## Supplementary Table 1: Gene Ontology enrichment analysis of co differentially expressed genes in Poly(ADP-ribose) polymerase inhibitors-treated ovarian cancer cells following 6-month exposure

| ID | ONTOLOGY | Description | GeneRatio | BgRatio | pvalue | p.adjust | qvalue | geneID | Count | bgCount | EnrichmentScore | group1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GO:0002065 | BP | columnar/cuboidal epithelial cell differentiation | 0.15151515 | 92/18800 | 5.35543E-07 | 0.000438609 | 0.000343875 | *EMX1, AGR2, TP63, FASN, CDH2* | 5 | 92 | 0.05434783 | merge1_down |
| GO:0002067 | BP | glandular epithelial cell differentiation | 0.12121212 | 54/18800 | 2.33815E-06 | 0.000957471 | 0.000750668 | *AGR2, TP63, FASN, CDH2* | 4 | 54 | 0.07407407 | merge1_down |
| GO:0030520 | BP | intracellular estrogen receptor signaling pathway | 0.09090909 | 54/18800 | 0.000114985 | 0.03139082 | 0.024610758 | *ESR1, PARP1, TP63* | 3 | 54 | 0.05555556 | merge1_down |
| GO:0060019 | BP | radial glial cell differentiation | 0.06060606 | 12/18800 | 0.000195047 | 0.037423326 | 0.029340311 | *EMX1, CDH2* | 2 | 12 | 0.16666667 | merge1_down |
| GO:0045109 | BP | intermediate filament organization | 0.09090909 | 68/18800 | 0.00022847 | 0.037423326 | 0.029340311 | *KRT5, KRT17, KRT14* | 3 | 68 | 0.04411765 | merge1_down |
| GO:0002064 | BP | epithelial cell development | 0.12121212 | 203/18800 | 0.000422539 | 0.037591726 | 0.029472338 | *ESR1, TP63, FASN, CDH2* | 4 | 203 | 0.01970443 | merge1_down |
| GO:0030540 | BP | female genitalia development | 0.06060606 | 18/18800 | 0.000449184 | 0.037591726 | 0.029472338 | *ESR1, TP63* | 2 | 18 | 0.11111111 | merge1_down |
| GO:0045104 | BP | intermediate filament cytoskeleton organization | 0.09090909 | 88/18800 | 0.000488459 | 0.037591726 | 0.029472338 | *KRT5, KRT17, KRT14* | 3 | 88 | 0.03409091 | merge1_down |
| GO:0060749 | BP | mammary gland alveolus development | 0.06060606 | 19/18800 | 0.000501479 | 0.037591726 | 0.029472338 | *ESR1, FOXB1* | 2 | 19 | 0.10526316 | merge1_down |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GO:0061377 | BP | mammary gland lobule development | 0.06060606 | 19/18800 | 0.000501479 | 0.037591726 | 0.029472338 | *ESR1, FOXB1* | 2 | 19 | 0.10526316 | merge1_down |
| GO:0045103 | BP | intermediate filament-based process | 0.09090909 | 89/18800 | 0.000504895 | 0.037591726 | 0.029472338 | *KRT5, KRT17, KRT14* | 3 | 89 | 0.03370787 | merge1_down |
| GO:0030324 | BP | lung development | 0.2727273 | 179/18800 | 0.000132397 | 0.02022558 | 0.01354211 | *PDPN, RBP4, MME* | 3 | 179 | 0.01675978 | merge1_up |
| GO:0030323 | BP | respiratory tube development | 0.2727273 | 183/18800 | 0.000141344 | 0.02022558 | 0.01354211 | *PDPN, RBP4, MME* | 3 | 183 | 0.01639344 | merge1_up |
| GO:0060541 | BP | respiratory system development | 0.2727273 | 203/18800 | 0.000192015 | 0.02022558 | 0.01354211 | *PDPN, RBP4, MME* | 3 | 203 | 0.01477833 | merge1_up |
| GO:0007565 | BP | female pregnancy | 0.19230769 | 185/18800 | 4.86166E-06 | 0.002573704 | 0.001788047 | *PSG9, PSG2, PSG7, PSG5, UCN* | 5 | 185 | 0.02702703 | merge2_up |
| GO:0044703 | BP | multi-organism reproductive process | 0.19230769 | 205/18800 | 8.01498E-06 | 0.002573704 | 0.001788047 | *PSG9, PSG2, PSG7, PSG5, UCN* | 5 | 205 | 0.02439024 | merge2_up |
| GO:0044706 | BP | multi-multicellular organism process | 0.19230769 | 213/18800 | 9.65139E-06 | 0.002573704 | 0.001788047 | *PSG9, PSG2, PSG7, PSG5, UCN* | 5 | 213 | 0.02347418 | merge2_up |
| GO:0038063 | BP | collagen-activated tyrosine kinase receptor signaling pathway | 0.07692308 | 12/18800 | 0.000120356 | 0.021706788 | 0.015080506 | *COL4A2, COL4A1* | 2 | 12 | 0.16666667 | merge2_up |
| GO:0045741 | BP | positive regulation of epidermal growth | 0.07692308 | 13/18800 | 0.000142118 | 0.021706788 | 0.015080506 | *AREG, EPGN* | 2 | 13 | 0.15384615 | merge2_up |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | factor-activated receptor activity | | | | | | | | | | |
| GO:0010838 | BP | positive regulation of keratinocyte proliferation | 0.07692308 | 14/18800 | 0.000165663 | 0.021706788 | 0.015080506 | *AREG, CDH3* | 2 | 14 | 0.14285714 | merge2_up |
| GO:0050679 | BP | positive regulation of epithelial cell proliferation | 0.15384615 | 211/18800 | 0.000189934 | 0.021706788 | 0.015080506 | *BMP5, AREG, CDH3, EPGN* | 4 | 211 | 0.01895735 | merge2_up |
| GO:0010566 | BP | regulation of ketone biosynthetic process | 0.07692308 | 17/18800 | 0.000246954 | 0.021951419 | 0.01525046 | *BMP5, EGR1* | 2 | 17 | 0.11764706 | merge2_up |
| GO:0038065 | BP | collagen-activated signaling pathway | 0.07692308 | 17/18800 | 0.000246954 | 0.021951419 | 0.01525046 | *COL4A2, COL4A1* | 2 | 17 | 0.11764706 | merge2_up |
| GO:0006700 | BP | C21-steroid hormone biosynthetic process | 0.07692308 | 20/18800 | 0.000344129 | 0.027530339 | 0.019126341 | *BMP5, EGR1* | 2 | 20 | 0.1 | merge2_up |
| GO:0046885 | BP | regulation of hormone biosynthetic process | 0.07692308 | 22/18800 | 0.000417678 | 0.030376558 | 0.021103714 | *BMP5, EGR1* | 2 | 22 | 0.09090909 | merge2_up |
| GO:0043567 | BP | regulation of insulin-like growth factor receptor signaling pathway | 0.07692308 | 24/18800 | 0.000498195 | 0.030658181 | 0.021299368 | *BMP5, CDH3* | 2 | 24 | 0.08333333 | merge2_up |
| GO:0120255 | BP | olefinic compound biosynthetic process | 0.07692308 | 24/18800 | 0.000498195 | 0.030658181 | 0.021299368 | *BMP5, EGR1* | 2 | 24 | 0.08333333 | merge2_up |
| GO:0098742 | BP | cell-cell adhesion via plasma-membrane adhesion molecules | 0.15384615 | 279/18800 | 0.00054858 | 0.031347409 | 0.0217782 | *PSG2, PECAM1, CDH3, PSG5* | 4 | 279 | 0.01433692 | merge2_up |
| GO:00 | BP | glomerulus | 0.07692308 | 27/18800 | 0.00063 | 0.03370 | 0.0234 | *PECAM1,* | 2 | 27 | 0.074074 | merge2_ |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 72012 | | vasculature development | | | 1961 | 4571 | 15807 | *EGR1* | | | 07 | up |
| GO:0061437 | BP | renal system vasculature development | 0.07692308 | 29/18800 | 0.000729744 | 0.034340902 | 0.02385789 | *PECAM1, EGR1* | 2 | 29 | 0.06896552 | merge2_up |
| GO:0061440 | BP | kidney vasculature development | 0.07692308 | 29/18800 | 0.000729744 | 0.034340902 | 0.02385789 | *PECAM1, EGR1* | 2 | 29 | 0.06896552 | merge2_up |
| GO:0007176 | BP | regulation of epidermal growth factor-activated receptor activity | 0.07692308 | 30/18800 | 0.000781205 | 0.034720199 | 0.024121401 | *AREG, EPGN* | 2 | 30 | 0.06666667 | merge2_up |
| GO:0072001 | BP | renal system development | 0.15384615 | 312/18800 | 0.000833677 | 0.035102191 | 0.024386785 | *PECAM1, EGR1, COL4A1, EPCAM* | 4 | 312 | 0.01282051 | merge2_up |
| GO:0010837 | BP | regulation of keratinocyte proliferation | 0.07692308 | 36/18800 | 0.001125646 | 0.039631925 | 0.027533758 | *AREG, CDH3* | 2 | 36 | 0.05555556 | merge2_up |
| GO:0032350 | BP | regulation of hormone metabolic process | 0.07692308 | 36/18800 | 0.001125646 | 0.039631925 | 0.027533758 | *BMP5, EGR1* | 2 | 36 | 0.05555556 | merge2_up |
| GO:0045742 | BP | positive regulation of epidermal growth factor receptor signaling pathway | 0.07692308 | 36/18800 | 0.001125646 | 0.039631925 | 0.027533758 | *AREG, EPGN* | 2 | 36 | 0.05555556 | merge2_up |
| GO:0008207 | BP | C21-steroid hormone metabolic process | 0.07692308 | 37/18800 | 0.001188958 | 0.039631925 | 0.027533758 | *BMP5, EGR1* | 2 | 37 | 0.05405405 | merge2_up |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GO:0048009 | BP | insulin-like growth factor receptor signaling pathway | 0.07692308 | 37/18800 | 0.001188958 | 0.039631925 | 0.027533758 | *BMP5, CDH3* | 2 | 37 | 0.05405405 | merge2_up |
| GO:1901186 | BP | positive regulation of ERBB signaling pathway | 0.07692308 | 38/18800 | 0.001253945 | 0.04011733 | 0.027870987 | *AREG, EPGN* | 2 | 38 | 0.05263158 | merge2_up |
| GO:0001655 | BP | urogenital system development | 0.15384615 | 352/18800 | 0.001303813 | 0.04011733 | 0.027870987 | *PECAM1, EGR1, COL4A1, EPCAM* | 4 | 352 | 0.01136364 | merge2_up |
| GO:0120178 | BP | steroid hormone biosynthetic process | 0.07692308 | 41/18800 | 0.001458917 | 0.043227156 | 0.030031498 | *BMP5, EGR1* | 2 | 41 | 0.04878049 | merge2_up |
| GO:0042181 | BP | ketone biosynthetic process | 0.07692308 | 43/18800 | 0.001603861 | 0.044244437 | 0.03073824 | *BMP5, EGR1* | 2 | 43 | 0.04651163 | merge2_up |
| GO:0071604 | BP | transforming growth factor beta production | 0.07692308 | 43/18800 | 0.001603861 | 0.044244437 | 0.03073824 | *PSG9, CDH3* | 2 | 43 | 0.04651163 | merge2_up |
| GO:2000273 | BP | positive regulation of signaling receptor activity | 0.07692308 | 45/18800 | 0.001755402 | 0.045435301 | 0.031565578 | *AREG, EPGN* | 2 | 45 | 0.04444444 | merge2_up |
| GO:0050678 | BP | regulation of epithelial cell proliferation | 0.15384615 | 382/18800 | 0.001760618 | 0.045435301 | 0.031565578 | *BMP5, AREG, CDH3, EPGN* | 4 | 382 | 0.0104712 | merge2_up |
| GO:0043616 | BP | keratinocyte proliferation | 0.07692308 | 47/18800 | 0.001913505 | 0.046388003 | 0.032227454 | *AREG, CDH3* | 2 | 47 | 0.04255319 | merge2_up |
| GO:0043618 | BP | regulation of transcription from | 0.07692308 | 47/18800 | 0.001913505 | 0.046388003 | 0.032227454 | *EGR1, EPAS1* | 2 | 47 | 0.04255319 | merge2_up |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | RNA polymerase II promoter in response to stress | | | | | | | | | | |
| GO:0045860 | BP | positive regulation of protein kinase activity | 0.15384615 | 396/18800 | 0.002007859 | 0.04724374 | 0.032821967 | *AREG, EGR1, EPGN, UCN* | 4 | 396 | 0.01010101 | merge2_up |
| GO:0050731 | BP | positive regulation of peptidyl-tyrosine phosphorylation | 0.11538462 | 190/18800 | 0.002225963 | 0.048632633 | 0.033786882 | *AREG, PECAM1, EPGN* | 3 | 190 | 0.01578947 | merge2_up |
| GO:0007157 | BP | heterophilic cell-cell adhesion via plasma membrane cell adhesion molecules | 0.07692308 | 51/18800 | 0.002249259 | 0.048632633 | 0.033786882 | *PSG2, PSG5* | 2 | 51 | 0.03921569 | merge2_up |
| GO:0045332 | BP | phospholipid translocation | 0.07692308 | 51/18800 | 0.002249259 | 0.048632633 | 0.033786882 | *ATP10A, ABCB1* | 2 | 51 | 0.03921569 | merge2_up |
| GO:0098644 | CC | complex of collagen trimers | 0.07407407 | 22/19594 | 0.000415277 | 0.034467979 | 0.027102279 | *COL4A2, COL4A1* | 2 | 22 | 0.09090909 | merge2_up |
| GO:0048018 | MF | receptor ligand activity | 0.25925926 | 489/18410 | 5.00318E-06 | 0.000236185 | 0.000135871 | *BMP5, DEFB103B, AREG, EBI3, CXCL16, EPGN, UCN* | 7 | 489 | 0.01431493 | merge2_up |
| GO:0030546 | MF | signaling receptor activator activity | 0.25925926 | 496/18410 | 5.49266E-06 | 0.000236185 | 0.000135871 | *BMP5, DEFB103B, AREG, EBI3, CXCL16, EPGN, UCN* | 7 | 496 | 0.0141129 | merge2_up |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GO:0140333 | MF | glycerophospholipid flippase activity | 0.07407407 | 14/18410 | 0.000186456 | 0.002984762 | 0.00171706 | *ATP10A, ABCB1* | 2 | 14 | 0.14285714 | merge2_up |
| GO:0005041 | MF | low-density lipoprotein particle receptor activity | 0.07407407 | 15/18410 | 0.000214947 | 0.002984762 | 0.00171706 | *OLR1, CXCL16* | 2 | 15 | 0.13333333 | merge2_up |
| GO:0140328 | MF | floppase activity | 0.07407407 | 16/18410 | 0.000245431 | 0.002984762 | 0.00171706 | *ATP10A, ABCB1* | 2 | 16 | 0.125 | merge2_up |
| GO:0008525 | MF | phosphatidylcholine transporter activity | 0.07407407 | 17/18410 | 0.000277904 | 0.002984762 | 0.00171706 | *ATP10A, ABCB1* | 2 | 17 | 0.11764706 | merge2_up |
| GO:0140327 | MF | flippase activity | 0.07407407 | 17/18410 | 0.000277904 | 0.002984762 | 0.00171706 | *ATP10A, ABCB1* | 2 | 17 | 0.11764706 | merge2_up |
| GO:0030228 | MF | lipoprotein particle receptor activity | 0.07407407 | 18/18410 | 0.000312359 | 0.002984762 | 0.00171706 | *OLR1, CXCL16* | 2 | 18 | 0.11111111 | merge2_up |
| GO:0046624 | MF | sphingolipid transporter activity | 0.07407407 | 18/18410 | 0.000312359 | 0.002984762 | 0.00171706 | *ATP10A, ABCB1* | 2 | 18 | 0.11111111 | merge2_up |
| GO:0005125 | MF | cytokine activity | 0.14814815 | 235/18410 | 0.000360548 | 0.003100716 | 0.001783765 | *BMP5, AREG, EBI3, CXCL16* | 4 | 235 | 0.01702128 | merge2_up |
| GO:0140326 | MF | ATPase-coupled intramembrane lipid transporter activity | 0.07407407 | 27/18410 | 0.000710778 | 0.005556993 | 0.003196802 | *ATP10A, ABCB1* | 2 | 27 | 0.07407407 | merge2_up |
| GO:0005154 | MF | epidermal growth factor receptor binding | 0.07407407 | 32/18410 | 0.000999875 | 0.007165769 | 0.004122291 | *AREG, EPGN* | 2 | 32 | 0.0625 | merge2_up |
| GO:0030020 | MF | extracellular matrix structural constituent | 0.07407407 | 41/18410 | 0.001639631 | 0.009604343 | 0.005525142 | *COL4A2, COL4A1* | 2 | 41 | 0.04878049 | merge2_up |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | conferring tensile strength | | | | | | | | | | |
| GO:0140303 | MF | intramembrane lipid transporter activity | 0.07407407 | 41/18410 | 0.001639631 | 0.009604343 | 0.005525142 | *ATP10A, ABCB1* | 2 | 41 | 0.04878049 | merge2_up |
| GO:0008083 | MF | growth factor activity | 0.11111111 | 162/18410 | 0.001675176 | 0.009604343 | 0.005525142 | *BMP5, AREG, EPGN* | 3 | 162 | 0.01851852 | merge2_up |
| GO:0005548 | MF | phospholipid transporter activity | 0.07407407 | 62/18410 | 0.003710157 | 0.019942096 | 0.011472197 | *ATP10A, ABCB1* | 2 | 62 | 0.03225806 | merge2_up |
| GO:0042379 | MF | chemokine receptor binding | 0.07407407 | 71/18410 | 0.004836191 | 0.024465435 | 0.014074363 | *DEFB103B, CXCL16* | 2 | 71 | 0.02816901 | merge2_up |
| GO:0038024 | MF | cargo receptor activity | 0.07407407 | 79/18410 | 0.005953036 | 0.028442281 | 0.016362145 | *OLR1, CXCL16* | 2 | 79 | 0.02531646 | merge2_up |
| GO:0005126 | MF | cytokine receptor binding | 0.11111111 | 272/18410 | 0.007178066 | 0.032490194 | 0.018690809 | *DEFB103B, EBI3, CXCL16* | 3 | 272 | 0.01102941 | merge2_up |
| GO:0001664 | MF | G protein-coupled receptor binding | 0.11111111 | 288/18410 | 0.008394504 | 0.036096368 | 0.020765353 | *DEFB103B, CXCL16, UCN* | 3 | 288 | 0.01041667 | merge2_up |
| GO:1990782 | MF | protein tyrosine kinase binding | 0.07407407 | 113/18410 | 0.01185854 | 0.048563527 | 0.027937402 | *PSG9, PSG7* | 2 | 113 | 0.01769912 | merge2_up |

BP, biological preocess; CC, cellular component; MF, molecular function; Merge1_up, DEGs that are up-regulated in both SKOV3_Nira_6M and SKOV3_Ola_6M; merge1_down, DEGs that are down-regulated in both SKOV3_Nira_6M and SKOV3_Ola_6M; merge2_up, DEGs that are up-regulated in both OVCAR8_Nira_6M and OVCAR8_Ola_6M

**Supplementary Table 2: Biological process enrichment analysis of co- differentially expressed genes in Poly(ADP-ribose) polymerase inhibitors-treated ovarian cancer cells**

| ID | term description | observed gene count | background gene count | strength | signal | false discovery rate | matching proteins in your network (labels) | group |
|---|---|---|---|---|---|---|---|---|
| GO:0030855 | Epithelial cell differentiation | 14 | 617 | 0.89 | 0.93 | 3.38E-05 | *KRT14, KRT5, EMX1, EPAS1, TP63, CDH2, PDPN, FASN, KRT17, ACTL8, FOXB1, WNT5B, AGR2, ESR1* | 22up&75down |
| GO:0060429 | Epithelium development | 16 | 1069 | 0.71 | 0.68 | 0.00033 | *KRT14, KRT5, EMX1, EPAS1, TP63, CDH2, PDPN, FASN, KRT17, ACTL8, CA9, AREG, FOXB1, WNT5B, AGR2, ESR1* | 22up&75down |
| GO:0009888 | Tissue development | 18 | 1723 | 0.56 | 0.45 | 0.0054 | *KRT14, MEST, KRT5, EMX1, EPAS1, TP63, CDH2, PDPN, FASN, KRT17, RBP4, ACTL8, CA9, AREG, FOXB1, WNT5B, AGR2, ESR1* | 22up&75down |
| GO:0048856 | Anatomical structure development | 32 | 5117 | 0.33 | 0.35 | 0.0055 | *KRT14, MEST, KRT5, EMX1, CDKN2C, RPS6KA6, EPAS1, TP63, CDH6, CDH2, PDPN, IGFBP7, UCN, TNFRSF11B, CLEC4E, UGT1A6, FASN, KRT17, EID2B, PARP1, LDOC1, RBP4, ACTL8, CA9, AREG, FOXB1, WNT5B, AGR2, ESR1, SYBU, MME, CPAMD8* | 22up&75down |

|  |  |  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|
| GO:0032502 | Developmental process | 33 | 5657 | 0.3 | 0.31 | 0.0132 | *KRT14, MEST, KRT5, EMX1, CDKN2C, RPS6KA6, EPAS1, TP63, CDH6, CDH2, PDPN, IGFBP7, UCN, TNFRSF11B, CLEC4E, UGT1A6, FASN, KRT17, EID2B, PARP1, LDOC1, RBP4, ACTL8, CA9, ADGRG2, AREG, FOXB1, WNT5B, AGR2, ESR1, SYBU, MME, CPAMD8* | 22up&75down |
| GO:0002065 | Columnar/cuboidal epithelial cell differentiation | 5 | 105 | 1.22 | 0.43 | 0.0424 | *EMX1, TP63, CDH2, FASN, AGR2* | 22up&75down |
| GO:0002064 | Epithelial cell development | 6 | 190 | 1.04 | 0.4 | 0.0471 | *EPAS1, TP63, CDH2, FASN, WNT5B, ESR1* | 22up&75down |
| GO:0098609 | Cell-cell adhesion | 8 | 542 | 0.95 | 0.44 | 0.0408 | *EPCAM, CDH3, OLR1, BMP5, PSG5, PSG2, PECAM1, PCDHGB5* | 44up&21down |

22up&75down, Persistently 22 up-regulated and 75 down-regulated differentially expressed genes (DEGs) following continuous exposure to olaparib and niraparib for 2, 3, or 6 months; 44up&21down, 44 specifically up-regulated and 21 down-regulated DEGs following 6-month exposure to olaparib and niraparib.

Supplementary Table 3: Results of the proportional hazards (PH) assumption test for the multivariable Cox model of *CPAMD8* and *EGR1*

| Index | Overall survival | | | Progression-free survival | | |
|---|---|---|---|---|---|---|
| | chisq | df | p | chisq | df | p |
| Aage | 4.7937 | 1 | 0.029 | 2.60E+00 | 1 | 0.1069 |
| Stage.status | 9.5507 | 4 | 0.049 | 2.77E+00 | 2 | 0.2505 |
| Drug treatment | 25.3412 | 1 | 4.80E-07 | 3.92E-07 | 1 | 0.9995 |
| BRCAmut.status | 0.252 | 1 | 0.616 | 3.32E+00 | 1 | 0.0686 |
| Grade | 19.0764 | 6 | 0.004 | 9.80E+00 | 6 | 0.1334 |
| *CPAMD8* | 0.0787 | 1 | 0.779 | 1.12E+00 | 1 | 0.2893 |
| *EGR1* | 4.2036 | 1 | 0.04 | 1.76E+00 | 1 | 0.1845 |
| Global | 73.1423 | 15 | 1.20E-09 | 2.86E+01 | 13 | 0.0076 |

Supplementary Table 4: Association of ***CPAMD8*** and ***EGR1*** with survival upon stratification by BRCA1/2 mutation status

| | exp(coef) | lower.95 | upper.95 | *p* |
|---|---|---|---|---|
| CPAMD8hig_BRCAwt | 0.5439 | 0.13356 | 2.215 | |
| CPAMD8low_BRCAmut | 0.3173 | 0.04447 | 2.264 | 0.1 |
| CPAMD8low_BRCAwt | 0.3968 | 0.09694 | 1.624 | |
| EGR1hig_BRCAwt | 1.261 | 0.25061 | 2.51 | |
| EGR1low_BRCAmut | 2.608 | 0.03962 | 3.711 | 0.3 |
| EGR1low_BRCAwt | 1.678 | 0.18691 | 1.9 | |

**Supplementary Table 5: Top 10 biological process enrichment analysis of *CPAMD8*, *DAPP1* and *EGR1***

| ID | term description | observed gene count | background gene count | strength | signal | false discovery rate | matching proteins in your network (labels) | *group* |
|---|---|---|---|---|---|---|---|---|
| GO:0062023 | Collagen-containing extracellular matrix | 7 | 407 | 1.21 | 1.07 | 0.00032 | *MYOC, P3H2, COL26A1, FBN1, ADAMTSL4, COL23A1, COL25A1* | *CPAMD8_biological process* |
| GO:0005788 | Endoplasmic reticulum lumen | 6 | 312 | 1.26 | 1.02 | 0.00076 | *P3H2, COL26A1, FBN1, ADAMTSL4, COL23A1, COL25A1* | *CPAMD8_biological process* |
| GO:0038095 | Fc-epsilon receptor signaling pathway | 5 | 23 | 2.59 | 3.96 | 2.86E-08 | *PLCG1, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0035556 | Intracellular signal transduction | 9 | 1518 | 1.03 | 1.06 | 2.45E-05 | *PLEK2, PLEK, PLCG1, RAC2, RAC3, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0002764 | Immune response-regulating signaling pathway | 6 | 312 | 1.54 | 1.77 | 2.85E-05 | *PLCG1, PIK3AP1, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0002224 | Toll-like receptor signaling pathway | 4 | 61 | 2.07 | 1.99 | 0.00011 | *PIK3AP1, LYN, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0002429 | Immune response-activating cell surface receptor signaling pathway | 5 | 197 | 1.66 | 1.71 | 0.00012 | *PLCG1, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |

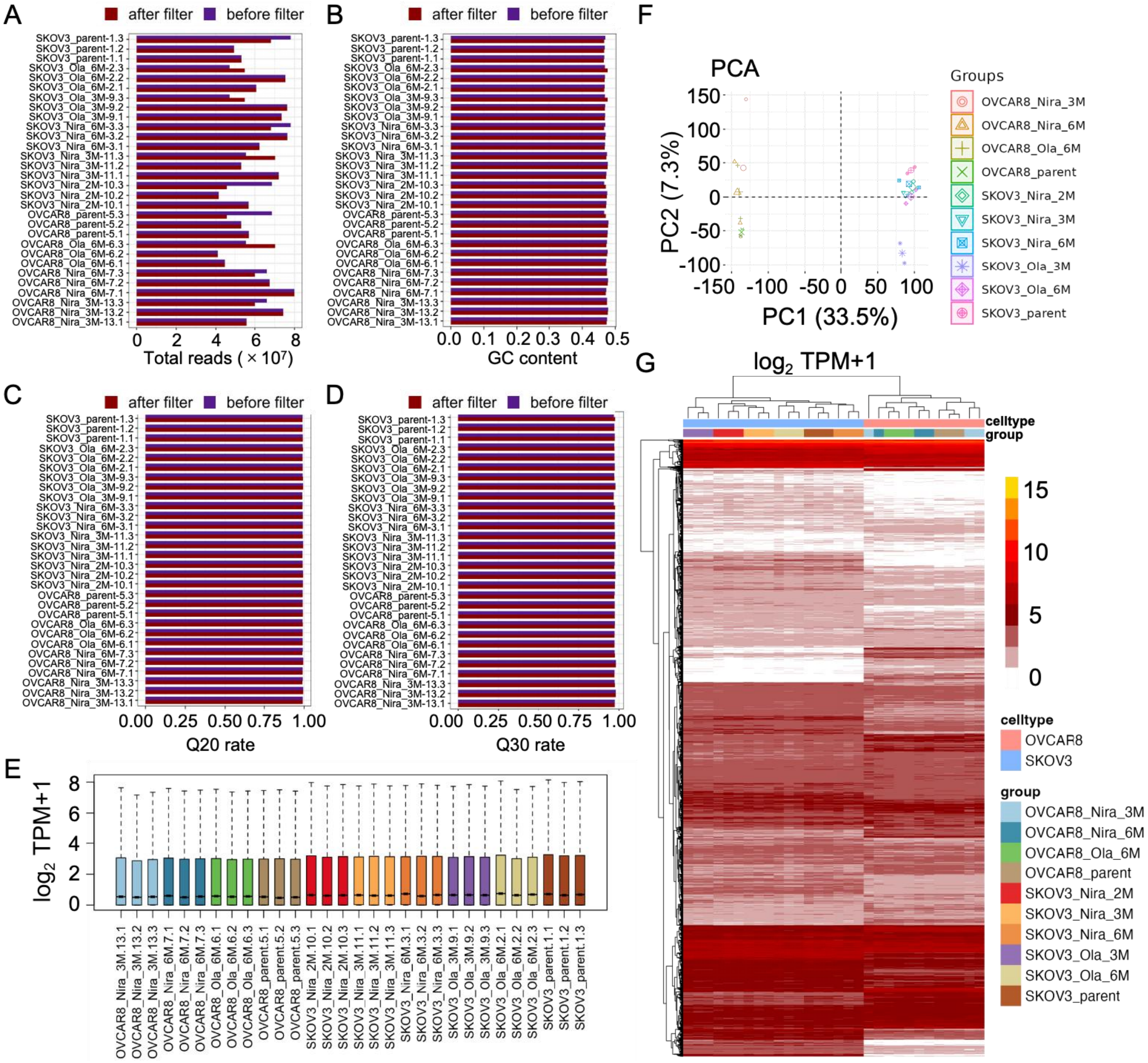
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| GO:0050776 | Regulation of immune response | 7 | 844 | 1.17 | 1.16 | 0.00015 | *PLCG1, RAC2, PIK3AP1, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0002703 | Regulation of leukocyte mediated immunity | 5 | 239 | 1.57 | 1.57 | 0.00019 | *RAC2, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0007165 | Signal transduction | 11 | 4714 | 0.62 | 0.53 | 0.00021 | *PLEK2, PLEK, PLCG1, RAC2, RAC3, PIK3AP1, DAPP1, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0002699 | Positive regulation of immune effector process | 5 | 264 | 1.53 | 1.49 | 0.00025 | *RAC2, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0032101 | Regulation of response to external stimulus | 7 | 964 | 1.11 | 1.05 | 0.00025 | *PLCG1, RAC2, PIK3AP1, LYN, VAV1, PLCG2, BTK* | *DAPP1_biological process* |
| GO:0045944 | Positive regulation of transcription by RNA polymerase II | 9 | 1250 | 1.11 | 1.24 | 7.93E-06 | *EGR1, EGR2, FOSB, JUND, MAPK3, TP53, JUNB, FOS, JUN* | *EGR1_biological process* |
| GO:0071248 | Cellular response to metal ion | 6 | 198 | 1.73 | 2.18 | 7.93E-06 | *FOSB, JUND, MAPK3, JUNB, FOS, JUN* | *EGR1_biological process* |
| GO:0071277 | Cellular response to calcium ion | 5 | 89 | 2 | 2.44 | 7.93E-06 | *FOSB, JUND, JUNB, FOS, JUN* | *EGR1_biological process* |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| GO:0006355 | Regulation of transcription, DNA-templated | 11 | 3460 | 0.76 | 0.71 | 1.53E-05 | *EGR1, EGR2, FOSB, JUND, MAPK3, TP53, NAB2, JUNB, FOS, NAB1, JUN* | *EGR1_biological process* |
| GO:0010243 | Response to organonitrogen compound | 8 | 963 | 1.17 | 1.3 | 1.53E-05 | *EGR1, EGR2, FOSB, JUND, MAPK3, TP53, FOS, JUN* | *EGR1_biological process* |
| GO:1902895 | Positive regulation of miRNA transcription | 4 | 48 | 2.17 | 2.39 | 1.90E-05 | *EGR1, TP53, FOS, JUN* | *EGR1_biological process* |
| GO:0007178 | Transmembrane receptor protein serine/threonine kinase signaling pathway | 5 | 206 | 1.64 | 1.85 | 3.69E-05 | *EGR1, MAPK3, TP53, FOS, JUN* | *EGR1_biological process* |
| GO:0009612 | Response to mechanical stimulus | 5 | 214 | 1.62 | 1.83 | 3.93E-05 | *FOSB, JUND, MAPK3, FOS, JUN* | *EGR1_biological process* |
| GO:0009719 | Response to endogenous stimulus | 8 | 1363 | 1.02 | 1.04 | 3.93E-05 | *EGR1, EGR2, FOSB, JUND, MAPK3, TP53, FOS, JUN* | *EGR1_biological process* |
| GO:0031325 | Positive regulation of cellular metabolic process | 10 | 3114 | 0.76 | 0.7 | 4.56E-05 | *EGR1, EGR2, FOSB, JUND, MAPK3, TP53, NAB2, JUNB, FOS, JUN* | *EGR1_biological process* |

**Supplementary Table 6: Spearman correlation of *CPAMD8* and *EGR1* expression with classical poly(ADP-ribose) polymerase inhibitors resistance gene signatures**

| Targets | Machine | Referenc | CPAMD8 | | EGR1 | |
|---|---|---|---|---|---|---|
| | | | *P* | *r* | *P* | *r* |
| ABCB1 | Drug transport | PMID: 30252484; PMID: 24962512 | 7.17E-12 | -0.904438764 | 2.79E-05 | -0.686616981 |
| CDK12 | Cell cycle checkpoint | PMID: 27880910; PMID: 37478560 | 0.000190046 | 0.640934372 | 3.91E-07 | 0.884315907 |
| ATR | HRR | PMID: 32709856; PMID: 35259479 | 5.39E-06 | -0.743715239 | 0.000464636 | -0.608898776 |
| BRCA1 | | PMID: 39103848; PMID: 32870734 | 0.00264529 | 0.535483871 | 1.52E-06 | 0.787319244 |
| BRD4 | | PMID: 36753396; PMID: 29533782 | 0.003722231 | 0.519021135 | 0.000118652 | 0.65650723 |
| CTC1 | | PMID: 40403056; PMID: 29768208 | 3.77E-05 | 0.691212458 | 4.97E-05 | 0.68320356 |
| DDB2 | | PMID: 31541611 | 0.047456287 | -0.36596218 | 0.002142695 | -0.545272525 |
| DNA2 | | PMID: 40127955; PMID: 37756561 | 6.35E-06 | -0.739265851 | 2.65E-06 | -0.764627364 |
| EXO1 | | PMID: 41323735; PMID: 40127955; PMID: 40054125 | 1.15E-06 | -0.806451613 | 9.48E-05 | -0.663626251 |
| FBXO5 | | PMID: 30554948; PMID: 33412559 | 8.29E-07 | -0.837152392 | 3.92E-06 | -0.752614016 |
| H2AX | | PMID: 38789420; PMID: 39588777 | 0.000965485 | 0.579977753 | 1.05E-05 | 0.725917686 |
| KLF5 | | PMID: 37702443; PMID: 38433576; PMID: 40307891 | 0.000407778 | 0.613793103 | 8.62E-07 | 0.833592881 |
| MDC1 | | PMID: 39677775; PMID: 38697125; PMID: 29656893 | 1.27E-06 | -0.798442714 | 8.75E-07 | -0.832258065 |
| PALB2 | | PMID: 35768576; PMID: 35926819 | 8.45E-06 | -0.731701891 | 0.003461839 | -0.522580645 |
| PDS5B | | PMID: 27924011 | 3.71E-05 | 0.691657397 | 8.79E-07 | 0.831813126 |
| POLE3 | | PMID: 38828775; PMID: 38753485 | 0.002451828 | 0.539043382 | 0.0007263 | 0.591546162 |
| POLE4 | | PMID: 38828775; PMID: 38753485 | 7.90E-06 | -0.733481646 | 8.38E-07 | -0.836262514 |
| RAD51 | | PMID: 29635390; PMID: 38007537 | 0.029057359 | -0.400667408 | 0.018239643 | -0.430923248 |

| | | | | | | |
|---|---|---|---|---|---|---|
| RAD51C | | PMID: 34321239; PMID: 23512992; PMID: 28588062 | 4.66E-06 | -0.747719689 | 0.007342949 | -0.483870968 |
| RAD51D | | PMID: 28588062; PMID: 37833926 | 0.000323855 | -0.622246941 | 0.013624561 | -0.448720801 |
| RADX | | PMID: 28735897 | 1.87E-06 | -0.77753059 | 0.000175618 | -0.643604004 |
| RBBP8 | | PMID: 35219381; PMID: 26713604; PMID: 24413181 | 0.000323855 | 0.622246941 | 4.87E-07 | 0.873637375 |
| RIF1 | | PMID: 38244928; PMID: 35177609 | 4.47E-05 | 0.686318131 | 1.11E-06 | 0.809121246 |
| RNF8 | | PMID: 29656893; PMID: 24240613 | 0.000149634 | 0.64894327 | 1.01E-06 | 0.818020022 |
| SHLD1 | | PMID: 30022168 | 0.015448761 | 0.441156841 | 0.000216428 | 0.636484983 |
| STN1 | | PMID: 40403056; PMID: 29768208 | 1.19E-06 | 0.80378198 | 0.004294113 | 0.511902113 |
| TOPBP1 | | PMID: 37878724; PMID: 26811421 | 2.91E-06 | -0.761512792 | 0.000216428 | -0.636484983 |
| TP53BP1 | | PMID: 27613518; PMID: 37002234; PMID: 39632881; PMID: 30686551 | 1.39E-06 | 0.792658509 | 9.95E-07 | 0.819799778 |
| TRIP13 | | PMID: 40115747; PMID: 35517402 | 0.031837435 | -0.394438265 | 0.007966328 | -0.47942158 |
| PARG | PARylation restore | PMID: 32029455; PMID: 29894693 | 0.014459012 | 0.44516129 | 0.001849614 | 0.551946607 |
| EZH2 | Stability and protection of replication fork | PMID: 32004442; PMID: 39562655 | 8.25E-07 | -0.83759733 | 3.42E-06 | -0.756618465 |
| HLTF | | PMID: 40548939 | 3.80E-06 | -0.753503893 | 0.000398126 | -0.614682981 |
| KMT2C | | PMID: 27443740; PMID: 33853832 | 8.54E-07 | -0.834482759 | 0.000293341 | -0.625806452 |
| MUS81 | | PMID: 37254810; PMID: 35910852; PMID: 29087384 | 0.001624478 | -0.557730812 | 9.34E-07 | -0.826028921 |
| ZRANB3 | | PMID: 28735897 | 0.000875882 | 0.583982202 | 2.62E-05 | 0.701446051 |



**Supplementary Fig. 1. Overview of transcriptome sequencing data following treatment with Olaparib and Niraparib for different durations**

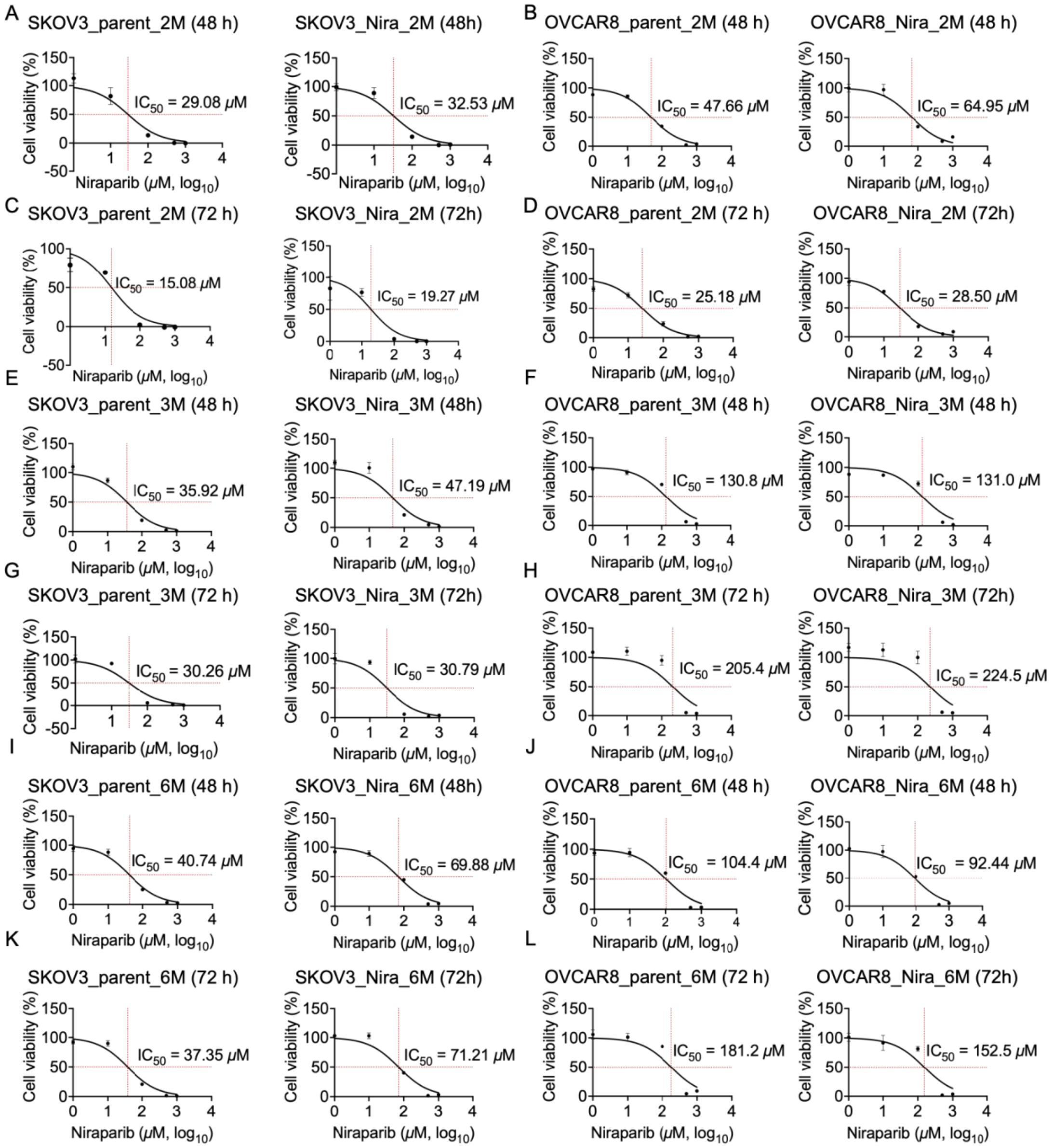
A-D) Total reads (A), GC content (B), Q20 value (C), and Q30 value (D) for each sample before and after filtering with fastp software.

E) Box plot displaying the range and median values of log2-transformed TPM for all genes across the30samples.

F) Distribution of 30 samples based on principal component analysis (PCA), showing separation along principal components 1 (PC1) and 2 (PC2).

G) Heatmap of gene expression profiles and hierarchical clustering of the 30 sequenced samples.

GC, Guanine and Cytosine content; Q20, Proportion of bases with a quality score greater than 20; Q30, Proportion of bases with a quality score greater than 30; TPM, Transcripts Per Million; OVCAR8_parent, Parental OVCAR8 cells cultured without drugs; OVCAR8_Nira_3M/OVCAR8_Nira_6M, OVCAR8 cells treated with Niraparib for 3 or 6 months; OVCAR8_Ola_6M, OVCAR8 cells treated with Olaparib for 6 months; SKOV3_parent, Parental SKOV3 cells cultured without drugs; SKOV3_Nira_2M/SKOV3_Nira_3M/SKOV3_Nira_6M, SKOV3 cells treated with Niraparib for 2, 3, or 6 months; SKOV3_Ola_3M/SKOV3_Ola_6M, SKOV3 cells treated with Olaparib for 3 or 6 months.

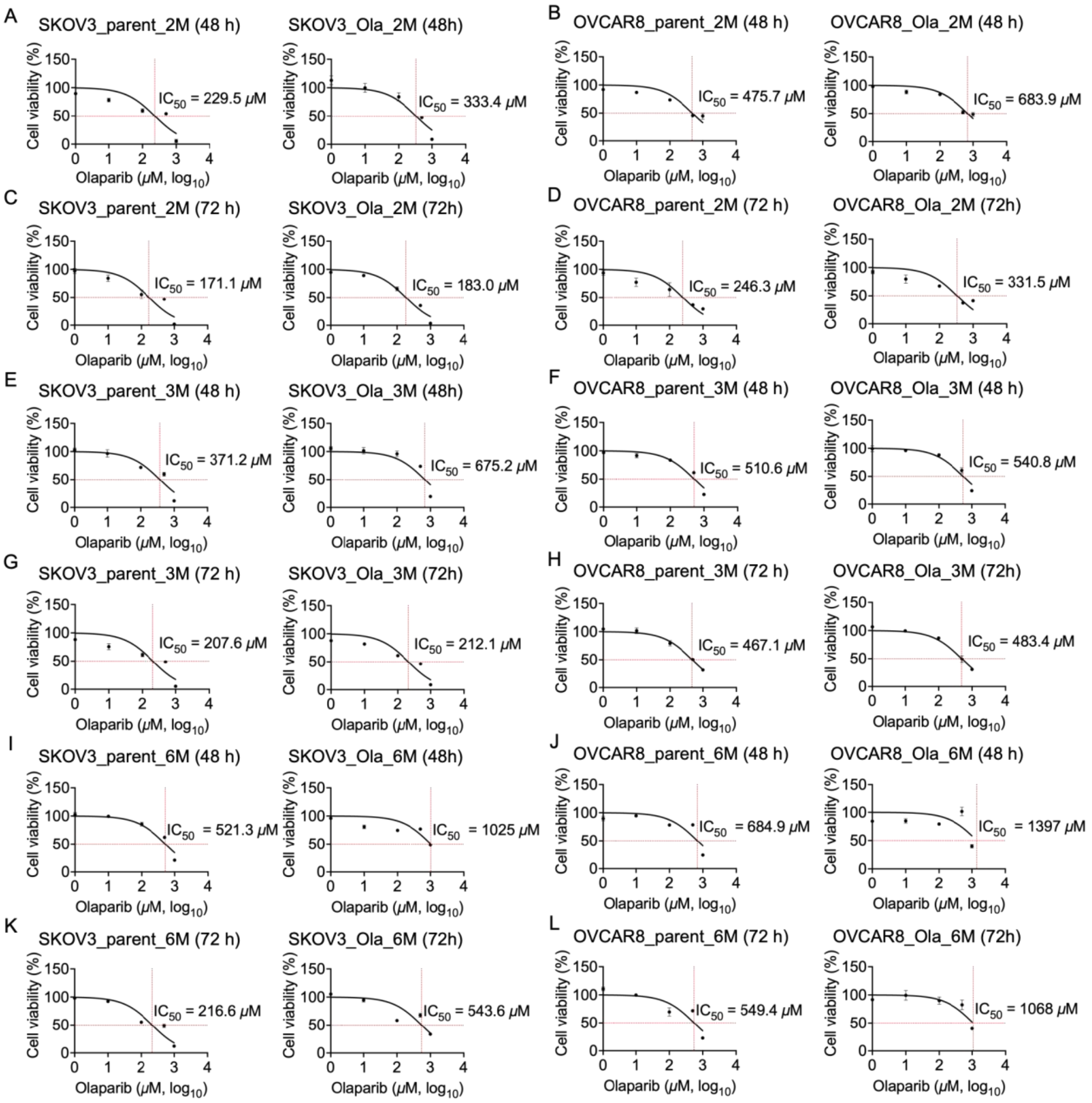


**Supplementary Fig. 2. Changes in the sensitivity of high-grade serous ovarian cancer cells to Niraparib after long-term culture**

A-D) Concentration-response curves of cell viability for SKOV3 and OVCAR8 cells after 2 months of maintenance culture with Niraparib (1, 10, 100, 500, 1000) treatment for 48 h (A, B) and 72 h (C, D).

E-H) Concentration-response curves of cell viability after 3 months of maintenance culture with Niraparib treatment for 48 h (E, F) and 72 h (G, H).

I-L) Concentration-response curves of cell viability after 6 months of maintenance culture with Niraparib treatment for 48 h (I, J) and 72 h (K, L).

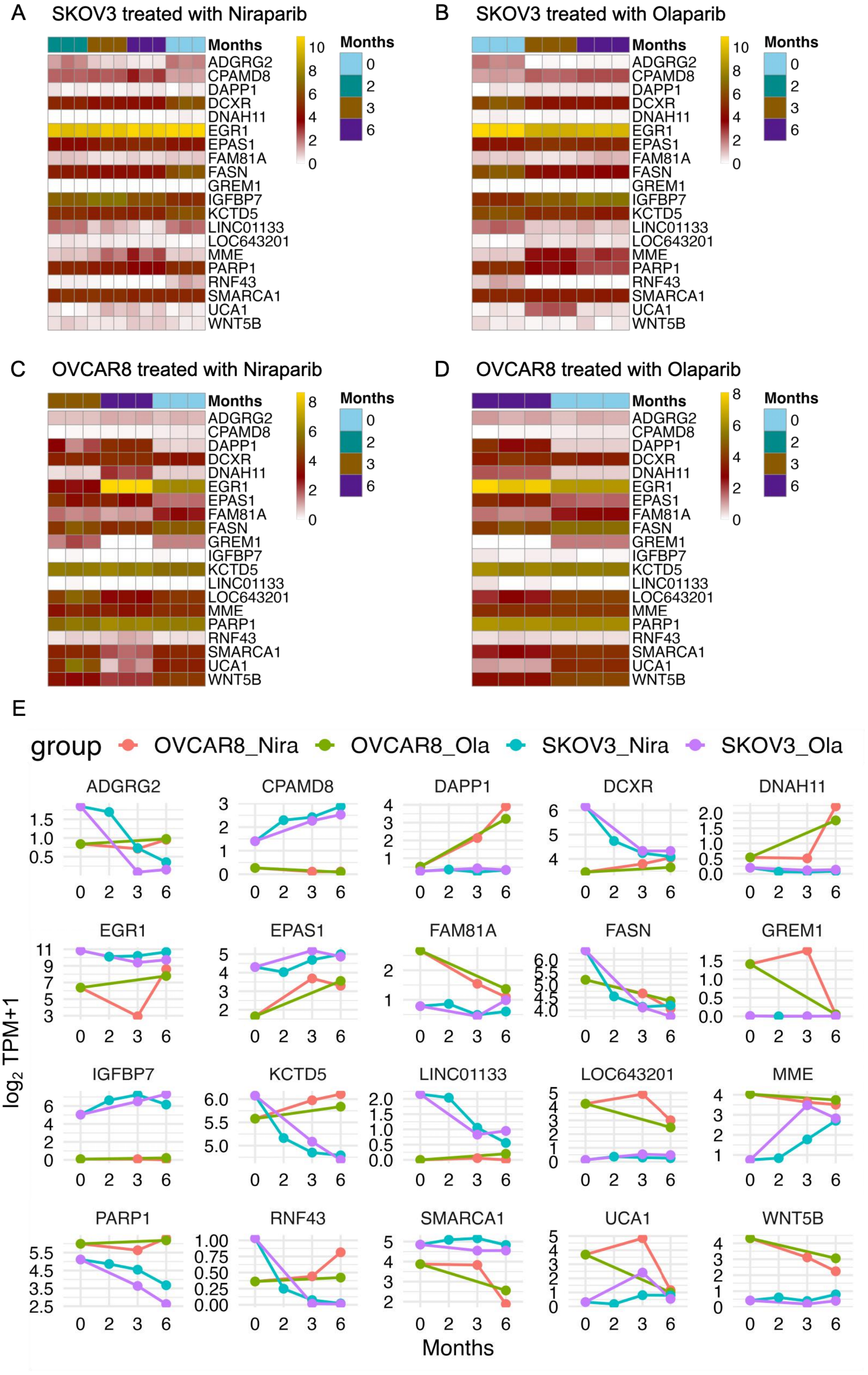


**Supplementary Fig. 3. Altered sensitivity of high-grade serous ovarian cancer cells to Olaparib following long-term culture.**

A-D) Dose-response curves of cell viability for SKOV3 and OVCAR8 cells treated with Olaparib (1-1000 μM) for 48 h (A, B) or 72 h (C, D) after 2 months of maintenance culture.

E-H) Dose-response curves after 3 months of maintenance culture, with Olaparib treatment for 48 h (E, F) or 72 h (G, H).

I-L) Dose-response curves after 6 months of maintenance culture, with Olaparib treatment for 48 h (I, J) or 72 h (K, L).



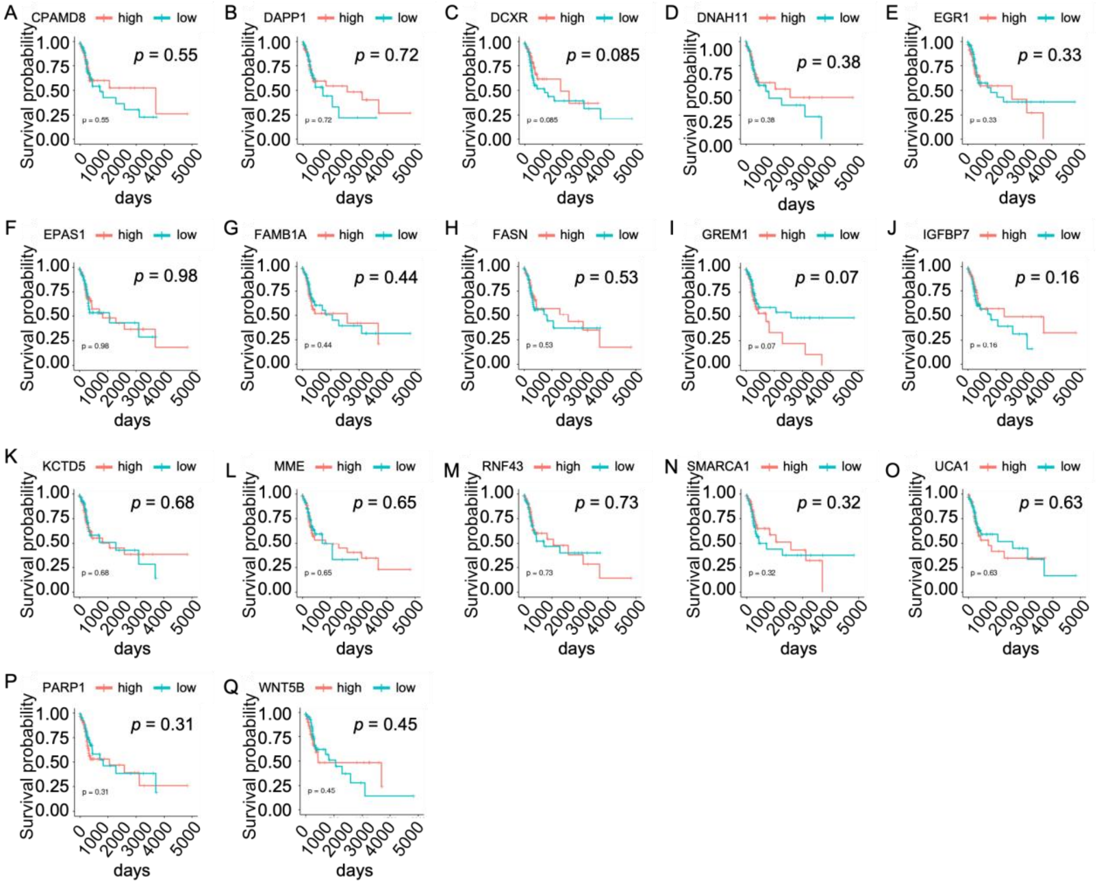
**Supplementary Fig. 4. Dynamic expression profiles of 20 significantly altered**

**significantly differentially expressed genes (DEGs) in Niraparib- or Olaparib- treated ovarian cancer cells**

A-B) Heatmaps showing expression patterns of 20 DEGs in SKOV3 cells after 0, 2, 3, and 6 months of exposure to niraparib (A) and olaparib (B)

C-D) Expression heatmaps of 20 DEGs in OVCAR8 cells treated with niraparib (C) and olaparib (D) for the different durations.

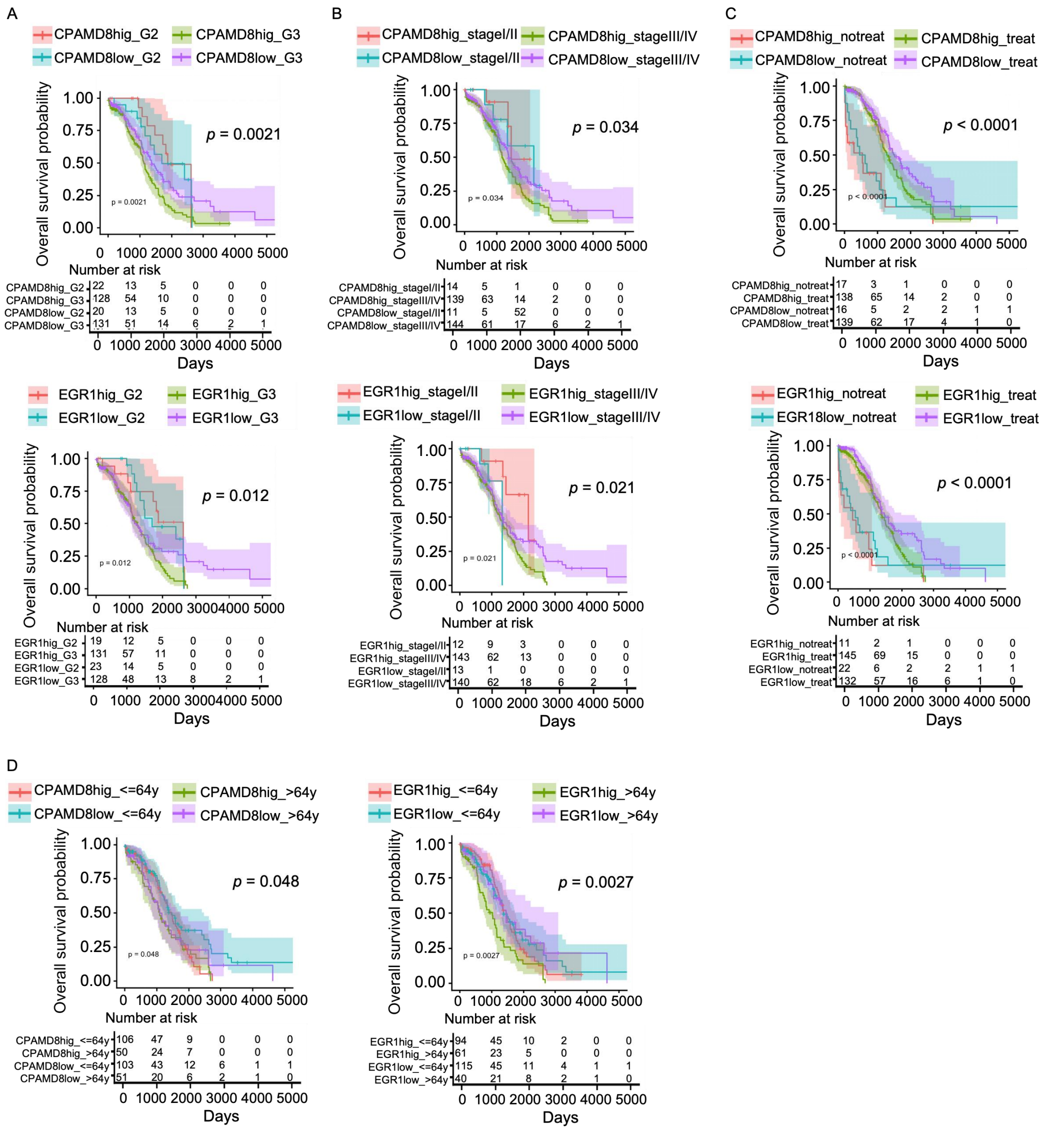
E) Time-course curves depicting the average expression trends of the 20 DEGs across 0-, 2-, 3-, and 6-month treatments.



**Supplementary Fig. 5. Disease-free survival (DFS) prognostic analysis of 20 overlapping significantly differentially expressed genes (DEGs)**

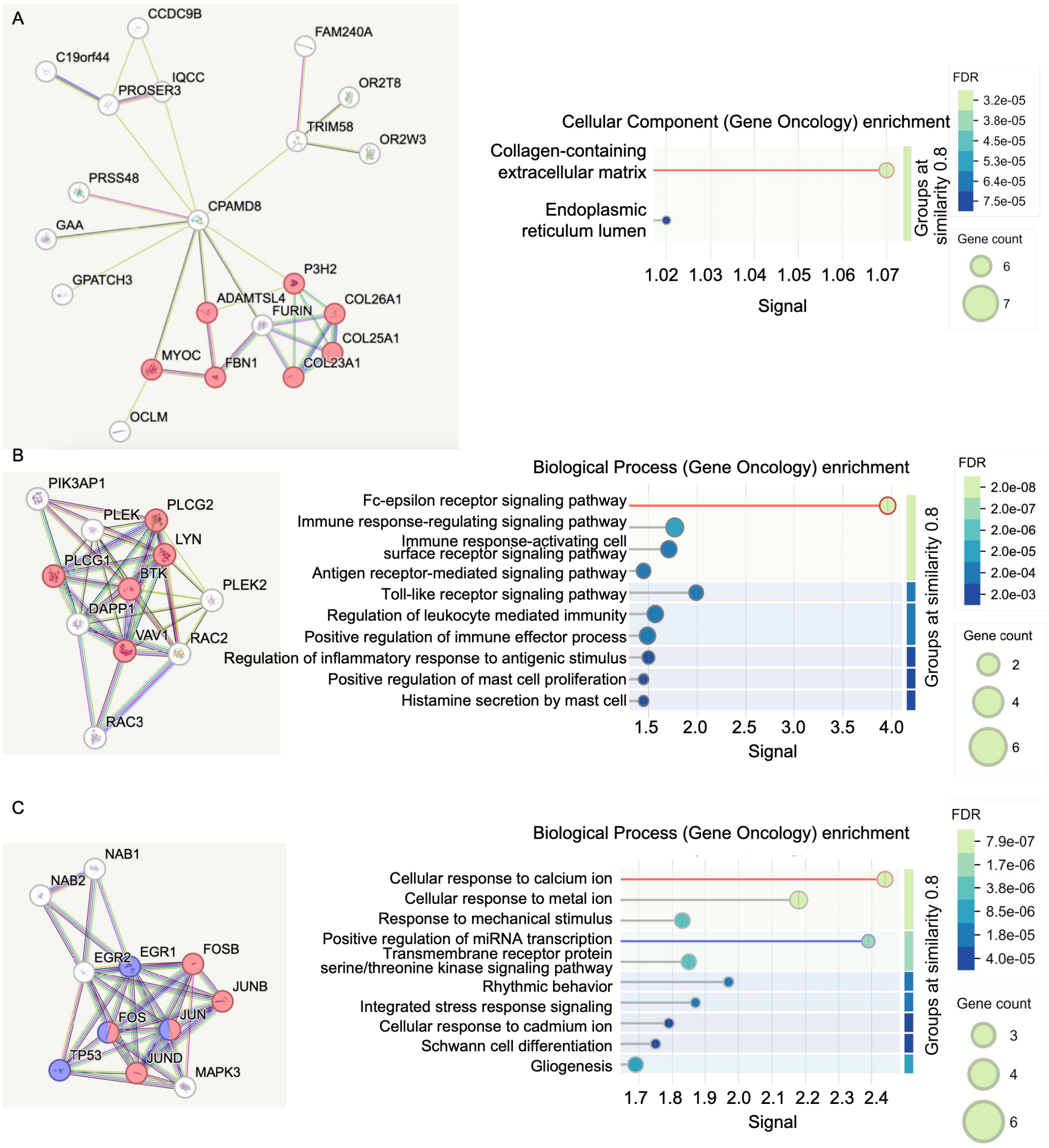
A-Q) Kaplan-Meier survival curves based on DFS for the following DEGs: *CPAMD8 (A), DAPP1 (B), DCXR (C), DNAH11 (D), EGR1 (E), EPAS1 (F), FAM81A (G), FASN (H), GREM1 (I), IGFBP7 (J), KCTD5 (K), MME (L), RNF43 (M), SMARCA1 (N), UCA1 (O),*

*PARP1 (P), WNT5B (Q).*



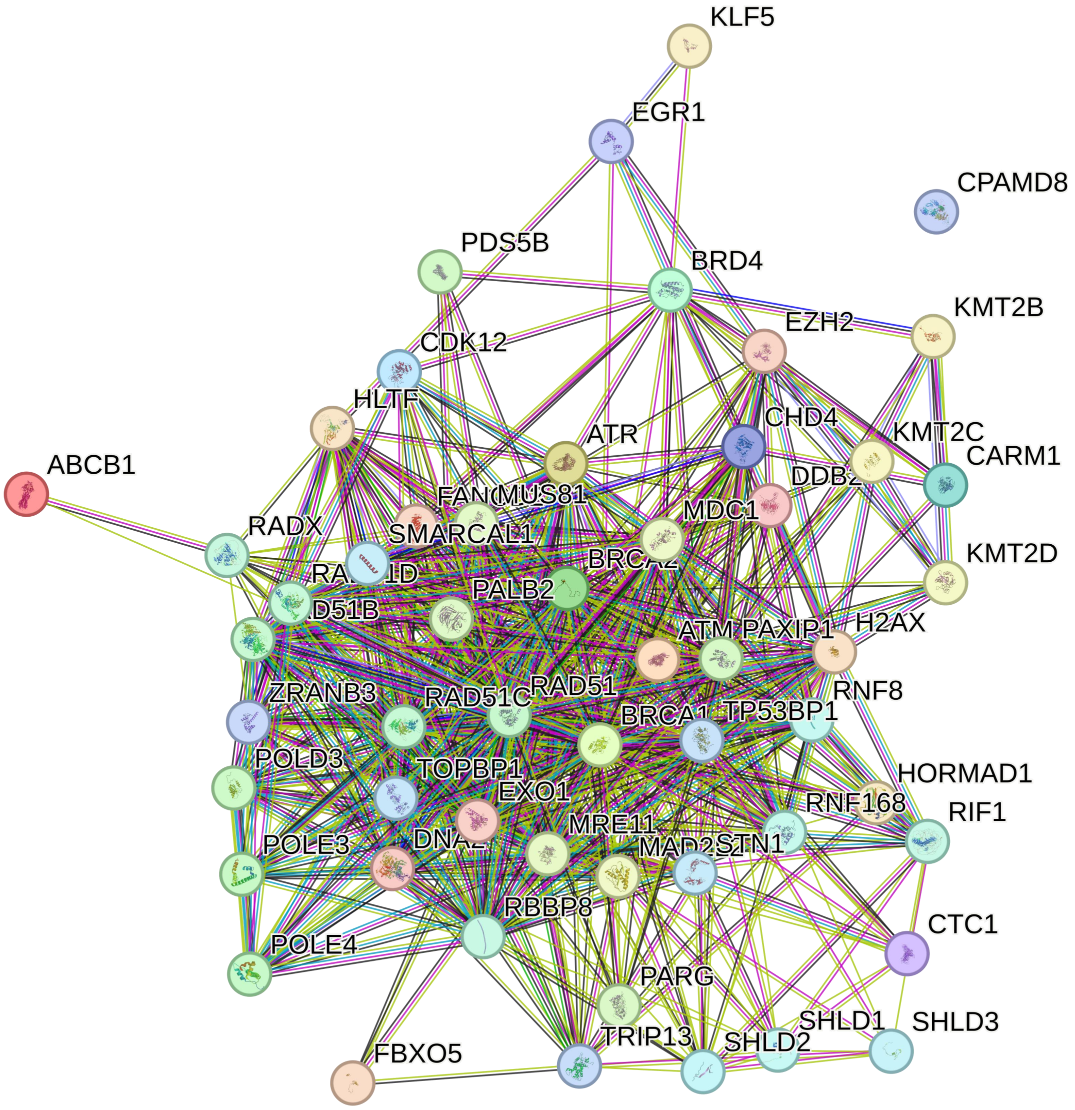
## Supplementary Fig. 6. Stratified Cox survival analysis of *CPAMD8* and *EGR1*.

A–E) *Kaplan–Meier* survival curves stratified by expression levels of *CPAMD8* (high/low) and *EGR1* (high/low) according to different grades (G2, G3; A), stages (stage I/II, stage III/IV; B), prior chemotherapy or targeted therapy (treated, untreated; C), and age groups (<35, 35–64, >64 years; D).



**Supplementary Fig. 7. Analysis of closely related genes and enriched signaling pathways of prognostic genes after long-term Olaparib and Niraparib treatment based on the string database**

A-C) Genes closely related to *CPAMD8* (A), DAPP1 (B), and *EGR1* (C) and their top 10 significantly enriched biological processes (BP).



**Supplementary Fig. 8. Potential interactions between *CPAMD8*, *EGR1* and 52 validated PARPi resistance genes**