**Identification of tumor mutation burden related differential gene expression (DEG) and differential methylation regions (DMR)**

In order to investigate the multi-omics data interaction, we investigated tumor mutation burden related differential gene expression (DEG) and differential methylation regions (DMR). In the TMB-related gene expression analysis, we compared the TMB values with difference of the each tumor sample from the corresponding normal sample. Meanwhile, in order to decrease the multiple test correction burden, we removed 30% small variant genes and high correlated genes (R2>0.6). Finally, we identified 26 interesting TMB related gene expression (P<5.0x10-4). xxxx here, you can talk about the function of some interesting genes xxx. Furthermore, in order to identify TMB-related DMRs, we binary the samples to high-TMB tumors and low-TMB tumors by the mean value of TMBs (V=4.05) and then we screen all the tumor DMRs. Finally, we identified 28 significant TMB-related DMRs with P<1.2x10-4 xxxx here, you can talk about the function of some interesting genes xxx.

Table 1. Tumor mutation burden significantly related gene expression

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Symbol | Estimate | Std..Error | t.value | P-value |
| RP11-693J15.5 | 7.865739706 | 1.453080678 | 5.413147269 | 1.47E-05 |
| NAAA | 0.242543606 | 0.048266117 | 5.025131938 | 3.90E-05 |
| H2BFS | 0.190097511 | 0.040760064 | 4.663817801 | 9.76E-05 |
| AC092299.8 | 0.674641714 | 0.145083043 | 4.650038345 | 0.000101111 |
| C1orf228 | -0.11168053 | 0.024030885 | -4.647374737 | 0.000101798 |
| OR1L3 | -2.807277446 | 0.604833346 | -4.641406541 | 0.000103356 |
| RPL6P25 | -0.073465495 | 0.016445187 | -4.467294507 | 0.00016096 |
| GBAS | -0.293093028 | 0.066403357 | -4.413828497 | 0.00018441 |
| FCGR1B | 1.055896106 | 0.242921051 | 4.346663667 | 0.000218755 |
| TMEM8C | -0.323871996 | 0.074931836 | -4.322221565 | 0.000232777 |
| CDH15 | -0.494421956 | 0.114728436 | -4.309497917 | 0.000240427 |
| RP11-281O15.5 | -1.101933942 | 0.257801079 | -4.274357376 | 0.000262881 |
| SPEM1 | 0.588555721 | 0.138007668 | 4.264659556 | 0.000269437 |
| CHRAC1 | -0.56757007 | 0.133828264 | -4.241032883 | 0.000286099 |
| LINC00989 | -6.559492333 | 1.548222328 | -4.23678965 | 0.000289198 |
| CYP4A22 | 1.876579898 | 0.444594259 | 4.220881984 | 0.000301116 |
| ROCK1 | -0.711684952 | 0.170425699 | -4.175925084 | 0.000337503 |
| PA2G4P1 | 1.430338751 | 0.343921536 | 4.158910098 | 0.000352386 |
| AOC3 | -0.306810346 | 0.074171427 | -4.136503236 | 0.000372984 |
| COMMD3-BMI1 | -0.115562458 | 0.028304292 | -4.082859956 | 0.000427278 |
| LINC00202-1 | -1.546288076 | 0.379148047 | -4.07832267 | 0.000432215 |
| SLC8A2 | -0.178007814 | 0.043661947 | -4.076955479 | 0.000433713 |
| KLF11 | -0.337891731 | 0.083010025 | -4.070493067 | 0.000440867 |
| RP11-773H22.2 | -1.778613467 | 0.438473154 | -4.056379393 | 0.000456899 |
| RP1-177I10.1 | -6.657732708 | 1.644877986 | -4.047554145 | 0.000467216 |
| ZNF859P | 4.571530836 | 1.13697826 | 4.020772424 | 0.000499958 |

* Linear regression was applied to test TMB and delta gene expression derived by difference between cancer samples compared with corresponding normal samples.

Table 2. Tumor mutation burden significantly related differential methylation regions

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| CHR | START | END | Estimate | Std..Error | t.value | P-value | Symbol |
| chr6 | 150983544 | 150983985 | 0.029831021 | 0.004680812 | 6.373044005 | 1.37E-06 | PLEKHG1 |
| chr1 | 224427563 | 224428113 | 0.037976364 | 0.006072106 | 6.254232657 | 1.83E-06 | NVL |
| chr1 | 22150064 | 22150561 | 0.061144871 | 0.010999333 | 5.558961654 | 1.02E-05 | HSPG2 |
| chr1 | 22150064 | 22150561 | 0.061144871 | 0.010999333 | 5.558961654 | 1.02E-05 | LDLRAD2 |
| chr15 | 99290335 | 99290927 | 0.029232405 | 0.005560851 | 5.25682253 | 2.17E-05 | IGF1R |
| chr5 | 135097961 | 135099845 | 0.038961648 | 0.007570319 | 5.146631982 | 2.87E-05 | SLC25A48 |
| chr18 | 55134480 | 55135151 | 0.044239913 | 0.008606869 | 5.140070192 | 2.92E-05 | ONECUT2 |
| chr14 | 24456264 | 24456641 | 0.033839233 | 0.00661441 | 5.115986845 | 3.10E-05 | DHRS4L2 |
| chr8 | 77585155 | 77586330 | 0.030396192 | 0.005944863 | 5.113018437 | 3.12E-05 | ZFHX4-AS1 |
| chr22 | 21283438 | 21283925 | 0.037378141 | 0.007415125 | 5.040797478 | 3.75E-05 | CRKL |
| chr12 | 41100864 | 41101403 | 0.020656768 | 0.004103872 | 5.033482171 | 3.82E-05 | CNTN1 |
| chr15 | 79324293 | 79324689 | 0.029426077 | 0.005894294 | 4.992298531 | 4.24E-05 | RASGRF1 |
| chr5 | 138120757 | 138121234 | 0.021332153 | 0.004316851 | 4.941600501 | 4.82E-05 | CTNNA1 |
| chr3 | 186447464 | 186447829 | 0.036594616 | 0.007484354 | 4.889481939 | 5.50E-05 | KNG1 |
| chr10 | 69591710 | 69592081 | 0.018148367 | 0.003734013 | 4.860285447 | 5.93E-05 | DNAJC12 |
| chr7 | 139878003 | 139878431 | 0.027312429 | 0.005628006 | 4.852949771 | 6.04E-05 | KDM7A-DT |
| chr17 | 30282979 | 30283420 | 0.029881143 | 0.006172145 | 4.841289715 | 6.22E-05 | SUZ12 |
| chr2 | 86757029 | 86757610 | 0.017335322 | 0.003615053 | 4.79531658 | 6.99E-05 | CHMP3 |
| chr2 | 86757029 | 86757610 | 0.017335322 | 0.003615053 | 4.79531658 | 6.99E-05 | RNF103 |
| chr7 | 140332774 | 140333187 | 0.028360582 | 0.005968894 | 4.751396269 | 7.81E-05 | DENND2A |
| chr8 | 30279176 | 30279589 | 0.016298338 | 0.003447256 | 4.727916066 | 8.29E-05 | RBPMS |
| chr15 | 78747163 | 78747894 | 0.027471138 | 0.005823407 | 4.717364866 | 8.52E-05 | IREB2 |
| chr2 | 88860670 | 88861129 | 0.016069512 | 0.00343534 | 4.67770618 | 9.42E-05 | EIF2AK3 |
| chr2 | 88860670 | 88861129 | 0.016069512 | 0.00343534 | 4.67770618 | 9.42E-05 | LOC101928371 |
| chr12 | 69233925 | 69234647 | 0.014444581 | 0.003096447 | 4.664889532 | 9.74E-05 | MDM2 |
| chr15 | 56492659 | 56493043 | 0.021343159 | 0.004593537 | 4.646344864 | 0.000102065 | RFX7 |
| chr4 | 149296260 | 149296635 | 0.019594553 | 0.004221345 | 4.641779975 | 0.000103257 | NR3C2 |
| chr1 | 45170458 | 45170919 | 0.035902119 | 0.007739252 | 4.638964919 | 0.000104 | ARMH1 |
| chr3 | 49671128 | 49671722 | 0.035580063 | 0.007709709 | 4.614968119 | 0.000110546 | BSN |
| chr14 | 72438036 | 72439575 | 0.04773642 | 0.010398825 | 4.59055923 | 0.000117629 | RGS6 |
| chr7 | 103191363 | 103191831 | 0.030582265 | 0.006677788 | 4.579700175 | 0.000120924 | RELN |

* Student t-test was applied to identify the relationship between TMB and fold change of methylation peak changes between cancer samples compared with corresponding normal samples.