Supplemental Materials and Methods

Preparation of histone-enriched cellular extracts

To prepare cell extracts for immunoblot analysis, 4 million cells were plated per 150mm plate for hypoxic conditions, and 2 million cells were plated per 150mm plate for normoxic conditions. The difference in plating takes into account the differences in proliferation rate, so that on the day of harvest, cells are approximately 70% confluent. The day after plating, the cells were incubated for 48 hours at normoxia or 0.2% oxygen. Cells were then scraped, collected, and pelleted by centrigugation. The cell pellet was resuspended in 3 volumes of cell lysis buffer (10mM Tris pH7.5, 10mM NaCl, 3mM $MgCl_2$, and 0.5% Triton X-100). Crude cell extract was discarded and the pellet was resuspended in 3 volumes of PH buffer (100mM KCl, 20mM Tris pH7.8, 0.05% Tween, 2mM DTT, 1X Calbiochem protease inhibitor cocktail set 1, and 2.5μM TSA). Samples were then homogenized with 40 strokes in a dounce homogenizer. Proteins were extracted from the homogenate with an additional 0.2M NaCl (0.3M total salt). The extract was discarded, and the remaining pellet was resuspended in 3 volumes of DNase I reaction buffer (40mM Tris pH 8.0, 10mM $MgSO_4$, and 1mM $CaCl_2$) and digested for 1 hour at 4°C with 1/10 pellet volume of 1unit/μl DNase I and 880 units of MNase per mL of pellet. Proteins were then extracted with 0.5M NaCl and used for immunoblotting.

Primary antibodies used for immunoblotting

Primary antibodies for the following proteins were incubated overnight at 4°C and used at the specified dilutions: H3K9ac (Upstate 06-942) 1:1000, H3K14ac (Upstate 06-911) 1:1000, H4ac (Upstate 06-866) 1:2000, R3H4R3me2 (Upstate 07-213) 1:500, H3K4me2 (Upstate 07-030) 1:2000, H3K4me3 (Novus NB 500-173) 1:2000, H3K9me2 (Abcam

ab7312, Upstate 07-212, and Lake Placid Biologicals AR-0108) 1:1000, H3K4me1 (Abcam ab8895) 1:500, H3K27me3 (Abcam ab6002) 1:1000, and H3K79me2 (Upstate 07-366) 1:1000.

Primers and PCR conditions used for quantitative RT-PCR

The following primers were used: *AFP* (forward primer, CAGGCAACAACCATTATTAAGC; reverse primer, 5'-TTCCTTGGCAACACTCCTC-3'), *VEGF* (forward primer, 5'-AGGCTGCTGTAACGATGAAG-3'; reverse primer, 5'-ATCTGCTGTGCTGTAGGAAG-3'), *EGR1* (forward primer, 5'-CCATGAACGCCCATATGCT-3'; reverse primer, 5'-TCATCCGAGCGAGAAAAGC-3'), 18S (forward primer, 5'-TCAAGAACGAAAGTCGGAGGTT-3'; reverse primer, 5'-GGACATCTAAGGGCATCACAG-3'), *Albumin* (forward primer, 5'-CTTAAACCGATGGGCGATCTCACT; reverse primer, 5'-CCCCACTAGCCTCAGGCAAAAT-3'). PCR products were amplified for 40 cycles of the following steps: 30 seconds at 95°C, 30 seconds at 55°C, 30 seconds at 72°C.

Antibodies, primers and PCR conditions for ChIP

The following antibodies were used: 10μl of H3K9AC (Upstate 06-942), 10μl of H3K9/27me2-Abcam (ab7312), 5μl of H3K9me2-Lake Placid Biologicals (AR-0108), 20μl of H3K4me3 (Novus NB 500-173), 5μl of H3 (Abcam ab1791), 5μl of normal sheep IgG (Upstate 12-515), 20μl of H3K27me3 (Abcam).

The following primers and Taqman probes were utilized to amplify the DNA: *AFP* core promoter (forward primer, 5'-GACTGCTCGAAACATCCCACTT-3'; reverse primer, 5'-TTCATGGCTGCTGGTTCCTT-3'; probe, FAM-CAGCACTGCCTGCG-MGB), *VEGF* core promoter (forward primer, 5'-GGGAGCCCCTAGGCCACTA-3'; reverse primer, 5'-AGGCCGTGGACCCTGGTA-3'; probe, FAM-TGGAAAGCTAAACCC-MGB), *EGR1* core

promoter (forward primer, 5’-TGCTGTTCCAGACCCTTGAAA-3’; reverse primer, 5’-GGCGGCTCCCCAAGTT-3’; probe, FAM-AGTCGCGAGAGATC-MGB), and *Brn3b* 3’UTR (forward primer, 5’-CCGGTTCACAATCTCTGATTT-3’; reverse primer, 5’-CAGACCAAGCCAGGAGCAA-3’; probe, FAM-CTCAGCTGCTTGCTT-MGB). These DNAs were amplified during a FAST run on an ABI 7500 FAST instrument. The core promoter region of *Albumin* was amplified during a standard run on an ABI FAST instrument using the following primers: (forward primer 5’-GGCAAAATGAAGTGGGTAACCTT-3’; reverse primer 5’-AAACACACCCCTGGAAAAAGC-3’).

Quantification of ChIP values

Each value was normalized to its representative input sample by subtracting the cT values generated from immunoprecipitated DNA from the cT values generated from input DNA (ddcT). The % of input bound by each histone modification was determined by applying the formula, 2^-ddCT, with input arbitrarily set as 100%. The % of input generated from IgG immunoprecipitation was subtracted from each value as a correction for background within normoxia and hypoxia, respectively. In figure 4, the % of input bound by the protein of interest was normalized to the % of input bound by H3 in order to generate % of input/ bound H3. Hypoxic % of input/ bound H3 values were divided by normoxic % of input/ bound H3 to generate the fold change observed during hypoxia.