**Figure S1.** MLL3/4 complex member expression analysis. (A-B) Gene expression analysis of SET/MLL complex member genes. (A) U-2 OS cells were treated with 10 µM SB-431542 inhibitor for 24 h and subsequently stimulated with 10 ng/ml TGF-β for 6 h as indicated. (B) U-2 OS cells were treated with 100 nM LDN-193189 inhibitor for 24 h and subsequently stimulated with 10 ng/ml BMPfor 6 h as indicated. (A-B) Samples were analyzed using qRT-PCR. Bars represent average expression corrected for ACTIN and normalized to the siNT control. Error bars represent standard deviation. Technical replication n = 3 for all samples.

**Figure S2.** UCSC genome browser tracks for TGF-β target genes SERPINE1 and PMEPA1. ChIP-seq tracks for SMAD3 in hESC BGO3 cells 1 and MLL4 in HCT116 cells 2. H3K4me1 and H3K4me3 abundance is shown for 8 and 9 different cell lines respectively. Co-occurrence of SMAD3 and MLL4 binding is highlighted in yellow.

**Supplemental references**

1. Mullen AC, Orlando DA, Newman JJ, Loven J, Kumar RM, Bilodeau S, et al. Master transcription factors determine cell-type-specific responses to TGF-beta signaling. Cell 2011; 147:565-76.

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