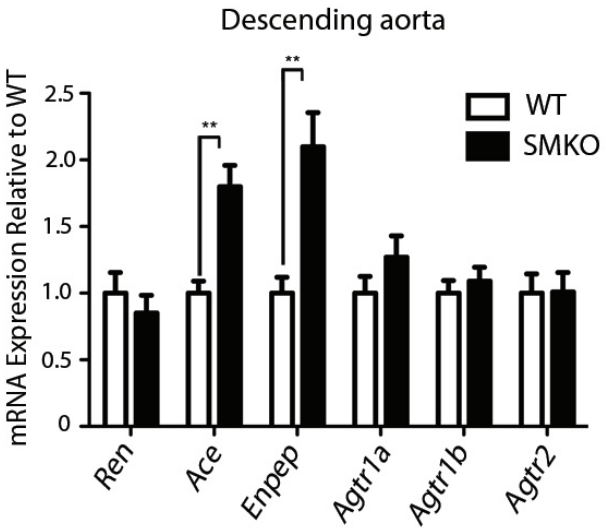

Fig. S1. qPCR analysis of the renin-angiotensin pathway in the descending aortas.

Descending aortas from control and SMKO mice were analyzed at 1 month old. N=4 per each genotype. Two-tailed Student *t*-test. Bars are mean ± SEM. ** $P < 0.005$.

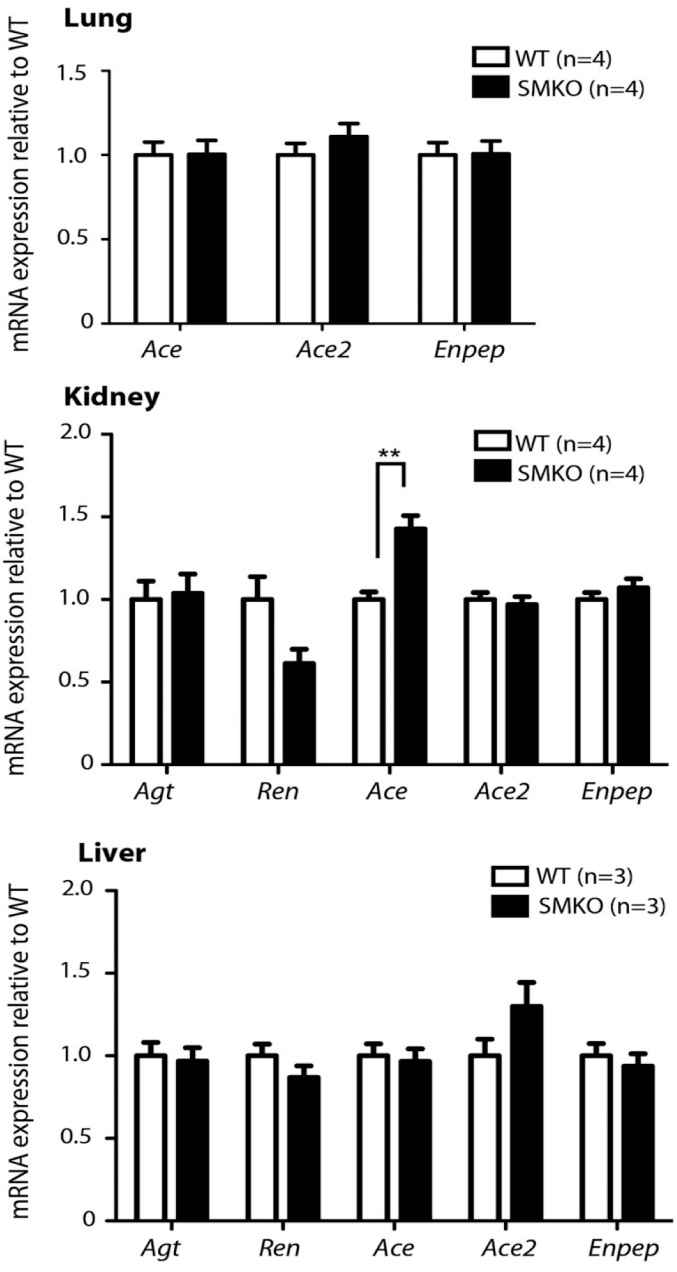

Fig. S2. qPCR analysis of the renin-angiotensin pathway in the lung, kidney and liver.

Indicated tissues from 3-month old WT and SMKO mice (n=4 per genotype) were analyzed. Two-tailed Student *t*-test. Bars are mean ± SEM. ** $P < 0.005$.

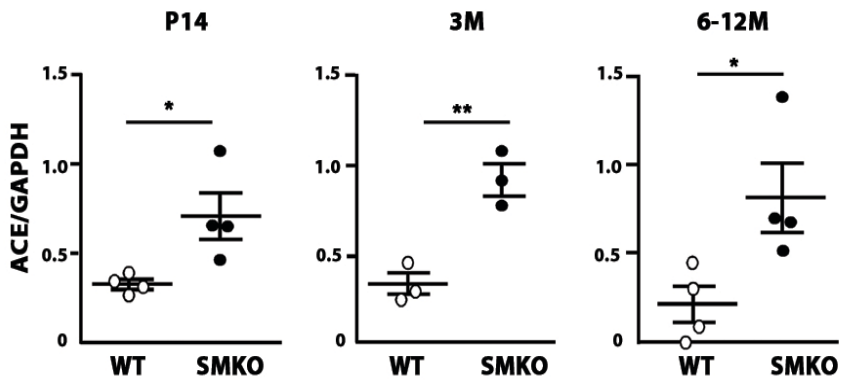

Fig. S3. Quantification of ACE in *Fbln4*^{SMKO} (SMKO) mice throughout postnatal and adult life. Aortas harvested from WT and SMKO mice at P14 (n=4 per genotype), 3 months (n=3 per genotype) and 6-12 months (n=4 per genotype) were analyzed. Signal intensity was quantified and expressed as a ratio to GAPDH. Two-tailed Student *t*-test. Bars are mean ± SEM. * $P<0.05$, ** $P < 0.005$.

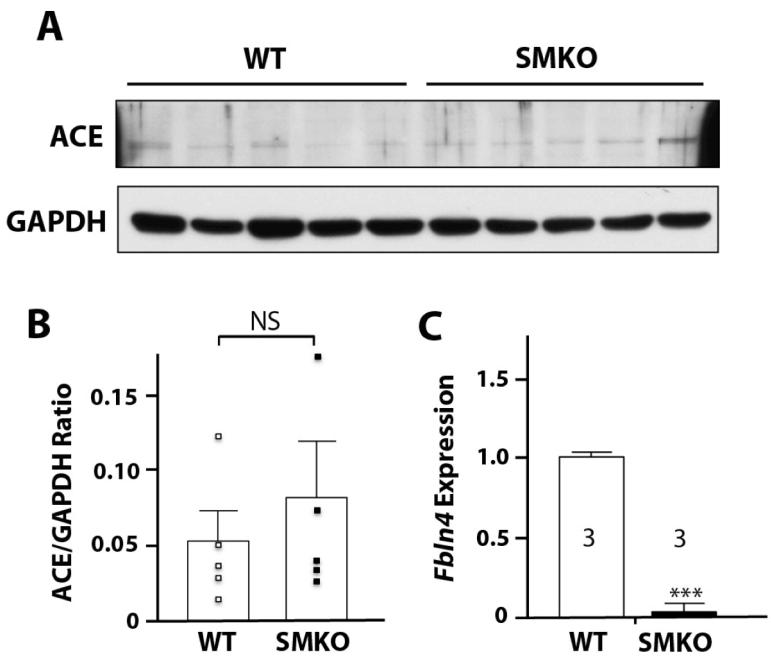

Fig. S4. ACE expression in primary *Fbln4*^{SMKO} SMCs. **A.** Western blot analysis of 5 independent SMCs established from P45 WT and SMKO aortas. **B.** Signal intensity was quantified and expressed as a ratio to GAPDH. **C.** qPCR confirming the absence of *Fbln4* transcripts in SMCs. N=3 per genotype. Two-tailed Student *t*-test. Bars are mean ± SEM. NS: not significant. *** $P < 0.001$.

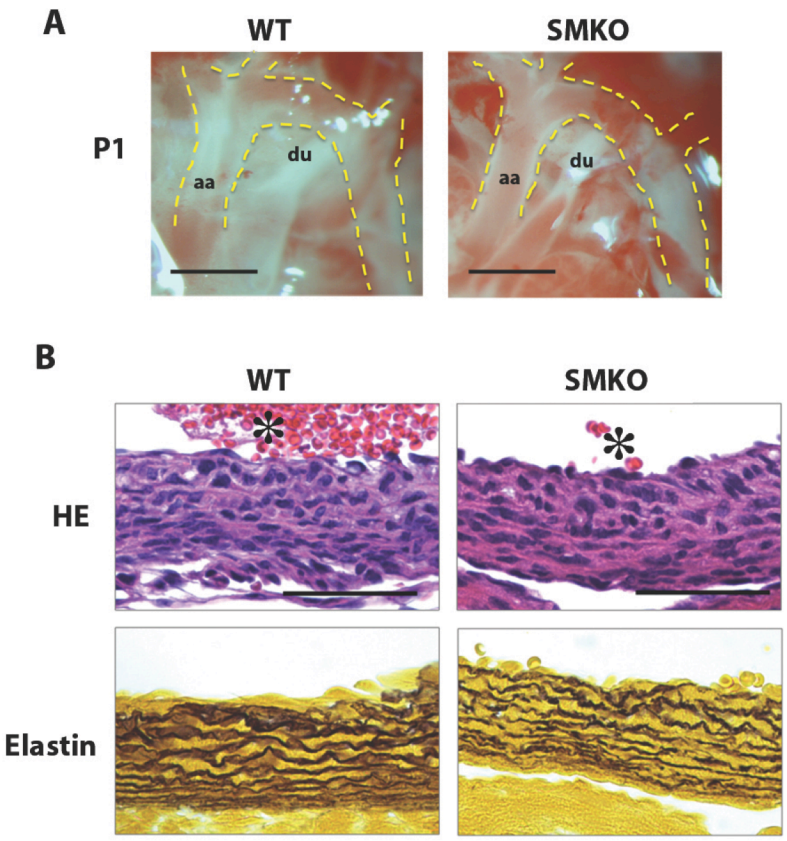

Fig. S5. Morphological analysis of *Fbln4*^{SMKO} ascending aorta at P1. **A.** Representative macroscopic images of WT and SMKO aortas at P1. aa: ascending aorta; du: ductus arteriosus. Bars are 1 mm. **B.** Histological images of cross sections of ascending aorta from WT and SMKO at P1 stained with H&E and Hart's for elastin. Bars are 50 µm.

Table S1. Animals used in morphometric analysis

Genotype & drug	Number of animals
Control (ut)	6*
Fbln4^{SMKO} (ut)	7
Fbln4^{SMKO} (d)	50
Captopril	
Midgestation-P90	5
Propranolol	
Midgestation-P90	7
Losartan	
Midgestation-P90	6
P7-P90	8
P30-P90	7
P7-P45	9
Control (ut)	5**
Agtr1a$^{-/-}$;*Fbln4*$^{+/+}$ (ut)	14
Agtr1a$^{+/+}$;*Fbln4*^{SMKO} (ut)	5
Agtr1a$^{+/-}$;*Fbln4*^{SMKO} (ut)	12
Agtr1a$^{-/-}$;*Fbln4*^{SMKO} (ut)	10
Agtr2$^{-/-}$;*Fbln4*$^{+/+}$ (ut)	5
Agtr2$^{-/-}$;*Fbln4*^{SMKO} (ut)	8
Agtr2$^{-/-}$;*Fbln4*$^{+/+}$ (d) Losartan (midgestation-P90)	5
Agtr2$^{-/-}$;*Fbln4*^{SMKO} (d) Losartan (midgestation-P90)	8

ut: untreated, d: drug-treated
* *Fbln4*$^{+/+}$ (n=2), *Fbln4*$^{fl/+}$ (n=2) and *Fbln4*$^{KO/+}$ (n=2)
** *Agtr1a*$^{+/+}$;*Fbln4*$^{+/+}$ (n=1) and *Atr1a*$^{+/-}$;*Fbln4*$^{+/+}$ (n=4)

Table S2. Animals used in blood pressure measurement

Genotype & drug	total
Control (ut)	6*
Fbln4^{SMKO} (ut)	6
Control (d)	19**
Captopril	6
Propranolol	8
Losartan	5
Fbln4^{SMKO} (d)	18
Captopril	6
Propranolol	7
Losartan	5

ut: untreated, d: drug-treated

* *Fbln4*$^{+/+}$ (n=2), *Fbln4*$^{KO/+}$ (n=2) and *Fbln4*$^{fl/+}$ (n=2)

** All *Fbln4*$^{+/+}$

Table S3. Animals used in vessel biomechanics

Genotype & drug	Number of animals
Control (ut)	9*
Fbln4^{SMKO} (ut)	9
Control (d)	25**
Captopril	5
Propranolol	8
Losartan	12
Fbln4^{SMKO} (d)	26
Captopril	10
Propranolol	6
Losartan	10

ut: untreated, d: drug-treated
* *Fbln4*$^{+/+}$ (n=5), *Fbln4*$^{KO/+}$ (n=2), and *Fbln4*$^{fl/+}$ (n=2)
** All *Fbln4*$^{+/+}$

Table S4. qPCR primer sequences

Gene	Forward primer 5'-3'	Reverse primer 5'-3'
Agt	cgagtgggagaggttctcaatag	gacgtggtcggctgttcct
Ace	gggcattgacctagagactgatg	cttgggctgtccggtcata
Ace2	tcttctgccatcggattttca	tgtcaatgcctgtttcagtagga
Enpep	ccccatgatagagacgtactttca	cctgccatcccagcaaatc
Agtr1a	actcacagcaaccctccaag	ctcagacactgttcaaaatgcac
Agtr1b	cgccagcagcactgtaga	ggagggggtgaattcaaaa
Agtr2	ccctctctgggcaacctattact	atcgacactcatgcaggtaataaaaa
Ren	ggatcagggagagtcaaaggttt	tcacagtgattccacccacagt
Acta2	atcgtccaccgcaaatgc	aaggaactggaggcgctg
Cnn1	aacttcatggatggcctcaaa	acccggctgcagcttgt
Mlck	agaagtcaaggaggtaaagaatgatgt	cgggtcgcttttcattgc
Myh11	tcaacgccaaccgcaggaagctg	tgctaagcagtctgctgggct
Myocd	caccccacgacatcaaatcc	tgcatcattcttgtcactttctga
Sm22	gcgcctgggcttcca	caggctgttcaccaatttgct
B2m	ccgagcccaagaccgtcta	aactggatttgtaattaagcaggttca
Gapdh	tgacgtgccgcctggagaaa	agtgtagcccaagatgcccttca