**Supplementary Figure Legends:**

**Supplementary Figure S1: mRNA expression profiles in resected metastases and matched primary tumors and normal tissues.** A) Venn diagram showing differentially regulated genes following an mRNA oligonucleotide microarray of resected normal and corresponding tumor and metastasis tissues. Arrays were performed on the HumanHT-12 v4 platform; B) List of differentially regulated genes common to all compartments. These genes were regarded as contributing to the common end point in our hypothesis generation.

**Supplementary Figure S2: Role of miR-218 investigated in additional cancer entities.** A) miR-218 mimics suppress N-Cadherin and ZEB2 expression at mRNA and protein levels, whereas miR-218 antagonists have the opposite effect. The A375 cell line with high endogenous expression of N-cadherin was used, mRNA and protein expression were evaluated at 48 hrs with qRT-PCR and Western blots, respectively; B, C) significantly decreased migration, invasion and metastasis was investigated using matrigel chamber assay and CAM assay respectively. The opposite effect was observed when miR-218 inhibitor was used in the study.

**Supplementary Figure S3: EMT following miR-135b/210 transfection.** Bright-field microscopy images showing mesenchymal transformation observed with miR-135b and -210 transfection in RKO cells. miRNAs were transfected at an end concentration of 100μM and images were acquired on a Cell Observer microscope (Zeiss, Germany) at 20X magnification 48hrs after transfection.

**Supplementary Figure S4: Cell line screening.** A) Endogenous expression of miR-218 in a SW480 and SW620 colorectal cancer cell lines. The low metastatic SW480 cell line has significantly high expression of miR-218 as compared to highly metastatic SW620 (real time PCR), and significantly lower expression of the pro-metastatic miRs -135b and -210.

**Supplementary Figure S5:** **FOXN3 significantly enhances survival in a small cohort of TCGA colorectal cancer samples.** Using all of the available data for patients in the TCGA colon data set of the Oncomine repository, who were deceased at 5 years or earlier, a significant difference in the median survival times for patients who had low vs high expression was observed (Mann Whitney two tailed test, *p* =0.044).

**Supplementary Figure S6:** **Independent *in vivo* validation of the novel miRNA-network in brain tumors in the Oncomine database.** A), miR-210 expression in the Northcott Brain 3 dataset showing a highly significant up-regulation of this miRNA in different subsets of brain tumors; column 1= classical medulloblastoma, 200 samples, column 2 = desmoplastic medulloblastoma, 21 samples, column 3= large cell medulloblastoma, 30 samples, column 4= medulloblastoma, 28 samples, column 5 = medulloblastoma with extensive nodularity, 6 samples. Almost all cases with very little exception showed an up-regulation of miR-210; B) MiR 218-1 expression in Northcott Brain 3 dataset showing a significant down-regulation of this miRNA in different subsets of brain tumors (column delineations, cancer subtypes and patient numbers are identical to that for miR-210).

**Supplementary Figure S7: TCGA colorectal cancer database analysis on selected target**s. A and B) MicroRNA concept filter analysis for miR-135b showing that SIAH1 and FOXN3 are significant targets using the TCGA colorectal cancer database. Individual patients are represented by a column, red and blue colors signify up and down regulation of the gene respectively. The Oncomine target filter analysis uses predictions from the picTar online *in silico* tool. C) A similar filter analysis for miR-210 showing SETD2 as significantly down regulated target.