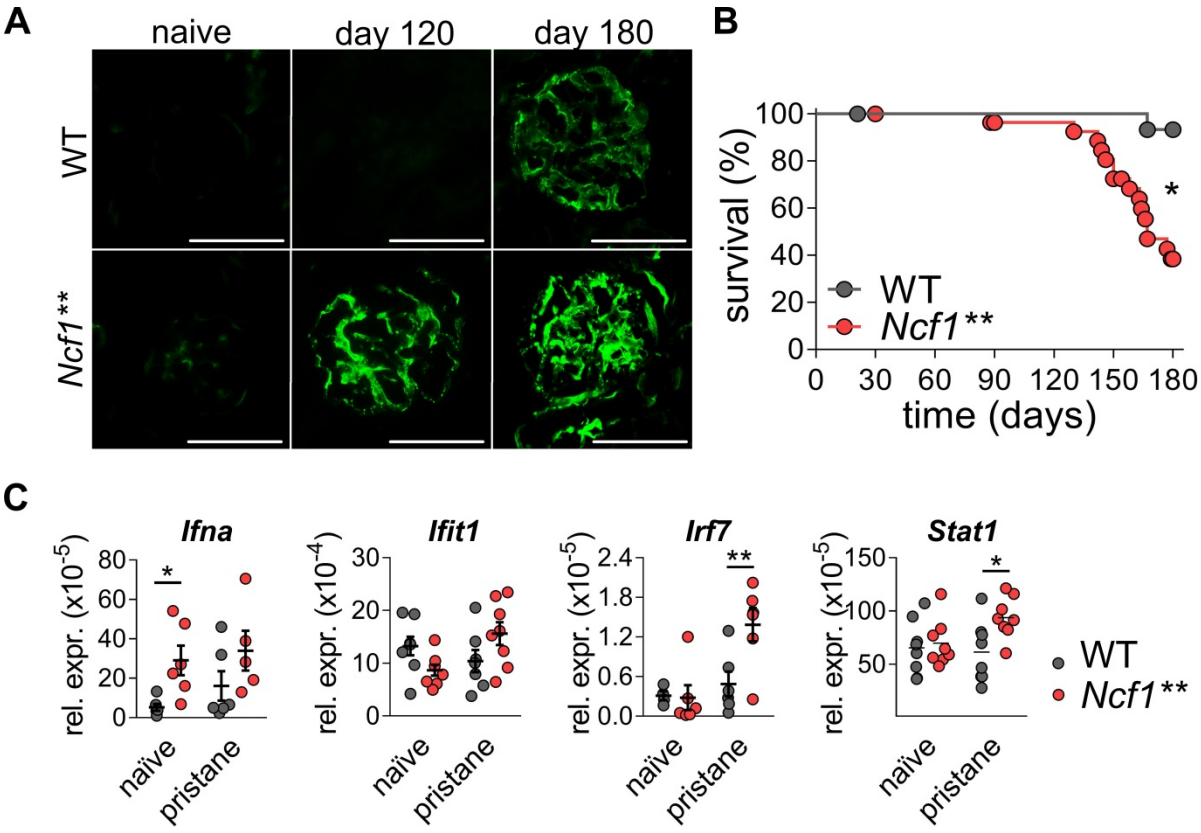
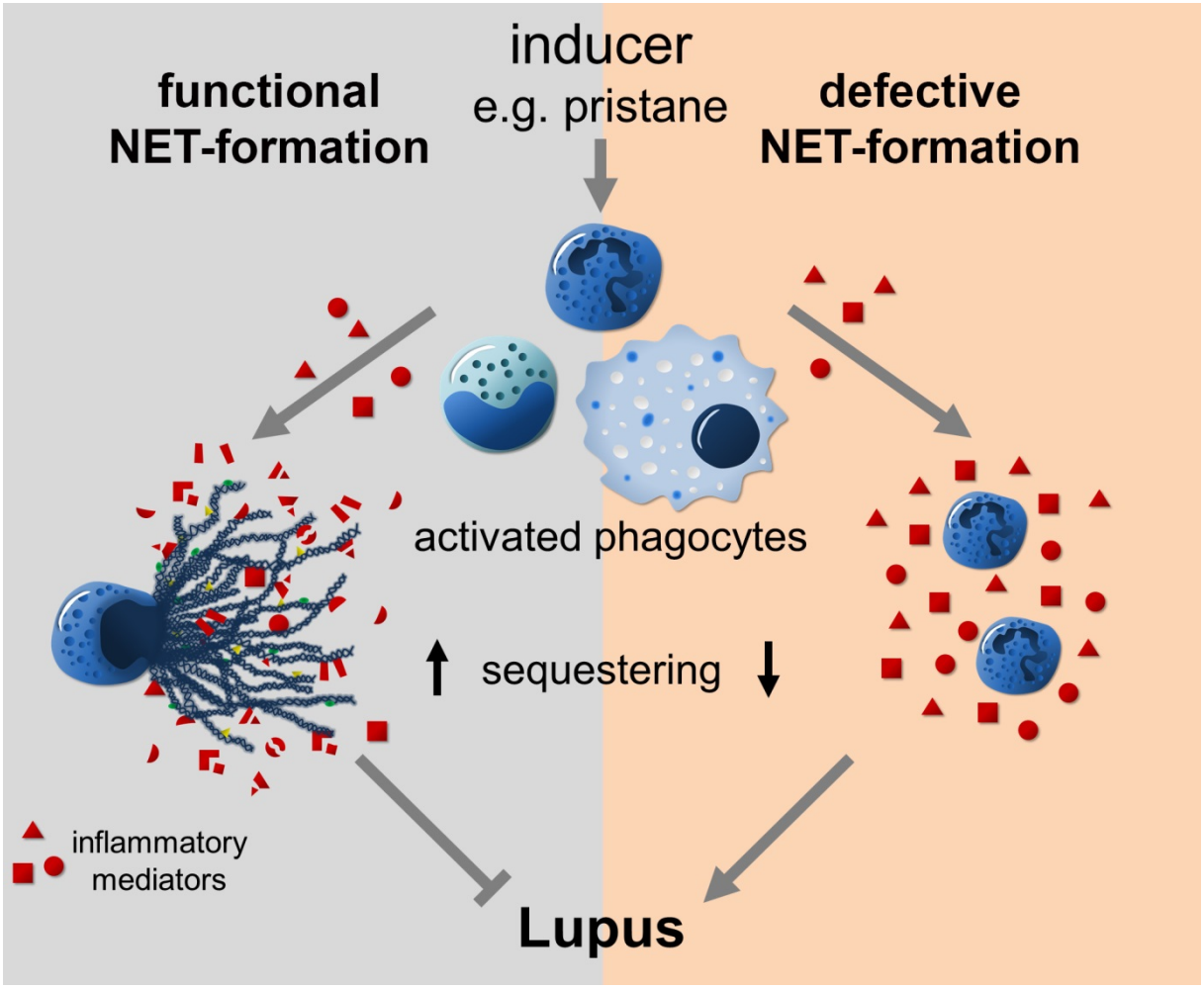
Supplemental figures



Supplemental Figure 1: Worsened kidney damage and accentuated interferon signature in BALB/c.*Ncf1* mice.** (**A**) Representative immunofluorescence images of complement C3 deposits in one out of seven BALB/c wild type (WT) and *Ncf1*** mice before and 4 and 6 months after pristane-injection, respectively. Scale bars, 100 µm. (**B**) Survival plot of BALB/c WT and *Ncf1*** mice after pristane-injection. The general clinical condition of the animals was graded according to an established scoring system (73), including also severe proteinuria, and animals were taken out of the experiment when demise was imminent. *P < 0.05 as determined by Mantel-Cox test, n = 17. (**C**) Expression of interferon alpha (*Ifna*) and IFN I–stimulated genes *Ifit1, Irf7*, and *Stat1* normalized to expression of *β-actin* in serum gained from mice before and 120 days after pristane-injection. Scatter plots show individual measurements, means and S.E.M., n = 6 - 8. *P < 0.05, **P < 0.01 as determined by ANOVA using Bonferroni´s post-hoc test.



Supplemental Figure 2. Impact of neutrophil extracellular traps (NETs) on the development of lupus. After injection of pristane or a similar trigger infiltrating monocytes and macrophages undergo apoptosis and necrosis. Nuclear autoantigens exposed on dead cell remnants in the setting of an altered cytokine milieu provided by activated phagocytes initiates autoimmunity and lead to development of lupus. In addition, in the presence of functional NOX2 and peptidyl arginine deiminase (PAD) 4 infiltrating neutrophils externalize their nuclear DNA and form NETs. NETs can attenuate inflammation and milden pristane-induced lupus by sequestering cytokines/chemokines via NET-associated proteases. In case of reactive oxygen species (ROS)- or PAD4-deficiency the abrogated degradation of inflammatory mediators in NETs exacerbates the development of lupus.

								Organ involvement*										Treatment								Assays	
Sample	Diagnosis	Sex	Age(y)	CRP (mg/l)	ESR 1h/2h	ANA titer	anti-dsDNA (U/ml)	arthritis	arthralgia	hematological inv.	vasculitis	serositis	skin	nephritis	fatigue	CNS	PNS	PDN	BEL	ASA	AZA	MTX	CQ/HCQ	MMF	LEF	ROS	NETosis
6	SLE	f	33	N.D.	N.D.	N.D.	N.D.			x													x			x	x
12	SLE	f	37	N.D.	N.D.	N.D.	N.D.	x															x			x	
13	SLE	f	28	N.D.	N.D.	N.D.	N.D.						x							x			x			x	
14	SLE	f	39	N.D.	N.D.	N.D.	N.D.		x								x						x			x	
15	SLE	f	21	N.D.	N.D.	N.D.	N.D.	x		x													x			x	
16	SLE	m	29	N.D.	N.D.	N.D.	N.D.														x		x			x	
21	SLE	m	56	4,40	7	1:320	0,1	x					x	x				x				x	x			x	
24	SLE	f	44	2,50	30	1:3200	0,1						x													x	
25	SLE	f	38	2,60	7/21	1:100	4,2		x				x							x			x			x	
26	SLE	m	50	1,40	9	N.D.	0,1		x			x	x					x				x	x				x
27	SLE	f	45	1,20	4/9	N.D.	0,1	x	x				x			x		x					x	x			x
28	SLE	f	27	1,70	3/11	1:320	6,2	x					x	x		x							x	x		x	
29	SLE	f	33	5,70	40	1:320	69,7	x	x								x					x	x			x	x
30	SLE	f	55	2,50	9/13	1:100	4,2													x			x	x		x	
31	SLE	f	30	10,60	36/66	1:1000	81,4	x					x										x	x		x	x
32	SLE	f	54	7,50	32/61	1:1000	6,3						x													x	x
33	SLE	f	57	4,00	21	1:100	0,1																x		x	x	
34	SLE	f	25	4,30	2/14	1:100	23,7								x					x			x	x		x	x
35	SLE	f	54	4,40	50	1:320	20,4						x					x					x				x
36	SLE	f	74	7,50	41	N.D.	2,7	x										x	x							x	x
37	SLE	f	36	3,50	N.D.	N.D.	1,7		x				x		x	x		x					x	x		x	x
38	SLE	f	49	3,20	38	N.D.	16	x	x				x					x		x						x	x
39	SLE	m	30	1,60	13	1:320	39,8							x	x			x			x		x			x	x
40	SLE	f	47	2,10	59	1:3200	7,3													x	x					x	x
41	SLE	m	44	15,70	41	1:100	4,5																x			x	x
42	SLE	f	47	1,60	13	1:100	8,9		x							x				x			x			x	x
43	SLE	f	45	1,60	8/17	1:320	7,9	x					x			x							x	x			x
44	SLE	m	41	2,90	11/80	1:320	7,1		x														x			x	x
45	SLE	f	21	8,70	42/59	1:320	20,4		x				x					x				x	x			x	x
46	SLE	f	21	5,60	13/25	1:1000	85																x				x
47	SLE	f	42	6,00	36	1:100	4,4																			x	x
48	SLE	m	63	4,90	17	1:3200	3,2		x											x			x	x		x	x
49	SLE	f	29	4,40	11	N.D.	0,1		x								x						x			x	x
50	SLE	f	41	3,00	57	1:1000	3,7		x								x			x		x	x			x	x
51	SLE	f	29	2,50	N.D.	N.D.	6,3																x			x	x
52	SLE	f	50	2,00	25	1:320	7,7														x		x			x	x
53	SLE	f	56	4,20	16	N.D.	0,1		x								x	x									x
54	SLE	m	75	2,90	6/14	N.D.	3,6															x	x			x	x
55	SLE	f	32	6,80	17/32	1:100	0,1																x	x		x	
56	SLE	f	53	3,10	N.D.	1:1000	4	x	x														x			x	
1	CGD	m	26	4,90	N.D.	N.D.	N.D.											Itraconazol, Cotrimoxazol, Candesartan, Cardevilol, Vit D3								x	
2	CGD	m	46	7,10	25	N.D.	N.D.											Posaconazol, Cotrimoxazol, Sultamicilin, Indapamid, Vit D3								x	
3	NHD	f	25																							x	x
4	NHD	f	24																							x	x
5	NHD	f	33																							x	x
6	NHD	f	25																							x	x
7	NHD	m	26																								x
8	NHD	m	39																							x	x
9	NHD	f	56																							x	x
10	NHD	m	54																							x	x
11	NHD	f	36																							x	x
12	NHD	f	15																							x	x
13	NHD	m	31																							x	x
14	NHD	f	33																							x	x
15	NHD	m	36																							x	x
16	NHD	f	32																							x	x

Supplemental Table 1: Serologic and clinical parameters and current treatment of individuals with systemic lupus erythematosus (SLE), chronic granulomatous disease (CGD) and normal healthy donors (NHD) enrolled in the study. CNS, involvement of the central nervous system; PNS, involvement of the peripheral nervous system; PDN, prednisone; AZA, azathioprine; MTX, methotrexate; CQ/NCQ, chloroquine or hydroxychloroquine; CTX, cyclophosphamide; MMF, mycophenolate mofetil; LEF, leflunomide; ASA, acetylsalicylic acid; N.D., not determined. *Organ involvement was taken into account for the study if it was apparent at the time of sample (serum) acquisition or max. 6 months prior.