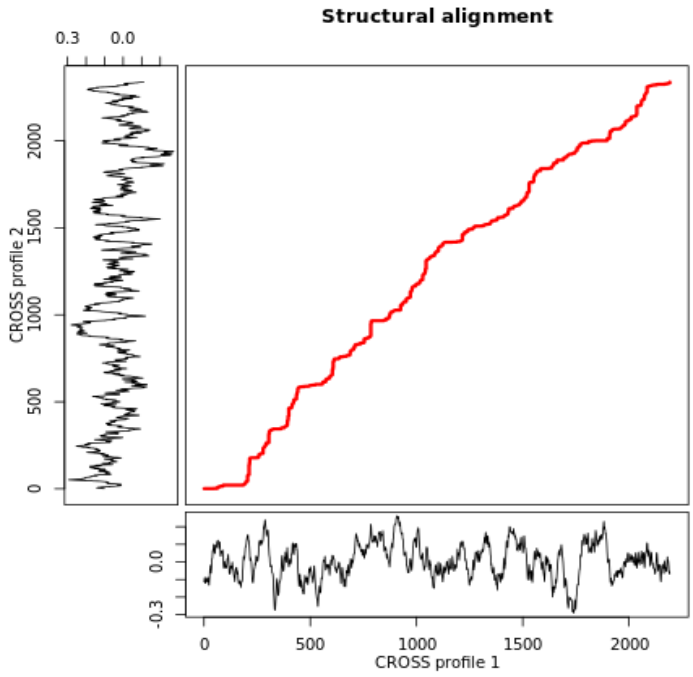
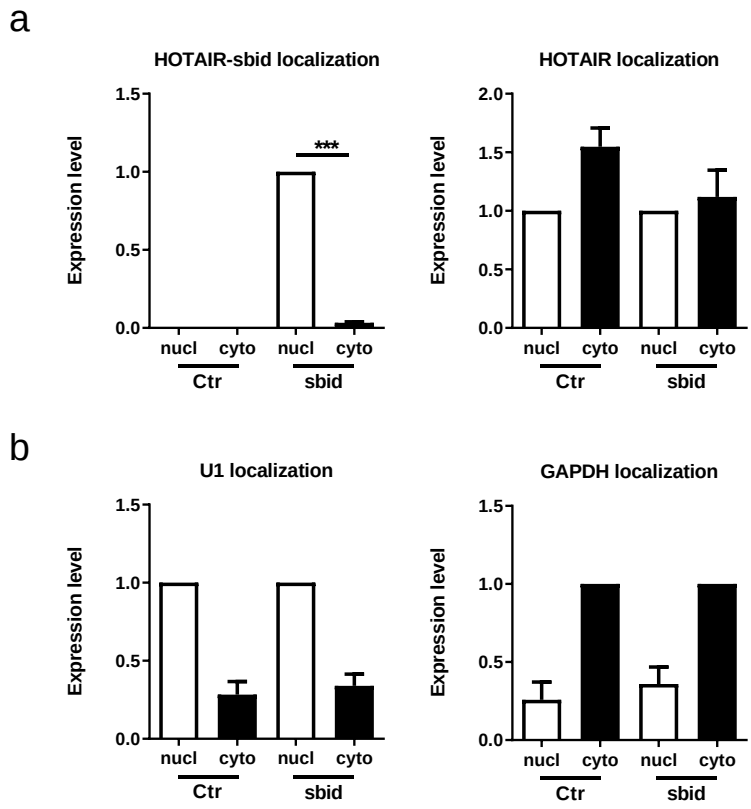
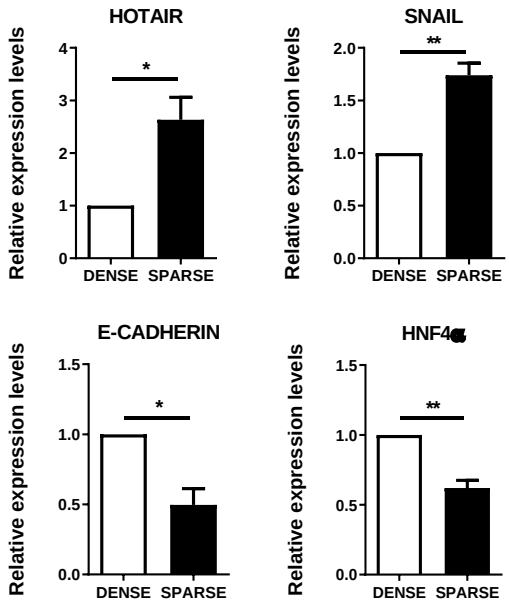


Supplementary Figure S1. Structure conservation between human and mouse HOTAIR. The most structurally conserved region in HOTAIR corresponds to Snail binding site predicted by catRAPID. The positions are relative to the alignments between the two sequences.

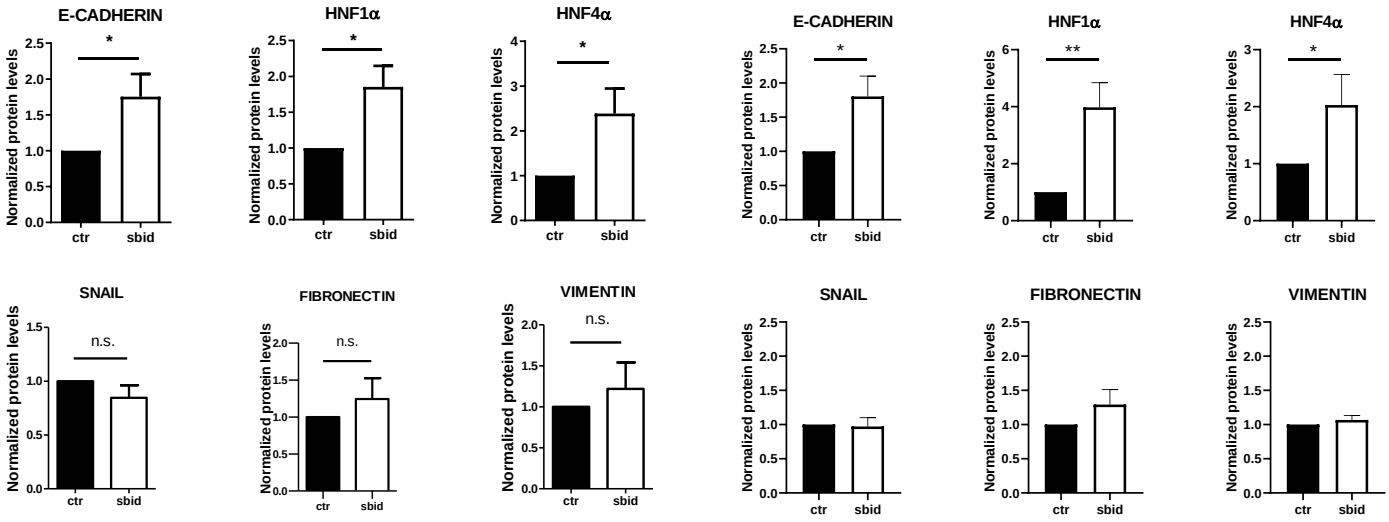


Supplementary Figure S2. HOTAIR-*sbid* retains a nuclear localization.

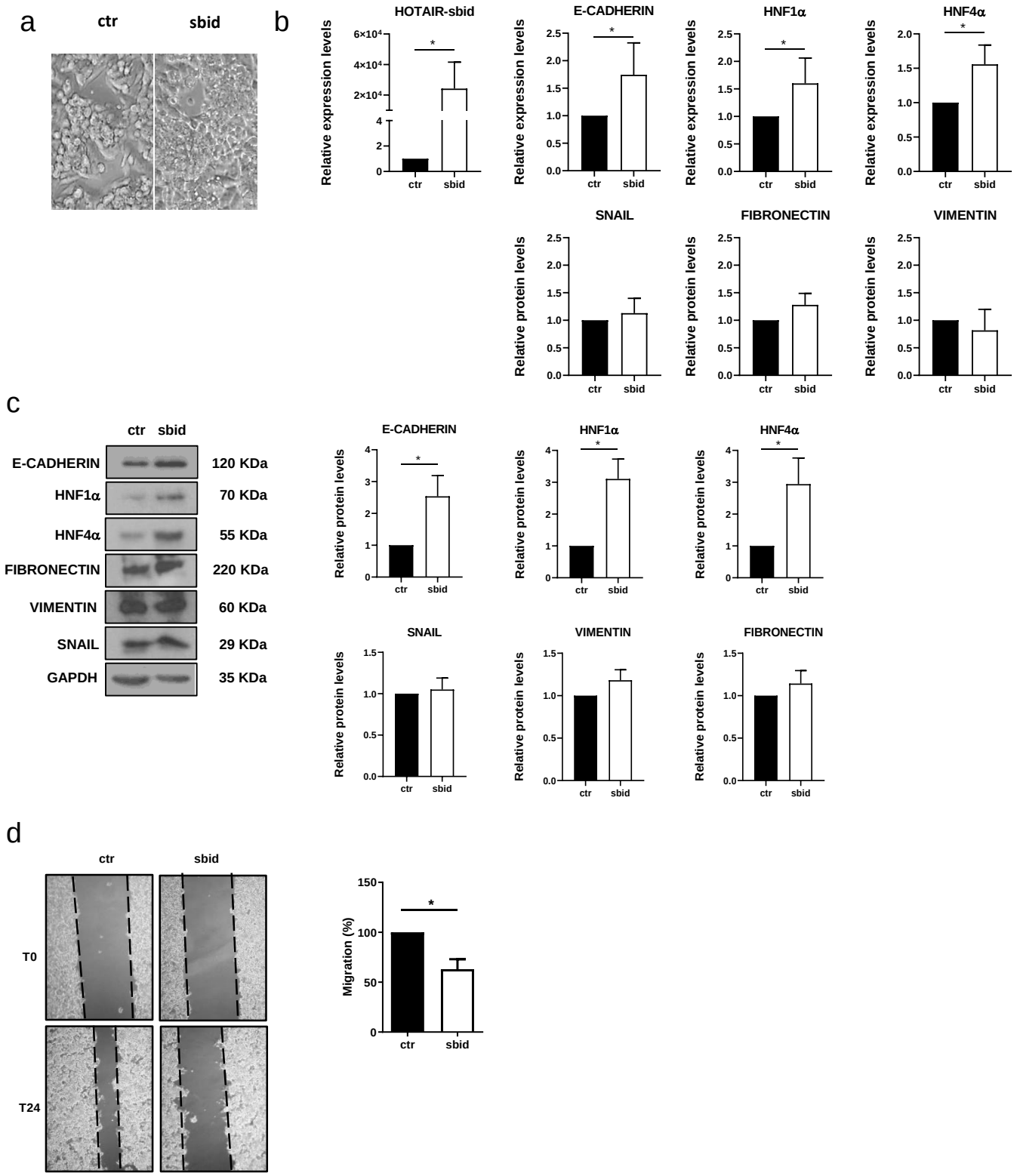
(**a**) qRT-PCRs on the Snail-binding domain of HOTAIR (HOTAIR-*sbid*) and on the endogenous HOTAIR in the nuclear (nucl) and cytoplasmic (cyto) fractions obtained from Hep3B cells expressing the HOTAIR-*sbid* (sbid) or the empty vector (Ctr) as a control. (**b**) qRT-PCR for U1 (nuclear marker) and of GAPDH (cytoplasmic marker) in the nuclear and cytoplasmic fractions using qRT-PCR. The error bars represent the calculated standard error of the mean based on three independent experiments.



Supplementary Figure S3. Hep3B grown at low density express HOTAIR and Snail and repress epithelial markers.
RT–qPCR analysis for the indicated mesenchymal (HOTAIR and SNAIL) and epithelial (E-CADHERIN, HNF4α) genes on human Hep3B cells grown at high (dense) or low density (sparse). The values are calculated by the $2(-\Delta Ct)$ method, expressed as fold of expression versus the control (arbitrary value=1) and shown as mean±s.e.m. Statistically significant differences are reported (*$P<0.05$, **$P<0.01$) for four independent experiments.

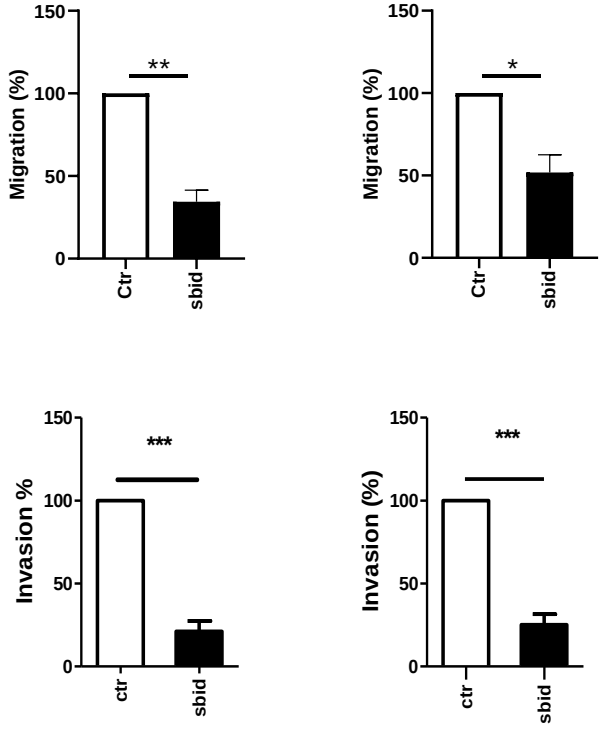


Supplementary Figure S4. Densitometric analysis of protein levels.
Densitometric analysis of protein levels in BW1J (left) and Hep3B (right) cells expressing HOTAIR-*sbid* or the empty vector as a control (Ctr). The values are expressed as fold of expression versus the control (arbitrary value=1) and shown as mean±s.e.m. Statistically significant differences are reported (*P<0.05, **P<0.01, ***P<0.001) for four (BW1J) and seven (Hep3B) independent experiments.

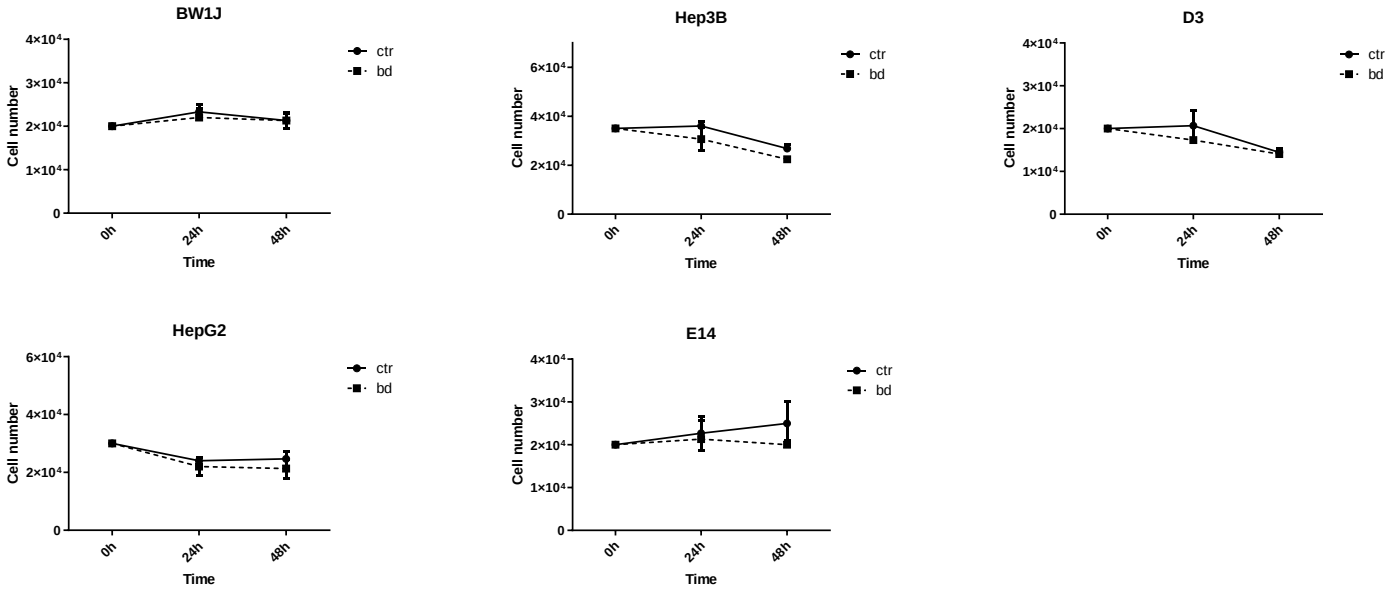


Supplementary Figure S5. HOTAIR-*sbid* interferes with the SNAIL/HOTAIR/EZH2-mediated functions

Analysis of HepG2 cells treated with TGFβ and expressing HOTAIR-*sbid* (sbid) or the empty vector as a control (ctr) as indicated. (a) Phase contrast micrographs; (b) RT–qPCR analysis for the indicated epithelial (e-cadherin, hnf4α, hnf1α) and mesenchymal (snail, vimentin and fibronectin) genes; the values are calculated by the 2(−ΔCt) method, expressed as fold of expression versus the control (arbitrary value=1) and shown as mean±s.e.m. Statistically significant differences are reported (*P<0.05) for four independent experiments; (c) *Left:* Western blot analysis (WB) for E-CADHERIN, HNF1α, HNF4α, FIBRONECTIN, VIMENTIN, SNAIL on protein extracts. GAPDH was used as a loading control. All the experiments have been performed four times and WB images represent one indicative experiment of the independent ones. *Right:* Densitometric analysis of protein expression relative to the independent experiments. (d) *Left:* Scratch assay at the indicted time. *Right:* quantification of migration ability relative to four independent experiments.

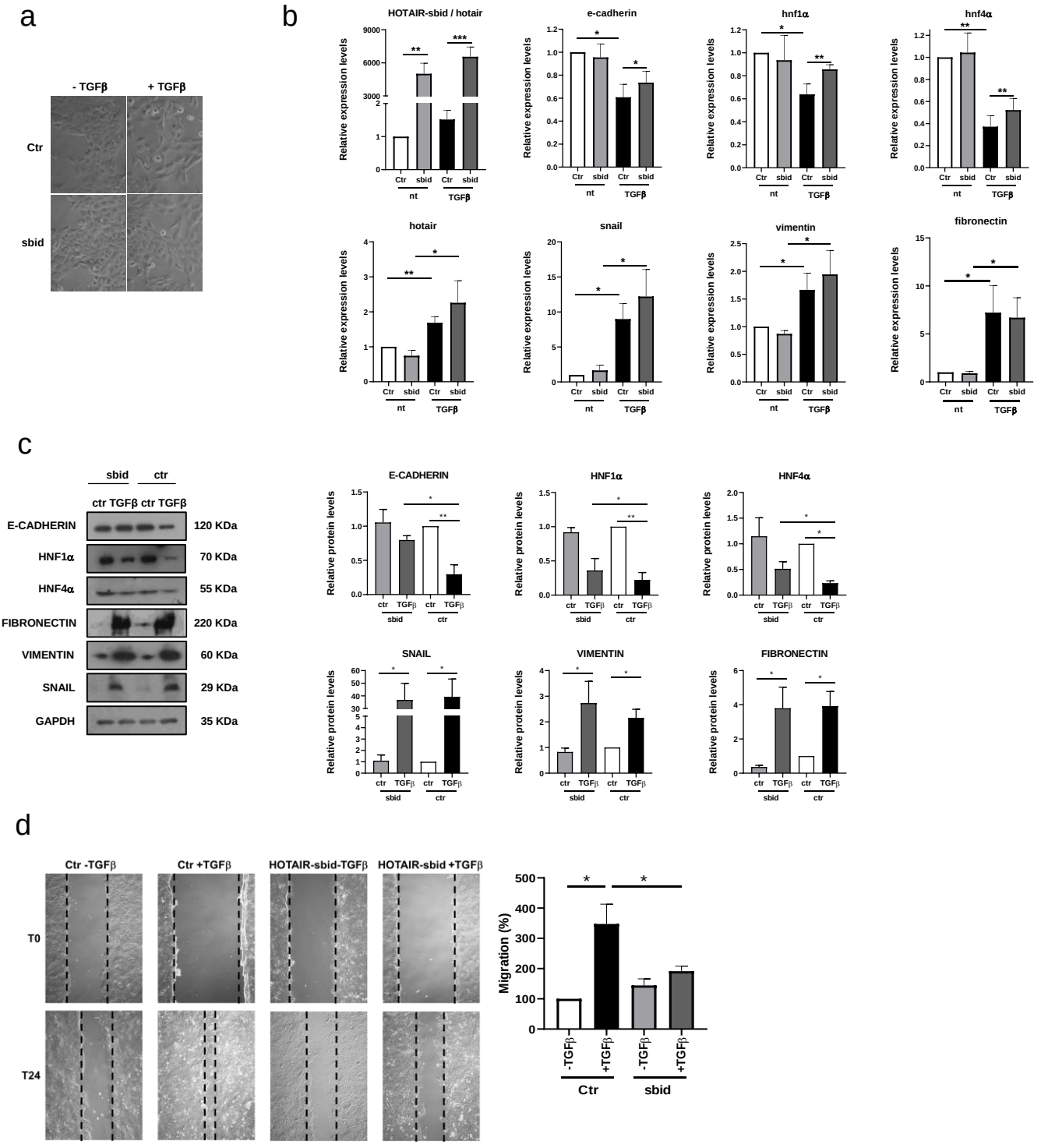


Supplementary Figure S6. Quantification of migration and invasion abilities.
Quantification of migrating ability (top) or invasive ability (bottom) in BW1J (left panels) and Hep3B (right panels) cells expressing HOTAIR-*sbid* or the empty vector as a control (Ctr). Statistically significant differences are reported (*P<0.05, **P<0.01, ***P<0.001) for three independent experiments (for invasion assays three fields for each experiment were analyzed).



Supplementary Figure S7. Proliferation assays

Proliferation assays in BW1J, Hep3B, D3, HepG2 and E14 cells expressing HOTAIR-*sbid* or the empty vector as a control (Ctr). Cells were grown in the absence of FBS to avoid proliferation as in Figure 3, 6 and Supplementary Figures S7 and S8. Differences are not statistically significant for three independent experiments.



Supplementary Figure S8. HOTAIR-*sbid* interferes with the SNAIL/HOTAIR/EZH2-mediated functions in EMT

E14 treated with TGFβ (+TGFβ) or left untreated (-TGFβ) and expressing HOTAIR-*sbid* or the empty vector as a control (Ctr). (a) Phase contrast micrographs; (b) RT–qPCR analysis for the indicated epithelial (e-cadherin, hnf4α, hnf1α), mesenchymal (snail, vimentin and fibronectin) genes and for HOTAIR and HOTAIR-*sbid*. The values are calculated by the 2(−ΔCt) method, expressed as fold of expression versus the control (arbitrary value=1) and shown as mean±s.e.m. Statistically significant differences are reported (*P<0.05, **P<0.01) for five independent experiments.

(c) *Left:* Western blot analysis (WB) for E-CADHERIN, HNF1α, HNF4α, FIBRONECTIN, VIMENTIN, SNAIL on protein extracts. GAPDH was used as a loading control. All the experiments have been performed three times and WB images represent one indicative experiment of the independent ones. *Right:* Densitometric analysis of protein expression relative to the independent experiments. (d) *Left:* Scratch assay at the indicted time; *Right:* quantification of migration abilities relative to four independent experiments.

List of primers used in RIP and gene expression analysis			
Gene name	Sequence	Efficiency (%)	r^2
HOTAIR-sbid FW	GAAGACACGCACGGAGAAAG	91	0,99
HOTAIR-sbid REV	ACTGGGGTTTGTCTGGAGTT		
hsa-L34 FW	GTCCCGAACCCCTGGTAATAG	107	0,992
hsa-L34 REV	GGCCCTGCTGACATGTTTCTT		
mmu-e-cadherin FW	CTACTGTTTCTACGGAGGAG	102,9	0,996
mmu-e-cadherin REV	CTCAAATCAAAGTCCTGGTC		
mmu-hnf4a FW	TCTTCTTTGATCCAGATGCC	90,7	0,988
mmu-hnf4a REV	GGTCGTTGATGTAATCCTCC		
mmu-hnf1a FW	TATCATGGCCTCGCTACCTG	97,1	0,995
mmu-hnf1a REV	ACTCCCCATGCTGTTGATGA		
mmu-snail FW	CCACTGCAACCGTGCTTTT	109,5	0,998
mmu-snail REV	CACATCCGAGTGGGTTTGG		
mmu-fibronectin FW	AGACCATACCTGCCGAATGTAG	95,3	0,996
mmu-fibronectin REV	GAGAGCTTCCTGTCCTGTAGAG		
mmu-vimentin FW	AGCAGTATGAAAGCGTGGCT	90,5	0,997
mmu-vimentin REV	CTCCAGGGACTCGTTAGTGC		
mmu-18S FW	ACGACCCATTCGAACGTCTG	94,7	0,996
mmu-18S REV	GCACGGCGACTACCATCG		
mmu-hotair FW	GCGCCAACGTAGACCAAAAG	109,4	0,989
mmu-hotair REV	TACCGATGTTGGGGACCTCT		
hsa-E-CADHERIN FW	TACGCCTGGGACTCCACCTA	*108,6*	0,981
hsa-E-CADHERIN REV	CCAGAAACGGAGGCCTGAT		
hsa- HNF4a FW	CATGGACATGGCCGACTACA	*110*	0,987
hsa-HNF4a REV	ATTGCCCATCGTCAACACCT		
hsa-HNF1a FW	GCCCACCAAGCAGGTCTTCA	104,5	0,985
hsa-HNF1a REV	AGGGTCCTGGCTGGGGAC		
hsa-SNAIL FW	CACTATGCCGCGCTCTTTC	*104,9*	0,985
hsa-SNAIL REV	GCTGGAAGGTAAACTCTGGATTAGA		
hsa-FIBRONECTIN FW	GGCTGACAGAGAAGATTCCCG	*96,9*	0,995
hsa-FIBRONECTIN REV	AGCTGGGTCTGCTAACATCAC		
hsa-VIMENTIN FW	GCTAACCAACGACAAAGCCC	*100,2*	0,997
hsa-VIMENTIN REV	GATTGCAGGGTGTTTTCGGC		
hsa-L32 FW	GGAGCGACTGCTACGGAAG	*90,8*	0,997
hsa-L32 REV	GATACTGTCCAAAAGGCTGGAA		
hsa-HOTAIR FW	CGGGACTTAGACCCTCAGGT	93,6	0,985
hsa-HOTAIR REV	GTTCCATTCCACTGCGAAGC		
hsa-U1 FW	TTTTCCCAGGGCGAGGCTTA	109,8	0,996
hsa-U1 REV	CCCCACTACCACAAATTATGCA		
hsa-GAPDH FW	GGGGAGATTCAGTGTGGTGG	93,3	0,982
hsa-GAPDH REV	GTGGCTGGCTCAGAAAAAGG		

Table S1. List of primers, sequence, primer pairs efficiency and r^2 values

List of primers used in ChIP analysis			
Promoter name	Sequence	Efficiency (%)	r^2
mmu-E-cadherin promoter Ebox FW	GAACGACCGTGGAATAGGAA	109,3	0,981
mmu-E-cadherin promoter Ebox REV	CTCCCACACCAGTGAGCAG		
mmu-hnf4a promoter Ebox FW	GGAGATGGAAACTGAGGCTTG	109,8	0,985
mmu-hnf4a promoter Ebox REV	GTCACATGCTTTGGGAACCG		
mmu-hnf1a promoter Ebox FW	GCACTTGGGAGCTAGAGGTA	97,3	0,988
mmu-hnf1a promoter Ebox REV	TGTGTGTGTATCTCTCTGTGTCT		
mmu-rpl30 promoter FW	TAAGGCAGGAAGATGGTGG	96,8	0,991
mmu-rpl30 promoter REV	CAGTGTGCTCAAATCTATCC		
hsa-E-cadherin promoter Ebox1 FW	GGCAAGACAGAGCGAGAC	100,5	0,991
hsa-E-cadherin promoter Ebox1 REV	TCGAACTCCTGGGCTGAA		
hsa-E-cadherin promoter Ebox2 FW	GGTGAACCCTCAGCCAATCA	91	0,993
hsa-E-cadherin promoter Ebox2 REV	CACAGGTGCTTTGCAGTTCC		
hsa-HNF1a promoter Ebox FW	TCAGAGCCTCGATTTCCTCC	105,4	0,986
hsa-HNF1a promoter Ebox REV	GACCCTTCCACCCCACTC		
hsa-HNF4a promoter Ebox FW	CAAGCAGGTGGTGAGATCC	107,5	0,993
hsa-HNF4a promoter Ebox REV	CGTCTCCTCTGGTCTCCTTC		
hsa-RPL30 promoter FW	GCAGGAAGATGGTGGCCGCAA	94,1	0,994
hsa-RPL30 promoter REV	AGTCTGCTTGTACCCCAGGACGT		

Table S2. List of primers, sequence, primer pairs efficiency and r^2 values