

SUPPLEMENTARY MATERIALS

Supplementary S1:

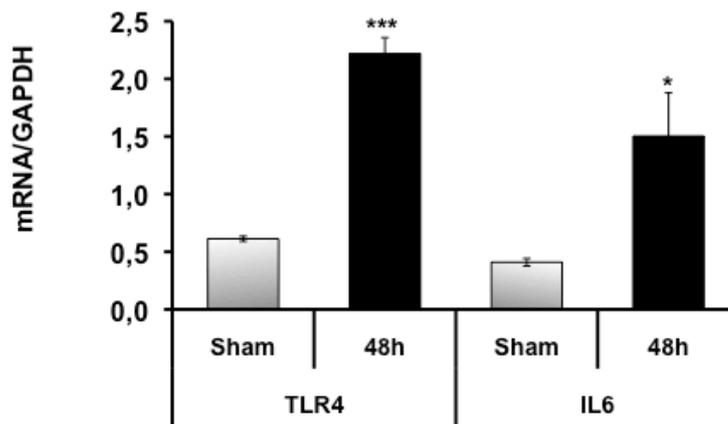


Figure S1: TLR4 and IL6 mRNA expressions in the kidney

The kidneys of Sham and 48-hour-infected WT mice were harvested, and the mRNA levels of both TLR4 and IL-6 were quantified by RT-qPCR. Data were normalized by GAPDH-mRNA levels. The results are the mean \pm s.e.m. of at least six individual mice in each group. * $P < 0.05$, *** $P < 0.0001$.

Supplementary S2:

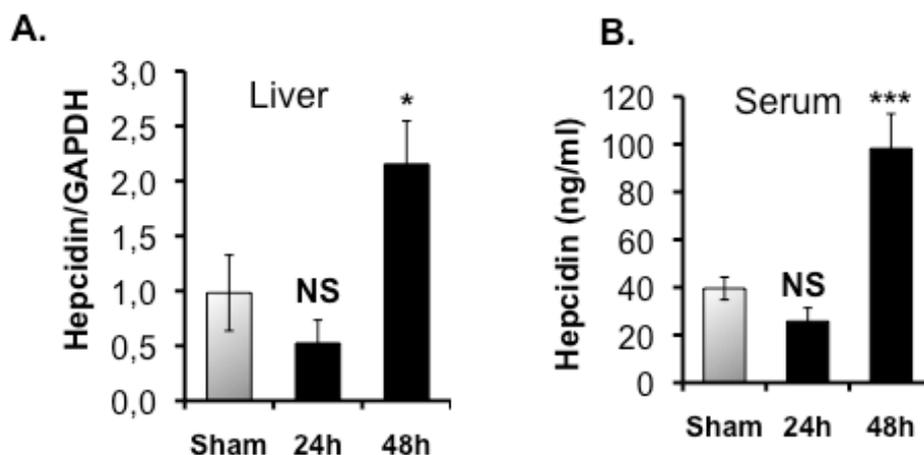


Figure S2:

CBA/J WT mice were infected with 10^9 CFUs of CFT073, and bacterial counts were performed on bladder and kidneys at 24 and 48 h postinfection. (A) Hepcidin mRNA quantification in WT liver at 24 and 48 hours postinfection. (B) WT serum hepcidin measured by LC-MS/MS at 24 and 48 hours post-infection. (Sham) means uninfected mice. The results are the mean \pm s.e.m. of at least six individual mice in each group. * $P < 0.05$, *** $P < 0.0001$. NS indicates non-significant.

Supplementary S3:

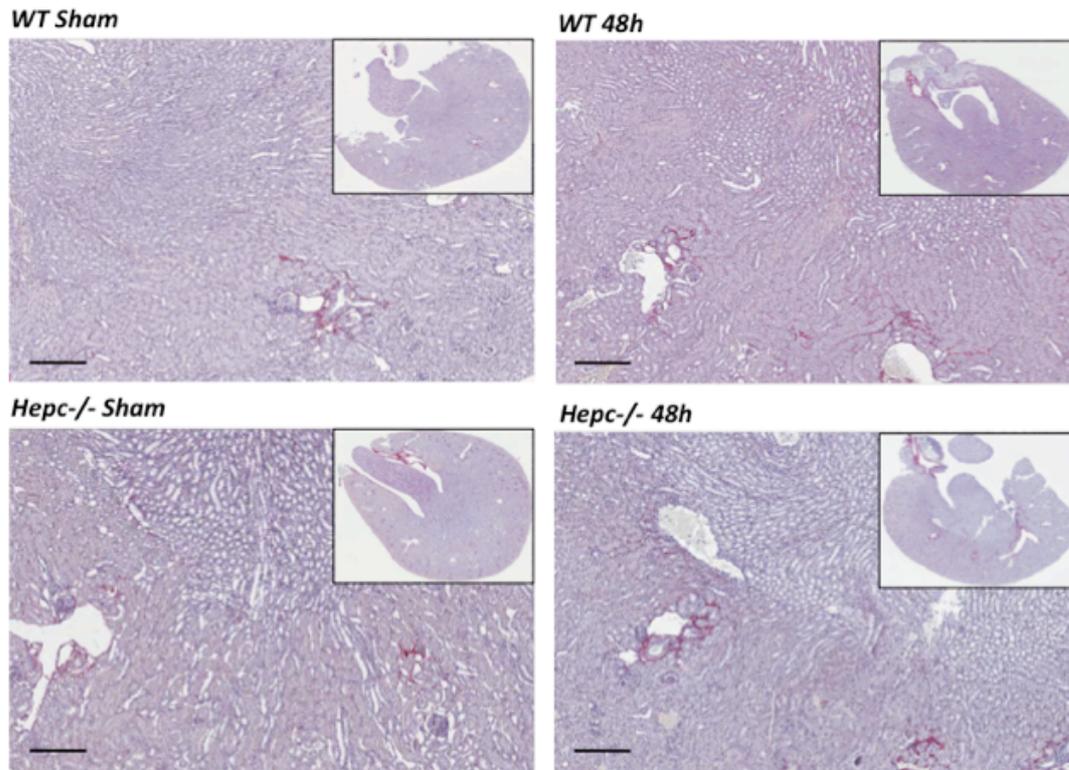


Figure S3:

Histologic examination

The kidneys were fixed in 4% formaldehyde, embedded in paraffin and sections of 4- μ m were then stained with picro-sirius red (PSR). Images were acquired using a ScanScope digital scanner (Aperio, TRIBVN, France). Morphologic assessments were conducted by two independent renal pathologists who were uninformed about the treatments and mice phenotypes.

Supplementary S4:

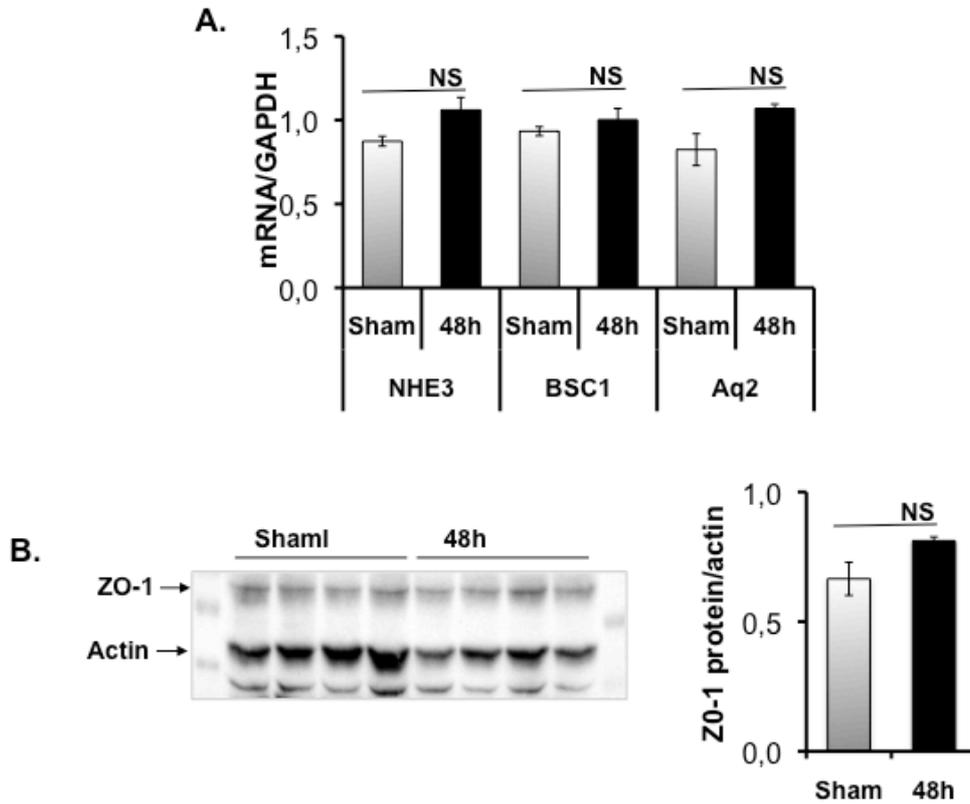


Figure S4: Renal cell damage evaluation

The kidneys of Sham and 48-hour-infected WT mice were harvested for the following studies. (A) The mRNA levels of Na⁺/H⁺ exchanger 3 (NHE3), bumetanide-sensitive Na⁺/K⁺/2Cl⁻ cotransporter 1 (BSC1) and the water channel aquaporin-2 (AQ2) were quantified by RT-qPCR. Data were normalized by GAPDH-mRNA levels. (B) Protein levels of tight junction ZO-1 were quantified by Western blot. The left panel shows a representative western blot, and the right panel shows the quantification. Data were normalized by β -actin protein level. The results are the mean \pm s.e.m. of at least six individual mice in each group. NS indicates non-significant

Supplementary S5:

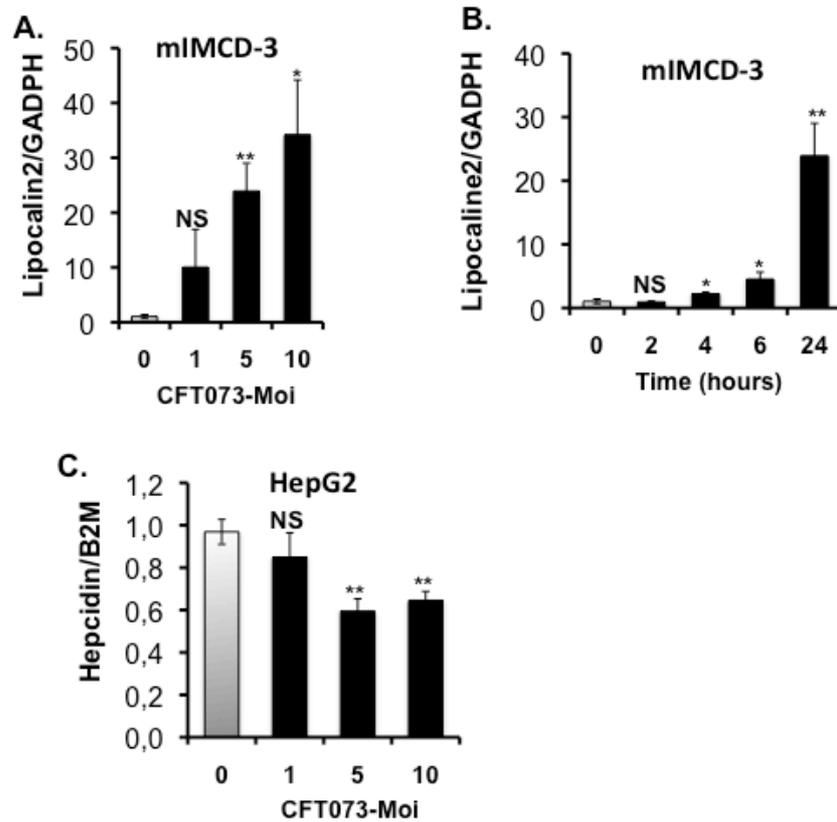


Figure S5: Effect of CFT073 on lipocalin-2 and hepcidin expressions in cultured renal mIMCD-3 and hepatic HepG2 cells respectively. mIMCD-3 and HepG2 cell lines were infected with PFA-fixed CFT073, and the mRNA level of lipocalin-2 was explored at different MOIs (MOI, multiplicity of infection, number of bacteria per number of monolayer cells) and different incubation times. (A) shows the effect of different MOIs on lipocalin-2 mRNA abundance in mIMCD-3 cells. (B) shows the time-course effect using an MOI of 5:1. (C) Hepcidin-mRNA repression in HepG2 cells in response to different MOIs of CFT073. All mRNA quantifications were determined by RT-qPCR. Data were normalized by GAPDH-mRNA levels. The results are the mean \pm s.e.m. of at least three independent cultures. *P < 0.05, **P < 0.03. NS indicates non-significant.

Table S1

	WT	Hepc ^{-/-}	Genotype (Sham)
(ng/ml)	Sham	Sham	<i>P</i> value
IL-6	15.9 ± 0.7	7.5 ± 4.4	NS
IFN- γ	51 ± 3.1	65.5 ± 5.6	NS
TNF- α	2.3 ± 0.3	5.3 ± 1.1	0.05
IL-1 α	272 ± 12.3	417 ± 19.3	0.002
CXCL2	12.6 ± 1.6	27.4 ± 4.2	NS
CCL5	58.1 ± 9.6	141.3 ± 18.8	NS

Table S1

Expression profile of inflammatory cytokines in WT and Hepc^{-/-} kidneys prior CFT073 infection (Sham). The results are the mean ± s.e.m. NS indicates non-significant.