Supplementary Fig. S1 Plasma apolipoprotein M (apoM) and sphingosine 1-phosphate (S1P) levels in the mice used in this study. (A, E) Ten-week-old wild-type mice (WT) or apoM knockout (KO) mice were analysed for the plasma apoM (A) and S1P levels (E) (n = 5). (B, C, D, F) Ten-week-old C57BL/6 mice were injected with adenovirus coding apoM (apoM) or GFP (GFP) (D) or siRNA against apoM (siapoM) or control siRNA (siCtl) (B, C, F). On the fifth day after the injection, the plasma apoM (B, C) and S1P levels (D, F) were examined (n = 5).

Supplementary Fig. S2 Modulation of basic parameters related to sepsis in response to the administration of lipopolysaccharide (LPS). Modulation of the survival rate (A), white blood cell (WBC) (B), platelet counts (C), plasma alanine aminotransferase (ALT) levels (D) and plasma creatinine levels (E) in surviving mice as shown in Fig. 1. *p < 0.01 versus vehicle, **p < 0.01 versus vehicle and p < 0.05 versus LPS10 or LPS25, †p < 0.01 versus LPS25 and p < 0.05 versus vehicle, ‡p < 0.01 versus other groups.
Supplementary Fig. S4 The effect of PNGase on the band of murine hepatic apolipoprotein M (apoM). Liver samples were prepared from the mice treated with lipopolysaccharide (LPS) at 25 mg/kg body weight (BW) and incubated with or without PNGase. Then they were subjected to a western blot analysis using anti-mouse apoM antibody.

Supplementary Fig. S5 Modulation of plasma alanine aminotransferase (ALT) and creatinine levels by the overexpression of apolipoprotein M (apoM). Ten-week-old C57BL/6 mice were injected with Ad-apoM or Ad-green fluorescent protein (GFP). On the fifth day after administration, the plasma ALT levels (A) and creatinine levels (B) were investigated (n = 5/group).

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Supplementary Fig. S6 Effects of the overexpression of apolipoprotein M (apoM) on the survival rate and organ injuries in mice treated with lipopolysaccharide (LPS). Ten-week-old C57BL/6 mice were injected with adenovirus coding Ad-apoM or Ad-green fluorescent protein (GFP). On the fifth day after injection, the mice were treated with LPS at a dose of 10 mg/kg body weight (BW) intraperitoneally (n = 8/group). After 24 hours, analyses of the surviving mice were performed (n = 7 for GFP, n = 8 for apoM). (A) Plasma apoM and albumin levels in the surviving mice. (B) Kaplan–Meier curve. (C) Plasma alanine aminotransferase (ALT) levels. (D) Plasma creatinine levels.

Supplementary Fig. S7 Modulation of inflammatory cytokines and plasminogen activator inhibitor-1 (PAI-1) by the administration of lipopolysaccharide (LPS). Modulation of the plasma interleukin (IL)-6 levels (A), plasma tumor necrosis factor (TNF)-α levels (B) and plasma PAI-1 levels (C) was measured in the surviving mice as shown in Fig. 1. * p < 0.01 versus other groups.
Supplementary Fig. S8 Effects of the overexpression, knockout or knockdown of apolipoprotein M (apoM) on plasma inflammatory cytokines in mice treated with lipopolysaccharide (LPS). The plasma tumor necrosis factor (TNF)-α levels (A) and interleukin (IL)-6 levels (B) were measured in plasma samples from the surviving mice as shown in ►Figs. 2–4, and ►Supplementary Fig. S6 [online only].
Supplementary Fig. S9: Effects of the overexpression of apolipoprotein M (apoM) on parameters related to pro-thrombosis. Platelet counts (A–C) and plasma plasminogen activator inhibitor-1 (PAI-1) levels (D, E) were investigated in the surviving mice. (A) Mice injected with Ad-apoM or Ad-green fluorescent protein (GFP) and treated with lipopolysaccharide (LPS) at a dose of 25 mg/kg body weight (BW) (n = 4 for GFP, n = 8 for apoM). (B, E) Mice injected with Ad-apoM or Ad-GFP and treated with LPS at a dose of 10 mg/kg BW intraperitoneally (n = 7 for GFP, n = 8 for apoM). (C) Mice injected with Ad-apoM or Ad-GFP with or without VPC23019 and treated with LPS at a dose of 25 mg/kg BW (C: n = 4 for GFP, n = 3 for GFP + VPC23019 [VPC], n = 8 for apoM, n = 4 for apoM + VPC). (D) Mice injected with Ad-apoM or Ad-GFP and treated with LPS at a dose of 50 mg/kg BW (n = 4 for GFP, n = 7 for apoM).
Supplementary Fig. S10 Modulation of the cleavage of caspase 3 by the administration of lipopolysaccharide (LPS). The cleavage of caspase 3 (cleaved/non-cleaved caspase 3) in the liver (A, B) and kidney (C, D) was investigated using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice, as shown in ► Fig. 1 (n = 6 for vehicle, n = 6 for LPS10, n = 7 for LPS25). ‘p < 0.01 versus other groups, **p < 0.01 versus vehicle and p < 0.05 versus LPS10 or LPS25.
Supplementary Fig. S11 Modulation of the phosphorylation of Akt by the overexpression of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). The phosphorylation of Akt in the liver (A–D), kidney (E–H) and heart (I–L) was investigated using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with ad-apoM or ad-green fluorescent protein (GFP) and treated with LPS at a dose of 50 mg/kg body weight (BW) (A, B, E, F, I, J; n = 4 for GFP, n = 7 for apoM) or in the surviving mice injected with ad-apoM or ad-GFP and treated with LPS at a dose of 10 mg/kg BW (C, D, G, H, K, L; n = 7 for GFP, n = 8 for apoM).
Supplementary Fig. S12 Modulation of the phosphorylation of Akt by the knockout of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). The phosphorylation of Akt in the liver (A, B), kidney (C, D) and heart (E, F) was investigated using a western blot, and the intensities of the bands were quantified using Image J in the surviving wild-type mice (WT) or apoM knockout (KO) mice treated with LPS at a dose of 10 mg/kg body weight (BW) (n = 6 for WT, n = 5 for KO).
Supplementary Fig. S13 Modulation of the phosphorylation of Akt by the knockdown of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). The phosphorylation of Akt in the liver (A, B), kidney (C, D) and heart (E, F) was investigated using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with siapoM or siCtl and treated with LPS at a dose of 25 mg/kg body weight (BW) (n = 11 for siCtl, n = 6 for siapoM).
Supplementary Fig. S14 Effects of LY294002 on the phosphorylation of Akt in mice treated with lipopolysaccharide (LPS). The phosphorylation of Akt in the liver (A, B), kidney (C, D) and heart (E, F) was investigated using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with ad-apoM or ad-green fluorescent protein (GFP) with or without LY294002 (LY) and treated with LPS at a dose of 25 mg/kg body weight (BW) \( (n = 5 \text{ for GFP, } n = 5 \text{ for GFP } + \text{LY, } n = 8 \text{ for apoM, } n = 6 \text{ for apoM } + \text{LY}) \). *\( p < 0.05 \) versus GFP and **\( p < 0.01 \) versus apoM, †\( p < 0.05 \) versus GFP and ‡\( p < 0.01 \) versus GFP. **\( p < 0.01 \) versus GFP + LY and apoM + LY.
Supplementary Fig. S15 Modulation of apoptosis markers by the overexpression of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). Apoptotic markers (Bcl-XL/BAX, Bcl-2/BAX and cleavage of caspase 3 [cleaved/non-cleaved caspase 3]) in the liver (A–C), kidney (D–F) and heart (G, H) were examined using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with ad-apoM or ad-green fluorescent protein (GFP) and treated with LPS at a dose of 25 mg/kg body weight (BW) (n = 4 for GFP, n = 8 for apoM). Black arrows indicate the bands corresponding to the proteins of interest, which were determined by the expected molecular weight.
Supplementary Fig. S16 Modulation of apoptosis markers by the overexpression of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). Apoptotic markers (Bcl-XL/BAX, Bcl-2/BAX and cleavage of caspase 3 [cleaved/non-cleaved caspase 3]) in the liver (A–C), kidney (D–F) and heart (G, H) were examined using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with ad-apoM or ad-green fluorescent protein (GFP) and treated intraperitoneally with LPS at a dose of 10 mg/kg body weight (BW) \((n = 7\) for GFP, \(n = 8\) for apoM). Black arrows indicate the bands corresponding to the proteins of interest, which were determined by the expected molecular weight.

Supplementary Fig. S17 Effects of VPC23019 on the modulation of apoptosis markers by the overexpression of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). Apoptotic markers (Bcl-XL/BAX, Bcl-2/BAX) in the heart were examined using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with Ad-apoM or Ad-green fluorescent protein (GFP) with or without VPC23019 and treated with LPS at a dose of 25 mg/kg body weight (BW) \((n = 4\) for GFP, \(n = 3\) for GFP + VPC23019 [VPC], \(n = 8\) for apoM, \(n = 4\) for apoM + VPC). \(^p < 0.05\) versus GFP and GFP + VPC.
Supplementary Fig. S18 Effects of LY294002 on the apoptosis markers modulated by the overexpression of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). Apoptotic markers (Bcl-XL/BAX, Bcl-2/BAX and cleavage of caspase 3) in the liver (A–D) and kidney (E–H) were examined using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with ad-apoM or ad-green fluorescent protein (GFP) with or without LY294002 (LY) and treated with LPS at a dose of 25 mg/kg body weight (BW) (n = 5 for GFP, n = 5 for GFP + LY, n = 8 for apoM, n = 6 for apoM + LY). Black arrows indicate the bands corresponding to the proteins of interest, which were determined by the expected molecular weight. *p < 0.05 versus other groups, **p < 0.05 versus GFP and GFP + LY, †p < 0.05 versus GFP, ‡p < 0.05 versus GFP + LY and apoM + LY.
Supplementary Fig. S19 Effects of LY294002 on the apoptosis markers modulated by the overexpression of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). Apoptotic markers (Bcl-XL/BAX and Bcl-2/BAX) in the heart were examined using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with ad-apoM or ad-green fluorescent protein (GFP) with or without LY294002 (LY) and treated with LPS at a dose of 25 mg/kg body weight (BW) ($n = 5$ for GFP, $n = 5$ for GFP + LY, $n = 8$ for apoM, $n = 6$ for apoM + LY). *p < 0.05 versus GFP and GFP + LY.

Supplementary Fig. S20 Modulation of apoptosis markers by the knockout of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). Apoptotic markers (Bcl-XL/BAX, Bcl-2/BAX and cleavage of caspase 3 [cleaved/non-cleaved caspase 3]) in the liver (A–C), kidney (D–F) and heart (G, H) were examined using a western blot, and the intensities of the bands were quantified using Image J in the surviving wild-type mice (WT) or apoM knockout (KO) mice treated with LPS at a dose of 10 mg/kg body weight (BW) ($n = 6$ for WT, $n = 5$ for KO).
Supplementary Fig. S21 Modulation of apoptosis markers by the knockdown of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). Apoptotic markers (Bcl-XL/BAX, Bcl-2/BAX and cleavage of caspase 3 [cleaved/non-cleaved caspase 3]) in the liver (A–C), kidney (D–F) and heart (G, H) were examined using a western blot, and the intensities of the bands were quantified using Image J in the surviving mice injected with siapoM or siCtl and treated with LPS at a dose of 25 mg/kg body weight (BW) (n = 11 for siCtl, n = 6 for siapoM).

Supplementary Fig. S22 Modulation of platelet counts by the administration of adenoviruses. Ten-week-old male mice were injected with phosphate-buffered saline (PBS), Ad-green fluorescent protein (GFP) or Ad-apolipoprotein M (apoM). On the fifth day after administration, the platelet counts were measured (n = 5–6/group). *p < 0.01 versus PBS.

Supplementary Fig. S23 Effects of LY294002 on the plasma plasminogen activator inhibitor-1 (PAI-1) levels modulated by the overexpression of apolipoprotein M (apoM) in mice treated with lipopolysaccharide (LPS). The plasma PAI-1 levels were examined using an enzyme-linked immunosorbent assay (ELISA) in the surviving mice injected with ad-apoM or ad-green fluorescent protein (GFP) with or without LY294002 (LY) and treated with LPS at a dose of 25 mg/kg body weight (BW) (n = 5 for GFP, n = 5 for GFP + LY, n = 8 for apoM, n = 6 for apoM + LY). *p < 0.05 versus GFP and **p < 0.01 versus GFP + LY.