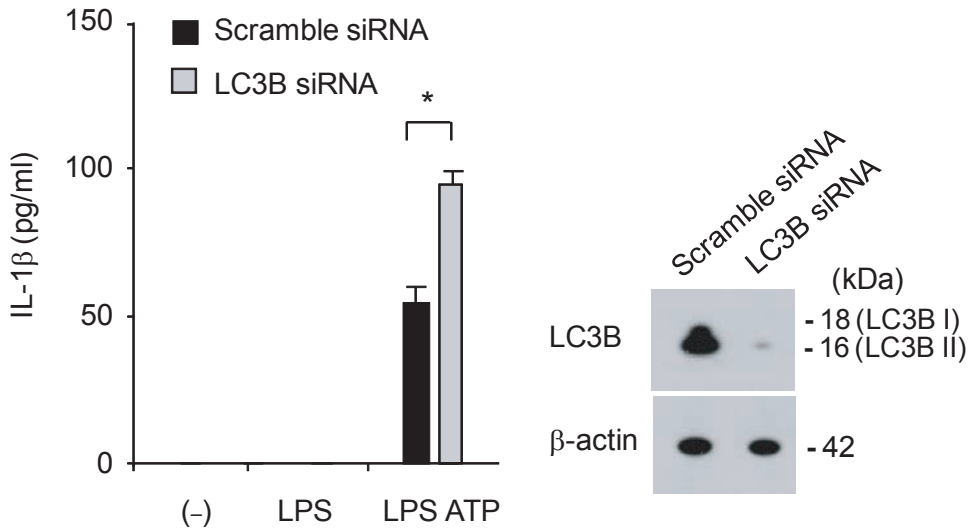

fig. S1 Gene silencing of LC3B by siRNA enhances IL-1β secretion. Peritoneal macrophages treated with siRNA against LC3B were incubated with LPS and then stimulated with ATP. Supernatants were analyzed by ELISA for IL-1β secretion. Protein levels of LC3B were analyzed by SDS-PAGE. Data are representative of three determinations per treatment group (mean and s.d.). Figure is representative of three independent experiments. Statistical significance was determined by the Student's *t*-test. $*P < 0.05$.

Nature Immunology: doi:10.1038/ni.1980

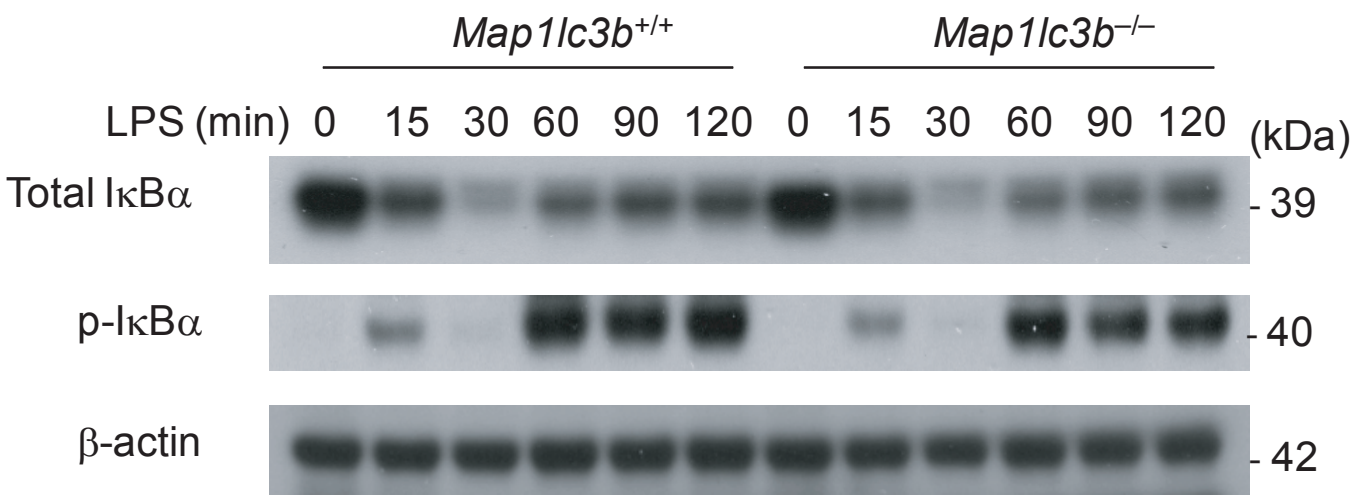

fig. S2 Absence of LC3B does not affect NF-κB signaling by LPS stimulation. BMDM from *Map1lc3b*$^{+/+}$ mice or *Map1lc3b*$^{-/-}$ mice were treated with LPS (10 ng/ml) and cells were harvested at indicated time points. Cell lysates were analyzed by immunoblotting for total IκB-α and phosphorylated IκB-α. Data are representative of three experiments.

Nature Immunology: doi:10.1038/ni.1980

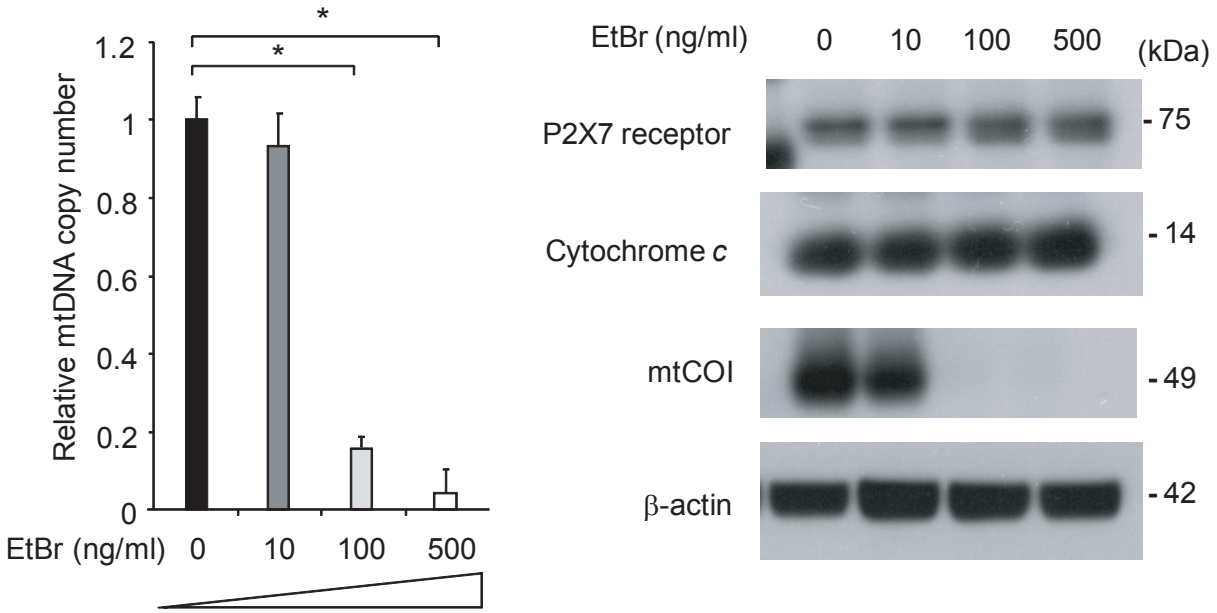

fig. S3 EtBr treatment depleted mtDNA in macrophages J774A.1 macrophages were exposed to EtBr at indicated doses. Total mtDNA copy number was measured by quantitative PCR. Cell lysates were analyzed by immunoblotting for mtCOI and cytochrome *c*. Statistical significance was determined by the Student's *t*-test. $*P < 0.05$. Data are representative of three experiments (mean and s.d.).

Nature Immunology: doi:10.1038/ni.1980

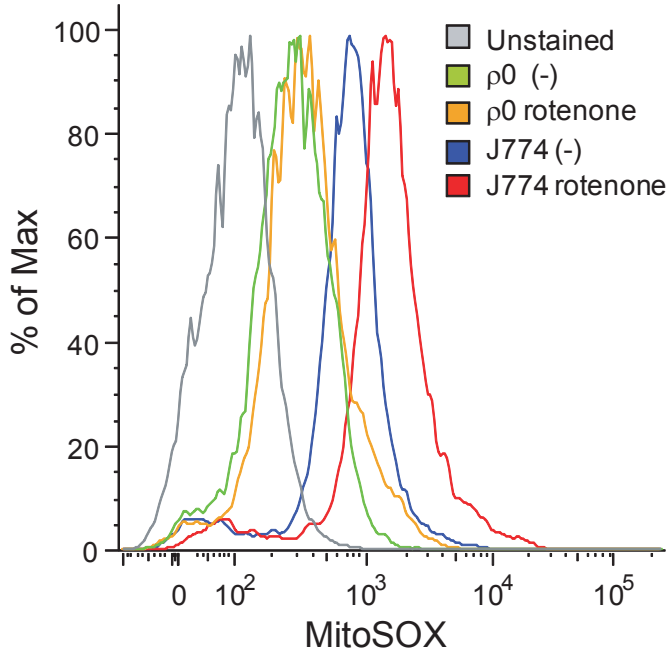

fig. S4 Mitochondrial ROS generation is impaired in ρ^0 macrophages. J774A.1 control or ρ^0 macrophages incubated with rotenone (5 mM) for 30 min were labeled with MitoSOX for 15 min. Representative flow cytometry plots are represented. Data are representative of three experiments.

Nature Immunology: doi:10.1038/ni.1980

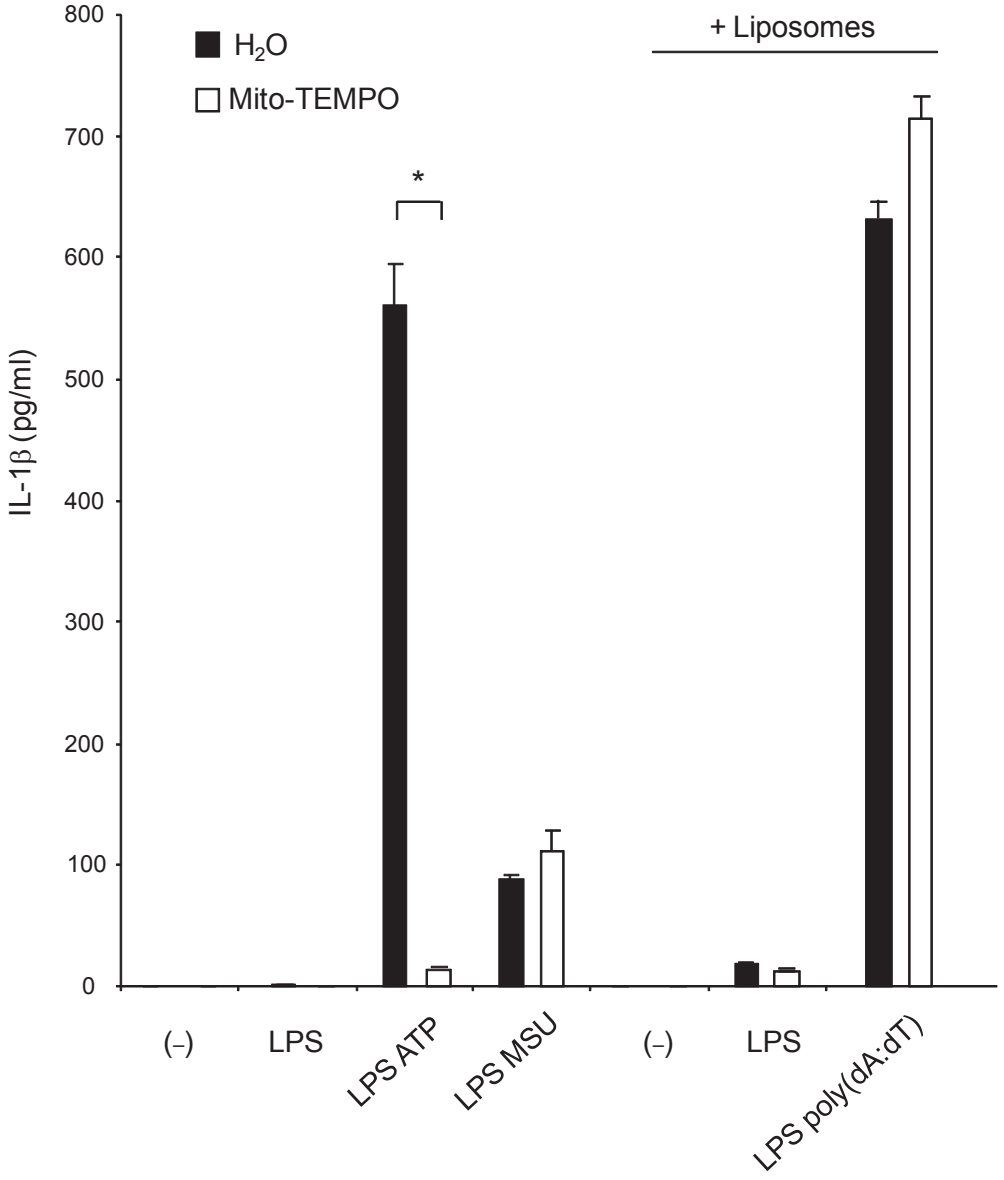

fig. S5 Differential effect of Mito-TEMPO on IL-1β secretion in macrophages. BMDM pre-incubated with Mito-TEMO (500 μM) were incubated with LPS for 4 h, and then stimulated with ATP, MSU or transfected with poly(dA:dT). IL-1β secretion into supernatants was analyzed by ELISA. Statistical significance was determined by the Student's *t*-test. **P* < 0.05. Data are representative of three experiments (mean and s.d.).

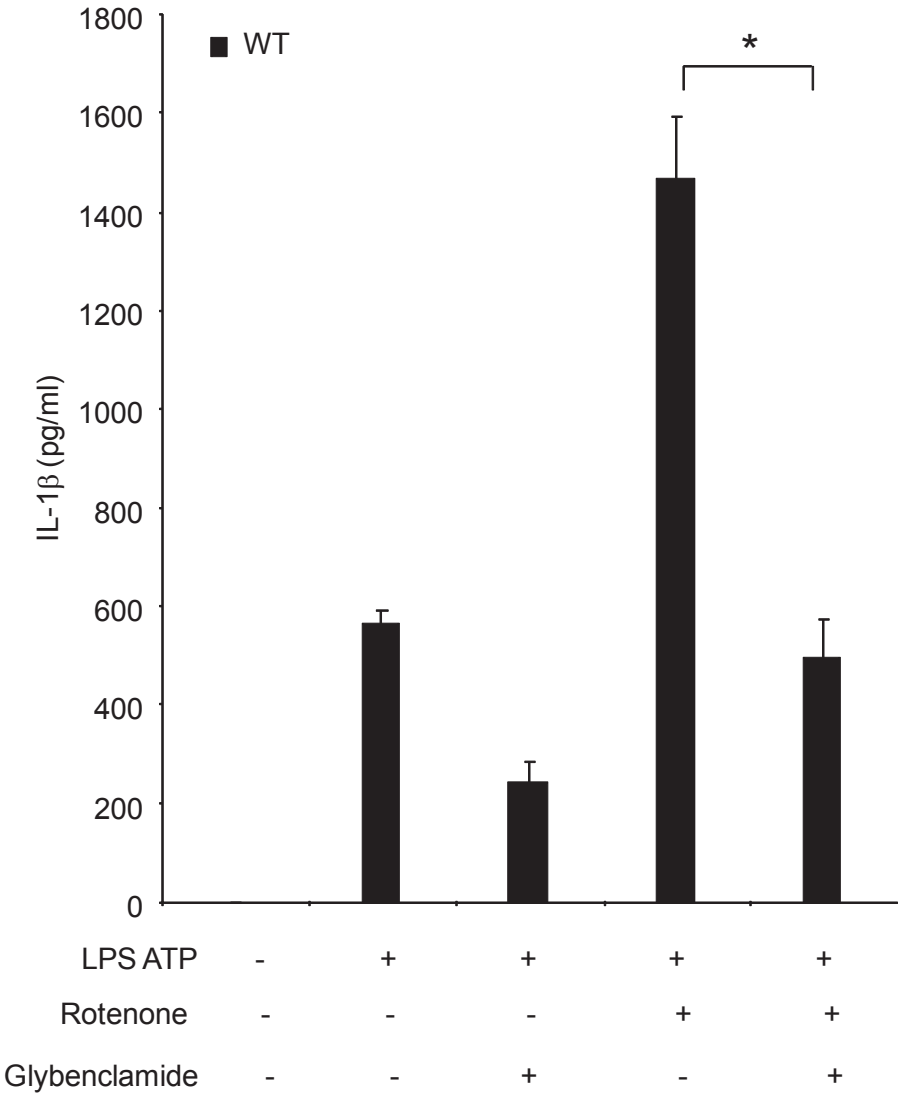

fig. S6 Glybenclamide treatment abrogated the effect of rotenone on IL-1b secretion

LPS-primed macrophages were incubated with rotenone in the presence or absence of glybenclamide (100 μM), followed by ATP stimulation for 1 h. IL-1β secretion into supernatants was analyzed by ELISA. Statistical significance was determined by the Student's *t*-test. *$P < 0.05$. Data are representative of three experiments (mean and s.d.).

Nature Immunology: doi:10.1038/ni.1980

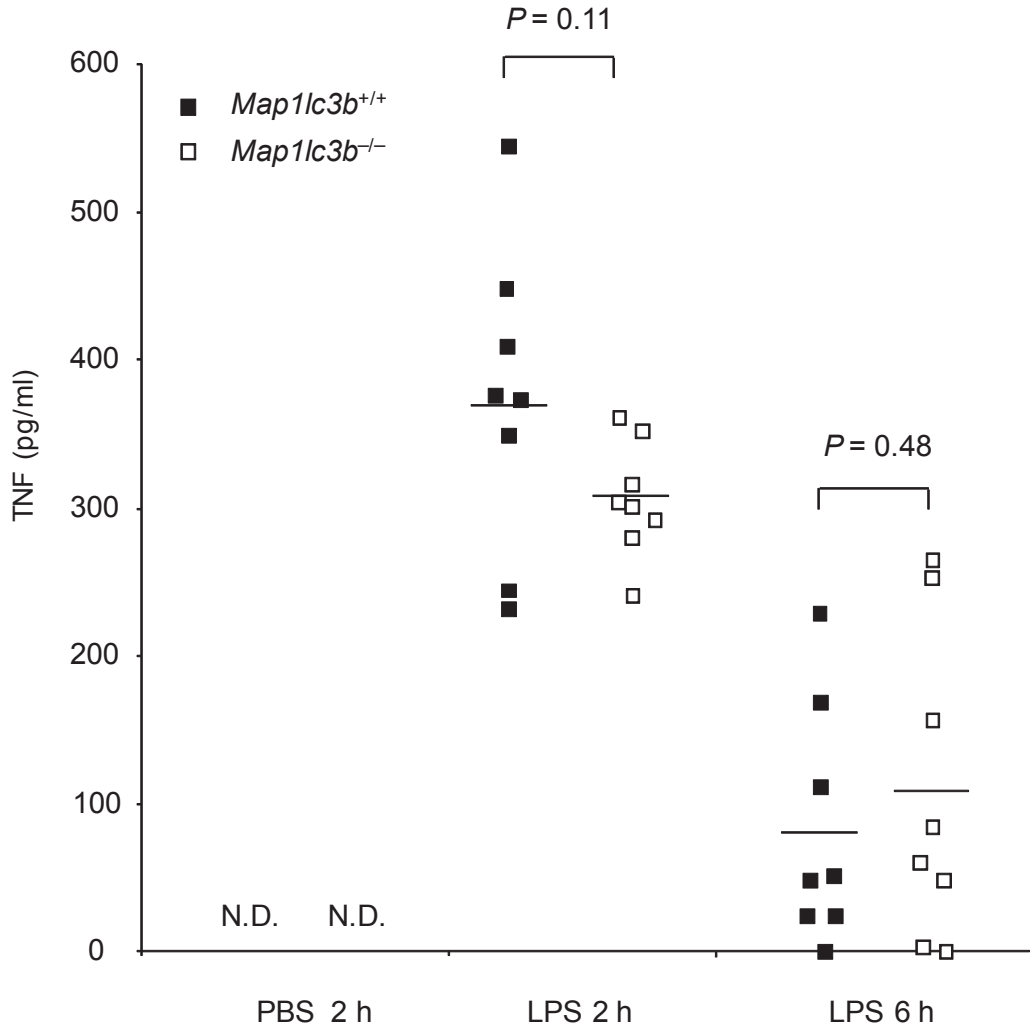

fig. S7 LC3B deficiency did not affect TNF production in serum after LPS administration. Male *Map1lc3b*$^{+/+}$ mice and *Map1lc3b*$^{-/-}$ mice (8-10 weeks of age) were intraperitoneally injected with 12 mg/kg LPS. Serum TNF at 2 and 6 h after injection was analyzed by ELISA. Data are representative of two experiments.

Nature Immunology: doi:10.1038/ni.1980

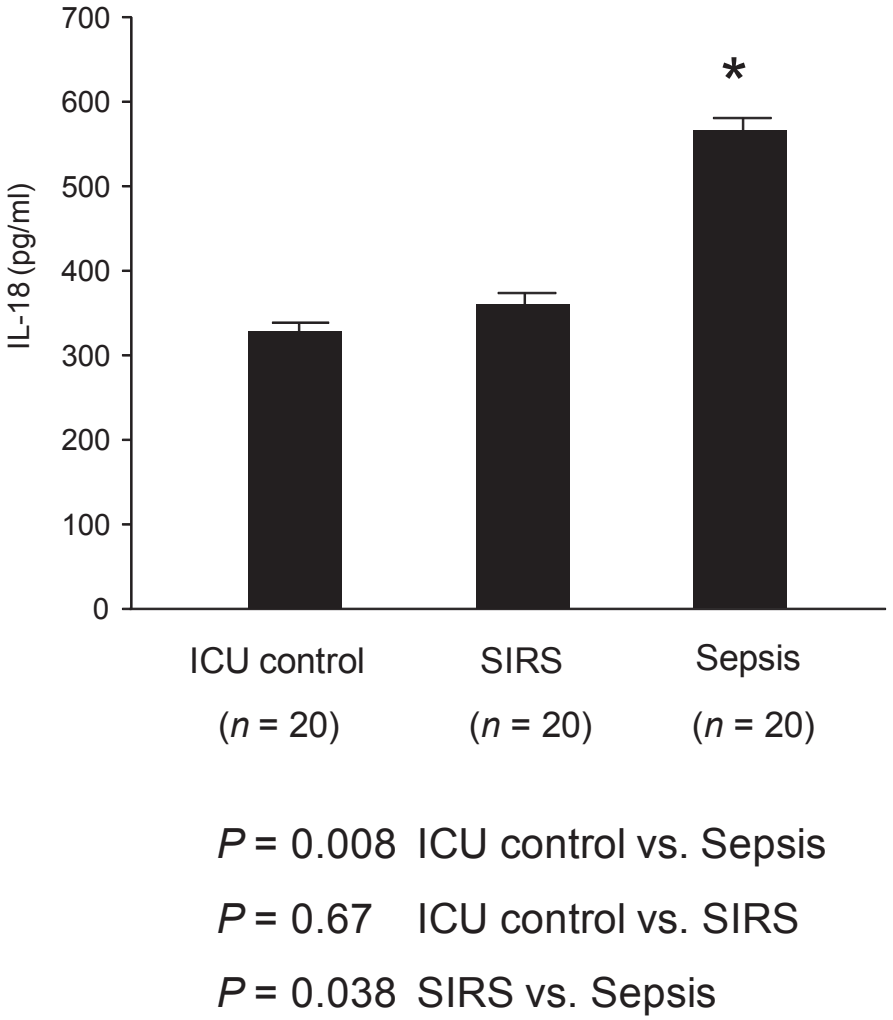

fig. S8 Increased level of IL-18 in plasma from patients with sepsis. Blood samples were collected from patients with sepsis within 48 hours following medical intensive care units (MICU) hospitalization. IL-18 concentration in plasma was analyzed by ELISA. Statistical analysis was performed by unpaired two-tailed Student's *t*-test.

The Research Registry and Human Sample Repository for the Study of the Biology of Critical Illness (abbreviated name: Registry of Critical Ilnness (RoCI)) collects demographic, clinical information and blood specimens from patients with critical illness in the medical intensive care unit of the Brigham and Women`s Hospital (BWH). RoCI is approved by Partners Human Research Committee and operates under 2008-P-000495 protocol.

Group	Age	Gender	Race	APACHE II	LOS
Control	60.8±17.7	11/9	4/0/15/1	19.8±6.6	6±4.5
SIRS	61.2±12.5	13/7	6/0/13/1	21.5±10.2	14±9.8
Sepsis	56.7±17.5	12/8	4/1/14/1	24.3±6.6	11±6.7

Age= mean Age (years)±SD,
Gender = Male/Female,
Race = Black, non-Hispanic/Asian-Pacific Islander/White non-Hispanic/Hispanic,
APACHE II = Acute Physiology and Chronic Health Evaluation II score,
LOS = length of hospital stay (days)±SD.
SIRS = Systemic Inflammatory Response Syndrome.
Control; *n* = 20 patients. SIRS; *n* = 20 patients. Sepsis; *n* = 20 patients

Supplementary Table 1. Demographics and clinical details of patients in the MICU.

Blood plasma samples were randomly selected from the Brigham and Women's Hospital Medical Intensive Care Unit (MICU), Registry of Critical Illness (RoCI), IRB Protocol number 2008-P-00495. In RoCI, controls are patients without signs of infection; Systemic inflammatory Response Syndrome (SIRS) patients meet at least two criteria for SIRS defined by the American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference; Sepsis patients have SIRS due to a culture positive infection or significant infection by observation.