

| Upstream from RAS activation   |                               |                |
|--------------------------------|-------------------------------|----------------|
| ERK only hits                  | ERK/GSK hits                  | GSK3 only hits |
| <i>slc10a4</i>                 | <i>ccdc32</i>                 |                |
| <i>tle3</i>                    | <i>metrnl</i>                 |                |
| <i>asb13</i>                   | <i>ctbp2</i>                  |                |
| <i>plekhf1</i>                 |                               |                |
| <i>nras</i>                    |                               |                |
| <i>serf2</i>                   |                               |                |
| <i>psmb3</i>                   |                               |                |
| <i>ddb2</i>                    |                               |                |
| Upstream from ERK activation   |                               |                |
| ERK only hits                  | ERK/GSK hits                  | GSK3 only hits |
| <i>3830406c13rik</i>           | <i>rab24</i>                  |                |
| <i>gmnn</i>                    | <i>ets1</i>                   |                |
| <i>pabpc1</i>                  | <i>pex11c</i>                 |                |
| <i>ppip5k1</i>                 | <i>tsc2</i>                   |                |
|                                | <i>ifna14</i>                 |                |
|                                | <i>sart3</i>                  |                |
| Downstream from ERK activation |                               |                |
| ERK only hits                  | ERK/GSK hits                  | GSK3 only hits |
| <i>kcnk13</i>                  | <i>il1f5</i>                  | <i>prkar1a</i> |
| <i>cacnb2</i>                  | <i>tssk3</i>                  | <i>sfpq</i>    |
| <i>ddc</i>                     | <i>robld3</i>                 | <i>odf2</i>    |
| <i>insrr</i>                   | <i>gsk3<math>\beta</math></i> | <i>acox1</i>   |
| <i>ddr1</i>                    | <i>mrpl49</i>                 | <i>dmbx1</i>   |
| <i>cdkn1a</i>                  | <i>idh3g</i>                  |                |
| <i>yipf1</i>                   | <i>hemt1</i>                  |                |
| <i>zfp420</i>                  | <i>5730528l13rik</i>          |                |
| <i>rnf215</i>                  | <i>2400001e08rik</i>          |                |
| <i>etv2</i>                    | <i>pou5f1</i>                 |                |
| <i>dnmt1</i>                   | <i>jun</i>                    |                |
| <i>edc4</i>                    | <i>rorb</i>                   |                |
|                                | <i>foxl2</i>                  |                |
|                                | <i>usf2</i>                   |                |
|                                | <i>mbd3</i>                   |                |
|                                | <i>jarid2</i>                 |                |
|                                | <i>smc4</i>                   |                |
|                                | <i>dhx9</i>                   |                |

**Table S4. Summary of the point of action of siRNAs with respect to the ERK signaling pathway.**