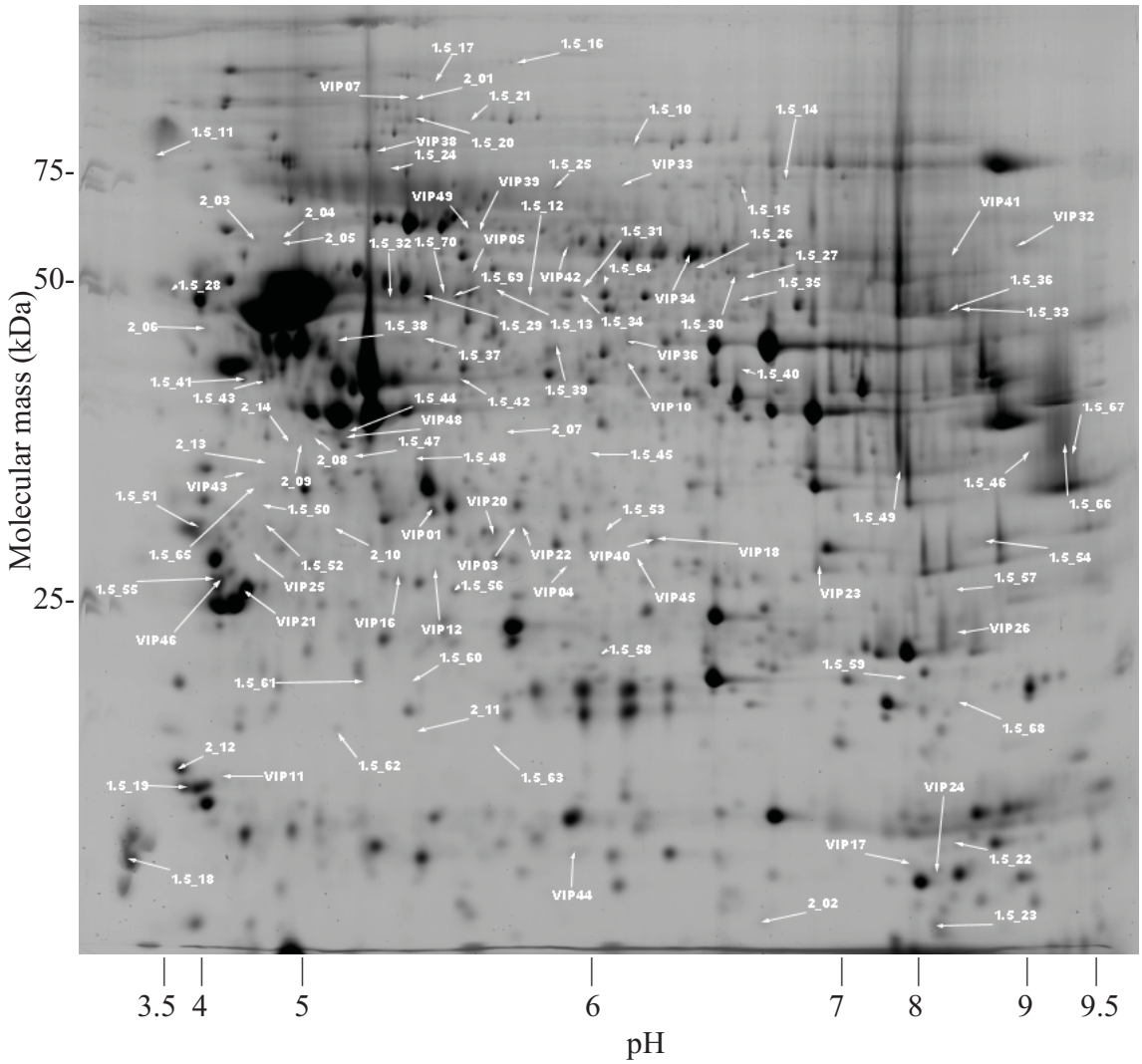
Fig. S1. Master two-dimensional gel image for A. epaulette shark cerebellum and B. rectal gland, formed by warping and fusing all individual gel images together in Delta 2D software. Protein mixtures were separated by isoelectric point (pH 3-10 nonlinear) in the horizontal dimension and molecular mass in the vertical dimension. Labels identify the the proteins whose abundance changed significantly following episodic anoxia or hypoxia, as determined from t-test and/or variable importance in the projection analyses (see Tables 4 and 5 and Supplemental Material, Tables S4 and S5).

A.



B.

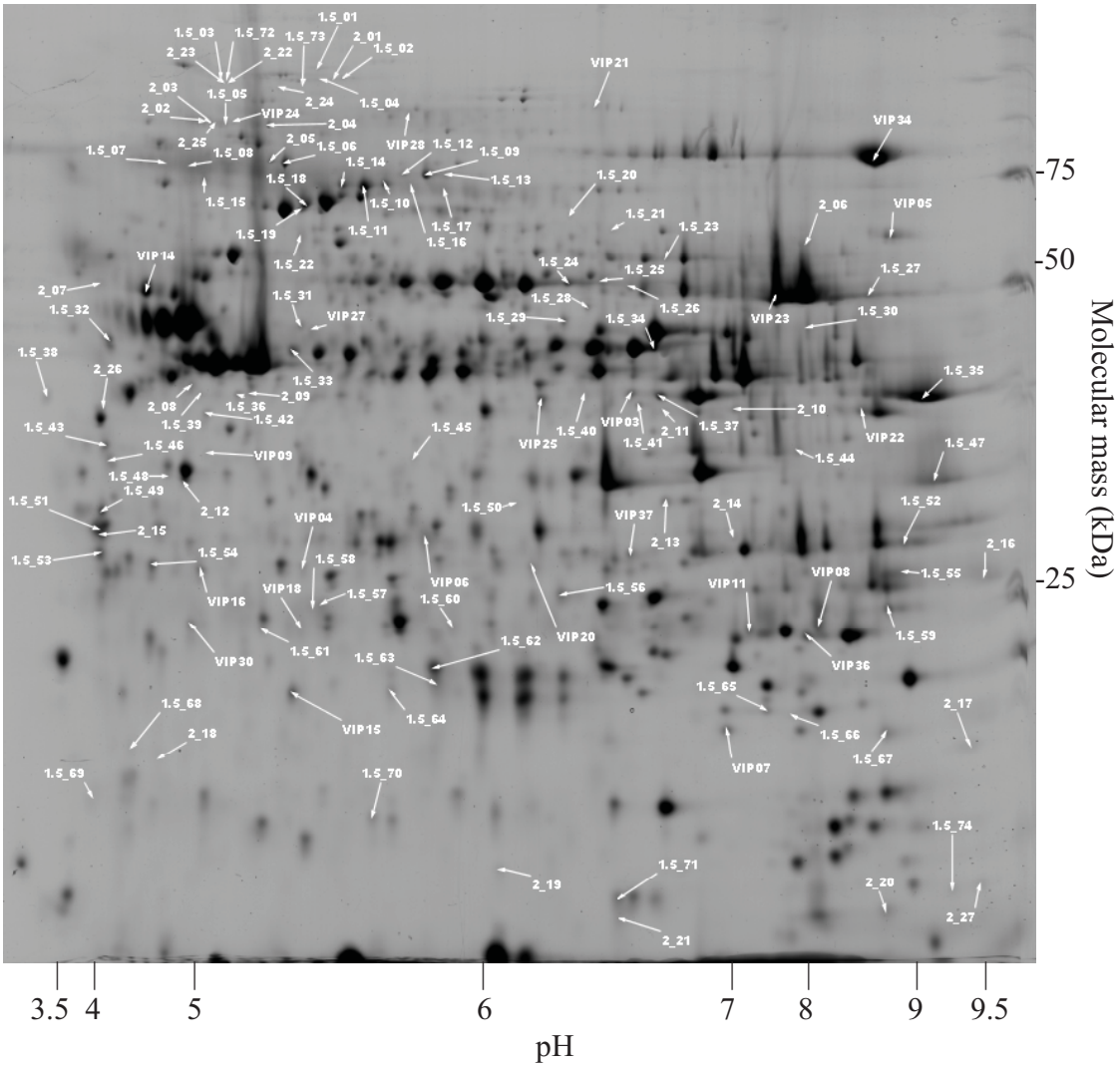


Fig. S2. Results of 200 permutations of the reduced epaulette shark PLS-DA models for A. cerebellum and B. rectal gland, in which the samples were randomly reassigned to the four treatments. R^2 represents the proportion of the variation in the protein expression dataset explained by the model, while Q^2 is a measure of the predictive ability of the model to assign a sample to a given treatment based on the expression pattern. The x-axis represents the correlation of the permutated dataset to the original dataset (for the original dataset x=1.0). In both tissues the reduced PLS-DA models perform far better than expected by chance (i.e., high relative Q^2 at x-axis=1).

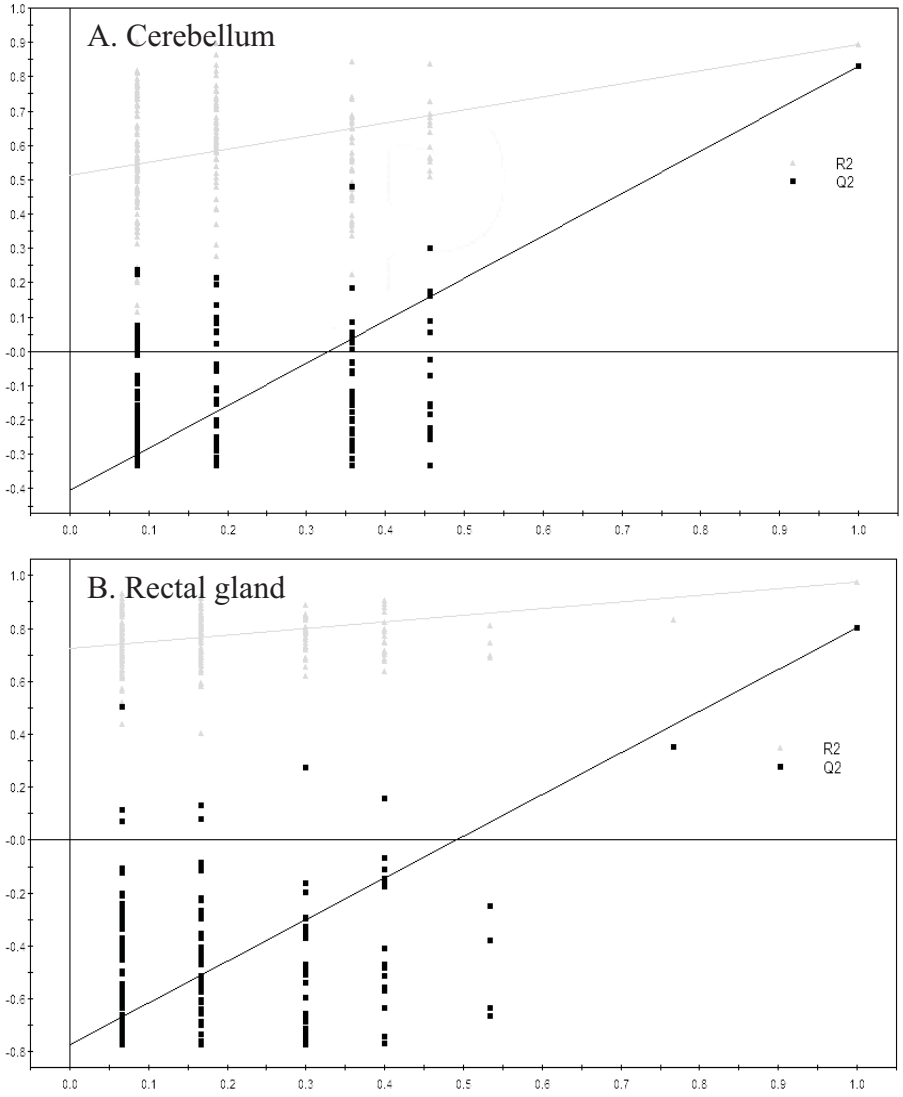


Fig. S3. (next page) Epaulette shark cerebellum master molecular interaction network generated by analysis in IPA software. Gray boxes represent proteins up- or downregulated following one or more experimental treatments. Bar charts adjacent to these boxes indicate relative expression level (relative to controls C1+24 h) for A1+24 h, H1+24 h, and H1+H2+24 h (left to right; red = upregulated, green = downregulated), regardless of statistical significance. Abbreviations for identified proteins as in Table 4. Key emergent nodes in the network: HTT=huntingtin; SLC2A4=solute carrier family 2 (facilitated glucose transporter), member 4; HNF4A=hepatocyte nuclear factor 4, alpha; TP53=tumor protein p53; PPARGC1A=peroxisome proliferator-activated receptor gamma, coactivator 1 alpha.

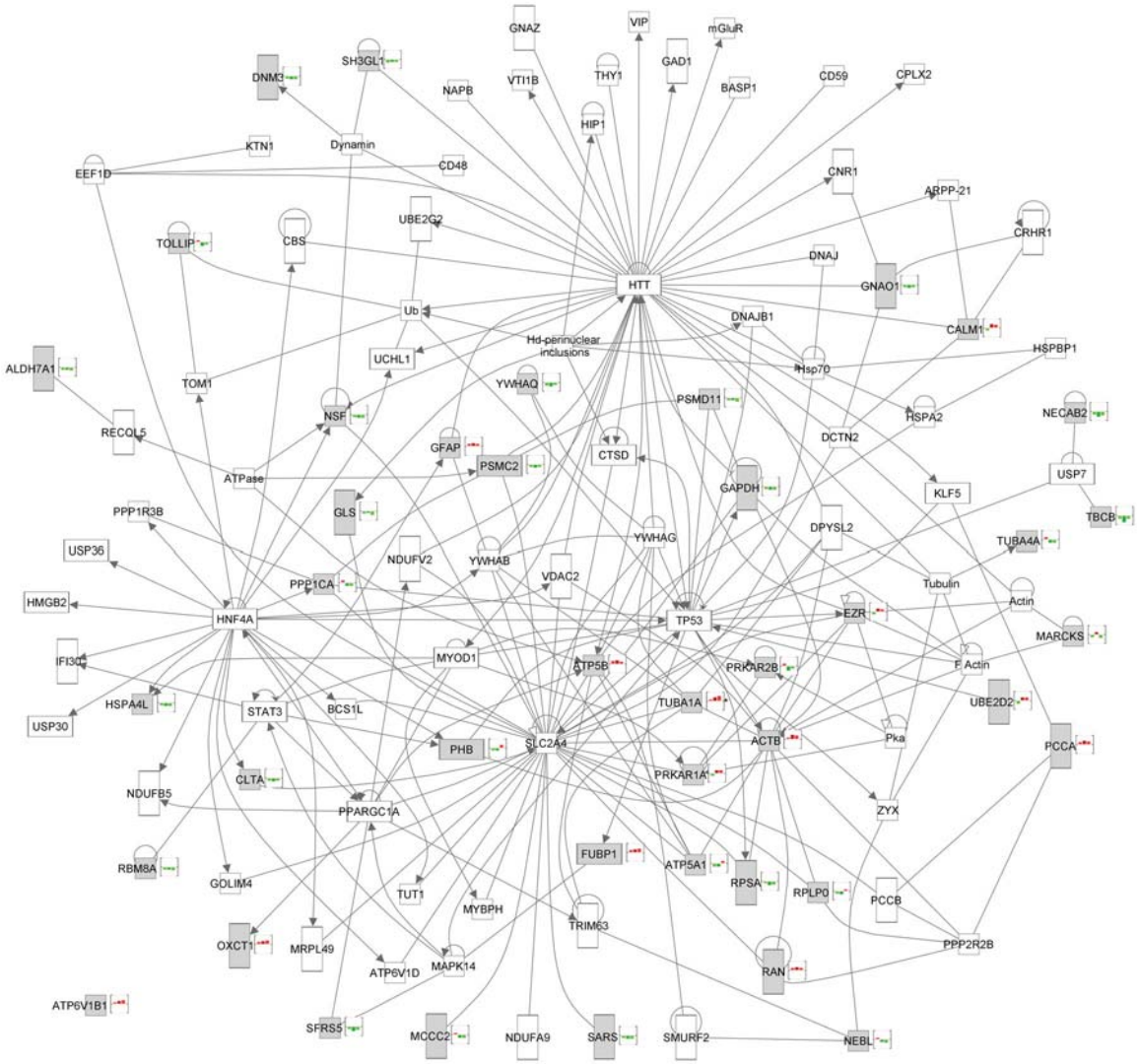
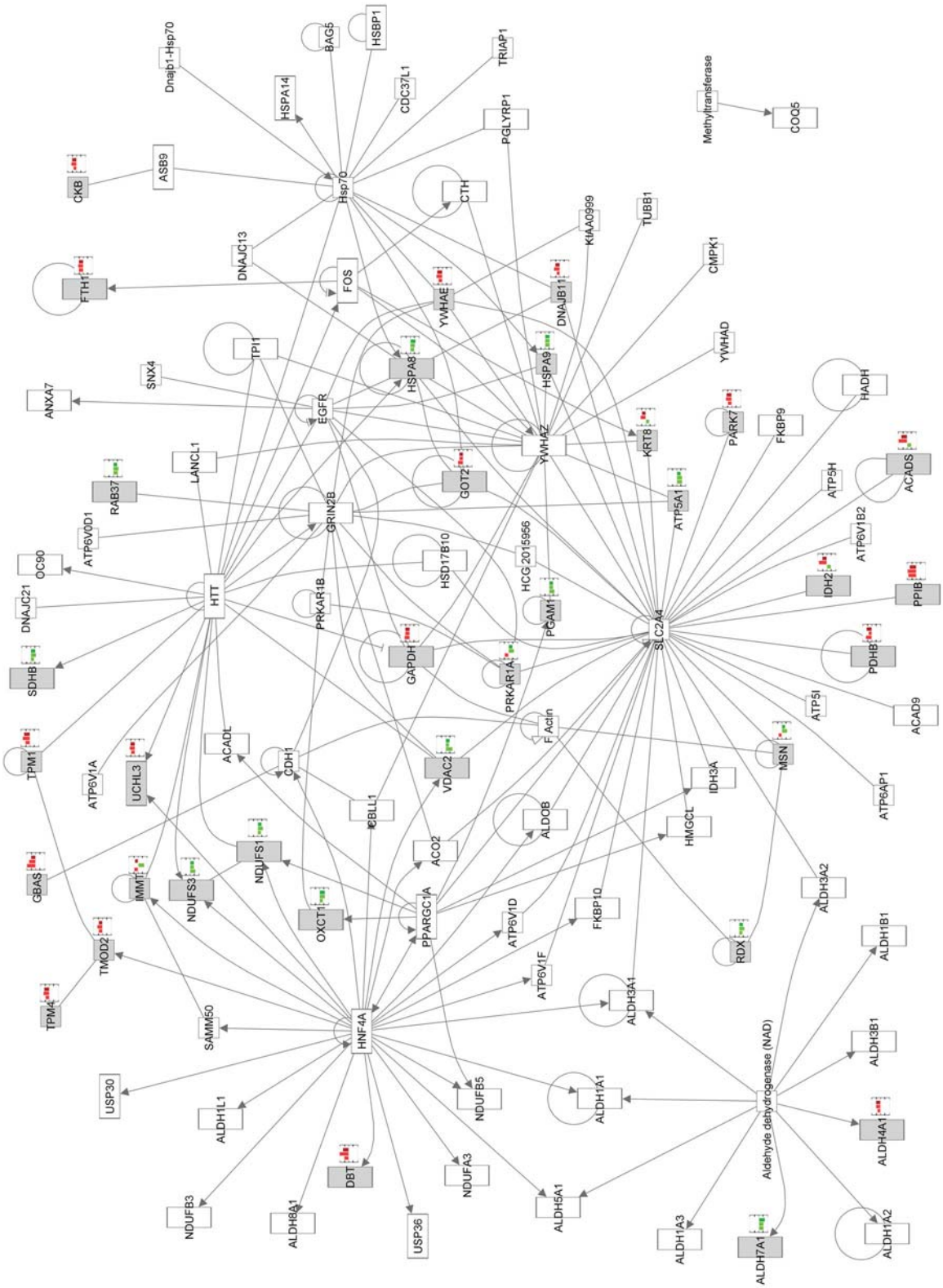

GNAZ
VIP
mGluR
SH3GL1
DNM3
NAPB
VTI1B
THY1
GAD1
BASP1
CD59
CPLX2
HIP1
KTN1
Dynamin
EEF1D
CD48
CNR1
ARPP-21
UBE2G2
CRHR1
TOLLIP
CBS
DNAJ
HTT
GNAO1
Ub
DNAJB1
CALM1
Hd-perinuclear inclusions
HSPBP1
ALDH7A1
UCHL1
Hsp70
TOM1
YWHAQ
PSMD11
HSPA2
NECAB2
RECQL5
NSF
DCTN2
GFAP
CTSD
PSMC2
USP7
ATPase
GAPDH
KLF5
PPP1R3B
GLS
TBCB
YWHAG
DPYSL2
USP36
NDUFV2
YWHAB
TUBA4A
VDAC2
Tubulin
Actin
HMGB2
PPP1CA
HNF4A
TP53
EZR
MARCKS
IFI30
MYOD1
ATP5B
PRKAR2B
F Actin
HSPA4L
STAT3
BCS1L
TUBA1A
UBE2D2
USP30
PHB
SLC2A4
ACTB
Pka
PCCA
CLTA
PRKAR1A
NDUFB5
PPARGC1A
ZYX
FUBP1
ATP5A1
RBM8A
RPSA
RPLP0
GDLIM4
TUT1
MYBPH
PCCB
TRIM63
OXCT1
MRPL49
PPP2R2B
MAPK14
ATP6V1D
RAN
ATP6V1B1
SFRS5
MCCC2
NDUFA9
SARS
SMURF2
NEBL

Fig. S4. (next page) Epaulette shark rectal gland master molecular interaction network generated by analysis in IPA software. Gray boxes represent proteins up- or downregulated following one or more experimental treatments. Bar charts adjacent to these boxes indicate relative expression level (relative to controls C1+24 h) for A1+24 h, H1+24 h, and H1+H2+24 h (left to right; red = upregulated, green = downregulated), regardless of statistical significance. Abbreviations for identified proteins as in Table 5. Key emergent nodes in the network: HTT=huntingtin; SLC2A4=solute carrier family 2 (facilitated glucose transporter), member 4; HNF4A=hepatocyte nuclear factor 4, alpha; GRIN2B=glutamate receptor, ionotropic, N-methyl D-aspartate 2B; EGFR=epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian); PPARGC1A=peroxisome proliferator-activated receptor gamma, coactivator 1 alpha.


Dnajb1-Hsp70
BAG5
HSBP1
HSPA14
CDC37L1
TRIAP1
PGLYRP1
Methyltransferase
COQ5
CKB
ASB9
Hsp70
CTH
KIAA0999
TUBB1
DNAJC13
FOS
CMPK1
FTH1
YWHAE
DNAJB11
YWHAD
TPI1
HSPA8
HSPA9
SNX4
ANXA7
EGFR
YWHAZ
KRT8
PARK7
FKBP9
HADH
LANCL1
GOT2
ACADS
RAB37
GRIN2B
ATP5A1
ATP5H
ATP6V0D1
HSD17B10
HCG 2015956
ATP6V1B2
OC90
HTT
PRKAR1B
PCAM1
IDH2
PPIB
DNAJC21
SLC2A4
SDHB
GAPDH
PRKAR1A
PDHB
F Actin
ATP5I
TPM1
ATP6V1A
UCHL3
ACADL
CDH1
VDAC2
MSN
ACAD9
IDH3A
CBLL1
ALDOB
ATP6AP1
HMGCL
GBAS
NDUFS1
ACO2
IMMT
NDUFS3
OXCT1
PPARGC1A
ATP6V1D
FKBP10
ALDH3A2
TMOD2
RDX
ATP6V1F
ALDH1B1
TPM4
ALDH3A1
SAMM50
HNF4A
ALDH3B1
USP30
NDUFB5
ALDH1A1
ALDH1L1
Aldehyde dehydrogenase (NAD)
ALDH4A1
DBT
NDUFA3
NDUFB3
ALDH6A1
ALDH5A1
USP36
ALDH1A3
ALDH7A1
ALDH1A2