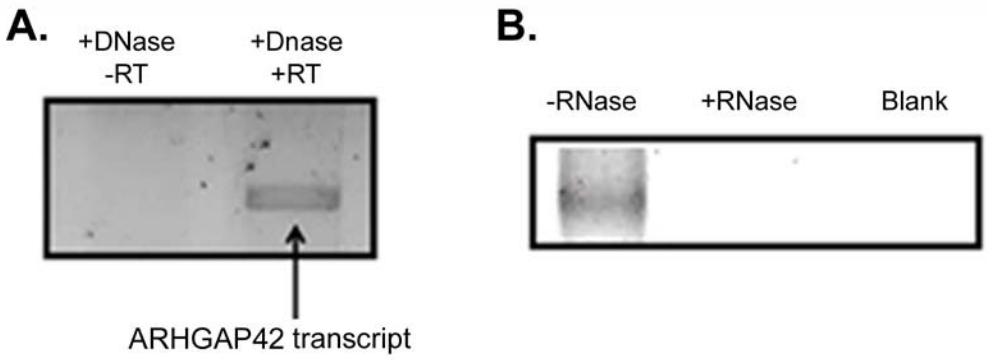
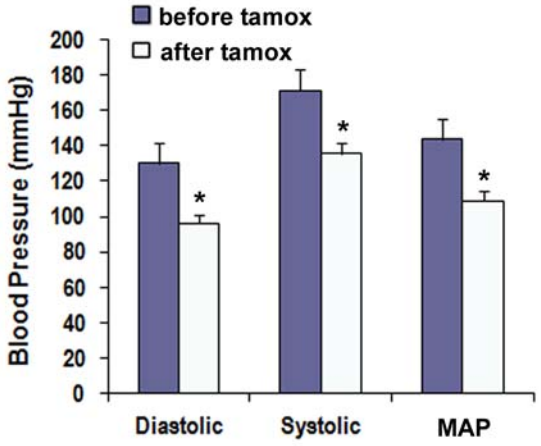
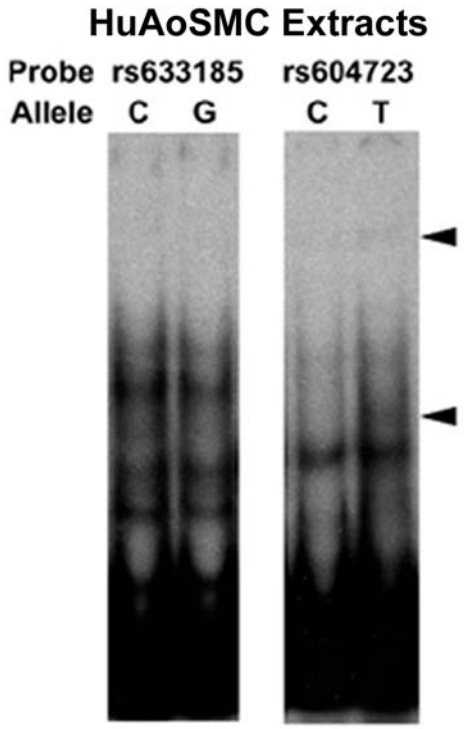


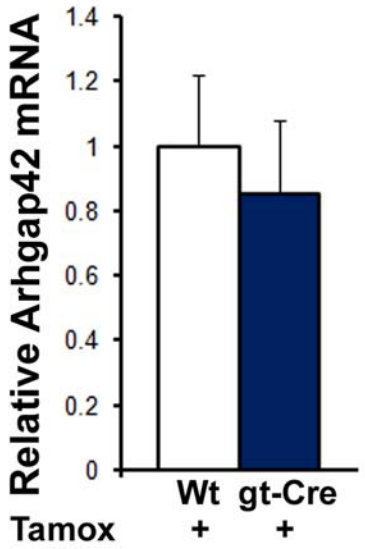
Supplemental Figure I. RNA used for allele-specific qPCR was not contaminated with genomic DNA. A) Total RNA isolated from HuAoSMC was treated with DNAse and then subjected to first strand synthesis +/- reverse transcriptase (RT). Reaction products were then used for PCR amplification of a 604 bp region encompassing the DHS2 region of the *ARHGAP42* gene. **B)** Same as A, except that one RNA sample was treated with RNAse before first strand synthesis. Data are representative of two separate experiments.



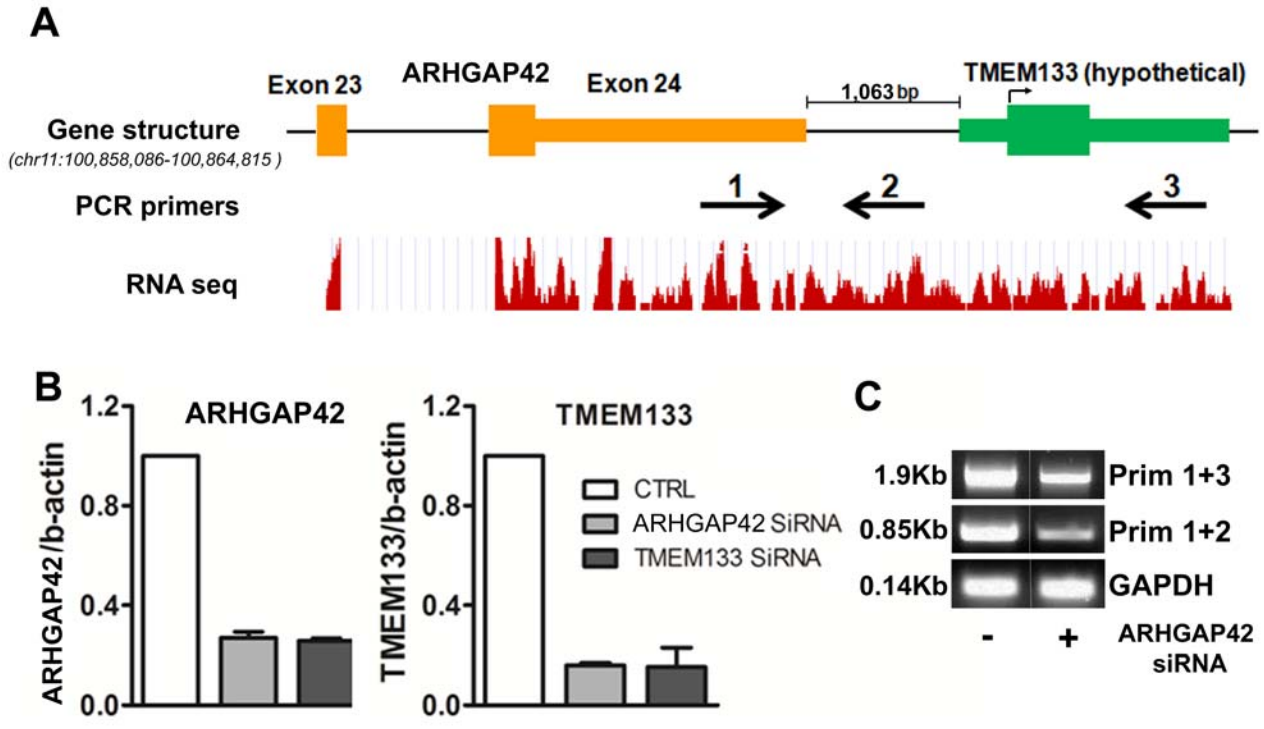
Supplemental Figure II. Tamoxifen treatment of *Arhgap42*$^{gt/gt}$SM-MHC^{creERT2} mice restored blood pressure homeostasis. Blood pressure was measured by tail cuff method before and two weeks after the start of tamoxifen treatment (100 mg/kg IP for 5 consecutive days). Data are expressed as mean ± SEM; n=5* $p<0.05$ vs before tamoxifen (student's t-test 2 tailed).



Supplemental Figure III. Gel shift assays were performed by combining nuclear lysates from HuAoSMC with radiolabeled 100 bp oligonucleotide probes containing the major or minor alleles at rs633185 and rs604723. Arrowheads mark allele-specific bands. Gel is representative of two individual experiments.



Supplemental Figure IV. Tamoxifen treatment of DOCA-salt-treated *Arhgap42*$^{gt/gt}$SMMHC^{creERT2} mice restored *ARHGAP42* expression in mesenteric arteries. Wt and *Arhgap42*$^{gt/gt}$SMMHC^{creERT2} mice were implantated with a 50mg slow-release DOCA pellet and then fed 0.9% NaCl in drinking water for 3 weeks. Ten days after the start of the DOCA-salt regimen, both groups were treated with tamoxifen by oral gavage of 1 mg for 3 consecutive days. Mice were sacrificed 12d after the start of tamoxifen treatment and Arhgap42 message was measured in isolated mesenteric arteries by qPCR. *ARHGAP42* expression was normalized to *GAPDH* and is expressed relative to Wt. Data are expressed as mean ± SEM; n=5 for Wt; n=7 for *Arhgap42*$^{gt/gt}$SMMHC^{creERT2} mice, p=0.6595 (student's t-test).



Supplemental Figure V. *TMEM133* is an extension of the *ARHGAP42* 3'UTR. A) RNA seq data from HuAoSMC near the genomic region containing *TMEM133*. **B)** siRNA targeted against *ARHGAP42* or *TMEM133* had identical effects on *ARHGAP42* and *TMEM133* mRNA levels as measured by qPCR. Data are expressed as mean ± SEM of three independent experiments. **C)** mRNA was isolated from HuAoSMCs +/- siRNA to *ARHGAP42*. Following DNase treatment, RT PCR was performed using the primers shown in A. Data represent three independent experiments.

Characteristic	Mean ± SD or percent
Age, mean (yrs)	48 ± 12
Age category, %	
30-44 yrs	44
45-64 yrs	45
65+ yrs	11
% female	53
Race, %	
White	77
Black	19
Other	4
Body mass index, mean (kg/m^2)	29 ± 6
Body mass index category, %	
Normal	27
Overweight	36
Obese	38
Total cholesterol (mg/dl), mean	200 ± 38
Current smoker, %	7
Office systolic BP (mm Hg), mean	130 ± 13
Office diastolic BP (mm Hg), mean	81 ± 9
Clinic hypertension, %	29

SD, standard deviation

Supplemental Table I. Characteristics of clinical cohort

rs604723	**C/C**	**C/T**	**T/T**	**MAF**
African American	326	32	0	*4.5%
Caucasian	359	274	40	26.3%

rs2055450	**A/A**	**A/T**	**T/T**	**MAF**
African American	311	47	0	*6.6%
Caucasian	346	290	37	27.0%

rs604723 vs rs2055450	**LD r^2**	**LD D'**
African American	0.56	0.89
Caucasian	0.83	0.92

Supplemental Table II. Analysis of *ARHGAP42* genotype in human populations. 1,031 patients from several clinical cohorts were genotyped at the rs604723 and rs2055450 variations using Taqman-based allelic discrimination assays. Linkage disequilibrium for these variations was calculated using R. * $p<0.001$ vs MAF in Caucasians; Chi-squared test.