

Supplemental Table 2 - Gene Set Enrichment Analysis. Positive enrichment: chronic *P. gingivalis*-treated group vs. chronic control group

Gene Set	Genes Contributing to Core Enrichment
1 BASAL CELL CARCINOMA	Trp53, Dvl2, Gli3, Wnt5b, Smo, Ctnnb1, Fzd1, Fzd6, Tcf7, Sufu, Fzd8, Ptch2, Gli1, Fzd5, Ptch1, Wnt16, Gli2, Wnt5a, Hhip, Tcf7l1, Wnt9a, Tcf7l2, Fzd2, Bmp4, Fzd7
3 NUCLEACHROMOSOME PART	H2afy, Cbx1, H1fnt, Pura, Syce1, Syce2, Ercc4, Atrx, Ube2i, Tipin, Pola1, Cbx5, 1110036O03Rik, Foxc1, H2afy2
5 REGULATION OF GENE EXPRESSION EPIGENETIC	Gpx1, Crebzf, Dmap1, Tnp1, H2afy, Dnmt1, Dicer1, Hmga1, Dgcr8, Rag1ap1, Smarcd1, Atf7ip, Atrx, Dnmt3a, Glmn, H2afy2
6 KEGG MELANOGENESIS	Mc1r, Dvl2, Camk2d, A, Wnt5b, Creb3l4, Ctnnb1, Fzd1, Gnai2, Adcy5, Fzd6, Tcf7, Gnaq, Creb3l2, Creb3l1, Plcb3, Fzd8, Adcy7, Mapk3, Fzd5, Wnt16, Adcy3, Prkacb, Plcb1, Gnai3, Wnt5a, Gnai1, Tcf7l1, Camk2b, Plcb4, Wnt9a, Camk2g, Tcf7l2, Fzd2, Fzd7
8 DNA REPLICATION 2 DNA DEPENDENT DNA REPLICATION 11 REGULATION OF DNA REPLICATION	² Orc2l, Rev1, ² Orc5l, ² Pura, ^{2,11} Enpp7, ² Rev3l, Pole3, Pot1a, ² Msh2, Terf2, ^{2,11} Cdt1, ² Msh6, Nae1, ² Mlh1, ^{2,11} Nbn, ² Polg2, Pold4, Terf2ip, ² Rfc1, Rad50, ^{2,11} Ccdc88a, Nap1l1, Pole2, ² Prim2, ^{2,11} S100a11, ^{2,11} Gli1, ² Pms2, ^{2,11} Gli2, Ptms, ^{2,11} Tipin, ² Pola1, ² Abl1, ² Mutyh, ² Orc4l, ² Prim1
9 PROTEINACEOUS EXTRACELLULAR MATRIX 4 EXTRACELLULAR MATRIX PART 7 BASEMENT MEMBRANE 13 EXTRACELLULAR MATRIX	^{4,7} Fbn1, ⁴ Col5a1, ^{4,7} Col4a3, Adamts5, ^{4,7} Lama4, ^{4,7} Col4a4, Prelp, ⁴ Col18a1, ^{4,7} Smc3, ^{4,7} Lamb2, ⁴ Col5a2, ⁴ Tnxb, ^{4,7} Magee1, Ltbp4, ^{4,7} Aplp1, ^{4,7} Agrn, ⁴ Col6a3, ⁴ Col3a1, ⁴ Col1a2, ⁴ Col15a1, ^{4,7} Efemp2, ^{4,7} Sntb2, Fbln5, Optc, Postn, ^{4,7} Sgce, Mmp11, Ecm2, ^{4,7} Dmd, ^{4,7} Sgcd, ^{4,7} Sntg2, ^{4,7} Sntb1, ^{4,7} Col4a5
10 KEGG HEDGEHOG SIGNALING PATHWAY	Gas1, Csnk1g3, Ihh, Gsk3b, Rab23, Gli3, Wnt5b, Smo, Csnk1a1, Csnk1g1, Sufu, Fbxw11, Ptch2, Gli1, Ptch1, Wnt16, Gli2, Prkacb, Wnt5a, Hhip, Wnt9a, Bmp4
12 REACTOME CELL EXTRACELLULAR MATRIX INTERACTIONS	Vasp, Fermt2, Itgb1, Parva, Lims2, Flna, Actn1, Rsu1, Fblim1, Ilk
14 REACTOME E2F MEDIATED REGULATION OF DNA REPLICATION	Dhfr, Orc2l, Orc5l, Ccna1, Cdc25a, Cdt1, Fbxo5, Pou5f1, Rrm2, Prim2, Tk2, Pola1, Orc4l, Prim1
15 REACTOME APOPTOTIC EXECUTION PHASE	Bcap31, Hist1h1c, Add1, 2610018G03Rik, H1f0, Vim, Dbnl, Ctnnb1, Casp3, Prkcd, Casp8, Dsg3, Pak2, Hist1h1b, Stk24, Hist1h1a, Dsg1b, Lmna, Tjp2, Rock1, Hist1h1e
16 COLLAGEN	Col11a1, Col13a1, Col16a1, Col10a1, Lum, Col7a1, Col9a2, Col9a1, Col5a1, Col4a3, Col4a4, Col18a1, Col5a2, Tnxb, Col6a3, Col3a1, Col1a2, Col15a1, Col4a5
17 REACTOME INACTIVATION OF APC VIA DIRECT INHIBITION OF THE AP COMPLEX	Anapc2, Cdc26, Bub3, Cdc27, Anapc5, Cdc16, Cdc23, Mad2l1, Anapc7, Anapc4
19 REACTOME SMOOTH MUSCLE	Acta2, Myl12b, Myl6b, Itgb5, Myl6, Mylk, Tln1, Itga1, Myh11, Lmod1, Tpm2, Vcl

CONTRACTION	
20 REACTOME CONVERSION FROM APC CDC20 TO APC CD1 IN LATE ANAPHASE	Cdc14a, Anapc4, Anapc7, Cdc23, Cdc16, Anapc5, Cdc27
21 REACTOME SIGNALING BY PDGF	Pik3cb, Plg, Col5a1, Col4a3, Col4a4, Col5a2, Col6a2, Pik3r2, Ywhab, Col6a1, Mapk3, Col6a3, Col3a1, Col1a2, Src, Col6a6, Plat, Pdgfc, Pdgfd, Thbs2, Pdgfa, Col4a5, Pdgfrb
22 KEGG LYSOSOME	Glb1, Lipa, Ap1s1, Abca2, Atp6v0d1, Ctsb, Idua, Ap1m2, Manba, Ap1s2, Aga, Gga3, Cd164, Ctso, Naglu, Tpp1, Ctsf, Sgsh, Fuca1, Gns, Arsg, Gm2a, Gga2, Atp6v1h, Gla, Cltc, Ap3m2, Abcb9, Ctsh, Sumf1, Cd63, Arsb, Slc17a5, Atp6v0d2, Ctsl, Ids, Ctsk, Asah1, Pla2g15, Ppt1, Hyal1, Hexb
23 MICROTUBULE CYTOSKELETON	Ranbp9, Pcm1, 6330503K22Rik, Akap9, Ccna1, 1700057K13Rik, Pkd2, Clasp2, Kif3c, Abca2, Sac3d1, Ctn3, Ckap5, Npm1, Esp1, Rpgr1p1, Tubgcp3, Brca2, Cep57, Katna1, Tsga14, Crocc, Fbxo5, Stau1, Dynll1, Cdk5rap2, Smc3, Cep63, Lyst, Cdc27, Rabgap1, Cdc16, Dnali1, Kifap3, Lats1, Mid1, Mark1, Atg4c, Gas8, Tubgcp5, Bbs4, Mtap1a, Alms1, Eml2, Ppp4r2, Sass6, Eml1, Mtap1b, Arhgef2, Sept9, Mapre1
24 CELL DIVISION 18 CYTOKINESIS	Pard3, Racgap1, Brca2, Tgfb2, ¹⁸ Anln, ¹⁸ Sept7, ¹⁸ Sept5, ¹⁸ Diap2, ¹⁸ Myh10, ¹⁸ Sept6
25 REACTOME CLASS B2 SECRETIN FAMILY RECEPTORS	Smo, Gngt1, Calcrl, Fzd1, Fzd6, Fzd8, Ptch2, Fzd5, Ptch1, Gng8, Wnt16, Vipr2, Wnt5a, Ramp1, Wnt9a, Gng12, Gnb4, Fzd2, Fzd7

The top 25 *P. gingivalis* gene sets whose member genes are predominantly upregulated with respect to the chronic control group. Column 1 includes the gene set name (bold) as provided by MSigDB and the rank of the gene set based on Normalized Enrichment Score (NES). Gene set names that are not in bold are gene sets that are redundant or partially redundant and included within larger bolded gene sets. The NES ranged from 2.32 (for Basal Cell Carcinoma, the top ranked gene set) to 1.66 (REACTOME Class B2 Secretin Family Receptors, the 25th-ranked gene set). FDR q range: 0.001-0.186. Column 2 lists those genes within the gene set that significantly contributed to the enrichment of the gene set. Genes within redundant gene sets are preceded by corresponding superscripts for the gene set to which they belong.

Supplemental Table 3 - Gene Set Enrichment Analysis. Negative enrichment: chronic *P. gingivalis*-treated group vs. chronic control group

Gene Set	Genes Contributing to Core Enrichment
2 REACTOME INTEGRATION OF ENERGY METABOLISM	Gm12251, Adcy6, Gnao1, Pdp2, Gm5506, Ndufv3, Snap25, Gpi1, Pfkfb3, Ndufb3, Pfkfb1, Ndufa6, Gng2, Ndufb6, Ndufa13, Ndufa2, Acaca, Tpi1, Pkm2, Gck, Gng11, Prkaa2, Acly, Ndufa1, Stradb, Etfa, Ndufb2, Rapgef3, Ndufa12, Pflk, Nnt, Suclg1, Sdhc, Cox8a, Pdhx, Pfkfb2, Ndufb11, Ndufc2, Abcc8, Dld, Cox6c, Ndufs8, Ndufv2, Adcy4, Ndufa7, Ndufb7, Atp5k, Prkar2b, Acsl1, Ndufa9, Fasn, Ndufs4, Ndufa4, Atp5o, Dlst, Cox7b, Atp5j2, Atp5d, Atp5f1, Atp5j, Aldoa, Gm4943, Kcnj11, Mlxipl, Ndufb9, Sucla2, Pdk2, Cs, Uqcr2, Idh3g, Cox4i1, Slc25a4, Idh3b, Ndufs7, Etfhd, Sdhc, Uqcr10, Sdha, Ndufs6, Ndufa5, Pdk1, Slc25a20, Rapgef4, Pcx, Ndufs1, Pdha1, Dlat, Cpt2, Idh2, Ndufc1, Atp5c1, Pdha, Ndufb8, Idh3a, Atp5a1, Atp5b, Fh1, Pfk, Ndufs2, Ndufa3, Ndufa8, Etfb, Uqcrs1, Cox6b1, Ogdh, Sdhb, Ndufb5, Ndufb10, Ndufa10, Cacna2d2, Pgam2, Ndufv1, Cyc1, Uqcr1, Acacb, Eno3, Cpt1b, Aco2, Mdh2, Pdk4, Cox5a, Uqcrq
4 KEGG OXIDATIVE PHOSPHORYLATION	Tcirg1, Atp6v0b, Cox4i2, Atp6v1e1, Cox6a1, Ndufs5, Ppa2, Ndufa4l2, Atp6v0a2, Atp6v1b2, Ndufv3, Cox17, Ndufb3, Ndufa6, Ndufb6, Ndufs3, Ndufa2, Ndufa1, Ndufb2, Sdhc, Cox8a, Cox7a2, Ndufa11, Ndufc2, Cox6c, Cox10, Ndufs8, Ndufv2, Ndufa7, Ndufb7, Atp5k, Ndufa9, Ndufs4, Ndufa4, Atp5o, Uqcrh, Atp5j2, Cox7b, Atp5d, Atp5f1, Atp5j, Ppa1, Ndufb9, Uqcr2, Cox4i1, Ndufs7, Sdhc, Uqcr10, Sdha, Ndufs6, Ndufa5, Atp5g3, Ndufs1, Ndufc1, Atp5c1, Ndufb8, Atp5a1, Atp5b, Ndufs2, Ndufa3, Ndufa8, Uqcrs1, Cox6b1, Sdhb, Ndufb5, Ndufb10, Ndufa10, Ndufv1, Cyc1, Uqcr1, Cox7a1, Cox6a2, Cox5a, Uqcrq
5 KEGG PARKINSONS DISEASE	Uba7, Ndufb3, Ndufa6, Ndufb6, Vdac2, Pink1, Ndufs3, Ndufa2, Ndufa1, Ndufb2, Sdhc, Cox8a, Cox7a2, Ndufc2, Cox6c, Ndufs8, Ube2g2, Ndufv2, Ndufa7, Ndufb7, Ndufa9, Ndufs4, Ndufa4, Atp5o, Uqcrh, Cox7b, Atp5d, Atp5f1, Atp5j, Vdac1, Ndufb9, Uqcr2, Cox4i1, Slc25a4, Ndufs7, Sdhc, Uqcr10, Sdha, Ndufs6, Ndufa5, Atp5g3, Ndufs1, Ndufc1, Atp5c1, Ndufb8, Atp5a1, Atp5b, Ndufs2, Ndufa3, Ndufa8, Uqcrs1, Cox6b1, Sdhb, Ndufb5, Ndufb10, Ndufa10, Ndufv1, Cyc1, Uqcr1, Cox7a1, Cox6a2, Cox5a, Uqcrq
7 MITOCHONDRIAL PART	Cox15, Acn9, Mrps10, Bckdk, Mrps18c, Gatm, Mrps24, Mrpl10, Mrps15, Slc25a22, Bcs1l, Timm44, Fis1, Timm50, Pin4, Mrps28, Aifm2, Ndufa6, Mrps35, Mrps18a, Mrps12, Ndufb6, Hccs, Alas2, Vdac2, Ndufa13, Opa1, Mrpl55, Ndufs3, Ndufa2, Timm8b, Aldh4a1, Ndufa1, Supv3l1, Mrpl51, Etfa, Abcb6, Ucp3, Nfs1, Abcb8, Oxa1l, Dnaja3, Phb, Nnt, Phb2, Slc25a3, Timm10, Immt, Slc25a11, Ndufs8, Grpel1, Bckdha, Ndufa9, Ndufs4, Atp5o, Atp5d, Atp5f1, Pmpca, Atp5j, Vdac1, Cs, Mrpl12, Acadm, Rhot2, Mrpl42, Ndufs7, Sdhc, Sdha, Atp5g3, Ndufs1, Mtx2, Atp5c1, Atp5a1, Mfn2, Atp5b, Ndufs2, Etfb, Ogdh, Ndufv1, Uqcr1
8 MITOCHONDRIAN 10 MITOCHONDRIAL MEMBRANE 11 MITOCHONDRIAL ENVELOPE 17 MITOCHONDRIAL MEMBRANE PART	Hsd17b10, Bckdk, Mrps18c, Arg2, Gatm, Gatz1, Mrps24, Mrpl10, Sco1, Ndufs5, Mrps15, Gcdh, Slc25a22, Mrps31, Spg7, Slc22a4, Oxsm, ^{10,17} Bcs1l, Polg, Timm44, ^{10,17} Fis1, Cln3, Mthfd2, Letm1, Lonp1, Fdx1, Pts, Mtch1, ^{10,17} Timm50, Pin4, Mrps28, Pccb, 0610009O20Rik, Tsfm, Mipep, Coq6, Aifm1, ^{10,11} Aifm2, ^{10,11,17} Ndufa6, Mrps35, Mrps18a, Pgs1, Bcl2l1, Mrps12, Msrp2, ^{10,11,17} Ndufb6, ^{10,11} Hccs, Ldhc, ^{10,11} Alas2, Clpx, ^{10,11} Vdac2, ^{10,11,17} Ndufa13, ^{10,11,17} Opa1, Pink1, Mrpl55, ^{10,11,17} Ndufs3, ^{10,11,17} Ndufa2, Glrx5, Diablo, CpoX, Tbrg4, 4930455C21Rik, ^{10,11,17} Timm8b, Aldh4a1, ^{10,11,17} Ndufa1, Supv3l1, Ptges2, D9Ertd402e, Mrpl51, Slc25a12, Mecr, Tmem126a, Etfa, ¹¹ Abcb6, ^{10,11} Ucp3, Nfs1, ¹¹ Abcb8, Acat1, Echs1, Hspe1, ^{10,11,17} Oxa1l, Tmem143, Lrpprc, Dnaja3, Ecsit, Pet112l, ^{10,11} Phb, Nt5m, Amacr, ^{10,11,17} Nnt, ^{10,11} Phb2, Suclg1, Sdhc, ^{10,11} Slc25a3, Ndufa11, Afg3l2, ^{10,11,17} Timm10, Dld, ^{10,11} Immt, Decr1, Acot2, ^{10,11} Slc25a11, ^{10,11,17} Ndufs8, Prdx5, Grpel1, Bckdha, Ghitm, Hspd1, ^{10,11,17} Ndufa9, Foxred1, ^{10,11,17} Ndufs4, Ndufa4, ^{10,11,17} Atp5o, Hint2, ^{10,11,17} Atp5d, Atp5f1, ^{10,11} Pmpca, ^{10,11} Atp5j, Coq7, ^{10,11} Vdac1, Sucla2, Cs, Bcat2, Hadh, Mrpl12, Acadm, Hspa9, Sod2, Acads, ^{10,11,17} Rhot2, Slc25a4, Idh3b, Mrpl42, ^{10,11,17} Ndufs7, Gbas, ^{10,11} Sdhc, Acadvl, ^{10,11,17} Sdha, Pdk1,

	Pcx, Chchd3, ^{10,11,17} Atp5g3, ^{10,11,17} Ndufs1, Pdha1, ^{10,11} Mtx2, Trak1, Idh2, Slc25a13, ^{10,11,17} Atp5c1, ^{10,11,17} Atp5a1, Me3, ^{10,11,17} Mfn2, ^{10,11,17} Atp5b, Fh1, ^{10,11,17} Ndufs2, Ndufa8, Etfb, ^{10,11} Ogdh, Sdhb, ^{10,11,17} Ndufv1, Cyc1, ^{10,11,17} Uqcrc1, Cox7a1, Cisd1, Cpt1b, Aco2, Pdk4, Ckmt2, 8430408G22Rik
9 KEGG CITRATE CYCLE TCA CYCLE	Mdh1, Idh2, Ogdh1, Sdhc, Fh1, Sdhc, Cs, Idh3b, Ogdh, Mdh2, Pdha1, Sdhb, Sdha, Dlat, Dlst, Dld, Idh3a, Idh3g, Sucla2, Pdhb, Suclg1, Aco2, Pck1, Pcx, Acly
12 KEGG ALZHEIMERS DISEASE	Ndufv3, Itpr3, Ppp3cc, Ndufb3, Ndufa6, Il1b, Ndufb6, Ndufs3, Ndufa2, Ndufa1, Ndufb2, Sdhc, Cox8a, Cox7a2, Ndufc2, Atf6, Cox6c, Ndufs8, Ndufv2, Ndufa7, Ndufb7, Itpr2, Ndufa9, Ndufs4, Ndufa4, Ryr3, Atp5o, Uqcrh, Cox7b, Atp5d, Atp5f1, Atp5j, Ndufb9, Uqcrc2, Cox4i1, Ndufs7, Sdhc, Uqcr10, Sdha, Ndufs6, Ndufa5, Atp5g3, Ndufs1, Ndufc1, Atp5c1, Ndufb8, Atp5a1, Atp5b, Ndufs2, Ndufa3, Atp2a2, Ndufa8, Uqcrc1, Cox6b1, Sdhb, Ndufb5, Ndufb10, Ndufa10, Ndufv1, Cyc1, Uqcrc1, Cox7a1, Cox6a2, Cox5a, Uqcrc1, Lpl
13 ORGANELLE INNER MEMBRANE 16 MITOCHONDRIAL INNER MEMBRANE	¹⁶ Timm50, ¹⁶ Ndufa6, ¹⁶ Ndufb6, ¹⁶ Hccs, ¹⁶ Alas2, ¹⁶ Ndufa13, ¹⁶ Opa1, ¹⁶ Ndufs3, ¹⁶ Ndufa2, Narf, ¹⁶ Timm8b, ¹⁶ Ndufa1, ¹⁶ Ucp3, ¹⁶ Oxa1l, ¹⁶ Phb, ¹⁶ Nnt, ¹⁶ Phb2, ¹⁶ Slc25a3, ¹⁶ Timm10, ¹⁶ Immt, ¹⁶ Slc25a11, ¹⁶ Ndufs8, ¹⁶ Ndufa9, ¹⁶ Ndufs4, ¹⁶ Atp5o, ¹⁶ Atp5d, ¹⁶ Pmpca, ¹⁶ Atp5j, ¹⁶ Ndufs7, ¹⁶ Sdhc, ¹⁶ Sdha, ¹⁶ Atp5g3, ¹⁶ Ndufs1, ¹⁶ Atp5c1, ¹⁶ Atp5a1, ¹⁶ Atp5b, ¹⁶ Ndufs2, ¹⁶ Ndufv1, ¹⁶ Uqcrc1
14 KEGG HUNTINGTONS DISEASE	Ndufb3, Ndufa6, Ndufb6, Vdac2, Ndufs3, Ndufa2, Ucp1, Ndufa1, Polr2e, Ndufb2, Sdhc, Cox8a, Cox7a2, Ndufc2, Cox6c, Ndufs8, Ndufv2, Pparg, Ndufa7, Ndufb7, Ndufa9, Ndufs4, Ndufa4, Atp5o, Uqcrh, Cox7b, Atp5d, Atp5f1, Atp5j, Vdac1, Ndufb9, Sod2, Uqcrc2, Cox4i1, Slc25a4, Ndufs7, Sdhc, Uqcr10, Sdha, Ndufs6, Ndufa5, Atp5g3, Ndufs1, Ndufc1, Atp5c1, Ndufb8, Atp5a1, Atp5b, Ndufs2, Ndufa3, Ndufa8, Uqcrc1, Cox6b1, Sdhb, Ndufb5, Ndufb10, Ndufa10, Ndufv1, Cyc1, Ppargc1a, Uqcrc1, Cox7a1, Cox6a2, Cox5a, Uqcrc1
15 REACTOME PYRUVATE METABOLISM AND TCA CYCLE 18 REACTOME CITRIC ACID CYCLE	Bsg, ¹⁸ Nnt, ¹⁸ Suclg1, ¹⁸ Sdhc, Pdhx, ¹⁸ Dld, ¹⁸ Dlst, ¹⁸ Sucla2, Pdk2, ¹⁸ Cs, Ldha, ¹⁸ Idh3g, Ldha, ¹⁸ Idh3b, ¹⁸ Sdhc, ¹⁸ Sdha, Pdk1, Pdha1, Dlat, ¹⁸ Idh2, Pdhb, ¹⁸ Idh3a, ¹⁸ Fh1, ¹⁸ Ogdh, ¹⁸ Sdhb, ¹⁸ Aco2, ¹⁸ Mdh2, Pdk4, Slc16a1
19 KEGG CARDIAC MUSCLE CONTRACTION	Cox8a, Cox7a2, Cox6c, Atp1a1, Uqcrh, Cox7b, Tnnt2, Uqcrc2, Cox4i1, Uqcr10, Tnni3, Myl2, Actc1, Atp1b1, Atp2a2, Myh6, Uqcrc1, Cox6b1, Ryr2, Cacna2d2, Cyc1, Uqcrc1, Cox7a1, Myl3, Cox6a2, Tnnc1, Cox5a, Uqcrc1, Myh7
20 REACTOME DIABETES PATHWAYS 1 REACTOME GLUCOSE REGULATION OF INSULIN SECRETION 3 REACTOME ELECTRON TRANSPORT CHAIN 6 REACTOME REGULATION OF INSULIN SECRETION	Dnajb11, ^{1,6} Ndufv3, ^{1,6} Snap25, ⁶ Itpr3, Hspa5, ^{1,6} Gpi1, Pappa, ^{1,6} Pfkfb3, ^{1,3,6} Ndufb3, ⁶ Gngt2, ^{1,6} Pfkfb1, ^{1,3,6} Ndufa6, ⁶ Gng2, ^{1,3,6} Ndufb6, ⁶ Glp1r, ^{1,3,6} Ndufa13, Pla2g7, Dnajb9, ^{1,3,6} Ndufs3, ^{1,3,6} Ndufa2, ^{1,6} Eno1, ^{1,6} Tpi1, Igf2, ^{1,6} Pkm2, ^{1,6} Gck, ⁶ Gng11, ^{1,3,6} Ndufa1, ^{1,3,6} Etfb, ^{1,3,6} Ndufb2, ^{1,6} Rapgef3, ^{1,3,6} Ndufa12, ^{1,6} Pfkl, ^{1,6} Nnt, ^{1,6} Suclg1, ^{1,3,6} Sdhc, ^{1,3,6} Cox8a, ^{1,6} Pdhx, ^{1,3,6} Ndufa11, ^{1,6} Pfkfb2, ^{1,3,6} Ndufb11, ^{1,3,6} Ndufc2, ^{1,6} Abcc8, Atf6, ^{1,6} Dld, ^{1,3,6} Cox6c, ^{1,3,6} Ndufs8, ^{1,3,6} Ndufv2, Herpud1, ^{1,3,6} Ndufa7, ^{1,3,6} Ndufb7, ⁶ Itpr2, ^{1,6} Atp5k, ⁶ Prkar2b, ^{1,3,6} Ndufa9, ^{1,3,6} Ndufs4, Igfbp3, ^{1,3,6} Ndufa4, ^{1,6} Atp5o, ^{1,6} Dlst, ^{1,3,6} Cox7b, ^{1,6} Atp5j2, ^{1,6} Atp5d, ^{1,6} Atp5f1, ^{1,6} Atp5j, ^{1,6} Aldoa, ^{1,6} Kcnj11, ^{1,3,6} Ndufb9, ^{1,6} Sucla2, ^{1,6} Cs, ^{1,3,6} Uqcrc2, ^{1,6} Idh3g, ^{1,3,6} Cox4i1, ^{1,6} Slc25a4, ^{1,6} Idh3b, ^{1,3,6} Ndufs7, ^{1,3,6} Etfb, ^{1,3,6} Sdhc, ^{1,3,6} Uqcr10, ^{1,3,6} Sdha, ^{1,3,6} Ndufs6, ^{1,3,6} Ndufa5, ^{1,6} Rapgef4, ^{1,6} Pcx, ^{1,3,6} Ndufs1, ^{1,6} Pdha1, ^{1,6} Dlat, ^{1,6} Idh2, ^{1,3,6} Ndufc1, ^{1,6} Atp5c1, ^{1,6} Pdha1, ^{1,3,6} Ndufb8, ^{1,6} Idh3a, ^{1,6} Atp5a1, ^{1,6} Atp5b, ^{1,6} Fh1, ^{1,6} Pfkm, ^{1,3,6} Ndufs2, ^{1,3,6} Ndufa3, ^{1,3,6} Ndufa8, ^{1,3,6} Etfb, ^{1,3,6} Uqcrc1, ^{1,3,6} Cox6b1, ^{1,6} Ogdh, ^{1,3,6} Sdhb, ^{1,3,6} Ndufb5, ^{1,3,6} Ndufb10, ^{1,3,6} Ndufa10, ^{1,6} Cacna2d2, ^{1,6} Pgam2, ^{1,3,6} Ndufv1, ^{1,3,6} Cyc1, ^{1,3,6} Uqcrc1, ^{1,6} Eno3, ^{1,6} Aco2, ^{1,6} Mdh2, ^{1,3,6} Cox5a, ^{1,3,6} Uqcrc1, ⁶ Kcng2
21 REACTOME GLUCOSE METABOLISM	Gpi1, Pfkfb3, Pfkfb1, Ugp2, Fbp2, Eno1, Tpi1, Pkm2, Slc25a12, Pgm2, Pygb, Gbe1, Pfkl, Gyg, Pfkfb2, Slc25a11, Agl, Pygl, Pck1, Gys1, Aldoa, Gys2, Pcx, Slc25a13, Pygm, Pfkm, Mdh1, Pgam2, Eno3, Mdh2, Got1
22 ENERGY DERIVATION BY OXIDATION OF ORGANIC COMPOUNDS	Gck, Gfpt2, Adrb3, Pygb, ²³ Oxa1l, ²³ Nnt, ²³ Sdhc, ²³ Ndufs4, ²³ Uqcrc2, ²³ Sdhc, Crat, Acadvl, Gys2, ²³ Sdha, ²³ Ndufs1, Pygm, ²³ Pdha1, ²³ Me3, ²³ Sdhb, ²³ Ppargc1a, ²³ Uqcrc1, ²³ Aco2

23 CELLULAR RESPIRATION	
24 REGULATION OF HEART CONTRACTION	Kcnj12, Kcne1, Tnnt2, Kcnq1, Hspb7, Actc1, Chrm2, Cacna1h, Myh6, Ryr2, Scn5a, Kcng2, Des, Myh7
25 KEGG PPAR SIGNALING PATHWAY	Angptl4, Dbi, Acsl5, Acsl6, Ucp1, Fabp7, Fabp4, Slc27a1, Scp2, Plin1, Pparg, Scd1, Acsl1, Acox1, Pck1, Adipoq, Acadm, Ppara, Slc27a2, Aqp7, Cpt2, Nr1h3, Rxrg, Acadl, Cpt1b, Sorbs1, Cd36, Lpl

The top 25 *P. gingivalis* gene sets whose member genes are predominantly downregulated with respect to the chronic control group. Column 1 includes the gene set name (bold) as provided by MSigDB and the rank of the gene set based on Normalized Enrichment Score (NES). Gene set names that are not in bold are gene sets that are redundant or partially redundant and included within larger bolded gene sets. The NES ranged from -3.24 (for REACTOME Integration of Energy Metabolism, the top ranked gene set) to -2.33 (KEGG PPAR Signaling Pathway, the 25th-ranked gene set). FDR $q < 1 \times 10^{-30}$. Column 2 includes those genes within the gene set that significantly contributed to the enrichment of the gene set. Genes within redundant gene sets are preceded by corresponding superscripts for the gene set to which they belong.

Supplemental Table 4 - Gene Set Enrichment Analysis. Positive enrichment: chronic *C. pneumoniae*-treated group vs. chronic control group

Gene Set	Genes Contributing to Core Enrichment
1 MICROBODY 2 PEROXISOME 20 PEROXISOME ORGANIZATION AND BIOGENESIS 7 KEGG PROPANOATE METABOLISM	Gnpat, Pipox, Peci, Amacr, Ide, Ech1, Crot, ²⁰ Pex12, Acot8, ²⁰ Pex1, ²⁰ Pex7, Acot4, Acox3, ²⁰ Pex19, Pnpla8, Scp2, Acad11, Lonp2, ⁷ Mlycd, ²⁰ Pex14, ²⁰ Pex6, Pex11a, Hsd17b4, Pmvk, Slc25a17, Pxmp4, ²⁰ Pex3, ²⁰ Pex13, ²⁰ Abcd3, ²⁰ Pex16, Hacl1, Abcd2, Ehhadh, Slc27a2
3 KEGG PEROXISOME 12 REACTOME PEROXISOMAL LIPID METABOLISM	Pipox, ¹² Acaa1a, Peci, ¹² Amacr, Ech1, ¹² Crot, Ddo, Pex12, ¹² Acot8, ¹² Abcd1, Sod1, Pex1, Pex7, ¹² Acox3, Ephx2, Pxmp3, Pex19, Mpv17l, Abcd4, ¹² Crat, ¹² Scp2, Pex5, Mlycd, Acsl1, Pex14, Acsl3, ¹² Acox1, Pex6, Pex11a, Pecr, ¹² Hsd17b4, Nudt12, Decr2, Pmvk, ¹² Slc25a17, Pxmp4, Pex3, Pex13, ¹² ldh1, Dhcr4, Cat, Abcd3, Pex16, ¹² Hacl1, Abcd2, Ehhadh, ¹² Slc27a2, Acsl5; (Gnpat – 12 ONLY)
4 KEGG PPAR SIGNALING PATHWAY	Apoc3, Fabp5, Cyp27a1, Acox3, Rxra, Acadm, Slc27a1, Acadl, Scp2, Gyk, Acsl1, Cpt2, Acsl3, Acox1, Nr1h3, Ppara, Dbi, Angptl4, Aqp7, Pparg, Scd1, Fabp4, Ehhadh, Slc27a2, Me1, Ucp1, Acsl5, Plin1, Adipoq, Pck1
5 REACTOME METABOLISM OF LIPIDS AND LIPOPROTEINS 6 REACTOME REGULATION OF LIPID METABOLISM BY PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR ALPHA 22 REACTOME CHOLESTEROL BIOSYNTHESIS 23 REACTOME SYNTHESIS OF BILE ACIDS AND BILE SALTS VIA 7ALPHA HYDROXYCHOLESTEROL	Crot, Cav1, Cyp46a1, Ldlr, Acat1, ²³ Acot8, Abcd1, Apoc3, Kdsr, Tm7sf2, Scarb1, Prkaca, Hsd11b1, Echs1, ²³ Cyp27a1, Hadha, Acox3, Sptlc1, ⁶ Abca1, ⁶ Rxra, ⁶ Acadm, ⁶ Slc27a1, Crat, Stard5, Abhd5, Acadl, Decr1, ^{6,23} Scp2, Gyk, Hadh, Prkd1, ²² Cyp51, ²³ Hsd3b7, ⁶ Acsl1, Dci, ⁶ Cpt2, Acads, Agpat1, ⁶ Acox1, Sgpl1, Gpam, ⁶ Nr1h3, ⁶ Ppara, Lass2, ⁶ Pex11a, ²³ Hsd17b4, ²² Dhcr7, Acadvl, ²² Pmvk, ⁶ Angptl4, Slc25a17, ²² Sqle, Agpat3, ²² Sc5d, ²² Fdft1, Idh1, ⁶ Srebf1, Slc25a20, ²² Lss, Acacb, ⁶ Plin2, ⁶ Scd1, Hacl1, ⁶ Fabp4, ⁶ Ehhadh, ⁶ Dgat1, ²² Dhcr24, ²³ Slc27a2, ⁶ Me1, ⁶ Ucp1, Lipe, Agpat2, ⁶ Plin1, Mgl1, ²² Nsdhl, ⁶ Acaca, Gpd1, ⁶ Fasn, Gpd2; (Amacr – 23 ONLY)
8 KEGG VALINE LEUCINE AND ISOLEUCINE DEGRADATION 7 KEGG PROPANOATE METABOLISM	⁷ Acat1, ⁷ Mcee, ⁷ Echs1, Hibadh, ⁷ Hadha, Aox1, Bcat2, Acaa2, ⁷ Acadm, Dld, Mccc1, Acad8, Acadsb, ⁷ Mut, Hadh, Bckdhd, Acads, Mccc2, ⁷ Aldh6a1, ⁷ Hibch, ⁷ Aldh2, ⁷ Aldh9a1, Bckdha, ⁷ Pccb, Dbt, ⁷ Pcca, ⁷ Ehhadh, ⁷ Acat2
9 KEGG FATTY ACID METABOLISM	Aldh3a2, Acaa1a, Peci, Adh5, Acat1, Echs1, Hadha, Acox3, Acaa2, Acadm, Acadsb, Acadl, Hadh, Adh7, Acsl1, Dci, Cpt2, Acads, Acsl3, Acox1, Acadvl, Aldh2, Aldh9a1, Ehhadh, Adh1, Acat2, Acsl5
10 REACTOME METABOLISM OF VITAMINS AND COFACTORS	Pank2, Nadsyn1, Aasdhppt, Rfk, Tpk1, Mthfd1, Ppcdc, Flad1, Shmt1, Slc25a16, Cyb5, Gsto2, Slc5a6, Slc25a32, Slc46a1, Nadk, Slc19a1, Coasy, Pank3, Pank1, Acp5, Fasn

11 KEGG PYRUVATE METABOLISM 7 KEGG PROPANOATE METABOLISM	Acat3, Haghl, ¹ Ldha, Hagh, Dlat, Acat1, Acyp1, Pdha1, Pdhb, Dld, Pkm2, Grhpr, Ldhd, Aldh2, Aldh9a1, ⁷ Acacb, Me1, Pcx, ⁷ Acss2, ⁷ Acaca, Pck1, Acat2
13 KEGG GLYCEROLIPID METABOLISM	Agpat9, Dgkb, Gyk, Agk, Agpat6, Agpat1, Gpam, Aldh2, Agpat3, Aldh9a1, Dgat2, Dgat1, Pnpla3, Agpat2, Mgl
15 LIPID CATABOLIC PROCESS 24 CELLULAR LIPID CATABOLIC PROCESS	²⁴ Smpd3, ²⁴ Prdx6, ²⁴ Aldh5a1, ²⁴ Ech1, ²⁴ Cyp46a1, ²⁴ Pla2g4c, Angptl3, ²⁴ Echs1, ²⁴ Acadm, ²⁴ Acads, ²⁴ Ppara, ²⁴ Acadvl, ²⁴ Hacl1, ²⁴ Pnpla3, Cidea
16 MITOCHONDRION LUMEN 17 MITOCHONDRIAL MATRIX 7 KEGG PROPANOATE METABOLISM	Timm8b, Spg7, Preld1, Trnt1, Polrmt, Car5a, Tomm22, Immt, Asah2, Caprin2, Hscb, Fdxr, Casp7, Dguok, Tmem186, Opa1, Ccdc39, Slc9a6, Cpt1b, Abcb6, Sdhd, Dnajc19, Atp5d, Ndufa1, Cisd1, Sco1, Gpx4, Fdx1, Tsfm, Hint2, Mrpl32, Mtx2, Supv31l, Fh1, Gcdh, Hsd3b1, Uqcrc1, Cox15, Cln3, Agpat5, Napg, ^{14,17} Polg2, Sod2, Tbrg4, ^{14,17} Mrpl40, ^{14,17} Timm44, Ndufb6, ^{14,17} Mrps24, Hspe1, Hspd1, Phb2, Cyc1, Sdhd, Mthfd1, Hsd17b10, Mtrf1, Peci, Afg3l2, Ndufs4, Mrps31, Glrx2, ^{14,17} Mrps15, Surf1, Aldh5a1, Amacr, ^{14,17} Cs, Idh3b, Slc25a15, Coq4, ^{14,17} Etfa, Ppox, ^{14,17} Mrps35, ^{14,17} Mrps18a, Pet112l, Ndufs3, ^{14,17} Etfb, Maob, D2hgdh, Ndufs8, Clpx, ^{14,17} Mrps11, ^{14,17} Dnaja3, Cox4nb, Slc22a4, Hspa9, Acat1, Tufm, Sdha, Oxsm, Sod1, Timm9, Pdha1, ^{14,17} Mrps22, Htra2, Mcat, ^{14,17} Nr3c1, Echs1, ^{14,17} Bckdk, Mosc2, Foxred1, Timm50, Ecsit, Cox11, Acn9, Mtif3, Thg1l, Ndufs5, Bcs1l, Casp8, Bcat2, Ptges2, Alas2, Glud1, ^{14,17} Acadm, Dld, Smcr7l, ^{14,17} Aldh4a1, Acp6, Mtif2, Acadsb, Aco2, Tfam, Abcb8, Tmem143, Ghitm, Aifm1, Aass, Glrx5, Mut, Decr1, Lonp1, Triap1, ⁷ Sucla2, Hadh, Bphl, Phb, Slc25a22, ^{14,17} Mrpl10, ⁷ Suclg1, Sars2, Bnip3l, Iscu, ^{14,17} Bckdhd, Txnrd2, Acads, Ak3, Gcsh, Cox18, ^{14,17} Grpel1, Ldhd, Pts, Acadvl, ^{14,17} Mrps21, Dhrr4, ^{14,17} Bckdha, Pccb, ^{14,17} Gm4459, Ucp3, Coq6, Pdk4, ^{14,17} Dbt, Aifm2, Gstz1, Letm1, Car5b, Nipsnap1, Mecr, Pcx, Slc25a1
18 REACTOME BRANCHED CHAIN AMINO ACID CATABOLISM	Auh, Hsd17b10, Acat1, Hibadh, Bcat2, Dld, Mccc1, Acad8, Acadsb, Bckdhd, Mccc2, Aldh6a1, Hibch, Bckdha, Dbt
19 COFACTOR METABOLIC PROCESS	Sdhd, Mocos, Fech, Acot3, Cox15, Gclc, Blvra, Gclm, Sdhd, Pdss2, Glrx2, Ppox, Alas1, Sdha, Oxsm, Sod1, Pgl, Acot4, Pdhd, Alas2, Aco2, Gpx1, Tspo, Alad, Mlycd, Iscu, Mocs2, Coasy Aldh11l, Me1, Pgd, Acly
21 KEGG BIOSYNTHESIS OF UNSATURATED FATTY ACIDS	Acot4, Hadha, Acox3, Acox1, Pecr, Elovl5, Hsd17b12, Scd1, Ptplb, Elovl6
25 VITAMIN METABOLIC PROCESS	Pgl, Rxra, Dhrr3, Retsat, Dhrr9, Me1, Pgd

The top 25 *C. pneumoniae* gene sets whose member genes are predominantly upregulated with respect to the chronic control group. Column 1 includes the gene set name (bold) as provided by MSigDB and the rank of the gene set based on Normalized Enrichment Score (NES). Gene set names that are not in bold are gene sets that are redundant or partially redundant and included within larger bolded gene sets. The NES ranged from 2.64 (for Microbody Peroxisome, the top ranked gene set) to 2.03 (Vitamin Metabolic Process, the 25th-ranked gene set). FDR q range: 0-0.001. Column 2 includes those genes within the gene set that significantly contributed to the enrichment of the gene set. Genes within redundant gene sets are preceded by corresponding superscripts for the gene set to which they belong.

Supplemental Table 5 - Gene Set Enrichment Analysis. Negative enrichment: chronic C. pneumoniae-treated group vs. chronic control group

Gene Set	Genes Contributing to Core Enrichment
1 KEGG HYPERTROPHIC CARDIOMYOPATHY	Cacna1d, Itga5, Itgb8, Tgfb1, Prkag3, Itga2, Cacna2d1, Sgcb, Cacnb2, Lama2, Prkaa2, Sgcg, Itgb6, Sgca, Slc8a1, Cacna1c, Atp2a2, Ryr2, Cacna2d2, Des, Actc1, Myh7, Tnni3, Myh6, Myl2, Myl3, Tnnc1, Ttn, Mybpc3, Tnnt2
2 KEGG DILATED CARDIOMYOPATHY	Prkx, Itga2, Cacna2d1, Sgcb, Cacnb2, Lama2, Sgcg, Itgb6, Sgca, Slc8a1, Cacna1c, Atp2a2, Ryr2, Cacna2d2, Des, Actc1, Myh7, Tnni3, Myh6, Myl2, Myl3, Tnnc1, Ttn, Mybpc3, Tnnt2
3 REACTOME MUSCLE CONTRACTION 4 REACTOME STRIATED MUSCLE CONTRACTION	⁴ Mybpc2, 2900073G15Rik, ⁴ Ttn, ⁴ Tnnt2, ⁴ Tnni3, ⁴ Tnni1, ⁴ Tnnc1, ⁴ Tmod1, ⁴ Tcap, Sorbs1, ⁴ Neb, ⁴ Myl2, ⁴ Myl3, ⁴ Myl4, ⁴ Myh6, ⁴ Mybpc3, ⁴ Des, ⁴ Actn2
5 MUSCLE DEVELOPMENT 21 SKELETAL MUSCLE DEVELOPMENT	Gaa, Tgfb1, Hbegf, ²¹ Svil, ²¹ Notch1, Sgcb, ²¹ Tbx3, Ache, Mstn, ²¹ Nrd1, ²¹ Cacnb2, Lama2, Sgcg, Sgca, ²¹ Mapk12, ²¹ Igfbp3, ²¹ Cacna1h, Itgb1bp2, ²¹ Acta1, Myh7, Tnni3, Myh6, ²¹ Ttn, Mybpc3, ²¹ Csrp3
6 ACTIN CYTOSKELETON	Fscn1, Gsn, Ablim1, Sep11, Capg, Pdlim5, Spna1, Amot, Sorbs1, Neb, Clic5, Dynll2, Myom1, 2900073G15Rik, Ablim2, Spnb1, Myo18b, Palld, Acta1, Myl4, Abra, Actc1, Myh7, Tnni3, Myh6, Myl3, Tnnc1, Actn2, Tnnt2, Myot
8 STRUCTURAL MOLECULE ACTIVITY 7 STRUCTURAL CONSTITUENT OF MUSCLE	Fbn2, Actl7b, Mybpc1, Strn4, Mtap7, Mtap4, Plp1, Mal, Epb4.114b, Spna1, Lama2, Lad1, ⁷ Neb, Fbln2, ⁷ Myom1, Comp, Chi3l1, ⁷ 2900073G15Rik, Fbln1, Dsp, Myoc, ⁷ Tcap, ⁷ Mybpc2, Acta1, Des, ⁷ Actc1, ⁷ Myh7, ⁷ Myom2, ⁷ Myh6, ⁷ Myl2, ⁷ Myl3, ⁷ Ttn, ⁷ Actn2, ⁷ Mybpc3, ⁷ Myot
9 REGULATION OF MULTICELLULAR ORGANISMAL PROCESS 12 REGULATION OF HEART CONTRACTION 25 REGULATION OF MUSCLE CONTRACTION	Grik2, ¹² Kcnj12, ²⁵ Sphk1, Tlr8, Icosl, ²⁵ 2900073G15Rik, ¹² Kcnq1, ¹² Kcne1, ¹² Scn5a, ²⁵ Ppp1r12b, Ptgds, ¹² Cacna1h, ¹² Ryr2, ¹² Hspb7, ¹² Kcng2, ¹² Chrm2, Ahsg, ¹² Des, ¹² Actc1, ¹² Myh7, ¹² Myh6, ²⁵ Myl2, ²⁵ Tnnc1, ²⁵ Mybpc3, ¹² Tnnt2
10 KEGG CARDIAC MUSCLE CONTRACTION	Slc8a1, Cacna1c, Atp1a1, Atp2a2, Ryr2, Cacna2d2, Atp1b1, Actc1, Myh7, Tnni3, Myh6, Myl2, Myl3, Tnnc1, Cox6a2, Tnnt2
11 CYTOSKELETAL PROTEIN BINDING 23 ACTIN BINDING	Myo9b, Tnnt1, Spnb2, Prnp, Ccr5, Rab11fip5, Apoe, Ezr, Kif5b, Mybpc1, Arfgef1, Baiap2, ²³ Svil, ²³ Ablim1, Ctnna1, Pacsin3, ²³ Egfr, ²³ Pdlim5, Tmod4, ²³ Shroom3, ²³ Spna1, ²³ Ssh2, Jup, ²³ Sorbs1, ²³ Scin, ²³ Fxyd5, Clip1, ²³ Nexn, Clasp1, ²³ Twf2, ²³ Spnb1, Trim63, Palld, Acta1, ²³ Abra, ²³ Tnni3, ²³ Nrap, Tnnc1, Ttn, Actn2, Mybpc3, ²³ Tnnt2
13 KEGG ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY ARVC	Cacna1d, Itga5, Itgb8, Itga2, Cacna2d1, Sgcb, Ctnna1, Ctnna3, Cacnb2, Lama2, Jup, Dsc2, Sgcg, Itgb6, Dsg2, Sgca, Slc8a1, Cacna1c, Dsp, Atp2a2, Pkp2, Ryr2, Cacna2d2, Cdh2, Des, Actn2
14 CONTRACTILE FIBER 15 CONTRACTILE FIBER PART 19 MYOFIBRIL	¹⁹ Neb, ¹⁹ Myom1, 2900073G15Rik, ¹⁹ Acta1, ¹⁹ Abra, ¹⁹ Des, ¹⁹ Myoz2, ¹⁹ Tnni3, Myl3, ¹⁹ Tnnc1, ¹⁹ Ttn, ¹⁹ Tnnt2

16 HEART DEVELOPMENT	Irx4, Fgf12, Gata4, Tbx5, Hand2, Alpk3, Casq2, Myh7, Myh6, Mybpc3
20 GATED CHANNEL ACTIVITY 17 VOLTAGE GATED CHANNEL ACTIVITY 18 VOLTAGE GATED CATION CHANNEL ACTIVITY	Trpc4, Kcnmb4, Chrb4, ^{17,18} Kcnd3, ^{17,18} Cacna1d, Htr3a, ^{17,18} Kcnk1, ^{17,18} Kcnk6, Nmur2, ^{17,18} Kcnh2, ^{17,18} Kcnb2, Clcn1, ^{17,18} Kcnj10, ^{17,18} Kcna5, ^{17,18} Cacna2d1, Trpc3, Chrna3, ^{17,18} Kcna6, ^{17,18} Scn4b, ^{17,18} Kcna1, ^{17,18} Scn7a, ^{17,18} Cacnb2, ^{17,18} Kcnj12, ^{17,18} Kcna4, ^{17,18} Scn4a, Ryr3, ^{17,18} Kcnq1, ^{17,18} Kcne1, Kcnn2, ^{17,18} Cacna1c, ^{17,18} Scn5a, ^{17,18} Cacna1g, ^{17,18} Kcnj5, ^{17,18} Cacna1h, ^{17,18} Kcnj3, Ryr2, ^{17,18} Kcng2
22 CATION CHANNEL ACTIVITY	Kcns1, Trpv5, Trpc4, Kcnmb4, Chrb4, Kcnd3, Cacna1d, Htr3a, Kcnk1, Kcnk6, Kcnh2, Kcnb2, Kcnj10, Kcna5, Cacna2d1, Trpc3, Chrna3, Kcna6, Scn4b, Kcna1, Scn7a, Cacnb2, Kcnj12, Kcna4, Scn4a, Ryr3, Kcnq1, Kcne1, Kcnn2, Cacna1c, Scn5a, Cacna1g, Kcnj5, Cacna1h, Kcnj3, Ryr2, Kcng2
24 CYTOSKELETAL PART	Nek2, Klc1, Myo9b, Gas2, Spnb2, Cenpf, Nefl, Dnaic2, Nedd9, Shroom4, Ezr, Kif5b, Mtap7, Kifc3, Mtap4, Sept11, Capg, Spna1, Amot, Drd2, Narf, Sorbs1, Dynll2, Clip1, Myom1, 2900073G15Rik, Cacna1c, Clasp1, Spnb1, Myo18b, Palld, Acta1, Myl4, Actc1, Myh7, Tnni3, Myh6, Myl3, Tnnc1, Actn2, Tnnt2

The top 25 *C. pneumoniae* gene sets whose member genes are predominantly downregulated with respect to the chronic control group. Column 1 includes the gene set name (bold) as provided by MSigDB and the rank of the gene set based on Normalized Enrichment Score (NES). Gene set names that are not in bold are gene sets that are redundant or partially redundant and included within larger bolded gene sets. The NES ranged from -2.79 (for KEGG Hypertrophic Cardiomyopathy, the top ranked gene set) to -2.23 (Regulation of Muscle Contraction, the 25th-ranked gene set). FDR $q < 1 \times 10^{-30}$. Column 2 includes those genes within the gene set that significantly contributed to the enrichment of the gene set. Genes within redundant gene sets are preceded by corresponding superscripts for the gene set to which they belong.

Supplemental Table 6 - Gene Set Enrichment Analysis. Positive enrichment: Western diet group vs. chronic control group

Gene Set	Genes Contributing to Core Enrichment
1 KEGG LYSOSOME	Arse, Ap3s2, Sumf1, Mcoln1, Ap1g1, Scarb2, Galns, Lamp1, Ap3b1, Nagpa, Gaa, Atp6v0b, Atp6v0a2, M6pr, Ctns, Naglu, Atp6v1h, Atp6ap1, Hgsnat, Naga, Ppt1, Ap1s2, Ap3m2, Ctsw, Cd63, Atp6v0a1, Tpp1, Atp6v0d1, Aga, Npc1, Gm2a, Lamp2, Ap1b1, Gba, Ap1s1, Slc17a5, Clta, Gnptab, Gns, Neu1, Ctsa, Acp2, Fuca1, Pla2g15, Psap, Ctsh, Igf2r, Acp5, Tcirg1, Asah1, Ctsk, Hexa, Cln3, Glb1, Hexb, Dnase2a, Manba, Ctsl, Man2b1, Ctso, Ctsb, Gla, Ctsd, Ctsc, Ctsz, Lgmn, Cln5, Galc, Slc11a1, Lipa, Npc2, Gusb, Atp6v0d2, Laptm5, Cd68, Ctss
2 REACTOME SIGNALING IN IMMUNE SYSTEM 10 REACTOME INNATE IMMUNITY SIGNALING 24 CELL SURFACE INTERACTIONS AT THE VASCULAR WALL	C920025E04Rik, ¹⁰ Nfkbib, Ppp2r5c, Map3k8, Angpt2, ¹⁰ Map2k4, Fyn, ¹⁰ Map2k6, Csk, Gas6, ¹⁰ Mapk14, ¹⁰ Ticam2, ¹⁰ Tlr6, ¹⁰ Ikbkg, ¹⁰ Ripk3, ¹⁰ Ikbke, ¹⁰ Mapkapk3, Itk, Jam2, Atp1b3, ¹⁰ Rps6ka2, ¹⁰ Tlr4, H2-Ob, Icosl, ¹⁰ Dusp7, Cd40, ²⁴ Esam, Icam2, ¹⁰ Map3k1, B2m, ²⁴ Cd244, ²⁴ F11r, ¹⁰ Rps6ka3, ²⁴ Fn1, ²⁴ Slc3a2, Cd28, Cd34, Cd3e, ¹⁰ Map2k1, Icam1, ²⁴ Kras, ²⁴ Lck, ²⁴ Itgal, Cd274, ¹⁰ Myd88, ²⁴ Nras, ²⁴ Slc7a8, ¹⁰ C2, Cd200r1, ²⁴ Slc16a3, Pak1, Ripk2, Grap2, ²⁴ Slc7a7, ¹⁰ Mapk3, ²⁴ Pf4, ¹⁰ Irak4, Tnfrsf14, H2-M3, ²⁴ Pecam1, ²⁴ Itga6, Cd8b1, ²⁴ Ptpn6, ¹⁰ Irak3, ²⁴ Cd47, ²⁴ Olr1, ²⁴ Pros1, Cd3g, ¹⁰ Tlr9, ¹⁰ Tlr2, ²⁴ Tek, ²⁴ Slc7a11, ¹⁰ Dusp6, ¹⁰ Irf7, ¹⁰ Tlr3, Was, ¹⁰ Rps6ka1, Cd4, ¹⁰ Ly96, Evi, Fyb, Cd86, ²⁴ Lyn, ¹⁰ Tlr7, ²⁴ Itgax, H2-Eb1, ²⁴ Selp, ²⁴ Itgam, ²⁴ Fcer1g, Lcp2, ¹⁰ Tlr1, ²⁴ Sirpa, Cd80, Fcgr2b, H2-Aa, ¹⁰ Cd180, Tyrobp, ¹⁰ Tlr8, Fcgr4, ¹⁰ C1ra, ²⁴ Inpp5d, ¹⁰ Lbp, H2-DMA, ¹⁰ C1qc, ¹⁰ C1qa, ¹⁰ C3, ²⁴ Cd84, ¹⁰ C1qb, Vcam1, Vav1, ¹⁰ Ly86, ¹⁰ Cfb, ¹⁰ Cd14, ²⁴ Cd48, ²⁴ Itga4, ²⁴ Itgb2, Ptprc, ²⁴ Selplg, ¹⁰ C6
3 KEGG NATURAL KILLER CELL MEDIATED CYTOTOXICITY	Grb2, Klrk1, Vav2, Gm10499, Bid, Nfatc3, Vav3, Fyn, Ppp3cc, Nfatc1, Tnf, Pik3r3, Icam2, Ppp3r1, Ifnar1, Cd244, Tnfsf10, Ppp3ca, Map2k1, Icam1, Kras, Lck, Itgal, Nras, Pak1, Mapk3, H2-M3, Pik3cd, Ptpn6, Ifngr1, Ifnar2, Sh2d1b1, Sh3bp2, Pik3cg, Pik3r5, Fcer1g, Prkcb, Lcp2, 2010110P09Rik, Rac2, Tyrobp, Fcgr4, Sykb, Plcg2, H2-T23, Vav1, Cd48, Ptk2b, Itgb2
4 KEGG SYSTEMIC LUPUS ERYTHEMATOSUS	Hist1h2bn, Tnf, H2-Ob, Cd40, Hist2h2ab, Cd28, Hist3h2a, C2, Hist2h2ac, Grin2a, Hist1h2bm, Hist1h2bg, H2afz, Hist1h2bb, Fcgr1, Cd86, Hist2h2bb, H2-Eb1, Cd80, Fcgr2b, H2-Aa, Fcgr4, Fcgr3, C1ra, H2-DMA, C1qc, C1qa, C3, C1qb, Hist1h2ak, C6
6 KEGG B CELL RECEPTOR SIGNALING PATHWAY	Akt1, Nfkb1, Malt1, Grb2, Vav2, Nfkbib, Nfatc3, Vav3, Ppp3cc, Nfatc1, Cd79b, Ikbkg, Rasgrp3, Pik3r3, Ppp3r1, Ppp3ca, Map2k1, Kras, Nras, Dapp1, Mapk3, Btk, Pik3cd, Ptpn6, Nfkbie, Cd22, Cd72, Lyn, Pik3cg, Blnk, Pik3r5, Prkcb, 2010110P09Rik, Fcgr2b, Rac2, Pik3ap1, Sykb, Inpp5d, Plcg2, Vav1
7 LEISHMANIA INFECTION	Nos2, Nfkbib, Mapk14, Jak2, Tlr4, Tnf, H2-Ob, Il1a, Myd88, Jak1, Mapk3, Irak4, Ptpn6, Tgfb1, Stat1, Ifngr1, Ncf1, Tlr2, Fcgr1, Cyba, H2-Eb1, Itgam, Ncf4, Prkcb, H2-Aa, Fcgr4, Fcgr3, H2-DMA, C3, Itga4, Itgb2
8 KEGG TOLL LIKE RECEPTOR SIGNALING PATHWAY	Tollip, Map3k8, Map2k4, Map2k6, Mapk14, Ticam2, Tlr6, Ikbkg, Ikbke, Tlr4, Tnf, Cd40, Pik3r3, Ifnar1, Map2k1, Myd88, Mapk3, Irak4, Pik3cd, Stat1, Cxcl10, Ctsk, Ccl5, Ifnar2, Tlr9, Tlr2, Irf7, Tlr3, Ly96, Cd86, Tlr7, Pik3cg, Irf5, Pik3r5, Tlr1, Cd80, Spp1, Tlr8, Lbp, Casp8, Cd14
9 IMMUNE SYSTEM PROCESS 5 IMMUNE RESPONSE	Cd79b, Ccr9, Ikbkg, Nlrc3, Il15, Cebpg, Lig1, Myh9, Cxcl13, Atp6v0a2, Tlr4, Map4k1, Icosl, ⁵ Mr1, ⁵ Fth1, ⁵ Ccl12, Cdk6, ⁵ Il18bp, ⁵ Ets1, ⁵ Ctsw, ⁵ Il6st, ⁵ Tcf7, ⁵ Preli1, ⁵ Cd28, Acvr1b, Cd34, Cd3e, Lck, Lrmp, ⁵ Psmb10, ⁵ Il18, ⁵ Ifitm2, ⁵ Cd274, ⁵ Rsad2, ⁵ Tapbp, ⁵ Ciita, ⁵ C2, ⁵ Cnr2, ⁵ Bst2, ⁵ Gbp2, ⁵ Ccr2, ⁵ Ccr1, ⁵ Il27ra, Pf4, ⁵ Tnfrsf14, Cklf, ⁵ Gpr65, ⁵ Il2ra, ⁵ Tgfb1, Clec7a, ⁵ Cxcl12, ⁵ Sema4d, ⁵ Ccl5, ⁵ Dpp4, Cd47, ⁵ Ifitm3, ⁵ Il4ra, Prex1, ⁵ Bnip3l, ⁵ Ptger4, ⁵ Il10rb, Hcls1, ⁵ Nfam1, ⁵ Cd22, ⁵ C5ar1, ⁵ Was, ⁵ Lat2, Cd4, ⁵ Ctsc, ⁵ Fcgr1, ⁵ Fyb, ⁵ Cd86, Lyn, ⁵ Tlr7, ⁵ Rgs1, ⁵ Aim2, ⁵ Irf8, ⁵ Blnk, ⁵ Cd74, ⁵ Ncf4, ⁵ Lcp2, Sfp1, ⁵ Fcgr2b, Saa3, ⁵ Tlr8, ⁵ Trem2, ⁵ Fcgr4, Sykb, ⁵ Arhgdib, ⁵ Ptafr, ⁵ Il7r, ⁵ Igsf6, ⁵ Ccr5, Dock2, Mafb, ⁵ Cd83, ⁵ Cx3cl1, ⁵ Ctss, ⁵ Ly86, ⁵ Bst1, ⁵ Il2rg, ⁵ Itgb2, ⁵ Ptprc, ⁵ Cxcr4
11 REACTOME TOLL RECEPTOR CASCADES	Ppp2ca, Tirap, Tab2, Ripk1, Mapk9, Nfkb1, Pik3c3, Irak1, Ppp2r1a, Nfkbib, Map2k4, Map2k6, Mapk14, Ticam2, Tlr6, Ikbkg, Ripk3, Ikbke, Mapkapk3, Rps6ka2, Tlr4, Dusp7, Map3k1, Rps6ka3, Map2k1, Myd88, Mapk3, Irak4, Irak3, Tlr9, Tlr2, Dusp6,

	Irf7, Tlr3, Rps6ka1, Ly96, Tlr7, Tlr1, Cd180, Tlr8, Lbp, Ly86, Cd14
13 REACTOME S PHASE 15 REACTOME SYNTHESIS OF DNA	¹⁵ Rpa1, ¹⁵ Pma3, ¹⁵ Psm2, ¹⁵ Pma2, ¹⁵ Psm9, ¹⁵ Prim2, ¹⁵ Psmc6, ¹⁵ Cdc6, ¹⁵ Psm1, ¹⁵ Psm2, ¹⁵ Orc5l, ¹⁵ Psm4, Cul1, ¹⁵ Psm13, ¹⁵ Mcm5, ¹⁵ Orc4l, ¹⁵ Pma6, ¹⁵ Psm6, ¹⁵ Rfc5, ¹⁵ Mcm3, ¹⁵ Psm3, ¹⁵ Orc2l, ¹⁵ Psm3, ¹⁵ Rb1, ¹⁵ Orc3l, ¹⁵ Pola1, ¹⁵ Pma1, Skp1a, ¹⁵ Gins1, ¹⁵ Rfc1, ¹⁵ Psm5, ¹⁵ Mcm4, ¹⁵ Lig1, Ccnh, ¹⁵ Rfc4, ¹⁵ Cdt1, ¹⁵ Pma4, ¹⁵ Pola2, Cdk4, ¹⁵ Gins4, ¹⁵ Psmf1, ¹⁵ Pold4, ¹⁵ Pold3, ¹⁵ Rfc2, ¹⁵ Psm8, ¹⁵ Mcm2, ¹⁵ Pma7, ¹⁵ Psm10, ¹⁵ Pole, ¹⁵ Psm10, ¹⁵ Dna2, ¹⁵ Psm14, ¹⁵ Rfc3, ¹⁵ Psm2, Ccnd1, Ccne2, ¹⁵ Rpa3, ¹⁵ Psm9, ¹⁵ Psm8, ¹⁵ Ccna2, ¹⁵ Pole2, ¹⁵ Mcm7
14 KEGG FC GAMMA R MEDIATED PHAGOCYTOSIS	Pik3r3, Arpc4, Arf6, Map2k1, Pak1, Mapk3, Arpc3, Pik3cd, Arpc5, Marcks, Ncf1, Was, Arpc1b, Hck, Fcgr1, Lyn, Pik3cg, Pik3r5, Prkcb, Fcgr2b, Rac2, Fcgr4, Sykb, Fcgr3, Inpp5d, Plcg2, Dock2, Vav1, Ptpcr
16 REACTOME HOST INTERACTIONS OF HIV FACTORS	Nup37, Psm6, Psmc4, Rac1, Psm12, Psmc1, Kpnb1, Nup210, Arf1, Psm1, Nup155, Nup54, Pma3, Psm2, Pma2, Nupl1, Nup205, Psm9, Psmc6, Aaas, Xpo1, Nup62, Psm1, Psm2, Psm4, Psm13, Pma6, Psm6, Psm3, Ap2s1, Cul5, Npm1, Psm3, Seh1l, Ap1g1, Pacs1, Ran, Fyn, Pma1, Tpr, Skp1a, Psm5, Nup50, Pma4, Ap2m1, Atp6v1h, Ap2b1, Tceb1, Ap1s2, Psmf1, B2m, Psm8, Ap2a2, Cd28, Pma7, Psm10, Lck, Psm10, Ap1b1, Ap1s1, Psm14, Psm2, Cd8b1, Psm9, Psm8, Elmo1, Cd4, Hck, Dock2
17 REACTOME M G1 TRANSITION 12 DNA REPLICATION PRE INITIATION	Psm1, Psmc2, Psm7, Pma5, Psm6, Psmc4, Psm12, Psmc1, ¹² Mcm6, ¹² Psm1, ¹² Pma3, ¹² Psm2, ¹² Pma2, ¹² Psm9, ¹² Psmc6, ¹² Cdc6, ¹² Psm1, ¹² Psm2, ¹² Orc5l, ¹² Psm4, ¹² Psm13, ¹² Mcm5, ¹² Orc4l, ¹² Pma6, ¹² E2f3, ¹² Psm6, ¹² Mcm3, ¹² Psm3, ¹² Orc2l, ¹² Psm3, ¹² Orc3l, ¹² Pma1, ¹² E2f1, ¹² Psm5, ¹² E2f2, ¹² Mcm4, ¹² Cdt1, ¹² Pma4, ¹² Psmf1, ¹² Psm8, ¹² Mcm2, ¹² Pma7, ¹² Psm10, ¹² Psm10, ¹² Psm14, ¹² Psm2, ¹² Psm9, ¹² Psm8, ¹² Mcm7
18 KEGG T CELL RECEPTOR SIGNALING PATHWAY	Mapk9, Akt1, Nfkb1, Malt1, Cbl, Grb2, Vav2, Nck1, Nfkbib, Map3k8, Nfatc3, Vav3, Fyn, Ppp3cc, Nfatc1, Mapk14, Ikbkg, Itk, Tnf, Cdk4, Pik3r3, Ppp3r1, Cd28, Cd3e, Ppp3ca, Map2k1, Kras, Lck, Nras, Pak1, Grap2, Mapk3, Pik3cd, Cd8b1, Ptpn6, Nfkbie, Cd3g, Tec, Cd4, Pik3cg, Pik3r5, Lcp2, 2010110P09Rik, Rasgrp1, Vav1, Ptpcr
19 DEFENSE RESPONSE	Cd40, Gata3, Clec1b, Irak2, F11r, Kng2, Hp, Tnfaip6, Nmi, Il1a, Nlr4, Cd5l, Rsad2, Lsp1, C2, Tnfrsf1a, Rnase6, Ripk2, Cbara1, Anxa1, Ccr2, Ccr1, Stab1, Tnip1, H2-M3, Nlrp3, Tgfb1, Sele, Tcigr1, Cxcl10, Ccl5, Ncf1, Bnip3l, Il10rb, C5ar1, Tlr3, Was, Cysltr1, Aif1, Ly96, Nod1, Clec5a, Cx3cr1, Tlr7, Ccl3, Cfp, Blnk, Il1r2, Csf3r, Ccl2, Tyrobp, Tlr8, Aoah, Ptafr, Lbp, Alox5ap, Ccr5, Cd84, Cd83, C3ar1, Cx3cl1, Cd48, Kcnn4, Lgals3bp, Ptpcr, Cxcr4, Pla2g7, Cybb
20 KEGG NOD LIKE RECEPTOR SIGNALING PATHWAY	Hsp90b1, Nfkbib, Mapk14, Ikbkg, Tnf, Ccl12, Sugt1, Erbb2ip, Xiap, Birc3, Card9, Nlr4, Il18, Card6, Ripk2, Casp1, Mapk3, Ccl7, Nlrp3, Pycard, Ccl5, Nod1, Pstpip1, Ccl2, Tnfaip3, Casp8
21 KEGG HEMATOPOIETIC CELL LINEAGE	Tnf, Cd5, Kit, Cd34, Cd3e, Il1a, Il2ra, Itga6, Cd8b1, Cd44, Il4ra, Cd3g, Cd22, Csf2ra, Cd4, Tfrc, Fcgr1, Cd38, H2-Eb1, Itgam, Csf3r, Anep, Csf1r, Il7r, Cd14, Cd37, Itga4
22 REACTOME G1 S TRANSITION 12 DNA REPLICATION PRE INITIATION	¹² Rpa1, ¹² Pma3, ¹² Psm2, ¹² Pma2, ¹² Psm9, ¹² Prim2, ¹² Psmc6, Fbxo5, ¹² Cdc6, ¹² Psm1, ¹² Psm2, ¹² Orc5l, ¹² Psm4, Cul1, ¹² Psm13, ¹² Mcm5, ¹² Orc4l, ¹² Pma6, ¹² E2f3, ¹² Psm6, ¹² Mcm3, ¹² Psm3, ¹² Orc2l, ¹² Psm3, Rb1, ¹² Orc3l, ¹² Pola1, ¹² Pma1, Skp1a, ¹² E2f1, ¹² Psm5, ¹² E2f2, ¹² Mcm4, Ccnh, ¹² Cdt1, ¹² Pma4, ¹² Pola2, Tys, ¹² Psmf1, ¹² Psm8, ¹² Mcm2, ¹² Pma7, ¹² Psm10, ¹² Pole, ¹² Psm10, Tk2, ¹² Psm14, ¹² Psm2, Ccne2, ¹² Rpa3, ¹² Psm9, ¹² Psm8, Ccna2, ¹² Dbf4, ¹² Pole2, ¹² Mcm7, Cdk1, Rrm2
23 KEGG CHEMOKINE SIGNALING PATHWAY	Ccr7, Gnb1, Grb2, Ccl22, Stat5b, Vav2, Gnai2, Nfkbib, Vav3, Adrbk1, Stat2, Cxcl5, Csk, Ccr9, Jak2, Ikbkg, Adcy4, Itk, Cxcl13, Jak3, Rap1a, Pik3r3, Cxcr6, Ccl12, Pxn, Gng11, Map2k1, Kras, Prkx, Gnai3, Nras, Pak1, Ccr2, Mapk3, Ccr1, Pf4, Gng2, Pik3cd, Ccl7, Stat1, Cxcl12, Cxcl10, Rap1b, Ccl5, Elmo1, Fgr, Prex1, Ncf1, Was, Hck, Arrb2, Cx3cr1, Arrb1, Lyn, Plcb2, Ccl3, Pik3cg, Pik3r5, Gngt2, Prkcb, Rac2, Ccl2, Cxcl16, Ccr5, Dock2, Cx3cl1, Vav1, Ptk2b, Cxcr4

25 REACTOME CELL CYCLE CHECKPOINTS	Hus1, Rpa1, Psma3, Psm2, Psma2, Psm9, Psmc6, Cdc6, Ube2d1, Psme1, Psm2, Orc5l, Psm4, Psm13, Cdc16, Mcm5, Anapc4, Orc4l, Psma6, Rad17, Psm6, Rfc5, Mcm3, Cdc27, Psm3, Orc2l, Rfd2, Trp53, Psme3, Orc3l, Psma1, Rad1, Atm, Psm5, Mcm4, Mdm2, Rfc4, Psma4, Psmf1, Rfc2, Psm8, Mcm2, Psma7, Psm10, Chek2, Psm10, Psm14, Rfc3, Psme2, Bub1b, Ccne2, Rpa3, Psm9, Psm8, Mad2l1, Dbf4, Ube2c, Mcm7, Cdk1, Ccnb2
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The top 25 Western diet gene sets whose member genes are predominantly upregulated with respect to the chronic control group. Column 1 includes the gene set name (bold) as provided by MSigDB and the rank of the gene set based on Normalized Enrichment Score (NES). Gene set names that are not in bold are gene sets that are redundant or partially redundant and included within larger bolded gene sets. The NES ranged from 2.97 (for KEGG Lysosome, the top ranked gene set) to 2.42 (REACTOME Cell Cycle Checkpoints, the 25th-ranked gene set). FDR $q < 1 \times 10^{-30}$. Column 2 includes those genes within the gene set that significantly contributed to the enrichment of the gene set. Genes within redundant gene sets are preceded by corresponding superscripts for the gene set to which they belong.

Supplemental Table 7 - Gene Set Enrichment Analysis. Negative enrichment: Western diet group vs. chronic control group

Gene Set	Genes Contributing to Core Enrichment
1 G PROTEIN COUPLED RECEPTOR ACTIVITY 6 RHODOPSIN LIKE RECEPTOR ACTIVITY 14 PEPTIDE RECEPTOR ACTIVITY	^{6,14} Mas1, ^{6,14} Sstr4, ^{6,14} Grpr, ⁶ Adra2b, Gpr125, Grm7, ⁶ Tas2r107, ⁶ Tas2r121, ^{6,14} Sstr1, ^{6,14} Bdkrb2, ⁶ Adra2a, ⁶ Adra2c, Lphn3, ⁶ Tas2r137, Tmem11, ⁶ Htr5a, ⁶ Htr1f, ^{6,14} Sstr2, ⁶ Tas1r2, Celsr3, ⁶ Tas2r119, Pth2r, Bai1, ^{6,14} Oprm1, ^{6,14} Brs3, ⁶ Fshr, ⁶ Gpr139, ⁶ Chrm1, ⁶ Tas2r140, ^{6,14} Hcrtr2, ⁶ Pdgfrl, ⁶ Drd4, ⁶ Tas2r108, ^{6,14} Mchr1, ⁶ Htr2a, Gpr143, Grm2, ⁶ Olf90, Gcgr, ^{6,14} Tacr2, ⁶ Tas2r130, ^{6,14} Oxtr, Grm3, Vipr2, Bai3, Grm5, ^{6,14} Sstr3, ^{6,14} Cckbr, ^{6,14} Mc3r, ^{6,14} Nmbr, ^{6,14} Galr3, Gpr123, ⁶ Mtnr1a, ^{6,14} Npbwr1, Gpr113, ^{6,14} Cckar, Gpr124, Gpr115, ⁶ Htr6, ^{6,14} Agtr2, ⁶ Pax8, Grm8, ^{6,14} Avpr1b, ⁶ Adra1d, ⁶ Htr1b, Lancl1, ⁶ Ghsr, ⁶ Olf159, ⁶ Htr1a, Gpr128, ⁶ Htr1d, ^{6,14} Tacr1, ⁶ Tas2r118, ⁶ Trhr, ⁶ Mtnr1b, Glp2r, ⁶ Drd3, Gpr110, ^{6,14} Mc5r, Gabbr1, ^{6,14} Mc4r, ⁶ Tbxa2r, ⁶ Olf15, ⁶ Olf410, ^{6,14} Sstr5, ⁶ Tas1r3, Ghrhr, ^{6,14} Oprk1, ^{6,14} Gpr17, ⁶ Chrm5, ^{6,14} Kiss1r, ⁶ Gnrhr, ^{6,14} Galr2, ^{6,14} Nmur2, Lphn1, ⁶ Drd5, ^{6,14} F2r13, ^{6,14} Avpr2
2 APICAL JUNCTION COMPLEX 3 APICOLATERAL PLASMA MEMBRANE	Cldn8, Cldn14, Cldn11, Cldn10a, Cldn4, Cldn17, Wnk4, Cldn6, Amotl1, Sorbs1, Pard3, Pard6a, Cldn1, Cldn18, Ash1l, Cldn3, Cldn12, Cldn16, Cldn23, Cldn19, Cldn7, Cldn20, Cldn9, Pdzd3, Cldn22
4 NEUROTRANSMITTER BINDING 5 NEUROPEPTIDE RECEPTOR ACTIVITY 7 NEUROTRANSMITTER RECEPTOR ACTIVITY 10 NEUROPEPTIDE BINDING	⁷ Gabra2, ⁷ Chrna7, ⁷ Gabra6, ⁷ Gabra4, ⁷ Nmur1, ⁷ Chrm4, Mrgprx2, ^{5,7,10} Galr1, ⁷ Drd1a, ^{5,7,10} Tacr3, Adrb2, ⁷ Chrna6, ^{5,7,10} Sstr4, ^{5,7,10} Sstr1, ⁷ Chrna1, ^{5,7,10} Sstr2, ⁷ Chrn4, ^{5,7,10} Brs3, ⁷ Gabrg2, ⁷ Chrm1, ^{5,7,10} Hcrtr2, ⁷ Drd4, ^{5,7,10} Mchr1, ^{5,7,10} Tacr2, ^{5,7,10} Sstr3, ^{5,7,10} Cckbr, ^{5,7,10} Nmbr, ^{5,7,10} Galr3, ^{5,7,10} Cckar, ⁷ Chrna5, ^{5,7,10} Tacr1, ⁷ Drd3, ^{5,7,10} Sstr5, ⁷ Chrne, ⁷ Chrm5, ^{5,7,10} Kiss1r, ^{5,7,10} Galr2, ^{5,7,10} Nmur2, ⁷ Drd5
9 KEGG NEUROACTIVE LIGAND RECEPTOR INTERACTION	Gipr, Chrna6, Npy2r, Mas1, Gabrg3, Sstr4, Grpr, Grid2, Taar9, Adra2b, Fshb, Grm7, Rxfp2, Sstr1, P2ry2, Bdkrb2, Adra2a, Adra2c, Gabrb2, Grik1, Grin2d, Ltb4r2, Chrna1, Htr5a, Htr1f, Taar2, Sstr2, Gabrb1, Fpr3, Grid1, Thra, Pth2r, Htr2c, Oprm1, Chrn4, P2ry4, Brs3, Fshr, Gabrg2, Chrm1, Hcrtr2, F2, Gpr50, Lhcg, Drd4, Pard3, Mchr1, Htr2a, Grm2, Chrn3, S1pr4, Taar6, Gpr83, Gcgr, Tacr2, S1pr5, Grin2b, Oxtr, Grm3, P2rx1, Vipr2, Taar5, Grm5, Ntsr2, Sstr3, Gabra1, Thrb, Cckbr, Mc3r, Nmbr, Galr3, Mtnr1a, Npbwr1, Cckar, Gzma, Htr6, Grin2c, Agtr2, Oprl1, Lpar2, Grm8, Avpr1b, Chrna5, Adra1d, Htr1b, Ghsr, Chrnd, Htr1a, Grik4, Grin3b, Gabre, Chrng, Calcrl, Htr1d, Tacr1, Trhr, Mtnr1b, Glp2r, Drd3, Mc5r, Gabrp, Gabbr1, Gria1, Mc4r, Tbxa2r, Grik5, Npffr1, Hrh4, Prss2, Hcrtr1, Sstr5, Ghrhr, Npffr2, Oprk1, Chrne, Prlhr, Npy1r, Chrm5, Kiss1r, Gnrhr, Galr2, Gabrd, Nmbr2, Lhb, Drd5, F2r13, Avpr2, Prl, P2rx5
11 REACTOME AMINE LIGAND BINDING RECEPTORS 24 AMINE RECEPTOR ACTIVITY	Taar1, ²⁴ Hrh3, ²⁴ Chrm4, ²⁴ Htr7, ²⁴ Adrb1, ²⁴ Adra1a, ²⁴ Drd1a, ²⁴ Hrh2, ²⁴ Adrb2, Taar9, ²⁴ Adra2b, Taar8c, ²⁴ Adra2a, ²⁴ Adra2c, ²⁴ Htr5a, ²⁴ Htr1f, Taar2, Htr2c, ²⁴ Chrm1, ²⁴ Drd4, ²⁴ Htr2a, Taar6, Taar5, ²⁴ Htr6, ²⁴ Adra1d, ²⁴ Htr1b, ²⁴ Htr1a, ²⁴ Htr1d, ²⁴ Drd3, Hrh4, ²⁴ Chrm5, ²⁴ Drd5; (Htr3b – 24 ONLY)
12 INTERCELLULAR JUNCTION 8 TIGHT JUNCTION	⁸ Cldn8, ⁸ Cldn14, ⁸ Cldn11, ⁸ Cldn10a, Pkp4, ⁸ Cldn4, ⁸ Cldn17, Vcl, Gjb1, ⁸ Wnk4, Dsc1, Bai1, ⁸ Cldn6, ⁸ Amotl1, Amtn, Sorbs1, ⁸ Pard3, Nrap, ⁸ Pard6a, ⁸ Cldn, ⁸ Cldn18, ⁸ Ash1l, ⁸ Cldn3, ⁸ Cldn12, ⁸ Cldn16, ⁸ Cldn23, Ctnna3, ⁸ Cldn19, Gjd3, Pdzd2, ⁸ Cldn7, ⁸ Cldn20, ⁸ Cldn9, Zyx, Pdzd3, ⁸ Cldn22
13 STRUCTURAL CONSTITUENT OF MUSCLE	Actn2, Actc1, Myl6b, 2900073G15Rik, Tcap, Myl6, Mybph, Mybpc3, Myh7, Myot, Asph, Myh11, Myl3, Mylpf, Smtn, Dmd, Tpm2, Myl2, Mybpc1, Mybpc2, Myom1

15 CALCIUM CHANNEL ACTIVITY	Cacna1e, Cacng5, Trpc5, Ryr1, Trpc1, Trpv6, Cacnb2, Cacnb1, Cacng1, Trpv5, Trpc4, Cacna1g, Cacng4, Cacna1c
16 FEEDING BEHAVIOR	Htr2c, Brs3, Hcrtr2, Npw, Mchr1, Ppy, Cckbr, Galr3, Cckar, Ghsh, Mc4r, Hcrtr1, Ghrl, Galr2, Nmur2
18 VOLTAGE GATED CHANNEL ACTIVITY 17 VOLTAGE GATED POTASSIUM CHANNEL ACTIVITY 20 VOLTAGE GATED CATION CHANNEL ACTIVITY	^{17,20} Kcnh1, ²⁰ Cacnb4, ^{17,20} Kcnj1, ²⁰ Cacna1a, ^{17,20} Kcnq2, ^{17,20} Kcnc3, ²⁰ Cacng2, ^{17,20} Kcns1, ^{17,20} Kcnh3, Clcn1, ²⁰ Cacna2d1, ²⁰ Nox1, ^{17,20} Kcnj12, ^{17,20} Kcnj6, ^{17,20} Kcne2, ^{17,20} Kcnb2, ²⁰ Scn2a1, Clcnka, ²⁰ Cacna1e, ²⁰ Cacng5, ^{17,20} Kcnj10, ^{17,20} Kcnk1, ^{17,20} Kcnc1, ²⁰ Scn11a, ^{17,20} Kcnq3, ^{17,20} Kcna5, ²⁰ Cacnb2, ²⁰ Cacnb1, ^{17,20} Kcns3, ²⁰ Cacng1, Clcn2, ^{17,20} Kcnq5, ^{17,20} Kcnc4, ^{17,20} Kcna1, ^{17,20} Kcnj14, Clcnkb, ²⁰ Cacna1g, ^{17,20} Kcna6, ²⁰ Cacng4, ^{17,20} Kcnd3, ^{17,20} Kcnh2, ²⁰ Cacna1c
19 KEGG BASAL CELL CARCINOMA	Fzd5, Wnt8b, Fzd2, Tcf7l2, Wnt11, Wnt1, Fzd9, Wnt10a, Fzd3, Wnt6, Wnt7b, Fzd10, Fzd8, Wnt10b, Wnt5a, Shh, Dvl1, Smo, Wnt4, Wnt3a, Wnt8a, Wnt7a, Tcf7l1, Wnt3, Dvl3, Ptch2, Gli1, Gli2, Stk36, Wnt2b, Hhip
21 CONTRACTILE FIBER	Tnni3, Ttn, Tpm3, Tnnt2, Des, Myl6b, 2900073G15Rik, Tnnc1, Vcl, Acta1, Cdk5r1, Svil, Myl3, Mylpf, Dmd, Tpm2, Mybpc1, Abra, Myom1
22 ANION TRANSMEMBRANE TRANSPORTER ACTIVITY	Slc20a1, Clcn1, Slc34a1, Slc4a2, Best1, Slc34a3, Slc17a2, Slc12a9, Fxyd1, Clca3, Clcnka, Slc5a5, Slc17a4, Abcc2, Slc12a3, Slc4a3, Slc22a8, Slc17a1, Slc12a4, Clcn2, Slc12a1, Abcc5, Slc34a2, Slc26a4, Slc17a3, Bsnd, Slc22a7, Slc13a4, Clcnkb, Nmur2
23 REACTOME TIGHT JUNCTION INTERACTIONS	Cldn8, Cldn14, Cldn11, Cldn10a, Crb3, Cldn4, Cldn17, Cldn6, Pard3, Pard6a, Cldn1, Cldn18, Cldn3, Cldn12, Cldn16, Cldn23, Cldn19, Cldn7, Cldn20, Cldn9, Cldn22
25 DIGESTION	Galr1, Slc15a1, Apoa4, Pgc, Sstr1, Ctrl, Akr1c21, Sstr2, Mep1b, Akr1d1, Ppy, Tff3, Cckbr, Npc111, Cckar, Tff2, Baat, Sst, Prss2, Galr2, Ppy, Ldlr

The top 25 Western diet gene sets whose member genes are predominantly downregulated with respect to the chronic control group. Column 1 includes the gene set name (bold) as provided by MSigDB and the rank of the gene set based on Normalized Enrichment Score (NES). Gene set names that are not in bold are gene sets that are redundant or partially redundant and included within larger bolded gene sets. The NES ranged from -3.43 (for G Protein Coupled Receptor Activity, the top ranked gene set) to -1.92 (Digestion, the 25th-ranked gene set). FDR q range: 0 – 0.015. Column 2 includes those genes within the gene set that significantly contributed to the enrichment of the gene set. Genes within redundant gene sets are preceded by corresponding superscripts for the gene set to which they belong.