**Supplementary Tables:**

**Table S1.** Clinicopathological characteristics of cases on two meningioma TMAs (HTMA283 & HTMA285).

**Table S2**. Detailed outcome and biomarker data for meningioma patients with samples on HTMA283 and HTMA285

**Table S3.** Clinicopathological information for 22 cases meningioma tissues used for RNAseq analysis.

**Table S4.** Clinicopathological characteristics of patients whose resections were used to generate meningioma PDCLs.

**Table S5**. Gene-gene correlation data from the Celsius database analyzed by UGET.

**Table S6**. The sequences of siRNAs used in pools to reduce expression of SIX1, FOXC1, FOXC2, FOXD1, BNC2, KLF5, MEOX2, PTGDR and EYA2.

**Table S7.** The sequences of lentivirus shRNA against SIX1, LEPR and LACZ control.

**Table S8**. Microarray expression profiling data from publicly available brain tumor microarray data in GEO.

**Table S9.** The ranked gene list between meningioma and other brain tumors from microarray expression profiling data from GEO.

**Table S10**. The differential expressed gene list between meningioma and other brain tumors from microarray expression profiling data from GEO.

**Table S11.** The median value per marker used for distinguishing low and high expressors.

**Table S12.** IHC analysis of SIX1, FOXC1, FOXC2, BNC2, MEOX2, KLF5, EMA and LEPR in meningioma TMA283&285 (separated into low and high expressors - relative to the median score for each marker for the entire cohort)

**Table S13.** RNAscope analysis of SIX1, FOXC2, FOXD1, KLF5, LEPR TOTAL and LEPR long in meningioma TMA283&285 (separated into low and high expressors - relative to the median score for each marker for the entire cohort)

**Table S14.** UGET correlation between PTGDR, LEPR and meningioma TFs.

**Table S15**. The values for PTGDR and LEPR from mRNA expression array data and RNA-seq data.

**Table S16.** The percentages of LEPR splice variants in meningioma samples analyzed by RNAseq.

**Table S17.** Clinical information for cohort of patients with pulmonary meningothelial nodules.

**Supplementary Figures:**

**Figure S1.** **Identification of transcription factors (TFs) that are highly enriched in meningioma.** Microarray data and RNAseq data indicated that eight transcriptional factors (SIX1, SIX2, FOXC1, FOXC2, FOXD1, BNC2, MEOX2 and KLF5) were highly expressed in meningioma. A. Microarray data. B. RNAseq data.

**Figure S2.** **Meningioma TFs are highly expressed in less common meningioma subtypes.** IHC data indicated that SIX1, FOXC1 and MEOX2 are highly expressed in angiomatous meningioma, chordoid meningioma, clear cell meningioma and papillary meningioma.

**Figure S3.** **Meningioma TFs are markers of meningothelial lineage**. **A.** Representative images of *in situ* hybridization data for mRNA from TFs SIX1, FOXC1 and MEOX2 in E14.5 mouse meninges obtained from publicly available data (GenePaint) 49. **B.** IHC and immunofluorescence (IF) data for SIX1, FOXC1 and MEOX2 from human meninges, from post-mortem brain. **C.** Representative images from H&E and IHC stained slides for SIX1, FOXC1 and MEOX2 protein from pulmonary meningothelial nodules.

**Figure S4. Meningioma TFs are expressed in E14.5 mouse meninges**. The *in situ* hybridization of TFs (SIX2, FOXC2, BNC2, FOXD1 and KLF5) in E14.5 mouse meninges from GenePaint.org.

**Figure S5.** **The expression pattern of meningioma TFs protein in meningioma.** **A**. Representative image of IHC staining for epithelial membrane antigen (EMA) in grade I and grade III samples. Semi-quantitative scoring data for EMA IHC from 178 meningiomas is plotted by tumor grade in a plot of the percentage of cases that were EMA high and low expressors. **B.** Semi-quantitative scoring IHC data for BNC2, MEOX2 and KLF5 from 178 meningiomas is plotted by tumor grade in a plot of the percentage of cases that were high and low expressors for each TF. **C.** Kaplan Meier plots show overall survival for patients with tumors that were high and low expressors for BNC2, MEOX2 and KLF5. **D**. tSNE plot visualize the distribution of each TF.

**Figure S6.** **The expression pattern of meningioma TFs RNA in meningioma.** Representative images of in situ hybridization using RNAscope probes to detect **A.** SIX1 mRNA transcripts, **B.** FOXC2 mRNA transcripts, and **C.** FOXD1 mRNA transcripts in grade I and grade III meningiomas. Digital scoring data of the in situ hybridization signals (average dots per cell) using RNAscope dots is shown in plots of the percentage of cases that were high and low expressors for each marker. **D**. tSNE plot visualize the distribution of each TF.

**Figure S7. The protein-RNA correlation of meningioma TFs**. The correlation of semi-quantitative scoring IHC data and digital scoring RNAscope data (average dots per cell) was analyzed. A. SIX1 IHC and SIX1 RNAscope, B. FOXC2 IHC and FOXC2 RNAscope

**Figure S8. Mast cells infiltrate in meningioma TMA283 & HTMA285.** Tryptase-positive mast cells were counted per core and the average number of infiltrated mast cells was calculated for each case (using all cores). An average number greater than the median value for all cases was considered “high infiltration” and less than or equal to the median value was considered “low infiltration”. A plot of the percentage of cases that were high infiltration and low infiltration was made.

**Figure S9.** **Six different LEPR splices and protein-RNA correlation of LEPR detected by IHC and RNAscope.** **A.** Schematics of Six different splices of LEPR and target regions for RNAscope and qPCR. **B.** Correlation between LEPR IHC and LEPR TOTAL RNAscope, LEPR IHC and LEPR LONG RNAscope, LEPR TOTAL RNAscope and LEPR LONG RNAscope were analyzed.

**Figure S10.** **LEPR and PTGDR expression were decreased in low SIX1 expression meningioma samples.** **A.** LEPR and PTGDR expression were decreased in low SIX1 IHC meningioma samples in TMA 283&285. **B.** LEPR and PTGDR expression were decreased in low SIX1 RNAscope meningioma samples in TMA 283&285

**Figure S11.** **LEPR and PTGDR expression were correlated with SIX1 expression in meningioma.** **A.** SIX1 protein correlated with LEPR IHC, LEPR TOTAL RNA, and LEPR LONG RNA and PTGDR RNA in TMA 283&285. **B.** SIX1 RNA correlated with LEPR IHC, LEPR TOTAL RNA, and LEPR LONG RNA and PTGDR RNA in TMA 283&285.

**Figure S12. Body mass index correlates with pulmonary meningothelial nodules.** A group of 46 patients with pulmonary resection from the same time period and with the same gender distribution (female>male) were selected as a control group. The body mass index of these patients prior to the surgery was ascertained from the medical record and analyzed in two groups.

**Figure S13. Meningioma TFs are fatefully expressed in meningioma PDCLs. A**. qPCR assay of meningioma TFs in primary meningioma cell line MG8, MG14 and MG15 and siRNA pools treated cell lines. **B**. IF of meningioma TFs SIX1, FOXC1 and FOXC2 in meningioma cell line MG14 and MG15 (scale bar 50μm).

**Figure S14.** **LEPR, PTGDR, and four members of the eyes absent (EYA) family are expressed in meningioma PDCLs.** qPCR assay LEPR TOTAL, LEPR LONG, PTGDR, EYA1, EYA2, EYA3, and EYA4 in PDCL MG8, MG14 and MG15.

**Figure S15.** **RNAseq assay in meningioma tissues and corresponding meningioma PDCLs MG1, MG5 and MG8.** A. Meningioma TFs (SIX1, FOXC1, FOXC2, BNC2, MEOX2 and KLF5). B. LEPR and PTGDR.

**Figure S16.** **Meningioma TFs, LEPR and PTGDR are maintained in meningioma PDCLs.**  A. qPCR assay of meningioma TFs and LEPR and PTGDR in meningioma cell lines MG1, MG2 and MG5. B. IF of meningioma TFs SIX1, FOXC1 and FOXC2 in meningioma cell line MG1, MG2 and MG5 (scale bar 10μm).

**Figure S17.** **EYA1 and EYA2 are highly enriched in meningioma.** Heat map of publicly available brain tumor microarray data in GEO (also used in Figure 1A), including meningioma TFs (SIX1, SIX2, FOXC1, FOXC2, FOXD1, BNC2, MEOX2, KLF5), LEPR, PTGDR, as well as four members of the eyes absent (EYA) family (EYA1, EYA2, EYA3 and EYA4).

**Figure S18**. **Inhibition of SIX1 and LEPR expression in lentivirus shSIX1 and shLEPR infected grade I meningioma cells.** **A**. SIX1 qPCR detection in stable lentivirus shSIX1 infected MG8, MG14 and MG15 cells. **B.** LEPR TOTAL and LEPR LONG qPCR detection in stable lentivirus shRNA-LEPR infected MG8 and MG15 cells.

**Figure S19**. **Induction of apoptosis and G2/M arrest in lentivirus shSIX1 infected grade I meningioma cells.** Apoptosis was detected by Annexin V stains in lentivirus shSIX infected MG15 cells. **A**. The percentage of early apoptotic cells was increased significantly in lentivirus shSIX1 infected MG15 cells. **B.** The percentage of early apoptotic / late apoptotic / necrotic cells was increased significantly in lentivirus shSIX1 infected MG15 cells. **C.** Representative flow cytometry plots for each group. Cell cycle assay was detected by propidium iodide (PI) stains in lentivirus shSIX1 infected MG15 cells. **D.** The percentage of G0/G1 cells was decreased significantly in lentivirus shSIX1 infected MG15 cells. **E.** The percentage of G2/M cells was increased significantly in lentivirus shSIX1 infected MG15 cells. **C.** Representative plots of cell cycle assay for each group.

**Figure S20. Recombinant leptin promotes cell growth in meningioma cell lines in dose dependent manner.** Cell viability was assessed following treatment of meningioma PDCLs (A) MG8, (B) MG14 and (C) MG15 that were incubated in serum-free media supplemented and refreshed with recombinant human leptin for 7 days at the indicated concentrations.