**Supplemental Section**

**Antibodies and molecular reagents:**

Monoclonal antibodies to MYC (SC-40, clone 9E10), VEGF (SC-7269) and VDR (SC-13133) and polyclonal antibodies to CCND1 (SC-718), phospho-EGFR (SC-16802), pan ErbB2 (SC-284), phospho-ErbB2 (SC-12352R), phospho-ERK 1 and ERK-2 (SC-7383), pan STAT3 (SC-482), angiotensinogen (SC-7419), ACE (SC-20791), renin (SC 133145) and AT1 (SC-1173) were obtained from Santa Cruz Biotechnology (Santa Cruz, CA). Antibodies to phospho-active ErbB2 recognize human ErbB2 phosphorylated on tyrosine 1248. Antibodies to phospho-active EGFR recognize human EGFR phosphorylated on tyrosine 1092. Polyclonal pan EGFR (#2232), pan ERK (#9102), pan AKT antibodies (#9271), pSTAT3 antibodies (#9138) and Snail antibodies (L70G2) were obtained from Cell Signaling Technology (Beverly, MA). Rat monoclonal anti-nestin1 (#556309) and mouse monoclonal anti-β-catenin antibodies (#610153) were obtained from BD Pharmingen (Palo Alto, CA). Monoclonal β-actin antibodies were purchased from Sigma-Aldrich (St. Louis, MO). Anti-CD68 antibodies (ab955) reactive to macrophages were obtained from Abcam Inc. (Cambridge, MA). Anti-Renin antibodies (14291-1-AP) were obtained from ProteinTech (Chicago IL). Ang II EIA kit (#EIA-ANGII-1) was obtained from Ray Biotech (Norcross, GA). The ELISA kit for mouse TNF-α was obtained from BD Biosciences (San Diego, CA) and the ELISA kit for human amphiregulin was obtained from R&D Systems (Minneapolis, MN). Losartan and Ang II were purchased from Sigma Aldrich (Saint Louis, MO). DNeasy kit (#69504) and miRNeasy Mini Kit (#217004) and HotStarTaq™ DNA polymerase were obtained from Qiagen (Valencia, CA). EGFR siRNA, (s564, Cat. #4390824), Lipofectamine™ RNAiMax reagent, RNAlater™ RNA storage solution, and DNA-free™ DNase-I kit were purchased from Ambion (Austin, TX). PCR reagents, including Moloney murine leukemia virus reverse transcriptase, random hexamers, high capacity reverse transcription kit and Fast SYBR green master mix were purchased from Applied Biosystems (Foster City, CA). TRIzol® RNA/DNA/Protein isolation reagents and SuperScript III Platinum Two-Step qRT-PCR kit were obtained from Invitrogen (Carlsbad, California).

**Cell culture conditions**

HCT116 and HT29 cells were maintained in McCoy’s 5A modified media with 10% serum and Dld1 cells were maintained in RPMI 1640 with 10% heat-inactivated serum. CCD-18Co cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM) containing 15% fetal bovine serum. Media was supplemented with penicillin and streptomycin 50 units/ml. Cells were tested and found to be negative for mycoplasma. Where appropriate, cell treatment conditions, including agonist, inhibitor and siRNA concentrations and incubation times are provided in figure legends.

**Real time PCR assay:**

RNA (100 ng) was reverse transcribed into cDNA using high capacity reverse transcription kit in 20 µL total volume. Incubation conditions were 25°C for 10 min, 37°C for 120 min, and 85°C for 5 min. The resulting first-strand complementary DNA (cDNA) was used as template for quantitative PCR in triplicate using fast SYBR green master mix kit. Where possible, oligonucleotide PCR primer pairs were designed to cross intron-exon boundaries from published mouse sequences in the GenBank database using Primer3 1. Primer sequences are provided in the Supplemental data Table 1S. Reverse transcribed cDNA (1:10 dilution) and primers were mixed with fast SYBR green master mixture in 20 µl. Reactants were initially heated to 95°C for 20 sec followed by 40 cycles as follows: denaturation step at 95°C for 10 sec, annealing step at 55°C for 15 sec and extension step at 60°C for 30 sec. PCR amplification was verified by melting curve and electrophoretic analysis of the PCR products on 3% agarose gel. There were no detectable amplifications in the negative control samples (reactions lacking reverse transcriptase or reactions without DNA template).

**Immunostaining**

Five-micron sections of formalin-fixed paraffin-embedded tissues were cut and mounted on Vectabond-coated Superfrost Plus slides. The slides were heated to 60°C for 1 hr, deparaffinized by three washes of 5 min each in xylene, hydrated in a graded series of ethanol washes and rinsed with distilled water. Epitope retrievals were achieved by microwave heating for 15 min in 0.01 M citrate buffer, pH 6. Following epitope retrieval, sections were washed three times for 2 min each in Tris-buffered saline (TBS) containing 0.1% Tween-20 (TBST). The endogenous peroxidase activity was quenched by incubation for 15 min in methanol/H2O2 solution (0.5%) protected from light. Sections were washed three times in TBST for 2 min each and nonspecific binding saturated using Protein Block (Dako, Carpinteria, CA) for 20 min. The sections were incubated with primary antibodies for 24 hrs at room temperature (1:150 dilution for anti‑‑catenin; 1:100 for anti-renin antibodies, 1:100 for anti-AT1 antibodies, 1:50 for anti-nestin-1 antibodies, 1:200 for anti-CD68 antibodies, 1:100 for anti-VDR antibodies and 1:50 for anti Snail1 antibodies). After three TBST washes, sections were incubated at room temperature for 30 min with 1:200 dilution of biotinylated secondary antibodies. Antigen-antibody complexes were detected using an HRP-labeled DAKO EnVision™+ System (DAKO LSAB™+ System), with 3,3’-diaminobenzidine as substrate. After washing with distilled water, sections were counterstained with Gill’s III hematoxylin, rinsed with water, dehydrated in ethanol and cleared with xylene. Tumors of comparable stage were used for immunostaining comparisons. For negative controls, primary antibodies were omitted or sections were incubated with isotype-matched non-immune antibodies. Negative control sections showed no specific staining.

**Western blotting:**

Proteins were separated by SDS-PAGE on 4-20% resolving polyacrylamide gradient gels and electroblotted to PVDF membranes. Blots were incubated overnight at 4°C with specific primary antibodies followed by 1 hr incubation with appropriate peroxidase-coupled secondary antibodies that were detected by enhanced chemiluminescence using X OMAT film. Xerograms were digitized using an Epson scanner (San Jose, CA) and band intensity quantified using UN-SCAN-IT gel software V 5.3 (Silk Scientific, Orem UT). Protein levels in *Vdr-/-* tumors were expressed as fold-Vdr+/+ tumors (mean ± SD). Separate aliquots were probed for β-actin to assess loading.

**ELISA**

Ang II was assayed in lysates prepared from colonic mucosa from left colon. Reagents, standards and samples (500 µg protein) were assayed as suggested by the manufacturer using the RayBioTech Angiotensin II EIA Kit (#EIA-ANGII-1). Ang II levels were determined from a standard curve.

TNF- was assayed using an ELISA following the manufacturer’s directions (BD Biosciences). Briefly, RAW264.7 cells plated on 96 well plates were treated for 48 hrs at 37°C with Ang II, vehicle or pre-treated with losartan. Assay wells were coated with capture antibody (1:250) at 4°C. Subsequent incubations were at room temperature. Wells were washed x5 and detection antibody (1:250 dilution) followed by 1:250 diluted horseradish peroxidase enzyme reagent (SAv-HRP). Tetramethylbenzidine substrate solution (100 µl) was added followed by 50 µl stop solution and absorbance read at 450 nm. TNF- levels were determined from a standard curve.

**Table 1S Primers for real time PCR**

mRenin-F: 5’-GAGGCCTTCCTTGACCAATC-3’

mRenin-R: 5’-TGTGAATCCCACAAGCAAGG-3’

mACE-F: 5’-CCCATCTGCTAGGGAACATGT-3’

mACE-R: 5’-GGTGTCCATCCCTGCTTTATCA-3’

mAGT-F: 5’-TCTTTGGCACCCTGGTCTCTTTCT-3’

mAGT-R: 5’:-TTCTCAGTGGCAAGAACTGGGTCA-’3

mAGTR1-F: 5’-CTGCTCTCCCGGACTTAACA-3’

mAGTR1-R: 5’-CTGGGTTGAGTTGGTCTCAGA-3’

mIL-1-F1: 5’-GCAACTGTTCCTGAACTCAACT-3’

mIL-1-R1: 5’-ATCTTTTGGGGTCCGTCAACT-3’

mTNF- F: 5’-TGTCCCTTTCACTCACTGGC-3’

mTNF- R: 5’-CATCTTTTGGGGGAGTGCCT-3’

IL-6 F: 5’-CCTCTCTGCAAGAGACTTCCA-3'

IL-6 R: 5’-AGAATTGCCATTGCACAACTCT-3'

**Supplemental Figure Legends**

**Fig S1. Tarceva, an EGFR inhibitor, blocks Ang II induced HT29 cell proliferation.** Cells (5,000) were plated on 96 well plates and allowed to adhere overnight. Cells were then treated with Tarceva (10 µM), or vehicle for 2 hrs followed by Ang II (50 nM) or vehicle for 24 hrs. Cell proliferation was determined by Wst1 assay as described in the “Materials and Methods” (\*,†p<0.05, compared to control; n=2 independent platings).

**Fig S2. EGF induces Snail in HT29 colon cancer cells.** Cells were plated on collagen-coated 6 well plates in 10% serum. Twenty-four hrs later cells were deprived of serum and treated with vehicle (phosphate-buffered saline), 10 ng/ml EGF or 40 ng/ml TGFβ. After 72 hrs cells were lysed and extracts probed for indicated proteins. Shown are blots representative of three independent platings.

**Fig S3. EGFR suppresses VDR expression in AOM rat tumors.** VDR expression in control colonic mucosa and AOM-induced tumord in rats fed AIN-76A chow alone, or chow supplemented with EGFR inhibitor Gefitinib (A+G). Note the decreased VDR expression in tumors from rats fed AIN-76A alone, compared to rats supplemented with Gefitinib. Shown are representative tumors from two rats in each group.

**References:**