

**Table S1. Differentially expressed signaling-related mRNAs in Dicer-deficient CD4 T cells identified by gene expression arrays**

| Signalling-related transcripts, up-regulated (q<0.05) |   |            |            |
|---|---|------------|------------|
| Gene Symbol   | Gene Name   | F-C (log2) | GO-ID      |
| <i>Gpr114</i>   | G protein-coupled receptor 114  | 3.30       | GO:0007165 |
| <i>Iigp1</i>  | interferon inducible GTPase 1   | 3.11       | GO:0019221 |
| <i>Ifitm3</i>   | interferon induced transmembrane protein 3  | 1.71       | GO:0060337 |
| <i>Nedd4</i>  | neural precursor cell expressed developmentally down-regulated gene 4             | 1.66       | GO:0014068 |
| <i>Pde2a</i>  | phosphodiesterase 2A, cGMP-stimulated   | 1.38       | GO:0007165 |
| <i>Itgb3</i>  | integrin beta 3   | 1.33       | GO:0007229 |
| <i>Abca1</i>  | ATP-binding cassette, sub-family A (ABC1), member 1                               | 1.31       | GO:0007186 |
| <i>Irf1</i>   | interferon regulatory factor 1  | 1.30       | GO:0007249 |
| <i>Stat1</i>  | signal transducer and activator of transcription 1                                | 1.29       | GO:0007259 |
| <i>Txnip</i>  | thioredoxin interacting protein   | 1.22       | GO:0048008 |
| <i>Il10rb</i>   | interleukin 10 receptor, beta   | 1.21       | GO:0019221 |
| <i>Nr1d1</i>  | nuclear receptor subfamily 1, group D, member 1                                   | 1.20       | GO:0034144 |
| <i>Arpp19</i>   | cAMP-regulated phosphoprotein 19  | 1.17       | GO:0046579 |
| <i>Tgfbr1</i>   | transforming growth factor, beta receptor I                                       | 1.17       | GO:0007165 |
| <i>Cacnb3</i>   | calcium channel, voltage-dependent, beta 3 subunit                                | 1.10       | GO:0050852 |
| <i>Sept2</i>  | septin 2  | 1.07       | GO:0007224 |
| <i>Tgfbr3</i>   | transforming growth factor, beta receptor III                                     | 1.07       | GO:0007179 |
| <i>Sgk1</i>   | serum/glucocorticoid regulated kinase 1   | 1.05       | GO:0043402 |
| <i>Igfbp4</i>   | insulin-like growth factor binding protein 4                                      | 1.01       | GO:0043410 |
| <i>Tlr1</i>   | toll-like receptor 1  | 0.98       | GO:0007165 |
| <i>Aplp2</i>  | amyloid beta (A4) precursor-like protein 2  | 0.97       | GO:0007176 |
| <i>Rab1</i>   | RAB1, member RAS oncogene family  | 0.96       | GO:0007264 |
| <i>Bcl3</i>   | B-cell leukemia/lymphoma 3  | 0.96       | GO:0007249 |
| <i>Cttnb1</i>   | catenin (cadherin associated protein), beta 1                                     | 0.90       | GO:0003136 |
| <i>Nfe2l2</i>   | nuclear factor, erythroid derived 2, like 2                                       | 0.90       | GO:0030968 |
| <i>Ifnar1</i>   | interferon (alpha and beta) receptor 1  | 0.90       | GO:0019221 |
| <i>Rab12</i>  | RAB12, member RAS oncogene family   | 0.87       | GO:0007264 |
| <i>Smurf2</i>   | SMAD specific E3 ubiquitin protein ligase 2                                       | 0.87       | GO:0030579 |
| <i>Mknk2</i>  | MAP kinase-interacting serine/threonine kinase 2                                  | 0.86       | GO:0007243 |
| <i>Msh6</i>   | mutS homolog 6 (E. coli)  | 0.85       | GO:0008630 |
| <i>Rab2a</i>  | RAB2A, member RAS oncogene family   | 0.85       | GO:0007264 |
| <i>Adam10</i>   | a disintegrin and metallopeptidase domain 10                                      | 0.84       | GO:0007219 |
| <i>Sema7a</i>   | sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A | 0.81       | GO:0007229 |
| <i>Itgb7</i>  | integrin beta 7   | 0.81       | GO:0007229 |
| <i>Dyrk2</i>  | dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2                  | 0.81       | GO:0007224 |
| <i>Hspa5</i>  | heat shock protein 5  | 0.78       | GO:0006983 |
| <i>Sel1l</i>  | sel-1 suppressor of lin-12-like (C. elegans)                                      | 0.77       | GO:0007219 |

|                 |  |      |            |
|-----------------|--|------|------------|
| <i>Adamts14</i> | a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 14 | 0.77 | GO:0007229 |
| <i>Psap</i>     | prosaposin   | 0.76 | GO:0043408 |
| <i>Spnb2</i>    | spectrin beta 2  | 0.76 | GO:0007182 |
| <i>Arl8b</i>    | ADP-ribosylation factor-like 8B  | 0.76 | GO:0007264 |
| <i>Pecam1</i>   | platelet/endothelial cell adhesion molecule 1  | 0.75 | GO:0007266 |
| <i>Stat3</i>    | signal transducer and activator of transcription 3   | 0.75 | GO:0007165 |
| <i>Calr</i>     | calreticulin   | 0.75 | GO:0033144 |
| <i>Mcl1</i>     | myeloid cell leukemia sequence 1   | 0.74 | GO:2001240 |
| <i>Il21r</i>    | interleukin 21 receptor  | 0.73 | GO:0007165 |
| <i>Pik3cd</i>   | phosphatidylinositol 3-kinase catalytic delta polypeptide                                      | 0.73 | GO:0007166 |
| <i>Itgav</i>    | integrin alpha V   | 0.72 | GO:0007229 |
| <i>Ddx58</i>    | DEAD (Asp-Glu-Ala-Asp) box polypeptide 58  | 0.72 | GO:0039529 |
| <i>Adcy6</i>    | adenylate cyclase 6  | 0.71 | GO:0007212 |
| <i>Gsn</i>      | gelsolin   | 0.71 | GO:0048015 |
| <i>Gata3</i>    | GATA binding protein 3   | 0.71 | GO:0007165 |
| <i>Nptn</i>     | neuroplastin   | 0.70 | GO:0045743 |
| <i>Ppp1r9b</i>  | protein phosphatase 1, regulatory subunit 9B   | 0.70 | GO:2000474 |
| <i>Itgb2</i>    | integrin beta 2  | 0.69 | GO:0007229 |
| <i>Jak1</i>     | Janus kinase 1   | 0.68 | GO:0007167 |
| <i>Smad5</i>    | MAD homolog 5 (Drosophila)   | 0.67 | GO:0007179 |
| <i>Tgfbr2</i>   | transforming growth factor, beta receptor II   | 0.67 | GO:0007178 |
| <i>Cd4</i>      | CD4 antigen  | 0.67 | GO:0007166 |
| <i>Ccr7</i>     | chemokine (C-C motif) receptor 7   | 0.64 | GO:0007165 |
| <i>Hbp1</i>     | high mobility group box transcription factor 1   | 0.64 | GO:0016055 |
| <i>Igf2r</i>    | insulin-like growth factor 2 receptor  | 0.64 | GO:0007186 |
| <i>Arhgef6</i>  | Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6   | 0.62 | GO:0035023 |
| <i>Rras2</i>    | related RAS viral (r-ras) oncogene homolog 2   | 0.62 | GO:0007165 |
| <i>Tnks2</i>    | tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase 2                            | 0.62 | GO:0016055 |
| <i>Stk4</i>     | serine/threonine kinase 4  | 0.61 | GO:0007165 |
| <i>Ece1</i>     | endothelin converting enzyme 1   | 0.61 | GO:0045745 |
| <i>Dnaja1</i>   | DnaJ (Hsp40) homolog, subfamily A, member 1  | 0.60 | GO:0030521 |
| <i>Nfkbia</i>   | nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha            | 0.59 | GO:0007253 |
| <i>Rac1</i>     | RAS-related C3 botulinum substrate 1   | 0.58 | GO:0007264 |
| <i>Gpr18</i>    | G protein-coupled receptor 18  | 0.57 | GO:0007165 |
| <i>Rab18</i>    | RAB18, member RAS oncogene family   fatty acid binding protein 5-like 2                        | 0.57 | GO:0007264 |
| <i>Ecm1</i>     | extracellular matrix protein 1   | 0.57 | GO:0001960 |
| <i>Dusp10</i>   | dual specificity phosphatase 10  | 0.56 | GO:0000188 |
| <i>Adam17</i>   | a disintegrin and metallopeptidase domain 17   | 0.56 | GO:0007173 |
| <i>Pik3r1</i>   | phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85 alpha)                   | 0.56 | GO:0007165 |
| <i>Atp2a2</i>   | ATPase, Ca <sup>++</sup> transporting, cardiac muscle, slow twitch 2                           | 0.55 | GO:0006984 |
| <i>Nfkb2</i>    | nuclear factor of kappa light polypeptide gene enhancer in B-cells 2, p49/p100                 | 0.54 | GO:0007165 |
| <i>Ubash3a</i>  | ubiquitin associated and SH3 domain containing, A  | 0.54 | GO:0050860 |
| <i>G3bp2</i>    | GTPase activating protein (SH3 domain) binding protein 2                                       | 0.53 | GO:0007264 |
| <i>Gng12</i>    | guanine nucleotide binding protein (G protein), gamma 12                                       | 0.53 | GO:0007165 |

|                |  |      |            |
|----------------|--|------|------------|
| <i>Lck</i>     | lymphocyte protein tyrosine kinase   | 0.52 | GO:0007166 |
| <i>Sh3glb1</i> | SH3-domain GRB2-like B1 (endophilin)   | 0.52 | GO:0007165 |
| <i>Sema4d</i>  | sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4D | 0.52 | GO:0014068 |
| <i>Rap1b</i>   | RAS related protein 1b similar to GTP-binding protein  | 0.51 | GO:0007165 |
| <i>Ksr1</i>    | kinase suppressor of ras 1   | 0.50 | GO:0035556 |
| <i>Zc3hav1</i> | zinc finger CCCH type, antiviral 1   | 0.47 | GO:0043123 |
| <i>Lats1</i>   | large tumor suppressor   | 0.47 | GO:0009755 |
| <i>BNIP2</i>   | BCL2/adenovirus E1B interacting protein 1, NIP2  | 0.46 | GO:0043410 |
| <i>Gna13</i>   | guanine nucleotide binding protein, alpha 13   | 0.45 | GO:0007165 |
| <i>Hif1a</i>   | hypoxia inducible factor 1, alpha subunit  | 0.45 | GO:0007165 |
| <i>Grhl3</i>   | grainyhead-like 3 (Drosophila)   | 0.45 | GO:0090179 |
| <i>Ncoa3</i>   | nuclear receptor coactivator 3   | 0.45 | GO:0033145 |
| <i>Socs3</i>   | suppressor of cytokine signaling 3   | 0.45 | GO:0007165 |
| <i>Aars</i>    | alanyl-tRNA synthetase   exosome component 6   | 0.45 | GO:0030968 |
| <i>Prkca</i>   | protein kinase C, alpha  | 0.44 | GO:0000188 |
| <i>Slc44a2</i> | solute carrier family 44, member 2   | 0.44 | GO:0007165 |
| <i>Lfng</i>    | LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase   | 0.43 | GO:0045747 |
| <i>Sirt1</i>   | sirtuin 1 (silent mating type information regulation 2, homolog) 1   | 0.42 | GO:0008630 |
| <i>Nrbp1</i>   | nuclear receptor binding protein 1   | 0.42 | GO:0007254 |
| <i>Rps6ka5</i> | ribosomal protein S6 kinase, polypeptide 5   | 0.42 | GO:0007243 |
| <i>Vav2</i>    | vav 2 oncogene   | 0.42 | GO:0007264 |
| <i>Itgal</i>   | integrin alpha L   | 0.42 | GO:0007166 |
| <i>Cflar</i>   | CASP8 and FADD-like apoptosis regulator  | 0.41 | GO:2001237 |
| <i>Ppp2r5a</i> | protein phosphatase 2, regulatory subunit B (B56), alpha isoform   | 0.41 | GO:0007165 |
| <i>Mapk1</i>   | mitogen-activated protein kinase 1   | 0.40 | GO:0000165 |
| <i>Ripk1</i>   | receptor (TNFRSF)-interacting serine-threonine kinase 1  | 0.40 | GO:0007165 |
| <i>P2rx4</i>   | purinergic receptor P2X, ligand-gated ion channel 4  | 0.40 | GO:0007165 |
| <i>Arf1</i>    | ADP-ribosylation factor 1  | 0.40 | GO:0007264 |
| <i>Rhot1</i>   | ras homolog gene family, member T1   | 0.39 | GO:0007264 |
| <i>Asb8</i>    | ankyrin repeat and SOCS box-containing protein 8   | 0.39 | GO:0035556 |
| <i>Tlr6</i>    | toll-like receptor 6   | 0.39 | GO:0002224 |
| <i>Crk</i>     | v-crk sarcoma virus CT10 oncogene homolog (avian)  | 0.38 | GO:0035020 |
| <i>Tbl1xr1</i> | transducin (beta)-like 1X-linked receptor 1  | 0.38 | GO:0060070 |
| <i>Med14</i>   | mediator complex subunit 14  | 0.37 | GO:0030518 |
| <i>Rhoa</i>    | ras homolog gene family, member A  | 0.37 | GO:0007229 |
| <i>Il12rb1</i> | interleukin 12 receptor, beta 1  | 0.37 | GO:0035722 |
| <i>Nfkb1</i>   | nuclear factor of kappa light polypeptide gene enhancer in B-cells 1, p105                                       | 0.36 | GO:0007165 |
| <i>Plcl2</i>   | phospholipase C-like 2   | 0.36 | GO:0007165 |
| <i>Pak2</i>    | p21 (CDKN1A)-activated kinase 2  | 0.36 | GO:2001238 |
| <i>Smarcc1</i> | SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1                | 0.35 | GO:0008286 |
| <i>Csnk2a1</i> | casein kinase 2, alpha 1 polypeptide   | 0.34 | GO:0016055 |
| <i>Asb3</i>    | ankyrin repeat and SOCS box-containing protein 3   | 0.34 | GO:0035556 |
| <i>Ldb1</i>    | LIM domain binding 1   | 0.33 | GO:0016055 |
| <i>Socs7</i>   | suppressor of cytokine signaling 7   | 0.32 | GO:0008286 |
| <i>Aak1</i>    | AP2 associated kinase 1  | 0.32 | GO:0045747 |
| <i>Dot1l</i>   | DOT1-like, histone H3 methyltransferase (S. cerevisiae)  | 0.31 | GO:0046425 |
| <i>Ppap2b</i>  | phosphatidic acid phosphatase type 2B  | 0.31 | GO:0030111 |

|                 |  |      |            |
|-----------------|--|------|------------|
| <i>Adcy7</i>    | adenylate cyclase 7  | 0.31 | GO:0035556 |
| <i>Vapa</i>     | vesicle-associated membrane protein, associated protein A        | 0.31 | GO:0007165 |
| <i>Gpsm2</i>    | G-protein signalling modulator 2 (AGS3-like, <i>C. elegans</i> ) | 0.30 | GO:0007165 |
| <i>Ncstn</i>    | nicastrin  | 0.30 | GO:0007219 |
| <i>Cdc42</i>    | cell division cycle 42 homolog ( <i>S. cerevisiae</i> )          | 0.29 | GO:0007264 |
| <i>Rab10</i>    | RAB10, member RAS oncogene family                                | 0.29 | GO:0007264 |
| <i>Rnf14</i>    | ring finger protein 14   | 0.28 | GO:0060765 |
| <i>Casp2</i>    | caspase 2  | 0.25 | GO:0006977 |
| <i>Map3k4</i>   | mitogen-activated protein kinase kinase kinase 4                 | 0.25 | GO:0007243 |
| <i>Nras</i>     | neuroblastoma ras oncogene                                       | 0.25 | GO:0007265 |
| <i>Prkd2</i>    | protein kinase D2  | 0.22 | GO:0007243 |
| <i>Mapkapk5</i> | MAP kinase-activated protein kinase 5                            | 0.22 | GO:0007265 |
| <i>Hdac4</i>    | histone deacetylase 4  | 0.19 | GO:0010882 |
| <i>Hipk3</i>    | homeodomain interacting protein kinase 3                         | 0.19 | GO:0043508 |
| <i>Stat5a</i>   | signal transducer and activator of transcription 5A              | 0.19 | GO:0007165 |
| <i>Raf1</i>     | v-raf-leukemia viral oncogene 1                                  | 0.15 | GO:0000165 |
| <i>Vmn2r20</i>  | vomeroneasal 2, receptor 20                                      | 0.12 | GO:0007165 |
| <i>Golph3</i>   | golgi phosphoprotein 3   | 0.11 | GO:0032008 |
| <i>Olfir919</i> | olfactory receptor 919   | 0.10 | GO:0007165 |

---

**Signalling related genes, down-regulated (q-value < 0.05)**

---

| Gene Symbol      | Gene Name  | F-C (log2) | GO-ID      |
|------------------|--|------------|------------|
| <i>Olfir628</i>  | olfactory receptor 628   | -0.06      | GO:0007165 |
| <i>Olfir1242</i> | olfactory receptor 1242  | -0.08      | GO:0007165 |
| <i>Scg2</i>      | secretogranin II   | -0.10      | GO:0000165 |
| <i>Gpr15</i>     | G protein-coupled receptor 15  | -0.10      | GO:0007165 |
| <i>Guca1a</i>    | guanylate cyclase activator 1a (retina)  | -0.10      | GO:0007602 |
| <i>Sept4</i>     | septin 4   | -0.12      | GO:2001244 |
| <i>Arl10</i>     | ADP-ribosylation factor-like 10  | -0.14      | GO:0007264 |
| <i>Nmu</i>       | neuromedin U   | -0.15      | GO:0007218 |
| <i>Klk1b4</i>    | kallikrein 1-related peptidase b4  | -0.16      | GO:0007264 |
| <i>Olfir1427</i> | olfactory receptor 1427  | -0.16      | GO:0007165 |
| <i>Olfir669</i>  | olfactory receptor 669   | -0.17      | GO:0007165 |
| <i>Nphs1</i>     | nephrosis 1 homolog, nephrin (human)   | -0.18      | GO:0000165 |
| <i>Carm1</i>     | coactivator-associated arginine methyltransferase 1                            | -0.18      | GO:0030518 |
| <i>Sox2</i>      | SRY-box containing gene 2  | -0.19      | GO:0030178 |
| <i>Baiap2l2</i>  | BAI1-associated protein 2-like 2   | -0.19      | GO:0007165 |
| <i>Htt</i>       | huntingtin   | -0.21      | GO:0007212 |
| <i>Cdkn2b</i>    | cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)                      | -0.23      | GO:0030511 |
| <i>Olfir95</i>   | olfactory receptor 95  | -0.25      | GO:0007165 |
| <i>Robo1</i>     | roundabout homolog 1 ( <i>Drosophila</i> )                                     | -0.28      | GO:0035385 |
| <i>Gabbr2</i>    | gamma-aminobutyric acid (GABA-C) receptor, subunit rho 2                       | -0.28      | GO:0007214 |
| <i>Il20rb</i>    | interleukin 20 receptor beta   | -0.30      | GO:0002765 |
| <i>Irak1</i>     | interleukin-1 receptor-associated kinase 1                                     | -0.31      | GO:0001959 |
| <i>Ppp2r1b</i>   | protein phosphatase 2 (formerly 2A), regulatory subunit A (PR65), beta isoform | -0.34      | GO:2001241 |

|                |  |       |            |
|----------------|--|-------|------------|
| <i>Ppp2r5c</i> | protein phosphatase 2. regulatory subunit B (B56). gamma isoform     | -0.36 | GO:0006977 |
| <i>Rcan3</i>   | regulator of calcineurin 3   | -0.38 | GO:0019722 |
| <i>Efnb3</i>   | ephrin B3  | -0.40 | GO:0048013 |
| <i>Kcnh2</i>   | potassium voltage-gated channel. subfamily H (eag-related). member 2 | -0.42 | GO:0000160 |
| <i>Mif</i>     | macrophage migration inhibitory factor                               | -0.43 | GO:0007166 |
| <i>Tmbim4</i>  | transmembrane BAX inhibitor motif containing 4                       | -0.45 | GO:0050848 |
| <i>Egr1</i>    | early growth response 1  | -0.49 | GO:0030509 |
| <i>S100a13</i> | S100 calcium binding protein A13                                     | -0.50 | GO:0043123 |
| <i>Srebf2</i>  | sterol regulatory element binding factor 2                           | -0.54 | GO:0035104 |
| <i>Timp2</i>   | tissue inhibitor of metalloproteinase 2                              | -0.80 | GO:0032487 |

---

**Table S2. Differentially expressed signaling-related proteins in Dicer-deficient CD4 T cells identified by quantitative proteomics**

| Gene   | Protein  | F-C  | GO-ID      |
|--|--|------|------------|
| <b>Signalling-related proteins up-regulated &gt;1.5 fold</b> |  |      |            |
| <i>Itgb3</i>   | Integrin beta-3  | 5.22 | GO:0007229 |
| <i>Hgs</i>   | Hepatocyte growth factor-regulated tyrosine kinase substrate | 4.33 | GO:0046426 |
| <i>Rasa1</i>   | RAS p21 protein activator 1                                  | 4.28 | GO:0007165 |
| <i>Crk</i>   | v-crk sarcoma virus CT10 oncogene homolog                    | 4.19 | GO:0035020 |
| <i>Iqgap2</i>  | IQ motif containing GTPase activating protein 2              | 3.59 | GO:0007165 |
| <i>Itgav</i>   | Integrin alpha V, CD51                                       | 3.35 | GO:0007229 |
| <i>Pde2a</i>   | phosphodiesterase 2A   | 3.28 | GO:0007165 |
| <i>Stap1</i>   | Signal-transducing adaptor protein 1                         | 3.21 | GO:0007169 |
| <i>Map2k4</i>  | mitogen-activated protein kinase kinase 4                    | 3.07 | GO:0007257 |
| <i>Macf1</i>   | microtubule-actin crosslinking factor 1                      | 3.07 | GO:0016055 |
| <i>Prex1</i>   | Phosphatidylinositol 3,4,5-dependent Rac exchanger 1 protein | 2.84 | GO:0035023 |
| <i>Rictor</i>  | Rapamycin-insensitive companion of mTOR                      | 2.56 | GO:0051896 |
| <i>Gsk3a</i>   | Glycogen synthase kinase-3 alpha                             | 2.54 | GO:0071879 |
| <i>Col4a3bp</i>  | Collagen type IV alpha-3-binding protein                     | 2.47 | GO:0007165 |
| <i>Rps6ka5</i>   | Ribosomal protein S6 kinase alpha-5                          | 2.46 | GO:0007243 |
| <i>Usp34</i>   | Ubiquitin carboxyl-terminal hydrolase 34                     | 2.40 | GO:0090263 |
| <i>Msh6</i>  | DNA mismatch repair protein Msh6                             | 2.35 | GO:0008630 |
| <i>Spn</i>   | Sialophorin, CD43 antigen                                    | 2.33 | GO:0007166 |
| <i>Arl8a</i>   | ADP-ribosylation factor-like protein 8A                      | 2.31 | GO:0007264 |
| <i>Camk4</i>   | Calcium/calmodulin-dependent protein kinase type IV          | 2.25 | GO:0007165 |
| <i>Casp8</i>   | Caspase-8  | 2.23 | GO:0097191 |
| <i>Prkcd</i>   | Protein kinase C delta                                       | 2.18 | GO:0035556 |
| <i>Mtor</i>  | FKBP12-rapamycin complex-associated protein                  | 2.16 | GO:0051897 |
| <i>Rbm38</i>   | RNA-binding protein 38                                       | 2.08 | GO:0006977 |
| <i>Atp2a2</i>  | Sarcoplasmic/endoplasmic reticulum calcium ATPase 2          | 1.98 | GO:0006984 |
| <i>Msh2</i>  | DNA mismatch repair protein Msh2                             | 1.93 | GO:0042771 |
| <i>Dnaja1</i>  | DnaJ homolog subfamily A member 1                            | 1.92 | GO:0030521 |
| <i>Ccdc109a</i>  | Coiled-coil domain-containing protein 109A                   | 1.86 | GO:0019722 |
| <i>Dgke</i>  | Diacylglycerol kinase epsilon                                | 1.80 | GO:0007205 |
| <i>Gng2</i>  | Guanine nucleotide-binding protein gamma-2                   | 1.79 | GO:0007165 |
| <i>Tlk1</i>  | Serine/threonine-protein kinase tousel-like 1                | 1.77 | GO:0035556 |
| <i>Rab14</i>   | Ras-related protein Rab-14                                   | 1.76 | GO:0007264 |
| <i>Ogt</i>   | UDP-N- acetylglucosaminyltransferase                         | 1.73 | GO:0048015 |
| <i>Nfatc1</i>  | Nuclear factor of activated T-cells, cytoplasmic 1           | 1.73 | GO:0035556 |
| <i>Tnik</i>  | Traf2 and NCK-interacting protein kinase                     | 1.71 | GO:0016055 |
| <i>Slc44a2</i>   | Choline transporter-like protein 2                           | 1.67 | GO:0007165 |
| <i>G3bp2</i>   | Ras GTPase-activating protein-binding protein 2              | 1.68 | GO:0007264 |
| <i>Aars</i>  | Alanyl-tRNA synthetase, cytoplasmic                          | 1.68 | GO:0030968 |
| <i>Smarcc1</i>   | SWI/SNF complex 155 kDa subunit                              | 1.67 | GO:0008286 |
| <i>Cul3</i>  | Cullin-3   | 1.67 | GO:0007229 |

|                |  |      |            |
|----------------|--|------|------------|
| <i>Itpr2</i>   | Inositol 1,4,5-triphosphate receptor 2               | 1.66 | GO:0048016 |
| <i>Arf6</i>    | ADP-ribosylation factor 6                            | 1.65 | GO:0007264 |
| <i>Fkbp1a</i>  | FK506-binding protein 1A                             | 1.62 | GO:0007165 |
| <i>Dgkz</i>    | Diacylglycerol kinase zeta                           | 1.63 | GO:0007205 |
| <i>Stat3</i>   | Signal transducer and activator of transcription 3   | 1.62 | GO:0045747 |
| <i>Casp2</i>   | Caspase-2  | 1.62 | GO:0006977 |
| <i>Igf2r</i>   | IGF2 receptor  | 1.62 | GO:0007186 |
| <i>Nr3c1</i>   | Glucocorticoid receptor subfamily 3 group C member 1 | 1.62 | GO:0043402 |
| <i>Aip</i>     | AH receptor-interacting protein                      | 1.60 | GO:0010738 |
| <i>Spag9</i>   | C-jun-amino-terminal kinase-interacting protein 4    | 1.60 | GO:0007257 |
| <i>Rock1</i>   | Rho-associated protein kinase 1                      | 1.58 | GO:0007165 |
| <i>Dnm1l</i>   | Dynamin-1-like protein                               | 1.58 | GO:2001244 |
| <i>Aak1</i>    | AP2-associated protein kinase 1                      | 1.57 | GO:0045747 |
| <i>Synj1</i>   | Synaptojanin-1                                       | 1.56 | GO:0048015 |
| <i>Nkiras2</i> | NF-kappa-B inhibitor-interacting Ras-like protein 2  | 1.56 | GO:0007165 |
| <i>Rab21</i>   | Ras-related protein Rab-21                           | 1.56 | GO:0007264 |
| <i>Ubr2</i>    | E3 ubiquitin-protein ligase UBR2                     | 1.53 | GO:0032007 |
| <i>Itgal</i>   | Integrin alpha L                                     | 1.53 | GO:0007229 |
| <i>Itgb2</i>   | Integrin beta-2                                      | 1.53 | GO:0007229 |
| <i>Mapk3</i>   | Mitogen-activated protein kinase 3                   | 1.52 | GO:0032872 |
| <i>Adcy7</i>   | Adenylate cyclase type 7                             | 1.51 | GO:0035556 |
| <i>Gna13</i>   | Guanine nucleotide-binding protein alpha-13          | 1.51 | GO:0007165 |
| <i>Ncor1</i>   | Nuclear receptor co-repressor 1                      | 1.50 | GO:0046329 |

**Signalling-related proteins down-regulated >1.5 fold**

| <i>Gene</i>     | Protein  | F-C   | GO-ID      |
|-----------------|--|-------|------------|
| <i>Eef1d</i>    | eukaryotic translation elongation factor 1 delta         | -1.50 | GO:0007165 |
| <i>Lrrfip2</i>  | Leucine-rich repeat flightless-interacting protein 2     | -1.51 | GO:0016055 |
| <i>Arrb1</i>    | Beta-arrestin-1  | -1.52 | GO:0007165 |
| <i>Txndc17</i>  | Thioredoxin domain-containing protein 17                 | -1.52 | GO:0033209 |
| <i>Cdk5</i>     | Cell division protein kinase 5                           | -1.57 | GO:2000273 |
| <i>Ikbkb</i>    | Inhibitor of nuclear factor kappa-B kinase beta          | -1.58 | GO:0023014 |
| <i>Ikbkg</i>    | Inhibitor of nuclear factor kappa-B kinase gamma         | -1.60 | GO:0007250 |
| <i>Ada</i>      | Adenosine deaminase                                      | -1.60 | GO:0060169 |
| <i>Irf3</i>     | Interferon regulatory factor 3                           | -1.60 | GO:0043123 |
| <i>Wdr12</i>    | WD repeat-containing protein 12                          | -1.61 | GO:0007219 |
| <i>Igbp1</i>    | Immunoglobulin-binding protein 1                         | -1.61 | GO:0032873 |
| <i>Rps6</i>     | 40S ribosomal protein S6                                 | -1.61 | GO:0031929 |
| <i>Prkca</i>    | Protein kinase C alpha                                   | -1.63 | GO:0035556 |
| <i>Arid1a</i>   | AT rich interactive domain 1A                            | -1.63 | GO:0042921 |
| <i>Arhgef18</i> | Rho guanine nucleotide exchange factor 18                | -1.64 | GO:0035023 |
| <i>Ryr2</i>     | Ryanodine receptor type 2                                | -1.64 | GO:0030509 |
| <i>Gnb2l1</i>   | Guanine nucleotide-binding protein subunit beta-2-like 1 | -1.65 | GO:0035556 |
| <i>Sgpl1</i>    | Sphingosine-1-phosphate lyase 1                          | -1.67 | GO:0048008 |
| <i>Rgs10</i>    | Regulator of G-protein signaling 10                      | -1.69 | GO:0009968 |

|                 |  |       |            |
|-----------------|--|-------|------------|
| <i>Npm1</i>     | Nucleophosmin  | -1.69 | GO:0043516 |
| <i>Pfdn5</i>    | Prefoldin subunit 5                                    | -1.73 | GO:0090090 |
| <i>Ripk3</i>    | Receptor-interacting serine/threonine-protein kinase 3 | -1.75 | GO:0023014 |
| <i>Pycard</i>   | Apoptosis-associated protein containing a CARD         | -1.76 | GO:0033209 |
| <i>Pacsin2</i>  | PKC and CK substrate in neurons protein 2              | -1.76 | GO:0007165 |
| <i>Mif</i>      | Macrophage migration inhibitory factor                 | -1.79 | GO:0030330 |
| <i>Stk38</i>    | Serine/threonine-protein kinase 38                     | -1.83 | GO:0043407 |
| <i>Cd247</i>    | T-cell surface glycoprotein CD3 zeta chain, CD247      | -1.99 | GO:0007165 |
| <i>Rps6ka1</i>  | Ribosomal protein S6 kinase alpha-1                    | -2.10 | GO:0007243 |
| <i>S100a4</i>   | Protein S100-A4  | -2.14 | GO:0043123 |
| <i>S100a13</i>  | Protein S100-A13                                       | -2.19 | GO:0043123 |
| <i>Tgfbrap1</i> | TGF beta receptor associated protein -1                | -2.24 | GO:0007165 |
| <i>Crlf3</i>    | Cytokine receptor-like factor 3                        | -2.44 | GO:0046427 |
| <i>Rasa3</i>    | RAS p21 protein activator 3                            | -2.44 | GO:0007165 |
| <i>Cdk6</i>     | Cell division protein kinase 6                         | -2.48 | GO:0007219 |
| <i>Arl3</i>     | ADP-ribosylation factor-like protein 3                 | -2.59 | GO:0007264 |
| <i>Ifi204</i>   | 7 Interferon-activable protein 204                     | -2.77 | GO:0042771 |
| <i>Ero1l</i>    | ERO1-like  | -2.79 | GO:0030968 |
| <i>Plcl2</i>    | Inactive phospholipase C-like protein 2                | -2.79 | GO:0007165 |
| <i>Gpx1</i>     | Glutathione peroxidase 1                               | -3.04 | GO:0051897 |
| <i>Stat4</i>    | Signal transducer and activator of transcription 4     | -3.18 | GO:0007165 |
| <i>Apbb1ip</i>  | Amyloid beta A4 precursor interacting protein          | -3.22 | GO:0007165 |
| <i>Rgs14</i>    | Regulator of G-protein signaling 14                    | -3.57 | GO:0048008 |
| <i>Pdap1</i>    | 28 kDa heat- and acid-stable phosphoprotein            | -3.73 | GO:0048008 |
| <i>Ubash3a</i>  | ubiquitin associated and SH3 domain containing, A      | -3.75 | GO:0050860 |
| <i>Anxa1</i>    | Annexin A1   | -4.87 | GO:0007165 |
| <i>Lsp1</i>     | Lymphocyte-specific protein 1                          | -5.91 | GO:0007165 |
| <i>Rasgrp2</i>  | RAS guanyl-releasing protein 2                         | -8.54 | GO:0035556 |
| <i>Dgka</i>     | Diacylglycerol kinase alpha                            | -14.2 | GO:0007205 |

---



**Table S3. Densitometry of western blots**

| pERK                       |                         | H57 ng/ml      | pERK/ERK Ratio |        |        |        |       |         |        |        |
|----------------------------|-------------------------|----------------|----------------|--------|--------|--------|-------|---------|--------|--------|
| Dicer lox/lox              |                         | 0              | 2.80           |        |        |        |       |         |        |        |
|                            |                         | 2              | 3.94           |        |        |        |       |         |        |        |
|                            |                         | 10             | 6.43           |        |        |        |       |         |        |        |
|                            |                         | 30             | 6.51           |        |        |        |       |         |        |        |
|                            |                         | 60             | 7.37           |        |        |        |       |         |        |        |
|                            |                         | 180            | 6.87           |        |        |        |       |         |        |        |
|                            |                         | 360            | 6.56           |        |        |        |       |         |        |        |
| CD4Cre<br>Dicer lox/lox    |                         | 0              | 1.03           |        |        |        |       |         |        |        |
|                            |                         | 2              | 1.56           |        |        |        |       |         |        |        |
|                            |                         | 10             | 4.80           |        |        |        |       |         |        |        |
|                            |                         | 30             | 6.51           |        |        |        |       |         |        |        |
|                            |                         | 60             | 7.18           |        |        |        |       |         |        |        |
|                            |                         | 180            | 7.75           |        |        |        |       |         |        |        |
|                            |                         | 360            | 5.36           |        |        |        |       |         |        |        |
|                            |                         | pERK/ERK Ratio |                |        |        |        |       |         |        |        |
|                            |                         |                | 1              | 2      | 3      | 4      | Mean  | SEM     | T-test |        |
| Dicer<br>lox/lox           | 0 min                   | 1.213          | 0.389          | 1.213  | 0.389  | 0.801  | 0.291 | 0.295   |        |        |
|                            | 15 min                  | 11.209         | 10.063         | 12.065 | 13.681 | 11.755 | 1.524 | 0.727   |        |        |
|                            | 120 min                 | 10.758         | 8.908          | 12.490 | 11.377 | 10.883 | 1.499 | 0.861   |        |        |
|                            | 480 min                 | 11.753         | 12.389         | 10.481 | 10.397 | 11.255 | 0.978 | 0.099   |        |        |
|                            |                         |                | 1              | 2      | 3      | 4      | Mean  | SEM     |        |        |
| CD4Cre<br>Dicer<br>lox/lox | 0 min                   | 1.155          | 1.002          | 1.150  | 1.002  | 1.078  | 0.108 |         |        |        |
|                            | 15 min                  | 17.996         | 16.383         | 7.800  | 8.803  | 12.746 | 5.190 |         |        |        |
|                            | 120 min                 | 11.419         | 14.347         | 8.125  | 8.440  | 10.583 | 2.916 |         |        |        |
|                            | 480 min                 | 16.720         | 20.381         | 11.363 | 12.838 | 15.325 | 4.058 |         |        |        |
| pAkt<br>pAkt S473/Akt      |                         |                |                | 1      | 2      | 3      | 4     | Mean    | SEM    | T-test |
| anti-TCR                   | Dicer lox/lox           |                |                |        |        |        |       |         |        |        |
|                            | 0h                      | 1.962          |                | 1      | 2.753  | 1.905  | 0.507 | 0.567   |        |        |
|                            | 2h                      | 7.339          |                | 9.542  | 8.727  | 8.536  | 0.643 | 0.155   |        |        |
|                            | 8h                      | 2.939          | 1.971          | 4.176  | 4.912  | 3.499  | 0.652 | 8.2E-05 |        |        |
| anti-TCR<br>+CD28          | 2h                      | 7.338          |                | 9.396  | 5.325  | 7.353  | 1.175 | 0.126   |        |        |
|                            | 8h                      | 0.267          | 1.660          | 3.212  | 6.833  | 2.993  | 1.414 | 0.005   |        |        |
|                            |                         |                | 1              | 2      | 3      | 4      | Mean  | SEM     |        |        |
| anti-TCR<br>+CD28          | CD4Cre<br>Dicer lox/lox |                |                |        |        |        |       |         |        |        |
|                            | 0h                      | 0              |                | 2.614  | 1.399  | 1.338  | 0.755 |         |        |        |
|                            | 2h                      | 12.051         |                | 31.980 | 14.619 | 19.550 | 6.259 |         |        |        |
|                            | 8h                      | 19.839         | 15.624         | 14.260 | 15.771 | 16.373 | 1.204 |         |        |        |
| CD28                       | 2h                      | 28.014         |                | 13.618 | 11.342 | 17.658 | 5.219 |         |        |        |
|                            | 8h                      | 34.309         | 28.956         | 12.284 | 22.704 | 24.563 | 4.730 |         |        |        |

| pAkt<br>T308/Akt        |               | 1     | 2     | 3     | 4     | Mean  | SEM   | T-test |
|-------------------------|---------------|-------|-------|-------|-------|-------|-------|--------|
| anti-TCR                | Dicer lox/lox |       |       |       |       |       |       |        |
|                         | 0h            | 0.999 |       | 1     | 1     | 1     | 0     | 0.103  |
|                         | 2h            | 3.842 |       | 2.532 | 2.526 | 2.966 | 0.438 | 0.722  |
| anti-TCR<br>+CD28       | 8h            | 1.844 | 2.108 | 1.597 | 2.237 | 1.947 | 0.164 | 0.016  |
|                         | 2h            | 3.049 |       | 2.568 | 2.220 | 2.612 | 0.240 | 0.420  |
|                         | 8h            | 0.460 | 1.243 | 1.965 | 1.987 | 1.414 | 0.417 | 0.009  |
| CD4Cre<br>Dicer lox/lox |               | 1     | 2     | 3     | 4     | Mean  | SEM   |        |
| anti-TCR                | 0h            | 0.117 |       | 0.964 | 0     | 0.36  | 0.304 |        |
|                         | 2h            | 4.656 |       | 3.206 | 2.040 | 3.30  | 0.757 |        |
|                         | 8h            | 9.858 | 4.202 | 7.341 | 4.388 | 6.447 | 1.553 |        |
| anti-TCR<br>+CD28       | 2h            | 6.268 |       | 2.286 | 2.735 | 3.763 | 1.259 |        |
|                         | 8h            | 6.723 | 4.570 | 2.770 | 5.110 | 4.793 | 0.941 |        |