

**iScience, Volume 25**

**Supplemental information**

**Premise and peril of Wnt signaling  
activation through GSK-3 $\beta$  inhibition**

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		CHIR (0.1)	CHIR (10)	AR (10)	TWS (3.3)	TWS (10)
PC3	Up	<i>BIN1</i> <i>LARGE</i>	<u><i>CIAPIN1</i></u> <u><i>EXOC3</i></u> <u><i>GNAI1</i></u> <u><i>MLF1</i></u> <u><i>RDH11</i></u> <u><i>SENP6</i></u> <u><i>ST7</i></u> <u><i>TM9SF3</i></u> <u><i>TMEM194A</i></u>	<u><i>CD9</i></u> <u><i>CPE</i></u> <u><i>FAM69A</i></u> <u><i>HLA-DOA1</i></u> <u><i>IGFBP5</i></u> <u><i>IGL@</i></u> <u><i>PCP4</i></u> <u><i>PLA2G4A</i></u> <u><i>SELENBP1</i></u> <u><i>TMEM158</i></u>	<u><i>PSPH</i></u>	<u><i>AIF1</i></u> <u><i>HIST1H2AC</i></u> <u><i>MMP1</i></u> <u><i>SERPINE1</i></u>
	Down	<u><i>KLF5</i></u> <u><i>SEPT7</i></u> <u><i>ZNF148</i></u>	<u><i>ADO</i></u> <u><i>EIF1AY</i></u> <u><i>RAB30</i></u>	<u><i>AGR2</i></u> <u><i>ANKRD10</i></u> <u><i>CDH2</i></u> <u><i>EIF5</i></u> <u><i>FOLR1</i></u> <u><i>HOXC6</i></u> <u><i>HSPA1A</i></u> <u><i>POLD4</i></u> <u><i>RPL37A</i></u> <u><i>SCD</i></u>	<u><i>ACLY</i></u> <u><i>CYP1B1</i></u> <u><i>DFFB</i></u> <u><i>ZDHHC6</i></u>	<u><i>ADO</i></u> <u><i>ALDH1A3</i></u> <u><i>C16ORF59</i></u> <u><i>C22ORF29</i></u> <u><i>CYP1B1</i></u> <u><i>DFFB</i></u> <u><i>FOSL1</i></u> <u><i>HNRNPU</i></u> <u><i>IER3</i></u> <u><i>IGFBP3</i></u> <u><i>IL8</i></u> <u><i>MAFF</i></u> <u><i>MMP11</i></u> <u><i>MYC</i></u> <u><i>PDLIM1</i></u> <u><i>PLEK</i></u> <u><i>SERPINE1</i></u> <u><i>TIPARP</i></u>

**Supplemental Table 1:** The genes documented in the L1000 database (Keenan *et al.*, 2018) are affected by three GSK-3 $\beta$  inhibitors, CHIR: CHIR-99021, AR: AR-A014418, and TWS: TWS-119, in PC3 cells. Underlined genes represent those that exhibit altered gene expression in both PC3 and HA1E (supplemental table 2) cells. Although PC3 and HA1E cells differ significantly in embryonic origin, a large portion of the affected genes shared between these two cell lines exhibit overlap when treated with these three GSK-3 $\beta$  inhibitors. The double-underlined and red-font genes exhibit altered gene expression in both PC3 and HA1E cell lines and are altered by at least one other perturbagen (CHIR-99021, AR-A014418, TWS-119). The concentrations (in  $\mu$ M) of the compounds used to treat the cells are indicated in the parentheses.

		CHIR (10)	AR (10)	TWS (1.1)	TWS (3.3)	TWS (10)
HA1E	Up	<u>CIAPIN1</u> <u>EIF3G</u> <u>EPAG</u> <u>GNAI1</u> <u>MAPK11P1L</u> <u>MLF1</u> <u>PCDH11Y</u> <u>RDH11</u> <u>SENP6</u> <u>SNX13</u> <u>ST7</u> <u>TM9SF3</u>	<u>ATF3</u> <u>CPE</u> <u>EMP1</u> <u>GPNMB</u> <u>HIST1H1C</u> <u>HLA-DOA1</u> <u>IGFBP5</u> <u>LAPTM5</u> <u>MMP9</u> <u>PCP4</u> <u>PLA2G4A</u> <u>RGS1</u> <u>S100A8</u> <u>SPARCL1</u> <u>TMEM158</u>	<u>AIF1</u> <u>ALDOB</u> <u>ATP5S</u> <u>RNF10</u>	<u>ALDOB</u> <u>ATP5S</u> <u>PSPH</u> <u>RNF10</u>	<u>CFB</u> <u>CXCR4</u> <u>HIST1H2AC</u> <u>PSPH</u> <u>RNF10</u> <u>S100A8</u> <u>ZMYND8</u>
	Down	<u>CRADD</u> <u>DFFB</u> <u>EIF1AY</u> <u>KLF5</u> <u>LPAR1</u> <u>PPP2R5D</u> <u>RSG1</u> <u>SLC16A3</u> <u>TRIM23</u> <u>VPS13A</u> <u>XPO6</u>	<u>CDH2</u> <u>EIF5</u> <u>GAS1</u> <u>NIPSNAP1</u> <u>POLD4</u> <u>PTGIS</u> <u>SCD</u> <u>SLC2A6</u> <u>TM4SF1</u> <u>TMEM5</u> <u>TNFAIP2</u> <u>TSPAN8</u>	<u>MMP1</u> <u>PLEK</u>	<u>ATP9B</u> <u>COPS6</u> <u>CXCR4</u> <u>EIF4E2</u> <u>HNRNPU</u> <u>MMP1</u> <u>MRPL18</u> <u>PDLIM1</u> <u>RAB30</u> <u>SQRDL</u> <u>TRIOBP</u> <u>UBE3B</u>	<u>ADQ</u> <u>ALDH1A3</u> <u>C16ORF59</u> <u>C22ORF29</u> <u>COPS6</u> <u>CXCR4</u> <u>CYP1B1</u> <u>DFFB</u> <u>DUSP4</u> <u>FOSL1</u> <u>HNRNPU</u> <u>IER3</u> <u>IGFBP3</u> <u>IL8</u> <u>LDLR</u> <u>MAFF</u> <u>MANBA</u> <u>MMP1</u> <u>MMP11</u> <u>MRPL18</u> <u>MYC</u> <u>PLEK</u> <u>RAB30</u> <u>SERPINE1</u> <u>SQRDL</u> <u>TIPARP</u> <u>UBE3B</u> <u>ZDHHC6</u>

**Supplemental Table 2:** The genes documented in the L1000 database (Keenan *et al.*, 2018) are affected by three GSK-3 $\beta$  inhibitors, CHIR: CHIR-99021, AR: AR-A014418, and TWS: TWS-119, in HA1E cells. Underlined genes represent those that exhibit altered gene expression in both HA1E and PC3 (supplemental table 1) cells. Although PC3 and HA1E cells differ significantly in embryonic origin, a

large portion of the affected genes shared between these two cell lines exhibit overlap when treated with these three GSK-3 $\beta$  inhibitors. The double-underlined and red-font genes exhibit altered gene expression in both PC3 and HA1E cell lines and are altered by at least one other perturbagen (CHIR-99021, AR-A014418, TWS-119). The concentrations (in  $\mu$ M) of the compounds used to treat the cells are indicated in the parentheses.