**Supplementary data:**

# Why All the Fuss about Oxidative Phosphorylation (OXPHOS)?

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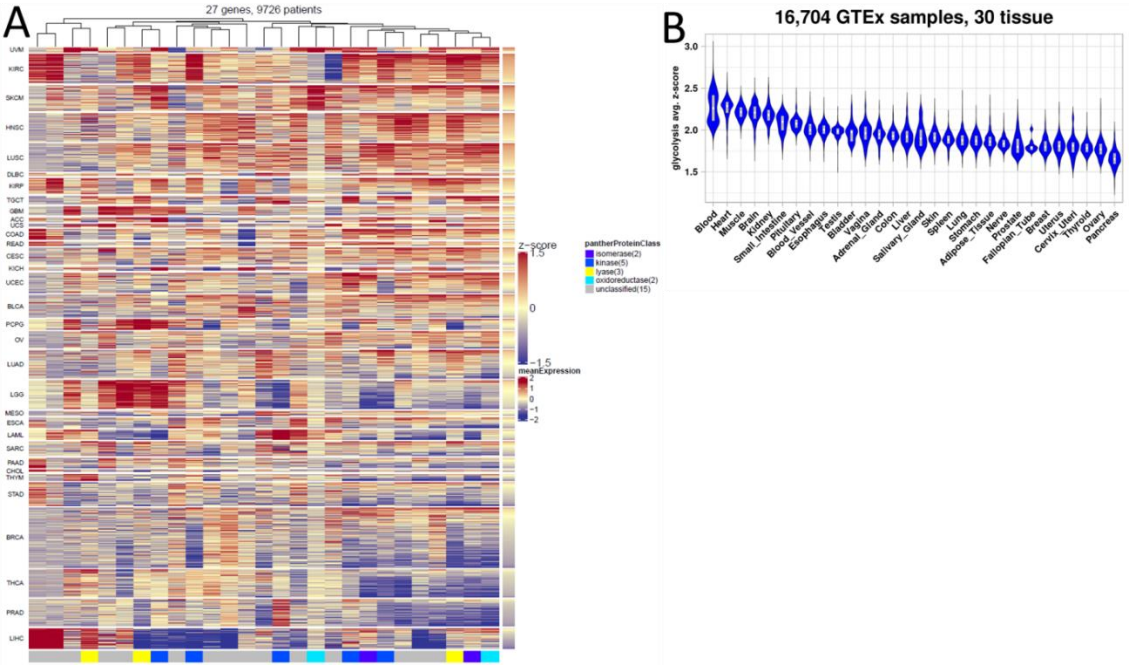
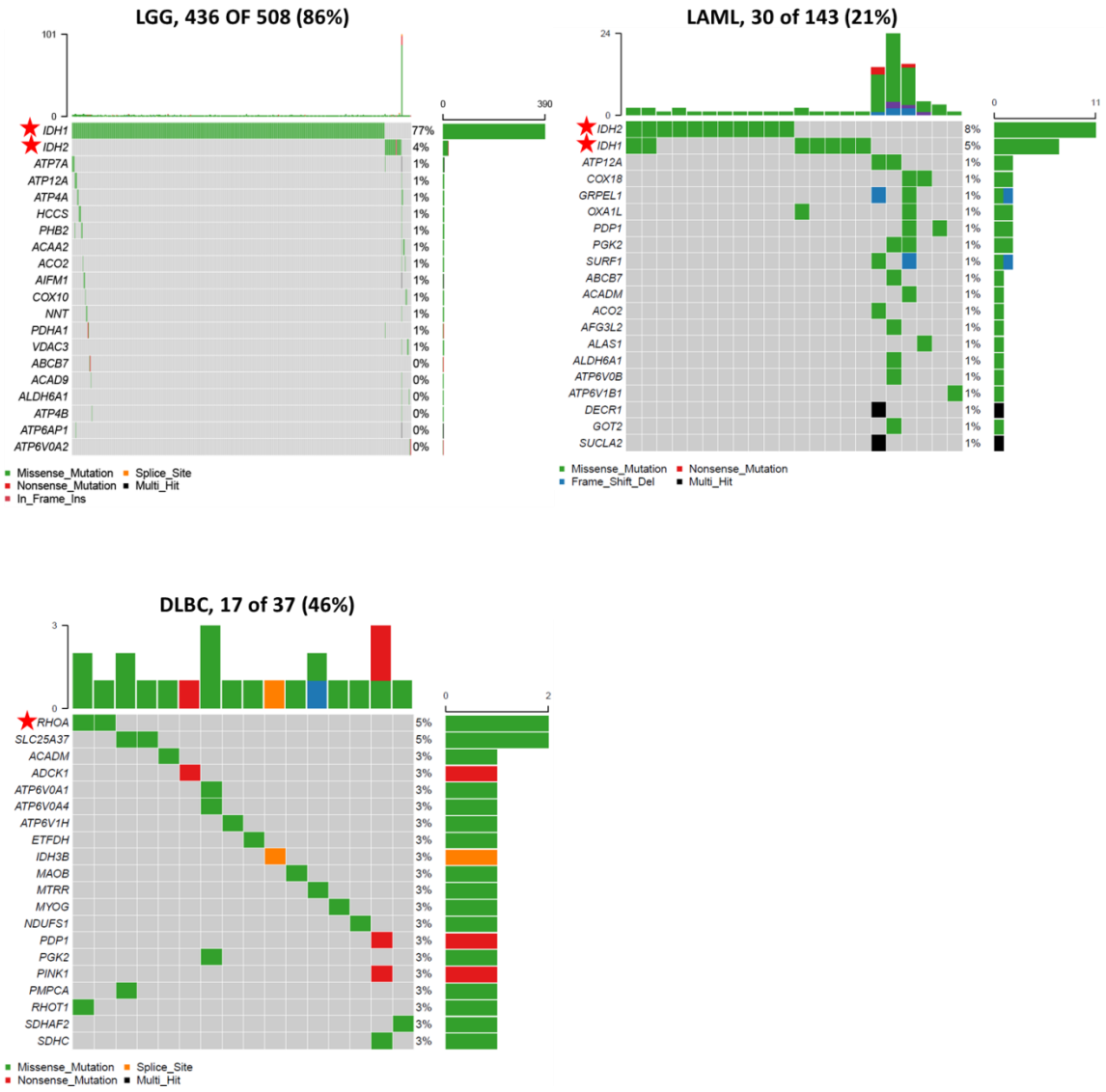



**Supplemental Figure 1**: (A) Pan-cancer TCGA heatmap showing z-score normalized expression of glycolysis genes with diseases ranked by average expression per disease. (B) Violin plot shows average z-score for glycolysis genes for GTEx tissue samples. Blood, heart, and muscle tissues have the highest average expression of glycolysis genes.




**Supplemental Figure 2**: Oncoprints for lower grade glioma (LGG), acute myeloid leukemia (LAML), and lymphoid neoplasm diffuse large B-cell lymphoma (DLBC) OXPHOS gene variants. Mutations from the top 20 mutated OXPHOS genes per disease are shown.

## Supplemental Table 1. OXPHOS structure genes

| Complex I nuclear genes | Complex I mtDNA genes | Complex II nuclear genes | Complex III nuclear genes | Complex III mtDNA genes | Complex IV nuclear genes | Complex IV mtDNA genes | Complex V nuclear genes | Complex V mtDNA genes |
|---|---|---|---|---|---|---|---|---|
| NDUFS1 | MT-ND1 | SDHA | CYC1 | CYTB | COX4I1 | MT-CO1 | ATP5F1A | ATP6 |
| NDUFS2 | MT-ND2 | SDHB | UQCRC1 | | COX4I2 | MT-CO2 | ATP5F1B | ATP8 |
| NDUFS3 | MT-ND3 | SDHC | UQCRC2 | | COX5A | MT-CO3 | ATP5F1C | |
| NDUFS7 | MT-ND4 | SDHD | UQCRFS1 | | COX5B | | ATP5F1D | |
| NDUFS8 | MT-ND4L | | UQCRH | | COX6A1 | | ATP5F1E | |
| NDUFV1 | MT-ND5 | | UQCRQ | | COX6A2 | | ATP5MC1 | |
| NDUFV2 | MT-ND6 | | TTC19 | | COX6B1 | | ATP5MC2 | |
| NDUFAB1 | | | UQCRB | | COX6B2 | | ATP5MC3 | |
| NDUFA1 | | | UQCR10 | | COX6C | | ATP5MD | |
| NDUFA2 | | | UQCR11 | | COX7A1 | | ATP5ME | |
| NDUFA3 | | | | | COX7A2 | | ATP5MF | |
| NDUFA5 | | | | | COX7B | | ATP5MG | |
| NDUFA6 | | | | | COX7B2 | | ATP5MPL | |
| NDUFA7 | | | | | COX7C | | ATP5PB | |
| NDUFA8 | | | | | COX8A | | ATP5PD | |
| NDUFA9 | | | | | COX8C | | ATP5PF | |
| NDUFA10 | | | | | | | ATP5PO | |
| NDUFA11 | | | | | | | ATP5IF1 | |
| NDUFA12 | | | | | | | | |
| NDUFA13 | | | | | | | | |
| NDUFB1 | | | | | | | | |
| NDUFB2 | | | | | | | | |
| NDUFB3 | | | | | | | | |
| NDUFB4 | | | | | | | | |
| NDUFB5 | | | | | | | | |
| NDUFB6 | | | | | | | | |
| NDUFB7 | | | | | | | | |
| NDUFB8 | | | | | | | | |
| NDUFB9 | | | | | | | | |
| NDUFB10 | | | | | | | | |
| NDUFB11 | | | | | | | | |
| NDUFC1 | | | | | | | | |
| NDUFC2 | | | | | | | | |
| NDUFS4 | | | | | | | | |
| NDUFS5 | | | | | | | | |
| NDUFS6 | | | | | | | | |
| NDUFV3 | | | | | | | | |

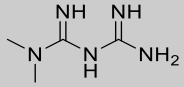
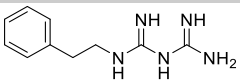
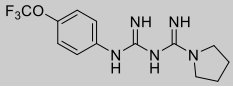
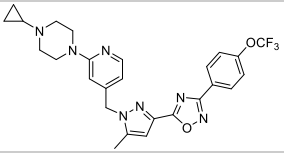
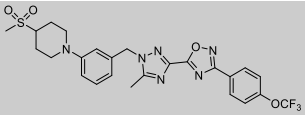
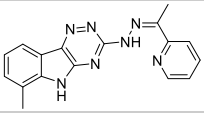
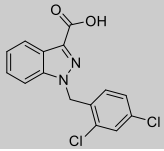
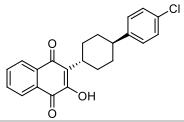
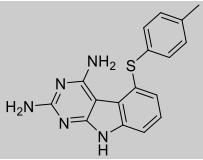
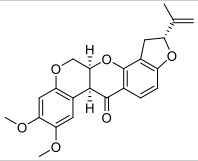
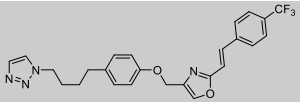
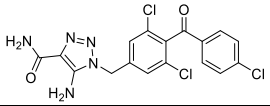
## Supplemental Table 2. OXPHOS assembly factors and biogenesis genes

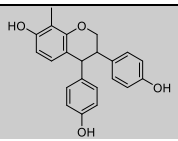
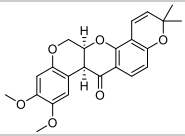
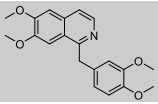
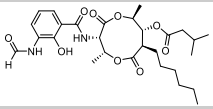
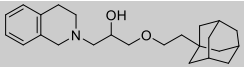
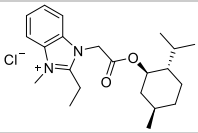
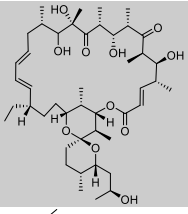
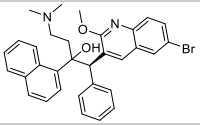
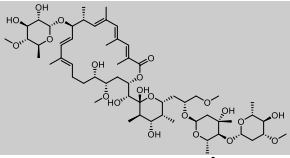
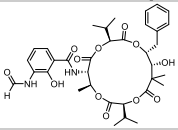
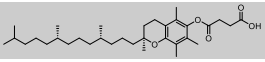
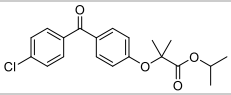
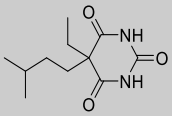
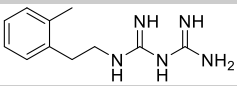
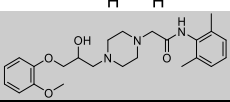
| Complex I Assembly factor genes | Complex II Assembly factor genes | Complex III Assembly factor genes | Complex IV Assembly factor genes | Complex V Assembly factor genes | Coenzyme Q10 (CoQ10) and Cytochrome-c (cyt-c) Biogenesis Genes | Fe-S Biogenesis Genes |
|---|---|---|---|---|---|---|
| NDUFAF1 | SDHAF1 | BCS1L | COX10 | ATPAF1 | ADCK1 | ABCB7 |
| NDUFAF2 | SDHAF2 | UQCC1 | COX11 | ATPAF2 | ADCK2 | FLRX5 |
| NDUFAF3 | SDHAF3 | UQCC2 | COX14 | TEME70 | ADCK3 | HSPA9 |
| NDUFAF4 | SDHAF4 | UQCC3 | COX15 | OXA1L | ADCK4 | ISCA1 |
| NDUFAF5 | | | COX17 | | ADCK5 | ISCA2 |
| NDUFAF6 | | | COX18 | | COQ2 | ISCU |
| NDUFAF7 | | | COX19 | | COQ3 | LYRM4 |
| C8orf38 | | | FASTKD2 | | COQ4 | SLC25A37 |
| C20orf7 | | | FDX1 | | COQ5 | SLC25A28 |
| ACAD9 | | | LRPPRC | | COQ6 | NUBPL |
| FOXRED1 | | | OXA1L | | COQ7 | NFS1 |
| OXA1L | | | PET191 | | COQ8 | NFU1 |
| NUBPL | | | RCF1 | | COQ9 | FXN |
| ECSIT | | | SCO1 | | COQ10A | |
| NUBPL | | | SCO2 | | COQ10B | |
| TEME126B | | | SURF1 | | CYCS | |
| | | | TACO1 | | HCCS | |
| | | | COA5 | | PDSS1 | |
| | | | | | PDSS2 | |

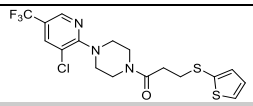
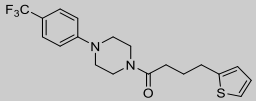
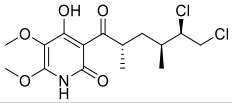
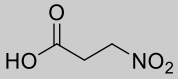
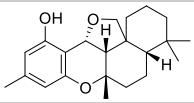
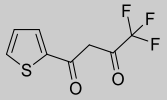
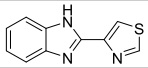
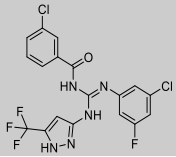
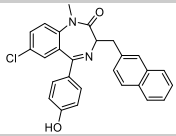
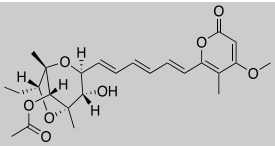
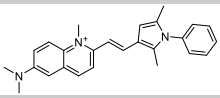
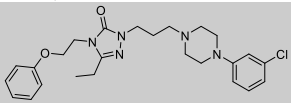
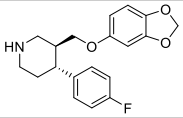
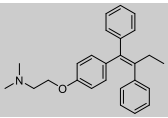
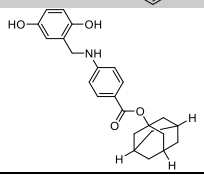
## Supplemental Table 3. Canonical glycolysis genes

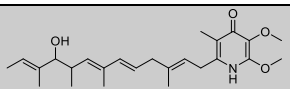
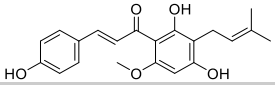
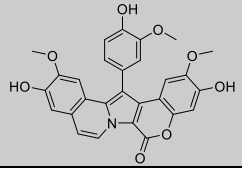
| Gene | Entrez | HGNC ID |
|---|---|---|
| ADPGK | 83440 | HGNC:25250 |
| ALDOA | 226 | HGNC:414 |
| ALDOB | 229 | HGNC:417 |
| ALDOC | 230 | HGNC:418 |
| BPGM | 669 | HGNC:1093 |
| ENO1 | 2023 | HGNC:3350 |
| ENO2 | 2026 | HGNC:3353 |
| ENO3 | 2027 | HGNC:3354 |
| FOXK1 | 221937 | HGNC:23480 |
| FOXK2 | 3607 | HGNC:6036 |
| GAPDH | 2597 | HGNC:4141 |
| GAPDHS | 26330 | HGNC:24864 |
| GCK | 2645 | HGNC:4195 |
| GPI | 2821 | HGNC:4458 |
| HK1 | 3098 | HGNC:4922 |
| HK2 | 3099 | HGNC:4923 |
| HK3 | 3101 | HGNC:4925 |
| PFKL | 5211 | HGNC:8876 |
| PFKM | 5213 | HGNC:8877 |
| PFKP | 5214 | HGNC:8878 |
| PGAM1 | 5223 | HGNC:8888 |
| PGAM2 | 5224 | HGNC:8889 |
| PGK1 | 5230 | HGNC:8896 |
| PGM2L1 | 283209 | HGNC:20898 |
| PKLR | 5313 | HGNC:9020 |
| PKM | 5315 | HGNC:9021 |
| TPI1 | 7167 | HGNC:12009 |

**Supplemental Table 4. List of physicochemical properties of 45 OXPHOS inhibitors**

| Name | | H-bond donor | H-bond acceptor | $Fsp^3$ | cLogP | TPSA | MW |
|---|---|---|---|---|---|---|---|
| **Metformin** |  | 4 | 5 | 0.5 | -0.92 | 88.99 | 129.17 |
| **Phenformin** |  | 5 | 5 | 0.2 | 0.833 | 97.78 | 205.27 |
| **IM156 (HL156A)** |  | 4 | 6 | 0.38 | 3.10 | 84.23 | 315.30 |
| **BAY 87-2243** |  | 0 | 7 | 0.38 | 6.25 | 85.34 | 525.54 |
| **IACS-010759** |  | 0 | 8 | 0.36 | 5.24 | 116.24 | 562.57 |
| **VLX600** |  | 2 | 6 | 0.12 | 2.97 | 91.74 | 317.36 |
| **Lonidamine** |  | 1 | 3 | 0.07 | 4.40 | 55.12 | 321.16 |
| **Atovaquone** |  | 1 | 3 | 0.27 | 5.00 | 54.37 | 366.84 |
| **AG311** |  | 3 | 4 | 0.06 | 3.85 | 93.61 | 321.4 |
| **Rotenone** |  | 0 | 6 | 0.35 | 3.32 | 63.22 | 394.42 |
| **Mubritinib** |  | 0 | 4 | 0.24 | 5.96 | 65.97 | 468.48 |
| **Carboxyamido triazole** |  | 2 | 5 | 0.06 | 4.16 | 116.89 | 424.67 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **ME344** |  | 3 | 4 | 0.18 | 4.82 | 69.92 | 348.40 |
| **Deguelin** |  | 0 | 6 | 0.35 | 3.30 | 63.22 | 394.42 |
| **Papaverine** |  | 0 | 5 | 0.25 | 3.08 | 49.81 | 339.39 |
| **Antimycin A** |  | 3 | 6 | 0.61 | 4.95 | 157.33 | 548.63 |
| **ADDA 5** |  | 1 | 3 | 0.75 | 0.75 | 32.7 | 369.55 |
| **Gboxin** |  | 0 | 1 | 0.64 | 0.73 | 35.11 | 362.97 |
| **Oligomycin A** |  | 5 | 10 | 0.8 | 7.45 | 180.05 | 791.08 |
| **Bedaquiline** |  | 1 | 4 | 0.22 | 7.13 | 45.59 | 555.52 |
| **Apoptolidin** |  | 8 | 20 | 0.81 | 4.24 | 289.67 | 1129.39 |
| **Neoantimcin F** |  | 4 | 8 | 0.49 | 5.23 | 203.86 | 684.74 |
| **α-TOS** |  | 1 | 4 | 0.76 | 10.24 | 72.83 | 530.79 |
| **Fenofibrate** |  | 0 | 3 | 0.3 | 5.28 | 52.6 | 360.83 |
| **Amobarbital** |  | 2 | 3 | 0.73 | 1.89 | 75.27 | 226.28 |
| **IM176OUT05** |  | 5 | 5 | 0.27 | 1.35 | 97.78 | 219.29 |
| **Ranolazine** |  | 2 | 6 | 0.46 | 2.83 | 74.27 | 427.55 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **RTB70** |  | 0 | 3 | 0.41 | 4.40 | 36.44 | 435.91 |
| **RTC1** |  | 0 | 2 | 0.42 | 4.67 | 23.55 | 382.45 |
| **Atpenin A5** |  | 2 | 5 | 0.6 | 2.64 | 84.86 | 366.24 |
| **3-Nitropropionic Acid** |  | 1 | 4 | 0.67 | -0.26 | 80.44 | 119.08 |
| **Siccanin** |  | 1 | 3 | 0.73 | 4.65 | 38.69 | 342.48 |
| **Thenoyltrifluoroacetone (TTFA)** |  | 0 | 2 | 0.25 | 2.80 | 34.14 | 222.18 |
| **Tiabendazole** |  | 1 | 2 | 0 | 2.33 | 41.57 | 201.25 |
| **Parimifasor (LYC-30937)** |  | 3 | 4 | 0.06 | 5.83 | 82.17 | 460.21 |
| **Bz-423** |  | 1 | 3 | 0.11 | 5.99 | 52.9 | 440.93 |
| **Aurovertin B** |  | 1 | 5 | 0.42 | 1.30 | 74.22 | 346.38 |
| **Pyrvinium** |  | 0 | 1 | 0.19 | 1.41 | 12.05 | 382.53 |
| **Nefazodone** |  | 0 | 5 | 0.44 | 4.65 | 51.62 | 470.01 |
| **Paroxetine** |  | 1 | 4 | 0.37 | 3.15 | 39.72 | 329.37 |
| **Tamoxifen** |  | 0 | 2 | 0.23 | 6.35 | 12.47 | 371.52 |
| **Adaphostin** |  | 3 | 4 | 0.46 | 4.66 | 78.79 | 393.48 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Piericidin A** |  | 2 | 5 | 0.48 | 4.82 | 67.79 | 415.57 |
| **Xanthohumol** |  | 3 | 3 | 0.19 | 5.20 | 86.99 | 354.40 |
| **Lamellarin D** |  | 3 | 7 | 0.11 | 3.74 | 119.09 | 499.48 |