Supplemental Data (2 Figures; 3 Tables)

Novel genomic targets of valosin-containing protein in protecting pathological cardiac hypertrophy

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Short title: Gene regulation of VCP against cardiac pressure overload

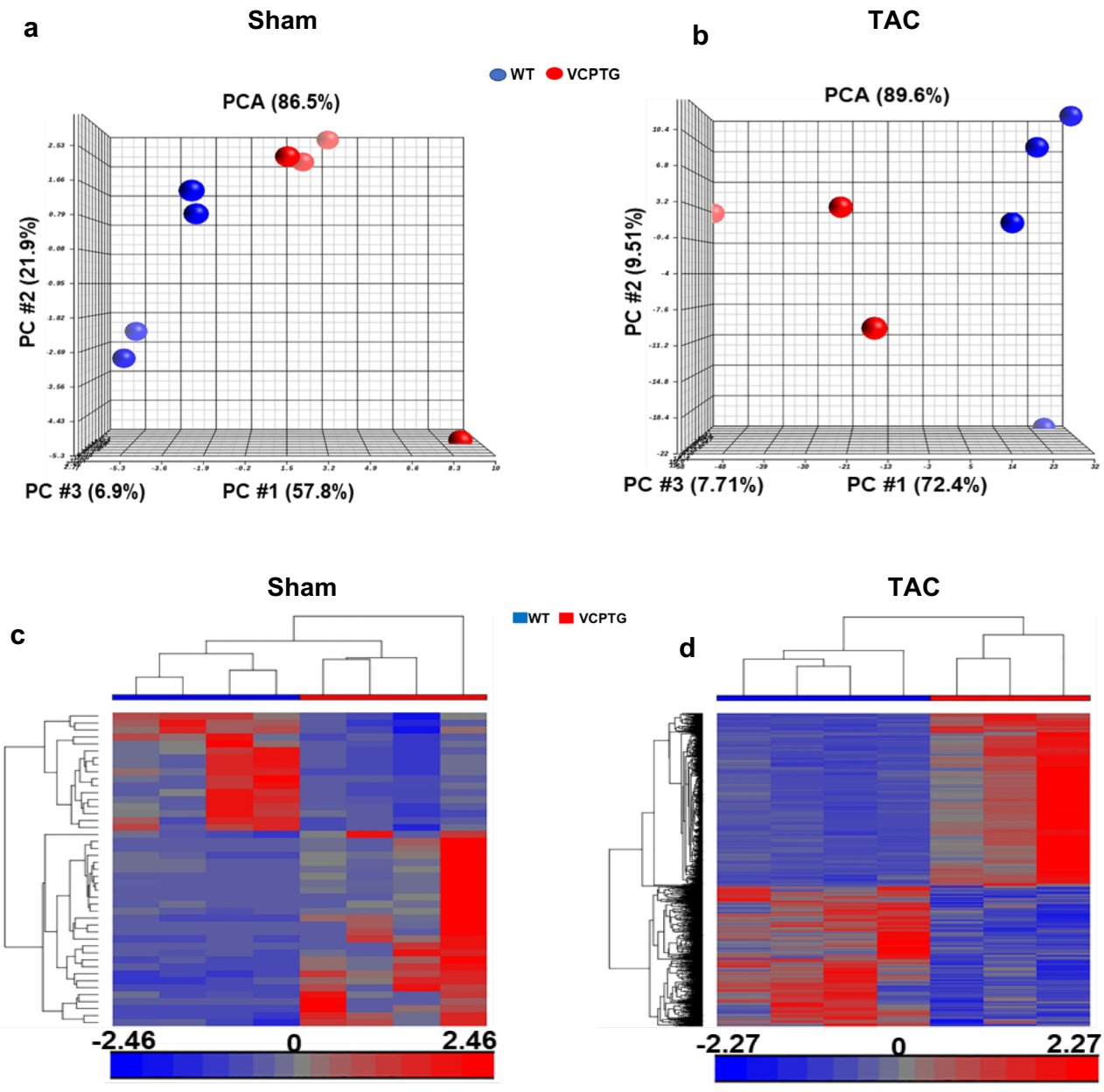

Figure S1. The profiles of the transcriptomic alterations between VCP TG and WT mice at the sham and 2 weeks TAC conditions. a-b. Principal component analysis (PCA) and **c-d.** Hierarchical clustering of differentially expressed genes (DEGs) between VCP TG and WT mice with FDR< 0.05 in sham (a and c) and 2W TAC (b and d). N=3-4/group.

Table S1. Top DEGs between VCP TG and WT by fold changes

sham					2 weeks TAC				
Transcript ID	**log2 FC**	**P value**	**FDR**	**Genes**	**Transcript ID**	**log2 FC**	**P value**	**FDR**	**Genes**
ENSMUSG00000030046	10.07	5.07E-07	2.312E-03	*Bmp10*	ENSMUSG00000099620	5.88	2.23E-04	9.00E-03	*Mrgprb13*
ENSMUSG00000083327	8.68	3.40E-08	4.620E-04	*Vcp-rs*	ENSMUSG00000102781	5.07	3.13E-03	4.40E-02	*Pla2r1*
ENSMUSG00000041616	5.11	3.90E-05	2.830E-02	*Nppa*	ENSMUSG00000009356	4.91	1.74E-04	7.00E-03	*Lpo*
ENSMUSG00000049436	4.32	3.31E-05	2.805E-02	*Upk1b*	ENSMUSG00000027376	4.81	8.93E-06	1.00E-03	*Prom2*
ENSMUSG00000069476	4.26	3.12E-05	2.805E-02	*Zfp616*	ENSMUSG00000020805	4.45	3.16E-04	1.10E-02	*Slc13a5*
ENSMUSG00000039419	3.90	4.50E-05	3.127E-02	*Cntnap2*	ENSMUSG00000042002	4.33	3.96E-04	1.20E-02	*Foxn4*
ENSMUSG00000027867	3.89	3.46E-05	2.805E-02	*Spag17*	ENSMUSG00000050201	4.07	2.81E-03	4.10E-02	*Otop2*
ENSMUSG00000039963	3.84	6.04E-07	2.312E-03	*Ccdc40*	ENSMUSG00000020159	3.64	4.51E-05	3.00E-03	*Gabrp*
ENSMUSG00000073940	3.67	9.86E-05	4.569E-02	*Hbb-bt*	ENSMUSG00000021441	3.61	1.22E-04	6.00E-03	*Cts6*
ENSMUSG00000025889	3.63	4.75E-08	4.620E-04	*Snca*	ENSMUSG00000017950	3.42	1.89E-03	3.20E-02	*Hnf4a*
ENSMUSG00000079014	-3.30	1.68E-05	1.814E-02	*Serpina3i*	ENSMUSG00000061295	3.40	1.65E-03	3.00E-02	*Olfr1261*
ENSMUSG00000043410	3.21	9.63E-05	4.568E-02	*Hfm1*	ENSMUSG00000073952	3.40	1.18E-03	2.40E-02	*Olfr597*
ENSMUSG00000006403	-3.05	5.35E-05	3.473E-02	*Adamts4*	ENSMUSG00000025576	3.38	1.65E-03	3.00E-02	*Rbfox3*
ENSMUSG00000030616	3.03	4.02E-06	7.120E-03	*Sytl2*	ENSMUSG00000000103	3.19	1.55E-03	2.80E-02	*Zfy2*
ENSMUSG00000075249	2.87	7.82E-06	1.015E-02	*Fsip2*	ENSMUSG00000061457	3.19	2.29E-04	9.00E-03	*Olfr871*
ENSMUSG00000025473	-2.79	4.56E-06	7.389E-03	*Adam8*	ENSMUSG00000034552	3.19	2.41E-05	2.00E-03	*Zswim2*
ENSMUSG00000034533	2.60	1.07E-06	2.597E-03	*Scn10a*	ENSMUSG00000040728	3.06	1.09E-04	5.00E-03	*Esrp1*
ENSMUSG00000062991	2.34	5.62E-05	3.527E-02	*Nrg1*	ENSMUSG00000022416	2.98	1.05E-03	2.30E-02	*Cacna1i*
ENSMUSG00000025902	-2.11	8.41E-06	1.023E-02	*Sox17*	ENSMUSG00000027457	2.98	7.27E-04	1.80E-02	*Snph*
ENSMUSG00000030748	-2.06	1.06E-05	1.216E-02	*Il4ra*	ENSMUSG00000096284	2.95	1.27E-03	2.50E-02	*Tcstv1*

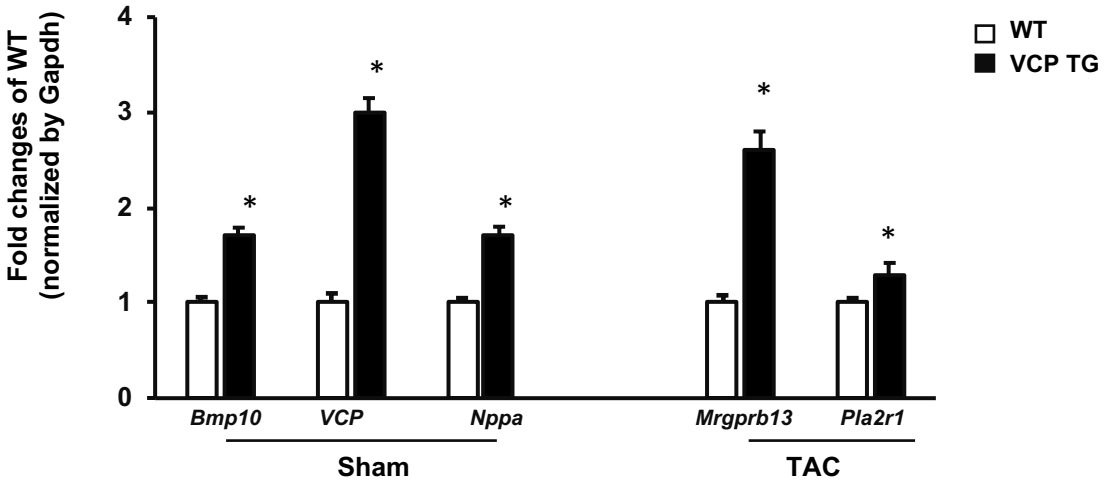

Figure S2. The validation of the alterations of the top DEGs between VCP TG vs WT by qPCR. *, p< 0.05 vs WT. N=4-5/groups

Table S2. DEGs detected between VCP TG vs WT at sham condition based on FDR<0.05 and their corresponding alterations under 2W TAC based on fold changes

Gene symbol	*Sham: VCP TG vs WT log2FoldChange*	*2W TAC: VCP TG vs WT log2FoldChange*	*WT: 2W TAC vs sham log2FoldChange*
Hlf	1.285	0.515	-0.461
Adamts4	-3.047	0.015	2.162
Rgcc	-1.864	-0.433	1.739
Angpt1	1.706	0.2	-1.103
Tfrc	1.083	0.26	-0.537
Fas	-1.835	-0.5	1.2
Adam8	-2.789	1.049	3.026
Snca	3.634	-0.516	-1.086
Sox17	-2.108	-0.042	2.336
Epha4	1.515	0.537	-0.482
Kcnj3	1.684	-0.108	-1.398
Mamdc4	**-1.65**	**1.066**	**1.577**
Spag17	3.887	0.373	-4.449
Vcp	1.051	0.78	-0.278
Tinagl1	-1.621	0.099	1.537
Lrrc47	-1.036	0.1	1.305
Bmp10	10.073	0.663	NA
Sytl2	3.031	0.454	-2.885
Il4ra	-2.064	-0.443	1.724
Tacc2	-1.417	0.252	1.383
Plscr2	-1.334	-0.591	1.213
Scn10a	2.602	0.892	NA
Aldh1b1	1.976	0.35	-1.104
Sh3tc1	-1.463	0.131	1.665
Prdm16	-0.941	-0.699	0.954
Cntnap2	**3.904**	**2.009**	**-2.954**
Ccdc40	3.843	-1.444	-3.652
Spns2	-1.425	0.139	1.474
Fam117b	**-1.548**	**-0.866**	**0.729**
Nppa	5.106	-1.122	NA
Hfm1	**3.215**	**1.731**	**-2.543**
BC049715	**3.858**	**1.93**	**-2.716**
Upk1b	4.315	-0.573	-6.224
2810025M15Rik	-1.382	0.202	0.619
Erbb4	1.614	-0.074	-1.216
Nrg1	2.342	-2.083	NA
Zfp616	**4.265**	**1.831**	**-3.345**
Hbb-bt	3.666	-0.084	-1.355
Dcdc5	1.746	0.04	-2.559
Fsip2	**2.874**	**1.969**	**-2.937**
Serpina3i	-3.295	-0.674	1.847
Gm7901	6.887	2.252	-4.217
Vcp-rs	8.68	2.728	NA
Gm3099	6.176	5.232	NA
Gm16513	4.469	1.65	-3.986

Table S3. The DETX between VCP TG and WT in different comparisons

Sham : VCP TG vs WT				2W TAC: VCP TG vs WT				WT: 2W TAC vs Sham			
ETX_cluster	DETX_gen	DETX	DETX_p.adj	DETX_cluster	DETX_ge	DETX	DETX_p.adj	DETX_cluster	DETX_ge	DETX	DETX_p.adju
chr4:clu_504_NA	*Asph*	10	0.00093	chr2:clu_3453_NA	***Ttn***	29	8.80E-10	chr4:clu_483_NA	*Asph*	10	2.0955E-06
chr7:clu_1121_NA	*Tacc2*	13	0.01753	chr11:clu_4241_NA	*Obscn*	23	0.00565	chr19:clu_2990_NA	***Sorbs1***	9	2.7497E-05
chr19:clu_2969_NA	***Sorbs1***	11	0.0169	chr2:clu_3460_NA	***Ttn***	7	8.55E-06	chr7:clu_883_NA	*Fxyd1*	5	1.3969E-05
chr17:clu_444_NA	*Ptprm*	5	0.01056	chr16:clu_2899_NA	*Eif4g1*	7	0.00344	chr8:clu_2265_NA	*Sorbs2*	8	0.00019223
chr4:clu_678_NA	*Epb4.1*	4	0.02129	chr7:clu_753_NA	*Fxyd1*	8	0.00565	chr16:clu_3533_NA	*Srl*	4	2.482E-05
chr15:clu_1439_NA	*Pacsin2*	4	0.02588	chr19:clu_2429_NA	***Sorbs1***	9	0.00913	chr3:clu_5013_NA	*Myoz2*	7	0.00050803
chr10:clu_3309_NA	*Sar1a*	2	0.0169	chr6:clu_3840_NA	*Wnk1*	7	0.00605	chr5:clu_2071_NA	*Myl2*	5	0.00037213
chr7:clu_1019_NA	*Serpinh1*	2	0.0169	chr1:clu_2117_NA	*Tns1*	5	0.00312	chr10:clu_3454_NA	*Mrpl42*	2	2.482E-05
chr17:clu_440_NA	*Ndufv2*	2	0.0169	chr16:clu_2939_NA	*Golgb1*	6	0.00673	chr5:clu_1878_NA	*Hadhb*	6	0.00137584
chr7:clu_1165_NA	*Nap1l4*	2	0.0169	chr19:clu_2423_NA	***Sorbs1***	6	0.02871	chr5:clu_1990_NA	*Sec31a*	6	0.00534863
chr8:clu_2450_NA	*Sipa1l2*	2	0.02356	chr9:clu_3257_NA	*Clasp2*	2	0.00312	chr17:clu_385_NA	*Apobec2*	3	0.00137584
chr16:clu_3560_NA	*Comt*	2	0.02588	chr11:clu_4296_NA	*Eno3*	5	0.0312	chr11:clu_5105_NA	*Ogdh*	2	0.00050803
chr18:clu_1748_NA	*Arap3*	2	0.02588	chr1:clu_2180_NA	*Ppip5k2*	5	0.03347	chr19:clu_2932_NA	*Prune2*	3	0.00156037
chr2:clu_4214_NA	***Ttn***	2	0.03074	chr8:clu_1774_NA	*Insr*	2	0.00497	chrX:clu_1175_NA	*Kdm6a*	4	0.00398873
chr16:clu_3590_NA	*Dlg1*	2	0.04115	chr10:clu_2689_NA	*Pln*	5	0.04452	chr1:clu_2687_NA	*Ppip5k2*	5	0.0129382
chr9:clu_3732_NA	*Dnm2*	2	0.04634	chr9:clu_3277_NA	*Trak1*	2	0.00789	chr10:clu_3439_NA	*Chpt1*	5	0.01333318
chr1:clu_2653_NA	*Hdac4*	1	0.04115	chr10:clu_2784_NA	*Chpt1*	4	0.03976	chr8:clu_2453_NA	*Zc3h18*	2	0.0011584
chr14:clu_176_NA	*Kctd9*	1	0.04479	chr7:clu_808_NA	*Pex11a*	4	0.04073	chr1:clu_2611_NA	*Tns1*	6	0.0237929
				chr14:clu_118_NA	*Hnrnpc*	3	0.02598	chr10:clu_3503_NA	*Naca*	2	0.00156037
				chr17:clu_266_NA	***Ndufv3***	2	0.01153	chr16:clu_3630_NA	*Golgb1*	6	0.03618515
				chr14:clu_132_NA	*Myh6*	3	0.0312	chr14:clu_124_NA	*Hnrnpc*	3	0.00535741
				chr10:clu_2781_NA	*Igf1*	2	0.01354	chr7:clu_802_NA	*Rdh13*	2	0.0026096
				chr18:clu_1458_NA	*Csnk1a*	2	0.0229	chr6:clu_4548_NA	*Ndufa5*	2	0.00269151
				chr4:clu_612_NA	*Hp1bp3*	3	0.04073	chr3:clu_5057_NA	*Nexn*	4	0.01661022
				chr14:clu_52_NA	*Ppif*	2	0.0256	chrX:clu_1212_NA	*Idh3g*	4	0.01661022
				chr1:clu_2166_NA	*Lrrfip1*	2	0.03951	chr2:clu_4202_NA	*March7*	2	0.003058
				chr5:clu_1565_NA	*Ppargc1*	2	0.03976	chr1:clu_2652_NA	*Sp100*	5	0.03618515
				chr17:clu_235_NA	*Hagh*	2	0.04073	chr17:clu_328_NA	*Brd2*	3	0.01228053
				chr7:clu_937_NA	*Tollip*	2	0.04361	chr16:clu_3601_NA	*Opa1*	2	0.00535741
				chr8:clu_1956_NA	*Chtf8*	2	0.04452	chr17:clu_360_NA	*Rcan2*	2	0.00535741
				chr5:clu_1585_NA	*Ociad1*	2	0.04452	chr17:clu_351_NA	*Rpp21*	2	0.00535741
				chr6:clu_3794_NA	*Iqsec1*	1	0.02477	chr11:clu_5302_NA	*Myo18a*	2	0.00811435
				chr4:clu_445_NA	*Npr2*	1	0.0256	chr1:clu_2803_NA	*Dcaf6*	2	0.00986572
				chr3:clu_3984_NA	*Mrpl24*	1	0.02598	chr7:clu_929_NA	*Ube3a*	2	0.01117853
				chr13:clu_1310_NA	***Ndufs6***	1	0.02851	chr12:clu_3050_NA	*Ncoa1*	4	0.04211347
				chr5:clu_1629_NA	*Nudt9*	1	0.03976	chr9:clu_3965_NA	*Rbm5*	2	0.01228053
				chr7:clu_916_NA	*Fam53b*	1	0.04073	chr18:clu_1752_NA	*Arap3*	2	0.01661022
				chr5:clu_1668_NA	*Tesc*	1	0.04073	chrX:clu_1233_NA	*Apoo*	2	0.01661022
				chr7:clu_862_NA	*Ipo7*	1	0.04073	chr2:clu_4203_NA	*Itgb6*	2	0.01661022
								chr14:clu_52_NA	*Ppif*	2	0.01661022
								chr10:clu_3331_NA	*Sar1a*	2	0.0176823
								chr16:clu_3590_NA	*Tra2b*	2	0.02135337
								chr8:clu_2335_NA	*Arhgap10*	2	0.02136414
								chr7:clu_997_NA	*Serpinh1*	3	0.04274286
								chr13:clu_1513_NA	*Mtr*	2	0.0237929
								chr16:clu_3657_NA	*Cblb*	3	0.04785809
								chr2:clu_4260_NA	*Ccdc141*	2	0.02739385
								chr5:clu_2007_NA	*Gbp6*	2	0.03065032
								chr2:clu_4165_NA	*Dab2ip*	2	0.03065032
								chr1:clu_2601_NA	*Acadl*	2	0.03068008
								chr2:clu_4250_NA	***Ttn***	2	0.03068008
								chr2:clu_4450_NA	*Rbm39*	2	0.03618515
								chr4:clu_575_NA	*Nfia*	2	0.03618515
								chrX:clu_1301_NA	*Msl3*	2	0.03826999
								chr18:clu_1807_NA	*Tcf4*	2	0.03826999
								chr7:clu_1145_NA	*Nap1l4*	2	0.03871731
								chr5:clu_1929_NA	*Pcdh7*	1	0.01654877
								chr18:clu_1778_NA	*Synpo*	2	0.0400688
								chr8:clu_2366_NA	*Dnase2a*	1	0.01661022
								chr15:clu_1354_NA	*Tmem65*	2	0.04211347
								chr7:clu_1083_NA	*Tgfb1i1*	2	0.04211347
								chr6:clu_4690_NA	*Setd5*	2	0.04274286
								chr7:clu_1052_NA	*Ndufab1*	2	0.04274286
								chr17:clu_318_NA	*Hnrnpm*	2	0.04274286
								chr12:clu_3149_NA	*Srsf5*	2	0.04274286
								chr18:clu_1781_NA	*Camk2a*	2	0.04274286
								chr1:clu_2686_NA	*Ppip5k2*	1	0.01741987
								chr19:clu_2970_NA	*Btaf1*	1	0.0176823
								chr3:clu_4935_NA	*Ubap2l*	2	0.04971823