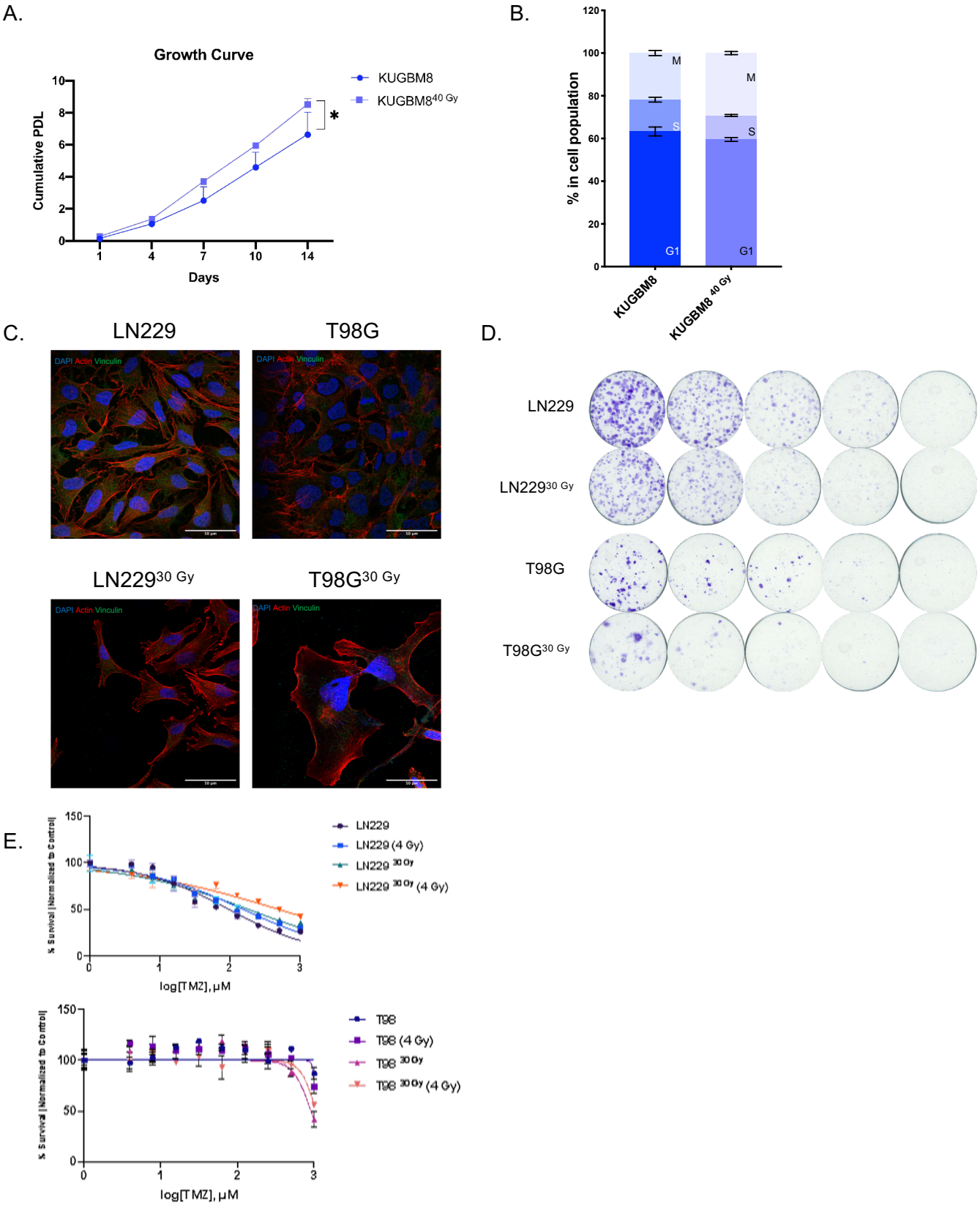
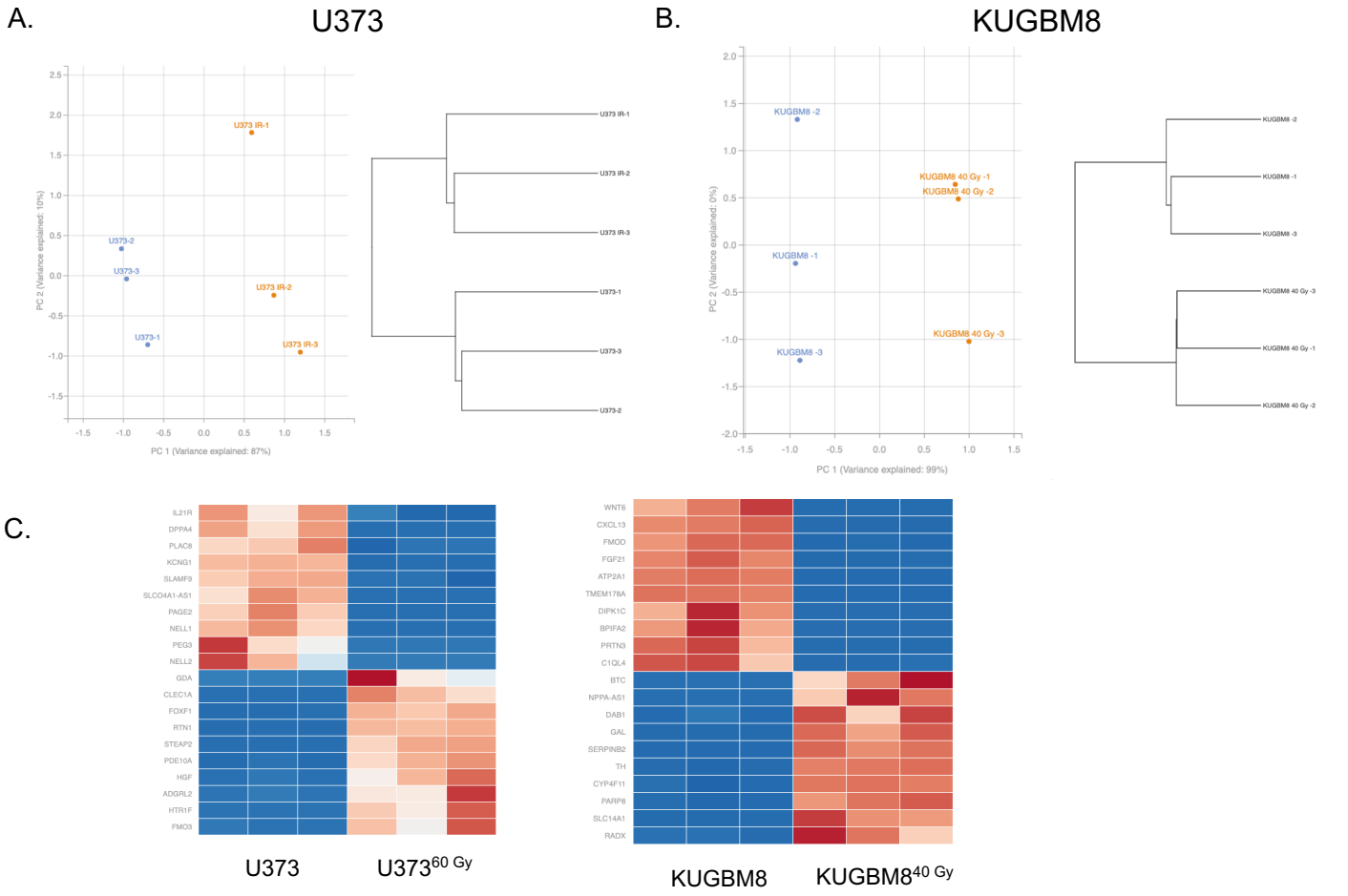


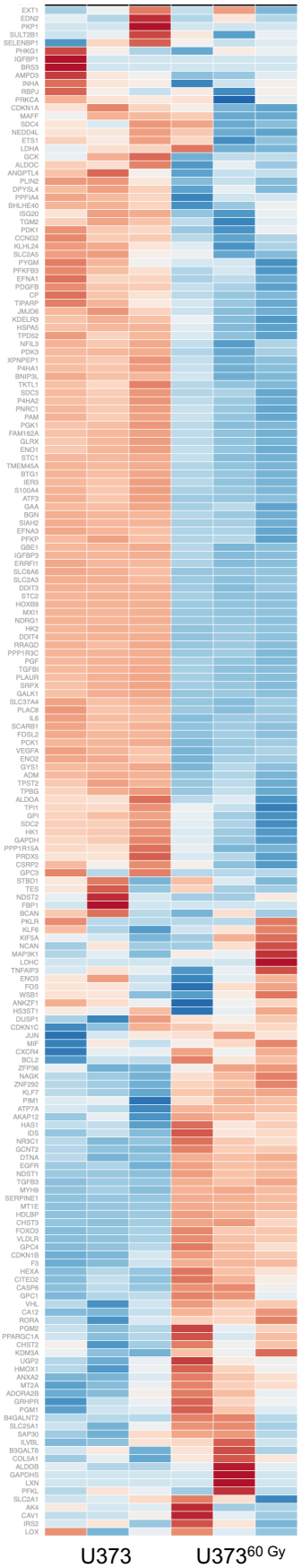

**Supplementary Figure S1. A.** Proliferation rates of KUGBM8 and KUGBM8$^{40\ Gy}$ cells. **B.** Cell cycle distributions of KUGBM8 and KUGBM8$^{40\ Gy}$ cells. **C.** Immunofluorescence staining for T98G and LN229 cells and their IR-Surv populations (DAPI: blue, Actin: red, Vinculin: Green). **D.** Representative images of clonogenic assay upon increasing doses of IR of T98G and LN229 cell lines. **E.** Dose-response curves of naïve and IR-Surv T98G and LN229 cells upon TMZ, IR or combination treatment.




**Supplementary Figure S2. A-B.** Principal component analysis (PCA) plots and representations of hierarchical clustering of U373-U373$^{60\ Gy}$ and KUGBM8-KUGBM8$^{40\ Gy}$ samples. **C.** Heatmap of top 10 differentially upregulated and downregulated genes in U373-U373$^{60\ Gy}$ and KUGBM8-KUGBM8$^{40\ Gy}$ cells. **D-E.** Hallmark GSEA and representative enrichment plots of U373 cells. **F-G.** Hallmark GSEA and representative enrichment plots of KUGBM8 cells.

A.

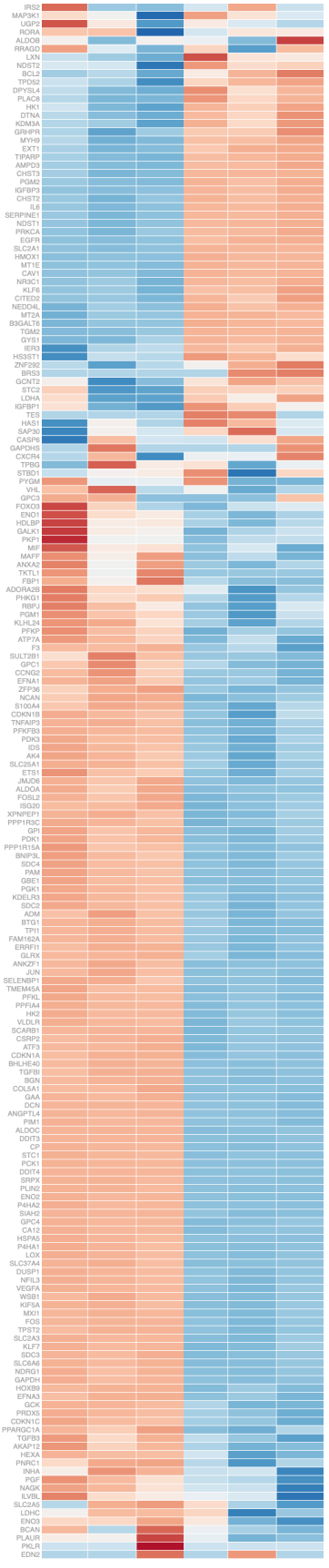
## Hallmark Hypoxia




| Gene | Log2(FC) | Gene | Log2(FC) |
|---|---|---|---|
| KDM3A | -0,02 | ISG20 | -0,97 |
| PGM1 | -0,02 | ATF3 | -0,98 |
| SLC25A1 | -0,03 | SRPX | -1,00 |
| MAP3K1 | -0,03 | SLC6A6 | -1,01 |
| GRHPR | -0,04 | NFIL3 | -1,01 |
| KLF6 | -0,06 | FAM162A | -1,05 |
| ILVBL | -0,07 | TPST2 | -1,05 |
| COL5A1 | -0,07 | TGM2 | -1,05 |
| SAP30 | -0,08 | GBE1 | -1,07 |
| CHST2 | -0,09 | ALDOC | -1,07 |
| PIM1 | -0,10 | ENO2 | -1,10 |
| B3GALT6 | -0,11 | GALK1 | -1,11 |
| CAV1 | -0,12 | EFNA3 | -1,11 |
| WSB1 | -0,12 | STC2 | -1,16 |
| DUSP1 | -0,12 | SLC2A5 | -1,17 |
| JUN | -0,12 | PDK3 | -1,20 |
| IRS2 | -0,14 | ADM | -1,20 |
| AK4 | -0,14 | PPFIA4 | -1,22 |
| TNFAIP3 | -0,15 | SLC2A3 | -1,22 |
| PFKL | -0,15 | HK2 | -1,24 |
| SLC2A1 | -0,16 | PLAUR | -1,25 |
| LOX | -0,16 | SCARB1 | -1,25 |
| FOS | -0,19 | SIAH2 | -1,30 |
| EXT1 | -0,19 | ANGPTL4 | -1,30 |
| RBPJ | -0,22 | PYGM | -1,32 |
| PRKCA | -0,22 | TGFBI | -1,34 |
| NEDD4L | -0,23 | PDGFB | -1,34 |
| STBD1 | -0,24 | GLRX | -1,40 |
| LDHA | -0,24 | TMEM45A | -1,49 |
| HS3ST1 | -0,26 | VEGFA | -1,50 |
| SDC4 | -0,26 | DDIT3 | -1,52 |
| ETS1 | -0,27 | BGN | -1,59 |
| PFKFB3 | -0,27 | MXI1 | -1,62 |
| ALDOA | -0,28 | PPP1R3C | -1,68 |
| CDKN1A | -0,30 | S100A4 | -1,71 |
| BHLHE40 | -0,30 | RRAGD | -1,79 |
| SDC3 | -0,32 | PGF | -1,95 |
| PDK1 | -0,35 | IER3 | -1,99 |
| ENO3 | -0,36 | NDRG1 | -2,00 |
| DPYSL4 | -0,37 | IGFBP3 | -2,07 |
| PFKP | -0,37 | HOXB9 | -2,26 |
| ANKZF1 | -0,39 | DDIT4 | -2,43 |
| MAFF | -0,39 | GCK | -2,50 |
| PPP1R15A | -0,40 | PCK1 | -2,83 |
| GAPDH | -0,40 | PLIN2 | -3,64 |
| HK1 | -0,42 | PLAC8 | -5,04 |
| GYS1 | -0,42 | UGP2 | 0,01 |
| GPI | -0,42 | IDS | 0,03 |
| CSRP2 | -0,43 | PGM2 | 0,04 |
| SULT2B1 | -0,43 | ADORA2B | 0,06 |
| TPI1 | -0,43 | GPC1 | 0,07 |
| KLHL24 | -0,43 | NR3C1 | 0,08 |
| PRDX5 | -0,44 | ZFP36 | 0,08 |
| TPBG | -0,45 | HEXA | 0,09 |
| CCNG2 | -0,45 | AKAP12 | 0,09 |
| SELENBP1 | -0,46 | NAGK | 0,09 |
| GAA | -0,46 | CDKN1B | 0,09 |
| PHKG1 | -0,49 | MT2A | 0,11 |
| HSPA5 | -0,50 | KIF5A | 0,12 |
| EFNA1 | -0,50 | CHST3 | 0,13 |
| KDELR3 | -0,52 | CDKN1C | 0,14 |
| TKTL1 | -0,52 | HMOX1 | 0,14 |
| XPNPEP1 | -0,54 | GPC4 | 0,15 |
| SDC2 | -0,55 | CITED2 | 0,16 |
| PAM | -0,55 | ANXA2 | 0,17 |
| JMJD6 | -0,56 | VHL | 0,18 |
| SLC37A4 | -0,56 | ATP7A | 0,21 |
| TPD52 | -0,58 | PPARGC1A | 0,21 |
| PNRC1 | -0,61 | DTNA | 0,25 |
| BNIP3L | -0,61 | KLF7 | 0,25 |
| TES | -0,63 | ZNF292 | 0,27 |
| ERRFI1 | -0,63 | NDST1 | 0,28 |
| BCAN | -0,64 | CASP6 | 0,28 |
| CP | -0,66 | F3 | 0,40 |
| TIPARP | -0,69 | VLDLR | 0,40 |
| ENO1 | -0,70 | GCNT2 | 0,41 |
| P4HA2 | -0,71 | MYH9 | 0,45 |
| NDST2 | -0,71 | HDLBP | 0,46 |
| INHA | -0,73 | RORA | 0,46 |
| FOSL2 | -0,73 | BCL2 | 0,49 |
| IL6 | -0,75 | MIF | 0,50 |
| P4HA1 | -0,75 | EGFR | 0,55 |
| AMPD3 | -0,79 | TGFB3 | 0,59 |
| PGK 1,00 | -0,80 | FOXO3 | 0,64 |
| BTG1 | -0,84 | CA12 | 0,78 |
| STC1 | -0,90 | CXCR4 | 1,07 |
| | | SERPINE1 | 1,52 |
| | | HAS1 | 1,96 |
| | | MT1E | 3,30 |

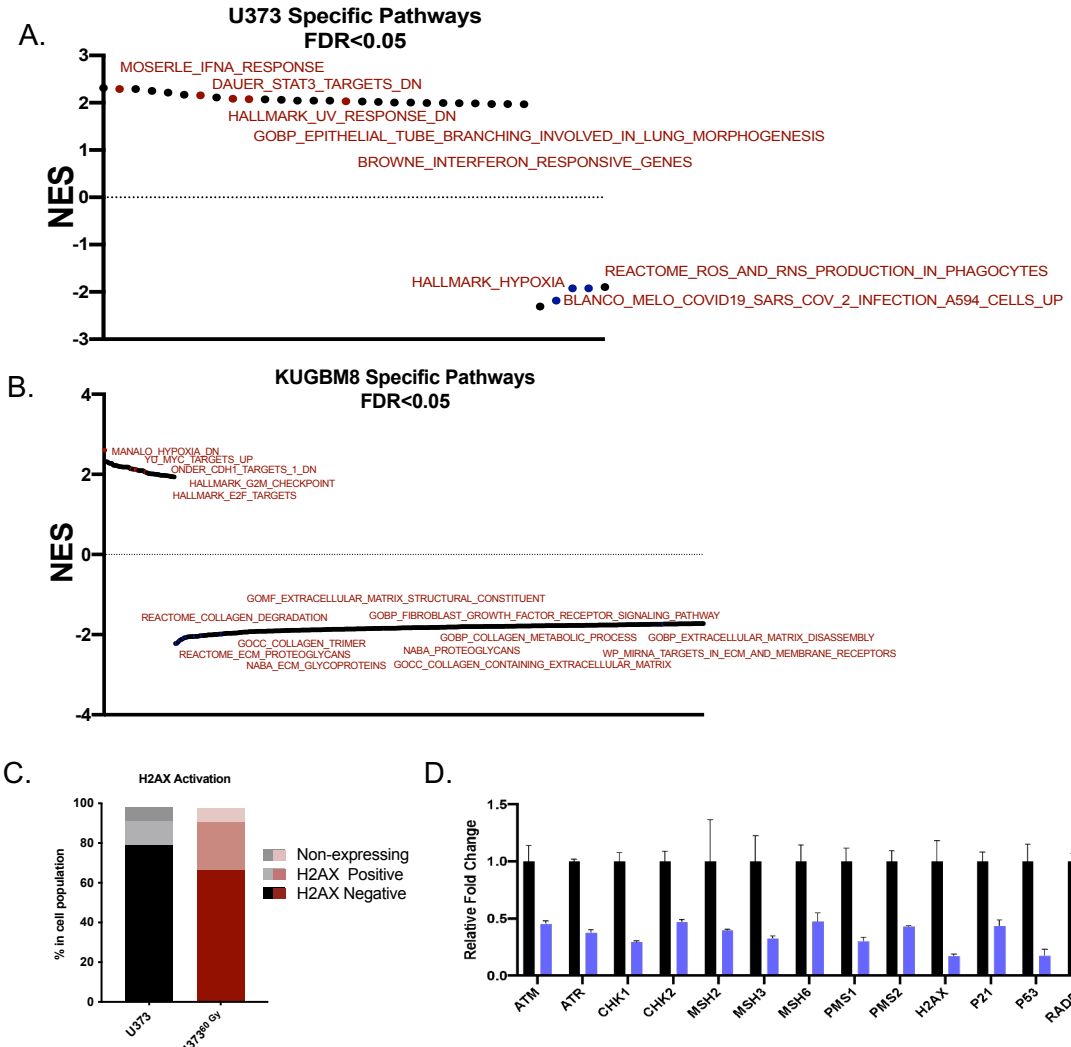
B.

## Hallmark Hypoxia




| Gene | Log2(FC) | Gene | Log2(FC) |
|---|---|---|---|
| GPC1 | 0,00 | VLDLR | -1,76 |
| HDLBP | 0,00 | SCARB1 | -1,84 |
| FOXO3 | -0,01 | BHLHE40 | -1,88 |
| PLAUR | -0,01 | CA12 | -1,92 |
| ANXA2 | -0,03 | SLC2A3 | -1,95 |
| VHL | -0,06 | SRPX | -1,96 |
| ILVBL | -0,07 | ISG20 | -2,01 |
| PGF | -0,09 | FAM162A | -2,03 |
| NAGK | -0,10 | PPP1R3C | -2,09 |
| ENO1 | -0,11 | PIM1 | -2,14 |
| PGM1 | -0,15 | PLIN2 | -2,22 |
| GPI | -0,17 | MXI1 | -2,22 |
| HEXA | -0,18 | PKP1 | -2,41 |
| KLHL24 | -0,18 | PPFIA4 | -2,42 |
| SLC2A5 | -0,20 | GAA | -2,49 |
| PNRC1 | -0,23 | P4HA1 | -2,52 |
| ADORA2B | -0,23 | CDKN1C | -2,54 |
| GALK1 | -0,26 | HSPA5 | -2,58 |
| ATP7A | -0,26 | KIF5A | -2,60 |
| RBPJ | -0,27 | NCAN | -2,62 |
| TGFB3 | -0,27 | CP | -2,79 |
| PFKP | -0,30 | EFNA3 | -2,93 |
| ENO3 | -0,32 | GCK | -2,96 |
| ADM | -0,33 | ENO2 | -3,16 |
| F3 | -0,34 | CSRP2 | -3,26 |
| XPNPEP1 | -0,36 | GPC4 | -3,45 |
| PPP1R15A | -0,38 | BGN | -3,48 |
| TNFAIP3 | -0,39 | DDIT3 | -3,62 |
| FOSL2 | -0,40 | FBP1 | -4,08 |
| TGFBI | -0,40 | DDIT4 | -4,08 |
| MAFF | -0,43 | ALDOC | -4,13 |
| JUN | -0,46 | TKTL1 | -4,21 |
| CDKN1B | -0,47 | DCN | -4,42 |
| SLC25A1 | -0,49 | SULT2B1 | -4,67 |
| PFKFB3 | -0,49 | HOXB9 | -5,20 |
| SDC3 | -0,49 | SELENBP1 | -5,68 |
| PYGM | -0,50 | ANGPTL4 | -5,73 |
| ETS1 | -0,50 | UGP2 | 0,08 |
| AKAP12 | -0,51 | TPBG | 0,08 |
| CCNG2 | -0,52 | RORA | 0,11 |
| TPI1 | -0,53 | RRAGD | 0,11 |
| PRDX5 | -0,54 | IRS2 | 0,11 |
| GAPDH | -0,57 | STBD1 | 0,15 |
| BNIP3L | -0,65 | STC2 | 0,18 |
| IDS | -0,65 | CASP6 | 0,18 |
| TPST2 | -0,66 | LDHA | 0,21 |
| NDRG1 | -0,70 | MAP3K1 | 0,24 |
| JMJD6 | -0,72 | SAP30 | 0,31 |
| SLC6A6 | -0,77 | DPYSL4 | 0,31 |
| COL5A1 | -0,78 | ZNF292 | 0,33 |
| PDK3 | -0,81 | HK1 | 0,34 |
| S100A4 | -0,86 | GRHPR | 0,39 |
| DUSP1 | -0,89 | DTNA | 0,40 |
| AK4 | -0,90 | CITED2 | 0,41 |
| PDK1 | -0,90 | EXT1 | 0,43 |
| PPARGC1A | -0,96 | KDM3A | 0,43 |
| PHKG1 | -0,97 | MYH9 | 0,44 |
| PAM | -0,98 | KLF6 | 0,55 |
| PFKL | -0,99 | GCNT2 | 0,57 |
| VEGFA | -1,02 | HAS1 | 0,61 |
| GBE1 | -1,06 | GYS1 | 0,63 |
| ANKZF1 | -1,07 | NEDD4L | 0,68 |
| ZFP36 | -1,08 | HS3ST1 | 0,71 |
| LDHC | -1,09 | PGM2 | 0,76 |
| HK2 | -1,10 | B3GALT6 | 0,78 |
| ERRFI1 | -1,11 | BCL2 | 0,81 |
| INHA | -1,11 | CXCR4 | 0,92 |
| GLRX | -1,14 | GFBP3 | 1,02 |
| SLC37A4 | -1,15 | NDST2 | 1,11 |
| KLF7 | -1,19 | NR3C1 | 1,11 |
| ALDOA | -1,20 | PRKCA | 1,11 |
| KDELR3 | -1,21 | IL6 | 1,12 |
| SDC4 | -1,23 | TIPARP | 1,14 |
| EFNA1 | -1,24 | CHST3 | 1,17 |
| CDKN1A | -1,26 | TPD52 | 1,20 |
| TMEM45A | -1,27 | SLC2A1 | 1,31 |
| BCAN | -1,29 | AMPD3 | 1,33 |
| FOS | -1,31 | IER3 | 1,37 |
| SIAH2 | -1,34 | LXN | 1,54 |
| SDC2 | -1,42 | HMOX1 | 1,56 |
| NFIL3 | -1,42 | GFBP1 | 1,57 |
| ATF3 | -1,46 | NDST1 | 1,59 |
| BTG1 | -1,50 | CHST2 | 1,70 |
| MIF | -1,53 | EGFR | 1,85 |
| LOX | -1,54 | CAV1 | 2,07 |
| PGK 1,00 | -1,57 | MT2A | 2,82 |
| P4HA2 | -1,64 | SERPINE1 | 2,95 |
| STC1 | -1,69 | TGM2 | 3,28 |
| WSB1 | -1,72 | PLAC8 | 3,98 |
| | | MT1E | 4,37 |

**Supplementary Figure S3**. **A-B**. Differential expression heat map of Hallmark Hypoxia gene set for U373 **(A)** and KUGBM8 **(B)** cells and DEG scores for each gene.




**Supplementary Figure S4**. **A.** Representation of U373-specific differentially enriched pathways (FDR cut-off <0.05) **B.** Representation of KUGBM8-specific differentially enriched pathways (FDR cut-off <0.05) **C.** Basal H2AX activation levels of U373 and U373$^{60\ Gy}$ cells. **D.** qRT-PCR results showing gene expression levels of different DNA damage response and repair elements in KUGBM8 cells.

**GOBP Regulation of DNA Repair**

| Gene | Log2(FC) | Gene | Log2(FC) |
|---|---|---|---|
| PARG | 0,00 | SHLD1 | 0,10 |
| EYA4 | 0,00 | RAD51 | 0,10 |
| BABAM2 | -0,01 | TWIST1 | 0,11 |
| PARP3 | -0,02 | UBR5 | 0,11 |
| RNF168 | -0,02 | NSD2 | 0,12 |
| UIMC1 | -0,02 | H2AX | 0,12 |
| MORF4L1 | -0,02 | UBE2V1 | 0,13 |
| SIRT1 | -0,03 | FMN2 | 0,13 |
| VPS72 | -0,03 | POT1 | 0,13 |
| PARPBP | -0,03 | WDR48 | 0,14 |
| HDGFL2 | -0,03 | OTUB1 | 0,14 |
| UBE2N | -0,04 | KDM4D | 0,15 |
| KDM1A | -0,05 | TFIP11 | 0,16 |
| MRNIP | -0,05 | HELB | 0,16 |
| CDK9 | -0,05 | OGG1 | 0,16 |
| SPIRE1 | -0,06 | RPA2 | 0,18 |
| ERCC8 | -0,06 | TERF2IP | 0,18 |
| WAS | -0,07 | ARID2 | 0,19 |
| SIRT6 | -0,07 | RNF169 | 0,20 |
| RAD51AP1 | -0,09 | CUL4A | 0,20 |
| YEATS4 | -0,10 | ACTR2 | 0,21 |
| RNF8 | -0,10 | ERCC6 | 0,21 |
| MORF4L2 | -0,14 | DEK | 0,23 |
| UBQLN4 | -0,15 | CHEK1 | 0,23 |
| TIGAR | -0,15 | BRD8 | 0,23 |
| RUVBL2 | -0,16 | PPP4R2 | 0,23 |
| MMS19 | -0,18 | SPIRE2 | 0,23 |
| AXIN2 | -0,20 | FOXM1 | 0,24 |
| MAGEF1 | -0,22 | BRCA1 | 0,24 |
| SHLD3 | -0,22 | SHLD2 | 0,25 |
| PNKP | -0,23 | RTEL1 | 0,26 |
| HSF1 | -0,25 | POLH | 0,26 |
| XRCC1 | -0,26 | EPC1 | 0,27 |
| MAD2L2 | -0,29 | POGZ | 0,28 |
| ACTL6A | -0,30 | TRIM28 | 0,28 |
| SPIDR | -0,33 | EYA3 | 0,29 |
| UBE2V2 | -0,34 | SMCHD1 | 0,29 |
| ZNF365 | -0,37 | NUDT16L1 | 0,31 |
| MIR221 | -0,40 | BRCC3 | 0,32 |
| SLF1 | -0,41 | RAD52 | 0,32 |
| MRGBP | -0,47 | FANCB | 0,32 |
| WRNIP1 | -0,48 | DHX9 | 0,33 |
| AUNIP | -0,50 | TP53BP1 | 0,36 |
| RMI2 | -0,50 | PPP4R3B | 0,37 |
| WRAP53 | -0,50 | FAM168A | 0,39 |
| RPS3 | -0,51 | POLQ | 0,40 |
| TMEM161A | -0,53 | ING3 | 0,43 |
| KMT5C | -0,56 | SETD2 | 0,43 |
| OTUB2 | -0,64 | TRRAP | 0,44 |
| CEBPG | -0,78 | EP400 | 0,45 |
| KLHL15 | -0,79 | ACTB | 0,48 |
| PRKCG | -1,24 | PML | 0,51 |
| MEAF6 | 0,00 | HDAC10 | 0,53 |
| PRKDC | 0,01 | EGFR | 0,55 |
| CYREN | 0,01 | SLF2 | 0,55 |
| KMT5B | 0,01 | DTX3L | 0,57 |
| PPP4C | 0,01 | PARP9 | 0,59 |
| DDX11 | 0,01 | SETMAR | 0,65 |
| FBH1 | 0,02 | NPAS2 | 0,66 |
| USP1 | 0,03 | PCNA | 0,74 |
| MBTD1 | 0,03 | ZCWPW1 | 0,75 |
| TIMELESS | 0,04 | TEX15 | 0,76 |
| PARP1 | 0,04 | RIF1 | 0,78 |
| RECQL5 | 0,05 | TRIP12 | 0,85 |
| BABAM1 | 0,05 | FUS | 0,88 |
| RUVBL1 | 0,06 | EPC2 | 0,89 |
| KAT5 | 0,06 | HMGA2 | 1,08 |
| TERF2 | 0,08 | EYA2 | 1,24 |
| SIRT7 | 0,08 | EYA1 | 1,37 |
| CCDC117 | 0,08 | RADX | 2,59 |
| HMGB1 | 0,09 | MGMT | 5,26 |
| DMAP1 | 0,09 | | |
| RBBP8 | 0,09 | | |
| KAT7 | 0,09 | | |
| FIGNL1 | 0,10 | | |

**Reactome DNA DSB Repair**

| Gene | Log2(FC) | Gene | Log2(FC) |
|---|---|---|---|
| EYA4 | 0,00 | DNA2 | 0,11 |
| BABAM2 | -0,01 | RFC1 | 0,12 |
| RAD51C | -0,02 | NSD2 | 0,12 |
| RNF168 | -0,02 | UBC | 0,12 |
| UIMC1 | -0,02 | H2AX | 0,12 |
| POLD2 | -0,03 | MUS81 | 0,13 |
| UBE2N | -0,04 | H2BC9 | 0,13 |
| H4C14 | -0,04 | BRIP1 | 0,14 |
| UBE2I | -0,05 | XRCC6 | 0,14 |
| NBN | -0,06 | H4-16 | 0,14 |
| H4C8 | -0,07 | FEN1 | 0,15 |
| TDP1 | -0,07 | EXO1 | 0,17 |
| SIRT6 | -0,07 | HUS1 | 0,17 |
| POLD3 | -0,08 | RPA2 | 0,18 |
| H4C5 | -0,09 | PIAS4 | 0,18 |
| RAD51AP1 | -0,09 | NHEJ1 | 0,18 |
| RNF8 | -0,10 | BAP1 | 0,19 |
| TOP3A | -0,12 | RAD1 | 0,19 |
| XRCC3 | -0,15 | EME2 | 0,19 |
| POLD1 | -0,15 | BLM | 0,20 |
| UBXN1 | -0,15 | H2BC21 | 0,21 |
| PARP2 | -0,16 | MAPK8 | 0,22 |
| H2BC5 | -0,17 | POLE | 0,22 |
| ERCC1 | -0,17 | CHEK1 | 0,23 |
| ABRAXAS1 | -0,18 | RPA3 | 0,23 |
| POLK | -0,19 | RFC3 | 0,23 |
| LIG3 | -0,19 | BAZ1B | 0,23 |
| UBA52 | -0,19 | PPP4R2 | 0,23 |
| RPS27A | -0,20 | BRCA1 | 0,24 |
| RAD9A | -0,22 | H2BC17 | 0,25 |
| H2BC15 | -0,24 | TDP2 | 0,25 |
| DCLRE1C | -0,24 | RMI1 | 0,25 |
| RAD17 | -0,25 | RNF4 | 0,26 |
| POLM | -0,25 | RTEL1 | 0,26 |
| RPA1 | -0,25 | H2BC4 | 0,26 |
| XRCC1 | -0,26 | POLH | 0,26 |
| UBB | -0,26 | SUMO2 | 0,27 |
| KDM4A | -0,27 | RFC5 | 0,28 |
| H2BC8 | -0,27 | EYA3 | 0,29 |
| ABL1 | -0,29 | H2BC11 | 0,30 |
| KDM4B | -0,32 | BRCA2 | 0,31 |
| SPIDR | -0,33 | BRCC3 | 0,32 |
| RAD51B | -0,33 | TOPBP1 | 0,32 |
| UBE2V2 | -0,34 | RAD52 | 0,32 |
| RFC4 | -0,42 | PALB2 | 0,33 |
| CHEK2 | -0,45 | LIG4 | 0,35 |
| EME1 | -0,46 | TP53BP1 | 0,36 |
| POLL | -0,48 | SUMO1 | 0,37 |
| RMI2 | -0,50 | KPNA2 | 0,39 |
| XRCC4 | -0,51 | CCNA2 | 0,40 |
| POLD4 | -0,58 | POLQ | 0,40 |
| H2BU1 | -0,63 | SMARCA5 | 0,40 |
| APBB1 | -0,82 | TIPIN | 0,40 |
| H2BC7 | -1,36 | ATM | 0,41 |
| ERCC4 | 0,00 | GEN1 | 0,42 |
| MRE11 | 0,00 | WRN | 0,44 |
| PRKDC | 0,01 | RAD50 | 0,46 |
| RAD51D | 0,01 | HERC2 | 0,48 |
| PPP4C | 0,01 | CLSPN | 0,55 |
| POLE2 | 0,01 | H4C9 | 0,59 |
| CDK2 | 0,03 | XRCC5 | 0,60 |
| XRCC2 | 0,04 | H2BC6 | 0,64 |
| RFC2 | 0,04 | ATR | 0,66 |
| TIMELESS | 0,04 | PCNA | 0,74 |
| PARP1 | 0,04 | BARD1 | 0,76 |
| BABAM1 | 0,05 | RIF1 | 0,78 |
| KAT5 | 0,06 | H2BC10 | 0,81 |
| MDC 1,00 | 0,07 | H2BC12 | 1,01 |
| POLE3 | 0,07 | H4C3 | 1,07 |
| TP53 | 0,07 | SLX1B | 1,18 |
| ATRIP | 0,08 | EYA2 | 1,24 |
| PAXIP1 | 0,08 | EYA1 | 1,37 |
| PPP5C | 0,08 | H2BC13 | 1,37 |
| RHNO1 | 0,09 | RAD9B | 1,49 |
| RBBP8 | 0,09 | CCNA1 | 1,77 |
| SLX4 | 0,10 | H4C4 | 3,18 |
| RAD51 | 0,10 | | |
| POLE4 | 0,11 | | |

**GOBP Regulation of DNA Repair**

| Gene | Log2(FC) | Gene | Log2(FC) |
|---|---|---|---|
| UBQLN4 | 0,00 | RNF169 | 0,21 |
| BABAM1 | -0,01 | RPS3 | 0,23 |
| CCDC117 | -0,01 | PARG | 0,23 |
| UBE2V2 | -0,01 | SPIRE1 | 0,24 |
| PARP1 | -0,02 | PARP3 | 0,24 |
| ACTR2 | -0,05 | DDX11 | 0,25 |
| KDM4D | -0,05 | OTUB1 | 0,26 |
| PARP9 | -0,06 | SLF1 | 0,26 |
| TIGAR | -0,07 | RNF8 | 0,26 |
| TERF2 | -0,07 | DEK | 0,28 |
| PNKP | -0,12 | UBE2N | 0,29 |
| RUVBL2 | -0,13 | SPIRE2 | 0,30 |
| POT1 | -0,13 | ERCC8 | 0,31 |
| SHLD3 | -0,14 | SETD2 | 0,32 |
| WRNIP1 | -0,17 | RAD51AP1 | 0,33 |
| FBH1 | -0,17 | XRCC1 | 0,35 |
| NUDT16L1 | -0,19 | ACTL6A | 0,36 |
| MORF4L1 | -0,20 | OGG1 | 0,37 |
| SPIDR | -0,24 | PARPBP | 0,37 |
| SIRT6 | -0,25 | SETMAR | 0,39 |
| UIMC1 | -0,28 | DMAP1 | 0,42 |
| EYA3 | -0,30 | NSD2 | 0,42 |
| POGZ | -0,30 | KMT5B | 0,44 |
| KDM1A | -0,30 | RBBP8 | 0,45 |
| MRGBP | -0,31 | HMGB1 | 0,49 |
| RUVBL1 | -0,34 | RAD51 | 0,51 |
| TERF2IP | -0,35 | YEATS4 | 0,51 |
| PPP4R2 | -0,39 | TFIP11 | 0,52 |
| VPS72 | -0,40 | ACTB | 0,54 |
| FAM168A | -0,41 | SHLD2 | 0,55 |
| MMS19 | -0,43 | USP1 | 0,57 |
| HSF1 | -0,45 | CUL4A | 0,67 |
| HDAC10 | -0,46 | PML | 0,67 |
| HDGFL2 | -0,46 | CGAS | 0,68 |
| HELB | -0,46 | BRD8 | 0,69 |
| PPP4C | -0,49 | ARID2 | 0,70 |
| CDK9 | -0,57 | DTX3L | 0,71 |
| RAD52 | -0,59 | AUNIP | 0,72 |
| MAD2L2 | -0,60 | RIF1 | 0,79 |
| MORF4L2 | -0,63 | EPC1 | 0,80 |
| TWIST1 | -0,63 | ZCWPW1 | 0,83 |
| ZNF365 | -0,64 | PRKDC | 0,84 |
| KLHL15 | -0,76 | TRIM28 | 0,85 |
| SHLD1 | -0,77 | PPP4R3B | 0,87 |
| UBE2V1 | -0,79 | TRIP12 | 0,87 |
| KMT5C | -0,79 | EYA4 | 0,87 |
| RMI2 | -0,80 | PCNA | 0,88 |
| TMEM161A | -0,88 | CHEK1 | 0,90 |
| BABAM2 | -0,92 | TIMELESS | 0,99 |
| RNF168 | -0,93 | RTEL1 | 1,00 |
| CEBPG | -1,02 | FOXM1 | 1,00 |
| MAGEF1 | -1,13 | BRCA1 | 1,02 |
| AXIN2 | -1,13 | TRRAP | 1,03 |
| EYA1 | -1,14 | SLF2 | 1,11 |
| NPAS2 | -1,74 | FMN2 | 1,12 |
| MGMT | -1,78 | BRCC3 | 1,13 |
| OTUB2 | -1,84 | EP400 | 1,17 |
| WAS | -2,01 | SMCHD1 | 1,22 |
| PRKCG | -3,15 | TEX15 | 1,23 |
| FGF10 | -5,59 | SIRT1 | 1,24 |
| WRAP53 | 0,02 | ING3 | 1,31 |
| MBTD1 | 0,05 | FUS | 1,37 |
| RECQL5 | 0,05 | ERCC6 | 1,40 |
| UBR5 | 0,06 | H2AX | 1,41 |
| POLQ | 0,08 | KAT5 | 1,41 |
| SIRT7 | 0,09 | CYREN | 1,53 |
| TP53BP1 | 0,11 | USP51 | 1,76 |
| POLH | 0,12 | FIGNL1 | 1,78 |
| RPA2 | 0,13 | EPC2 | 1,82 |
| MEAF6 | 0,14 | DHX9 | 1,83 |
| KAT7 | 0,14 | EGFR | 1,85 |
| MRNIP | 0,16 | MIR221 | 2,69 |
| WDR48 | 0,18 | HMGA2 | 3,04 |
| FANCB | 0,20 | RADX | 6,67 |

**Reactome DNA DSB Repair**

| Gene | Log2(FC) | Gene | Log2(FC) |
|---|---|---|---|
| BABAM1 | -0,01 | PIAS4 | 0,27 |
| UBE2V2 | -0,01 | MRE11 | 0,28 |
| MAPK8 | -0,02 | KDM4A | 0,29 |
| PARP1 | -0,02 | H2BC5 | 0,29 |
| UBB | -0,05 | RHNO1 | 0,29 |
| POLM | -0,05 | UBE2N | 0,29 |
| POLK | -0,07 | RAD9A | 0,29 |
| BAP1 | -0,08 | KPNA2 | 0,32 |
| SUMO1 | -0,09 | RAD17 | 0,32 |
| RAD9B | -0,09 | H4C4 | 0,33 |
| UBC | -0,13 | H2BC17 | 0,33 |
| UBE2I | -0,14 | RAD51AP1 | 0,33 |
| POLL | -0,15 | XRCC1 | 0,35 |
| POLD1 | -0,15 | RFC3 | 0,37 |
| POLD3 | -0,16 | PALB2 | 0,39 |
| SUMO2 | -0,19 | RMI1 | 0,39 |
| ERCC1 | -0,20 | NSD2 | 0,42 |
| POLD4 | -0,22 | UBXN1 | 0,42 |
| SPIDR | -0,24 | XRCC6 | 0,43 |
| SIRT6 | -0,25 | TDP1 | 0,44 |
| RPA1 | -0,28 | POLD2 | 0,44 |
| H4C5 | -0,28 | XRCC5 | 0,45 |
| UIMC1 | -0,28 | RBBP8 | 0,45 |
| RAD1 | -0,29 | PPP5C | 0,47 |
| RFC4 | -0,29 | TIPIN | 0,50 |
| EYA3 | -0,30 | RPS27A | 0,50 |
| RAD51B | -0,35 | RAD51 | 0,51 |
| PPP4R2 | -0,39 | BARD1 | 0,57 |
| H2BC15 | -0,44 | H4C14 | 0,59 |
| H2BC9 | -0,46 | TOPBP1 | 0,60 |
| TOP3A | -0,47 | POLE2 | 0,61 |
| PPP4C | -0,49 | WRN | 0,73 |
| KDM4B | -0,57 | FEN1 | 0,73 |
| RFC1 | -0,57 | POLE | 0,74 |
| RAD52 | -0,59 | RIF1 | 0,79 |
| EME1 | -0,59 | BAZ1B | 0,80 |
| H2BC7 | -0,60 | ABRAXAS1 | 0,82 |
| XRCC4 | -0,60 | MUS81 | 0,83 |
| PARP2 | -0,63 | HUS1 | 0,83 |
| CCNA1 | -0,73 | ATM | 0,84 |
| CDK2 | -0,78 | PRKDC | 0,84 |
| RMI2 | -0,80 | EYA4 | 0,87 |
| XRCC3 | -0,81 | RAD51D | 0,87 |
| BABAM2 | -0,92 | CCNA2 | 0,87 |
| RNF168 | -0,93 | PCNA | 0,88 |
| APBB1 | -1,02 | DCLRE1C | 0,89 |
| CHEK2 | -1,04 | BLM | 0,89 |
| H2BC10 | -1,09 | CHEK1 | 0,90 |
| H2BC21 | -1,13 | POLE4 | 0,92 |
| EYA1 | -1,14 | ATRIP | 0,95 |
| LIG3 | -1,20 | HERC2 | 0,97 |
| H2BC8 | -1,49 | TP53 | 0,97 |
| H2BC13 | -1,55 | EME2 | 0,99 |
| UBA52 | 0,01 | TIMELESS | 0,99 |
| ERCC4 | 0,01 | RTEL1 | 1,00 |
| SMARCA5 | 0,04 | BRCA1 | 1,02 |
| ABL1 | 0,06 | BRIP1 | 1,07 |
| POLQ | 0,08 | CLSPN | 1,09 |
| RFC2 | 0,10 | H4-16 | 1,11 |
| TP53BP1 | 0,11 | ATR | 1,12 |
| SLX4 | 0,12 | PAXIP1 | 1,13 |
| POLH | 0,12 | BRCC3 | 1,13 |
| RPA2 | 0,13 | NBN | 1,22 |
| RPA3 | 0,14 | DNA2 | 1,33 |
| RAD51C | 0,14 | BRCA2 | 1,37 |
| RFC5 | 0,15 | H2AX | 1,41 |
| LIG4 | 0,17 | KAT5 | 1,41 |
| H4C3 | 0,18 | RAD50 | 1,43 |
| TDP2 | 0,20 | H4C9 | 1,48 |
| POLE3 | 0,20 | XRCC2 | 1,57 |
| EXO1 | 0,22 | H2BC11 | 1,82 |
| RNF4 | 0,23 | H2BC12 | 2,02 |
| MDC 1,00 | 0,26 | NHEJ1 | 2,03 |
| RNF8 | 0,26 | GEN1 | 2,27 |
| | | H4C8 | 2,34 |
| | | H2BC4 | 3,01 |

**Supplementary Table S1. A-B.** DEG scores list of GOBP Regulation of DNA Repair **(A)** and Reactome DNA DSB Repair **(B)** gene sets for U373 cells. **C-D**. DEG Scores list of GOBP Regulation of DNA Repair **(C)** and Reactome DNA DSB Repair **(D)** gene sets for KUGBM8 cells.

| Gene | Sequence of Forward Primer (5'-3') | Sequence of Reverse Primer (5'-3') |
|---|---|---|
| GAPDH | AGCCACATCGCTCAGACAC | GCCCAATACGACCAAATCC |
| ATM | CATCGCATGTGATTAAAGCA | TTCTGATAGGAATCAGGGC |
| ATR | CAATTGTGGAGGAGATTTCC | CTTCTGAGAACTCTTGTATCTG |
| CHK1 | CGGTATAATAATCGTGAGCG | TTCCAAGGGTTGAGGTATGT |
| CHK2 | CTCGGGAGTCGGATGTTGAG | GAGTTTGGCATCGTGCTGGT |
| MSH2 | TTGATGGCCAGAGACAGGTT | CCATGTCTCCAGCAGTCTCT |
| MSH3 | CCATCATGGCTCAGATTGGC | ATCATGAGTGCTCGTCCCTC |
| MSH6 | ACTTCAGCAGGGACGTAACA | ACTTCAGCAGGGACGTAACA |
| PMS1 | ATGAGTGGAGCAGGGGAAAT | CACTTGCTGACATGGGTTTCT |
| PMS2 | ACTTCCGTGGATTCTGAGGG | GTGTTTGGGGTTGCGAGATT |
| MLH1 | CTACTTCCAGCAACCCCAGA | AGAACCTCATGTCCCTGCTC |
| H2AX | ACTCAACTGGGCAATCCAAG | GGGTTAGCTGCAGAATTCCA |
| p21 | GGCAGACCAGCATGACAGATTT | AAGATGTAGAGCGGGCCTTTGA |
| TP53 | GGTGACACGCTTCCCTGGATT | AGGGGGACAGAACGTTGTTTTCAG |
| RAD51 | TGCGGACCGAGTAATGGCA | TCCTTCTTTGGCGCATAGGCA |
| VEGFA | TGTGAATGCAGACCAAAGAAAGA | ACCAACGTACACGCTCCAG |
| MGMT | GGATTGCCTCTCATTGCTCC | CCCGTTTTCCAGCAAGAGTC |

**Supplementary Table S2.** List of primers and sequences used in qRT-PCR

| Antibody | Brand/Catalog Number |
|---|---|
| Phospho-ATR Ser428 | Cell Signaling/5161 |
| ATR Total | Cell Signaling/2790 |
| Phospho-ATM Ser1981 | Cell Signaling/13050 |
| ATM total | Cell Signalling/11G12 |
| Phospho-CHK1 Ser345 | Cell Signalling/133D3 |
| CHK1 | Cell Signalling/23605 |
| Phospho-CHK2 Ser19 | Cell Signalling/2666 |
| CHK2 | Cell Signalling/2662S |
| $\gamma$H2AX | EMD Millipore/05-636 |
| RAD51 | Abcam/ab213 |
| MSH2 | Abcam/ab52266 |
| MSH6 | Abcam/ab92471 |
| PMS1 | Abcam/ab129020 |
| PMS2 | Abcam/ab110638 |
| MLH1 | Abcam/ab92312 |
| MSH3 | Abcam/ab111107 |
| $\alpha$-tubulin | Abcam/ab15246 |
| GAPDH | Abcam/ab9485 |

**Supplementary Table S3.** List of primary antibodies used in Western Blot

| Antibody | Brand/ Catalog Number |
|---|---|
| Anti-vinculin | Abcam/ab73412 |
| Rhodamin-phalloidin | Thermo R415 |
| Mounting medium with DAPI | Abcam/ab104139 |
| Phosphor-Histone H2A.X (Ser139) | Millipore/05-636 |
| 53BP1 | Novus/NB100-304 |
| Alexa Fluor® 488 Anti- IgG Secondary Antibody | Invitrogen |
| Alexa Fluor® 594 Anti- IgG Secondary Antibody | Invitrogen |

**Supplementary Table S4.** List of primary and secondary antibodies used in immunofluorescence staining