### Supplemental Table S3. Top Upstream Regulators

| Upstream regulator | Expression log ratio | Molecule type                  | Predicted activation state | Activation z-score | P value of overlap | Target molecules in dataset          |
|--------------------|----------------------|--------------------------------|---------------------------|--------------------|-------------------|--------------------------------------|
| CTNNB1             | –0.389               | Transcription regulator        |                           |                    |                   | BMP4, CCND1, LEF1, PLS3, PTCH1, TOB2, TSC22D1, UGCG, VCAN |
| RARB               |                      | Ligand-dependent nuclear receptor | –1                        | 0.00015            |                   | ARHGP4, HOXA5, IFI27, IGFBP6          |
| PGR                | –0.667               | Ligand-dependent nuclear receptor | –1.287                    | 0.00024            |                   | CCND1, CDKN1C, FBKP5, ID1, IFI27, KRT18, UGCG, VCAN |
| GLI1               |                      | Transcription regulator        | Inhibited –2.607          | 0.00025            |                   | CCND1, NAV3, NR2F2, NREP, PDZRN3, PTCH1, SESN3 |
| MAFB               | –0.326               | Transcription regulator        |                           | 0.00024            |                   | ALCAM, FBLN5, GATM, OLFML3, SLC7A8    |
| CLOCK              | –0.514               | Transcription regulator        |                           | 0.00034            |                   | CCND1, ITM2C, KANK2, NR1D1, PER3, SERINC5, TAF9B |
| NR3C1              | –0.462               | Ligand-dependent nuclear receptor | –1.103                    | 0.000681           |                   | C1QTNF1, CDC42EP3, CDKN1C, FBKP5, MAOA, NAV3, NGFR, PI3KR1, PRKCD, RBMS3, STK17B, TIMP3 |
| TCF7L2             | –0.681               | Transcription regulator        |                           | 0.000747           |                   | ADGRG1, CAMK2N1, CCND1, STK17B       |
| HDAC7              | –0.321               | Transcription regulator        |                           | 0.000775           |                   | CCND1, RPRM                          |
| KHDRBS1            | –0.333               | Transcription regulator        |                           | 0.000775           |                   | CCND1, SMN1/SMN2                      |
| ESR2               |                      | Ligand-dependent nuclear receptor | –1.153                    | 0.00147            |                   | BMP4, C3, CCND1, FBLN1                |
| IRF2               | –0.329               | Transcription regulator        | Inhibited –2              | 0.00162            |                   | C1QTNF1, CCND1, CES1, FGG, ID1       |
| SREBF1             | 0.147                | Transcription regulator        |                           | 0.0017             |                   | ADGRG1, BHLHE41, MK, PCK2, PLS3, SORBS3 |
| PRDM5              | –0.793               | Transcription regulator        |                           | 0.00216            |                   | DKK3, EMID1, ISLR, NREP, SIK1/SIK1B   |
| HLX                |                      | Transcription regulator        |                           | 0.00223            |                   | CDKN1C, CLDN1, ELK1                   |
| DYRK1B             | –0.337               | Kinase                         |                           | 0.00265            |                   | CCND1, SOD3                          |
| RXRG               |                      | Ligand-dependent nuclear receptor | –1.53                     | 0.00265            |                   | IGBP6, TIMP3                         |
| MYOCD              |                      | Transcription regulator        | –1.103                    | 0.00341            |                   | ECM2, LMOD1, SIK1/SIK1B, TNNC1        |
| RARG               | –0.98                | Ligand-dependent nuclear receptor |                           | 0.00351            |                   | HOXA5, IGBP6                         |
| HMGA1              |                      | Transcription regulator        |                           | 0.00438            |                   | CCND1, ELK1, KITLG                    |
| SPDEF              |                      | Transcription regulator        | Activated 2               | 0.00442            |                   | CD34, COL16A1, DKK3, LEF1             |
| NUPR1              | –0.377               | Transcription regulator        | –0.277                    | 0.00498            |                   | ADGRG1, AVP1, CAMK2N1, CARMIL1, GRAMD2B, KANK2, NGFR, NR1D1, PER3, PHLDLA1, PI3KR1, SIK1/SIK1B, SYTL2 |
| HIC1               |                      | Transcription regulator        |                           | 0.00499            |                   | CCND1, CDKN1C, CDO1, NOV              |
| AR                 |                      | Ligand-dependent nuclear receptor | –1.281                    | 0.00595            |                   | CCND1, FBKP5, LMOD1, MAOA, PLS3, PRKCD, VCAN |
| HAND2              |                      | Transcription regulator        |                           | 0.00806            |                   | ECM2, SIK1/SIK1B, TNNC1               |
| ETV5               | –0.841               | Transcription regulator        |                           | 0.00806            |                   | ALCAM, CCND1, CLDN1                   |
| CBX5               | –0.69                | Transcription regulator        | Activated 2.219           | 0.00849            |                   | LEF1, RORA, SELENBP1, SLC7A8, SYTL2   |
| TCF4               | –0.515               | Transcription regulator        |                           | 0.0087             |                   | CCND1, LEF1, VCAN                    |
| TBX5               |                      | Transcription regulator        |                           | 0.00937            |                   | ECM2, SIK1/SIK1B, TNNC1               |