

**Table S1. TaqMan Assays for mRNA quantification by qPCR**

| Genes         | Names                                             | Dyes | TaqMan Assay ID | Amplicon | Ref. Sequence         |
|---------------|---------------------------------------------------|------|-----------------|----------|-----------------------|
| <b>PPIA</b>   | Cyclophilin A                                     | VIC  | Hs_99999904_m1  | 98       | NM_021130.3           |
| <b>DVL2</b>   | Dishevelled segment polarity protein 2            | FAM  | Hs_1005253_m1   | 55       | <u>NM_004422.2</u>    |
| <b>ETS1</b>   | <i>ETS proto-oncogene 1, transcription factor</i> | FAM  | Hs_00428293_m1  | 99       | <u>NM_001143820.1</u> |
| <b>IL1RAP</b> | Interleukin 1 receptor accessory protein          | FAM  | Hs_00370509_m1  | 113      | <u>NM_001167928.1</u> |

**Table S2. miR-221-3p and miR-222-3p Target Gene aliases and names**

| VALIDATED GENES | NAMES                                                      |
|-----------------|------------------------------------------------------------|
| <b>ABLIM1</b>   | Actin-binding LIM protein 1                                |
| <b>ACTB</b>     | Actin, cytoplasmic 1                                       |
| <b>ACTG1</b>    | Actin, cytoplasmic 2                                       |
| <b>ADAM1A</b>   | Adam Metallopeptidase Domain 1A (Pseudogene)               |
| <b>ARHGAP42</b> | Rho GTPase-activating protein 42                           |
| <b>C19orf12</b> | Protein C19orf12                                           |
| <b>CABYR</b>    | Calcium-binding tyrosine phosphorylation-regulated protein |
| <b>CDKN1C</b>   | Cyclin-dependent kinase inhibitor 1C                       |
| <b>CHORDC1</b>  | Cysteine and histidine-rich domain-containing protein 1    |
| <b>CIAPIN1</b>  | Anamorsin                                                  |
| <b>COG5</b>     | Conserved oligomeric Golgi complex subunit 5               |
| <b>CORO1A</b>   | Coronin-1A                                                 |
| <b>CPSF6</b>    | Cleavage and polyadenylation specificity factor subunit 6  |
| <b>CSTF2T</b>   | Cleavage stimulation factor subunit 2 tau variant          |
| <b>DDIT4</b>    | DNA damage-inducible transcript 4 protein                  |
| <b>DDX6</b>     | Probable ATP-dependent RNA helicase DDX6                   |
| <b>DERL2</b>    | Derlin-2                                                   |

|                 |                                                             |
|-----------------|-------------------------------------------------------------|
| <i>DIRAS3</i>   | GTP-binding protein Di-Ras3                                 |
| <i>DKK2</i>     | Dickkopf-related protein 2                                  |
| <i>ETS1</i>     | Protein C-ets-1                                             |
| <i>EXOC8</i>    | Exocyst complex component 8                                 |
| <i>FAM35A</i>   | Protein FAM35A                                              |
| <i>FAM84A</i>   | Protein FAM84A                                              |
| <i>FBXL18</i>   | F-box/LRR-repeat protein 18                                 |
| <i>FOS</i>      | Proto-oncogene c-Fos                                        |
| <i>GCN1L1</i>   | Alternative protein GCN1L1                                  |
| <i>HNRNPD</i>   | Heterogeneous nuclear ribonucleoprotein D0                  |
| <i>KPNA6</i>    | Importin subunit alpha-7                                    |
| <i>MAT2A</i>    | S-adenosylmethionine synthase isoform type-2                |
| <i>MGMT</i>     | Methylated-DNA--protein-cysteine methyltransferase          |
| <i>MKKS</i>     | McKusick-Kaufman/Bardet-Biedl syndromes putative chaperonin |
| <i>OBFC1</i>    | CST complex subunit STN1                                    |
| <i>OIP5</i>     | Protein Mis18-beta                                          |
| <i>PGPEP1</i>   | Pyroglutamyl-peptidase 1                                    |
| <i>PIWIL1</i>   | Piwi-like protein 1                                         |
| <i>PRPS1L1</i>  | Ribose-phosphate pyrophosphokinase 3                        |
| <i>RBMS2</i>    | RNA-binding motif, single-stranded-interacting protein 2    |
| <i>RNF4</i>     | E3 ubiquitin-protein ligase RNF4                            |
| <i>SAPCD2</i>   | Suppressor APC domain-containing protein 2                  |
| <i>SELE</i>     | E-selectin                                                  |
| <i>SLC25A36</i> | Solute carrier family 25 member 36                          |
| <i>SMC2</i>     | Structural maintenance of chromosomes protein 2             |
| <i>SNX4</i>     | Sorting nexin-4                                             |
| <i>STAT5A</i>   | Signal transducer and activator of transcription 5A         |
| <i>TIMP3</i>    | Metalloproteinase inhibitor 3                               |
| <i>TIPARP</i>   | TCDD-inducible poly [ADP-ribose] polymerase                 |
| <i>TMCC1</i>    | Transmembrane and coiled-coil domains protein 1             |
| <i>TNFSF10</i>  | Tumor necrosis factor ligand superfamily member 10          |
| <i>TRAT1</i>    | T-cell receptor-associated transmembrane adapter 1          |
| <i>TSPAN13</i>  | Tetraspanin-13                                              |
| <i>ZEB2</i>     | Zinc finger E-box-binding homeobox 2                        |
| <i>ZFP30</i>    | Zinc finger protein 30 homolog                              |
| <i>ZNF236</i>   | Zinc finger protein 236                                     |

| <b>PREDICTED</b> | <b>NAME</b>                                     |
|------------------|-------------------------------------------------|
| <i>AKT3</i>      | RAC-gamma serine/threonine-protein kinase       |
| <i>APAF1</i>     | Apoptotic protease-activating factor 1          |
| <i>BCL2</i>      | Apoptosis regulator Bcl-2                       |
| <i>CASP10</i>    | Caspase 10                                      |
| <i>CELF1</i>     | CUGBP Elav-like family member 1                 |
| <i>CREB1</i>     | Cyclic AMP-responsive element-binding protein 1 |

|                |                                                                                |
|----------------|--------------------------------------------------------------------------------|
| <b>DVL2</b>    | Segment polarity protein disheveled homolog DVL-2                              |
| <b>IKBKG</b>   | NF-kappa-B essential modulator                                                 |
| <b>IL1RAP</b>  | Interleukin-1 receptor accessory protein                                       |
| <b>LIFR</b>    | Leukemia inhibitory factor receptor                                            |
| <b>NCK1</b>    | Cytoplasmic protein NCK1                                                       |
| <b>PDGFD</b>   | Platelet-derived growth factor D                                               |
| <b>PIK3CD</b>  | Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta isoform |
| <b>PPP3R1</b>  | Calcineurin subunit B type 1                                                   |
| <b>PRKCB</b>   | Protein kinase C beta type                                                     |
| <b>STAT2</b>   | Signal transducer and activator of transcription 2                             |
| <b>TNFSF10</b> | Tumor necrosis factor ligand superfamily member 10                             |

**Table S3. Binding sites of miR-221-3p and miR-222-3p within the selected target genes**

| GENE        | ID                | 3' UTR length | miRNA          | Position  | seed match | Context ++ score | Context ++ score Percentile | Pct  |
|-------------|-------------------|---------------|----------------|-----------|------------|------------------|-----------------------------|------|
| <b>ETS1</b> | ENST00000531611.1 | 3774          | hsa-miR-221-3p | 3581-3587 | 7mer-m8    | -0.09            | 65                          | 0.10 |
| <b>ETS1</b> | ENST00000531611.1 | 3774          | hsa-miR-222-3p | 3581-3587 | 7mer-m8    | -0.11            | 70                          | 0.1  |
| <b>ETS1</b> | ENST00000531611.1 | 3774          | hsa-miR-221-3p | 1231-1237 | 7mer-1A    | -0.09            | 65                          | <0.1 |
| <b>ETS1</b> | ENST00000531611.1 | 3774          | hsa-miR-222-3p | 1231-1237 | 7mer-1A    | -0.1             | 67                          | <0.1 |
| <b>ETS1</b> | ENST00000345075.4 | 3600          | hsa-miR-221-3p | 3403-3409 | 7mer-m8    | -0.08            | 62                          | 0.10 |
| <b>ETS1</b> | ENST00000345075.4 | 3600          | hsa-miR-222-3p | 3403-3409 | 7mer-m8    | -0.10            | 68                          | 0.10 |
| <b>ETS1</b> | ENST00000345075.4 | 3600          | hsa-miR-221-3p | 3403-3409 | 7mer-1A    | -0.08            | 64                          | <0.1 |

|                                  |                       |      |                        |               |             |       |    |          |
|----------------------------------|-----------------------|------|------------------------|---------------|-------------|-------|----|----------|
| <b><i>ETS1</i></b>               | ENST00000345075.<br>4 | 3600 | hsa-<br>miR-<br>222-3p | 3403-<br>3409 | 7mer-<br>1A | -0.10 | 67 | <0.<br>1 |
| <b><i>IL1RA</i><br/><i>P</i></b> | ENST00000422485.<br>1 | 3005 | hsa-<br>miR-<br>221-3p | 199-205       | 7mer-<br>m8 | -0.28 | 94 | <0.<br>1 |
| <b><i>IL1RA</i><br/><i>P</i></b> | ENST00000422485.<br>1 | 3005 | hsa-<br>miR-<br>222-3p | 199-205       | 7mer-<br>m8 | -0.29 | 94 | <0.<br>1 |
| <b><i>IL1RA</i><br/><i>P</i></b> | ENST00000317757.<br>3 | 1447 | hsa-<br>miR-<br>221-3p | 865-871       | 7mer-<br>m8 | -0.07 | 56 | <0.<br>1 |
| <b><i>IL1RA</i><br/><i>P</i></b> | ENST00000317757.<br>3 | 1447 | hsa-<br>miR-<br>222-3p | 865-871       | 7mer-<br>m8 | -0.1  | 67 | <0.<br>1 |
| <b><i>DVL2</i></b>               | ENST00000005340.<br>5 | 524  | hsa-<br>miR-<br>221-3p | 449-455       | 7mer-<br>m8 | -0.11 | 70 | <0.<br>1 |
| <b><i>DVL2</i></b>               | ENST00000005340.<br>5 | 524  | hsa-<br>miR-<br>222-3p | 449-455       | 7mer-<br>m8 | -0.12 | 72 | <0.<br>1 |

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