

Title: Molecular elucidation of brain lipofuscin in aging and Neuronal Ceroid Lipofuscinosis

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Data Description: This file contains the underlying numerical data and UniProt IDs for molecules constituting canonical pathways identified by Ingenuity Pathway Analysis (IPA). These data include the top 10 canonical pathways for (**Fig. 3E**) consensus lipofuscin proteome hits (n = 688), (**Fig. S6A**) consensus PPT1 KO lipofuscin proteins across timepoints (n = 745), (**Fig. S6B**) consensus WT lipofuscin proteins across timepoints (n = 957), (**Fig. S6C**) significantly upregulated lipofuscin proteins in PPT1 KO 7-month/WT 24-month samples (n = 83), and (Fig. S6D) significantly downregulated lipofuscin proteins in PPT1 KO 7-month/WT 24-month samples (n = 348).

Fig. 3E - Consensus Lipofuscin Proteome Top 10 Canonical Pathways

Ingenuity Canonical Pathways	-log(p-value)	Ratio	Molecules
Mitochondrial Dysfunction	71	0.285	ACADL,AC02,AIFM1,ATP1A1,ATP1A2,ATP1A3,ATP1B1,ATP1B2,Atp5e,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5MF,ATP5PB,ATP5PD,ATP5PF,ATP5PO,CACN A2D1,CACNG8,Calm1 (includes others),CAMK2A,CAMK2B,CAMK2G,CAPN2,COX4I1,COX5A,COX6B1,Cox6c,Cox7a2/Cox7a2l2,CYC1,CYCS,DLAT,DLD,DNM1L,FIS1,GPD2,GSTP1,HSD17 B10,IDH2,ITPR1,MAOA,MAOB,MAPT,MCU,MFN2,MT-CO2,MT-CO3,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,Ndufs6,NDUFS7,NDUFV1,NDUFV2,OGDH,OPA1,PDHA1,PDHB,PPP3CA,PPP3R1,PRDX6,PR KAR2A,PRKAR2B,RHOT1,SAMM50,SDHA,SDHB,SNCA,SOD1,SOD2,TOMM22,TOMM70,UQCRC1,UQCRC2,UQCRFS1,UQCRQ,VDAC1,VDAC2,VDAC3
Electron transport, ATP synthesis, and heat production by uncoupling proteins	49	0.422	ACAD9,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5MF,ATP5PB,ATP5PD,ATP5PF,ATP5PO,COX4I1,COX5A,COX6B1,CYC1,CYCS,ETFA,ETFB,ETFDH,LRPPRC, MT-CO2,MT-CO3,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFC2,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS7,NDUFV1,NDUFV2,SDHA,SDHB,TRAP1,UQCRC1,UQCRC2,UQCRFS1,U QCRQ
Oxidative Phosphorylation	46.9	0.446	Atp5e,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5MF,ATP5PB,ATP5PD,ATP5PF,ATP5PO,COX4I1,COX5A,COX6B1,Cox6c,Cox7a2/Cox7a2l2,CYC1,CYCS,MT- CO2,MT-CO3,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS7,NDUFV1,NDUFV2,SDHA,SDHB,UQCRC1,UQCRC2,UQCRFS1,UQCRQ
Sirtuin Signaling Pathway	36.9	0.216	ACADL,ACLY,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5PB,ATP5PF,CYC1,GLS,GLUD1,GOT2,IDH2,LDHB,NDUFA10,NDUFA11,NDUFA12,NDUFA13,ND UFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3, NDUFS4,Ndufs6,NDUFS7,NDUFV1,NDUFV2,PDHA1,PK1,PFKM,PGAM1,PGK1,SDHA,SDHB,SIRT2,SLC25A4,SLC25A5,SOD1,SOD2,TIMM44,TIMM50,TIMM 9,TOMM22,TOMM70,TUBA4A,UQCRC2,UQCRFS1,VDAC1,VDAC2,VDAC3
Estrogen Receptor Signaling	30.5	0.161	ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5PB,CACNA2D1,CACNG8,CFL1,CTBP1,CYC1,DLG4,GNAI1,GNAI2,GNAO1,GNAQ,GNAS,GNB1,GNB2,GN B4,GNB5,GNG12,GNG2,HSP90AA1,HSP90AB1,HSP90B1,MAP2K1,MCU,MYL6,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUF A6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS7,NDUFV1 ,NDUFV2,PDIA3,PLCB1,PRKAR2A,PRKAR2B,PRKCG,RALA,RHOA,SDHA,SDHB,SOD2,UQCRC2,UQCRFS1
Synaptogenesis Signaling Pathway	28	0.177	ACTR2,ACTR3,AP2A1,AP2A2,AP2B1,AP2M1,ARPC1A,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CACNA2D1,CADM1,Calm1 (includes others),CAMK2A,CAMK2B,CAMK2G,CDH13,CDH2,CFL1,CNTNAP1,CNTNAP2,CPLX2,CTNNB1,DLG4,DNAJC5,FARP1,GRIN1,HSPA8,ITPR1,LRP1,MAP1B,M APT,NAPA,NAPB,NRXN1,NSF,PRKAR2A,PRKAR2B,RAB3A,RAB5C,RALA,RHOA,SNAP25,SNCA,SNCB,STX1A,STX1B,STXBP1,SYN1,SYN2,SYNGAP1,SYT1,SYT2, VAMP2
The citric acid (TCA) cycle and respiratory electron transport	23.9	0.455	ACO2,BSG,CS,DLAT,DLD,DLST,FH,IDH2,IDH3A,IDH3G,LDHB,MDH2,ME2,ME3,MPC1,OGDH,PDHA1,PDHB,PKD1,SDHA,SDHB,SUCLA2,SUCLG1,SUCLG2, VDAC1
GABAergic Receptor Signaling Pathway (Enhanced)	23	0.252	ABAT,ALDH5A1,CACNA2D1,CACNG8,CNTNAP1,CNTNAP2,GABBR1,GABBR2,GABRA1,GAD1,GLS,GLUD1,GLUL,GNAI1,GNAI2,GNAO1,GNB1,GNB2,GNB4, GNB5,GNG12,GNG2,GOT1,GOT2,GPHN,GRIN1,ITPR1,NRXN1,PRKAR2A,PRKAR2B,SLC12A5,SLC32A1,SLC38A3,SLC6A1,SLC6A11
Granzyme A Signaling	22.5	0.36	NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB 7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,Ndufs6,NDUFS7,NDUFV1,NDUFV2,NME1

Fig. S6A - PPT1 KO-2-4-7 Consensus Proteome Top 10 Upregulated Canonical Pathways

Ingenuity Canonical Pathways	-log(p-value)	Ratio	Molecules
Mitochondrial Dysfunction	82.5	0.313	ACADL,ACO2,AIFM1,ATP1A1,Atp1a2,ATP1A3,ATP1B1,ATP1B2,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5ME,ATP5MF,ATP5PB,ATP5PD,ATP5PF,ATP5PO,CACNA2D1,CACNG8,CALM1,CAMK2A,CAMK2B,CAMK2D,CAMK2G,CAPN2,COX4I1,COX5A,COX5B,COX6B1,COX6C,COX7A2,CYB5R3,CYC1,CYCS,DLAT,DLD,DNM1L,FIS1,GPD2,Gstp1 (includes others),HSD17B10,HTRA2,IDH2,ITPR1,MAOA,MAOB,MAPT,MCU,MFN2,MT-CO2,MT-CO3,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2,OGDH,OPA1,PDHA1,PDHB,PDHX,PPP3CA,PPP3R1,PRDX6,PRKAR2A,PRKAR2B,RHOT1,SAMM50,SDHA,SDHB,SNCA,SOD1,SOD2,TOMM22,TOMM70,UQCRCB,UQCRC1,UQCRC2,UQCRFS1,UQCRQ,VDAC1,VDAC2,VDAC3
Mitochondrial protein degradation	64.1	0.592	ACAD8,ACADSB,ACAT1,ACO2,AFG3L2,ALDH18A1,ALDH1B1,ALDH2,ATP5F1A,ATP5F1B,ATP5F1C,ATP5PD,ATP5PF,ATP5PO,BDH1,COX4I1,COX5A,COX5B,CS,DBT,DLD,EC11,FECH,FH,GLUD1,HADH,HSD17B10,HSPA9,HSPD1,HTRA2,IARS2,IDH2,IDH3A,LONP1,MDH2,ME2,MRPL12,MT-CO2,MT-ND5,NADK2,NDUFA13,NDUFA2,NDUFS1,NDUFS3,NDUFV1,OGDH,OPA1,OXCT1,PCCB,PDHA1,PDHB,PDK1,SLC25A5,SUCLG2,TIMM10,TIMM9,UQCRC2,UQCRQ
Oxidative Phosphorylation	57.1	0.514	ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5ME,ATP5MF,ATP5PB,ATP5PD,ATP5PF,ATP5PO,COX4I1,COX5A,COX5B,COX6B1,COX6C,COX7A2,CYC1,CYCS,MT-CO2,MT-CO3,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2,SDHA,SDHB,UQCRCB,UQCRC1,UQCRC2,UQCRFS1,UQCRQ
Respiratory electron transport	54	0.568	COX4I1,COX5A,COX5B,COX6B1,COX6C,COX7A2,CYC1,CYCS,ETFA,ETFB,ETFDH,MT-CO2,MT-CO3,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFC2,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2,SDHA,SDHB,TRAP1,UQCRCB,UQCRC1,UQCRC2,UQCRFS1,UQCRQ
Sirtuin Signaling Pathway	44.8	0.238	ACADL,ACLY,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5PB,ATP5PF,CYC1,GLS,GLUD1,GOT2,IDH2,LDHA,LDHB,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2,PCK2,PDHA1,PDK1,PFKM,PGAM1,PGK1,PPID,SDHA,SDHB,SIRT2,SLC25A4,SLC25A5,SOD1,SOD2,TIMM10,TIMM13,TIMM44,TIMM50,TIMM9,TOMM22,TOMM70,Tuba4a,UQCRC2,UQCRFS1,VDAC1,VDAC2,VDAC3
Parkinson's Signaling Pathway	39.8	0.215	ACTG1,ALDH18A1,ALDH1B1,ALDH1L1,ALDH2,AlDH3a2,ALDH4A1,ALDH5A1,ALDH6A1,ALDH7A1,ALDH9A1,ATP6V0A1,ATP6V0D1,ATP6V1A,ATP6V1B2,ATP6V1C1,ATP6V1D,ATP6V1E1,ATP6V1G2,ATP6V1H,CACNA2D1,CACNG8,CALM1,CAMK2A,CAMK2B,CAMK2D,CAMK2G,GRIA1,GRIA2,GRIN1,HSPA5,ITPR1,MAOA,MAOB,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2,SLC1A2,SNCA,TUBB,TUBB3,TUBB4A,UCHL1
Estrogen Receptor Signaling	36.7	0.177	ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5PB,ATP5PF,CACNA2D1,CACNG8,CFL1,CFL2,CTBP1,CYC1,DLG4,GNAI1,GNAI2,GNAO1,GNAQ,GNAS,GNB1,GNB2,GNB4,GNB5,GNG12,GNG2,HSP90AA1,HSP90AB1,HSP90B1,MAP2K1,MCU,MT-ND5,MYL6,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2,PDIA3,PLCB1,PRKAR2A,PRKAR2B,PRKCG,RALA,RAP1A,RHOA,SDHA,SDHB,SOD2,UQCRC2,UQCRFS1
Synaptogenesis Signaling Pathway	33.8	0.196	ACTR2,ACTR3,AP2A1,AP2A2,AP2B1,AP2M1,ARPC1A,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CACNA2D1,CADM1,CALM1,CAMK2A,CAMK2B,CAMK2D,CAMK2G,CDH13,CDH2,CFL1,CNTNAP1,CNTNAP2,CPLX2,CTNBB1,DLG4,DNAJC5,FARP1,GRIA1,GRIA2,GRI1,N1,HSPA8,ITPR1,LRP1,MAP1B,MAPT,MARCKS,NAPA,NAPB,NAPG,NRXN1,NSF,PRKAR2A,PRKAR2B,RAB3A,RAB5C,RALA,RAP1A,RHOA,SNAP25,SNCA,SNCB,STX1A,STX1B,STXBP1,SYN1,SYN2,SYNGAP1,SYT1,SYT2,VAMP2
Complex I biogenesis	28.2	0.441	ACAD9,HSPA9,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFC2,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2
Neutrophil Extracellular Trap Signaling Pathway	27	0.15	ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5PB,ATP5PF,C1QB,CYC1,ITPR1,MAP2K1,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB4,NDUFB5,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFV1,NDUFV2,PDIA3,PLCB1,PPID,PPP3CA,PPP3R1,PRDX6,PRKCG,SDHA,SDHB,SLC25A4,SLC25A5,TIMM10,TIMM13,TIMM44,TIMM50,TIMM9,TOMM22,TOMM70,UQCRC2,UQCRFS1,VDAC1,VDAC2,VDAC3

Fig. S6B - WT-12-18-24 Consensus Proteome Top 10 Upregulated Canonical Pathways

Ingenuity Canonical Pathways	-log(p-value)	Ratio	Molecules
Mitochondrial Dysfunction	89.7	0.359	ACADL,ACO2,AIFM1,ATP1A1,Atp1a2,ATP1A3,ATP1B1,ATP1B2,ATP1B3,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5ME,ATP5MF,ATP5MG,ATP5PB,ATP5PD,ATP5PF,ATP5PO,CACNA1E,CACNA2D1,CACNA2D2,CACNA2D3,CACNG8,CALM1,CAMK2A,CAMK2B,CAMK2G,CAPN2,COX411,COX5A,COX6B1,COX6C,COX7A2,CYB5R3,CYC1,CYCS,DLAT,DLD,DN M1L,FIS1,GPD2,GPX4,Gstp1 (includes others),GSTZ1,HSD17B10,IDH2,ITPR1,MAOA,MAOB,MAPT,MCU,MFN2,MGST3,MT-CO2,MT-CO3,MT-ND1,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,OGDH,OPA1,PARK7,PDHA1,PDHB,PDHX,PPP3CA,PPP3R1,PRDX6,PRKAR2A,PRKAR2B,RHOT1,SAMM50,SDHA,SDHB,SDHC,SNCA,SOD1,SOD2,TOMM22,TOMM70,UQCR10,UQCR11,UQCRB,UQCRC1,UQCRC2,UQCRFS1,UQCRH,UQCRQ,VDAC1,VDAC2,VDAC3
Oxidative Phosphorylation	66.6	0.606	ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5ME,ATP5MF,ATP5MG,ATP5PB,ATP5PD,ATP5PF,ATP5PO,COX411,COX5A,COX6B1,COX6C,COX7A2,CYC1,CYCS,MT-CO2,MT-CO3,MT-ND1,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,SDHA,SDHB,SDHC,UQCR10,UQCR11,UQCRB,UQCRC1,UQCRC2,UQCRFS1,UQCRH,UQCRQ
Respiratory electron transport	65.3	0.682	COX4I1,COX5A,COX6B1,COX6C,COX7A2,CYC1,CYCS,ETFA,ETFB,ETFDH,MT-CO2,MT-CO3,MT-ND1,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFC2,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,SDHA,SDHB,SDHC,TMEM186,TRAP1,UQCR10,UQCR11,UQCRB,UQCRC1,UQCRC2,UQCRFS1,UQCRH,UQCRQ
Mitochondrial protein degradation	62.6	0.622	ACAD8,ACADS8,ACAT1,ACO2,AFG3L2,ALDH18A1,ALDH1B1,ALDH2,ATP5F1A,ATP5F1B,ATP5F1C,ATP5MG,ATP5PD,ATP5PF,ATP5PO,BDH1,COX4I1,COX5A,CS,DBT,DLD,ECI1,FECH,FH,GLUD1,HADH,HSD17B10,HSPA9,HSPD1,IARS2,IDH2,IDH3A,LONP1,MDH2,ME2,MRPL12,MT-CO2,MT-ND1,MT-ND5,NADK2,NDUFA13,NDUFA2,NDUFB6,NDUFS1,NDUFS3,NDUFV1,NDUFV3,OGDH,OPA1,OXCT1,PCCB,PDHA1,PDHB,PDK1,SHMT2,SLC25A5,SUCLG2,TIMM22,TIMM9,UQCRC2,UQCRQ
Sirtuin Signaling Pathway	47.5	0.272	ACADL,ACLY,ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5PB,ATP5PF,CYC1,GLS,GLUD1,GOT2,H1-4,IDH2,LDHA,LDHB,MAPK1,MT-ND1,MT-ND5,NDRG1,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,PDHA1,PKD1,PFKM,PGAM1,PGK1,SDHA,SDHB,SDHC,SIRT2,SLC25A4,SLC25A5,SLC2A1,SOD1,SOD2,TIMM22,TIMM44,TIMM50,TIMM9,TOMM22,TOMM40L,TOMM70,TUBA1A,Tuba4a,UQCRC2,UQCRFS1,VDAC1,VDAC2,VDAC3
Estrogen Receptor Signaling	45.1	0.221	ATP5F1A,ATP5F1B,ATP5F1C,ATP5F1D,ATP5F1E,ATP5PB,ATP5PF,CACNA1E,CACNA2D1,CACNA2D2,CACNA2D3,CACNG8,CFL1,CTBP1,CYC1,DLG4,GNAI1,GNA13,GNAI1,GNAI2,GNAL,GNAO1,GNAQ,GNAS,GNAZ,GNB1,GNB2,GNB4,GNB5,GNNG12,GNNG2,HRAS,HSP90AA1,HSP90AB1,HSP90B1,MAP2K1,MAPK1,MCU,MT-ND1,MT-ND5,MYL12B,MYL6,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,PAK1,PDIA3,PLCB1,PRKAR2A,PRKAR2B,PRKCB,PRKCG,RALA,RAP2B,RHOA,ROCK2,SDHA,SDHB,SDHC,SOD2,UQCRC2,UQCRFS1
Parkinson's Signaling Pathway	43.4	0.25	ACTG1,ALDH18A1,Aldh1a1,ALDH1B1,ALDH1L1,ALDH2,Aldh3a2,ALDH4A1,ALDH5A1,ALDH6A1,ALDH7A1,ALDH9A1,ATP6V0A1,ATP6V0D1,ATP6V1A,ATP6V1B2,ATP6V1C1,ATP6V1D,ATP6V1E1,ATP6V1G2,ATP6V1H,CACNA1E,CACNA2D1,CACNA2D2,CACNA2D3,CACNG8,CALM1,CAMK2A,CAMK2B,CAMK2G,GRIN1,GRIN2B,HSPA5,ITPR1,MAOA,MAOB,MAPK1,MT-ND1,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,PARK7,SLC1A2,SNCA,TUBA1A,TUBB,TUBB3,TUBB4A,Uchl1
Synaptogenesis Signaling Pathway	41.3	0.243	ACTR2,ACTR3,AP2A1,AP2A2,AP2B1,AP2M1,ARPC1A,ARPC2,ARPC3,ARPC4,ARPC5,ARPC5L,CACNA2D1,CACNA2D2,CALM1,CALM1,CAMK2A,CAMK2B,CAMK2G,CDC42,CDH13,CDH2,CFL1,CLASP2,CNTNAP1,CNTNAP2,CPLX2,CTNNA1,DLG4,DNAJC5,FARP1,GRIN1,GRIN2B,GRM1,GRM2,GRM3,GRM5,HRAS,HSPA8,ITPR1,LRP1,MAP1B,MAPK1,MAPT,MARCKS,NAPA,NAPB,NAPG,NLGN2,NLGN3,NRXN1,NSF,PAFAH1B1,PAK1,PRKAR2A,PRKAR2B,RAB3A,RAB5B,RAB5C,RAC1,RALA,RAP2B,RHOA,SNAP25,SNCA,SNCB,STX1A,STX1B,STXBP1,STXBP5,SYN1,SYN2,SYNGAP1,SYT1,SYT2,VAMP2,YKT6
Complex I biogenesis	35	0.544	ACAD9,HSPA9,MT-ND1,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFA10,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFC2,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,TMEM186
Granzyme A Signaling	32.9	0.493	H1-4,MBP,MT-ND1,MT-ND5,NDUFA10,NDUFA11,NDUFA12,NDUFA13,NDUFA2,NDUFA3,NDUFA4,NDUFA5,NDUFA6,NDUFA7,NDUFA8,NDUFA9,NDUFAB1,NDUFB10,NDUFB11,NDUFB4,NDUFB5,NDUFB6,NDUFB7,NDUFB8,NDUFB9,NDUFS1,NDUFS2,NDUFS3,NDUFS4,NDUFS5,NDUFS6,NDUFS7,NDUFS8,NDUFV1,NDUFV2,NDUFV3,Nme1

Fig. S6C - PPT1-7 vs WT-24 DEGs Top 10 Upregulated Canonical Pathways

Ingenuity Canonical Pathways	-log(p-value)	Ratio	Molecules
Electron transport, ATP synthesis, and heat production by uncoupling proteins	7.95	0.0625	ATP5F1D,ATP5MF,ATP5PO,NDUFA2,NDUFA5,NDUFA6,NDUFB7,TMEM186
Oxidative Phosphorylation	7.01	0.0625	ATP5F1D,ATP5MF,ATP5PO,NDUFA2,NDUFA5,NDUFA6,NDUFB7
Signaling by Rho Family GTPases	6.57	0.0337	ARPC3,GFAP,GNG12,GNG2,MSN,RHOB,SEPTIN11,SEPTIN2,VIM
Sirtuin Signaling Pathway	6.26	0.0309	ATP5F1D,NDUFA2,NDUFA5,NDUFA6,NDUFB7,SLC25A4,TIMM10,TIMM22,TOMM22
Mitochondrial Dysfunction	5.66	0.0262	ATP5F1D,ATP5MF,ATP5PO,HTRA2,NDUFA2,NDUFA5,NDUFA6,NDUFB7,TOMM22
Neutrophil Extracellular Trap Signaling Pathway	5.12	0.0225	ATP5F1D,NDUFA2,NDUFA5,NDUFA6,NDUFB7,SLC25A4,TIMM10,TIMM22,TOMM22
Neutrophil degranulation	4.53	0.0189	ASAH1,CTSD,DYNLL1,LAMP1,PSAP,PSMA5,SCAMP1,SYNGR1,VAT1
Huntington's Disease Signaling	4.33	0.0246	ATP5F1D,CTSD,GNG12,GNG2,GRIN2B,HRAS,PSMA5
Mitochondrial protein import	4.2	0.0625	SLC25A4,TIMM10,TIMM22,TOMM22
Estrogen Receptor Signaling	4.18	0.0196	ATP5F1D,GNG12,GNG2,HRAS,NDUFA2,NDUFA5,NDUFA6,NDUFB7

Fig. S6D - WT-24 vs. PPT1-7 DEGs Top 10 Upregulated Canonical Pathways

Ingenuity Canonical Pathways	-log(p-value)	Ratio	Molecules
Mitochondrial Dysfunction	17.3	0.0959	ACADL,ATP5F1E,CACNG8,CAMK2B,CAMK2G,CAPN2,COX7A2,CYCS,DLD,DNM1L,FIS1,G PX4,GSTZ1,HSD17B10,IDH2,ITPR1,MCU,MFN2,MT- CO3,NDUFA8,NDUFA9,NDUFAB1,NDUFB5,NDUFB6,NDUFB8,NDUFS2,NDUFS7,PPP3CA ,PRKAR2B,SOD1,SOD2,UQCRB,UQCRCQ
Clathrin-mediated endocytosis	14.6	0.154	AAK1,ACTG1,AMPH,AP2A1,AP2B1,AP2M1,ARFGAP1,ARPC1A,ARPC2,BIN1,CTTN,DNAJC6, DNM1,DNM3,EP515L1,NECAP1,PACSIN1,SNAP91,SYNJ1,SYT2
Neurexins and neuroligins	12	0.228	CASK,DLG2,DLG4,DLGAP1,DLGAP4,EPB41L1,EPB41L2,GRIN1,NRXN1,SHANK1,SHANK2, SHANK3,SYT2
Parkinson's Signaling Pathway	11.6	0.0814	ACTG1,ALDH1A1,ALDH1L1,ALDH4A1,ALDH6A1,ALDH7A1,ALDH9A1,ATP6V0D1,ATP6V1 D,ATP6V1G2,CACNG8,CAMK2B,CAMK2G,GRIN1,ITPR1,NDUFA8,NDUFA9,NDUFAB1,NDU FB5,NDUFB6,NDUFB8,NDUFS2,NDUFS7,TUBB3,UCHL1
Opioid Signalling	11.6	0.167	AHCYL1,CAMK2B,CAMK2G,GNAI1,GNAI2,GNB2,GNB5,GRK2,ITPR1,PLCB1,PPP2 R1A,PPP3CA,PRKAR2B,PRKCG
Clathrin-mediated Endocytosis Signaling	11.6	0.101	AAK1,ACTG1,AMPH,AP1B1,AP2A1,AP2B1,AP2M1,AP3B2,AP3D1,ARPC1A,ARPC2,ARPC5L, CDC42,CTTN,DNM1,DNM1L,DNM3,PPP3CA,SH3GLB2,SNAP91,SYNJ1
Electron transport, ATP synthesis, and heat production by uncoupling proteins	11.4	0.133	ACAD9,ATP5F1E,CYCS,ETFA,LRPPRC,MT- CO3,NDUFA8,NDUFA9,NDUFAB1,NDUFB5,NDUFB6,NDUFB8,NDUFS2,NDUFS7,TRAP1, UQCRB,UQCRCQ
Synaptogenesis Signaling Pathway	11.4	0.0794	AP2A1,AP2B1,AP2M1,ARPC1A,ARPC2,ARPC5L,CAMK2B,CAMK2G,CDC42,CNTNAP1,CNT NAP2,DLG4,GRIN1,ITPR1,LRP1,NAPA,NRXN1,PAFAH1B1,PRKAR2B,SNAP25,SNCB,SYN1, SYN2,SYNGAP1,SYT2
Netrin Signaling	11.2	0.11	ABLIM1,ARPC1A,ARPC2,ARPC5L,CACNG8,CAMK2B,CAMK2G,CDC42,CRMP1,DPYSL2,D PYSL4,DPYSL5,ITPR1,NAPA,PGK1,PPP3CA,PRKAR2B,PRKCG,SNAP25
Glycolysis I	10.1	0.333	ENO1,ENO2,PFKL,PFKM,PFKP,PGAM1,PGK1,PKM,TPI1