Supplemental Materials

Relative adrenal insufficiency is a risk factor and endotype of sepsis - A proof-ofconcept study to support a precision medicine approach to guide glucocorticoid therapy for sepsis

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Tables S1. List of cytokines that did not show significant difference between SR-BI^{fl/fl} mice and SF1creSR-BI^{fl/fl} mice treated with CLP. SR-BI^{fl/fl} and SF1creSR-BI^{fl/fl} littermates were treated with CLP (25G, full ligation) for 4 and 20h. Plasma was harvested and analyzed for cytokines levels. Data comparing SR-BI^{fl/fl} and SF1creSR-BI^{fl/fl} littermates were analyzed by student t-test. n = 6.

List of cytoking	nes with a p	o>0.05 (pg	ı/ml)	
	SR-Blflf/fl		SF1creS	R-Blflf/fl
	4h	20h	4h	20h
G-CSF	32557.00	35645.13	39040.77	39308.02
IFNy	8.13	4.96	0.64	90.36
IL-1a	250.41	215.48	96.77	405.77
IL-3	2.55	5.35	1.07	8.00
IL-4	0.46	4.58	0.18	0.72
IL-7	7.75	49.49	8.02	39.80
IL-9	11.02	9.08	24.81	34.83
IL-10	70.64	108.75	76.94	188.74
IL-12 (p70)	63.19	136.97	57.93	86.53
IL-15	39.05	225.37	43.92	632.52
IL-17	35.37	71.03	5.04	118.91
IP-10	149.23	782.85	278.13	1085.23
LIF	4.35	22.17	4.72	1187.72
LIX	1009.24	138.83	799.75	3782.94
MCP-1	206.35	1146.57	364.40	8872.91
M-CSF	12.37	15.37	5.50	33.31
MIG	54.33	96.93	94.84	770.34
MIP-1B	310.13	559.29	90.24	1013.04
MIP-2	907.53	1987.45	1451.05	11816.06
RANTES	63.87	74.55	38.62	158.17

Major Resource Tables

Mouse Breeding: SF1cre mice in FVB/NJ background were from the Jackson Laboratory (#012462). SR-BI^{fl/fl} mice in 8x C57BL/6J background were from Dr. Chieko Mineo (University of Texas Southwestern Medical Center). SR-BI^{fl/fl} mice were further backcrossed to C57BL/6J mice for two generations. The SF1cre mice were backcrossed for 4 generations against C57BL/6J mice and subsequently interbred with SR-BI^{fl/fl} mice for three rounds to yield SF1creSR-BI^{fl/fl} and SR-BI^{fl/fl} littermates.

	Vendor or Source	Breeding Strategy	Background Strain
Parent - Male	In house	SF1cre mice	7x C57BL/6J
Parent - Female	In house	SR-BI ^{fl/fl} mice	10x C57BL/6J

Mouse Models (in vivo studies)

Mouse Model	Vendor or Source	Sex
SF1creSR-BI ^{fl/fl} mice	In house breeding	male & female
SR-BI ^{fl/fl} mice	—— in flouse breeding	maie & Iemaie

Mouse Housing Conditions

	Mouse Housing Conditions	Note
Set Temperature range	22 °C	
Set Humidity range	50%	
Light Cycle (Mouse)	14 hours : 10 hours	
Water	RO Water	ad libitum
Standard Feed	Teklad Irradiated Global 18% Protein Rodent Diet (Envigo); Diet # 2918	ad libitum
Standard Bedding	P.J. Murphy Coarse SaniChip	
Experimental Feed	Teklad Irradiated Global 18% Protein Rodent Diet (Envigo); Diet # 2918	ad libitum
SPF	Yes	

Major Resources Table

Reagents or Resources	Source	Identifier	
Antibodies			
anti-SR-BI	Sigma-Genosys	Customer made	
anti-mouse CD16/CD32 (Fc)	Biolegend	101302;RRID:AB_312801	
PE/Cy7-conjugated anti-F4/80 (BM8)	Biolegend	123114;RRID:AB_893478	
PE-conjugated anti-Ly6g (1A8)	Biolegend	127608;RRID:AB_1186099	
Percp-cy5.5-conjugated anti- CD11b (M1/70)	BD Bioscience	550993; RRID:AB_394002	

APC-cy7-conjugated anti-CD45 (30F11)	Biolegend	103116; RRID:AB_312981
Critical Commercial Assays		
Corticosterone ELISA Kit	ENZO Life	ADI-900-097;
	Sciences	RRID:AB_2307314
Mouse IL-6 ELISA Ready-SET- Go!®	eBioscience	88-7064; RRID:AB_2574987
Mouse TNF alpha ELISA Ready- SET-Go!®	eBioscience	88-7324; RRID:AB_2575077
Mouse Cytokine Array /	Eve	
Chemokine Array 31-Plex (MD31)	Technologies	
Liquid ALT (SGPT)	POINTE	A7526-01-881
Reagent Set	SCIENTIFIC	
QuantiChromTM Urea Assay Kit	QuantiChrom	DIUR-100
RNeasy Mini Kit	QIAGEN	74104
iScript™ Reverse Transcription	Bio-Rad	1708840
Supermix		
Chemicals and Recombinant Proteins		
BODIPY ™ FL-conjugated	Life	E2864
Escherichia coli BioParticles	technologies	
Hydrocortisone (water-soluble)	Sigma	H0396
LPS (LPS-EK; <i>E. coli</i> K-12)	invioviGen	tlrl-eklps

Primers

Gene	Primer	Vendor or Source	
MKP-1	5'-GTTGTTGGATTGTCGCTCCTT and	Integrated DNA	
	5'-TTGGGCACGATATGCTCCAG	Technologies IDT	
U36B4	5'-CGTCCTCGTTGGAGTGCA and 5'-	Integrated DNA	
	CGGTGCGTCAGGGATTG	Technologies IDT	