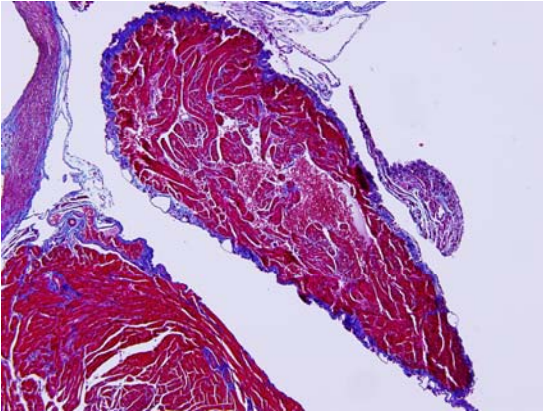
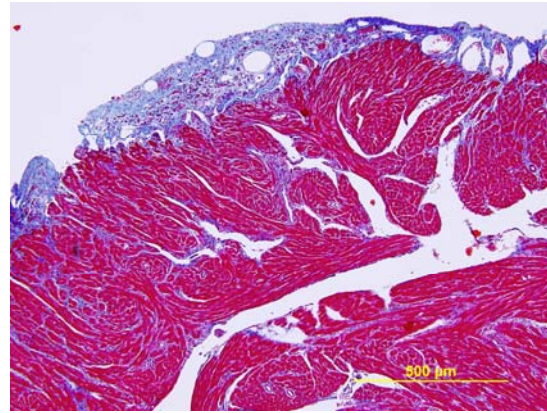
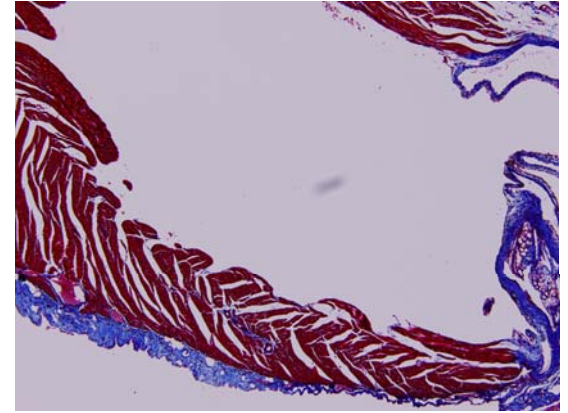
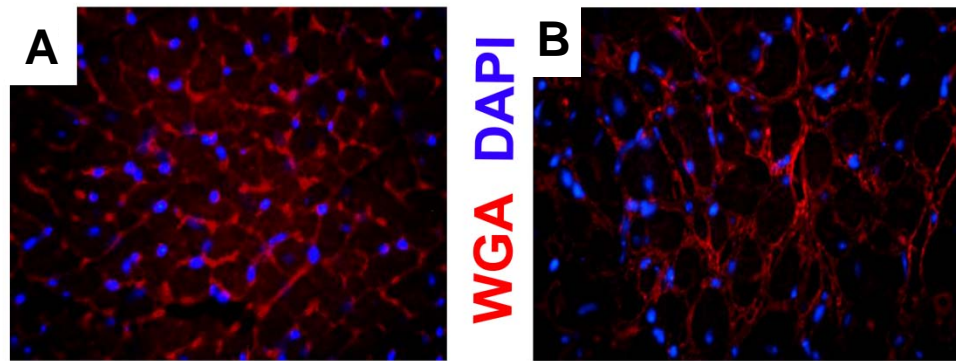


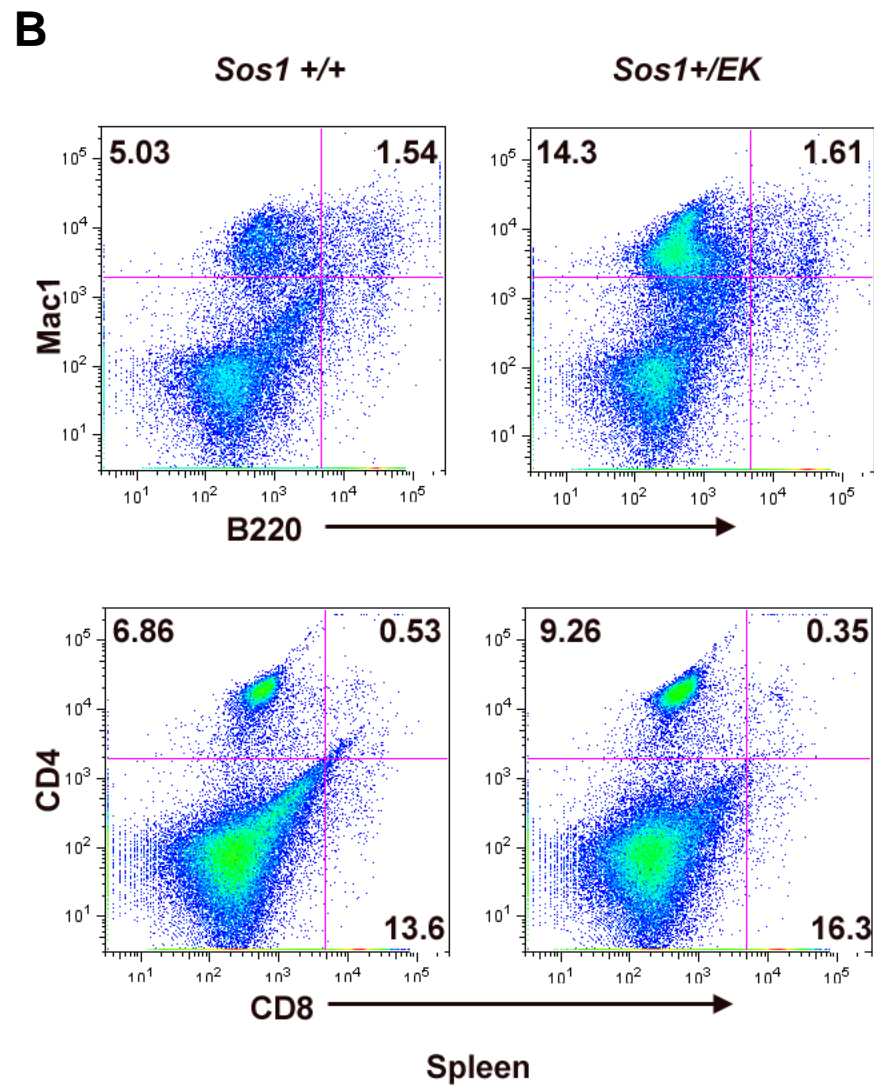
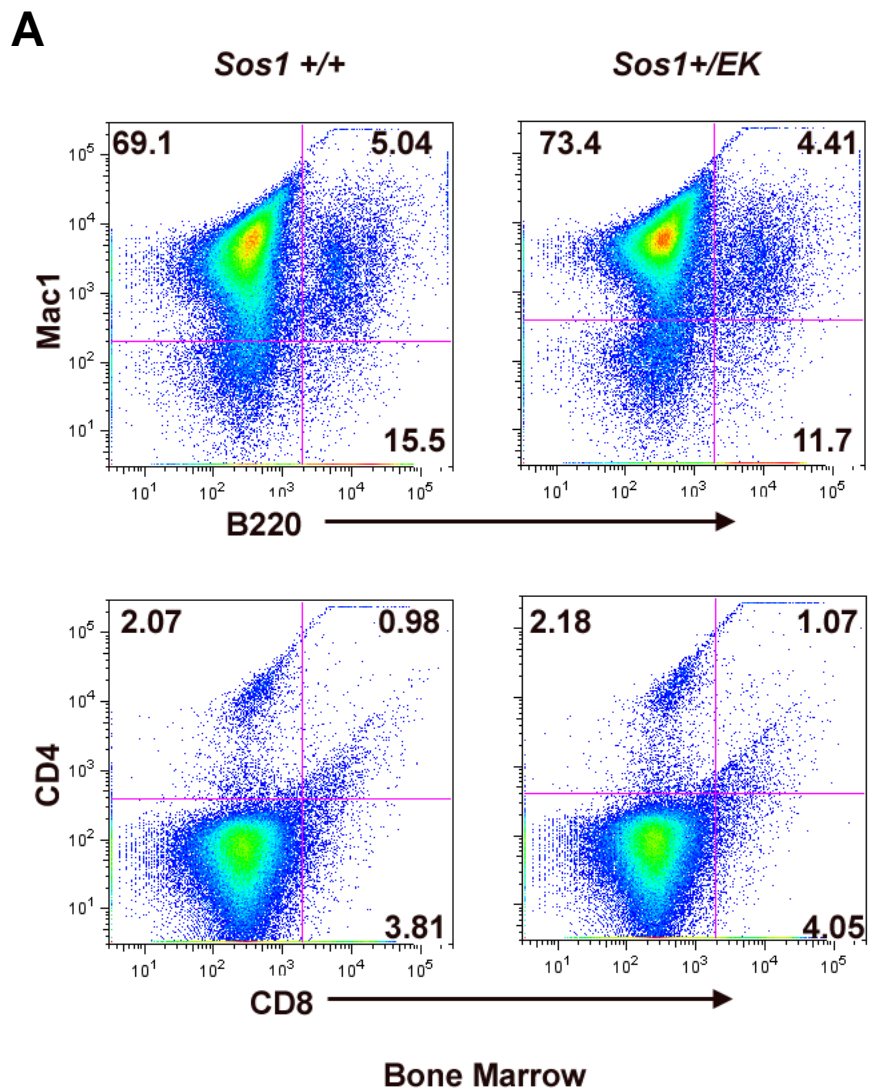
Supplementary Figure 1 Immunohistochemistry staining of *Sos1* with hematoxylin counterstaining. Note brown cytoplasmic staining of *Sos1* in E13.5 (**A**) *Wt* and (**B**) *Sos1*^{+/*EK*} embryos. Right panels show higher magnification. Arch, arch of aorta; PV, pulmonary valve; aAo, ascending aorta; PT, pulmonary trunk; AVSS, aortica-pulmonary spiral septum; dAo, descending aorta; AV, aortic valve; TV, tricuspid valve; AVC, atrioventricular cushion; MV, mitral valve; VSD, ventricular septal defect; *, site of fusion of the bulbar ridges with the interventricular septum.

A**B****C**

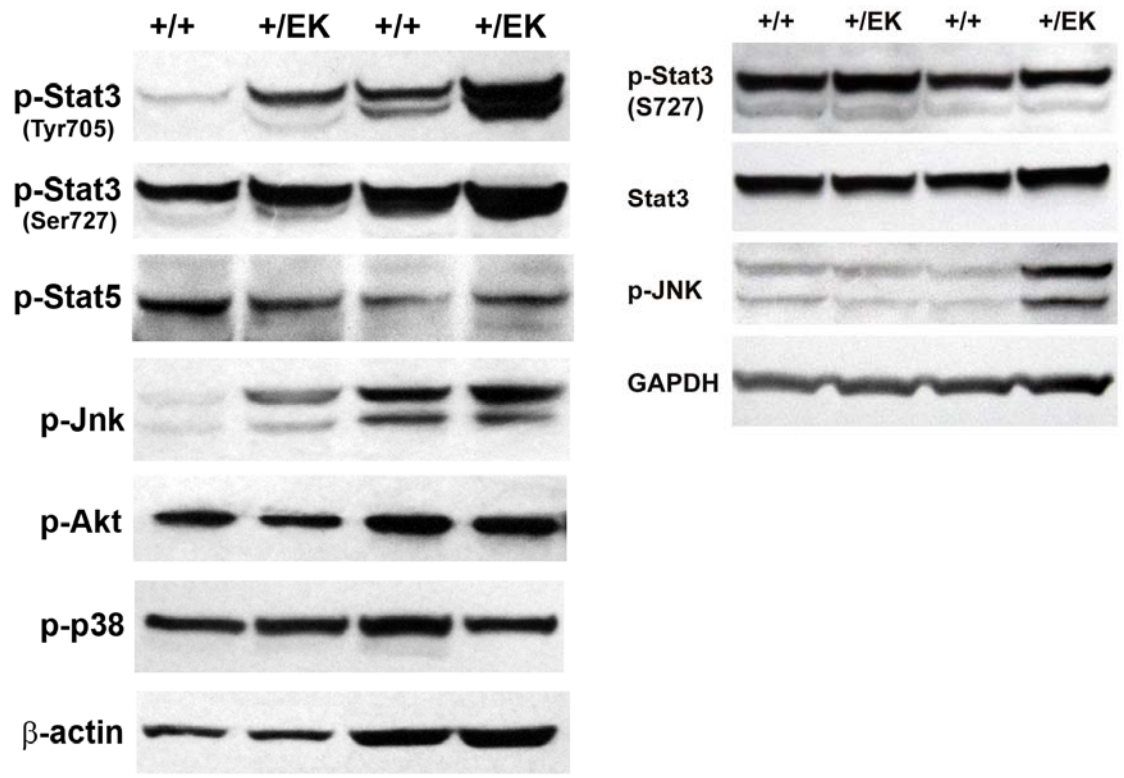
Supplementary Figure 2 Masson-Trichrome staining of heart tissue showing fibrosis in 4-month old *Sos1^{EK/EK}* mice. Note blue collagen staining in (A) right atrial epicardium, (B) left ventricular epicardium and myocardium and (C) right ventricular epicardium.



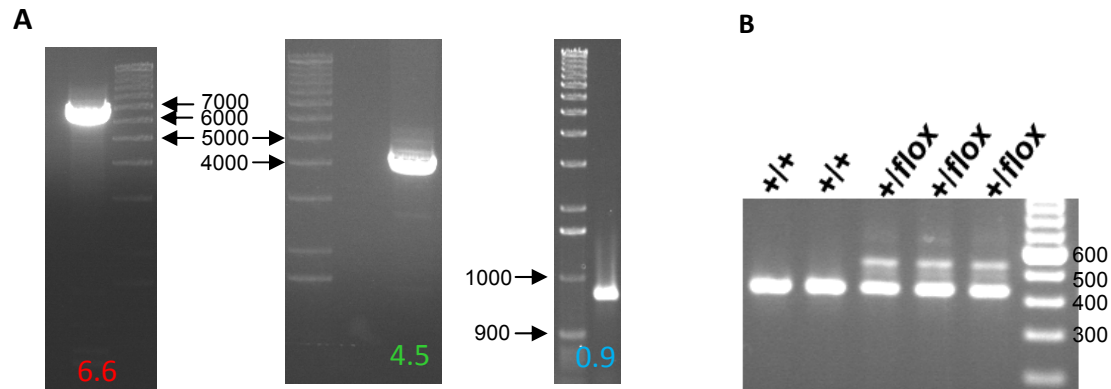
Supplementary Figure 3 Wheat germ agglutinin (WGA) staining of left ventricular wall sections in 9-month-old (A) *Wt* and (B) *Sos1^{+/EK}* mice. Note larger size and disorganized structure of *Sos1^{+/EK}* cardiomyocytes.



Supplementary Figure 4 Flow cytometric analysis of (A) bone marrow and (B) spleen of 5-month-old *Wt* and *Sos1*^{+/*EK*} mice.



Supplementary Figure 5 Representative immunoblotting of phospho-proteins in *Sos1* heart tissue.



Supplementary Figure 6 (A) Representative results of long-range PCR screening of a positive ES cell clone carrying the targeted *Sos1^{EK}* allele. Primer pairs are indicated in Fig. 1A in respective red, green and blue color, numbers indicate the size of PCR bands in kilo-base pairs (bp). Numbers indicate bp of DNA ladder. **(B)** Representative PCR results for genotyping *Sos1^{EK}* targeted locus using primer pairs indicated in purple in Fig. 1A. The mutant allele rendered a band that is ~100 bp more than the *Wt* allele due to the presence of *loxP* construction site. Numbers indicate bp of DNA ladder.

Supplementary Table 1 Blood pressure of *Sos1* mice

	<u><i>Sos1</i>^{+/+} (n=5)</u>	<u><i>Sos1</i>^{+/EK} (n=5)</u>	p
Systolic-5month (mmHg)	127.97 ±9.06	114.7 ±9.13	0.82
Systolic-8month (mmHg)	117.79 ±5.83	108.6 ±6.02	0.83

Supplementary Table 2 Complete blood count of 5-month-old *Sos1* mice

	<i>Sos1</i> ^{+/+} (n=4)		<i>Sos1</i> ^{+/<i>EK</i>} (n=6)		
	Mean number x10 ³ /μl	SD	Mean number x10 ³ /μl	SD	
WBC	2.06	1.08	4.74	3.37	*
NE	0.48	0.22	1.57	1.03	
LY	1.38	0.71	2.68	1.97	
MO	0.15	0.07	0.44	0.51	
EO	0.04	0.07	0.04	0.03	
BA	0.01	0.02	0.02	0.02	
RBC	7.95	0.63	7.24	3.38	
Hb	11.63	0.89	12.00	1.56	
HCT	43.88	2.57	44.70	5.73	
MCV	55.33	2.97	53.35	3.25	
MCH	14.65	1.04	14.28	0.30	
MCHC	26.58	2.54	26.83	1.20	
RDW	17.98	1.58	20.05	3.36	
PLT	704.25	119.98	463.67	292.66	
MPV	5.25	0.13	6.02	0.72	

WBC, total white blood cells; NE, neutrophils; LY, lymphocytes; MO, monocytes; EO, eosinophils; BA, basophils; RBC, total red blood cells; Hb, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red blood cell distribution width; PLT, platelet; MPV, mean platelet volume; *, p<0.05.

Supplementary Table 3 Primer sequences

Name/Gene	Forward	Reversed
846-ex15-ex16-F	GGTTTGAGAAATGTATTGTA	
846-ex17-R		AGGCACACACGGTGGATTA
ANF	GGCCATATTGGAGCAAATCCTGTG	CATGACCTCATCTTCTACCGGCAT
BNP	TGGGAAGTCCTAGCCAGTCTC	CTGTCTCTGGGCCATTTCT
β -MHC	GAGGGAGACCTGAAGCTGAC	CTCATCCAACCTGCTGCTTGT