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**Supplemental information**

**Role of extracellular microRNA-146a-5p  
in host innate immunity and bacterial sepsis**

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**Table S1. Demographic and Laboratory Data of Septic Patients and Healthy Volunteers, Related to Figure 1.**

	<b>Control (n = 8)</b>	<b>Sepsis (n = 10)</b>
Age, years	54 [46-65]	55 [49 – 66]
Sex, male	6 (75%)	7 (70%)
Ethnicity		
White	4 (50%)	5 (50%)
Asian	0 (0%)	2 (20%)
Black	4 (50%)	3 (30%)
Hematology Labs		
INR ( $\leq 1.1$ )	N/A	1.35 [1.1 - 2.1]
PTT (25-38 sec)	N/A	28 [25 - 40]
Platelets ( $153\text{-}367 \times 10^3/\mu\text{L}$ )	N/A	164 [94 – 206]
Plasma IL-6 (pg/ml)	N.D.	1955.6 $\pm$ 2803.1
Plasma TNF $\alpha$ (pg/ml)	N.D.	11.39 $\pm$ 16.4
Plasma RNA (ng/ml)	40.4 $\pm$ 6.1	109.2 $\pm$ 60.7*

Patient demographics, coagulation parameters, and plasma markers were measured at 24 hours after sepsis diagnosis. Data are displayed as median [interquartile range], number (percentage), or mean  $\pm$  SD. N/A, not available. N.D., not detectable. \*  $p < 0.05$ .

**Table S2. Target genes and their function regulated by selected miRNAs identified in septic mice and humans, Related to Figure 1.**

	<b>Target Genes</b>	<b>Functions</b>	<b>References</b>
<b>miR-146a-5p</b>	Irak1, Traf6	Macrophage activity	(Boldin et al., 2011)
	Hes1, Notch1	Macrophage polarization	(Huang et al., 2016)
	Relb	Monocyte activity	(Etzrodt et al., 2012)
	Ifng, Nos2	Lymphocyte activity	(Dai et al., 2008)
	Egr1	B cell proliferation	(Contreras et al., 2015)
	Stat1	Treg activity	(Lu et al., 2010)
<b>miR-22-3p</b>	Cdc25c, Erbb3, Mecom	Breast cancer metastasis	(Patel et al., 2011)
	Irf8, Bcl2	Dendritic cell development	(Li et al., 2012; Min et al., 2013)
	Ppara, Sirt1, Hdac4	Cardiac hypertrophy	(Gurha et al., 2013; Huang et al., 2013)
	Max	Cell cycle length	(Berenguer et al., 2013)
<b>miR-122-5p</b>	Slc7a1	Amino acids transportation	(Chang et al., 2004)
	Noct	Liver circadian	(Kojima et al., 2010)
	Hfe, Hju, Bmpr1a, Hamp	Systemic iron metabolism	(Castoldi et al., 2011)
	Klf6	Hepatocarcinogenesis	(Tsai et al., 2012)
	c-Myc	Liver growth	(Yarushkin et al., 2017)
<b>miR-10a-5p</b>	Hdac4	Smooth muscle cell differentiation	(Huang et al., 2010)
	Bim	Apoptosis	(Ho et al., 2011)
	Klf4	Activate wnt signal	(Stadthagen et al., 2013)

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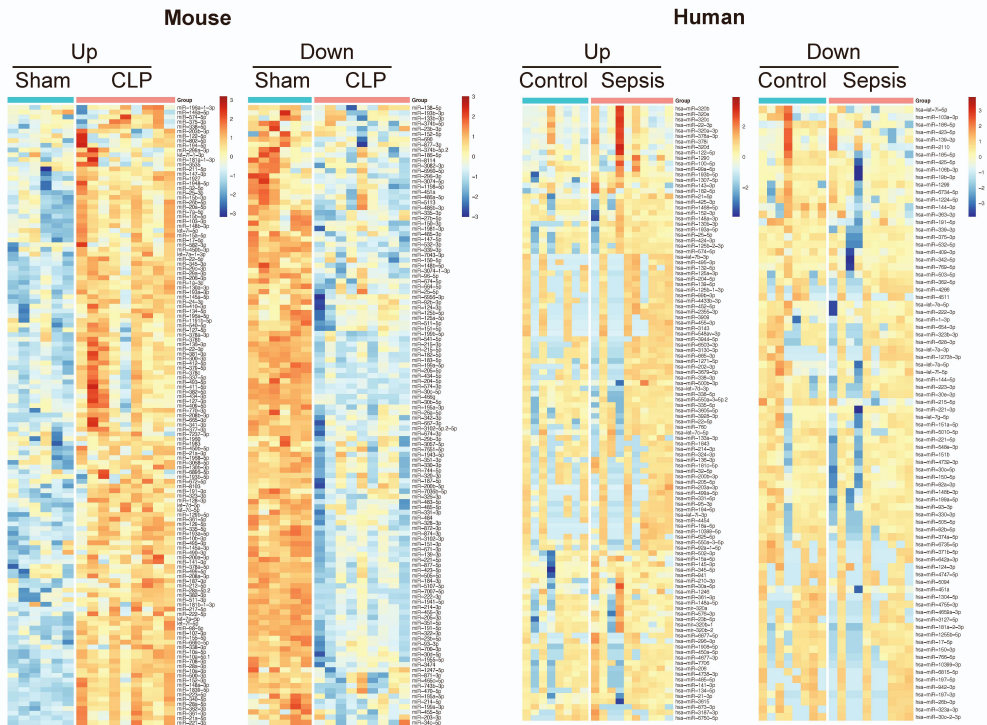
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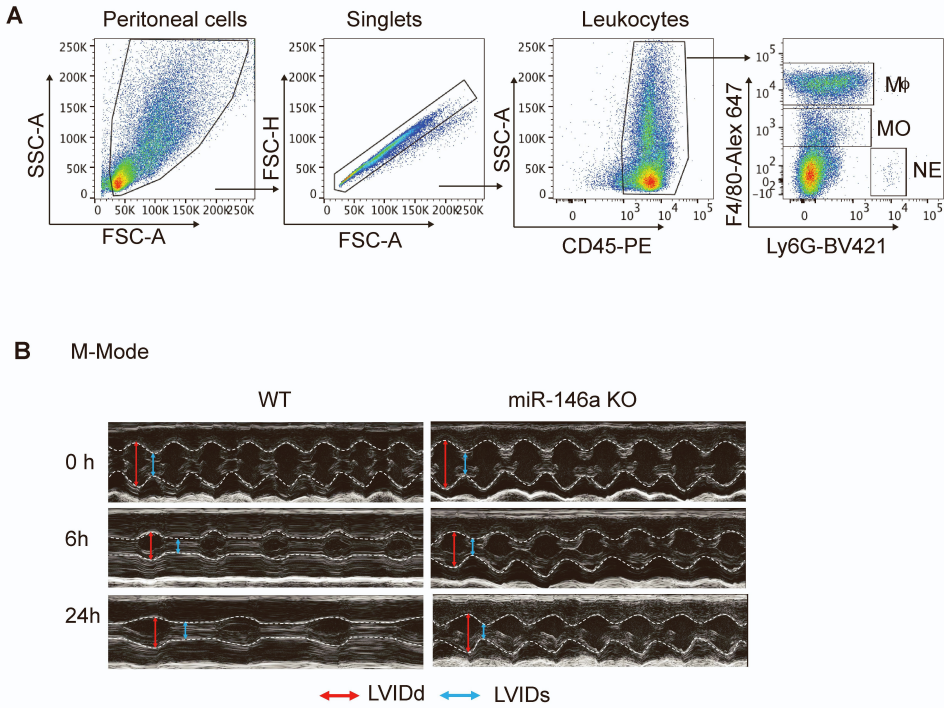
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**Table S3. Primer sequences, Related to Figure 2, Figure 3, Figure 4, and Figure 6.**

<b>Genes (Mouse)</b>	<b>Primer Sequence</b>
<i>Gapdh</i>	Forward 5'-AACTTTGGCATTGTGGAAGG-3' Reverse 5'-GGATGCAGGGATGATGTTCT-3'
<i>Il-1<math>\beta</math></i>	Forward 5'-GCCCATCCTCTGTGACTCAT-3' Reverse 5'-AGGCCACAGGTATTTTGTCTG-3'
<i>Il-6</i>	Forward 5'-AGTTGCCTTCTTGGGACTGA-3' Reverse 5'-TCCACGATTTCCCAGAGAAC-3'
<i>Il-10</i>	Forward 5'-GCTCTTACTGACTGGCATGAG-3' Reverse 5'-CGCAGCTCTAGGAGCATGTG-3'
<i>Cxcl2</i>	Forward 5'-CCGCTGTTGTGGCCAGTGAAGTGC-3' Reverse 5'-TTAGCCTTGCCTTTGTTTCAGTAT-3'
<i>Tnfa</i>	Forward 5'-CTGGGACAGTGACCTGGACT-3' Reverse 5'-GCACCTCAGGGAAGAGTCTG-3'
<i>Irak-1</i>	Forward 5'-GCCACCTGAGTTCTATCACA-3' Reverse 5'-GCCACCTGAGTTCTATCACA-3'
<i>Kim-1</i>	Forward 5'-CATTTAGGCCTCATACTGC-3' Reverse 5'-ACAAGCAGAAGATGGGCATT-3'

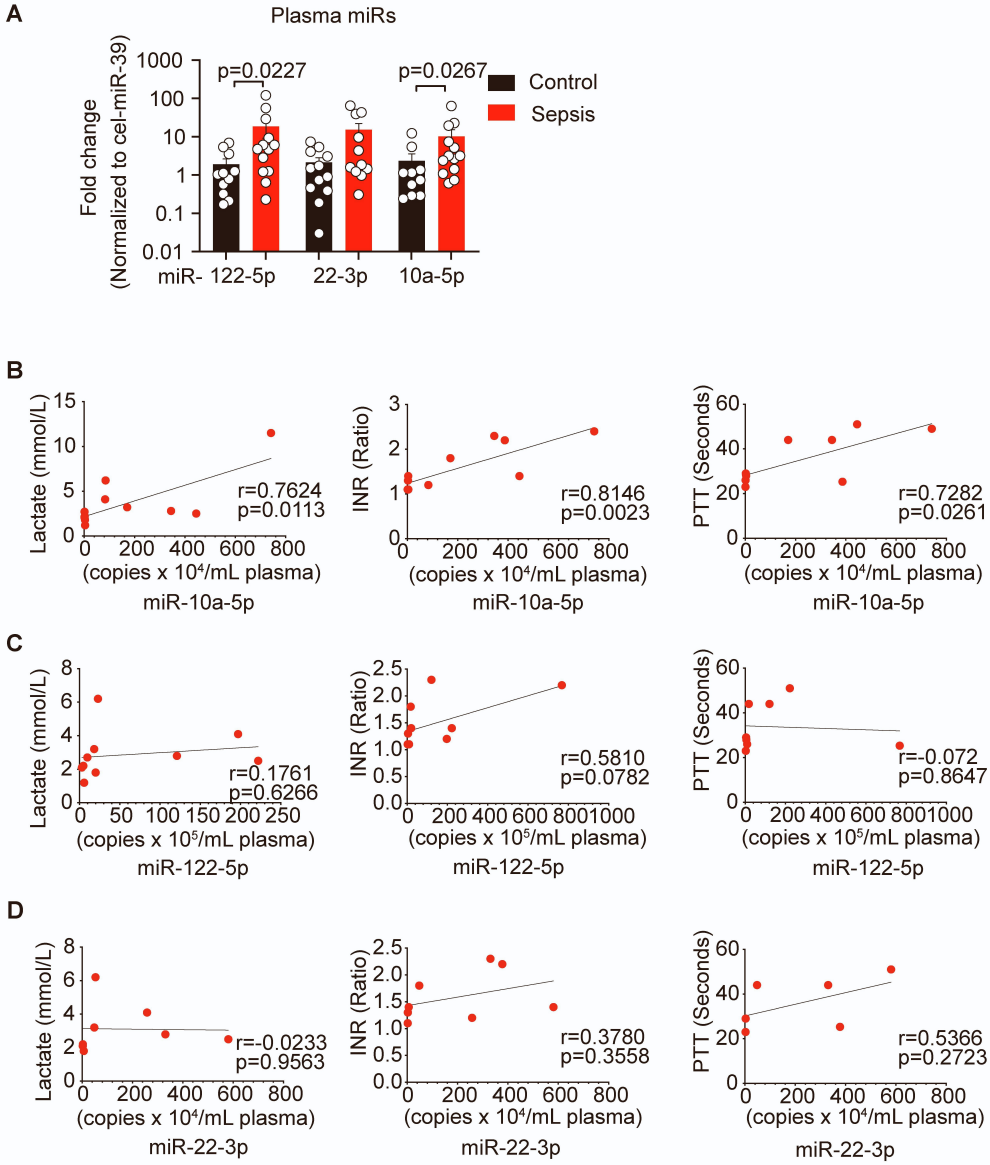


**Figure S1.** Heatmap showing differential expression of plasma miRNAs between control and sepsis in mice and humans, Related to Figure 1.



**Figure S2.** (A) Gating strategy of flow cytometry in peritoneal cells. Macrophages were characterized as CD45<sup>+</sup>F4/80<sup>high</sup>Ly6G<sup>-</sup>, neutrophils CD45<sup>+</sup>F4/80<sup>+</sup>Ly6G<sup>+</sup>, and monocytes CD45<sup>+</sup>F4/80<sup>low</sup>Ly6G<sup>-</sup>; Related to Figure 2. (B) Representative M-mode images of transthoracic echocardiography of WT and miR-146a<sup>-/-</sup> mice at baseline (0 hour), 6 hours, and 24 hours after CLP procedure. LVIDd: left ventricular internal dimension at end-diastole; LVIDs: left ventricular internal dimension at end-systole, Related to Figure 6.





**Figure S3.** Pearson's correlation between the plasma miRNA (miR-10a-5p, miR-122a-5p, miR-22-3p) concentrations and the clinical parameters - serum lactate, blood international normalized ratio (INR), and partial thromboplastin time (PTT) in septic humans. n=11-13. Related to Figure 6.