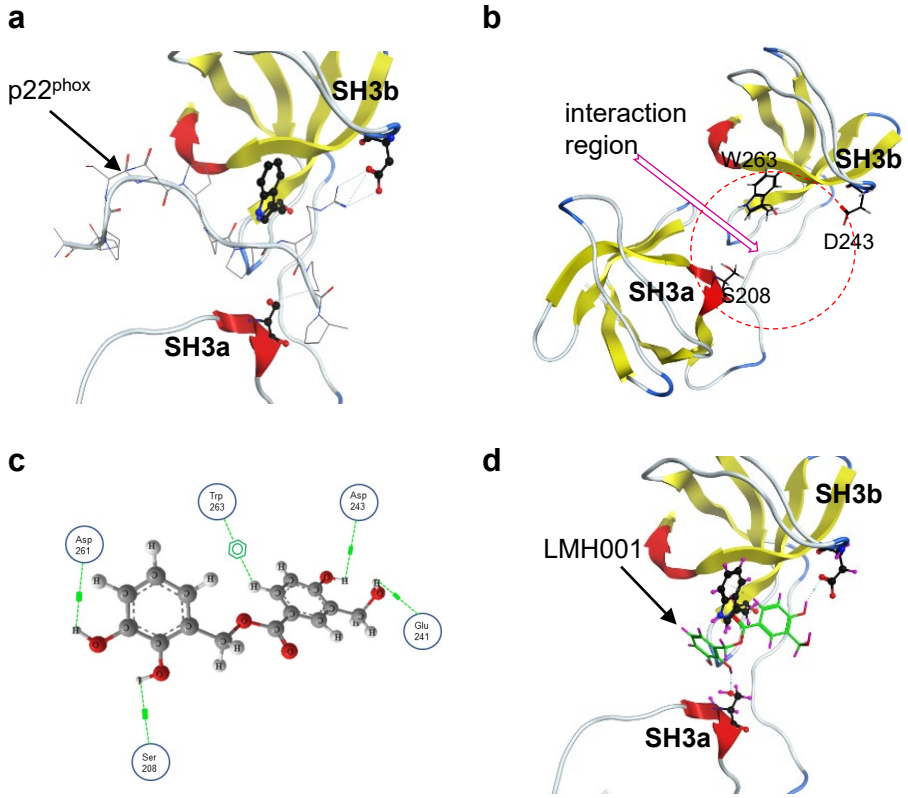
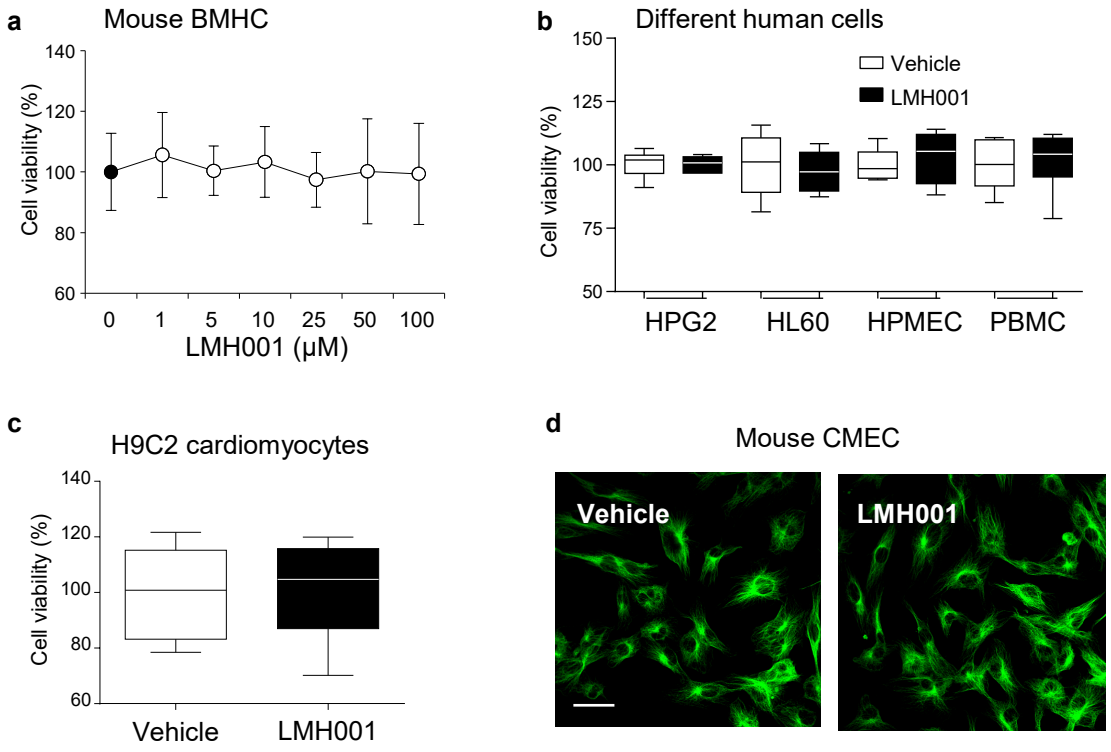
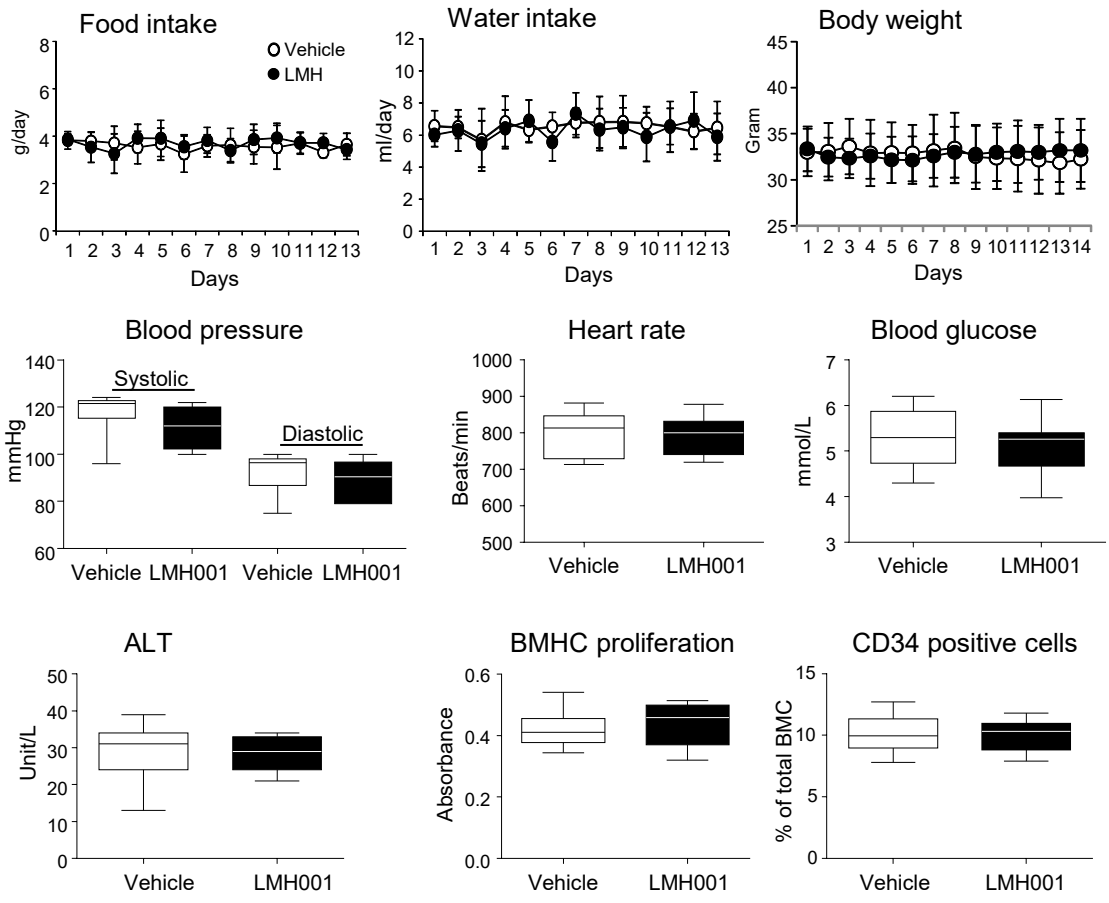


Supplementary Fig. 1: Illustration of LMH001 design and inhibition of p47^{phox}/p22^{phox} interaction.

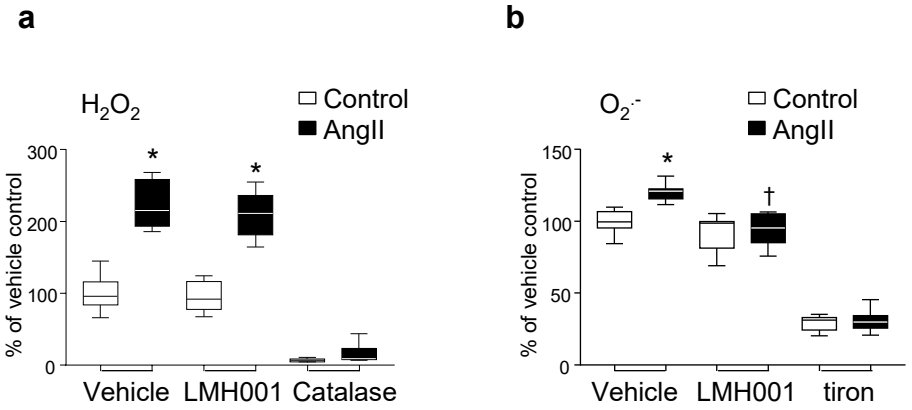
a. Computer model of p22^{phox} C-terminal proline rich region (sequence: QPPSNPPPRPP) integration with phosphorylated p47^{phox} tandem SH3 domain. **b.** Pharmacophore identified in p47^{phox} crystal structure (PDBe 1ov3) for its interaction with p22^{phox} (Trp263, Asp243 and Ser208 depicted in black stick format) and used for inhibitor design. **c.** Illustration of LMH001 structure and model interactions (dashed lines) with Ser208, Asp243, Glu 241 and Asp261 (side-chain hydrogen bonding) and with Trp-263 (π-π stacking). d**.** Model of LMH001 docked in the p47^{phox} SH3 (a and b) binding pocket. Detailed methods of computer modeling and molecular dynamics of p47^{phox} phosphorylation and interaction with p22^{phox} had been published and referenced in the main text.



Supplementary Fig. 2. In vitro tests of LMH001 cytotoxicity. Cell viability was tested by both MTS and MTT assays with similar results. Data displayed here were from MTS assay and were expressed as % of control (without LMH001). **a.** Primary mouse bone marrow hematopoietic cells (BMHC). LMH001 was added in the culture medium at the dose indicated for 48 h. **b.** Human cell viability. LMH001 (20 μM) was added in the culture medium for 48 h. HPG2: human liver cell line; HL60: human peripheral leucocyte cell line; HPMEC: human pulmonary microvascular endothelial cell line, PBMC: freshly isolated human peripheral blood mononuclear cells. **c.** Cardiomyocyte viability. H9C2: rat embryoid cardiac myocytes. **d** Morphology and tubulin staining (green) of mouse primary coronary microvascular endothelial cells (CMEC) after 14 d culture with LMH001 (10 μM, refreshed every other day) by immunofluorescence.



Supplementary Fig. 3. in vivo test of LMH001 safety. LMH001 (5 mg/kg/day. once) was injected intraperitonially for 14 days in mice. The measurements were labelled above the figures. ALT: serum alanine aminotransferase. The bone marrow hemopoietic cells (BMHC) were isolated from these mice and cell proliferation was tested by MTS assay. The % of CD34 (a stem cell marker) positive cells in BMHC was examined by flow cytometry. The results were expressed as % of vehicle injected controls. n=6-8 mice/group.



Supplementary Fig. 4. **LMH001 effects on ROS production by primary mouse aortic vascular smooth cells.** **a.** H_2O_2 production detected by amplex red assay. **b.** $O_2^{\cdot -}$ production detected by lucigenin-chemiluminescence. *P<0.05 for indicated values versus vehicle control (or control) values. †P<0.05 for indicated values versus vehicle AngII (or AngII) values . n=6 independent cell cultures or isolations.

Supplementary Table 1. Comparison of measurements with or without LMH001 treatment

Parameter	Day	Saline control group			AngII 0.8mg/kg/d for 14d		
		Vehicle	LMH	p47KO	Vehicle	LMH	p47KO
Body Weight (g)	d 0	32.8±1.7	32.5±1.4	31.9±1.6	32.1±2.3	32.1±2.1	32.8±1.5
	d 14	33.6±1.9	33.3±1.3	32.4±1.5	28.1±1.4*†	31.2±2.0#	30.8±1.3#
Heart weight (mg)	d 14	149±7.5	150±6.5	150±5.7	174±4.5†	152±5.5#	159±7.2†#
sBP (mm/Hg)	d0	123±3.1	120±5.6	125±5.6	124±7.8	125±8	117±10.8
	d14	128±6.1	124±6.4	125±6.3	188±9.3*†	130±7.5#	147±7.0*#
Glucose (mM)	d14	6.6±1.1	6.5±0.5	6.7±0.7	6.1±0.9	6.2±0.7	6.0±0.9
Mice had aortic aneurysm	d14	0/12	0/12	0/12	8/12†	1/12#	3/12#

Results were presented as mean±SD of 12 mice/per group. Two-way ANOVA with Tukey multiple comparison was used for statistics of body weight, heart weight and BP. Fisher's exact test was used for mice with aneurysm. * $P<0.05$ for indicated d14 values versus d0 value in the same treatment group; † $P<0.05$ for indicated AngII values versus saline vehicle values at d14; # $P<0.05$ for indicated value versus vehicle value under the same dose of AngII treatment.