Supplemental Methods

Western blot analysis and quantification of pulmonary COX2-expression. Snap frozen lung tissue (30 mg) or endothelial cells were lyzed and Western blotting performed employing either anti-mouse COX2 (C-20, 1:200, Santa Cruz, Santa Cruz, CA, USA) and anti-β-Actin (A5441, 1:20.000, Sigma Aldrich) or anti-human COX2 (AF4198, R&D Systems, Minneapolis, MN) or GAPDH (R&D Systems) antibodies. Quantitative analysis of COX2 expression was performed densitometrically. All signals were normalized to the β-Actin signal of the corresponding sample. Tumor necrosis factor (TNF)alpha (R&D Systems) was employed at 10ng/mL.

In vitro pulmonary endothelial cell migration. $1x10^4$ human pulmonary microvascular endothelial cells (HPMECs, PromoCell, Heidelberg, Germany) were grown on 12-well cell-culture dishes until confluency. Employing a pipette tip, endothelial monolayers were wounded horizontally and vertically as described previously (Wagner NM et al., Arterioscler Thromb Vasc Biol, 2013) and incubated in the presence of either simvastatin or pravastatin or vehicle control. Pictures from scratch-crosses were taken immediately and following 8 hours of incubation. Cell-free area was quantified employing ImageProPlus and GraphPadPrism 6.0 software.

In vitro pulmonary endothelial cell capillary formation. $1x10^4$ endothelial cells were seeded in duplicate on growth factor reduced Matrigel™ (BD Bioscience, San Jose, CA) in a 96-well format and incubated in the presence of either statins or vehicles as described previously (8). Experiments were performed in duplicate and averaged per independent experiment. Following 8 hours of incubation, pictures were taken from 4 random fields per well and tube length was determined employing Image Pro Plus software.

Endothelial cell apoptosis and necrosis. Following incubation with either statin or vehicle for 24 hours, pulmonary endothelial cells were detached, washed and resuspended at $1x10^6$ cells per mL. Volumes of 100 µL cell suspension were incubated with reagents of the BD AnnexinV: FITC Apoptosis Detection Kit I according to manufacturer's instructions and analyzed employing a Becton Dickinson flow cytometer (Bedford, MA, USA).

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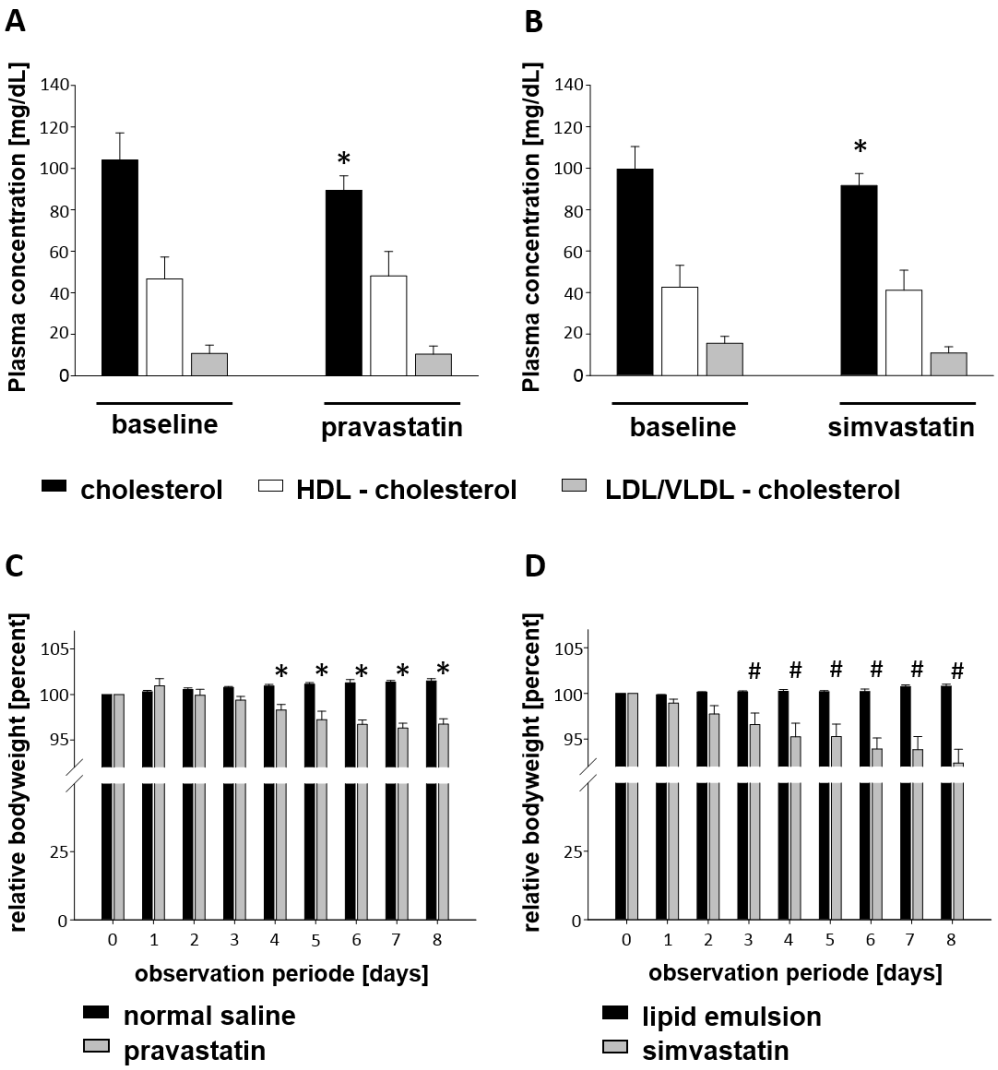
Supplemental Figure 1 Plasma cholesterol concentration and relative bodyweight in response to intravenous statin treatment.

A, B Cholesterol plasma levels in mice following one week of statin treatment. Mean±SD, *P<0.05 vs. baseline; n=7 mice, analysis by Kolmogorov-Smirnov test for normal distribution, paired t-test, mean±SD. **C, D** Bodyweight during one week of statin treatment. *P<0.05 pravastatin vs. saline, #P<0.05 simvastatin vs. lipid emulsion, analysis by Kolmogorov-Smirnov test for normal distribution, repeated measures ANOVA, mean±SD.



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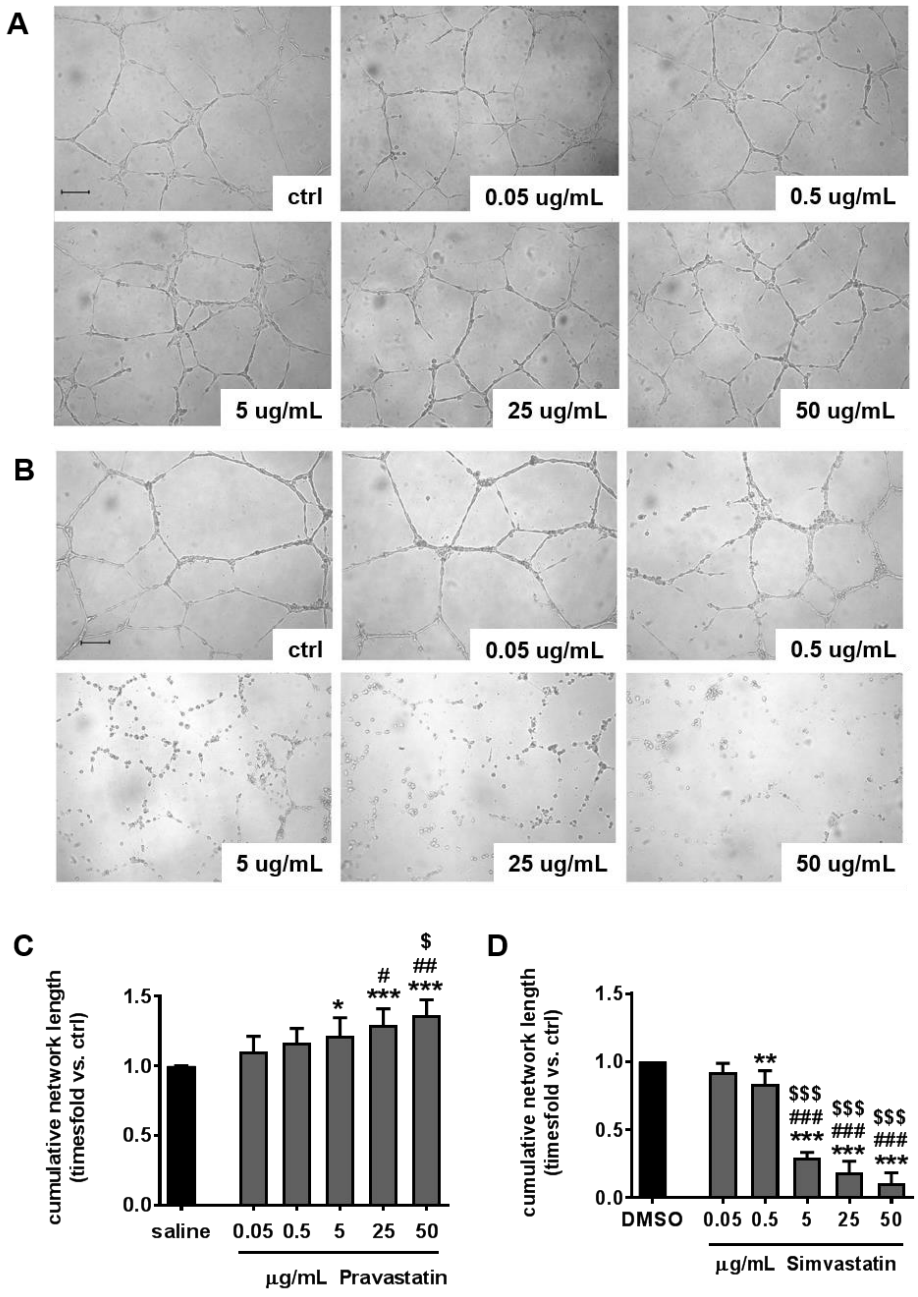
Supplemental Figure 2 Pravastatin augments and simvastatin impairs endothelial cell capillary formation *in vitro*.

A, **C** Capillary tube formation on Matrigel after 8h in the presence of pravastatin. *P<0.05, ***P<0.001 vs. saline (ctrl), #P<0.05, ##P<0.01 vs. 0.05µg/mL and $P<0.05 vs. 0.5µg/mL pravastatin, n=6. **B, D** Capillary tube formation in the presence of simvastatin. **P<0.01, ***P<0.001 vs. DMSO, ###P<0.001 vs. 0.05µg/mL and $$$P<0.001 vs. 0.5µg/mL simvastatin, n=6. Scale bars indicate 200µm. Mean±SD, data analysis by ANOVA/Bonferroni.



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Supplemental Table 1

Physiological and experimental parameters of resuscitation

	CA/CPR 10 min		CA/CPR 10 min	
	normal saline	pravastatin	simvastatin	lipid emulsion
	n = 31	n = 31	n = 30	n = 32
Baseline (preparation) before CA/CPR				
bodyweight [g]	22.65 [±2.2]	21.8 [±2.0]	20.19 [±2.1]	20.76 [±1.7]
heart rate [1/min]	245 [±27]	238 [±31]	219 [±27]	226 [±30]
MAP [mm Hg]	103 [±10]	105 [±12]	85 [±12]	84 [±12]
body temperature [°C]	36.0 [±0.1]	36.0 [±0.1]	35.9 [±0.1]	35.9 [±0.1]
Parameter of CA/CPR				
ROSC time [s]	87 [±25]	70 [±25]	71 [±28]	68 [±19]
ROSC rate [%]	100	100	100	100
Epinephrine [µg]	15 [±5]	15[±5]	12.5[±5]	12.5 [±2.5]
Weaning [min]	138 [±12]	133 [±8]	156 [±21]	145 [±15]
1 hour after CA/CPR				
heart rate [1 / min]	440 [±33]	430 [±28]	378 [±49]	383 [±48]
MAP [mm Hg]	75 [±10]	80 [±12]	65 [±8]	63 [±9]
body temperature [°C]	36.3 [±0.2]	36.4 [±0.1]	36.2 [±0.3]	36.2 [±0.2]
2 hours after CA/CPR				
heart rate [1 / min]	320 [±40]	305 [±37]	290 [±53]	283 [±49]
MAP [mm Hg]	65 [±7.5]	65 [±8]	61 [±6]	58 [±6]
body temperature [°C]	36.0 [±0.1]	36.0 [±0.1]	36.0 [±0.1]	36.0 [±0.2]

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Supplemental Table 2

Results of the NeuroScore

(max. 12 Points)	saline	pravastatin	simvastatin	lipid emulsion
	n=31	n=30	n=30	n=32
day 0	12[12-12]	12[12-12]	12[12-12]	12[12–12]
day 1	11[9.5-12]	11.5[10-12]	10[8.25-10]	10[8–11]
day 2	12[10-12]	12 [10-12]	10[10-11]	10[9.75–12]
day 3	12[11-12]	12[12-12]	11[10-12]	12[9-12]
day 5	12[12-12]	12[12-12]	12[11-12]	12[12–12]

Supplemental Table 3

Results of the RotaRod test

(time[sec])	saline	pravastatin	simvastatin	lipid emulsion
	n=31	n=30	n=30	n=32
day0	851[671-900]	900[682-900]	900[845-900]	900[812-900]
day1	38[5-620]	41[9-385]	22[7-99]	15[7-190]
day2	391[98-598]	303[16-696]	67[13-209]	56[8-363]
day3	401[138-734]	664[231-881]	236[31-384]	489[34-737]
day4	610[227-900]	900[723-900]*****	312[125-589]	351[152-605]
day5	810[578-894]	900[696-900]*****	531[225-781]	657[580-834]

*P<0.05 vs. saline. Median and [25–75] percentiles, Mann-Whitney U-test.

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Supplemental Table 4

Blood gas analysis 8 hours after CA/CPR

	saline	pravastatin	simvastatin	lipid emulsion
	n=31	n=31	n=30	n=32
p_aO_2[mm Hg]	104.1[±3.9]	138.3[±12.1]*****	107.1[±6.7]	111.8[±5.2]
Horowitz-ratio	495.9[±18.6]	658.5[±57.6] *****	509.9[±31.7]	532.3[±24.7]
p_aCO_2[mm Hg]	46.6[±1.4]	43.3[±1.8]	39.6[±2.2]	42.1[±1.1]
pH	7.30[±0.02]	7.30[±0.06]	7.32[±0.04]	7.33[±0.04]
HCO_3^-[mmol/L]	21.9[±0.9]	20.6[±2.8]	22.5[±1.4]	21.7[±1.5]
Base excess[mmo/L]	-3.8[±1.3]	-6.3[±4.1]	-2.4[±1.9]	-4.3[±2.3]
K^+[mmol/L]	3.8[±0.1]	4.3[±0.2]	4.1[±0.1]	4.0[±0.2]

*P<0.05 vs. saline. Mean ± SD, data analysis by ANOVA/Bonferroni

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