Table SI. Functional clustering by mRNA expression ratio (tumor/normal; T/N) and DNA methylation (Δβ) for all 66 candidate genes.

A, Group A (T/N<0.1 and Δβ>0.1), 5 genes

| Gene symbol | T/N | Δβ | Description | Function (UniProt) |
|---|---|---|---|---|
| *CTTNBP2* | 0.046474983 | 0.126641348 | Cortactin binding protein 2 | Growth factor |
| *ID4* | 0.094123798 | 0.143371386 | Inhibitor of DNA binding 4, dominant negative helix-loop-helix protein | Growth factor |
| *KRT4* | 0.062651366 | 0.185101375 | Keratin 4 | Structure |
| *PDE6A* | 0.055492042 | 0.170563917 | Phosphodiesterase 6A, cGMP-specific, rod, alpha | Signal |
| *PRR4* | 0.09230861 | 0.174528072 | Proline-rich 4 (lacrimal), transcript variant 2 | Adhesion |

B, Group B (T/N>10 and Δβ>0.1), 22 genes

| Gene symbol | T/N | Δβ | Description | Function (UniProt) |
|---|---|---|---|---|
| *ACTA1* | 76.7808690487 | 0.2413933517 | Actin, alpha 1, skeletal muscle | Structure |
| *ACTN2* | 30.1225359676 | 0.2697856283 | Actinin, alpha 2 | Structure |
| *AJAP1* | 12.72493561 | 0.170383578 | Adherens junctions-associated protein 1, transcript variant 1 | Adhesion |
| *C1QTNF6* | 11.81205156 | 0.2002445 | C1q and tumor necrosis factor related protein 6, transcript variant 1 | Immune/inflammation |
| *CCL7* | 13.79784112 | 0.117473304 | Chemokine (C-C motif) ligand 7 | Signal |
| *CGB1* | 14.68078975 | 0.192942457 | Chorionic gonadotropin, beta polypeptide 1 | Signal |
| *CSF2* | 26.0082585199 | 0.1131973583 | Colony stimulating factor 2 (granulocyte-macrophage) | Growth factor |
| *CXCL13* | 135.1941882092 | 0.1312700667 | Chemokine (C-X-C motif) ligand 13 (B-cell chemoattractant) | Signal |
| *FSCN1* | 19.72305927 | 0.107002422 | Fascin homolog 1, actin-bundling protein (Strongylocentrotus purpuratus) | Adhesion |
| *FSTL3* | 14.40239918 | 0.122337249 | Follistatin-like 3 (secreted glycoprotein) | Growth factor |
| *GLDC* | 63.8204524590 | 0.1210649675 | Glycine dehydrogenase (decarboxylating) | Enzyme |
| *GREM1* | 10.40692335 | 0.185049141 | Gremlin 1, cysteine knot superfamily, homolog (Xenopus laevis) | Signal |
| *GRP* | 18.13726263 | 0.204426325 | Gastrin-releasing peptide, transcript variant 1 | Signal |
| *HOXD10* | 10.89073607 | 0.241879033 | Homeobox D10 | Signal |
| *KRT24* | 10.39678035 | 0.113224267 | Keratin 24 | Structure |
| *LHX2* | 22.1837618830 | 0.1107520367 | LIM homeobox 2 | Signal |
| *MMP11* | 32.4300605647 | 0.1595691732 | Matrix metallopeptidase 11 (stromelysin 3) | Enzyme |
| *PACSIN1* | 10.19954821 | 0.215395687 | Protein kinase C and casein kinase substrate in neurons 1 | Structure |
| *PLA2G7* | 15.91459725 | 0.192194565 | Phospholipase A2, group VII (platelet-activating factor acetylhydrolase, plasma) | Enzyme |
| *SERPINA3* | 14.53320371 | 0.127161615 | Serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3 | Enzyme |
| *SOX11* | 22.5603549704 | 0.1317415482 | SRY (sex determining region Y)-box 11 | Transcriptional factor |
| *TNFRSF17* | 71.2474598502 | 0.1831412333 | Tumor necrosis factor receptor superfamily, member 17 | Signal |

C, Group C (T/N > 10 and Δβ < -0.1), 39 genes

| Gene symbol | T/N | Δβ | Description | Function (UniProt) |
|---|---|---|---|---|
| *AIM2* | 19.6217124 | -0.217970098 | Absent in melanoma 2 | Growth factor |
| *AZGP1* | 15.14100236 | -0.180976358 | Alpha-2-glycoprotein 1, zinc-binding | Adhesion |
| *BLK* | 15.87772918 | -0.167095193 | B lymphoid tyrosine kinase | Enzyme |
| *BST2* | 20.3898517378 | -0.3484786992 | Bone marrow stromal cell antigen 2 | Immune/inflammation |

Table SI. Continued.

C, Group C (T/N > 10 and Δβ < -0.1), 39 genes

| Gene symbol | T/N | Δβ | Description | Function (UniProt) |
|---|---|---|---|---|
| *CALB1* | 55.0002978101 | -0.1093218617 | Calbindin 1, 28 kDa | Metabolism |
| *CCL8* | 13.19396768 | -0.265696985 | Chemokine (C-C motif) ligand 8 | Signal |
| *CDSN* | 63.2763605196 | -0.1181656758 | Corneodesmosin | Growth factor |
| *DEFB103A* | 16.37311905 | -0.125522273 | Defensin, beta 103A | Immune/inflammation |
| *DKK1* | 16.92536015 | -0.126459913 | Dickkopf homolog 1 (Xenopus laevis) | Signal |
| *FCGR3B* | 10.13229106 | -0.137753942 | Fc fragment of IgG, low affinity IIIb, receptor (CD16b) | Immune/inflammation |
| *GBP5* | 33.2380782353 | -0.1109470775 | Guanylate binding protein 5 | Immune/inflammation |
| *GFI1* | 10.09558923 | -0.137140478 | Growth factor independent 1 transcription repressor | Growth factor |
| *GJB7* | 21.2001494041 | -0.1136051583 | Gap junction protein, beta 7, 25 kDa | Transportation |
| *GNLY* | 14.94594066 | -0.168183 | Granulysin, transcript variant NKG5 | Immune/inflammation |
| *IGJ* | 31.9503473103 | -0.1295257750 | Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides | Immune/inflammation |
| *IGLL1* | 136.4124102143 | -0.1344653383 | Immunoglobulin lambda-like polypeptide 1, transcript variant 1 | Immune/inflammation |
| *IL12RB2* | 11.06056928 | -0.207640713 | Interleukin 12 receptor, beta 2 | Immune/inflammation |
| *IL2RA* | 19.01117519 | -0.323533125 | Interleukin 2 receptor, alpha | Immune/inflammation |
| *LAIR2* | 12.69447317 | -0.102877801 | Leukocyte-associated immunoglobulin-like receptor 2, transcript variant 1 | Immune/inflammation |
| *MAGEA1* | 18.4626044 | -0.118301511 | Melanoma antigen family A, 1 (directs expression of antigen MZ2-E) | Growth factor |
| *MAGEC2* | 12.51059687 | -0.152597578 | Melanoma antigen family C, 2 | Signal |
| *MMP13* | 250.9824673732 | -0.1116719583 | Matrix metallopeptidase 13 (collagenase 3) | Enzyme |
| *MYH7* | 24.8015332005 | -0.1860270050 | Myosin, heavy chain 7, cardiac muscle, beta | Structure |
| *MYL1* | 29.4306344251 | -0.1106252500 | Myosin, light chain 1, alkali; skeletal, fast, transcript variant 1f | Structure |
| *OLFM4* | 40.7686369333 | -0.1801804950 | Olfactomedin 4 | Adhesion |
| *OSM* | 10.09295695 | -0.148159558 | Oncostatin M | Growth factor |
| *OSTbeta* | 18.02041425 | -0.156318441 | Organic solute transporter beta | Transportation |
| *PAGE2* | 29.6983745678 | -0.1145915392 | P antigen family, member 2 (prostate associated) | Unknown |
| *PFTK1* | 10.623217 | -0.112921867 | PFTAIRE protein kinase 1 | Signal |
| *PI3* | 12.01545048 | -0.232030383 | Peptidase inhibitor 3, skin-derived (SKALP) | Enzyme |
| *PIK3R5* | 14.495631 | -0.10109523 | Phosphoinositide-3-kinase, regulatory subunit 5 | Signal |
| *PIP* | 15.17028015 | -0.212125542 | Prolactin-induced protein | Transportation |
| *PLUNC* | 17.34791478 | -0.125113619 | Palate, lung and nasal epithelium-associated, transcript variant 1 | Immune/inflammation |
| *PNOC* | 11.28327184 | -0.210293025 | Prepronociceptin | Signal |
| *POU2AF1* | 10.49018407 | -0.187083537 | POU class 2 associating factor 1 | Signal |
| *TREM1* | 10.26454338 | -0.144586192 | Triggering receptor expressed on myeloid cells 1 | Immune/inflammation |
| *UBD* | 18.6851743 | -0.148723942 | Ubiquitin D | Signal |
| *VTCN1* | 10.18126512 | -0.10736898 | V-set domain containing T-cell activation inhibitor 1 | Immune/inflammation |
| *WARS* | 15.03172176 | -0.141310829 | Tryptophanyl-tRNA synthetase, transcript variant 1 | Immune/inflammation |

mRNA expression ratio (T/N) and DNA methylation score (Δβ) were calculated as expression score in tumor tissue (T) normal tissue (N), and methylation score in tumor tissue (T) - normal tissue (N), respectively. We set up the threshold of T/N and Δβ (Fig. 1), and performed functional clustering (Fig. 2). When the thresholds were T/N>10 and Δβ>0.1 or <-0.1, 66 genes were identified as candidate genes suggested to be regulated via altered aberrant DNA methylation. There were also certain cancer prognostic genes (lower part of Table I). All 66 candidate genes are shown in this table. According to the patterns of T/N and Δβ, each group was defined as follows: Group A: T/N<0.1 and Δβ>0.1, group B: T/N>10 and Δβ>0.1, group C: T/N>10 and Δβ<-0.1.