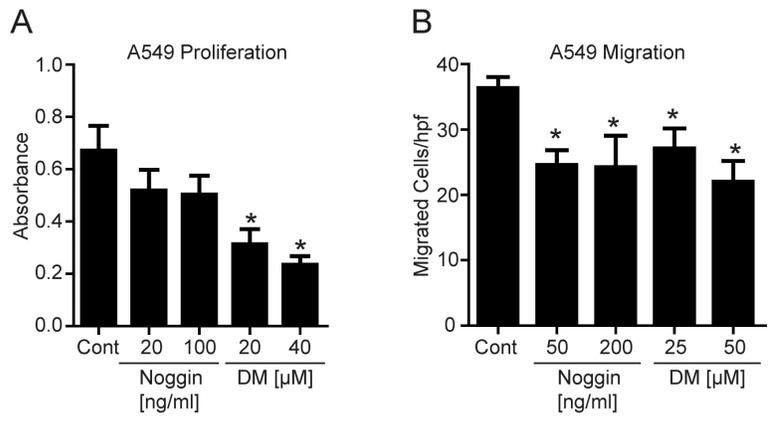
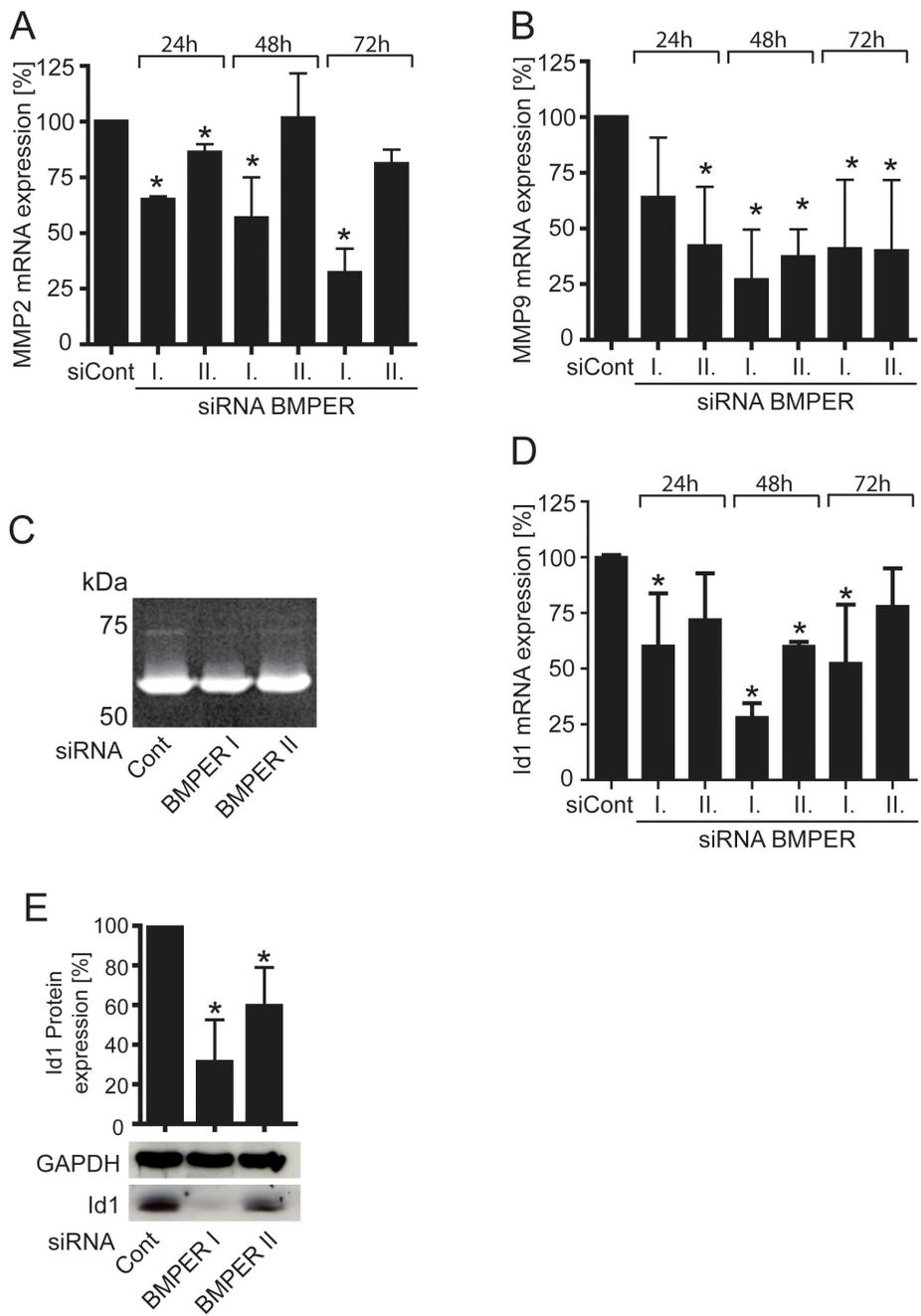


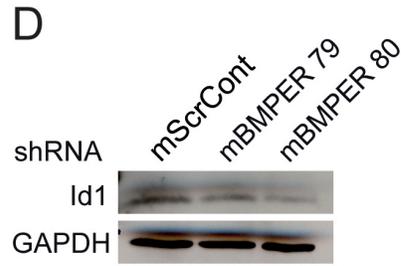
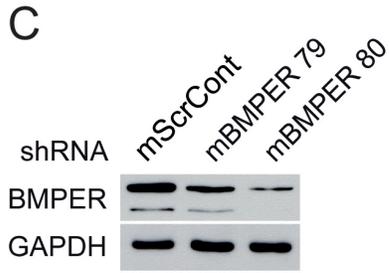
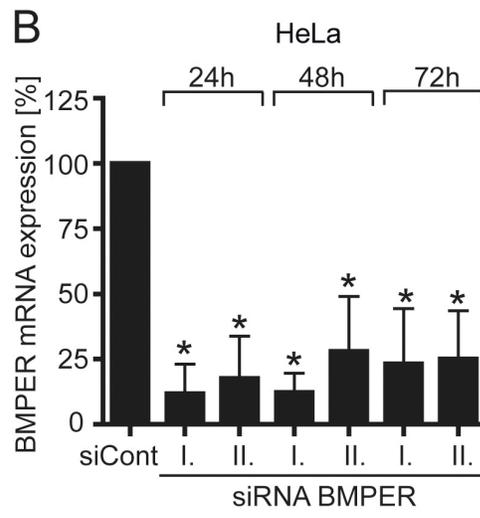
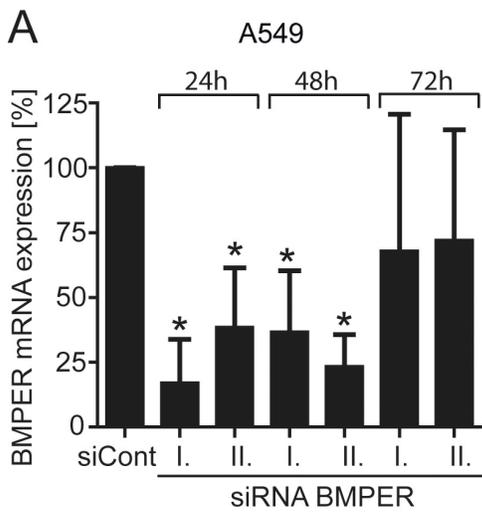
Supplemental Figure 1: Impact of BMPER on HeLa carcinoma cell proliferation, migration, invasion and on endothelial cell sprout formation.



Supplemental Figure 2: Impact of BMP antagonists on A549 carcinoma cell proliferation and migration.



Supplemental Figure 3: Lack of BMPER in HeLa carcinoma cells influences expression of BMP target gene Id1 and expression of MMPs.



Supplemental Figure 4: BMPER reduction and effects in tumor cells.

Supplementary Online Information

Supplementary Online Material and Methods

SiRNA Sequences

siBMPER I: forward: 5'-UGAAGGAGCUGUUAUAGGUAUUUCC-3', reverse 5'-GGAAAUACCUAUAACAGCUCCUUCA-3'; siBMPER II: forward: 5'-CAGAGGAAAGUGUUUGACCUCCCUU-3', reverse: 5'-AAGGGAGGUCAAACACUUUCCUCUG-3'.

Primer Sequences

BMPER (forward primer: 5'-AGG ACA GTG CTG CCC CAA ATG-3' and reverse primer: 5'-TAC TGA CAC GTC CCC TGA AAG-3'), human RNA-Polymerase II (hRP) (forward primer: 5'-GCA CCA CGT CCA ATG ACA T-3' and reverse primer: 5'-GTG CGG CTG CTT CCA TAA-3'), Id1 (forward primer: 5'-CAC CCT CAA CGG CGA GAT C-3' and reverse primer: 5'-CCA CAG AGC ACG TAA TTC CTC-3'), MMP-2 (forward primer: 5'-CTG GGA GCA TGG CGA TGG ATA C-3' and reverse primer: 5'-GGA AGC GGA ATG GAA ACT TG-3') and MMP-9 (forward primer: 5'-GAT GAC GAG TTG TGG TCC CT-3' and reverse primer: 5'-GCC TTG GAA GAT GAA TGG AA-3').

Supplementary Online Figure Legends

Supplementary Online Figure 1: *Impact of BMPER on HeLa carcinoma cell proliferation, migration and invasion.* (A) Proliferation was determined by BrdU assay. Triplicates of HeLa cells were incubated for 24 hours with BrdU and increasing concentrations of BMPER. Cells with BrdU and medium served as negative control. (B) HeLa cells were transfected in triplicates with either one of two BMPER specific siRNAs or scrambled siRNA control. 48 hours post-transfection the BrdU ELISA was performed. (C) HeLa cells were serum-starved

overnight and trans-migration was assayed with or without BMPER at indicated concentrations or EGF (50 ng/ml final concentration) as positive control. Triplicates were fixed after 4 hours and for each 5 random microscopic fields were counted. **(D)** HeLa cells were transfected with either one of two BMPER specific siRNAs or scrambled siRNA control. 48 hours post-transfection tumor cell migration was quantified. **(E)** 24 hours post-transfection of HeLa cell invasion into matrix was quantified. Triplicates were fixed after 24 hours and 5 random microscopic fields were counted. Mean \pm SD; *= P<0.05 versus the respective control. hpf=high power field. **(F–G)** BMPER reduction in HeLa cells effects tube formation of endothelial cells. HUVECs were incubated with the supernatant of HeLa cells, which were transfected with one of two specific siRNA against BMPER or negative control siRNA, respectively. Thereafter HUVECs were subjected to matrigel assay. **(F)** Cumulative sprout length and **(G)** branch points of capillary-like structures were measured after 3 hours and quantified. Mean \pm SD; * = P<0.001 versus control siRNA.

Supplemental Online Figure 2: *Impact of BMP antagonists on A549 carcinoma cell proliferation and migration.* **(A)** Proliferation was determined by BrdU assay. Triplicates of A549 cells were incubated for 24 hours with BrdU and indicated concentrations of Noggin or dorsomorphin. Cells with BrdU and medium served as negative control. **(B)** For trans-migration A549 cells were serum-starved overnight and assayed with indicated concentrations of Noggin or dorsomorphin. Triplicates were fixed after 4 hours and 5 random microscopic fields were counted. Mean \pm SD; *= P<0.01 versus the respective control. hpf=high power field.

Supplementary Online Figure 3: *Lack of BMPER in HeLa carcinoma cells modulates expression of MMPs and expression of the BMP target gene Id1.* **(A–B&D)** mRNA expression of MMP2, MMP9 and Id1 in HeLa cells after 24, 48 and 72 hours post-transfection with

siRNA BMPER I or II was analyzed compared to scrambled siRNA control. mRNA content was quantified by real-time (q)PCR using specific primers for MMP-2, MMP-9, Id1 and hRP as internal control. Knock-down efficiency was calculated using $\Delta\Delta C_T$ method. Mean \pm SD; * = $P < 0.05$ versus control. (C) Representative gelatin zymography assay of conditioned media collected from siRNA-transfected HeLa cells 72 hours post-transfection. MMPs degrade gelatin and produce a white band in the coomassie-stained gelatin SDS gel. The size of approximately 68kDa indicates the proenzyme and of 62kDa indicates the activated form of MMP2. (E) Western blot analysis for Id1 was performed 48 hours post-transfection. GAPDH served as loading control. Densitometric analysis of Id protein expression for three independent experiments is shown. Mean \pm SD; *= $P < 0.05$ versus control.

Supplemental Online Figure 4: BMPER reduction and effects in tumor cells. (A-B) BMPER mRNA expression in A549 and HeLa cells after 24, 48 and 72 hours post-transfection with siRNA BMPER I or II was analyzed compared to scrambled siRNA control. mRNA content was quantified by real-time (q)PCR using specific primers for BMPER and hRP as internal control. Knock-down efficiency was calculated using $\Delta\Delta C_T$ method. Mean \pm SD; * = $P < 0.05$ versus control. (C) After clonal selection of LLCs transduced with lentiviral particles encoding either a scrambled shRNA (ScrCont) or one of two different shRNAs targeted against BMPER (mBMPER79 or 80) BMPER protein knock-down efficiency was analyzed by western blot. (D) Western blot analysis of Id1 protein expression of stable shRNA expressing LLC clones. GAPDH served as loading control.