



**Figure S4. SFRP2 and WLS are two major SOX2 targets in hESCs, functioning as WNT antagonist and agonist, respectively, in mediating Wnt pathway induced non-neural lineage differentiation. Related to Figure 6.**

(A) RT-qPCR results showing decreased *SFRP2* expression and unaffected *WLS* expression in hNPCs on day 3 of SOX2 KD under neuronal differentiation conditions.

(B) ChIP-qPCR validation of SOX2 binding at *SFRP2* promoter in hNPCs.

(C) ChIP-qPCR validation of SOX2 binding at *SFRP2* and *WLS* promoter in hESCs.

(D and E) RT-qPCR results showing that knock down of *SFRP2* by siRNA (D) or reduction of its activity by a neutralizing antibody (E) enhanced the induction in the expression of non-neural lineage markers with WNT3A (50 ng/ml) treatment for 3 days in H9 hESCs.

(F) RT-qPCR results in relation to Figure 6D and 6E. Rescue effects of *SFRP2* supplement and *WLS* knock down on SOX2/3 knock down caused increase of various markers are shown with additional SOX2/3 siRNAs and *WLS* stable knock down H9 cell lines. Scale bar represents  $\log_2$  of expression level.