**Supplementary Table S6.** Pathways identified by GSEA as enriched in high-hypoxia tumors from the French training cohort

|  |  |  |  |
| --- | --- | --- | --- |
| NAME | SIZE | NES | FDR q-val |
| ROSTY\_CERVICAL\_CANCER\_PROLIFERATION\_CLUSTER | 136 | 2.772621 | 0 |
| MENSE\_HYPOXIA\_UP | 94 | 2.729226 | 0 |
| SOTIRIOU\_BREAST\_CANCER\_GRADE\_1\_VS\_3\_UP | 140 | 2.593809 | 0 |
| HARRIS\_HYPOXIA | 78 | 2.59126 | 0 |
| ELVIDGE\_HYPOXIA\_BY\_DMOG\_UP | 123 | 2.589598 | 0 |
| SHEDDEN\_LUNG\_CANCER\_POOR\_SURVIVAL\_A6 | 424 | 2.583794 | 0 |
| ELVIDGE\_HIF1A\_TARGETS\_DN | 86 | 2.582839 | 0 |
| NAKAYAMA\_SOFT\_TISSUE\_TUMORS\_PCA2\_UP | 86 | 2.581241 | 0 |
| WINTER\_HYPOXIA\_UP | 81 | 2.578937 | 0 |
| WINTER\_HYPOXIA\_METAGENE | 226 | 2.557733 | 0 |
| KOBAYASHI\_EGFR\_SIGNALING\_24HR\_DN | 234 | 2.546267 | 0 |
| ELVIDGE\_HIF1A\_AND\_HIF2A\_TARGETS\_DN | 99 | 2.546146 | 0 |
| ELVIDGE\_HYPOXIA\_UP | 159 | 2.529292 | 0 |
| QI\_HYPOXIA | 133 | 2.527242 | 0 |
| VANTVEER\_BREAST\_CANCER\_METASTASIS\_DN | 108 | 2.524836 | 0 |
| CHANG\_CYCLING\_GENES | 137 | 2.509404 | 0 |
| KIM\_HYPOXIA | 24 | 2.448844 | 0 |
| SEMENZA\_HIF1\_TARGETS | 34 | 2.439188 | 0 |
| LEONARD\_HYPOXIA | 45 | 2.409583 | 0 |
| VECCHI\_GASTRIC\_CANCER\_EARLY\_UP | 384 | 2.39393 | 0 |
| ZHAN\_MULTIPLE\_MYELOMA\_PR\_UP | 43 | 2.387739 | 0 |
| FARDIN\_HYPOXIA\_11 | 30 | 2.377227 | 0 |
| LEE\_EARLY\_T\_LYMPHOCYTE\_UP | 96 | 2.367318 | 0 |
| CROONQUIST\_NRAS\_SIGNALING\_DN | 72 | 2.36024 | 0 |
| KONG\_E2F3\_TARGETS | 90 | 2.359015 | 0 |
| REACTOME\_GLYCOLYSIS | 26 | 2.341999 | 0 |
| KANG\_DOXORUBICIN\_RESISTANCE\_UP | 52 | 2.341144 | 0 |
| DUTERTRE\_ESTRADIOL\_RESPONSE\_24HR\_UP | 302 | 2.328301 | 0 |
| REACTOME\_GLUCOSE\_METABOLISM | 62 | 2.324387 | 0 |
| WINNEPENNINCKX\_MELANOMA\_METASTASIS\_UP | 151 | 2.31927 | 0 |
| SHIPP\_DLBCL\_VS\_FOLLICULAR\_LYMPHOMA\_UP | 42 | 2.297002 | 0 |
| WHITEFORD\_PEDIATRIC\_CANCER\_MARKERS | 110 | 2.295661 | 0 |
| MISSIAGLIA\_REGULATED\_BY\_METHYLATION\_DN | 114 | 2.283461 | 0 |
| RUIZ\_TNC\_TARGETS\_DN | 131 | 2.271131 | 0 |
| PRAMOONJAGO\_SOX4\_TARGETS\_UP | 51 | 2.270425 | 0 |
| MORI\_IMMATURE\_B\_LYMPHOCYTE\_DN | 87 | 2.263043 | 0 |
| CHEMNITZ\_RESPONSE\_TO\_PROSTAGLANDIN\_E2\_UP | 131 | 2.260914 | 0 |
| ODONNELL\_TFRC\_TARGETS\_DN | 129 | 2.250758 | 0 |
| FOURNIER\_ACINAR\_DEVELOPMENT\_LATE\_2 | 256 | 2.234073 | 0 |
| KEGG\_FRUCTOSE\_AND\_MANNOSE\_METABOLISM | 33 | 2.231426 | 0 |
| RHODES\_UNDIFFERENTIATED\_CANCER | 66 | 2.225542 | 0 |
| CROONQUIST\_IL6\_DEPRIVATION\_DN | 98 | 2.22504 | 0 |
| CHIANG\_LIVER\_CANCER\_SUBCLASS\_PROLIFERATION\_UP | 164 | 2.22369 | 0 |
| MARTORIATI\_MDM4\_TARGETS\_NEUROEPITHELIUM\_UP | 155 | 2.223373 | 0 |
| HOFFMANN\_LARGE\_TO\_SMALL\_PRE\_BII\_LYMPHOCYTE\_UP | 149 | 2.222841 | 0 |
| PID\_HIF1\_TFPATHWAY | 65 | 2.212369 | 0 |
| FERREIRA\_EWINGS\_SARCOMA\_UNSTABLE\_VS\_STABLE\_UP | 149 | 2.199161 | 0 |
| WANG\_RESPONSE\_TO\_GSK3\_INHIBITOR\_SB216763\_DN | 323 | 2.197625 | 0 |
| SARRIO\_EPITHELIAL\_MESENCHYMAL\_TRANSITION\_UP | 161 | 2.190648 | 0 |
| MARTORIATI\_MDM4\_TARGETS\_FETAL\_LIVER\_UP | 201 | 2.18686 | 0 |
| WU\_APOPTOSIS\_BY\_CDKN1A\_VIA\_TP53 | 52 | 2.182998 | 0 |
| BURTON\_ADIPOGENESIS\_3 | 101 | 2.179957 | 0 |
| WONG\_EMBRYONIC\_STEM\_CELL\_CORE | 318 | 2.17703 | 0 |
| WHITFIELD\_CELL\_CYCLE\_LITERATURE | 44 | 2.171037 | 0 |
| MOOTHA\_GLYCOLYSIS | 20 | 2.155306 | 0 |
| BASAKI\_YBX1\_TARGETS\_UP | 267 | 2.153959 | 0 |
| GREENBAUM\_E2A\_TARGETS\_UP | 33 | 2.145845 | 0 |
| FARMER\_BREAST\_CANCER\_CLUSTER\_2 | 32 | 2.140396 | 0 |
| VANDESLUIS\_COMMD1\_TARGETS\_GROUP\_3\_UP | 84 | 2.129941 | 0 |
| AMUNDSON\_GAMMA\_RADIATION\_RESPONSE | 39 | 2.129818 | 0 |
| ZHOU\_CELL\_CYCLE\_GENES\_IN\_IR\_RESPONSE\_6HR | 82 | 2.126611 | 0 |
| KRIEG\_HYPOXIA\_VIA\_KDM3A | 50 | 2.120327 | 0 |
| LIEN\_BREAST\_CARCINOMA\_METAPLASTIC\_VS\_DUCTAL\_UP | 76 | 2.117474 | 0 |
| WANG\_ADIPOGENIC\_GENES\_REPRESSED\_BY\_SIRT1 | 25 | 2.116553 | 0 |
| FURUKAWA\_DUSP6\_TARGETS\_PCI35\_DN | 66 | 2.115399 | 0 |
| ODONNELL\_TARGETS\_OF\_MYC\_AND\_TFRC\_DN | 45 | 2.111408 | 0 |
| ZHANG\_TLX\_TARGETS\_DN | 83 | 2.093721 | 3.12E-05 |
| FRASOR\_RESPONSE\_TO\_SERM\_OR\_FULVESTRANT\_DN | 49 | 2.089645 | 3.08E-05 |
| NIELSEN\_LEIOMYOSARCOMA\_CNN1\_UP | 19 | 2.087955 | 3.03E-05 |
| MOLENAAR\_TARGETS\_OF\_CCND1\_AND\_CDK4\_DN | 51 | 2.086041 | 2.99E-05 |
| REACTOME\_MUSCLE\_CONTRACTION | 45 | 2.083972 | 4.43E-05 |
| REACTOME\_SMOOTH\_MUSCLE\_CONTRACTION | 22 | 2.083461 | 4.37E-05 |
| REACTOME\_GLUCONEOGENESIS | 31 | 2.081169 | 5.71E-05 |
| MORI\_LARGE\_PRE\_BII\_LYMPHOCYTE\_UP | 82 | 2.073474 | 7.02E-05 |
| KEGG\_PENTOSE\_PHOSPHATE\_PATHWAY | 26 | 2.060951 | 1.11E-04 |
| DELPUECH\_FOXO3\_TARGETS\_DN | 39 | 2.060713 | 1.09E-04 |
| REICHERT\_MITOSIS\_LIN9\_TARGETS | 26 | 2.059284 | 1.21E-04 |
| GRAHAM\_CML\_DIVIDING\_VS\_NORMAL\_QUIESCENT\_UP | 177 | 2.05798 | 1.20E-04 |
| ZHANG\_TLX\_TARGETS\_60HR\_DN | 253 | 2.056499 | 1.32E-04 |
| GRAHAM\_NORMAL\_QUIESCENT\_VS\_NORMAL\_DIVIDING\_DN | 86 | 2.054364 | 1.43E-04 |
| GAVIN\_FOXP3\_TARGETS\_CLUSTER\_P6 | 87 | 2.054354 | 1.41E-04 |
| ISHIDA\_E2F\_TARGETS | 51 | 2.054121 | 1.39E-04 |
| MOOTHA\_GLUCONEOGENESIS | 32 | 2.051652 | 1.50E-04 |
| FOURNIER\_ACINAR\_DEVELOPMENT\_LATE\_DN | 20 | 2.042302 | 1.61E-04 |
| OXFORD\_RALA\_OR\_RALB\_TARGETS\_UP | 45 | 2.014794 | 2.69E-04 |
| BENPORATH\_PROLIFERATION | 136 | 2.005694 | 3.51E-04 |
| HORIUCHI\_WTAP\_TARGETS\_DN | 288 | 2.004785 | 3.59E-04 |
| NIELSEN\_LIPOSARCOMA\_DN | 19 | 2.001899 | 3.55E-04 |
| PID\_PLK1\_PATHWAY | 43 | 1.992884 | 3.86E-04 |
| SONG\_TARGETS\_OF\_IE86\_CMV\_PROTEIN | 59 | 1.992636 | 3.81E-04 |
| YU\_MYC\_TARGETS\_UP | 39 | 1.990344 | 3.88E-04 |
| GROSS\_HIF1A\_TARGETS\_DN | 22 | 1.989183 | 3.96E-04 |
| KEGG\_GLYCOLYSIS\_GLUCONEOGENESIS | 60 | 1.988793 | 3.92E-04 |
| MANALO\_HYPOXIA\_UP | 199 | 1.975619 | 5.65E-04 |
| KAMMINGA\_EZH2\_TARGETS | 41 | 1.970872 | 6.14E-04 |
| KAUFFMANN\_MELANOMA\_RELAPSE\_UP | 56 | 1.964084 | 6.62E-04 |
| BOYAULT\_LIVER\_CANCER\_SUBCLASS\_G3\_UP | 177 | 1.960707 | 7.09E-04 |
| TANG\_SENESCENCE\_TP53\_TARGETS\_DN | 57 | 1.954325 | 8.39E-04 |
| CHANG\_CORE\_SERUM\_RESPONSE\_UP | 199 | 1.949775 | 9.04E-04 |
| KEGG\_STARCH\_AND\_SUCROSE\_METABOLISM | 34 | 1.94775 | 9.16E-04 |
| REACTOME\_REGULATION\_OF\_HYPOXIA\_INDUCIBLE\_FACTOR\_HIF\_BY\_OXYGEN | 23 | 1.943826 | 0.001041 |
| REACTOME\_CHROMOSOME\_MAINTENANCE | 98 | 1.942287 | 0.001041 |
| KAN\_RESPONSE\_TO\_ARSENIC\_TRIOXIDE | 119 | 1.935722 | 0.001173 |
| EGUCHI\_CELL\_CYCLE\_RB1\_TARGETS | 23 | 1.934484 | 0.001212 |
| SMIRNOV\_RESPONSE\_TO\_IR\_6HR\_DN | 109 | 1.932369 | 0.00126 |
| SABATES\_COLORECTAL\_ADENOMA\_UP | 126 | 1.93184 | 0.001258 |
| BLUM\_RESPONSE\_TO\_SALIRASIB\_DN | 324 | 1.931785 | 0.001246 |
| MITSIADES\_RESPONSE\_TO\_APLIDIN\_DN | 236 | 1.931128 | 0.001283 |
| GROSS\_HYPOXIA\_VIA\_ELK3\_AND\_HIF1A\_UP | 137 | 1.928592 | 0.001319 |
| LANDIS\_ERBB2\_BREAST\_PRENEOPLASTIC\_UP | 18 | 1.923963 | 0.001449 |
| OXFORD\_RALA\_OR\_RALB\_TARGETS\_DN | 21 | 1.921057 | 0.001549 |
| OLSSON\_E2F3\_TARGETS\_DN | 43 | 1.920617 | 0.001573 |
| GRAESSMANN\_RESPONSE\_TO\_MC\_AND\_SERUM\_DEPRIVATION\_DN | 75 | 1.91999 | 0.001596 |
| HOOI\_ST7\_TARGETS\_DN | 110 | 1.913579 | 0.00191 |
| RICKMAN\_TUMOR\_DIFFERENTIATED\_WELL\_VS\_MODERATELY\_DN | 102 | 1.904257 | 0.002168 |
| WEST\_ADRENOCORTICAL\_TUMOR\_MARKERS\_UP | 21 | 1.901338 | 0.002212 |
| PUJANA\_BRCA\_CENTERED\_NETWORK | 114 | 1.900447 | 0.002256 |
| GRAESSMANN\_APOPTOSIS\_BY\_SERUM\_DEPRIVATION\_DN | 213 | 1.898702 | 0.002298 |
| CREIGHTON\_AKT1\_SIGNALING\_VIA\_MTOR\_DN | 22 | 1.897483 | 0.002331 |
| REACTOME\_DEPOSITION\_OF\_NEW\_CENPA\_CONTAINING\_NUCLEOSOMES\_AT\_THE\_CENTROMERE | 43 | 1.897245 | 0.002329 |
| SMID\_BREAST\_CANCER\_LUMINAL\_A\_DN | 17 | 1.896513 | 0.002336 |
| PUJANA\_XPRSS\_INT\_NETWORK | 157 | 1.879695 | 0.003361 |
| SHAFFER\_IRF4\_TARGETS\_IN\_ACTIVATED\_B\_LYMPHOCYTE | 68 | 1.879217 | 0.003376 |
| REN\_BOUND\_BY\_E2F | 59 | 1.879194 | 0.003349 |
| PEDERSEN\_TARGETS\_OF\_611CTF\_ISOFORM\_OF\_ERBB2 | 70 | 1.877679 | 0.00343 |
| LE\_EGR2\_TARGETS\_UP | 105 | 1.874444 | 0.003576 |
| LY\_AGING\_MIDDLE\_DN | 16 | 1.871823 | 0.003712 |
| PID\_HIF2PATHWAY | 32 | 1.869956 | 0.003814 |
| SCIAN\_CELL\_CYCLE\_TARGETS\_OF\_TP53\_AND\_TP73\_DN | 22 | 1.865569 | 0.004091 |
| MIYAGAWA\_TARGETS\_OF\_EWSR1\_ETS\_FUSIONS\_DN | 201 | 1.865228 | 0.004116 |
| ZAMORA\_NOS2\_TARGETS\_UP | 60 | 1.855308 | 0.004825 |
| FINETTI\_BREAST\_CANCER\_KINOME\_RED | 16 | 1.847636 | 0.005271 |
| KEGG\_DNA\_REPLICATION | 36 | 1.843635 | 0.00564 |
| NAKAMURA\_CANCER\_MICROENVIRONMENT\_DN | 42 | 1.842256 | 0.005737 |
| LANDIS\_BREAST\_CANCER\_PROGRESSION\_UP | 43 | 1.840163 | 0.005826 |
| BENPORATH\_ES\_1 | 346 | 1.839361 | 0.005844 |
| VERNELL\_RETINOBLASTOMA\_PATHWAY\_UP | 67 | 1.838275 | 0.005947 |
| LI\_WILMS\_TUMOR\_VS\_FETAL\_KIDNEY\_1\_DN | 152 | 1.837221 | 0.005978 |
| QI\_HYPOXIA\_TARGETS\_OF\_HIF1A\_AND\_FOXA2 | 34 | 1.835512 | 0.006107 |
| YOKOE\_CANCER\_TESTIS\_ANTIGENS | 31 | 1.833583 | 0.006256 |
| MANALO\_HYPOXIA\_DN | 264 | 1.826833 | 0.006901 |
| MORI\_PRE\_BI\_LYMPHOCYTE\_UP | 76 | 1.825082 | 0.007028 |
| PID\_AURORA\_B\_PATHWAY | 39 | 1.824365 | 0.007052 |
| SIMBULAN\_PARP1\_TARGETS\_DN | 17 | 1.823556 | 0.007111 |
| HENDRICKS\_SMARCA4\_TARGETS\_UP | 52 | 1.822728 | 0.007134 |
| LINDGREN\_BLADDER\_CANCER\_CLUSTER\_3\_UP | 298 | 1.822521 | 0.00712 |
| DANG\_REGULATED\_BY\_MYC\_UP | 64 | 1.821507 | 0.007179 |
| GARGALOVIC\_RESPONSE\_TO\_OXIDIZED\_PHOSPHOLIPIDS\_RED\_UP | 17 | 1.819385 | 0.007382 |
| MATTHEWS\_AP1\_TARGETS | 16 | 1.819157 | 0.007375 |
| BOYAULT\_LIVER\_CANCER\_SUBCLASS\_G23\_UP | 48 | 1.818352 | 0.007402 |
| BIDUS\_METASTASIS\_UP | 202 | 1.816538 | 0.007525 |
| GHANDHI\_BYSTANDER\_IRRADIATION\_UP | 77 | 1.815944 | 0.007578 |
| BROWNE\_HCMV\_INFECTION\_2HR\_DN | 48 | 1.81532 | 0.007611 |
| WELCSH\_BRCA1\_TARGETS\_DN | 133 | 1.814874 | 0.007595 |
| REACTOME\_TELOMERE\_MAINTENANCE | 59 | 1.813176 | 0.007727 |
| KIM\_WT1\_TARGETS\_8HR\_UP | 158 | 1.809537 | 0.008184 |
| ZHOU\_CELL\_CYCLE\_GENES\_IN\_IR\_RESPONSE\_24HR | 121 | 1.809076 | 0.008204 |
| FUJII\_YBX1\_TARGETS\_DN | 195 | 1.80602 | 0.008454 |
| SU\_TESTIS | 74 | 1.805539 | 0.00844 |
| JEON\_SMAD6\_TARGETS\_DN | 18 | 1.804783 | 0.008544 |
| SCIBETTA\_KDM5B\_TARGETS\_DN | 76 | 1.802617 | 0.008847 |
| RHODES\_CANCER\_META\_SIGNATURE | 63 | 1.802032 | 0.008876 |
| SUNG\_METASTASIS\_STROMA\_DN | 47 | 1.800779 | 0.008988 |
| MOOTHA\_PGC | 395 | 1.799984 | 0.009016 |
| LIAO\_METASTASIS | 495 | 1.799278 | 0.009075 |
| AMIT\_EGF\_RESPONSE\_480\_MCF10A | 41 | 1.796628 | 0.00936 |
| GRADE\_COLON\_AND\_RECTAL\_CANCER\_UP | 262 | 1.796569 | 0.009311 |
| CHIARADONNA\_NEOPLASTIC\_TRANSFORMATION\_KRAS\_CDC25\_UP | 55 | 1.792634 | 0.009665 |
| NES: normalized enrichment score; FDR q-val: false discovery rate corrected P value | | | |