTPN20B	2.94171532	-1.313082288	0.038386336
PXYLP1	0.499923138	-0.352277215	-0.433462452
RAB11FIP2	2.127390354	-0.433404898	-0.122797454
RAD51D	1.213788252	-0.216227473	-0.245051943
RARB	1.012707794	-0.423717259	-0.301253515
RBAK	0.540556946	-0.443785932	-0.376492103
RCC1	1.130006967	-0.469695548	-0.288044272
RERE	0.454117538	-0.307021967	-0.337946865
RGD1304982	0.820903518	-0.429621186	-0.308870541
RGD1305587	2.608939547	-0.751975387	0.122447658
RGD1306926	0.379785094	-0.393728737	-0.498607565
RGD1309651	0.63220649	-1.382823375	-1.860659235
RGD1310852	0.960743094	-0.290012698	-0.215465603
RGD1311756	1.104877455	-0.379713543	-0.185186499
RGD1560242	0.262042127	1.625062695	2.567256737
RGD1561795	0.527782336	2.128543805	1.527312748
RGD1561998	2.513939307	-2.138110963	-0.832733601
RGD1563528	0.976447623	-1.853480736	-1.524228882
RGD1564036	0.646962688	-0.148263279	-0.497917644
RGD1565170	0.596368014	-0.311783165	-0.804344723
RGD1565222	1.734527301	0.113682264	0.168994698
RGD1566084	0.827882852	-0.259750736	-0.522398898
RIMBP2	0.569204579	-0.949367785	-0.829355616
RIN2	0.868765479	-0.559609802	-0.38610434
RN50_16_0006.1	1.987584056	-0.512533039	-0.058864211
RN50_8_0646.1	0.583371383	-0.676342791	-0.358973125
RNF141	0.816550909	-0.457664599	-0.276685482
RNF170	0.891366501	-0.46735298	-0.132848429
RNF213	0.326095506	-0.750847864	-0.623079984
RNF43	1.941916143	-0.243380431	-0.12008096

RPA1	0.588172735	-0.235776068	-0.252652504
RPS6KA6	2.691508718	-0.537307582	0.04404992
RSPH3	1.212135674	-0.091183108	-0.229037914
RXRA	1.003698355	-0.517536663	-0.352111474
RXRG	2.196709151	-1.538034704	-0.95320121
SAMD10	0.492718585	-0.292068304	-0.331774213
SAMD11	0.972838946	-0.515826585	-0.610372528
SCAI	1.622301841	-0.218030558	-0.123468583
SCN1B	0.399834778	-0.554660459	-0.648866202
SDF2L1	0.61232086	-0.556433441	-0.460578769
SEC11C	0.644269592	-0.323176613	-0.23587982
SEC16B	0.528891204	-0.869906325	-0.619129166
SECISBP2	0.693384254	-0.228923337	-0.193318177
SFMBT1	1.393841703	-0.430067126	-0.200770666
SGCD	1.239555012	-0.562978483	-0.152875723
SGOL2	1.712642835	-0.671717795	-0.44509447
SH3BP5	0.810911632	-0.504579315	-0.351132134
SHCBP1	1.178008288	-0.668994164	-0.632425179
SHROOM2	1.80940481	-0.701867784	-0.353894202
SIX5	0.469608815	-0.295527273	-0.332322867
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SPATA6L	2.345180871	-0.529572634	-0.288598816
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STARD8	1.218460535	-0.193589501	0.021550986
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TMEM179	1.41844221	-0.083226387	-0.196934825
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VEPH1	0.939662316	-1.530224086	-1.278604834
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CAR4	-0.779477944	2.341029808	2.153103714
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CATSPERG1	-1.408581022	1.103201011	0.134986777
CCL20	-0.445192861	1.265086659	1.379048577
CCL27	-0.715243453	0.383769591	0.210152956
CCL3	-1.220377422	1.974909363	0.600310131
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CD14	-0.604316756	1.153764326	0.581726141
CD163	-0.689090354	1.834443563	1.910869096
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CEP19	-0.492017134	0.536104356	0.292906267
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CHAC1	-0.79396953	0.8177193	0.971464382
CISH	-0.45169606	1.000156254	0.743310504
CLEC10A	-1.114678635	1.937629812	1.434871162
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COL16A1	-0.652437687	0.448069016	0.302569396
COX4I2	-1.511927729	1.193868286	0.776798981
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CSF2RB	-0.860347342	1.470252411	0.74826856
CTSS	-1.394825505	1.945472211	1.082856057
CYBA	-0.733928698	0.566271807	0.05900701
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DAAM2	-0.643302092	0.88960828	0.704363265
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DIAPH1	-0.396770857	0.334834454	0.370870286
DLK1	-0.698391243	3.099667748	2.802779649
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EBF1	-0.61884185	0.482629659	0.503765938
EBP	-0.5747632	0.580916525	0.384770482
EDAR	-1.036583944	1.443114113	0.776746871
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ELOF1	-0.350174952	0.444924292	0.286814186
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ENPP3	-0.884677397	1.742673555	1.075523766
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ERO1L	-0.552157662	0.227500029	0.490066613
ERRF1	-0.498557339	1.592081155	1.578723247
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RGD1561137	-0.430503198	0.405165323	0.173937171
RGD1561444	-0.627996193	0.711049701	0.829741806
RGD1561916	-2.200948693	1.957881371	0.41435022
RGS1	-2.0508268	1.780906148	-0.045728335
RGS17	-0.79703688	0.731684456	0.693308143
RGS4	-1.266044328	-0.244540356	-0.239221338
RN50_10_0291.1	-0.480083123	0.197736728	0.242125312
RN50_4_2163.2	-0.633820896	0.476560719	-0.026446027
RNASE4	-0.470581045	1.108283134	0.805772755
RND1	-0.789658137	1.168297212	1.191214027
RNF113A1	-0.641680651	0.268002091	0.002569553
RNF186	-0.775767646	1.074717183	0.759500908
RPL35A	-0.483476409	0.648543657	0.213628358
RT1-CE3	-0.857306886	0.513780463	0.049882939
RT1-S2	-0.535248243	0.383777786	0.123670233
RTN4RL2	-1.403772105	1.580844372	1.11812744
SAT1	-0.545208802	0.613066889	0.497383874
SCGB1A1	-1.597141141	2.79399688	1.565596622
SCLY	-0.621363276	0.323894316	-0.14484069
SCX	-0.373449274	-0.629787727	-0.810340128
SEMA6B	-1.015443529	0.343853787	0.437932058
SERINC2	-0.960728214	1.220771157	0.884912369
SERPINF1	-0.464243568	0.4747772	0.403173373
SFRP1	-0.654052365	0.521383956	0.45100709
SH2B3	-0.42211649	0.21301886	0.172000352
SIK1	-0.803495564	0.587552705	0.483752643
SIK3	-0.429617676	0.271422553	0.270096319

SLC11A1	-1.251739422	1.448667791	0.87564179
SLC1A4	-0.561271486	0.275821021	0.283053902
SLC1A5	-0.595958433	0.473769601	0.290613831
SLC28A2	-0.347182963	1.827334494	1.56379169
SLC2A1	-0.526514557	0.471309314	0.390626209
SLC47A2	-0.638518496	0.794458648	0.55678989
SLC4A11	-0.87037051	0.402478501	0.125573953
SNTG2	-0.991919217	1.54177138	0.316821195
SPATC1	-1.585085542	2.053502019	0.941450548
SPP1	-0.673805323	0.955471731	0.820991848
SPRN	-0.713871564	0.626333122	0.544167085
SRPX	-0.606518243	0.960753939	0.708217309
STARD5	-0.459004886	0.570805444	0.599636878
STK40	-0.487901306	0.142065194	0.304396052
STMN4	-2.567315433	0.513695223	-0.406874902
STS	-0.49781755	0.386860909	0.339033197
SYT3	-0.499353888	0.385325023	0.340880712
TACR1	-3.115641439	0.734945374	-0.910296847
TAGLN2	-0.42557246	0.440181963	0.311720779
TBX2	-1.00247754	0.576768536	-0.037301907
TCEAL3	-1.270772383	1.882377979	0.368823663
TGM1	-0.439210789	1.549766306	1.176373835
TIFA	-0.828170461	0.33569514	-0.306260742
TLR4	-0.730079213	0.804878351	0.21377106
TLR7	-1.465720589	1.635275054	1.241725831
TLR8	-1.547326652	1.9445964	0.401279094
TMBIM1	-0.531919592	0.758110061	0.682266271
TMEM120B	-0.429999298	0.690015897	0.551558845
TMPRSS5	-1.119218096	1.422115327	0.306673032
TNFAIP8L2	-1.495010964	0.48876072	-0.150642549
TNFRSF1B	-0.637870366	0.644423844	0.374231798
TNFRSF26	-0.590080349	0.650838074	0.539933504
TRAF3IP2	-0.634884435	0.435807325	0.084682363
TREM1	-1.761008549	1.288165014	0.603427725
TRIM10	-2.110419982	2.548218925	1.145102533
TRIM66	-0.97888769	2.250490145	2.450373263
TRIP10	-0.568035088	0.065619848	0.018619097
TSSK4	-0.597139666	1.086226427	0.915526216
TTL9	-0.451121056	1.7007334	1.223980917
TYROBP	-1.884855833	1.477044825	0.12328372
UBXN11	-0.648685098	0.435541187	0.298139532
UHRF1BP1L	-0.389444519	0.377070271	0.448205239
UQCRCQ	-0.373380429	0.461015601	0.35909834

VSIG4	-1.352539995	1.832340592	0.916812531
WDR54	-0.55985468	0.349861389	0.130541552
WDR93	-2.276426257	0.327957345	-0.662531106
WHAMM	-0.431698119	0.235511155	0.178396266
WNT10B	-1.177577068	0.23519146	0.043513277
XDH	-0.668133186	1.465718577	1.073262961
YWHAH	-0.426606735	0.400122116	0.397271828
ZDHC9	-0.470264773	0.660695858	0.574098012
ZFP593	-0.377633385	0.222369539	0.283788286
ZNRF2	-0.488858977	0.156115214	0.303354419

Figure Legends

Figure S1. PDE5 is Expressed in Pediatric RV Cardiomyocytes

(A) Sectioned NF and SV tissue was stained with fluorescently labeled secondary antibodies to primary sarcomeric α actinin (red), primary PDE5 (green) and nuclei were stained with DAPI (blue). The merged confocal laser microscopy images demonstrate that PDE5 is expressed in cardiomyocytes. All images are at 60X magnification, scale bar = 20 μ M. (B) Representative FV-1000 colocalization analysis scattergram demonstrating significant overlap of α -actinin and PDE5 channels.

Figure S2. Top Canonical Pathways Activated by SV Serum Treatment *in vitro*

Activation z-scores of the top 6 most significantly activated canonical pathways in NF versus SV serum-treated NRVMs compared to NF+PDE5i vs SV+PDE5i serum-treated NRVMs.; Fisher's exact test, $-\log_{10}(\text{p-value}) > 2.9$ or $p < 0.001$ n=3 NF, n=3 NF+PDE5i, n=3 SV, n=3 SV+PDE5i in a total of 3 NRVM preparations.

Table S1. Subject Characteristics

Characteristics for all patients included in this study. M = Male, F = Female, ACEi = angiotensin-converting enzyme inhibitor, β -B = β -Blocker, PDEi = phosphodiesterase inhibitor, PDA = patent ductus arteriosus, PA = pulmonary artery, PLE = protein losing enteropathy, NA = not available. *Non-PDEi Inotrope includes: dopamine, dobutamine, epinephrine, norepinephrine.

Table S2. RT-qPCR Primer Sequences

Listed are the species specific [rat (r) or human (h)] forward (F) and reverse (R) primer sequences used for each target gene. All primers are presented in 5'-3' orientation.

Table S3. Differentially Expressed Transcripts

List of all differentially expressed transcripts, NF vs SV, $p < 0.05$.

Table S4. Differentially Expressed Transcripts Normalized by PDE5i

List of all differentially expressed genes (NF vs SV, $p < 0.05$) that were normalized by PDE5i (NF+PDE5i vs SV+PDE5i, $p > 0.05$).