**Supplementary File 1: PGC-1α supports therapeutic resistance across several cancer types**

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| **Cancer type** | **Drug** | **PGC-1α role in resistance** | **Mechanism** | **Reference** |
| Non-Small Cell Lung Cancer | Cisplatin | Promotes | Resistant cells overexpress PGC-1α and PGC-1β to promote mitochondrial biogenesis, thereby overcoming reduced OXPHOS inefficiency caused by mtDNA mutations | (1) |
| Ovarian cancer | Cisplatin | Promotes | Resistant cells overexpress PGC-1α and are dependent on OXPHOS | (2) |
| Ovarian cancer | Cisplatin or Paclitaxel | Promotes | Treatment increases ROS, which increases PGC-1α and reprograms metabolism | (3) |
| Breast cancer | Metformin | Promotes | Metformin-resistant cells show elevated PGC-1α and high-PGC-1α tumors are resistant to metformin | (4) |
| Colon cancer | Oxaliplatin and 5-FU | Promotes | Chemotherapy induces a SIRT1/PGC1α-dependent increase in OXPHOS that promotes tumor survival during treatment | (5) |
| Breast cancer | PI3K/mTOR inhibitors | Promotes | PGC-1α and ERRα promote lactate oxidation, which is a pathway preferred by resistant cells | (6) |
| Melanoma | Piperlongumine | Promotes | Subset of tumors show high PGC1α, increased mitochondrial capacity and resistance to oxidative stress | (7) |
| Glioblastoma stem cells | Radiation | Promotes | Resistant cells overexpress PGC-1α | (8) |
| Melanoma | Selumetenib | Promotes | Subset of resistant melanomas show high PGC1α and OXPHOS; mTORC1/2 inhibitors are effective against this subset. | (9) |
| Ovarian cancer | Carboplatin or Paclitaxel | Sensitizes | High PGC-1α subset are more sensitive | (10) |
| Ovarian cancer | Cisplatin | Sensitizes | Resistant cells diminished PGC-1α, although high-grade serous carcinomas had elevated PGC-1α | (11) |
| Acute Myeloid Leukemia | Cytarabine and doxorubicin, and VEGFR2 inhibition | Sensitizes to new treatment | Presence of PGC-1α is required for VEGFR2 inhibition to resensitize cells to chemotherapy | (12) |
| Clear Cell Renal Cell Carcinoma | Doxorubicin or radiation | Sensitizes | Resistant cells respond better with elevated PGC-1α, cells with elevated PGC-1α are more sensitive | (13) |
| Pancreatic TICs | Metformin | Sensitizes | High PGC-1α leads to higher OXPHOS and better response to metformin | (14) |
| Breast cancer | Methotrexate | Sensitizes | Increasing PGC-1α increases sensitivity by diminishing expression of the target pathway | (15) |

**Supplementary References**

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