

**Supp Fig 1 : SFRP1 methylation with coculture:** DNA methylation analysis shows hypermethylation of selected loci (marked by arrows) in the SFRP1 promoter in the HS27 stromal cells that are co-cultured with KG1a cells.



Supp Fig 2 : Validation of methylation changes with stroma and leukemic cell coculture: DNA methylation analysis shows hypermethylation of selected loci (marked by arrows) in the TNF-alpha promoter in the HS27 stromal cells that are co-cultured with KG1a cells. Hypermethylation was confirmed by Massarray bisulfite epityper analysis (lowerpanel).

## MDS22 Isotype 20x MDS22 UnTx FRZB 20x MDS22 Aza FRZB 20x MDS23 Isotype 20x MDS23 UnTx FRZB 20x MDS23 Aza FRZB 20x

**Supp Fig 3: FRZB upregulation in MDS stroma after 5-Azacytidine treatment:** Immunohistochemistry shows increase expression of FRZB in MDS stroma treated with 5-Aza (.5uM) for 5 days. **Supp Fig 4: FRZB knockdown leads to partial inhibition of erythroid differentiation induced by treatment of MDS stroma with 5-Aza** : siRNA mediated knockdown of FRZB was achieved in primary MDS stromal cells via siRNAs with scrambled siRNAs as controls. MDS stromal cells were then pretreated with 5-Aza for 5. Co-culture of healthy CD34 cells with MDS stroma was performed for 14 days and FACS analysis done (A,B). 5-Aza pretreatment of MDS stroma led to increase in Glycophorin A positive cells that was partially inhibited with FRZB knockdown (B).



Supp Fig 5: The expression of WNT signature genes in MDS and control marrow derived CD34+ cells is shown in the heatmap. The genes that are significantly differentially expressed in MDS when compared to controls are marked with asterix. Subtypes of MDS are indicated below

