TableS1. Clinical data of ovarian cancer patients from TCGA and ICGC

|  |  |  |
| --- | --- | --- |
| Characteristics | TCGA | ICGC |
| Number of samples | 533 | 79 |
| Age (%) |  |  |
| <60 | 274 (51.4) | 42 (53.2) |
| ≥60 | 259 (48.6) | 37 (46.8) |
| Stage (%) |  |  |
| I | 12 ( 2.3) | - |
| II | 25 ( 4.7) | - |
| III | 409 (77.3) | 67 (84.8) |
| IV | 83 (15.7) | 12 (15.2) |
| Grade (%) |  |  |
| G1&G2/G2 | 70 (13.5) | 15 (19.0) |
| G3&G4/G3 | 450 (86.5) | 64 (81.0) |

TableS2.Identified DNA driver methylation (DNAme) in TCGA, ICGC and GSE146556.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **TCGA** | | | | |
| Hugo | Rank | Sample\_Size | Pvalue | Padjust |
| BHMT | 1 | 546 | 1.86E-16 | 6.91E-13 |
| FAIM2 | 2 | 550 | 1.44E-15 | 2.13E-12 |
| SPAG6 | 3 | 550 | 1.73E-15 | 2.13E-12 |
| CLIC6 | 4 | 550 | 1.10E-14 | 1.02E-11 |
| TRH | 5 | 550 | 6.58E-14 | 4.88E-11 |
| HNF1B | 6 | 550 | 8.27E-13 | 5.11E-10 |
| NID2 | 7 | 550 | 1.13E-12 | 6.01E-10 |
| LEP | 8 | 550 | 1.58E-12 | 7.32E-10 |
| ZNF560 | 9 | 550 | 2.06E-12 | 8.49E-10 |
| SLC38A4 | 10 | 389 | 3.37E-12 | 1.25E-09 |
| TNXB | 11 | 550 | 7.35E-12 | 2.48E-09 |
| PRLHR | 12 | 550 | 8.43E-12 | 2.60E-09 |
| GRIK2 | 13 | 550 | 7.22E-11 | 2.06E-08 |
| HAAO | 14 | 550 | 2.95E-10 | 7.82E-08 |
| TLX3 | 15 | 531 | 5.13E-10 | 1.27E-07 |
| NEFM | 16 | 550 | 7.87E-10 | 1.82E-07 |
| WBP2NL | 17 | 550 | 9.06E-10 | 1.98E-07 |
| SLC26A5 | 18 | 550 | 1.16E-09 | 2.32E-07 |
| SALL3 | 19 | 550 | 1.24E-09 | 2.32E-07 |
| OTX2 | 20 | 550 | 1.25E-09 | 2.32E-07 |
| GPR26 | 21 | 550 | 1.56E-09 | 2.76E-07 |
| PAX3 | 22 | 550 | 3.40E-09 | 5.49E-07 |
| SLC6A3 | 23 | 550 | 3.41E-09 | 5.49E-07 |
| NPY | 24 | 550 | 4.54E-09 | 7.01E-07 |
| DIO3 | 25 | 550 | 5.43E-09 | 7.96E-07 |
| PCDHA13 | 26 | 550 | 5.58E-09 | 7.96E-07 |
| HAPLN1 | 27 | 550 | 5.96E-09 | 8.19E-07 |
| CPT1C | 28 | 550 | 9.58E-09 | 1.27E-06 |
| FERD3L | 29 | 550 | 1.29E-08 | 1.61E-06 |
| SCRG1 | 30 | 550 | 1.32E-08 | 1.61E-06 |
| RTEL1 | 31 | 550 | 1.35E-08 | 1.61E-06 |
| SLC18A2 | 32 | 550 | 1.69E-08 | 1.96E-06 |
| LYPD5 | 33 | 550 | 1.99E-08 | 2.24E-06 |
| MOXD1 | 34 | 550 | 2.38E-08 | 2.59E-06 |
| ENPP2 | 35 | 550 | 2.76E-08 | 2.92E-06 |
| FILIP1 | 36 | 550 | 2.85E-08 | 2.93E-06 |
| DDO | 37 | 550 | 6.73E-08 | 6.74E-06 |
| MTA3 | 38 | 547 | 7.33E-08 | 7.15E-06 |
| PENK | 39 | 550 | 8.05E-08 | 7.65E-06 |
| MEGF10 | 40 | 550 | 8.43E-08 | 7.81E-06 |
| CD8B | 41 | 550 | 8.85E-08 | 8.00E-06 |
| PRICKLE2 | 42 | 550 | 9.19E-08 | 8.10E-06 |
| TCF15 | 43 | 550 | 1.03E-07 | 8.84E-06 |
| AMBP | 44 | 550 | 1.09E-07 | 9.10E-06 |
| GYPC | 45 | 550 | 1.10E-07 | 9.10E-06 |
| ASB3 | 46 | 550 | 1.14E-07 | 9.19E-06 |
| SLITRK1 | 47 | 550 | 1.21E-07 | 9.57E-06 |
| GPR75 | 48 | 550 | 1.27E-07 | 9.77E-06 |
| ANXA13 | 49 | 550 | 1.53E-07 | 1.16E-05 |
| TBX5 | 50 | 550 | 1.78E-07 | 1.32E-05 |
| RBM24 | 51 | 550 | 1.83E-07 | 1.33E-05 |
| TCERG1L | 52 | 550 | 2.06E-07 | 1.46E-05 |
| IGF2BP1 | 53 | 550 | 2.23E-07 | 1.56E-05 |
| ACTN2 | 54 | 550 | 2.43E-07 | 1.67E-05 |
| LGALS12 | 55 | 550 | 2.69E-07 | 1.81E-05 |
| SULT1C4 | 56 | 550 | 2.88E-07 | 1.90E-05 |
| GDF10 | 57 | 550 | 3.18E-07 | 2.07E-05 |
| KL | 58 | 550 | 3.49E-07 | 2.23E-05 |
| NKX6-2 | 59 | 550 | 3.65E-07 | 2.29E-05 |
| FBXW10 | 60 | 550 | 4.76E-07 | 2.94E-05 |
| ABCA6 | 61 | 550 | 4.90E-07 | 2.98E-05 |
| PTGDR | 62 | 550 | 5.32E-07 | 3.18E-05 |
| FOXL1 | 63 | 550 | 5.71E-07 | 3.36E-05 |
| LDHD | 64 | 550 | 7.10E-07 | 4.11E-05 |
| ARHGEF15 | 65 | 550 | 8.04E-07 | 4.58E-05 |
| RAB22A | 66 | 550 | 9.93E-07 | 5.58E-05 |
| KCTD8 | 67 | 550 | 1.04E-06 | 5.74E-05 |
| CYP26C1 | 68 | 550 | 1.05E-06 | 5.74E-05 |
| RHOJ | 69 | 550 | 1.17E-06 | 6.29E-05 |
| NUAK1 | 70 | 550 | 1.24E-06 | 6.55E-05 |
| FOXI2 | 71 | 550 | 1.33E-06 | 6.95E-05 |
| LEFTY2 | 72 | 550 | 1.40E-06 | 7.22E-05 |
| DCT | 73 | 547 | 1.68E-06 | 8.54E-05 |
| SEMA3E | 74 | 550 | 1.77E-06 | 8.85E-05 |
| TBX20 | 75 | 550 | 1.79E-06 | 8.85E-05 |
| EPX | 76 | 550 | 1.83E-06 | 8.93E-05 |
| PSKH2 | 77 | 550 | 2.25E-06 | 0.000108 |
| CXCL6 | 78 | 550 | 2.42E-06 | 0.000115 |
| CTNNBL1 | 79 | 550 | 2.49E-06 | 0.000116 |
| COL11A1 | 80 | 550 | 2.50E-06 | 0.000116 |
| CADPS | 81 | 550 | 2.66E-06 | 0.00012 |
| CDH9 | 82 | 550 | 2.66E-06 | 0.00012 |
| PON1 | 83 | 550 | 2.97E-06 | 0.000132 |
| KLHL1 | 84 | 550 | 3.00E-06 | 0.000132 |
| ACTA1 | 85 | 550 | 3.04E-06 | 0.000133 |
| DMGDH | 86 | 550 | 3.56E-06 | 0.000154 |
| MLNR | 87 | 550 | 3.95E-06 | 0.000168 |
| MOS | 88 | 550 | 4.48E-06 | 0.000189 |
| SALL4 | 89 | 482 | 4.63E-06 | 0.000193 |
| TAC1 | 90 | 550 | 4.93E-06 | 0.000203 |
| CMBL | 91 | 550 | 5.07E-06 | 0.000206 |
| COL14A1 | 92 | 550 | 5.10E-06 | 0.000206 |
| NMBR | 93 | 550 | 5.98E-06 | 0.000238 |
| ADRA1A | 94 | 550 | 6.11E-06 | 0.000241 |
| LIN7A | 95 | 550 | 8.92E-06 | 0.000348 |
| EVX1 | 96 | 550 | 9.40E-06 | 0.000363 |
| VSX2 | 97 | 550 | 9.94E-06 | 0.00038 |
| PAK2 | 98 | 546 | 1.08E-05 | 0.000409 |
| LAMA3 | 99 | 549 | 1.16E-05 | 0.000434 |
| HOXD3 | 100 | 550 | 1.20E-05 | 0.000444 |
| CXCL12 | 101 | 550 | 1.24E-05 | 0.000455 |
| PTPRR | 102 | 550 | 1.25E-05 | 0.000455 |
| TM4SF4 | 103 | 550 | 1.33E-05 | 0.000478 |
| EFEMP1 | 104 | 550 | 1.40E-05 | 0.000499 |
| LARP1 | 105 | 550 | 1.43E-05 | 0.000504 |
| HCN1 | 106 | 550 | 1.59E-05 | 0.000556 |
| KCNA1 | 107 | 550 | 1.64E-05 | 0.000568 |
| TFAP2B | 108 | 550 | 1.90E-05 | 0.000651 |
| TOX2 | 109 | 550 | 2.05E-05 | 0.000698 |
| ZNF177 | 110 | 492 | 2.22E-05 | 0.000747 |
| SYT10 | 111 | 550 | 2.29E-05 | 0.000765 |
| ENG | 112 | 550 | 2.37E-05 | 0.000784 |
| OLIG2 | 113 | 550 | 2.43E-05 | 0.000797 |
| EREG | 114 | 550 | 2.88E-05 | 0.000936 |
| WDR88 | 115 | 550 | 3.41E-05 | 0.0011 |
| NKX3-1 | 116 | 550 | 3.49E-05 | 0.001114 |
| CD47 | 117 | 550 | 3.59E-05 | 0.001136 |
| PCSK1 | 118 | 550 | 3.62E-05 | 0.001136 |
| SRGN | 119 | 550 | 3.66E-05 | 0.001139 |
| UBE4A | 120 | 550 | 3.88E-05 | 0.001197 |
| HPSE2 | 121 | 550 | 4.14E-05 | 0.001267 |
| MYH6 | 122 | 550 | 4.59E-05 | 0.001394 |
| SIM1 | 123 | 550 | 4.81E-05 | 0.00145 |
| ONECUT2 | 124 | 550 | 5.14E-05 | 0.001537 |
| THNSL2 | 125 | 550 | 5.25E-05 | 0.001556 |
| CACNG6 | 126 | 550 | 5.53E-05 | 0.001628 |
| BCL11B | 127 | 550 | 5.66E-05 | 0.001652 |
| SCUBE2 | 128 | 550 | 6.29E-05 | 0.001822 |
| MASP1 | 129 | 550 | 6.38E-05 | 0.001832 |
| PHACTR2 | 130 | 550 | 6.44E-05 | 0.001835 |
| RERG | 131 | 550 | 6.88E-05 | 0.001946 |
| DCHS2 | 132 | 539 | 7.37E-05 | 0.002069 |
| IRX2 | 133 | 550 | 8.02E-05 | 0.002236 |
| SCG3 | 134 | 550 | 9.00E-05 | 0.002488 |
| SERPING1 | 135 | 550 | 0.000101 | 0.002768 |
| COL5A2 | 136 | 550 | 0.000104 | 0.002845 |
| CKMT2 | 137 | 550 | 0.000122 | 0.003296 |
| MAPRE3 | 138 | 550 | 0.000126 | 0.003372 |
| COL3A1 | 139 | 550 | 0.000129 | 0.003443 |
| KRT72 | 140 | 530 | 0.000143 | 0.003797 |
| PHYHIP | 141 | 550 | 0.000157 | 0.004121 |
| GRIK1 | 142 | 547 | 0.000162 | 0.004226 |
| CDH6 | 143 | 550 | 0.000166 | 0.004299 |
| FBXL22 | 144 | 550 | 0.000168 | 0.004327 |
| GRIA4 | 145 | 550 | 0.000183 | 0.004666 |
| CLEC14A | 146 | 540 | 0.000188 | 0.004762 |
| MCHR2 | 147 | 550 | 0.000191 | 0.004813 |
| MYO16 | 148 | 550 | 0.000204 | 0.005107 |
| SH2D4B | 149 | 550 | 0.000206 | 0.005129 |
| PLD5 | 150 | 550 | 0.000223 | 0.005503 |
| ACSS1 | 151 | 550 | 0.000242 | 0.005937 |
| APCDD1L | 152 | 550 | 0.00025 | 0.006089 |
| KCNS2 | 153 | 550 | 0.000274 | 0.006626 |
| SLC25A18 | 154 | 550 | 0.000288 | 0.006925 |
| ADRA2B | 155 | 550 | 0.000297 | 0.007108 |
| CDH16 | 156 | 550 | 0.000311 | 0.007387 |
| DYNC1I1 | 157 | 546 | 0.000319 | 0.007538 |
| TTLL11 | 158 | 550 | 0.000325 | 0.007624 |
| POU4F1 | 159 | 550 | 0.000337 | 0.007856 |
| ZCCHC14 | 160 | 550 | 0.000342 | 0.007924 |
| CD226 | 161 | 550 | 0.00036 | 0.008286 |
| JPH4 | 162 | 550 | 0.000386 | 0.008833 |
| SLC22A3 | 163 | 549 | 0.000446 | 0.010136 |
| ABCG1 | 164 | 550 | 0.000453 | 0.010238 |
| TSPYL5 | 165 | 550 | 0.000467 | 0.01049 |
| CD96 | 166 | 550 | 0.000478 | 0.010668 |
| PTHLH | 167 | 550 | 0.000502 | 0.011132 |
| MRGPRF | 168 | 550 | 0.000535 | 0.011803 |
| SLC2A3 | 169 | 550 | 0.00059 | 0.012939 |
| ITGAD | 170 | 549 | 0.000604 | 0.01316 |
| KLF14 | 171 | 550 | 0.00064 | 0.013873 |
| CSMD3 | 172 | 549 | 0.000658 | 0.01417 |
| MBP | 173 | 550 | 0.00069 | 0.014701 |
| MAL | 174 | 550 | 0.000692 | 0.014701 |
| LIPE | 175 | 548 | 0.000694 | 0.014701 |
| SCG5 | 176 | 550 | 0.000733 | 0.015439 |
| NAV1 | 177 | 550 | 0.000754 | 0.015791 |
| BVES | 178 | 509 | 0.000784 | 0.016317 |
| TEX14 | 179 | 538 | 0.000831 | 0.017204 |
| CH25H | 180 | 550 | 0.000863 | 0.017746 |
| HS3ST2 | 181 | 550 | 0.000867 | 0.017746 |
| ZIC5 | 182 | 550 | 0.000896 | 0.018245 |
| LYN | 183 | 550 | 0.000977 | 0.019781 |
| CTNNA3 | 184 | 550 | 0.000998 | 0.020099 |
| TRPC4 | 185 | 550 | 0.00108 | 0.021627 |
| SLC5A7 | 186 | 550 | 0.001089 | 0.021631 |
| GRIN3A | 187 | 550 | 0.001091 | 0.021631 |
| PMP22 | 188 | 538 | 0.001148 | 0.022634 |
| COG2 | 189 | 550 | 0.001171 | 0.022969 |
| RBP7 | 190 | 549 | 0.001234 | 0.024078 |
| KCNS1 | 191 | 550 | 0.001313 | 0.025482 |
| SCUBE3 | 192 | 550 | 0.001342 | 0.025911 |
| PTF1A | 193 | 550 | 0.001399 | 0.026826 |
| PEX5L | 194 | 550 | 0.001404 | 0.026826 |
| TRHDE | 195 | 550 | 0.001456 | 0.027671 |
| ZNF44 | 196 | 550 | 0.001464 | 0.027689 |
| FBXO44 | 197 | 550 | 0.001478 | 0.027798 |
| FAP | 198 | 550 | 0.001494 | 0.027967 |
| HSD17B6 | 199 | 550 | 0.001529 | 0.028473 |
| RHOH | 200 | 550 | 0.001633 | 0.030144 |
| SOX14 | 201 | 550 | 0.001635 | 0.030144 |
| HAND2 | 202 | 550 | 0.001673 | 0.030693 |
| LUM | 203 | 550 | 0.001725 | 0.031499 |
| COL6A3 | 204 | 550 | 0.001874 | 0.034046 |
| MED15 | 205 | 550 | 0.001911 | 0.03455 |
| FIBCD1 | 206 | 550 | 0.001983 | 0.035679 |
| KNG1 | 207 | 550 | 0.001999 | 0.035796 |
| MMP26 | 208 | 550 | 0.002131 | 0.037974 |
| SLC15A2 | 209 | 550 | 0.002276 | 0.04035 |
| PES1 | 210 | 550 | 0.00236 | 0.041644 |
| ST8SIA5 | 211 | 550 | 0.002386 | 0.041913 |
| PI15 | 212 | 550 | 0.002406 | 0.042055 |
| OTP | 213 | 550 | 0.00242 | 0.042097 |
| SLC17A8 | 214 | 550 | 0.002475 | 0.042862 |
| TSHR | 215 | 550 | 0.002567 | 0.044252 |
| RHBDD1 | 216 | 550 | 0.00262 | 0.044957 |
| SOX11 | 217 | 550 | 0.002643 | 0.045139 |
| SLC5A8 | 218 | 550 | 0.002668 | 0.045355 |
| CEACAM6 | 219 | 550 | 0.002723 | 0.046073 |
| CDH13 | 220 | 550 | 0.002787 | 0.046949 |
| RAB11FIP4 | 221 | 550 | 0.002809 | 0.047101 |
| GARNL3 | 222 | 549 | 0.002822 | 0.04711 |
| SPARC | 223 | 550 | 0.002905 | 0.048278 |
| PID1 | 224 | 550 | 0.002946 | 0.048745 |
| HLA-G | 225 | 550 | 0.003017 | 0.049688 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ICGC** | | | | |
| Hugo | Rank | Sample\_Size | Pvalue | Padjust |
| MMP23B | 1 | 79 | 4.85E-20 | 1.71E-16 |
| FILIP1 | 2 | 76 | 5.42E-19 | 9.53E-16 |
| PXDNL | 3 | 79 | 6.92E-18 | 8.11E-15 |
| TRH | 4 | 79 | 3.87E-17 | 3.41E-14 |
| PCDHGA3 | 5 | 79 | 5.69E-17 | 4.01E-14 |
| CPNE8 | 6 | 79 | 9.75E-17 | 5.72E-14 |
| MRGPRF | 7 | 79 | 3.53E-16 | 1.78E-13 |
| PCDHA10 | 8 | 76 | 8.48E-15 | 3.73E-12 |
| BHMT | 9 | 79 | 7.53E-14 | 2.94E-11 |
| F10 | 10 | 79 | 9.76E-14 | 3.44E-11 |
| TRIM61 | 11 | 79 | 1.28E-13 | 4.11E-11 |
| PCDHA6 | 12 | 79 | 2.53E-13 | 7.42E-11 |
| SLC22A8 | 13 | 79 | 7.61E-13 | 2.06E-10 |
| PCDHGA6 | 14 | 79 | 1.88E-12 | 4.45E-10 |
| GYPC | 15 | 79 | 1.90E-12 | 4.45E-10 |
| PCDHGB2 | 16 | 78 | 2.15E-12 | 4.73E-10 |
| PCDHGA2 | 17 | 79 | 4.10E-12 | 8.48E-10 |
| HLA-DPA1 | 18 | 79 | 5.85E-12 | 1.14E-09 |
| PCDHGA5 | 19 | 79 | 6.67E-12 | 1.24E-09 |
| COLEC11 | 20 | 79 | 8.53E-12 | 1.50E-09 |
| CMBL | 21 | 79 | 9.21E-12 | 1.54E-09 |
| FAIM2 | 22 | 79 | 1.13E-11 | 1.80E-09 |
| XAF1 | 23 | 79 | 3.76E-11 | 5.76E-09 |
| DNHD1 | 24 | 79 | 7.05E-11 | 1.03E-08 |
| HNF1B | 25 | 79 | 7.84E-11 | 1.10E-08 |
| IFT80 | 26 | 79 | 4.74E-10 | 6.41E-08 |
| MOV10L1 | 27 | 79 | 7.34E-10 | 9.56E-08 |
| CPT1C | 28 | 79 | 1.52E-09 | 1.91E-07 |
| UBASH3A | 29 | 79 | 1.70E-09 | 2.07E-07 |
| HOXB3 | 30 | 79 | 4.30E-09 | 5.05E-07 |
| ZIC4 | 31 | 79 | 4.78E-09 | 5.43E-07 |
| COL5A2 | 32 | 79 | 7.81E-09 | 8.59E-07 |
| TBX20 | 33 | 78 | 9.47E-09 | 1.01E-06 |
| HORMAD2 | 34 | 79 | 1.05E-08 | 1.09E-06 |
| PCDHGB4 | 35 | 79 | 1.32E-08 | 1.31E-06 |
| TTLL10 | 36 | 79 | 1.34E-08 | 1.31E-06 |
| NETO1 | 37 | 79 | 1.52E-08 | 1.44E-06 |
| RGS22 | 38 | 79 | 1.71E-08 | 1.56E-06 |
| COL1A2 | 39 | 79 | 1.73E-08 | 1.56E-06 |
| OTX2 | 40 | 79 | 2.11E-08 | 1.85E-06 |
| STAG3 | 41 | 79 | 4.15E-08 | 3.49E-06 |
| CYP26C1 | 42 | 79 | 4.23E-08 | 3.49E-06 |
| DIO3 | 43 | 79 | 4.26E-08 | 3.49E-06 |
| IRX2 | 44 | 79 | 4.73E-08 | 3.79E-06 |
| PCDHGA1 | 45 | 79 | 5.34E-08 | 4.17E-06 |
| SIM1 | 46 | 79 | 7.13E-08 | 5.45E-06 |
| SOX1 | 47 | 79 | 8.51E-08 | 6.37E-06 |
| CD302 | 48 | 79 | 1.05E-07 | 7.67E-06 |
| KIF25 | 49 | 79 | 1.25E-07 | 9.00E-06 |
| ZNF560 | 50 | 79 | 1.51E-07 | 1.06E-05 |
| TBPL2 | 51 | 79 | 1.77E-07 | 1.22E-05 |
| KCNK2 | 52 | 78 | 2.04E-07 | 1.38E-05 |
| SERPING1 | 53 | 78 | 2.32E-07 | 1.54E-05 |
| TBX5 | 54 | 79 | 2.83E-07 | 1.85E-05 |
| ZNF69 | 55 | 79 | 3.11E-07 | 1.99E-05 |
| MCHR2 | 56 | 79 | 4.51E-07 | 2.84E-05 |
| SALL3 | 57 | 79 | 5.59E-07 | 3.42E-05 |
| PHOX2B | 58 | 79 | 5.64E-07 | 3.42E-05 |
| PCDHGA4 | 59 | 79 | 5.89E-07 | 3.49E-05 |
| ESRRG | 60 | 79 | 5.95E-07 | 3.49E-05 |
| PIGZ | 61 | 79 | 9.76E-07 | 5.63E-05 |
| NID2 | 62 | 79 | 1.05E-06 | 5.95E-05 |
| ZNF486 | 63 | 79 | 1.25E-06 | 7.01E-05 |
| ITGAE | 64 | 79 | 1.31E-06 | 7.21E-05 |
| TMEM140 | 65 | 79 | 1.34E-06 | 7.26E-05 |
| PHYHIP | 66 | 79 | 1.72E-06 | 9.17E-05 |
| FOXG1 | 67 | 79 | 1.79E-06 | 9.41E-05 |
| CDH3 | 68 | 79 | 1.99E-06 | 0.000101 |
| ITGAL | 69 | 79 | 1.99E-06 | 0.000101 |
| BARX1 | 70 | 79 | 2.12E-06 | 0.000106 |
| NEFM | 71 | 79 | 2.79E-06 | 0.000138 |
| SMOC2 | 72 | 79 | 2.88E-06 | 0.000141 |
| PCDH8 | 73 | 79 | 3.24E-06 | 0.000156 |
| KCNC2 | 74 | 79 | 3.29E-06 | 0.000157 |
| CTNND1 | 75 | 76 | 3.63E-06 | 0.000171 |
| PHLDB1 | 76 | 78 | 4.68E-06 | 0.000217 |
| LDHD | 77 | 79 | 7.26E-06 | 0.000332 |
| AKAP12 | 78 | 79 | 8.36E-06 | 0.000377 |
| FOXL2 | 79 | 79 | 8.87E-06 | 0.000395 |
| BNC1 | 80 | 79 | 9.69E-06 | 0.000426 |
| KCNJ12 | 81 | 79 | 1.48E-05 | 0.000645 |
| FERD3L | 82 | 79 | 1.54E-05 | 0.000663 |
| SEMA5A | 83 | 79 | 1.70E-05 | 0.000723 |
| APOD | 84 | 75 | 1.75E-05 | 0.000733 |
| PRLHR | 85 | 79 | 2.29E-05 | 0.000946 |
| KHDRBS2 | 86 | 79 | 2.31E-05 | 0.000946 |
| NUAK1 | 87 | 79 | 2.45E-05 | 0.00099 |
| QRICH2 | 88 | 79 | 2.50E-05 | 0.000998 |
| AKT2 | 89 | 79 | 2.52E-05 | 0.000998 |
| PAX9 | 90 | 79 | 2.84E-05 | 0.001112 |
| FOXD4L1 | 91 | 79 | 2.89E-05 | 0.001119 |
| OLIG3 | 92 | 79 | 3.42E-05 | 0.00131 |
| HOXA10 | 93 | 79 | 3.51E-05 | 0.00133 |
| DNAH1 | 94 | 79 | 4.03E-05 | 0.001508 |
| FN1 | 95 | 79 | 4.29E-05 | 0.00159 |
| CD93 | 96 | 79 | 4.80E-05 | 0.001758 |
| GALNT13 | 97 | 79 | 5.53E-05 | 0.002006 |
| RASL11B | 98 | 79 | 5.60E-05 | 0.00201 |
| IRS1 | 99 | 79 | 5.74E-05 | 0.002042 |
| GHSR | 100 | 79 | 5.89E-05 | 0.002075 |
| NPY | 101 | 79 | 6.75E-05 | 0.002336 |
| SLC10A4 | 102 | 79 | 6.77E-05 | 0.002336 |
| ZNF177 | 103 | 79 | 6.94E-05 | 0.002373 |
| CA10 | 104 | 79 | 7.10E-05 | 0.002384 |
| CXCL5 | 105 | 79 | 7.11E-05 | 0.002384 |
| PENK | 106 | 79 | 7.90E-05 | 0.002625 |
| ZIC5 | 107 | 79 | 8.99E-05 | 0.002956 |
| GJB6 | 108 | 79 | 9.51E-05 | 0.003097 |
| UPB1 | 109 | 79 | 9.59E-05 | 0.003097 |
| BAALC | 110 | 79 | 0.000105 | 0.00334 |
| ABLIM3 | 111 | 79 | 0.000105 | 0.00334 |
| LPIN2 | 112 | 79 | 0.000118 | 0.003699 |
| PRDM14 | 113 | 79 | 0.000138 | 0.004306 |
| GATM | 114 | 79 | 0.000147 | 0.004549 |
| PTGIS | 115 | 79 | 0.00015 | 0.004604 |
| PSKH2 | 116 | 79 | 0.000152 | 0.004624 |
| EVX1 | 117 | 79 | 0.000158 | 0.004713 |
| SIX3 | 118 | 79 | 0.000158 | 0.004713 |
| STXBP5L | 119 | 78 | 0.000177 | 0.005231 |
| PAX3 | 120 | 79 | 0.000187 | 0.005458 |
| GRIK2 | 121 | 79 | 0.000188 | 0.005458 |
| HS3ST2 | 122 | 79 | 0.000199 | 0.005755 |
| RNF212 | 123 | 79 | 0.00022 | 0.006302 |
| MAL | 124 | 79 | 0.000237 | 0.006735 |
| MSX1 | 125 | 79 | 0.000249 | 0.007022 |
| HCN1 | 126 | 79 | 0.000262 | 0.007324 |
| HCK | 127 | 79 | 0.000272 | 0.007551 |
| ASPG | 128 | 79 | 0.000284 | 0.007823 |
| RASGRF2 | 129 | 79 | 0.000288 | 0.007848 |
| BPI | 130 | 79 | 0.000301 | 0.008158 |
| LAMA4 | 131 | 79 | 0.000324 | 0.008713 |
| GPR155 | 132 | 79 | 0.000327 | 0.008732 |
| SLC4A11 | 133 | 79 | 0.000368 | 0.009734 |
| TMEM26 | 134 | 79 | 0.000371 | 0.009748 |
| CHN2 | 135 | 79 | 0.000383 | 0.009982 |
| PLEKHB1 | 136 | 79 | 0.000392 | 0.010152 |
| PRSS16 | 137 | 79 | 0.000431 | 0.011029 |
| TOX | 138 | 79 | 0.000432 | 0.011029 |
| FBN1 | 139 | 79 | 0.000546 | 0.013821 |
| HPCAL1 | 140 | 79 | 0.000551 | 0.013858 |
| SFRP1 | 141 | 79 | 0.000573 | 0.014309 |
| RADIL | 142 | 79 | 0.000604 | 0.014964 |
| DLGAP1 | 143 | 79 | 0.000623 | 0.015347 |
| DRGX | 144 | 79 | 0.000656 | 0.016044 |
| MLNR | 145 | 79 | 0.000679 | 0.01648 |
| COG5 | 146 | 79 | 0.000714 | 0.017216 |
| TLX3 | 147 | 79 | 0.000729 | 0.017451 |
| KRT72 | 148 | 79 | 0.000771 | 0.018339 |
| MKX | 149 | 79 | 0.000828 | 0.019571 |
| HSPA1B | 150 | 79 | 0.00087 | 0.020426 |
| PAX6 | 151 | 79 | 0.000909 | 0.021185 |
| BBX | 152 | 79 | 0.000925 | 0.021432 |
| CDX2 | 153 | 79 | 0.000936 | 0.021489 |
| SCG5 | 154 | 79 | 0.00094 | 0.021489 |
| CALD1 | 155 | 79 | 0.000973 | 0.022101 |
| KCNS1 | 156 | 79 | 0.000984 | 0.022183 |
| APBB1IP | 157 | 79 | 0.000989 | 0.022183 |
| CYP7B1 | 158 | 79 | 0.001197 | 0.026674 |
| TRPC4 | 159 | 79 | 0.001212 | 0.026832 |
| VAX1 | 160 | 79 | 0.001257 | 0.027665 |
| MRGPRE | 161 | 79 | 0.001302 | 0.028456 |
| SLITRK1 | 162 | 79 | 0.001416 | 0.030668 |
| TFAP2A | 163 | 79 | 0.00142 | 0.030668 |
| ZSWIM2 | 164 | 79 | 0.00144 | 0.030908 |
| OXTR | 165 | 79 | 0.001537 | 0.032773 |
| PTGDR | 166 | 79 | 0.001546 | 0.032773 |
| POU4F1 | 167 | 79 | 0.00167 | 0.035069 |
| NEFL | 168 | 78 | 0.001674 | 0.035069 |
| DHRS7C | 169 | 79 | 0.001707 | 0.03556 |
| ASCL2 | 170 | 79 | 0.001901 | 0.039363 |
| PCDHGB1 | 171 | 79 | 0.001949 | 0.040125 |
| PPP1R3C | 172 | 79 | 0.001991 | 0.040656 |
| SLC7A14 | 173 | 79 | 0.001998 | 0.040656 |
| PTPRN2 | 174 | 79 | 0.002219 | 0.04489 |
| ZCCHC14 | 175 | 79 | 0.002339 | 0.046823 |
| TFAP2B | 176 | 79 | 0.002341 | 0.046823 |
| KLF14 | 177 | 79 | 0.002399 | 0.047708 |
| CADPS | 178 | 79 | 0.00242 | 0.047781 |
| TFAP2D | 179 | 79 | 0.00243 | 0.047781 |
| ZNF300 | 180 | 74 | 0.002479 | 0.048484 |
| LYNX1 | 181 | 79 | 0.002559 | 0.049759 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **GSE146556** | | | | |
| Hugo | Rank | Sample\_Size | Pvalue | Padjust |
| FAIM2 | 1 | 20 | 1.81E-24 | 6.14E-21 |
| CMBL | 2 | 20 | 1.25E-21 | 2.12E-18 |
| MMP23B | 3 | 20 | 1.14E-20 | 1.29E-17 |
| CPNE8 | 4 | 20 | 5.09E-20 | 4.31E-17 |
| FILIP1 | 5 | 20 | 2.05E-15 | 1.39E-12 |
| PXDNL | 6 | 20 | 1.40E-14 | 7.21E-12 |
| TRH | 7 | 20 | 1.49E-14 | 7.21E-12 |
| HNF1B | 8 | 20 | 4.39E-14 | 1.86E-11 |
| SALL3 | 9 | 20 | 4.50E-13 | 1.69E-10 |
| OTX2 | 10 | 20 | 2.29E-12 | 7.45E-10 |
| NETO1 | 11 | 20 | 2.42E-12 | 7.45E-10 |
| TRIM61 | 12 | 20 | 4.57E-12 | 1.29E-09 |
| MRGPRF | 13 | 20 | 2.05E-11 | 5.34E-09 |
| BHMT | 14 | 20 | 2.49E-11 | 6.02E-09 |
| MOV10L1 | 15 | 20 | 3.97E-11 | 8.98E-09 |
| PHOX2B | 16 | 20 | 4.49E-11 | 9.51E-09 |
| NID2 | 17 | 20 | 4.94E-11 | 9.84E-09 |
| HLA-DPA1 | 18 | 20 | 9.01E-11 | 1.70E-08 |
| F10 | 19 | 20 | 1.32E-10 | 2.36E-08 |
| SIM1 | 20 | 20 | 1.45E-10 | 2.45E-08 |
| CPT1C | 21 | 20 | 3.57E-10 | 5.77E-08 |
| IRX2 | 22 | 20 | 4.20E-10 | 6.47E-08 |
| CYP26C1 | 23 | 20 | 9.89E-10 | 1.46E-07 |
| HSPA1B | 24 | 20 | 1.16E-09 | 1.64E-07 |
| SOX1 | 25 | 20 | 1.26E-09 | 1.71E-07 |
| GYPC | 26 | 20 | 1.36E-09 | 1.78E-07 |
| TBX20 | 27 | 20 | 4.07E-09 | 5.10E-07 |
| GHSR | 28 | 20 | 7.30E-09 | 8.84E-07 |
| FERD3L | 29 | 20 | 8.15E-09 | 9.52E-07 |
| BST1 | 30 | 20 | 8.66E-09 | 9.79E-07 |
| DNHD1 | 31 | 20 | 1.20E-08 | 1.31E-06 |
| UBASH3A | 32 | 20 | 1.25E-08 | 1.32E-06 |
| SLC22A8 | 33 | 20 | 1.77E-08 | 1.82E-06 |
| PAX3 | 34 | 20 | 2.21E-08 | 2.20E-06 |
| IRAK2 | 35 | 20 | 2.70E-08 | 2.62E-06 |
| XAF1 | 36 | 20 | 2.88E-08 | 2.64E-06 |
| TBX5 | 37 | 20 | 2.89E-08 | 2.64E-06 |
| ZIC4 | 38 | 20 | 2.99E-08 | 2.67E-06 |
| ASPG | 39 | 20 | 3.61E-08 | 3.13E-06 |
| DIO3 | 40 | 20 | 5.96E-08 | 4.98E-06 |
| TFAP2D | 41 | 20 | 6.02E-08 | 4.98E-06 |
| COLEC11 | 42 | 20 | 6.47E-08 | 5.22E-06 |
| TBPL2 | 43 | 20 | 7.55E-08 | 5.95E-06 |
| MCHR2 | 44 | 20 | 7.81E-08 | 6.02E-06 |
| ITGAL | 45 | 20 | 2.05E-07 | 1.54E-05 |
| CD40 | 46 | 20 | 3.93E-07 | 2.89E-05 |
| KCNC2 | 47 | 20 | 4.34E-07 | 3.13E-05 |
| OLIG3 | 48 | 20 | 5.24E-07 | 3.70E-05 |
| HORMAD2 | 49 | 20 | 5.76E-07 | 3.98E-05 |
| ESRRG | 50 | 20 | 6.18E-07 | 4.19E-05 |
| CDH8 | 51 | 20 | 8.74E-07 | 5.81E-05 |
| CADPS | 52 | 20 | 1.03E-06 | 6.74E-05 |
| HOXA10 | 53 | 20 | 1.15E-06 | 7.35E-05 |
| PTGDR | 54 | 20 | 1.30E-06 | 8.18E-05 |
| PSKH2 | 55 | 20 | 1.40E-06 | 8.65E-05 |
| PENK | 56 | 20 | 2.09E-06 | 0.000126 |
| KHDRBS2 | 57 | 20 | 2.62E-06 | 0.000156 |
| ZNF560 | 58 | 20 | 2.73E-06 | 0.000159 |
| TLX3 | 59 | 20 | 2.92E-06 | 0.000168 |
| FOXL2 | 60 | 20 | 4.27E-06 | 0.000241 |
| HCK | 61 | 20 | 4.48E-06 | 0.000246 |
| UNC5D | 62 | 20 | 4.50E-06 | 0.000246 |
| SLC10A4 | 63 | 20 | 4.62E-06 | 0.000249 |
| ZNF300 | 64 | 20 | 5.30E-06 | 0.000281 |
| GALNT13 | 65 | 20 | 6.62E-06 | 0.000345 |
| HCN1 | 66 | 20 | 7.61E-06 | 0.000391 |
| SIX3 | 67 | 20 | 8.81E-06 | 0.000442 |
| NPY | 68 | 20 | 8.87E-06 | 0.000442 |
| ZNF486 | 69 | 20 | 9.55E-06 | 0.000469 |
| BNC1 | 70 | 20 | 9.97E-06 | 0.000483 |
| NEFM | 71 | 20 | 1.08E-05 | 0.000514 |
| PRLHR | 72 | 20 | 1.21E-05 | 0.00057 |
| PAX9 | 73 | 20 | 1.31E-05 | 0.000599 |
| FOXD4L1 | 74 | 20 | 1.31E-05 | 0.000599 |
| ITGAE | 75 | 20 | 1.97E-05 | 0.000891 |
| KCNJ3 | 76 | 20 | 2.00E-05 | 0.000893 |
| MAGI2 | 77 | 20 | 2.14E-05 | 0.000941 |
| HOXB3 | 78 | 20 | 2.22E-05 | 0.000965 |
| STAG3 | 79 | 20 | 2.64E-05 | 0.001133 |
| ZIC5 | 80 | 20 | 2.82E-05 | 0.001182 |
| SLC4A11 | 81 | 20 | 2.83E-05 | 0.001182 |
| SCG5 | 82 | 20 | 3.26E-05 | 0.001345 |
| CCDC105 | 83 | 20 | 3.65E-05 | 0.001491 |
| CA10 | 84 | 20 | 3.80E-05 | 0.001535 |
| PCDH8 | 85 | 20 | 4.07E-05 | 0.001588 |
| OLIG2 | 86 | 20 | 4.07E-05 | 0.001588 |
| BDNF | 87 | 20 | 4.08E-05 | 0.001588 |
| DRGX | 88 | 20 | 4.57E-05 | 0.001762 |
| PLEKHB1 | 89 | 20 | 5.45E-05 | 0.002073 |
| CLDN5 | 90 | 20 | 5.79E-05 | 0.002181 |
| FOXG1 | 91 | 20 | 7.38E-05 | 0.002748 |
| VSX2 | 92 | 20 | 7.55E-05 | 0.002781 |
| SLC7A14 | 93 | 20 | 7.67E-05 | 0.002795 |
| PRDM14 | 94 | 20 | 8.17E-05 | 0.002946 |
| PIGZ | 95 | 20 | 8.70E-05 | 0.003102 |
| POU4F1 | 96 | 20 | 9.59E-05 | 0.003386 |
| TTLL10 | 97 | 20 | 9.74E-05 | 0.003403 |
| COL5A2 | 98 | 20 | 0.0001 | 0.003453 |
| SLITRK1 | 99 | 20 | 0.000101 | 0.003453 |
| CACNA2D3 | 100 | 20 | 0.000102 | 0.003453 |
| ADRA1A | 101 | 20 | 0.000118 | 0.003959 |
| NEFL | 102 | 20 | 0.000119 | 0.003961 |
| AKR1B1 | 103 | 20 | 0.000122 | 0.004001 |
| PAM | 104 | 20 | 0.000142 | 0.004618 |
| EVX1 | 105 | 20 | 0.000149 | 0.00482 |
| MEGF10 | 106 | 20 | 0.000152 | 0.004842 |
| MLNR | 107 | 20 | 0.000153 | 0.004842 |
| ZNF69 | 108 | 20 | 0.000156 | 0.004889 |
| ZNF177 | 109 | 20 | 0.000177 | 0.005472 |
| FAM180A | 110 | 20 | 0.000178 | 0.005472 |
| HS3ST2 | 111 | 20 | 0.000236 | 0.007192 |
| ITGA8 | 112 | 20 | 0.000251 | 0.007586 |
| MSX1 | 113 | 20 | 0.000275 | 0.008254 |
| AKAP12 | 114 | 20 | 0.000289 | 0.008605 |
| IFT80 | 115 | 20 | 0.000293 | 0.00863 |
| STXBP5L | 116 | 20 | 0.000304 | 0.008885 |
| SLC8A3 | 117 | 20 | 0.000325 | 0.009423 |
| DUSP22 | 118 | 20 | 0.000328 | 0.009423 |
| SMOC2 | 119 | 20 | 0.000394 | 0.011234 |
| DLGAP1 | 120 | 20 | 0.000404 | 0.011422 |
| NEFH | 121 | 20 | 0.000427 | 0.011951 |
| IGF2BP1 | 122 | 20 | 0.000434 | 0.01207 |
| P2RX5 | 123 | 20 | 0.000508 | 0.013986 |
| CDX2 | 124 | 20 | 0.000516 | 0.014106 |
| GJB6 | 125 | 20 | 0.000567 | 0.015361 |
| TMEM26 | 126 | 20 | 0.0006 | 0.016149 |
| RGS22 | 127 | 20 | 0.000691 | 0.01845 |
| TBX18 | 128 | 20 | 0.000698 | 0.018474 |
| PAX6 | 129 | 20 | 0.000741 | 0.019479 |
| FSTL1 | 130 | 20 | 0.000756 | 0.019707 |
| SEMA5A | 131 | 20 | 0.000763 | 0.019748 |
| NUAK1 | 132 | 20 | 0.000798 | 0.020476 |
| PTF1A | 133 | 20 | 0.000829 | 0.021133 |
| AJAP1 | 134 | 20 | 0.000847 | 0.021428 |
| AKT2 | 135 | 20 | 0.000951 | 0.023865 |
| FBN1 | 136 | 20 | 0.000971 | 0.024189 |
| ALX1 | 137 | 20 | 0.00104 | 0.025724 |
| DNAH1 | 138 | 20 | 0.001076 | 0.026431 |
| OR2L13 | 139 | 20 | 0.001109 | 0.027018 |
| ABLIM3 | 140 | 20 | 0.001116 | 0.027018 |
| PTPRN2 | 141 | 20 | 0.001158 | 0.027837 |
| MKX | 142 | 20 | 0.0012 | 0.028645 |
| CHN2 | 143 | 20 | 0.001305 | 0.030935 |
| POU4F2 | 144 | 20 | 0.001338 | 0.031498 |
| PTGIS | 145 | 20 | 0.001455 | 0.034004 |
| CDH3 | 146 | 20 | 0.001483 | 0.034433 |
| RASGRF2 | 147 | 20 | 0.001507 | 0.034741 |
| TAC1 | 148 | 20 | 0.001528 | 0.034996 |
| MAL | 149 | 20 | 0.001717 | 0.039045 |
| PRSS16 | 150 | 20 | 0.001759 | 0.039741 |
| CTNND1 | 151 | 20 | 0.001786 | 0.04008 |
| ZSWIM2 | 152 | 20 | 0.00181 | 0.040293 |
| KRT72 | 153 | 20 | 0.001819 | 0.040293 |
| PROM1 | 154 | 20 | 0.001877 | 0.041311 |
| RASL11B | 155 | 20 | 0.00199 | 0.043512 |
| HOXD1 | 156 | 20 | 0.002066 | 0.044672 |
| PCDH17 | 157 | 20 | 0.002079 | 0.044672 |
| IRS1 | 158 | 20 | 0.002083 | 0.044672 |
| RNF212 | 159 | 20 | 0.002103 | 0.044832 |
| COX19 | 160 | 20 | 0.00217 | 0.045955 |
| LAMA4 | 161 | 20 | 0.002262 | 0.047616 |

TableS3. The correlation between DNAme and corresponding mRNA expression in TCGA, ICGC and GSE146556.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| DNA methylation & mRNA expression | TCGA | | ICGC | | GSE146556 | |
| Pearson r | *P* | Pearson r | *P* | Pearson r | *P* |
| FILIP1 | -0.109 | 0.012 | -0.241 | 0.032 | -0.156 | 0.523 |
| TRH | -0.015 | 0.735 | -0.09 | 0.432 | 0.314 | 0.19 |
| MRGPRF | -0.233 | <0.001 | -0.264 | 0.019 | -0.314 | 0.19 |
| BHMT | -0.03 | 0.49 | 0.058 | 0.613 | -0.536 | 0.018 |
| GYPC | -0.435 | <0.001 | -0.515 | <0.001 | -0.355 | 0.136 |
| CMBL | -0.654 | <0.001 | -0.52 | <0.001 | -0.529 | 0.02 |
| FAIM2 | 0.059 | 0.173 | 0.014 | 0.902 | -0.05 | 0.838 |
| HNF1B | -0.363 | <0.001 | -0.317 | 0.004 | -0.268 | 0.267 |
| CPT1C | -0.309 | <0.001 | -0.353 | 0.001 | -0.439 | 0.06 |
| COL5A2 | 0.058 | 0.18 | 0.266 | 0.018 | -0.253 | 0.295 |
| TBX20 | -0.121 | 0.005 | 0.089 | 0.437 | 0.239 | 0.324 |
| OTX2 | 0.04 | 0.361 | 0.256 | 0.023 | 0.123 | 0.615 |
| CYP26C1 | 0.061 | 0.16 | 0.204 | 0.071 | 0.27 | 0.263 |
| DIO3 | 0.07 | 0.107 | -0.002 | 0.988 | 0.286 | 0.236 |
| IRX2 | 0.05 | 0.253 | -0.22 | 0.051 | -0.242 | 0.319 |
| SIM1 | -0.056 | 0.195 | -0.008 | 0.944 | -0.03 | 0.901 |
| ZNF560 | -0.516 | <0.001 | -0.707 | <0.001 | -0.32 | 0.182 |
| TBX5 | -0.046 | 0.288 | 0.233 | 0.039 | 0.184 | 0.45 |
| MCHR2 | -0.033 | 0.45 | -0.189 | 0.095 | 0.051 | 0.836 |
| SALL3 | 0.034 | 0.429 | 0.054 | 0.635 | -0.106 | 0.667 |
| NID2 | -0.045 | 0.303 | 0.058 | 0.614 | -0.35 | 0.142 |
| NEFM | -0.076 | 0.078 | -0.15 | 0.188 | -0.111 | 0.65 |
| FERD3L | 0.01 | 0.811 | 0.106 | 0.354 | 0.08 | 0.745 |
| PRLHR | 0.048 | 0.268 | -0.148 | 0.194 | 0.023 | 0.924 |
| NUAK1 | -0.321 | <0.001 | -0.291 | 0.009 | -0.364 | 0.125 |
| NPY | -0.092 | 0.034 | 0.132 | 0.248 | -0.043 | 0.861 |
| ZNF177 | 0.064 | 0.142 | 0.126 | 0.27 | -0.266 | 0.272 |
| PENK | -0.069 | 0.11 | -0.159 | 0.162 | 0.265 | 0.272 |
| ZIC5 | 0.113 | 0.009 | -0.191 | 0.092 | -0.263 | 0.276 |
| PSKH2 | -0.022 | 0.616 | 0.077 | 0.5 | 0.348 | 0.144 |
| EVX1 | -0.027 | 0.537 | 0.146 | 0.199 | -0.207 | 0.394 |
| PAX3 | 0.067 | 0.125 | 0.144 | 0.205 | -0.102 | 0.677 |
| HS3ST2 | 0.119 | 0.006 | -0.171 | 0.133 | -0.004 | 0.988 |
| MAL | -0.326 | <0.001 | -0.481 | <0.001 | -0.42 | 0.074 |
| HCN1 | -0.039 | 0.374 | -0.132 | 0.245 | -0.144 | 0.555 |
| MLNR | 0.07 | 0.105 | -0.045 | 0.691 | 0.256 | 0.289 |
| TLX3 | 0.026 | 0.555 | -0.048 | 0.673 | 0.085 | 0.728 |
| KRT72 | -0.042 | 0.335 | -0.175 | 0.122 | -0.048 | 0.844 |
| SCG5 | -0.471 | <0.001 | -0.491 | <0.001 | -0.469 | 0.043 |
| SLITRK1 | -0.039 | 0.373 | -0.103 | 0.367 | -0.288 | 0.232 |
| PTGDR | 0.124 | 0.004 | 0.216 | 0.055 | -0.053 | 0.83 |
| POU4F1 | 0.116 | 0.007 | 0.276 | 0.014 | 0.059 | 0.809 |
| CADPS | -0.08 | 0.066 | -0.09 | 0.43 | -0.195 | 0.423 |

TableS4.Analysis of pathway enrichment (KEGG) and Gene Ontology (GO) of DNAme-associated mRNA in TCGA.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| KEGG | | | | | | | | |
| ID | Description | GeneRatio | BgRatio | pvalue | p.adjust | qvalue | geneID | Count |
| hsa04145 | Phagosome | 38/532 | 152/8104 | 2.74E-13 | 8.53E-11 | 6.38E-11 | 10952/7037/79659/3684/3122/3689/2213/7099/929/3115/2212/3123/64581/3678/4973/4688/7097/3113/3135/3111/718/7846/3134/4689/347733/1520/6890/3106/3133/11151/7058/7057/2214/4481/203068/537/83547/3105 | 38 |
| hsa04612 | Antigen processing and presentation | 22/532 | 78/8104 | 2.74E-09 | 4.26E-07 | 3.19E-07 | 3122/920/3115/3123/3113/3135/3111/567/3134/4261/6892/972/1520/6890/3106/3133/3303/5720/4800/3105/10437/3306 | 22 |
| hsa05152 | Tuberculosis | 35/532 | 180/8104 | 4.12E-09 | 4.27E-07 | 3.19E-07 | 7042/5601/3684/3122/2207/3689/2213/7099/929/3115/2212/3687/3587/3123/7096/64581/7097/3113/3111/718/4261/8767/3717/972/1520/64127/11151/2214/3553/3656/4615/843/3654/4800/537 | 35 |
| hsa05133 | Pertussis | 21/532 | 76/8104 | 9.48E-09 | 7.37E-07 | 5.51E-07 | 5601/3684/3689/7099/929/834/23643/716/3678/718/3659/3394/727/3553/114548/4615/3654/714/10392/713/712 | 21 |
| hsa05140 | Leishmaniasis | 21/532 | 77/8104 | 1.23E-08 | 7.62E-07 | 5.70E-07 | 7042/3684/3122/3689/7099/3115/2212/3123/4688/7097/3113/3111/718/4689/3717/2214/3553/3676/4615/3654/6885 | 21 |
| hsa04640 | Hematopoietic cell lineage | 23/532 | 99/8104 | 6.73E-08 | 3.49E-06 | 2.61E-06 | 7037/3684/3122/920/3575/929/3115/3123/3678/1436/3113/3111/3590/960/3566/951/3553/3676/914/915/916/1435/3815 | 23 |
| hsa05416 | Viral myocarditis | 17/532 | 60/8104 | 1.66E-07 | 6.55E-06 | 4.90E-06 | 3122/942/3689/3115/3123/3113/3135/3111/3134/3106/3133/3383/3683/284217/3105/5551/2534 | 17 |
| hsa05150 | Staphylococcus aureus infection | 22/532 | 96/8104 | 1.69E-07 | 6.55E-06 | 4.90E-06 | 3684/3122/3689/2213/3115/2212/3123/716/719/3113/3111/718/727/2214/2357/3383/3683/1672/714/713/712/6404 | 22 |
| hsa05332 | Graft-versus-host disease | 14/532 | 42/8104 | 2.22E-07 | 7.68E-06 | 5.74E-06 | 3122/942/355/3115/3123/3113/3135/3111/3134/3106/3133/3553/3105/5551 | 14 |
| hsa05169 | Epstein-Barr virus infection | 34/532 | 202/8104 | 2.81E-07 | 8.30E-06 | 6.21E-06 | 5601/8503/695/3122/355/3115/4067/3123/7097/3113/3135/3111/567/3134/4609/6892/29760/1647/960/6890/3106/3133/915/3383/3683/916/4615/3066/8517/3654/6885/1021/3105/3627 | 34 |
| hsa04940 | Type I diabetes mellitus | 14/532 | 43/8104 | 3.10E-07 | 8.30E-06 | 6.21E-06 | 3122/942/355/3115/3123/3113/3135/3111/3134/3106/3133/3553/3105/5551 | 14 |
| hsa04514 | Cell adhesion molecules | 28/532 | 149/8104 | 3.20E-07 | 8.30E-06 | 6.21E-06 | 3684/3122/942/5788/3689/920/3115/3123/3113/7412/3135/3111/3134/4684/3106/3133/6402/80380/3676/914/3383/1462/3683/9074/1001/3105/1000/6404 | 28 |
| hsa05330 | Allograft rejection | 13/532 | 38/8104 | 4.29E-07 | 9.56E-06 | 7.15E-06 | 3122/942/355/3115/3123/3113/3135/3111/3134/3106/3133/3105/5551 | 13 |
| hsa05417 | Lipid and atherosclerosis | 35/532 | 215/8104 | 4.30E-07 | 9.56E-06 | 7.15E-06 | 5601/8503/355/7099/929/834/23643/4067/4973/4688/7097/7412/8743/4689/5335/5330/6347/6648/3717/4217/3553/6352/114548/3383/3303/4615/8517/3654/6885/23236/25833/2932/5332/335/3306 | 35 |
| hsa05142 | Chagas disease | 22/532 | 102/8104 | 5.20E-07 | 1.08E-05 | 8.07E-06 | 7042/5601/8503/7048/355/7099/7097/718/5330/6347/3553/6352/915/916/4615/8517/3654/23236/5332/714/713/712 | 22 |
| hsa05145 | Toxoplasmosis | 23/532 | 112/8104 | 7.25E-07 | 1.35E-05 | 1.01E-05 | 7042/5601/3122/5294/7099/3115/3587/23643/3123/330/7097/3113/3111/4261/3717/240/3303/284217/4615/8517/3654/6885/3306 | 23 |
| hsa05132 | Salmonella infection | 38/532 | 249/8104 | 7.40E-07 | 1.35E-05 | 1.01E-05 | 7295/5601/79659/5788/5294/7099/929/834/23643/330/3071/7097/837/7846/8743/4609/8767/347733/83439/23191/5585/10540/5217/3553/114548/79443/4615/382/8517/3654/6885/2318/203068/3839/83547/10392/10810/399 | 38 |
| hsa04621 | NOD-like receptor signaling pathway | 31/532 | 184/8104 | 9.31E-07 | 1.61E-05 | 1.20E-05 | 7295/5601/118429/2634/7099/834/330/837/115361/8767/5330/84674/6347/5585/64127/51393/3553/6352/114548/3428/4615/5580/8517/79184/2635/6885/23236/5332/10392/2633/115362 | 31 |
| hsa05144 | Malaria | 14/532 | 50/8104 | 2.42E-06 | 3.95E-05 | 2.96E-05 | 7042/3820/3689/7099/7097/7412/2995/6347/7058/7057/3553/3383/3683/4615 | 14 |
| hsa04659 | Th17 cell differentiation | 21/532 | 108/8104 | 5.51E-06 | 8.57E-05 | 6.41E-05 | 861/5601/3561/7048/3122/920/3115/3123/3113/196/3111/5335/3717/3566/3553/915/916/8517/50615/2625/3662 | 21 |
| hsa04933 | AGE-RAGE signaling pathway in diabetic complications | 20/532 | 100/8104 | 5.88E-06 | 8.72E-05 | 6.52E-05 | 7042/5601/8503/7048/7412/5335/5330/6347/1906/3717/4313/1278/3553/1281/2335/3383/5580/23236/5332/1287 | 20 |
| hsa05323 | Rheumatoid arthritis | 19/532 | 93/8104 | 7.26E-06 | 0.000103 | 7.67E-05 | 7042/3122/942/3689/7099/3115/3123/7097/3113/3111/10673/6347/1513/3553/6352/3383/3683/1435/537 | 19 |
| hsa04380 | Osteoclast differentiation | 23/532 | 128/8104 | 8.00E-06 | 0.000108 | 8.09E-05 | 7042/5601/8503/695/7048/3937/2213/2212/4688/1436/4689/29760/7305/54209/1513/140885/2214/3553/11006/1435/8517/6885/2534 | 23 |
| hsa04613 | Neutrophil extracellular trap formation | 29/532 | 190/8104 | 1.55E-05 | 0.000201 | 0.00015 | 8503/51311/3684/3689/7099/834/2212/64581/4688/51284/7097/1183/837/718/4689/5335/55506/5330/10013/727/366/2214/2357/3683/3066/6885/23236/5332/6404 | 29 |
| hsa05340 | Primary immunodeficiency | 11/532 | 38/8104 | 2.08E-05 | 0.000259 | 0.000193 | 695/3561/5788/920/3575/4261/29760/6890/915/916/8517 | 11 |
| hsa05320 | Autoimmune thyroid disease | 13/532 | 53/8104 | 2.67E-05 | 0.00032 | 0.000239 | 3122/942/355/3115/3123/3113/3135/3111/3134/3106/3133/3105/5551 | 13 |
| hsa04610 | Complement and coagulation cascades | 17/532 | 85/8104 | 2.93E-05 | 0.000338 | 0.000253 | 3684/3689/3687/716/719/718/2/5265/1361/727/5329/5328/11326/1191/714/713/712 | 17 |
| hsa04064 | NF-kappa B signaling pathway | 19/532 | 104/8104 | 3.85E-05 | 0.000413 | 0.000309 | 695/7099/929/23643/4067/330/7412/10673/5335/29760/1647/3553/3383/597/5328/4615/8517/3654/6885 | 19 |
| hsa04620 | Toll-like receptor signaling pathway | 19/532 | 104/8104 | 3.85E-05 | 0.000413 | 0.000309 | 5601/8503/51311/942/7099/929/23643/7096/51284/7097/1513/3553/6352/4615/8517/3654/6885/3627/4283 | 19 |
| hsa05321 | Inflammatory bowel disease | 14/532 | 65/8104 | 6.29E-05 | 0.000652 | 0.000488 | 7042/3561/3122/7099/3115/3123/7097/3113/3111/64127/3566/3553/50615/2625 | 14 |
| hsa05135 | Yersinia infection | 22/532 | 137/8104 | 7.58E-05 | 0.000761 | 0.000569 | 5601/8503/3937/920/7099/834/2212/3678/5335/6347/5585/3553/3676/2335/7456/114548/4615/382/8517/3654/6885/2932 | 22 |
| hsa05130 | Pathogenic Escherichia coli infection | 28/532 | 197/8104 | 8.05E-05 | 0.000782 | 0.000585 | 5601/4542/355/7099/834/2212/3071/4644/837/7846/8743/55930/347733/23191/3553/7456/114548/8936/4615/9074/382/8517/4430/3654/6885/203068/10810/2534 | 28 |
| hsa05143 | African trypanosomiasis | 10/532 | 37/8104 | 9.45E-05 | 0.00089 | 0.000666 | 355/7412/5330/8542/3553/3383/4615/23236/5332/335 | 10 |
| hsa04668 | TNF signaling pathway | 19/532 | 112/8104 | 0.00011 | 0.001004 | 0.000751 | 5601/8503/355/330/7412/3659/6347/1906/4217/64127/3553/6352/3383/1435/8517/843/6885/7133/3627 | 19 |
| hsa04936 | Alcoholic liver disease | 22/532 | 142/8104 | 0.000131 | 0.001163 | 0.00087 | 5601/355/7099/929/23643/719/718/83439/4217/126129/727/3553/4615/8517/3654/6885/2932/714/713/712/6319/6720 | 22 |
| hsa04060 | Cytokine-cytokine receptor interaction | 36/532 | 295/8104 | 0.000207 | 0.001787 | 0.001337 | 7042/658/3561/7048/920/355/3575/3587/1436/655/8743/10673/3590/10220/93/6347/1230/91/8764/9180/3566/3553/6352/3603/3597/1435/7133/55504/3627/10563/50615/4283/1439/608/939/729230 | 36 |
| hsa05146 | Amoebiasis | 17/532 | 102/8104 | 0.000311 | 0.002611 | 0.001953 | 7042/8503/3684/3689/7099/929/7097/5330/1278/3553/1281/2335/284217/384/23236/5332/1287 | 17 |
| hsa05166 | Human T-cell leukemia virus 1 infection | 28/532 | 222/8104 | 0.000612 | 0.005012 | 0.003749 | 4488/7042/5601/8503/3561/7048/3122/3689/920/3115/3123/8829/2113/3113/3135/3111/567/3134/4609/83660/3106/3133/915/3383/3683/916/8517/3105 | 28 |
| hsa05162 | Measles | 20/532 | 139/8104 | 0.000702 | 0.0056 | 0.004189 | 5601/8503/3561/2213/355/7099/51284/7097/4478/3553/915/916/3303/4615/8517/3654/6885/2932/1021/3306 | 20 |
| hsa05164 | Influenza A | 23/532 | 171/8104 | 0.000761 | 0.005913 | 0.004423 | 8503/3122/355/7099/3115/834/3123/51284/3113/3111/8743/4261/8480/6347/3717/3553/6352/114548/3383/4615/8517/1021/3627 | 23 |
| hsa05205 | Proteoglycans in cancer | 26/532 | 205/8104 | 0.000873 | 0.006487 | 0.004853 | 2066/7042/8503/355/7099/3678/7097/4478/8826/4609/5335/960/4313/4060/7057/1634/1278/2335/5329/5328/7481/8322/2318/10855/7474/2260 | 26 |
| hsa04658 | Th1 and Th2 cell differentiation | 15/532 | 92/8104 | 0.000876 | 0.006487 | 0.004853 | 5601/3561/3122/920/3115/3123/3113/3111/5335/3717/3566/915/916/8517/2625 | 15 |
| hsa05134 | Legionellosis | 11/532 | 57/8104 | 0.001021 | 0.007382 | 0.005522 | 3684/3689/7099/929/834/7097/718/3553/3303/4615/3306 | 11 |
| hsa05170 | Human immunodeficiency virus 1 infection | 26/532 | 212/8104 | 0.001435 | 0.010143 | 0.007587 | 5601/8503/920/355/7099/54331/7097/3135/567/3134/5335/6892/140564/6890/85417/3106/3133/915/916/4615/8517/3654/6885/7133/3105/162 | 26 |
| hsa04010 | MAPK signaling pathway | 33/532 | 294/8104 | 0.001632 | 0.011117 | 0.008316 | 2066/7042/5601/7048/355/929/4208/1436/51347/4609/7786/1647/10125/4217/9254/2252/5156/3553/3303/1435/784/9448/4615/8517/3654/3925/51701/6885/2318/2260/3815/11184/3306 | 33 |
| hsa04512 | ECM-receptor interaction | 14/532 | 88/8104 | 0.001644 | 0.011117 | 0.008316 | 3678/3694/960/9900/7058/7057/1278/22801/1293/3676/2335/284217/1287/3371 | 14 |
| hsa05167 | Kaposi sarcoma-associated herpesvirus infection | 24/532 | 194/8104 | 0.001918 | 0.01269 | 0.009492 | 5601/8503/942/355/5294/54331/4067/3135/718/3134/4609/5335/3717/1230/83439/3106/3133/9976/3383/3055/8517/2932/1021/3105 | 24 |
| hsa04650 | Natural killer cell mediated cytotoxicity | 18/532 | 131/8104 | 0.002172 | 0.014071 | 0.010525 | 8503/3937/2207/3689/355/3135/8743/5335/7305/3106/3133/2214/3383/3683/962/3105/5551/2534 | 18 |
| hsa05171 | Coronavirus disease - COVID-19 | 27/532 | 232/8104 | 0.002529 | 0.016054 | 0.012008 | 5601/8503/51311/7099/834/2212/716/8829/51284/7097/719/718/51065/5335/6347/727/3553/114548/4615/8517/6132/3654/6885/714/713/712/3627 | 27 |
| hsa04611 | Platelet activation | 17/532 | 124/8104 | 0.00292 | 0.01816 | 0.013584 | 8503/695/3937/2207/5294/2212/4067/6916/54518/5330/83660/10125/1278/1281/23236/5332/2534 | 17 |
| hsa04670 | Leukocyte transendothelial migration | 16/532 | 114/8104 | 0.003018 | 0.018406 | 0.013768 | 8503/3684/3689/4688/7412/4478/4689/5335/83593/4313/3702/3676/3383/3683/9074/399 | 16 |
| hsa05131 | Shigellosis | 28/532 | 247/8104 | 0.003113 | 0.01862 | 0.013928 | 5601/8503/7099/929/834/3678/837/718/5335/8767/5330/83660/960/5217/3553/6352/114548/8936/4615/5580/382/8517/6885/23048/23236/2932/5332/10392 | 28 |
| hsa05415 | Diabetic cardiomyopathy | 24/532 | 203/8104 | 0.003502 | 0.02055 | 0.015372 | 6262/7042/5601/5160/8503/7048/4688/4689/5330/5164/4313/1278/1281/9945/4731/1349/1537/5580/1345/4694/23236/2932/7381/5332 | 24 |
| hsa04062 | Chemokine signaling pathway | 23/532 | 192/8104 | 0.003572 | 0.02057 | 0.015386 | 2870/8503/1794/5294/54331/4067/5335/5330/6347/3717/1230/3702/6352/3055/5580/8517/23236/2932/5332/3627/10563/4283/729230 | 23 |
| hsa04672 | Intestinal immune network for IgA production | 9/532 | 49/8104 | 0.004091 | 0.022763 | 0.017027 | 3122/942/3115/3123/3113/3111/10673/3676/608 | 9 |
| hsa05412 | Arrhythmogenic right ventricular cardiomyopathy | 12/532 | 77/8104 | 0.004112 | 0.022763 | 0.017027 | 6262/3678/3694/83439/9254/22801/3676/284217/784/2010/1000/5318 | 12 |
| hsa05418 | Fluid shear stress and atherosclerosis | 18/532 | 139/8104 | 0.004172 | 0.022763 | 0.017027 | 7295/5601/8503/658/4208/4688/7412/93/6347/1906/4217/4313/3162/3553/3383/445/8517/6885 | 18 |
| hsa04151 | PI3K-Akt signaling pathway | 36/532 | 354/8104 | 0.005474 | 0.028906 | 0.021622 | 2066/8503/3561/5294/3575/7099/54331/3678/1436/7097/4609/3694/3717/9180/5585/7533/118788/3566/2252/7058/7057/5156/1278/22801/1293/3676/2335/1435/284217/8517/2932/1021/2260/1287/3815/3371 | 36 |
| hsa04061 | Viral protein interaction with cytokine and cytokine receptor | 14/532 | 100/8104 | 0.005484 | 0.028906 | 0.021622 | 3561/3587/1436/8743/6347/1230/8764/6352/1435/7133/3627/10563/4283/729230 | 14 |
| hsa05163 | Human cytomegalovirus infection | 25/532 | 225/8104 | 0.006545 | 0.033927 | 0.025378 | 8503/355/54331/3587/3135/567/5732/3134/4609/6892/5330/6347/1230/6890/3106/3133/5156/3553/6352/8517/23236/2932/5332/1021/3105 | 25 |
| hsa05225 | Hepatocellular carcinoma | 20/532 | 168/8104 | 0.006806 | 0.034701 | 0.025957 | 7042/8503/7048/6602/4040/4609/5335/83439/1647/1856/3162/7481/6605/6604/8322/2932/7474/8110/1021/6595 | 20 |
| hsa04210 | Apoptosis | 17/532 | 136/8104 | 0.007532 | 0.037782 | 0.028261 | 5601/8503/355/1512/330/7846/8743/1647/1520/4217/1513/597/8517/843/10039/1439/5551 | 17 |
| hsa04660 | T cell receptor signaling pathway | 14/532 | 104/8104 | 0.007763 | 0.03832 | 0.028664 | 5601/8503/5788/3937/920/5335/10125/3702/915/916/8517/6885/2932/2534 | 14 |
| hsa04810 | Regulation of actin cytoskeleton | 24/532 | 218/8104 | 0.008525 | 0.041424 | 0.030986 | 8503/3684/9459/3689/3687/3678/3071/4478/8826/79837/3694/55740/23191/5217/2252/5156/22801/3676/2335/3683/1131/8936/10788/2260 | 24 |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GO | | | | | | | | |
| ID | Description | GeneRatio | BgRatio | pvalue | p.adjust | qvalue | geneID | Count |
| GO:0007159 | leukocyte cell-cell adhesion | 67/973 | 328/17913 | 1.94E-21 | 1.04E-17 | 7.82E-18 | 861/7037/7048/942/5788/84868/26191/3689/6793/920/2213/199/3575/3115/10457/4067/2113/3678/3071/3113/7412/3135/4478/81704/655/634/10673/3485/3659/8767/1949/1803/6347/3958/972/8764/10125/8876/960/64127/3133/6402/80380/11151/3566/4907/3553/11006/3676/6352/114548/3383/3683/916/11326/301/445/3654/384/57045/64332/2625/6404/939/54900/729230/2534 | 67 |
| GO:0042110 | T cell activation | 75/973 | 443/17913 | 7.99E-19 | 2.14E-15 | 1.61E-15 | 861/7037/7048/942/5788/84868/1794/26191/920/2213/199/5294/3575/3115/10875/10457/4067/64581/3071/3113/7412/5873/54518/3135/3111/567/4478/81704/3936/634/10673/3485/3659/8767/1949/1803/6347/3958/972/8764/10125/8876/960/64127/3133/80380/11151/3566/3702/3553/11006/914/6352/114548/915/3383/3683/639/916/11326/301/384/57045/7133/1021/64332/3815/399/114836/2625/3662/939/54900/729230/2534 | 75 |
| GO:1903037 | regulation of leukocyte cell-cell adhesion | 59/973 | 295/17913 | 1.51E-18 | 2.70E-15 | 2.02E-15 | 861/7037/7048/942/5788/84868/26191/3689/920/2213/199/3575/3115/10457/4067/2113/3071/3113/7412/3135/81704/634/10673/3485/3659/8767/1949/1803/6347/3958/972/8764/10125/8876/960/64127/3133/80380/11151/3566/3553/11006/3676/6352/114548/3383/916/11326/301/445/3654/384/57045/64332/2625/939/54900/729230/2534 | 59 |
| GO:0002694 | regulation of leukocyte activation | 79/973 | 492/17913 | 2.31E-18 | 3.10E-15 | 2.32E-15 | 861/7037/695/3684/7048/942/5788/2207/84868/26191/3689/920/2213/199/3575/7099/3115/64092/8832/4208/10457/4067/4332/3071/3113/7412/196/3135/3111/81704/634/3134/10673/3485/3659/8767/1949/1803/6347/3958/10193/972/8764/7305/10125/8876/54209/5585/120892/64127/3133/80380/11151/3566/7057/3162/3553/11006/914/6352/114548/639/916/11326/301/384/10039/57045/7474/7133/712/64332/2625/56833/3662/939/54900/729230/2534 | 79 |
| GO:0071346 | cellular response to interferon-gamma | 41/973 | 153/17913 | 5.24E-18 | 5.62E-15 | 4.22E-15 | 3122/2634/199/7099/3115/834/3123/7097/3113/7412/3135/567/3134/4684/4261/115361/3659/7726/10346/6347/1906/3717/3394/960/4502/3106/3133/140885/6352/3383/3055/445/5580/252983/7474/84166/2633/115362/3105/10437/3662 | 41 |
| GO:0051249 | regulation of lymphocyte activation | 69/973 | 401/17913 | 8.71E-18 | 7.78E-15 | 5.84E-15 | 861/7037/695/7048/942/5788/84868/26191/920/2213/199/3575/7099/3115/64092/4208/10457/4067/4332/3071/3113/7412/196/3135/3111/81704/634/3134/10673/3485/3659/8767/1949/1803/6347/3958/10193/972/8764/7305/10125/8876/5585/64127/3133/80380/11151/3566/3553/11006/914/6352/114548/639/916/11326/301/384/10039/57045/7133/64332/2625/56833/3662/939/54900/729230/2534 | 69 |
| GO:1903039 | positive regulation of leukocyte cell-cell adhesion | 48/973 | 214/17913 | 2.07E-17 | 1.47E-14 | 1.11E-14 | 861/7037/7048/942/5788/84868/3689/920/199/3575/3115/4067/2113/3071/3113/7412/3135/81704/10673/3485/8767/1949/1803/6347/972/8764/10125/8876/960/64127/3133/80380/11151/3566/3553/11006/3676/6352/114548/3383/916/301/3654/64332/2625/939/729230/2534 | 48 |
| GO:0045785 | positive regulation of cell adhesion | 67/973 | 388/17913 | 2.20E-17 | 1.47E-14 | 1.11E-14 | 861/7037/7042/7048/942/5788/84868/3689/920/199/3575/3115/4067/8829/2113/3678/3071/3113/7412/54518/3135/81704/8826/655/10673/3485/8767/1949/57669/1803/6347/3717/972/8764/10125/8876/960/64127/3133/80380/11151/3566/3553/11006/3676/2335/1295/6352/114548/3383/151887/916/301/1435/9448/3654/2932/7474/1021/64332/335/342184/10563/2625/939/729230/2534 | 67 |
| GO:0022407 | regulation of cell-cell adhesion | 67/973 | 389/17913 | 2.52E-17 | 1.50E-14 | 1.13E-14 | 861/7037/7048/942/5788/84868/26191/3689/920/2213/199/3575/3115/10457/4067/2113/3071/3113/7412/3135/81704/655/634/10673/3485/3659/8767/1949/57669/1803/6347/3717/3958/972/8764/10125/8876/960/64127/3133/80380/11151/3566/3553/11006/3676/6591/6352/114548/3383/916/11326/301/445/5580/3654/384/57045/7474/64332/335/10563/2625/939/54900/729230/2534 | 67 |
| GO:0034341 | response to interferon-gamma | 42/973 | 173/17913 | 1.03E-16 | 5.55E-14 | 4.16E-14 | 3122/2634/199/7099/3115/834/3123/7097/3113/7412/3135/567/3134/4684/4261/115361/3659/7726/10346/6347/1906/3717/3394/960/4502/3106/3133/140885/6352/3383/3055/445/51667/5580/252983/7474/84166/2633/115362/3105/10437/3662 | 42 |
| GO:0022409 | positive regulation of cell-cell adhesion | 51/973 | 251/17913 | 1.69E-16 | 8.24E-14 | 6.19E-14 | 861/7037/7048/942/5788/84868/3689/920/199/3575/3115/4067/2113/3071/3113/7412/3135/81704/655/10673/3485/8767/1949/1803/6347/972/8764/10125/8876/960/64127/3133/80380/11151/3566/3553/11006/3676/6352/114548/3383/916/301/3654/7474/64332/10563/2625/939/729230/2534 | 51 |
| GO:0050863 | regulation of T cell activation | 57/973 | 307/17913 | 2.04E-16 | 9.11E-14 | 6.84E-14 | 861/7037/7048/942/5788/84868/26191/920/2213/199/3575/3115/10457/4067/3071/3113/7412/3135/3111/81704/634/10673/3485/3659/8767/1949/1803/6347/3958/972/8764/10125/8876/64127/3133/80380/11151/3566/3553/11006/914/6352/114548/639/916/11326/301/384/57045/7133/64332/2625/3662/939/54900/729230/2534 | 57 |
| GO:0050867 | positive regulation of cell activation | 58/973 | 319/17913 | 2.99E-16 | 1.23E-13 | 9.25E-14 | 861/7037/695/3684/7048/942/5788/2207/84868/3689/920/199/3575/7099/3115/4208/4067/5341/3071/3113/7412/3135/81704/3134/10673/3485/8767/1949/1803/6347/3717/972/8764/7305/10125/8876/54209/120892/64127/3133/80380/11151/3566/7057/3553/11006/914/6352/114548/916/301/7474/712/64332/2625/939/729230/2534 | 58 |
| GO:0002696 | positive regulation of leukocyte activation | 56/973 | 305/17913 | 6.30E-16 | 2.41E-13 | 1.81E-13 | 861/7037/695/3684/7048/942/5788/2207/84868/3689/920/199/3575/7099/3115/4208/4067/3071/3113/7412/3135/81704/3134/10673/3485/8767/1949/1803/6347/972/8764/7305/10125/8876/54209/120892/64127/3133/80380/11151/3566/7057/3553/11006/914/6352/114548/916/301/7474/712/64332/2625/939/729230/2534 | 56 |
| GO:0070661 | leukocyte proliferation | 52/973 | 270/17913 | 9.01E-16 | 3.22E-13 | 2.42E-13 | 7037/695/7048/5788/84868/1794/26191/920/2213/199/5294/3575/7099/3115/4208/10457/4067/4332/1436/3071/3113/7412/196/3135/4478/81704/10673/3485/3659/8767/3958/972/7305/5585/3133/80380/11151/3553/6352/916/11326/301/1435/5580/1191/384/57045/7133/3815/3251/729230/2534 | 52 |
| GO:0002460 | adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | 54/973 | 295/17913 | 2.41E-15 | 8.07E-13 | 6.06E-13 | 7037/695/51311/5788/2207/84868/920/2213/3575/7099/10875/4208/1512/716/23180/5873/3135/567/718/634/3134/10673/11118/8767/54795/10384/972/163486/5585/3133/727/3566/3553/114548/3383/301/5580/1191/10039/6885/89857/714/7133/713/712/64332/3251/10563/114836/2625/3662/5551/939/729230 | 54 |
| GO:0032943 | mononuclear cell proliferation | 48/973 | 246/17913 | 6.94E-15 | 2.19E-12 | 1.64E-12 | 7037/695/7048/5788/84868/1794/26191/920/2213/199/5294/3575/7099/3115/4208/10457/4332/3071/3113/7412/196/3135/4478/81704/10673/3485/3659/8767/3958/972/7305/5585/3133/80380/11151/3553/6352/916/11326/301/1435/5580/384/57045/7133/3251/729230/2534 | 48 |
| GO:0001819 | positive regulation of cytokine production | 68/973 | 446/17913 | 8.44E-15 | 2.51E-12 | 1.89E-12 | 861/10555/51311/942/5788/2207/84868/26191/920/199/7099/929/3115/834/23643/330/7096/1436/51284/7097/719/3113/3135/567/718/3134/3659/8767/3717/972/7305/10125/3394/54209/120892/64127/3133/727/4060/3566/57493/7057/3162/10631/3553/914/114548/916/55959/301/3303/3428/7481/4615/3066/1191/3654/6885/23236/10855/7474/10392/115362/114836/2625/3662/5434/729230 | 68 |
| GO:0050870 | positive regulation of T cell activation | 42/973 | 198/17913 | 1.70E-14 | 4.79E-12 | 3.60E-12 | 861/7037/7048/942/5788/84868/920/199/3575/3115/4067/3071/3113/7412/3135/81704/10673/3485/8767/1949/1803/6347/972/8764/10125/8876/64127/3133/80380/11151/3566/3553/11006/6352/114548/916/301/64332/2625/939/729230/2534 | 42 |
| GO:0060333 | interferon-gamma-mediated signaling pathway | 28/973 | 91/17913 | 2.16E-14 | 5.65E-12 | 4.24E-12 | 3122/2634/3115/3123/3113/7412/3135/567/3134/4684/4261/3659/7726/10346/3717/3394/960/4502/3106/3133/3383/3055/5580/84166/2633/3105/10437/3662 | 28 |
| GO:0046651 | lymphocyte proliferation | 47/973 | 244/17913 | 2.21E-14 | 5.65E-12 | 4.24E-12 | 7037/695/7048/5788/84868/1794/26191/920/2213/199/5294/3575/7099/3115/4208/10457/4332/3071/3113/7412/196/3135/4478/81704/10673/3485/3659/8767/3958/972/7305/5585/3133/80380/11151/3553/6352/916/11326/301/5580/384/57045/7133/3251/729230/2534 | 47 |
| GO:0030198 | extracellular matrix organization | 56/973 | 334/17913 | 3.68E-14 | 8.97E-12 | 6.74E-12 | 2683/7042/2296/3684/3689/3687/2113/3678/7412/6624/3936/2/3694/4237/1803/1361/1520/960/4313/1513/4060/2191/7057/5156/1634/1278/22801/1293/1289/8038/3676/1281/2335/1295/4015/81621/3383/1462/3683/151887/6678/83716/1290/2200/55959/284217/5650/2201/56999/8751/7133/9508/1287/5268/23768/3371 | 56 |
| GO:0043062 | extracellular structure organization | 60/973 | 387/17913 | 1.60E-13 | 3.72E-11 | 2.79E-11 | 2683/7042/2296/3684/3689/3687/2113/3678/7412/655/6624/3936/2/3694/4237/1803/1361/1520/960/4313/1513/4060/2191/7057/5156/1634/1278/22801/1293/1289/8038/3676/1281/2335/1295/4015/81621/3383/1462/3683/151887/6678/83716/1290/2200/55959/284217/5650/2201/56999/8751/8694/341/7133/9508/1287/5268/23768/335/3371 | 60 |
| GO:0051251 | positive regulation of lymphocyte activation | 47/973 | 258/17913 | 1.93E-13 | 4.30E-11 | 3.23E-11 | 861/7037/695/7048/942/5788/84868/920/199/3575/7099/3115/4208/4067/3071/3113/7412/3135/81704/3134/10673/3485/8767/1949/1803/6347/972/8764/7305/10125/8876/64127/3133/80380/11151/3566/3553/11006/6352/114548/916/301/64332/2625/939/729230/2534 | 47 |
| GO:0032944 | regulation of mononuclear cell proliferation | 40/973 | 200/17913 | 5.47E-13 | 1.17E-10 | 8.81E-11 | 7037/695/7048/5788/84868/26191/920/2213/199/7099/3115/4208/10457/4332/3071/3113/7412/196/3135/10673/3485/3659/8767/3958/972/7305/5585/3133/80380/11151/3553/6352/916/11326/301/1435/384/57045/7133/729230 | 40 |
| GO:0070663 | regulation of leukocyte proliferation | 41/973 | 214/17913 | 1.23E-12 | 2.54E-10 | 1.91E-10 | 7037/695/7048/5788/84868/26191/920/2213/199/7099/3115/4208/10457/4067/4332/3071/3113/7412/196/3135/10673/3485/3659/8767/3958/972/7305/5585/3133/80380/11151/3553/6352/916/11326/301/1435/384/57045/7133/729230 | 41 |
| GO:0045088 | regulation of innate immune response | 63/973 | 440/17913 | 1.51E-12 | 2.99E-10 | 2.24E-10 | 695/51311/3684/2207/84868/26191/3689/2213/7099/929/23643/4067/330/7096/64581/4332/51284/7097/23180/3135/5696/634/3134/2/55198/3659/8767/3717/1520/10125/64127/3133/5698/10225/118788/1513/6352/3055/11326/3303/3656/3428/57402/4615/81622/5580/5720/57142/8517/4582/3654/7804/60343/6885/7474/10392/22841/84166/115362/114836/56833/3662/2534 | 63 |
| GO:0002521 | leukocyte differentiation | 67/973 | 485/17913 | 1.56E-12 | 2.99E-10 | 2.24E-10 | 861/7037/695/7048/942/5788/2207/1794/26191/920/2213/3575/7099/2124/55619/4208/4067/1436/3071/7097/7412/3135/3111/567/634/4609/3659/8767/29760/10193/1230/972/7305/10125/8876/54209/3566/9770/11006/3676/914/114548/915/639/916/2200/301/1435/6988/3930/2101/3428/133522/84456/537/714/1021/4495/64332/3815/399/114836/2625/56833/3662/939/729230 | 67 |
| GO:0050670 | regulation of lymphocyte proliferation | 39/973 | 199/17913 | 2.09E-12 | 3.86E-10 | 2.90E-10 | 7037/695/7048/5788/84868/26191/920/2213/199/7099/3115/4208/10457/4332/3071/3113/7412/196/3135/10673/3485/3659/8767/3958/972/7305/5585/3133/80380/11151/3553/6352/916/11326/301/384/57045/7133/729230 | 39 |
| GO:1902105 | regulation of leukocyte differentiation | 46/973 | 267/17913 | 2.74E-12 | 4.89E-10 | 3.67E-10 | 861/695/7048/942/5788/920/2213/3575/7099/2124/4067/3071/3135/3111/634/4609/3659/8767/10193/1230/972/7305/10125/8876/54209/3566/9770/11006/914/114548/639/2200/301/1435/6988/2101/133522/537/714/1021/64332/2625/56833/3662/939/729230 | 46 |
| GO:0002819 | regulation of adaptive immune response | 33/973 | 150/17913 | 3.85E-12 | 6.66E-10 | 5.00E-10 | 7037/695/5788/2207/84868/920/2213/3575/64092/4208/3135/567/718/634/3134/10673/3659/8767/54795/8764/5585/3133/3566/3553/114548/962/301/10039/6885/7133/64332/2625/729230 | 33 |
| GO:0042119 | neutrophil activation | 67/973 | 499/17913 | 5.83E-12 | 9.76E-10 | 7.32E-10 | 23250/10555/26578/2683/3684/3903/9535/5788/2207/1794/3689/6793/2213/929/10875/11031/963/2212/3687/1512/79895/4332/4973/11010/3071/7097/719/5873/567/1992/8826/718/634/3958/116844/5265/23191/1520/7305/8876/960/9961/6402/140885/7130/2357/6352/4069/5329/51411/3683/83716/5328/240/3303/5580/3934/1774/3482/10788/203068/10855/30/8694/7133/968/10043 | 67 |
| GO:0002449 | lymphocyte mediated immunity | 48/973 | 293/17913 | 6.03E-12 | 9.80E-10 | 7.35E-10 | 7037/695/51311/5788/2207/84868/2213/3575/10875/1512/716/23180/5873/3135/567/718/634/3134/11118/54795/10384/972/10125/163486/3133/727/11151/10225/3566/3553/114548/3383/5580/1191/10039/6885/203068/714/7133/713/712/3251/114836/57823/2625/5551/939/729230 | 48 |
| GO:0002440 | production of molecular mediator of immune response | 37/973 | 191/17913 | 1.11E-11 | 1.74E-09 | 1.31E-09 | 7037/7042/695/5788/2207/2213/3575/7099/10875/7097/3135/567/3134/10673/56259/54795/972/163486/5585/64127/3133/10225/3566/3162/3553/114548/5650/2590/10039/6885/7474/7133/3815/335/2625/54900/729230 | 37 |
| GO:0002237 | response to molecule of bacterial origin | 49/973 | 309/17913 | 1.22E-11 | 1.87E-09 | 1.41E-09 | 4064/84868/26191/2213/9450/7099/929/834/3587/23643/4208/4067/7096/7097/7412/10949/567/5732/259230/1312/8767/6347/1906/3717/3394/54209/64127/10225/140885/1634/3553/6352/114548/3383/6678/3055/3656/445/57402/3066/249/3934/3654/7474/92140/7133/968/3627/1439 | 49 |
| GO:0043312 | neutrophil degranulation | 65/973 | 485/17913 | 1.32E-11 | 1.95E-09 | 1.47E-09 | 23250/10555/26578/2683/3684/3903/9535/5788/2207/1794/3689/6793/929/10875/11031/963/2212/3687/1512/79895/4332/4973/11010/3071/7097/719/5873/567/1992/8826/718/634/3958/116844/5265/23191/1520/7305/8876/960/9961/6402/140885/7130/2357/4069/5329/51411/3683/83716/5328/240/3303/5580/3934/1774/3482/10788/203068/10855/30/8694/7133/968/10043 | 65 |
| GO:0002683 | negative regulation of immune system process | 62/973 | 451/17913 | 1.35E-11 | 1.95E-09 | 1.47E-09 | 861/7042/695/5788/2207/84868/26191/2213/3575/7099/929/10875/64092/8832/23643/10457/4067/4332/3135/3111/5094/634/3134/2/4609/6895/3659/6347/3958/972/8764/7305/5585/3133/727/80380/10225/3566/7057/3162/11006/1281/11326/2200/301/6988/3428/384/60343/10039/23236/57045/714/1021/84166/2633/968/335/56833/3662/54900/729230 | 62 |
| GO:0002283 | neutrophil activation involved in immune response | 65/973 | 488/17913 | 1.74E-11 | 2.45E-09 | 1.84E-09 | 23250/10555/26578/2683/3684/3903/9535/5788/2207/1794/3689/6793/929/10875/11031/963/2212/3687/1512/79895/4332/4973/11010/3071/7097/719/5873/567/1992/8826/718/634/3958/116844/5265/23191/1520/7305/8876/960/9961/6402/140885/7130/2357/4069/5329/51411/3683/83716/5328/240/3303/5580/3934/1774/3482/10788/203068/10855/30/8694/7133/968/10043 | 65 |
| GO:0050900 | leukocyte migration | 63/973 | 467/17913 | 2.08E-11 | 2.86E-09 | 2.15E-09 | 2683/7042/3684/2207/3689/6793/199/5294/4354/3687/8832/4067/3678/4973/3071/719/7412/2995/3269/4478/81704/634/5335/6347/54795/1906/3958/1230/972/960/54209/727/6402/11151/140885/7057/1278/3162/3676/2335/914/6352/3383/3603/3683/962/3055/301/1435/57402/80270/23604/23236/7474/3627/3815/10563/9123/2625/56833/6404/729230/2534 | 63 |
| GO:0002456 | T cell mediated immunity | 24/973 | 88/17913 | 2.77E-11 | 3.71E-09 | 2.79E-09 | 5788/2213/3575/1512/23180/5873/3135/567/634/3134/11118/54795/10384/163486/3133/3553/114548/3383/6885/7133/3251/2625/5551/729230 | 24 |
| GO:1903557 | positive regulation of tumor necrosis factor superfamily cytokine production | 23/973 | 81/17913 | 2.90E-11 | 3.79E-09 | 2.84E-09 | 942/5788/2207/84868/7099/929/23643/7096/7097/8767/3717/7305/10125/120892/64127/3133/7057/914/3066/1191/7474/10392/729230 | 23 |
| GO:0045089 | positive regulation of innate immune response | 54/973 | 373/17913 | 4.05E-11 | 5.16E-09 | 3.87E-09 | 695/51311/3684/2207/84868/26191/3689/7099/929/23643/4067/330/7096/64581/4332/51284/7097/23180/3135/5696/3134/55198/3659/8767/1520/10125/64127/3133/5698/118788/1513/6352/3055/3303/3656/3428/57402/4615/81622/5580/5720/57142/8517/4582/3654/6885/7474/10392/22841/84166/115362/114836/3662/2534 | 54 |
| GO:0002697 | regulation of immune effector process | 60/973 | 441/17913 | 4.47E-11 | 5.58E-09 | 4.19E-09 | 7037/7042/695/3684/942/5788/2207/84868/3689/2213/3575/7099/10875/8832/4067/330/716/719/3135/567/718/5094/634/3134/2/55198/6895/8767/54795/3958/972/1361/10125/5585/64127/3133/727/10225/3566/3162/3553/114548/11326/301/5650/1191/10039/6885/7474/714/7133/713/712/64332/335/114836/2625/56833/3662/729230 | 60 |
| GO:0002446 | neutrophil mediated immunity | 65/973 | 499/17913 | 4.63E-11 | 5.63E-09 | 4.23E-09 | 23250/10555/26578/2683/3684/3903/9535/5788/2207/1794/3689/6793/929/10875/11031/963/2212/3687/1512/79895/4332/4973/11010/3071/7097/719/5873/567/1992/8826/718/634/3958/116844/5265/23191/1520/7305/8876/960/9961/6402/140885/7130/2357/4069/5329/51411/3683/83716/5328/240/3303/5580/3934/1774/3482/10788/203068/10855/30/8694/7133/968/10043 | 65 |
| GO:0019882 | antigen processing and presentation | 39/973 | 220/17913 | 5.22E-11 | 6.22E-09 | 4.67E-09 | 3122/2213/3115/10875/3123/1512/4688/23180/3113/5873/3135/3111/567/5696/3134/4689/6892/3797/972/51762/1520/54209/6890/3106/10540/64127/3133/5698/7057/3383/55016/5720/8517/83547/10392/3105/968/10437/162 | 39 |
| GO:0002224 | toll-like receptor signaling pathway | 31/973 | 147/17913 | 5.48E-11 | 6.38E-09 | 4.79E-09 | 695/51311/3684/84868/26191/3689/7099/929/23643/4067/330/7096/51284/7097/23180/55198/3659/8767/1520/118788/1513/3656/57402/4615/81622/57142/8517/3654/6885/22841/3662 | 31 |
| GO:0032103 | positive regulation of response to external stimulus | 48/973 | 315/17913 | 8.31E-11 | 9.48E-09 | 7.12E-09 | 695/4064/3684/2207/84868/3689/9450/199/5294/7099/23643/8829/2113/51284/3071/7097/719/718/8767/1906/3717/347733/1230/972/1361/54209/9180/120892/64127/3133/7057/3553/6352/3603/1435/5650/57402/4615/23604/7474/10392/712/115362/2260/64332/3627/10563/729230 | 48 |
| GO:0032760 | positive regulation of tumor necrosis factor production | 22/973 | 78/17913 | 9.01E-11 | 1.01E-08 | 7.55E-09 | 5788/2207/84868/7099/929/23643/7096/7097/8767/3717/7305/10125/120892/64127/3133/7057/914/3066/1191/7474/10392/729230 | 22 |
| GO:0032496 | response to lipopolysaccharide | 46/973 | 295/17913 | 9.38E-11 | 1.03E-08 | 7.70E-09 | 4064/84868/26191/9450/7099/929/834/3587/23643/4208/4067/7097/7412/10949/5732/259230/1312/8767/6347/1906/3717/3394/54209/64127/10225/140885/1634/3553/6352/114548/3383/6678/3055/3656/445/57402/3066/249/3934/3654/7474/92140/7133/968/3627/1439 | 46 |
| GO:0042098 | T cell proliferation | 34/973 | 177/17913 | 9.63E-11 | 1.03E-08 | 7.75E-09 | 7037/7048/5788/84868/1794/920/199/5294/3115/10457/3071/3113/7412/3135/4478/81704/10673/3485/3659/8767/3958/3133/80380/11151/3553/6352/916/11326/301/384/57045/7133/729230/2534 | 34 |
| GO:0002822 | regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains | 29/973 | 135/17913 | 1.43E-10 | 1.50E-08 | 1.13E-08 | 7037/695/5788/2207/84868/920/2213/3575/4208/3135/567/718/634/3134/10673/8767/54795/5585/3133/3566/3553/114548/301/10039/6885/7133/64332/2625/729230 | 29 |
| GO:0071219 | cellular response to molecule of bacterial origin | 34/973 | 183/17913 | 2.46E-10 | 2.54E-08 | 1.90E-08 | 4064/84868/26191/2213/9450/7099/929/834/23643/4208/4067/7096/7097/259230/8767/6347/3394/54209/64127/140885/3553/6352/114548/3383/3055/3656/445/3934/3654/7474/92140/7133/968/3627 | 34 |
| GO:0006909 | phagocytosis | 46/973 | 308/17913 | 4.07E-10 | 4.12E-08 | 3.09E-08 | 3561/3684/5788/2207/1794/3689/2213/199/7099/929/11031/2212/4067/64581/4688/3071/7097/5873/23208/718/4689/55198/5335/6347/9777/23191/7305/3394/54209/11151/140885/7057/2214/4481/3553/7456/51411/3683/3055/301/4615/5580/79767/22841/335/2534 | 46 |
| GO:0071216 | cellular response to biotic stimulus | 36/973 | 206/17913 | 4.35E-10 | 4.32E-08 | 3.24E-08 | 695/4064/84868/26191/2213/9450/7099/929/834/23643/4208/4067/7096/7097/259230/8767/6347/3394/54209/64127/140885/3553/6352/114548/3383/3055/3656/445/3934/3654/2932/7474/92140/7133/968/3627 | 36 |
| GO:0002221 | pattern recognition receptor signaling pathway | 35/973 | 197/17913 | 4.79E-10 | 4.66E-08 | 3.50E-08 | 695/51311/3684/84868/26191/3689/7099/929/23643/4067/330/7096/64581/51284/7097/23180/55198/3659/8767/1520/64127/118788/1513/3303/3656/57402/4615/81622/57142/8517/3654/6885/10392/22841/3662 | 35 |
| GO:0050777 | negative regulation of immune response | 29/973 | 143/17913 | 6.07E-10 | 5.81E-08 | 4.36E-08 | 7042/5788/84868/2213/3575/64092/8832/4067/3135/634/3134/2/3958/8764/3133/10225/3566/3162/1281/11326/301/3428/384/60343/10039/84166/335/56833/729230 | 29 |
| GO:0002367 | cytokine production involved in immune response | 24/973 | 101/17913 | 6.25E-10 | 5.87E-08 | 4.41E-08 | 7042/695/2207/7099/7097/3135/567/3134/54795/972/163486/64127/3133/10225/3162/3553/114548/6885/7474/7133/3815/335/2625/729230 | 24 |
| GO:0007254 | JNK cascade | 35/973 | 200/17913 | 7.31E-10 | 6.75E-08 | 5.07E-08 | 5601/9459/26191/2213/7099/9839/51347/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/153769/140885/9770/3553/203447/3656/9448/8517/3654/8322/6885/23236/7474/10392/55504/221472/11184/939 | 35 |
| GO:1903555 | regulation of tumor necrosis factor superfamily cytokine production | 30/973 | 155/17913 | 1.01E-09 | 9.15E-08 | 6.87E-08 | 942/5788/2207/84868/26191/7099/929/23643/10457/7096/7097/23208/8767/3717/7305/10125/54209/120892/64127/3133/140885/7057/914/3066/1191/384/7474/10392/729230/54206 | 30 |
| GO:0002700 | regulation of production of molecular mediator of immune response | 28/973 | 138/17913 | 1.18E-09 | 1.06E-07 | 7.94E-08 | 7037/7042/695/5788/2207/2213/7099/3135/567/3134/54795/972/5585/64127/3133/10225/3566/3162/3553/114548/5650/10039/6885/7474/7133/335/2625/729230 | 28 |
| GO:0050851 | antigen receptor-mediated signaling pathway | 37/973 | 224/17913 | 1.28E-09 | 1.12E-07 | 8.44E-08 | 861/695/3122/5788/3937/26191/920/2213/3115/4208/4067/3123/4332/3071/23180/3113/5696/634/5335/8767/3958/163486/5698/3702/11006/915/916/784/5720/8517/6885/89857/2633/64332/2625/54900/2534 | 37 |
| GO:0042129 | regulation of T cell proliferation | 29/973 | 149/17913 | 1.67E-09 | 1.44E-07 | 1.08E-07 | 7037/7048/5788/84868/920/199/3115/10457/3071/3113/7412/3135/10673/3485/3659/8767/3958/3133/80380/11151/3553/6352/916/11326/301/384/57045/7133/729230 | 29 |
| GO:0002718 | regulation of cytokine production involved in immune response | 21/973 | 83/17913 | 2.16E-09 | 1.83E-07 | 1.38E-07 | 7042/695/2207/7099/3135/567/3134/54795/972/64127/3133/10225/3162/3553/114548/6885/7474/7133/335/2625/729230 | 21 |
| GO:0046330 | positive regulation of JNK cascade | 26/973 | 124/17913 | 2.21E-09 | 1.85E-07 | 1.39E-07 | 2213/7099/9839/51347/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/153769/9770/3553/203447/8322/6885/23236/7474/10392/221472/11184/939 | 26 |
| GO:0032680 | regulation of tumor necrosis factor production | 29/973 | 151/17913 | 2.31E-09 | 1.90E-07 | 1.43E-07 | 5788/2207/84868/26191/7099/929/23643/10457/7096/7097/23208/8767/3717/7305/10125/54209/120892/64127/3133/140885/7057/914/3066/1191/384/7474/10392/729230/54206 | 29 |
| GO:0071706 | tumor necrosis factor superfamily cytokine production | 30/973 | 161/17913 | 2.59E-09 | 2.11E-07 | 1.58E-07 | 942/5788/2207/84868/26191/7099/929/23643/10457/7096/7097/23208/8767/3717/7305/10125/54209/120892/64127/3133/140885/7057/914/3066/1191/384/7474/10392/729230/54206 | 30 |
| GO:0050808 | synapse organization | 52/973 | 394/17913 | 2.66E-09 | 2.12E-07 | 1.59E-07 | 2066/2895/3684/2213/55619/3587/4208/8829/7097/4644/718/7846/10611/57549/1627/9746/347902/4131/8997/23191/10013/1108/120892/9254/5217/56132/7058/6678/8828/4744/8936/57633/6623/382/4038/7804/9118/23767/11202/203068/29904/221935/7474/714/10810/713/712/1000/1287/23768/3371/2534 | 52 |
| GO:0050663 | cytokine secretion | 37/973 | 230/17913 | 2.71E-09 | 2.14E-07 | 1.60E-07 | 51311/3937/84868/26191/2213/199/7099/929/834/4067/7096/1436/7097/23208/1992/11118/8767/3694/10125/120892/64127/727/3566/5552/10631/3553/2335/914/114548/301/384/7474/7133/2633/115362/335/2625 | 37 |
| GO:0002573 | myeloid leukocyte differentiation | 34/973 | 201/17913 | 3.18E-09 | 2.47E-07 | 1.86E-07 | 861/7037/7048/2207/920/7099/2124/4208/4067/1436/7097/634/4609/1230/972/7305/54209/9770/11006/2200/1435/6988/3930/2101/3428/133522/84456/537/714/1021/4495/3815/2625/3662 | 34 |
| GO:1903706 | regulation of hemopoiesis | 58/973 | 468/17913 | 3.51E-09 | 2.68E-07 | 2.02E-07 | 861/2296/695/7048/942/5788/920/2213/3575/7099/2124/4208/4067/2113/3071/3135/3111/567/5696/634/4609/3659/8767/3958/10193/1230/91/972/7305/10125/8876/54209/5698/3566/9770/7057/11006/914/4015/114548/639/2200/301/3303/1435/6988/2101/5720/133522/537/714/1021/64332/2625/56833/3662/939/729230 | 58 |
| GO:0002218 | activation of innate immune response | 45/973 | 319/17913 | 3.99E-09 | 3.01E-07 | 2.26E-07 | 695/51311/3684/2207/84868/26191/3689/7099/929/23643/4067/330/7096/64581/4332/51284/7097/23180/5696/55198/3659/8767/1520/64127/5698/118788/1513/3055/3303/3656/3428/57402/4615/81622/5580/5720/57142/8517/4582/3654/6885/10392/22841/3662/2534 | 45 |
| GO:0032640 | tumor necrosis factor production | 29/973 | 155/17913 | 4.32E-09 | 3.22E-07 | 2.42E-07 | 5788/2207/84868/26191/7099/929/23643/10457/7096/7097/23208/8767/3717/7305/10125/54209/120892/64127/3133/140885/7057/914/3066/1191/384/7474/10392/729230/54206 | 29 |
| GO:0002758 | innate immune response-activating signal transduction | 43/973 | 298/17913 | 4.43E-09 | 3.25E-07 | 2.44E-07 | 695/51311/3684/2207/84868/26191/3689/7099/929/23643/4067/330/7096/64581/51284/7097/23180/5696/55198/3659/8767/1520/64127/5698/118788/1513/3055/3303/3656/57402/4615/81622/5580/5720/57142/8517/4582/3654/6885/10392/22841/3662/2534 | 43 |
| GO:0070304 | positive regulation of stress-activated protein kinase signaling cascade | 29/973 | 156/17913 | 5.04E-09 | 3.65E-07 | 2.74E-07 | 7042/2213/7099/4067/9839/51347/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/54910/153769/9770/3553/203447/8322/6885/23236/7474/10392/221472/11184/939 | 29 |
| GO:0002703 | regulation of leukocyte mediated immunity | 32/973 | 185/17913 | 5.25E-09 | 3.75E-07 | 2.81E-07 | 7037/695/3684/5788/2207/84868/3689/2213/3575/7099/8832/4067/3135/567/718/634/3134/54795/10125/64127/3133/10225/3566/3162/3553/114548/10039/6885/7133/114836/2625/729230 | 32 |
| GO:0071222 | cellular response to lipopolysaccharide | 31/973 | 176/17913 | 5.81E-09 | 4.10E-07 | 3.07E-07 | 4064/84868/26191/9450/7099/929/834/23643/4208/4067/7097/259230/8767/6347/3394/64127/140885/3553/6352/114548/3383/3055/3656/445/3934/3654/7474/92140/7133/968/3627 | 31 |
| GO:0032609 | interferon-gamma production | 23/973 | 105/17913 | 7.66E-09 | 5.33E-07 | 4.00E-07 | 51311/84868/26191/7099/929/3115/51284/3113/11118/8767/10125/3394/80380/10225/140885/3702/3553/914/916/7474/114836/2625/729230 | 23 |
| GO:0060326 | cell chemotaxis | 38/973 | 253/17913 | 1.16E-08 | 7.90E-07 | 5.93E-07 | 7042/3689/199/5294/4354/4067/8829/3071/719/7412/3269/6347/54795/1906/3958/1230/972/727/11151/7057/5156/6352/4015/3603/51411/301/1435/57402/5580/80270/23604/7474/2260/3627/3815/10563/56833/729230 | 38 |
| GO:0050707 | regulation of cytokine secretion | 33/973 | 201/17913 | 1.16E-08 | 7.90E-07 | 5.93E-07 | 51311/84868/26191/2213/199/7099/929/834/4067/7096/1436/7097/23208/1992/8767/10125/120892/64127/727/3566/5552/10631/3553/2335/914/114548/301/384/7474/7133/2633/335/2625 | 33 |
| GO:1902107 | positive regulation of leukocyte differentiation | 27/973 | 143/17913 | 1.20E-08 | 7.96E-07 | 5.97E-07 | 861/695/7048/942/5788/920/3575/2124/3071/3135/8767/1230/972/7305/10125/8876/54209/3566/11006/114548/301/1435/133522/537/64332/2625/939 | 27 |
| GO:0002698 | negative regulation of immune effector process | 24/973 | 116/17913 | 1.20E-08 | 7.96E-07 | 5.97E-07 | 7042/5788/84868/2213/3575/10875/8832/3135/5094/634/3134/2/6895/3958/3133/10225/3566/3162/11326/301/10039/335/56833/729230 | 24 |
| GO:1903708 | positive regulation of hemopoiesis | 31/973 | 182/17913 | 1.32E-08 | 8.65E-07 | 6.50E-07 | 861/2296/695/7048/942/5788/920/3575/2124/2113/3071/3135/8767/1230/91/972/7305/10125/8876/54209/3566/11006/114548/301/3303/1435/133522/537/64332/2625/939 | 31 |
| GO:0032612 | interleukin-1 production | 23/973 | 108/17913 | 1.36E-08 | 8.75E-07 | 6.57E-07 | 51311/84868/7099/834/1992/634/8767/3717/7305/54209/64127/140885/3553/114548/301/3428/3066/384/7474/10392/115362/335/54206 | 23 |
| GO:0033627 | cell adhesion mediated by integrin | 17/973 | 61/17913 | 1.51E-08 | 9.60E-07 | 7.21E-07 | 7042/5294/4067/3678/3071/3694/1803/22801/3676/6591/6352/3383/916/5328/2200/4582/10563 | 17 |
| GO:0032663 | regulation of interleukin-2 production | 16/973 | 54/17913 | 1.52E-08 | 9.60E-07 | 7.21E-07 | 861/942/5788/84868/920/8767/3553/916/11326/301/6885/2633/2625/3662/729230/89795 | 16 |
| GO:0031098 | stress-activated protein kinase signaling cascade | 40/973 | 278/17913 | 1.66E-08 | 1.04E-06 | 7.78E-07 | 7042/5601/9459/26191/2213/355/7099/4067/9839/51347/4609/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/54910/153769/140885/9770/3553/203447/3656/9448/8517/3654/8322/6885/23236/7474/10392/55504/221472/11184/939 | 40 |
| GO:0032874 | positive regulation of stress-activated MAPK cascade | 28/973 | 155/17913 | 1.78E-08 | 1.10E-06 | 8.23E-07 | 7042/2213/7099/9839/51347/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/54910/153769/9770/3553/203447/8322/6885/23236/7474/10392/221472/11184/939 | 28 |
| GO:0001818 | negative regulation of cytokine production | 41/973 | 290/17913 | 1.84E-08 | 1.12E-06 | 8.40E-07 | 7042/695/51311/5788/84868/26191/2213/7099/8832/10457/3071/23208/1992/5094/634/3134/55198/23607/7305/54209/80380/10225/140885/7057/5552/3162/2335/114548/11326/301/7481/384/57045/1001/84166/2633/2260/335/2625/89795/54206 | 41 |
| GO:0032649 | regulation of interferon-gamma production | 21/973 | 93/17913 | 1.94E-08 | 1.17E-06 | 8.75E-07 | 51311/84868/26191/7099/929/3115/51284/3113/8767/10125/3394/80380/10225/140885/3553/914/916/7474/114836/2625/729230 | 21 |
| GO:0032623 | interleukin-2 production | 17/973 | 62/17913 | 1.98E-08 | 1.17E-06 | 8.75E-07 | 861/942/5788/2207/84868/920/8767/3553/916/11326/301/6885/2633/2625/3662/729230/89795 | 17 |
| GO:0032729 | positive regulation of interferon-gamma production | 17/973 | 62/17913 | 1.98E-08 | 1.17E-06 | 8.75E-07 | 51311/84868/26191/7099/929/3115/51284/3113/8767/10125/3394/3553/914/916/7474/114836/729230 | 17 |
| GO:0002755 | MyD88-dependent toll-like receptor signaling pathway | 13/973 | 36/17913 | 2.38E-08 | 1.38E-06 | 1.04E-06 | 695/51311/7099/929/23643/7096/51284/7097/3659/3656/4615/3654/6885 | 13 |
| GO:0051403 | stress-activated MAPK cascade | 39/973 | 271/17913 | 2.50E-08 | 1.44E-06 | 1.08E-06 | 7042/5601/9459/26191/2213/355/7099/9839/51347/4609/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/54910/153769/140885/9770/3553/203447/3656/9448/8517/3654/8322/6885/23236/7474/10392/55504/221472/11184/939 | 39 |
| GO:0002699 | positive regulation of immune effector process | 32/973 | 198/17913 | 2.85E-08 | 1.62E-06 | 1.22E-06 | 7037/695/3684/942/5788/2207/3689/7099/8832/4067/3135/567/718/3134/55198/8767/972/10125/64127/3133/3566/3162/3553/114548/301/5650/6885/7474/64332/114836/2625/729230 | 32 |
| GO:0030595 | leukocyte chemotaxis | 31/973 | 188/17913 | 2.90E-08 | 1.64E-06 | 1.23E-06 | 7042/3689/199/5294/4354/4067/3071/719/3269/6347/54795/1906/3958/1230/972/727/11151/7057/6352/3603/301/1435/57402/80270/23604/7474/3627/3815/10563/56833/729230 | 31 |
| GO:0046328 | regulation of JNK cascade | 29/973 | 169/17913 | 3.27E-08 | 1.83E-06 | 1.37E-06 | 26191/2213/7099/9839/51347/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/153769/140885/9770/3553/203447/9448/8322/6885/23236/7474/10392/221472/11184/939 | 29 |
| GO:0032652 | regulation of interleukin-1 production | 21/973 | 96/17913 | 3.51E-08 | 1.92E-06 | 1.44E-06 | 51311/84868/7099/834/1992/634/8767/3717/7305/54209/64127/140885/114548/301/3428/3066/384/7474/10392/335/54206 | 21 |
| GO:0042116 | macrophage activation | 21/973 | 96/17913 | 3.51E-08 | 1.92E-06 | 1.44E-06 | 51311/3684/5788/84868/3689/2213/199/7099/7096/51284/7097/972/7305/54209/120892/3566/7057/11326/1191/7474/712 | 21 |
| GO:0043410 | positive regulation of MAPK cascade | 58/973 | 499/17913 | 3.62E-08 | 1.96E-06 | 1.47E-06 | 2066/7042/5788/84868/26191/920/2213/5294/7099/10457/8829/9839/1436/51347/8826/5151/8767/1906/3717/7786/1230/1647/972/1856/10125/960/54209/4217/57216/5585/120892/64127/54910/727/153769/9770/7057/5156/3553/2357/3383/203447/3656/8517/3654/8322/6885/23236/23286/537/7474/10392/221472/2260/1000/3815/11184/939 | 58 |
| GO:0070302 | regulation of stress-activated protein kinase signaling cascade | 34/973 | 222/17913 | 4.18E-08 | 2.24E-06 | 1.68E-06 | 7042/26191/2213/355/7099/4067/9839/51347/4609/8767/1906/7786/1647/1856/10125/4217/57216/5585/64127/54910/153769/140885/9770/3553/203447/9448/8322/6885/23236/7474/10392/221472/11184/939 | 34 |

TableS5. Univariate Cox regression analysis of DNAme-associated mRNA. (*P* < 0.05)

|  |  |  |  |
| --- | --- | --- | --- |
| Gene | P | HR | 95%CI |
| ZCCHC6 | 0.0137 | 1.3108 | 1.0571~1.6254 |
| EIF4E3 | 0.0011 | 0.7587 | 0.6430~0.8952 |
| PRR15 | 0.0255 | 0.8011 | 0.6594~0.9732 |
| TGFBR2 | 0.0027 | 1.4076 | 1.1261~1.7595 |
| FAS | 0.0331 | 1.1906 | 1.0141~1.3979 |
| FCGR2A | 0.0219 | 1.1799 | 1.0243~1.3593 |
| SH3D19 | 0.0417 | 1.22 | 1.0075~1.4773 |
| ATP8B4 | 0.017 | 1.2681 | 1.0433~1.5414 |
| DSE | 0.0032 | 1.312 | 1.0956~1.5713 |
| TGFBI | 0.0132 | 1.1886 | 1.0367~1.3627 |
| ITGA5 | 0.0356 | 1.1982 | 1.0122~1.4183 |
| SLC9A9 | 0.0442 | 1.1961 | 1.0047~1.4240 |
| CSF1R | 0.0429 | 1.1713 | 1.0051~1.3650 |
| TLR2 | 0.0163 | 1.2318 | 1.0391~1.4602 |
| MYO5A | 0.0063 | 1.3396 | 1.0863~1.6519 |
| CHD6 | 0.01 | 1.3001 | 1.0648~1.5875 |
| CMBL | 0.0017 | 0.825 | 0.7316~0.9304 |
| PANK3 | 0.0304 | 1.4469 | 1.0355~2.0216 |
| PSMB8 | 0.0144 | 0.8105 | 0.6849~0.9590 |
| CBX2 | 0.0063 | 0.7126 | 0.5590~0.9085 |
| MYL6B | 0.0258 | 0.7636 | 0.6024~0.9680 |
| TMOD3 | 0.033 | 1.2456 | 1.0179~1.5243 |
| ASRGL1 | 0.0033 | 0.8462 | 0.7570~0.9458 |
| PLEKHF2 | 0.0064 | 1.3294 | 1.0834~1.6313 |
| PDLIM5 | 0.0043 | 1.3873 | 1.1083~1.7366 |
| HLA-F | 0.0323 | 0.8553 | 0.7414~0.9869 |
| EYA4 | 0.002 | 1.1562 | 1.0545~1.2677 |
| AAAS | 0.0178 | 0.7165 | 0.5438~0.9440 |
| TARBP2 | 0.0199 | 0.7368 | 0.5698~0.9529 |
| GDF11 | 0.0444 | 0.8775 | 0.7726~0.9967 |
| PRCC | 0.035 | 0.6909 | 0.4899~0.9744 |
| FAM69B | 0.0366 | 0.7958 | 0.6424~0.9859 |
| SGMS2 | 0.0484 | 1.1828 | 1.0012~1.3974 |
| DHX35 | 0.0313 | 1.2633 | 1.0212~1.5629 |
| SLC4A8 | 0.0207 | 0.8008 | 0.6635~0.9666 |
| DPP4 | 0.0365 | 1.1102 | 1.0066~1.2246 |
| BTN3A3 | 0.0112 | 0.8293 | 0.7175~0.9584 |
| PRSS16 | 0.0017 | 0.6623 | 0.5119~0.8568 |
| GJB1 | 4.00E-04 | 0.789 | 0.6917~0.9000 |
| ENO2 | 0.0471 | 1.2041 | 1.0024~1.4464 |
| MAN2A1 | 0.0068 | 1.3269 | 1.0812~1.6283 |
| SMUG1 | 0.0027 | 0.6623 | 0.5062~0.8666 |
| MYO9A | 0.0443 | 1.2089 | 1.0048~1.4544 |
| TAP1 | 0.0072 | 0.8465 | 0.7496~0.9560 |
| MAPRE1 | 0.0231 | 1.3222 | 1.0392~1.6823 |
| NDRG3 | 0.0054 | 1.3886 | 1.1020~1.7498 |
| PSMB9 | 0.0491 | 0.911 | 0.8303~0.9996 |
| PDCL2 | 0.0496 | 0.8807 | 0.7759~0.9998 |
| SH3RF2 | 0.0226 | 0.7576 | 0.5967~0.9618 |
| CTSK | 0.0317 | 1.0871 | 1.0073~1.1731 |
| FAP | 0.0111 | 1.0899 | 1.0198~1.1648 |
| FGF7 | 0.0021 | 1.214 | 1.0727~1.3739 |
| THBS2 | 0.0477 | 1.0807 | 1.0008~1.1670 |
| TNFAIP6 | 0.0368 | 1.1223 | 1.0071~1.2507 |
| OMD | 0.0341 | 1.1539 | 1.0108~1.3172 |
| NT5E | 0.0445 | 1.0948 | 1.0022~1.1959 |
| ASPN | 0.0212 | 1.0996 | 1.0143~1.1922 |
| PDGFRA | 0.0062 | 1.192 | 1.0511~1.3518 |
| CD163 | 0.0322 | 1.1144 | 1.0092~1.2306 |
| PTGIS | 0.0264 | 1.157 | 1.0172~1.3160 |
| ADAM12 | 0.0229 | 1.1363 | 1.0179~1.2684 |
| MSR1 | 0.0481 | 1.1288 | 1.0010~1.2730 |
| BICC1 | 0.0123 | 1.1464 | 1.0301~1.2758 |
| RGS4 | 0.0094 | 1.2074 | 1.0474~1.3918 |
| WISP1 | 0.0344 | 1.2146 | 1.0144~1.4542 |
| COL3A1 | 0.0494 | 1.0856 | 1.0002~1.1782 |
| FN1 | 0.0267 | 1.104 | 1.0115~1.2049 |
| SVEP1 | 0.0195 | 1.1279 | 1.0195~1.2478 |
| RGS18 | 0.0372 | 1.3242 | 1.0167~1.7247 |
| LOX | 0.0403 | 1.1001 | 1.0042~1.2051 |
| CD3D | 0.0288 | 0.8502 | 0.7351~0.9833 |
| GFPT2 | 0.003 | 1.2496 | 1.0785~1.4477 |
| TMOD2 | 5.00E-04 | 1.4443 | 1.1742~1.7766 |
| VCAN | 0.0488 | 1.0844 | 1.0004~1.1754 |
| CCDC80 | 0.0014 | 1.1513 | 1.0560~1.2553 |
| COL5A2 | 0.0155 | 1.1215 | 1.0221~1.2306 |
| VSIG4 | 0.0018 | 1.2256 | 1.0784~1.3929 |
| FBN1 | 0.0192 | 1.1169 | 1.0182~1.2252 |
| ECM2 | 0.0266 | 1.2816 | 1.0293~1.5957 |
| NEXN | 0.0112 | 1.4584 | 1.0893~1.9524 |
| HSPA1A | 0.0273 | 0.9135 | 0.8430~0.9899 |
| USP42 | 0.0379 | 1.3761 | 1.0180~1.8601 |
| ADCK5 | 0.0066 | 0.6819 | 0.5172~0.8990 |
| ATRIP | 0.011 | 0.593 | 0.3964~0.8872 |
| CCDC88A | 0.0488 | 1.2062 | 1.0010~1.4534 |
| MACROD1 | 0.0334 | 0.7937 | 0.6415~0.9820 |
| CAPN6 | 0.0461 | 0.887 | 0.7884~0.9979 |
| NUAK1 | 0.0255 | 1.1963 | 1.0222~1.4000 |
| CCDC91 | 0.0074 | 1.311 | 1.0753~1.5982 |
| ATP1A3 | 0.025 | 1.2312 | 1.0264~1.4769 |
| SAMD12 | 0.0124 | 1.3402 | 1.0653~1.6861 |
| TMEM45A | 0.0272 | 1.1221 | 1.0131~1.2429 |
| CLDN6 | 0.0175 | 0.9228 | 0.8636~0.9860 |
| ALPL | 0.0036 | 0.85 | 0.7618~0.9484 |
| PPP1R16A | 0.0111 | 0.7009 | 0.5328~0.9219 |
| ADCK2 | 0.0111 | 0.7603 | 0.6154~0.9394 |
| RAI14 | 0.009 | 1.2221 | 1.0514~1.4206 |
| PXK | 0.0036 | 1.388 | 1.1128~1.7312 |
| FSTL1 | 0.0199 | 1.1724 | 1.0255~1.3403 |
| PRDM5 | 0.0056 | 1.2797 | 1.0746~1.5238 |
| RAB40B | 4.00E-04 | 0.6191 | 0.4740~0.8087 |
| IGF2R | 0.0402 | 1.2454 | 1.0098~1.5359 |
| TPST1 | 0.0421 | 1.2694 | 1.0085~1.5977 |
| TUBB | 0.0497 | 0.7465 | 0.5575~0.9996 |
| PKHD1 | 0.0334 | 0.7894 | 0.6348~0.9816 |
| MTDH | 0.0381 | 1.3094 | 1.0148~1.6896 |
| NLRC5 | 0.0383 | 0.7825 | 0.6205~0.9869 |
| ZMYM2 | 0.0357 | 1.2418 | 1.0146~1.5199 |
| PRTG | 0.0399 | 1.2027 | 1.0085~1.4343 |
| USP51 | 0.007 | 0.6795 | 0.5131~0.8998 |
| ADORA3 | 0.0226 | 1.2231 | 1.0287~1.4543 |
| CYP24A1 | 0.0224 | 1.1205 | 1.0162~1.2355 |
| CXCL13 | 0.0108 | 0.8748 | 0.7892~0.9696 |
| KCNA3 | 0.0265 | 0.7894 | 0.6405~0.9728 |
| ACSL1 | 0.0381 | 1.158 | 1.0081~1.3302 |
| MCTP1 | 0.0309 | 1.2588 | 1.0214~1.5513 |
| SLAMF7 | 0.0212 | 0.8688 | 0.7708~0.9792 |
| NEK6 | 0.0383 | 1.319 | 1.0150~1.7139 |
| CXCL9 | 0.0346 | 0.9067 | 0.8279~0.9929 |
| FCRL5 | 0.0119 | 0.7052 | 0.5372~0.9257 |
| IRF4 | 0.0216 | 0.7575 | 0.5977~0.9601 |
| CD27 | 0.0167 | 0.7812 | 0.6382~0.9562 |
| LAX1 | 0.0258 | 0.8086 | 0.6708~0.9747 |
| DERL3 | 0.0134 | 0.7322 | 0.5719~0.9374 |
| ETV1 | 0.0261 | 1.1795 | 1.0198~1.3641 |

TableS6. Analysis of pathway enrichment (KEGG) and Gene Ontology (GO) of prognostic significance DNAme-associated mRNA in TCGA

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| KEGG | | | | | | | | |
| ID | Description | GeneRatio | BgRatio | pvalue | p.adjust | qvalue | geneID | Count |
| hsa04145 | Phagosome | 8/55 | 152/8104 | 7.35E-06 | 0.001293 | 0.001129 | 2212/3678/7097/3134/6890/7058/4481/203068 | 8 |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GO | | | | | | | | |
| ID | Description | GeneRatio | BgRatio | pvalue | p.adjust | qvalue | geneID | Count |
| GO:0030198 | extracellular matrix organization | 13/118 | 334/17913 | 3.13E-07 | 0.000694 | 0.000652 | 3678/1803/1513/2191/5156/8038/1281/2335/4015/1462/151887/1290/2200 | 13 |
| GO:0043062 | extracellular structure organization | 13/118 | 387/17913 | 1.64E-06 | 0.001818 | 0.001707 | 3678/1803/1513/2191/5156/8038/1281/2335/4015/1462/151887/1290/2200 | 13 |

TableS7.Clinicopathological information of DNAme-associated subtypes in TCGA

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Features | S1 | S2 | S3 | *P* |
| n | 154 | 238 | 141 |  |
| Age (%) |  |  |  | 0.017 |
| <60 | 66 (42.9) | 137 (57.6) | 71 (50.4) |  |
| ≥60 | 88 (57.1) | 101 (42.4) | 70 (49.6) |  |
| Stage (%) |  |  |  | 0.02 |
| I | 3 (2.0) | 9 (3.8) | 0 (0.0) |  |
| II | 8 (5.3) | 16 (6.7) | 1 (0.7) |  |
| III | 122 (80.3) | 175 (73.5) | 112 (80.6) |  |
| IV | 19 (12.5) | 38 (16.0) | 26 (18.7) |  |
| Grade (%) |  |  |  | 0.062 |
| G1&G2 | 25 (16.3) | 22 (9.5) | 23 (16.9) |  |
| G3&G4 | 128 (83.7) | 209 (90.5) | 113 (83.1) |  |

TableS7.Clinicopathological information of DNAme-associated subtypes in ICGC

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Features | S1 | S2 | S3 | *P* |
| n | 18 | 33 | 28 |  |
| Age (%) |  |  |  |  |
| <60 | 8 (44.4) | 18 (54.5) | 16 (57.1) | 0.686 |
| ≥60 | 10 (55.6) | 15 (45.5) | 12 (42.9) |  |
| Stage (%) |  |  |  |  |
| III | 16 (88.9) | 28 (84.8) | 23 (82.1) | 0.824 |
| IV | 2 (11.1) | 5 (15.2) | 5 (17.9) |  |
| Grade (%) |  |  |  |  |
| G2 | 6 (33.3) | 5 (15.2) | 4 (14.3) | 0.209 |
| G3 | 12 (66.7) | 28 (84.8) | 24 (85.7) |  |

TableS8.Gene set enrichment analysis (GSEA) of three subtypes in TCGA

GSEA analysis in S1

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GS follow link to MSigDB | SIZE | ES | NES | NOM p-val | FDR q-val | FWER p-val | RANK AT MAX | LEADING EDGE |
| HALLMARK\_WNT\_BETA\_CATENIN\_SIGNALING | 40 | 0.49 | 1.56 | 0.048 | 0.374 | 0.397 | 4416 | tags=63%, list=33%, signal=93% |
| HALLMARK\_SPERMATOGENESIS | 102 | 0.48 | 1.49 | 0.031 | 0.296 | 0.514 | 3142 | tags=42%, list=24%, signal=55% |
| HALLMARK\_E2F\_TARGETS | 160 | 0.43 | 1.1 | 0.406 | 1 | 0.97 | 4413 | tags=57%, list=33%, signal=84% |
| HALLMARK\_G2M\_CHECKPOINT | 167 | 0.39 | 1.04 | 0.462 | 1 | 0.984 | 4432 | tags=58%, list=33%, signal=86% |
| HALLMARK\_MYC\_TARGETS\_V2 | 48 | 0.31 | 1 | 0.48 | 0.925 | 0.989 | 5252 | tags=46%, list=39%, signal=75% |
| HALLMARK\_MITOTIC\_SPINDLE | 182 | 0.28 | 0.88 | 0.602 | 1 | 0.998 | 2549 | tags=28%, list=19%, signal=34% |
| HALLMARK\_HEDGEHOG\_SIGNALING | 34 | 0.3 | 0.85 | 0.675 | 0.969 | 0.998 | 1047 | tags=21%, list=8%, signal=22% |
| HALLMARK\_KRAS\_SIGNALING\_DN | 159 | 0.25 | 0.82 | 0.8 | 0.907 | 0.999 | 966 | tags=13%, list=7%, signal=14% |
| HALLMARK\_NOTCH\_SIGNALING | 30 | 0.26 | 0.78 | 0.737 | 0.876 | 1 | 2858 | tags=30%, list=21%, signal=38% |
| HALLMARK\_MYC\_TARGETS\_V1 | 161 | 0.22 | 0.73 | 0.697 | 0.864 | 1 | 5165 | tags=45%, list=39%, signal=72% |
| HALLMARK\_DNA\_REPAIR | 125 | 0.19 | 0.71 | 0.792 | 0.82 | 1 | 3757 | tags=30%, list=28%, signal=41% |

GSEA analysis in S2

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GS follow link to MSigDB | SIZE | ES | NES | NOM p-val | FDR q-val | FWER p-val | RANK AT MAX | LEADING EDGE |
| HALLMARK\_INTERFERON\_GAMMA\_RESPONSE | 174 | 0.76 | 1.7 | 0.008 | 0.324 | 0.176 | 1636 | tags=66%, list=12%, signal=74% |
| HALLMARK\_INTERFERON\_ALPHA\_RESPONSE | 80 | 0.84 | 1.7 | 0.006 | 0.162 | 0.177 | 1595 | tags=80%, list=12%, signal=90% |
| HALLMARK\_REACTIVE\_OXYGEN\_SPECIES\_PATHWAY | 42 | 0.51 | 1.62 | 0.035 | 0.212 | 0.291 | 4067 | tags=55%, list=31%, signal=79% |
| HALLMARK\_ALLOGRAFT\_REJECTION | 171 | 0.63 | 1.49 | 0.097 | 0.402 | 0.538 | 1758 | tags=53%, list=13%, signal=61% |
| HALLMARK\_IL6\_JAK\_STAT3\_SIGNALING | 80 | 0.58 | 1.45 | 0.113 | 0.389 | 0.595 | 2660 | tags=54%, list=20%, signal=67% |
| HALLMARK\_ESTROGEN\_RESPONSE\_EARLY | 177 | 0.42 | 1.45 | 0.043 | 0.329 | 0.602 | 1991 | tags=39%, list=15%, signal=45% |
| HALLMARK\_INFLAMMATORY\_RESPONSE | 184 | 0.55 | 1.42 | 0.109 | 0.321 | 0.641 | 2013 | tags=47%, list=15%, signal=55% |
| HALLMARK\_PEROXISOME | 93 | 0.38 | 1.39 | 0.073 | 0.343 | 0.703 | 2266 | tags=28%, list=17%, signal=33% |
| HALLMARK\_ESTROGEN\_RESPONSE\_LATE | 187 | 0.39 | 1.29 | 0.098 | 0.467 | 0.817 | 1991 | tags=33%, list=15%, signal=38% |
| HALLMARK\_P53\_PATHWAY | 173 | 0.34 | 1.27 | 0.175 | 0.473 | 0.85 | 1765 | tags=24%, list=13%, signal=28% |
| HALLMARK\_HEME\_METABOLISM | 164 | 0.28 | 1.26 | 0.155 | 0.449 | 0.859 | 2712 | tags=24%, list=20%, signal=30% |
| HALLMARK\_COMPLEMENT | 180 | 0.43 | 1.21 | 0.245 | 0.485 | 0.892 | 917 | tags=24%, list=7%, signal=26% |
| HALLMARK\_TNFA\_SIGNALING\_VIA\_NFKB | 177 | 0.47 | 1.2 | 0.279 | 0.482 | 0.908 | 1996 | tags=36%, list=15%, signal=41% |
| HALLMARK\_FATTY\_ACID\_METABOLISM | 137 | 0.34 | 1.19 | 0.246 | 0.469 | 0.913 | 2671 | tags=33%, list=20%, signal=41% |
| HALLMARK\_IL2\_STAT5\_SIGNALING | 174 | 0.37 | 1.15 | 0.299 | 0.496 | 0.939 | 2779 | tags=34%, list=21%, signal=43% |
| HALLMARK\_OXIDATIVE\_PHOSPHORYLATION | 156 | 0.37 | 1.12 | 0.398 | 0.514 | 0.957 | 4083 | tags=43%, list=31%, signal=61% |
| HALLMARK\_CHOLESTEROL\_HOMEOSTASIS | 65 | 0.34 | 1.07 | 0.373 | 0.583 | 0.977 | 1966 | tags=28%, list=15%, signal=32% |
| HALLMARK\_ADIPOGENESIS | 169 | 0.3 | 1.06 | 0.391 | 0.575 | 0.98 | 1890 | tags=25%, list=14%, signal=29% |
| HALLMARK\_UV\_RESPONSE\_UP | 142 | 0.28 | 1.03 | 0.379 | 0.582 | 0.984 | 2315 | tags=27%, list=17%, signal=33% |
| HALLMARK\_PI3K\_AKT\_MTOR\_SIGNALING | 92 | 0.25 | 1.01 | 0.443 | 0.595 | 0.989 | 946 | tags=11%, list=7%, signal=12% |
| HALLMARK\_ANDROGEN\_RESPONSE | 90 | 0.3 | 1 | 0.446 | 0.578 | 0.99 | 1020 | tags=19%, list=8%, signal=20% |
| HALLMARK\_APOPTOSIS | 147 | 0.31 | 0.95 | 0.519 | 0.633 | 0.998 | 1046 | tags=22%, list=8%, signal=23% |
| HALLMARK\_BILE\_ACID\_METABOLISM | 102 | 0.25 | 0.87 | 0.68 | 0.74 | 0.999 | 1946 | tags=25%, list=15%, signal=30% |
| HALLMARK\_XENOBIOTIC\_METABOLISM | 179 | 0.25 | 0.84 | 0.72 | 0.771 | 1 | 1934 | tags=23%, list=15%, signal=26% |
| HALLMARK\_MYC\_TARGETS\_V2 | 48 | 0.24 | 0.8 | 0.624 | 0.804 | 1 | 4957 | tags=38%, list=37%, signal=59% |
| HALLMARK\_PANCREAS\_BETA\_CELLS | 28 | 0.3 | 0.8 | 0.794 | 0.777 | 1 | 4217 | tags=54%, list=32%, signal=78% |
| HALLMARK\_KRAS\_SIGNALING\_DN | 159 | 0.23 | 0.76 | 0.937 | 0.811 | 1 | 2591 | tags=28%, list=19%, signal=35% |
| HALLMARK\_MTORC1\_SIGNALING | 179 | 0.2 | 0.63 | 0.924 | 0.942 | 1 | 1066 | tags=11%, list=8%, signal=11% |
| HALLMARK\_DNA\_REPAIR | 125 | 0.1 | 0.35 | 1 | 0.998 | 1 | 5303 | tags=32%, list=40%, signal=53% |

GSEA analysis in S3

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GS follow link to MSigDB | SIZE | ES | NES | NOM p-val | FDR q-val | FWER p-val | RANK AT MAX | LEADING EDGE |
| HALLMARK\_APICAL\_JUNCTION | 184 | 0.61 | 2.11 | 0 | 0 | 0 | 1078 | tags=26%, list=8%, signal=27% |
| HALLMARK\_UV\_RESPONSE\_DN | 128 | 0.7 | 2.05 | 0 | 0.001 | 0.002 | 1400 | tags=34%, list=10%, signal=38% |
| HALLMARK\_TGF\_BETA\_SIGNALING | 51 | 0.62 | 2.04 | 0 | 0.002 | 0.004 | 2116 | tags=33%, list=16%, signal=39% |
| HALLMARK\_HYPOXIA | 178 | 0.6 | 1.97 | 0 | 0.005 | 0.012 | 2169 | tags=39%, list=16%, signal=46% |
| HALLMARK\_EPITHELIAL\_MESENCHYMAL\_TRANSITION | 185 | 0.87 | 1.96 | 0 | 0.006 | 0.016 | 1220 | tags=69%, list=9%, signal=75% |
| HALLMARK\_APOPTOSIS | 147 | 0.63 | 1.93 | 0 | 0.007 | 0.022 | 1697 | tags=33%, list=13%, signal=37% |
| HALLMARK\_KRAS\_SIGNALING\_UP | 172 | 0.71 | 1.9 | 0 | 0.008 | 0.028 | 1410 | tags=44%, list=11%, signal=48% |
| HALLMARK\_COAGULATION | 114 | 0.68 | 1.89 | 0 | 0.007 | 0.031 | 1341 | tags=39%, list=10%, signal=43% |
| HALLMARK\_TNFA\_SIGNALING\_VIA\_NFKB | 177 | 0.72 | 1.87 | 0.002 | 0.008 | 0.039 | 1395 | tags=38%, list=10%, signal=42% |
| HALLMARK\_COMPLEMENT | 180 | 0.65 | 1.84 | 0.002 | 0.011 | 0.055 | 2191 | tags=46%, list=16%, signal=54% |
| HALLMARK\_ANGIOGENESIS | 33 | 0.81 | 1.83 | 0 | 0.011 | 0.057 | 745 | tags=39%, list=6%, signal=42% |
| HALLMARK\_MYOGENESIS | 180 | 0.53 | 1.8 | 0.002 | 0.015 | 0.08 | 1414 | tags=26%, list=11%, signal=28% |
| HALLMARK\_IL2\_STAT5\_SIGNALING | 174 | 0.57 | 1.79 | 0.004 | 0.014 | 0.084 | 1664 | tags=34%, list=12%, signal=38% |
| HALLMARK\_INFLAMMATORY\_RESPONSE | 184 | 0.69 | 1.79 | 0.002 | 0.015 | 0.091 | 1679 | tags=47%, list=13%, signal=53% |
| HALLMARK\_ALLOGRAFT\_REJECTION | 171 | 0.7 | 1.68 | 0.014 | 0.037 | 0.202 | 1743 | tags=45%, list=13%, signal=51% |
| HALLMARK\_IL6\_JAK\_STAT3\_SIGNALING | 80 | 0.66 | 1.66 | 0.02 | 0.039 | 0.22 | 1446 | tags=41%, list=11%, signal=46% |
| HALLMARK\_ADIPOGENESIS | 169 | 0.46 | 1.64 | 0.014 | 0.045 | 0.257 | 1264 | tags=14%, list=9%, signal=15% |
| HALLMARK\_GLYCOLYSIS | 184 | 0.44 | 1.59 | 0.02 | 0.063 | 0.344 | 2545 | tags=27%, list=19%, signal=32% |
| HALLMARK\_ANDROGEN\_RESPONSE | 90 | 0.48 | 1.59 | 0.01 | 0.06 | 0.344 | 2617 | tags=46%, list=20%, signal=56% |
| HALLMARK\_P53\_PATHWAY | 173 | 0.42 | 1.58 | 0.037 | 0.061 | 0.358 | 2227 | tags=25%, list=17%, signal=30% |
| HALLMARK\_XENOBIOTIC\_METABOLISM | 179 | 0.44 | 1.53 | 0.014 | 0.085 | 0.451 | 2076 | tags=25%, list=16%, signal=29% |
| HALLMARK\_CHOLESTEROL\_HOMEOSTASIS | 65 | 0.5 | 1.51 | 0.048 | 0.087 | 0.465 | 2773 | tags=37%, list=21%, signal=46% |
| HALLMARK\_HEDGEHOG\_SIGNALING | 34 | 0.52 | 1.5 | 0.041 | 0.093 | 0.491 | 1940 | tags=41%, list=15%, signal=48% |
| HALLMARK\_APICAL\_SURFACE | 39 | 0.49 | 1.49 | 0.034 | 0.093 | 0.502 | 2320 | tags=36%, list=17%, signal=43% |
| HALLMARK\_MTORC1\_SIGNALING | 179 | 0.46 | 1.48 | 0.1 | 0.093 | 0.508 | 2917 | tags=37%, list=22%, signal=47% |
| HALLMARK\_UV\_RESPONSE\_UP | 142 | 0.39 | 1.42 | 0.05 | 0.125 | 0.62 | 2038 | tags=18%, list=15%, signal=21% |
| HALLMARK\_INTERFERON\_GAMMA\_RESPONSE | 174 | 0.63 | 1.41 | 0.124 | 0.129 | 0.653 | 2825 | tags=47%, list=21%, signal=59% |
| HALLMARK\_UNFOLDED\_PROTEIN\_RESPONSE | 97 | 0.37 | 1.38 | 0.14 | 0.145 | 0.697 | 3602 | tags=35%, list=27%, signal=48% |
| HALLMARK\_PROTEIN\_SECRETION | 87 | 0.46 | 1.36 | 0.158 | 0.154 | 0.726 | 3163 | tags=49%, list=24%, signal=64% |
| HALLMARK\_NOTCH\_SIGNALING | 30 | 0.42 | 1.31 | 0.156 | 0.189 | 0.786 | 3329 | tags=50%, list=25%, signal=66% |
| HALLMARK\_FATTY\_ACID\_METABOLISM | 137 | 0.36 | 1.24 | 0.193 | 0.241 | 0.859 | 2536 | tags=23%, list=19%, signal=29% |
| HALLMARK\_MITOTIC\_SPINDLE | 182 | 0.39 | 1.23 | 0.269 | 0.251 | 0.878 | 3124 | tags=33%, list=23%, signal=42% |
| HALLMARK\_PI3K\_AKT\_MTOR\_SIGNALING | 92 | 0.29 | 1.19 | 0.204 | 0.282 | 0.904 | 3513 | tags=37%, list=26%, signal=50% |
| HALLMARK\_BILE\_ACID\_METABOLISM | 102 | 0.34 | 1.18 | 0.194 | 0.277 | 0.906 | 1528 | tags=16%, list=11%, signal=18% |
| HALLMARK\_ESTROGEN\_RESPONSE\_EARLY | 177 | 0.34 | 1.17 | 0.237 | 0.287 | 0.915 | 1884 | tags=21%, list=14%, signal=24% |
| HALLMARK\_HEME\_METABOLISM | 164 | 0.24 | 1.06 | 0.342 | 0.403 | 0.972 | 2048 | tags=18%, list=15%, signal=21% |
| HALLMARK\_ESTROGEN\_RESPONSE\_LATE | 187 | 0.31 | 1.04 | 0.4 | 0.422 | 0.98 | 1802 | tags=21%, list=14%, signal=24% |
| HALLMARK\_INTERFERON\_ALPHA\_RESPONSE | 80 | 0.5 | 1.02 | 0.496 | 0.437 | 0.987 | 2802 | tags=38%, list=21%, signal=47% |
| HALLMARK\_PANCREAS\_BETA\_CELLS | 28 | 0.35 | 0.9 | 0.619 | 0.591 | 0.997 | 583 | tags=14%, list=4%, signal=15% |
| HALLMARK\_REACTIVE\_OXYGEN\_SPECIES\_PATHWAY | 42 | 0.22 | 0.7 | 0.8 | 0.867 | 1 | 3178 | tags=21%, list=24%, signal=28% |
| HALLMARK\_WNT\_BETA\_CATENIN\_SIGNALING | 40 | 0.21 | 0.66 | 0.91 | 0.893 | 1 | 2249 | tags=23%, list=17%, signal=27% |
| HALLMARK\_OXIDATIVE\_PHOSPHORYLATION | 156 | 0.14 | 0.45 | 0.951 | 0.988 | 1 | 9452 | tags=95%, list=71%, signal=322% |

TableS8.Gene set enrichment analysis (GSEA) of three subtypes in ICGC

GSEA analysis in S1

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GS follow link to MSigDB | SIZE | ES | NES | NOM p-val | FDR q-val | FWER p-val | RANK AT MAX | LEADING EDGE |
| HALLMARK\_SPERMATOGENESIS | 102 | 0.35 | 1.26 | 0.143 | 1 | 0.805 | 3046 | tags=39%, list=23%, signal=50% |
| HALLMARK\_KRAS\_SIGNALING\_DN | 159 | 0.26 | 1.03 | 0.41 | 1 | 0.934 | 2231 | tags=28%, list=17%, signal=33% |
| HALLMARK\_WNT\_BETA\_CATENIN\_SIGNALING | 40 | 0.31 | 0.94 | 0.539 | 1 | 0.957 | 2567 | tags=28%, list=19%, signal=34% |
| HALLMARK\_NOTCH\_SIGNALING | 30 | 0.3 | 0.88 | 0.594 | 1 | 0.971 | 1156 | tags=23%, list=9%, signal=25% |
| HALLMARK\_MYC\_TARGETS\_V1 | 161 | 0.18 | 0.84 | 0.562 | 1 | 0.982 | 4727 | tags=36%, list=35%, signal=55% |
| HALLMARK\_HEDGEHOG\_SIGNALING | 34 | 0.27 | 0.81 | 0.702 | 0.95 | 0.985 | 1795 | tags=24%, list=13%, signal=27% |
| HALLMARK\_DNA\_REPAIR | 125 | 0.15 | 0.69 | 0.828 | 1 | 0.998 | 2447 | tags=17%, list=18%, signal=20% |
| HALLMARK\_MYC\_TARGETS\_V2 | 48 | 0.17 | 0.62 | 0.838 | 0.986 | 0.998 | 4045 | tags=31%, list=30%, signal=45% |
| HALLMARK\_E2F\_TARGETS | 160 | 0.14 | 0.4 | 0.951 | 0.987 | 0.998 | 4506 | tags=34%, list=34%, signal=50% |

GSEA analysis in S2

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GS follow link to MSigDB | SIZE | ES | NES | NOM p-val | FDR q-val | FWER p-val | RANK AT MAX | LEADING EDGE |
| HALLMARK\_OXIDATIVE\_PHOSPHORYLATION | 156 | 0.38 | 1.54 | 0.136 | 0.458 | 0.474 | 3324 | tags=47%, list=25%, signal=62% |
| HALLMARK\_INTERFERON\_ALPHA\_RESPONSE | 80 | 0.58 | 1.41 | 0.186 | 0.453 | 0.663 | 2930 | tags=63%, list=22%, signal=80% |
| HALLMARK\_MYC\_TARGETS\_V2 | 48 | 0.37 | 1.29 | 0.205 | 0.492 | 0.792 | 2954 | tags=40%, list=22%, signal=51% |
| HALLMARK\_ESTROGEN\_RESPONSE\_LATE | 187 | 0.29 | 1.13 | 0.285 | 0.673 | 0.905 | 1731 | tags=29%, list=13%, signal=33% |
| HALLMARK\_PEROXISOME | 93 | 0.24 | 1.03 | 0.425 | 0.728 | 0.947 | 2205 | tags=27%, list=17%, signal=32% |
| HALLMARK\_REACTIVE\_OXYGEN\_SPECIES\_PATHWAY | 42 | 0.28 | 1.01 | 0.428 | 0.637 | 0.953 | 3197 | tags=40%, list=24%, signal=53% |
| HALLMARK\_INTERFERON\_GAMMA\_RESPONSE | 174 | 0.38 | 1.01 | 0.484 | 0.552 | 0.953 | 2032 | tags=39%, list=15%, signal=45% |
| HALLMARK\_FATTY\_ACID\_METABOLISM | 137 | 0.23 | 0.98 | 0.472 | 0.532 | 0.966 | 2835 | tags=34%, list=21%, signal=42% |
| HALLMARK\_MYC\_TARGETS\_V1 | 161 | 0.18 | 0.85 | 0.542 | 0.652 | 0.984 | 10193 | tags=98%, list=76%, signal=412% |
| HALLMARK\_DNA\_REPAIR | 125 | 0.12 | 0.55 | 0.975 | 0.931 | 0.998 | 2649 | tags=22%, list=20%, signal=28% |

GSEA analysis in S3

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| GS follow link to MSigDB | SIZE | ES | NES | NOM p-val | FDR q-val | FWER p-val | RANK AT MAX | LEADING EDGE |
| HALLMARK\_COAGULATION | 114 | 0.57 | 2.07 | 0 | 0.078 | 0.029 | 1633 | tags=33%, list=12%, signal=38% |
| HALLMARK\_EPITHELIAL\_MESENCHYMAL\_TRANSITION | 185 | 0.73 | 1.99 | 0.006 | 0.061 | 0.05 | 1821 | tags=60%, list=14%, signal=69% |
| HALLMARK\_KRAS\_SIGNALING\_UP | 172 | 0.6 | 1.92 | 0 | 0.053 | 0.064 | 2469 | tags=45%, list=19%, signal=54% |
| HALLMARK\_ADIPOGENESIS | 169 | 0.41 | 1.84 | 0.002 | 0.071 | 0.109 | 2498 | tags=24%, list=19%, signal=29% |
| HALLMARK\_ANGIOGENESIS | 33 | 0.65 | 1.84 | 0.002 | 0.057 | 0.11 | 1701 | tags=45%, list=13%, signal=52% |
| HALLMARK\_APICAL\_JUNCTION | 184 | 0.47 | 1.82 | 0 | 0.052 | 0.12 | 3741 | tags=45%, list=28%, signal=62% |
| HALLMARK\_COMPLEMENT | 180 | 0.53 | 1.8 | 0.006 | 0.051 | 0.134 | 4376 | tags=59%, list=33%, signal=87% |
| HALLMARK\_UV\_RESPONSE\_DN | 128 | 0.57 | 1.78 | 0.002 | 0.053 | 0.152 | 3547 | tags=58%, list=27%, signal=78% |
| HALLMARK\_TGF\_BETA\_SIGNALING | 51 | 0.6 | 1.77 | 0.006 | 0.048 | 0.154 | 3355 | tags=57%, list=25%, signal=76% |
| HALLMARK\_INFLAMMATORY\_RESPONSE | 184 | 0.62 | 1.76 | 0.008 | 0.046 | 0.166 | 2314 | tags=49%, list=17%, signal=59% |
| HALLMARK\_IL2\_STAT5\_SIGNALING | 174 | 0.5 | 1.74 | 0.014 | 0.05 | 0.191 | 3460 | tags=45%, list=26%, signal=61% |
| HALLMARK\_HEME\_METABOLISM | 164 | 0.38 | 1.68 | 0 | 0.068 | 0.256 | 3672 | tags=40%, list=28%, signal=54% |
| HALLMARK\_APOPTOSIS | 147 | 0.45 | 1.65 | 0.027 | 0.076 | 0.295 | 4501 | tags=50%, list=34%, signal=74% |
| HALLMARK\_ALLOGRAFT\_REJECTION | 171 | 0.64 | 1.64 | 0.066 | 0.077 | 0.314 | 2314 | tags=52%, list=17%, signal=62% |
| HALLMARK\_HYPOXIA | 178 | 0.45 | 1.64 | 0.019 | 0.072 | 0.315 | 3435 | tags=40%, list=26%, signal=54% |
| HALLMARK\_TNFA\_SIGNALING\_VIA\_NFKB | 177 | 0.56 | 1.62 | 0.037 | 0.077 | 0.352 | 4465 | tags=66%, list=33%, signal=97% |
| HALLMARK\_XENOBIOTIC\_METABOLISM | 179 | 0.38 | 1.6 | 0.017 | 0.083 | 0.382 | 3116 | tags=30%, list=23%, signal=39% |
| HALLMARK\_IL6\_JAK\_STAT3\_SIGNALING | 80 | 0.59 | 1.57 | 0.057 | 0.089 | 0.427 | 2839 | tags=54%, list=21%, signal=68% |
| HALLMARK\_MYOGENESIS | 180 | 0.41 | 1.57 | 0.023 | 0.086 | 0.434 | 2232 | tags=26%, list=17%, signal=31% |
| HALLMARK\_ANDROGEN\_RESPONSE | 90 | 0.46 | 1.54 | 0.025 | 0.098 | 0.481 | 3835 | tags=40%, list=29%, signal=56% |
| HALLMARK\_P53\_PATHWAY | 173 | 0.37 | 1.52 | 0.042 | 0.108 | 0.526 | 4504 | tags=42%, list=34%, signal=62% |
| HALLMARK\_HEDGEHOG\_SIGNALING | 34 | 0.51 | 1.51 | 0.038 | 0.104 | 0.527 | 3221 | tags=53%, list=24%, signal=70% |
| HALLMARK\_GLYCOLYSIS | 184 | 0.34 | 1.43 | 0.094 | 0.157 | 0.654 | 4181 | tags=34%, list=31%, signal=49% |
| HALLMARK\_APICAL\_SURFACE | 39 | 0.44 | 1.41 | 0.062 | 0.16 | 0.671 | 3376 | tags=44%, list=25%, signal=58% |
| HALLMARK\_FATTY\_ACID\_METABOLISM | 137 | 0.33 | 1.41 | 0.099 | 0.16 | 0.683 | 3381 | tags=25%, list=25%, signal=33% |
| HALLMARK\_WNT\_BETA\_CATENIN\_SIGNALING | 40 | 0.45 | 1.4 | 0.102 | 0.158 | 0.689 | 2951 | tags=35%, list=22%, signal=45% |
| HALLMARK\_UNFOLDED\_PROTEIN\_RESPONSE | 97 | 0.31 | 1.37 | 0.135 | 0.176 | 0.723 | 5355 | tags=42%, list=40%, signal=70% |
| HALLMARK\_INTERFERON\_GAMMA\_RESPONSE | 174 | 0.52 | 1.34 | 0.246 | 0.188 | 0.74 | 4364 | tags=54%, list=33%, signal=79% |
| HALLMARK\_MITOTIC\_SPINDLE | 182 | 0.41 | 1.34 | 0.187 | 0.185 | 0.744 | 5487 | tags=56%, list=41%, signal=94% |
| HALLMARK\_PI3K\_AKT\_MTOR\_SIGNALING | 92 | 0.33 | 1.33 | 0.116 | 0.185 | 0.755 | 5024 | tags=47%, list=38%, signal=74% |
| HALLMARK\_NOTCH\_SIGNALING | 30 | 0.45 | 1.32 | 0.163 | 0.186 | 0.758 | 4539 | tags=60%, list=34%, signal=91% |
| HALLMARK\_PROTEIN\_SECRETION | 87 | 0.39 | 1.31 | 0.215 | 0.191 | 0.766 | 4121 | tags=45%, list=31%, signal=64% |
| HALLMARK\_ESTROGEN\_RESPONSE\_EARLY | 177 | 0.35 | 1.28 | 0.142 | 0.206 | 0.792 | 3695 | tags=36%, list=28%, signal=49% |
| HALLMARK\_CHOLESTEROL\_HOMEOSTASIS | 65 | 0.35 | 1.27 | 0.204 | 0.213 | 0.806 | 5357 | tags=51%, list=40%, signal=84% |
| HALLMARK\_BILE\_ACID\_METABOLISM | 102 | 0.31 | 1.24 | 0.147 | 0.228 | 0.822 | 3381 | tags=30%, list=25%, signal=40% |
| HALLMARK\_UV\_RESPONSE\_UP | 142 | 0.28 | 1.23 | 0.186 | 0.232 | 0.833 | 5606 | tags=44%, list=42%, signal=76% |
| HALLMARK\_REACTIVE\_OXYGEN\_SPECIES\_PATHWAY | 42 | 0.33 | 1.22 | 0.242 | 0.238 | 0.843 | 3823 | tags=29%, list=29%, signal=40% |
| HALLMARK\_PANCREAS\_BETA\_CELLS | 28 | 0.35 | 1.1 | 0.34 | 0.343 | 0.917 | 1856 | tags=21%, list=14%, signal=25% |
| HALLMARK\_MTORC1\_SIGNALING | 179 | 0.26 | 1.09 | 0.376 | 0.341 | 0.922 | 5781 | tags=45%, list=43%, signal=79% |
| HALLMARK\_INTERFERON\_ALPHA\_RESPONSE | 80 | 0.42 | 1 | 0.499 | 0.437 | 0.955 | 6378 | tags=68%, list=48%, signal=129% |
| HALLMARK\_ESTROGEN\_RESPONSE\_LATE | 187 | 0.22 | 0.9 | 0.601 | 0.554 | 0.979 | 3658 | tags=26%, list=27%, signal=35% |
| HALLMARK\_G2M\_CHECKPOINT | 167 | 0.27 | 0.82 | 0.615 | 0.65 | 0.991 | 5697 | tags=48%, list=43%, signal=83% |
| HALLMARK\_PEROXISOME | 93 | 0.18 | 0.76 | 0.83 | 0.719 | 0.991 | 4990 | tags=34%, list=37%, signal=55% |
| HALLMARK\_E2F\_TARGETS | 160 | 0.13 | 0.39 | 0.961 | 0.99 | 1 | 5436 | tags=36%, list=41%, signal=59% |

**Table S9.** Abbreviations list

|  |  |  |  |
| --- | --- | --- | --- |
| AUC | Area under the curve | IE/F | Immune-Enriched Fibrotic |
| BCR | B-cell receptor | IPS | Immunophenoscore |
| CTA | Cancer testis antigens | ITH | Intratumor heterogeneity |
| D | Desert | KEGG | Kyoto Encyclopedia of Genes and Genomes |
| DNAme | DNA driver methylation | KNN | K-nearest neighbor |
| EMA | European Medicines Agency | LOH | Loss of heterozygosity |
| EMT | Epithelial-to-mesenchymal transition | NES | Normalized enrichment score |
| F | Fibrotic | NMF | Negative matrix factorization |
| FDA | Food and Drug Administration | OC | Ovarian cancer |
| GDSC | Genomics of Drug Sensitivity in Cancer | PARP | poly (ADP-ribose) polymerase |
| GEO | Gene Expression Omnibus | PCA | Principal component analysis |
| GO | Gene ontology | SNF | Similarity network fusion |
| GSEA | Gene set enrichment analysis | SOC | Serous ovarian cancer |
| GTEx | The Genotype-Tissue Expression | ssGSEA | Single sample gene set enrichment analysis |
| HGSOC | High grade serous ovarian cancer | Submap | Subclass Mapping |
| HRD | Homologous recombination deficiency | TCGA | The Cancer Genome Atlas Project |
| IC50 | Half-maximal inhibitory concentration | TCR | T-cell receptor |
| ICGC | International Cancer Genome Consortium | TIDE | Tumor Immune Dysfunction and Exclusion |
| IE | Immune-Enriched Non-Fibrotic | TME | Tumor microenvironment |