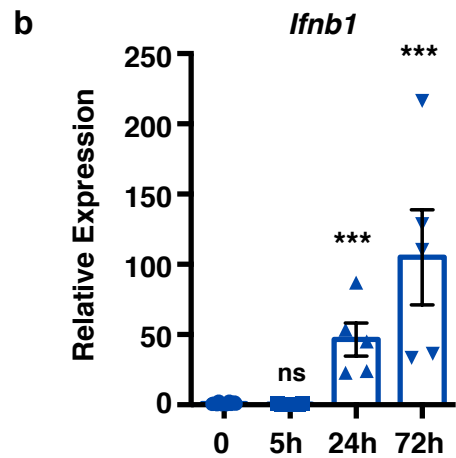
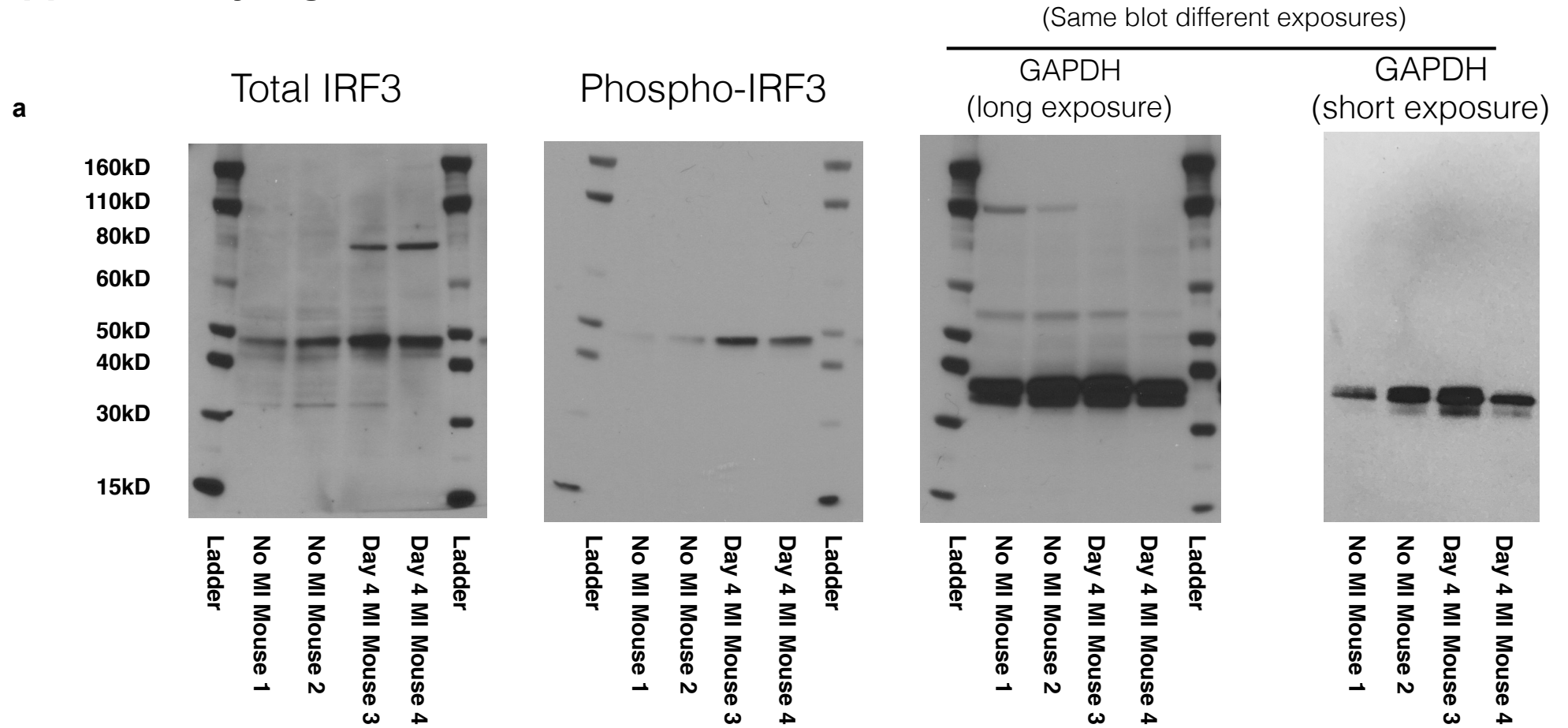


**IRF3 and Type I Inteferons
Fuel a Fatal Response to Myocardial Infarction
(NMED-L84840A)**

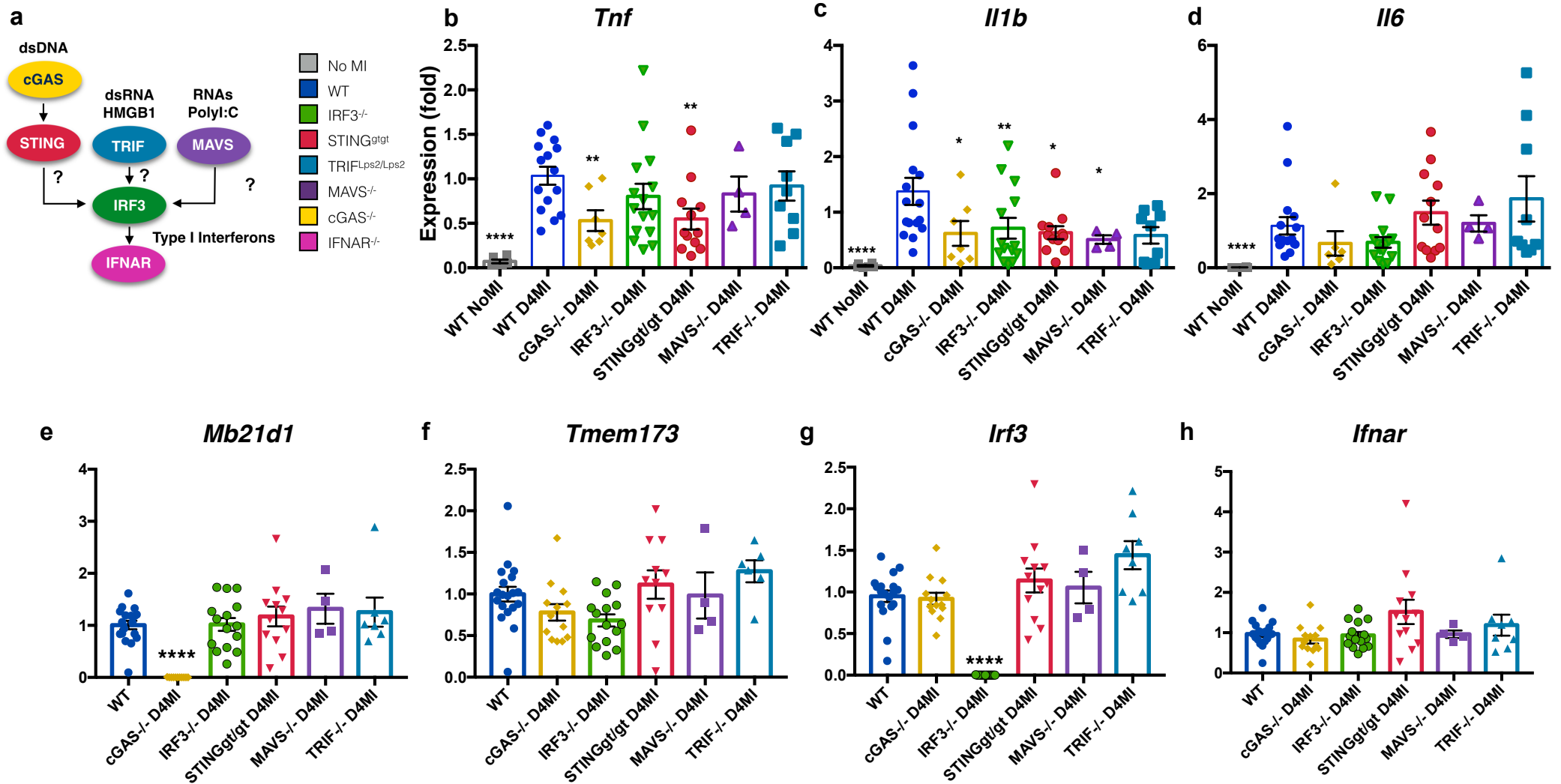
Supplementary Figures

Supplementary Fig. 1



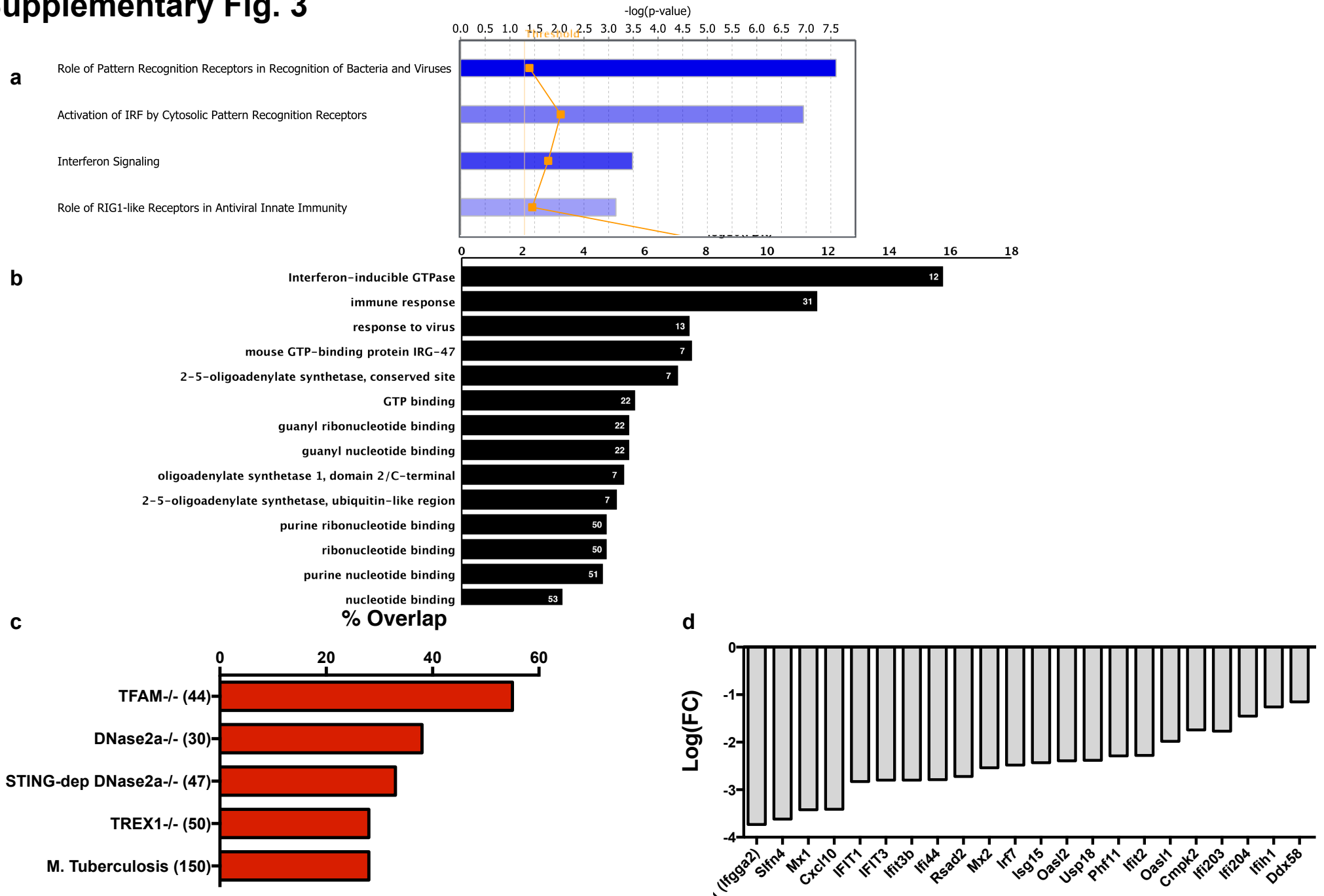
Supplementary Fig. 1 (a) Full gel images of western blot for total IRF3, Phospho-IRF3, and GAPDH loading control at 2 exposures (n=4 mice, 2 with no MI, 2 from day 4 MI). **(b)** Expression of *Ifnb1* from WT whole infarct tissue at various times (5h, 24h, 72h) after MI (n=5 per group). Mean \pm s.e.m. *** $P < 0.001$

Supplementary Fig. 2



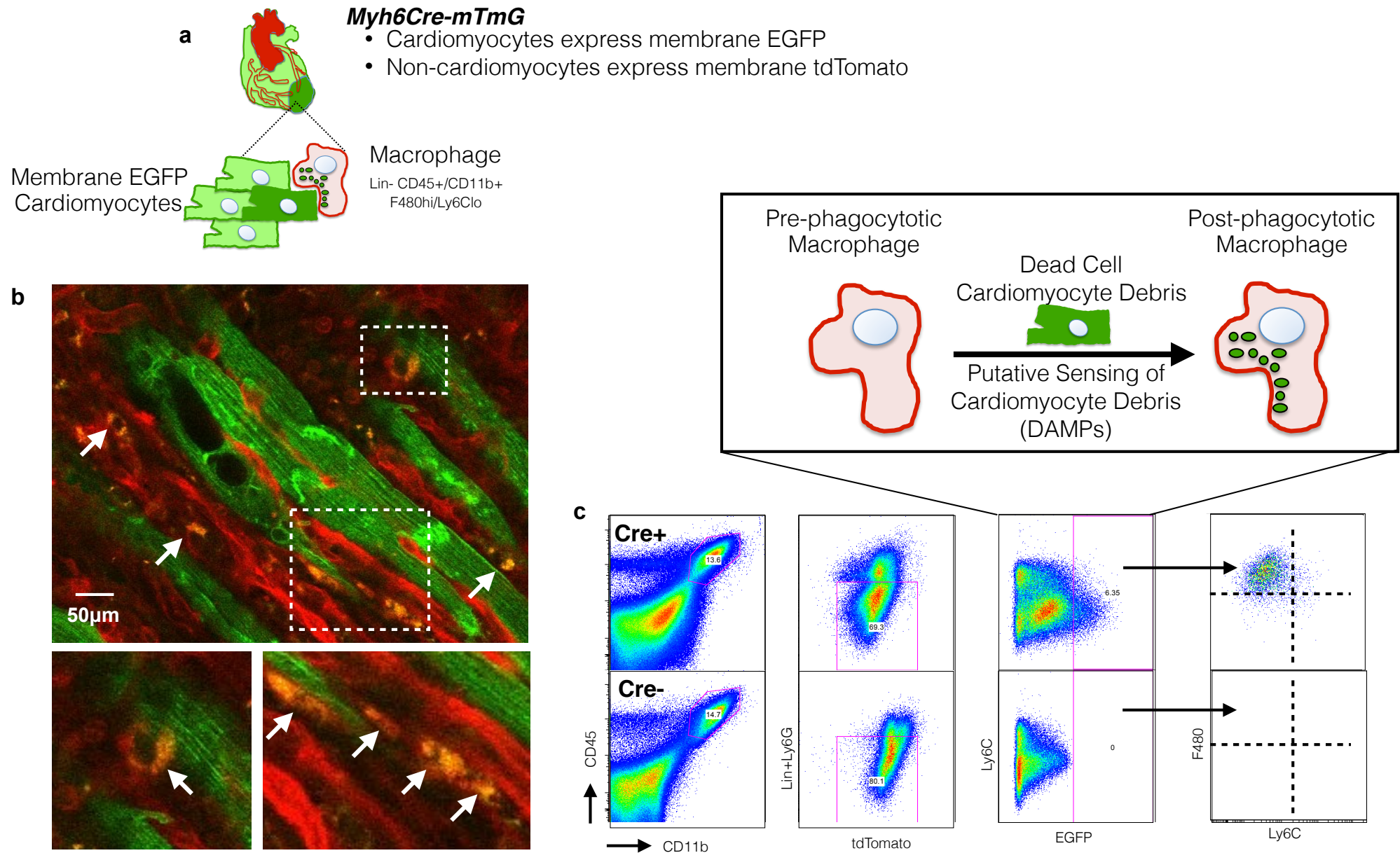
Supplementary Fig. 2. Gene expression from mice deficient in key molecules of the IRF3-activating pathways on day 4 after MI. **(a)** Schematic of IRF3-activating pathways. Quantitative PCR measurement of **(b)** *Tnf* **(c)** *Il1b* **(d)** *Il6*, **(e)** *Mb21d1* (cGAS), **(f)** *Tmem173* (*STING*), **(g)** *Irf3*, and **(h)** *Ifnar* from infarct tissue of various knockout mice on day 4 after MI. WT (n=16, dark blue), *cGAS*^{-/-} (n=7, yellow), *Irf3*^{-/-} (n=15, green), *STING*^{glt} (n=12, red), *Mavs*^{-/-} (n=4, purple), and *Trif*^{Lps2} (n=9, light blue). **P* < 0.05, ***P* < 0.01, Mean ± s.e.m.

Supplementary Fig. 3



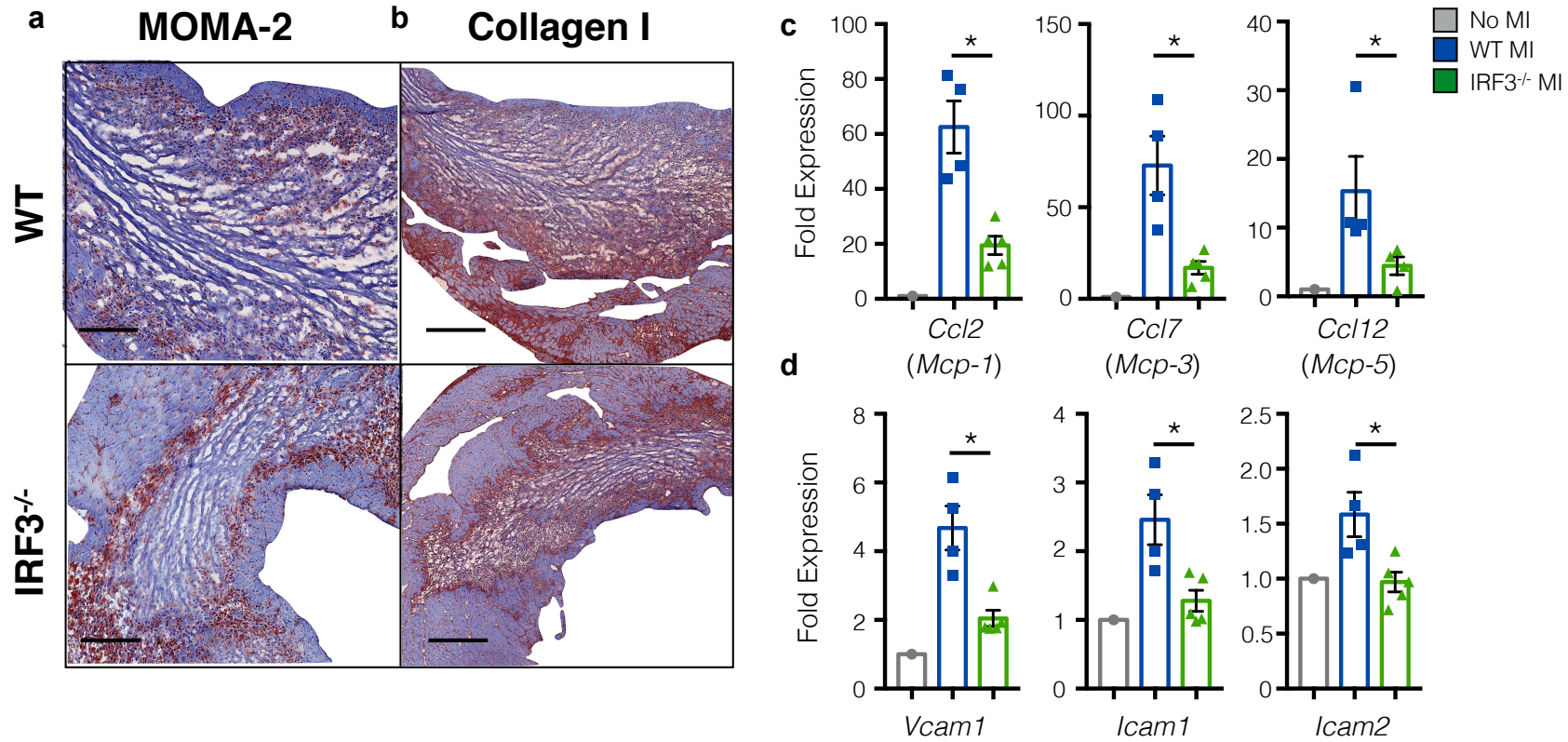
Supplementary Fig. 3 RNA Seq genome wide expression profiling of MI-induced IRF3- dependent genes. Genes differentially expressed by *WT* and *Irf3*^{-/-} mice (n=3) on day 4 after MI were classified by **(a)** Ingenuity Pathway Analysis and **(b)** DAVID Functional Classification Tools. **(c-d)** Comparison of MI-induced IRF3-dependent genes with prior studies implicating cytosolic DNA sensing. **(c)** Percent overlap (red bars) of *Irf3*^{-/-} vs. *WT* mice MI-induced differentially expressed genes (DEGs) compared to DEGs from published studies implicating cytosolic DNA as an inducer of the type I IFN response (number of genes in reference study is indicated in parenthases). **(d)** MI-induced IRF3-dependent DEGs found in 3 or more prior studies implicating cytosolic DNA sensing as the inducing stimulus.

Supplementary Fig. 5



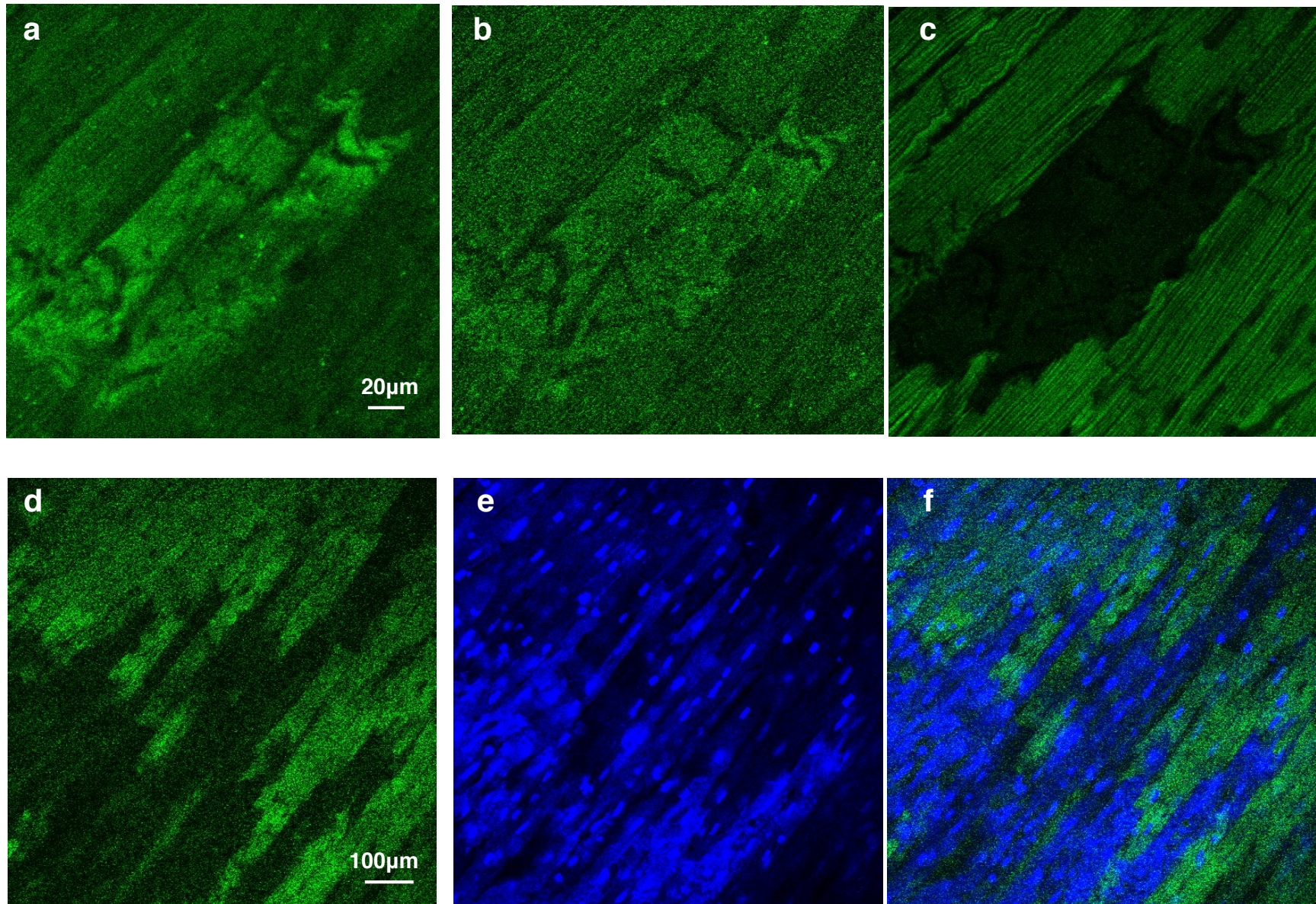
Supplementary Fig. 5 (a) Schematic of gating strategy for Myh6Cre-mTmG reporter strategy for sorting leukocytes most likely to be interacting with cardiomyocyte DAMPs such as DNA. **(b)** Two-photon microscopy of infarct borderzone on day 4 after MI. Cardiomyocytes express membrane EGFP (green) after Myh6-Cre mediated recombination. All other cells express membrane tdTomato (red). Arrows highlight cells with yellow cytoplasmic fluorescence. **(c)** Sorting and gating strategy to collect leukocytes most likely to have interacted with or phagocytosed cardiomyocyte DAMPs. A stringent background fluorescence is identified in the EGFP channel using an infarcted Cre⁻ mouse to account of cellular autofluorescence. This enables sorting of cells from a Cre⁺ mouse (in which cardiomyocytes express EGFP) that have taken up or are interacting with cardiomyocyte debris (have EGFP fluorescence above the stringent background established by the Cre⁻ cells).

Supplementary Fig. 6



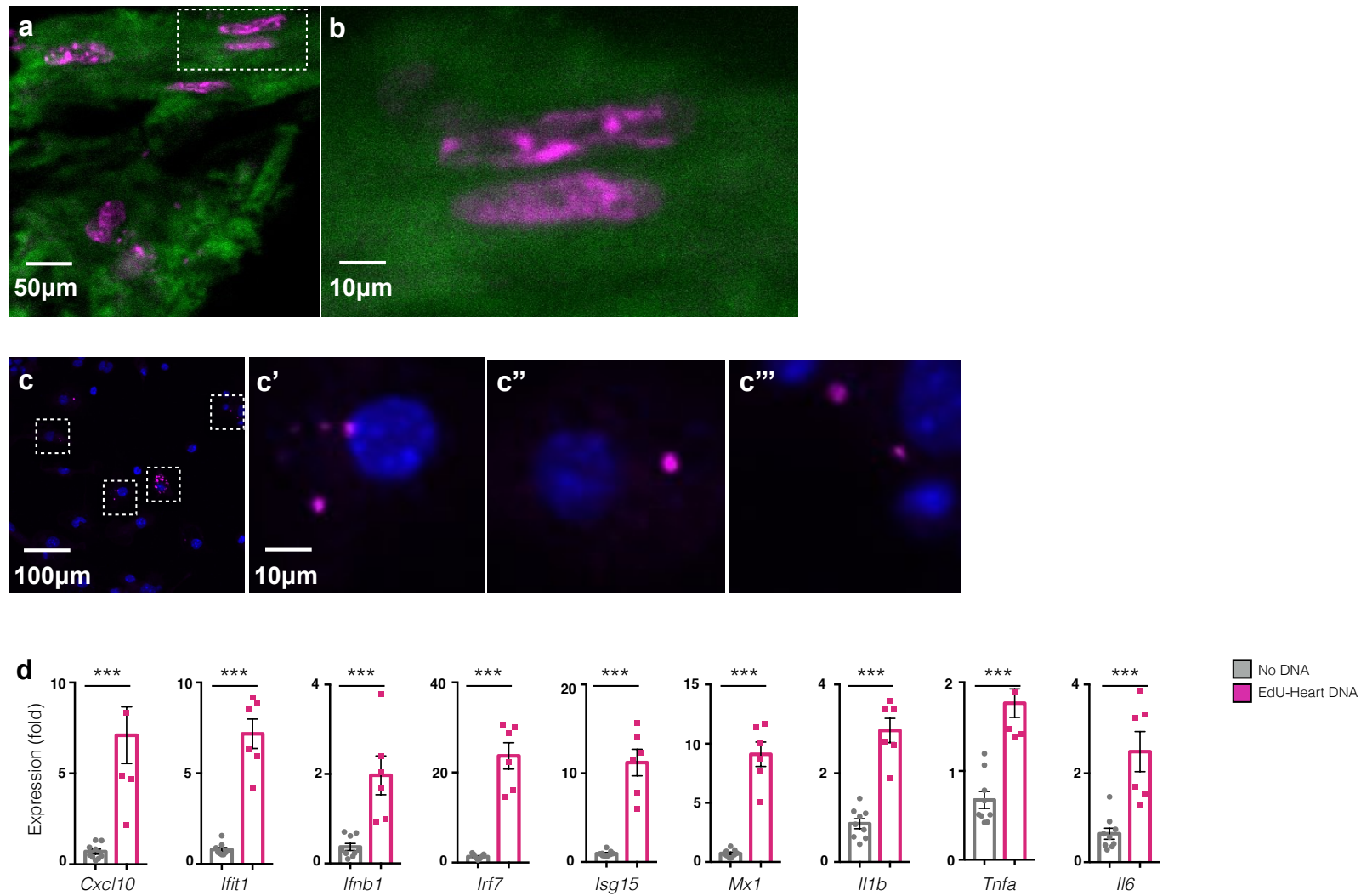
Supplementary Fig. 6. Immunohistochemical staining of *WT* and *Irf3*^{-/-} mice on day 4 after MI for **(a)** Monocyte/macrophage (MOMA-2) and **(b)** collagen I immunohistochemical staining in the borderzones and infarcts. **(c)** Expression of chemokines (*Ccl2*, *Ccl7*, and *Ccl12*) **(d)** and cell adhesion molecules (*Vcam1*, *Icam1*, and *Icam2*) were more highly induced in *WT* mice than *Irf3*^{-/-} mice.

Supplementary Fig. 7



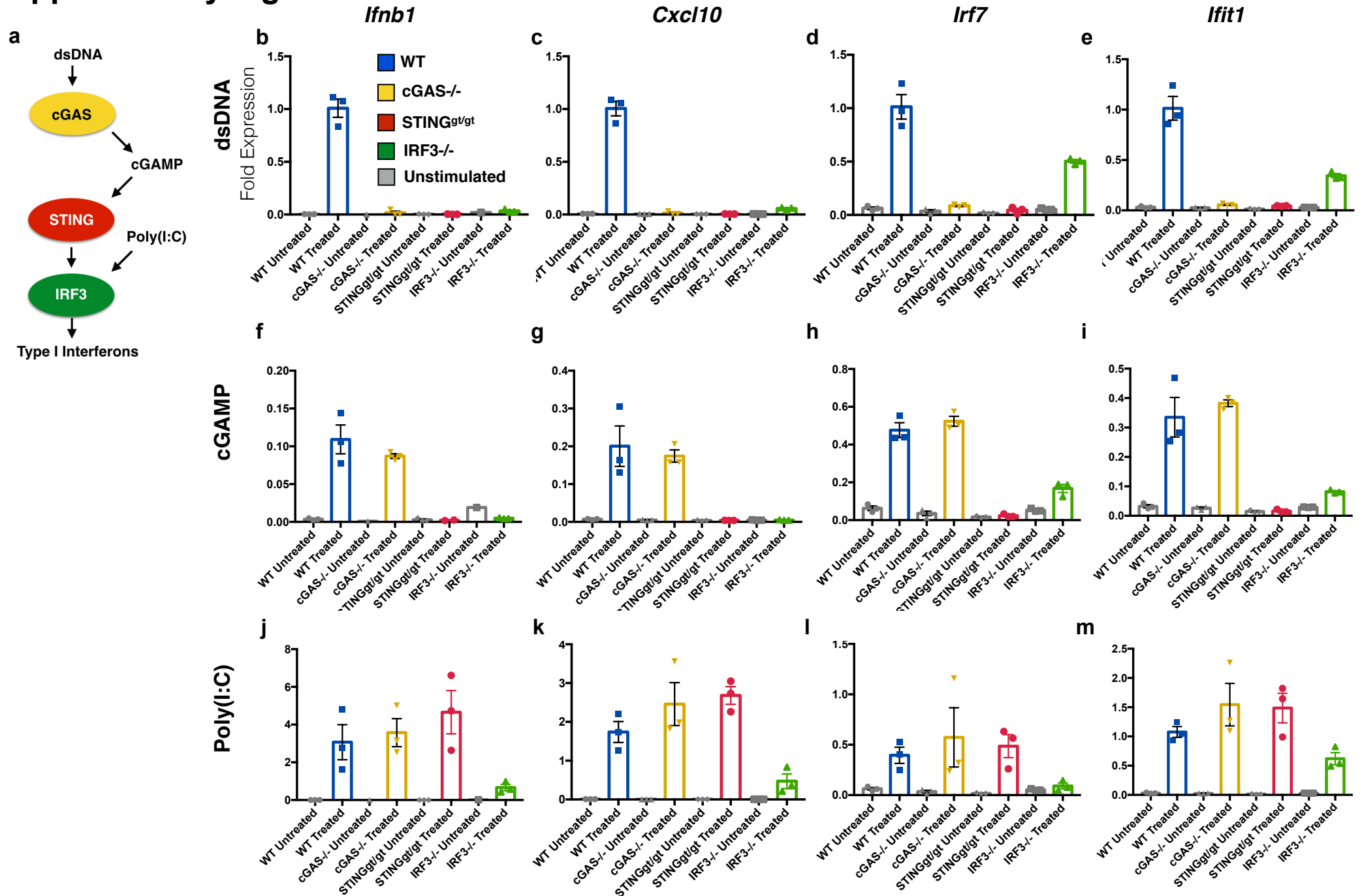
Supplementary Fig. 7 Fluorescence microscopy of dsDNA release from injured cardiomyocyte after MI. **(a-c)** Ex vivo imaging of injured cardiomyocyte autofluorescence with characteristic contraction bands are demonstrated by **(a)** confocal microscopy (460nm excitation) **(b)** two photon microscopy (910nm), and **(c)** two photon imaging at 750nm excitation. Imaging at 750nm shows complete loss of autofluorescence in injured cells. **(d-f)** Borderzone of an infarct after coronary ligation and topical application of the double-stranded DNA fluorescence probe, Pico Green. **(d)** Two photon autofluorescence at 750nm excitation illustrates loss of NADH autofluorescence in injured cells at the infarct borderzone. **(e)** dsDNA-bound PicoGreen fluorescence. **(f)** Overlay of NADH autofluorescence and dsDNA-bound PicoGreen.

Supplementary Fig. 8



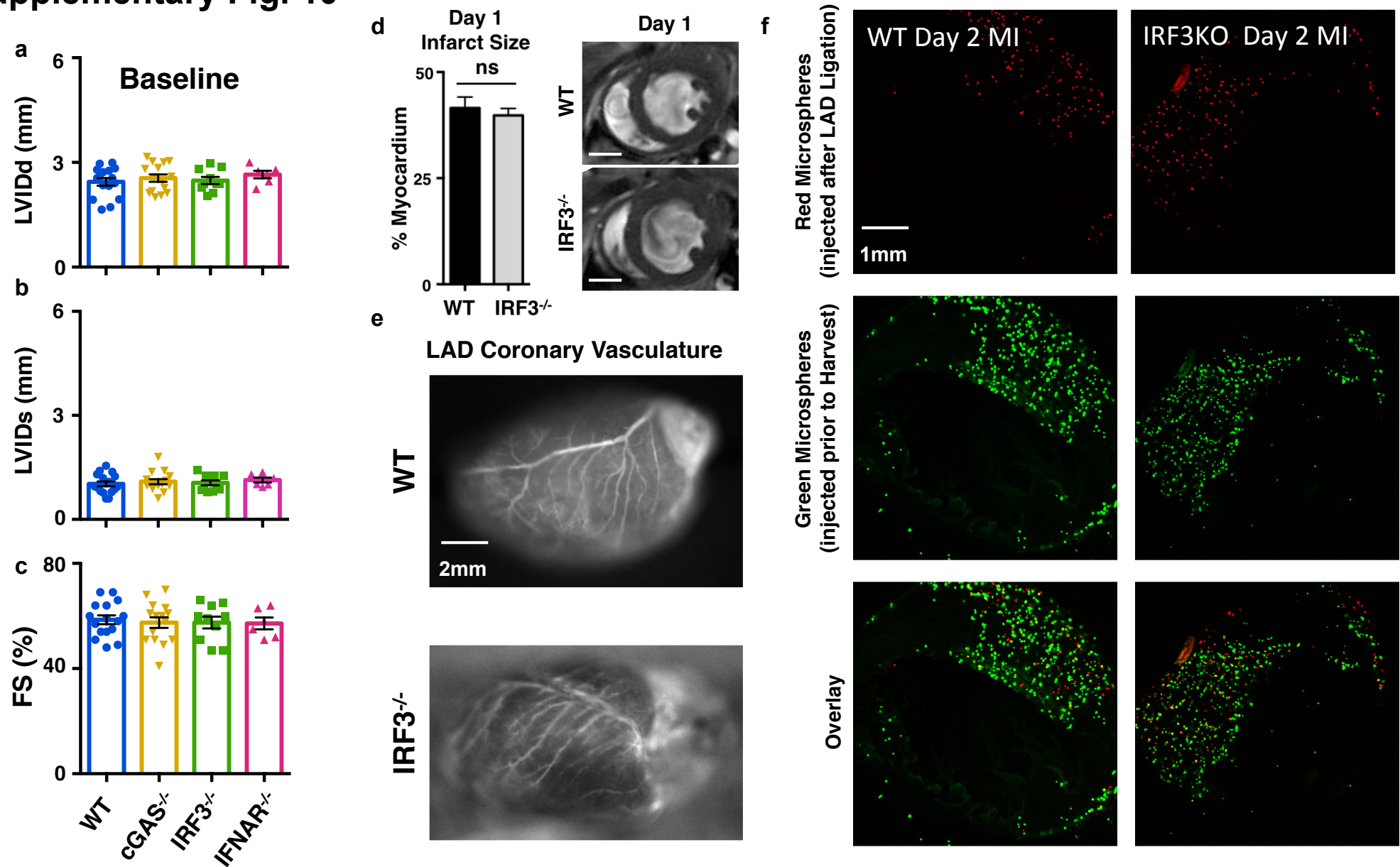
Supplementary Fig. 8. EdU labeling of adult cardiomyocyte nuclei and DNA uptake. Pregnant mice are injected with EdU on post-conception days 12, 16, and 20 to label offspring in utero. **(a)** EdU stained hearts from 10 week-old offspring click reacted to alexafluor 647 azide. **(b-c)** dsDNA was isolated from hearts of mice labeled in utero with EdU and delivered to cultured bone marrow derived macrophage (BMDM) with LTX Lipofectamine. BMDM were either **(b)** fixed, permeabilized, and click reacted with azide alexafluor 647 for imaging, or **(c)** lysed for RNA extraction and RT-PCR for interferon stimulated gene expression.

Supplementary Fig. 9



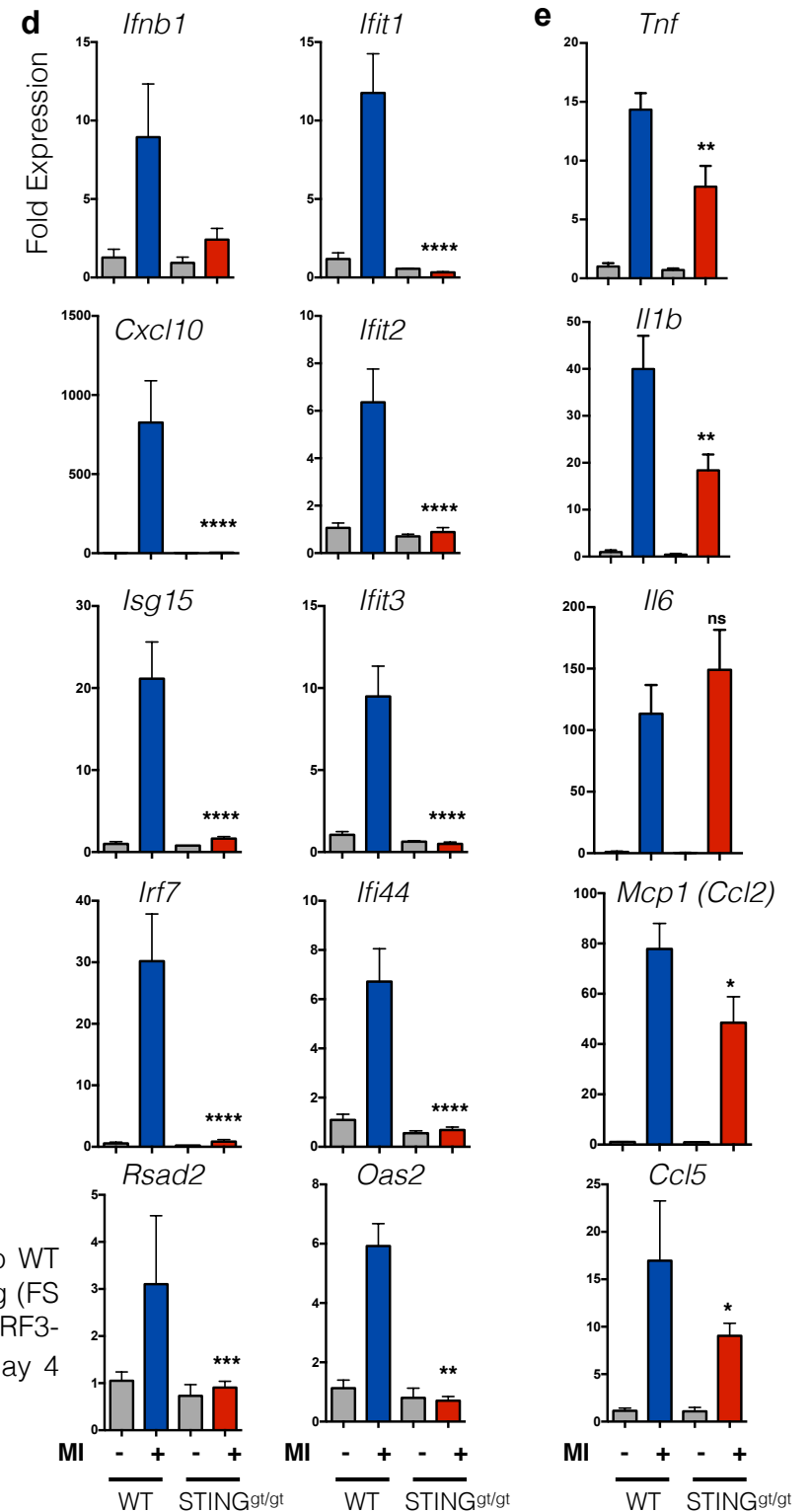
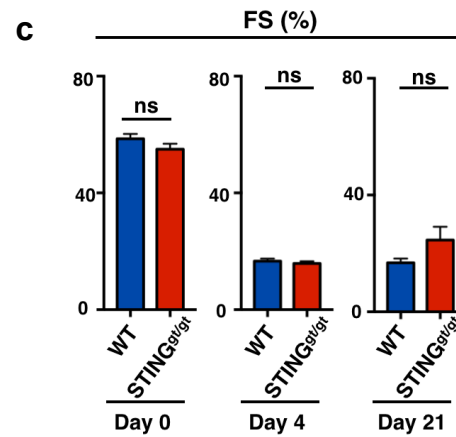
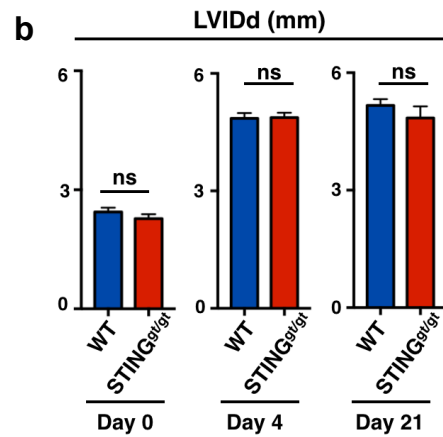
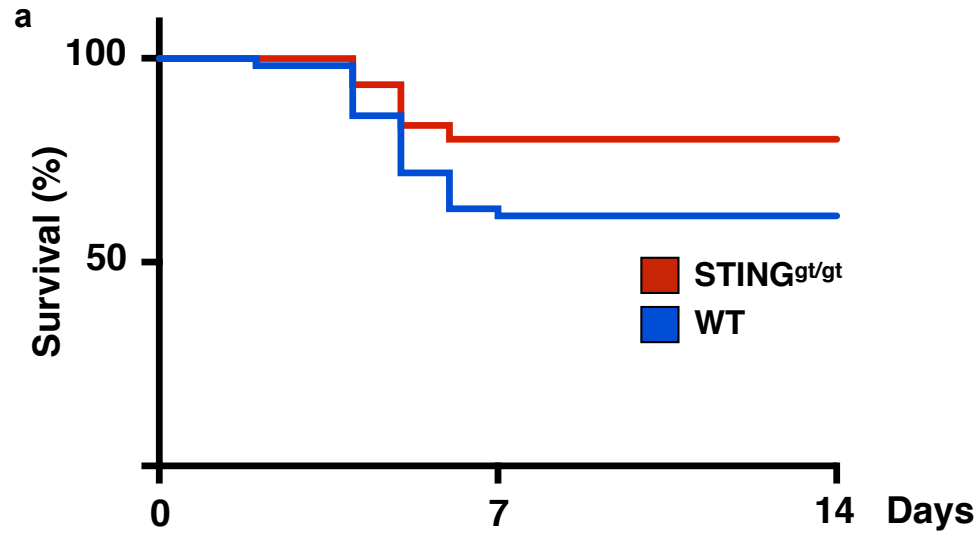
Supplementary Fig. 9 Bone marrow derived macrophages (BMDMs) cytosolic DNA sensing pathway activation by extracellular stimuli. **(a)** Schematic of cytosolic DNA sensing pathway. **(b-m)** BMDM from various mouse strains stimulated with inerte immune stimuli such as dsDNA **(b-e)**, the STING agonist cGAMP **(f-i)** or the STING-independent IRF3 activator Poly(I:C) **(j-m)** for 24 hours. Quantitative PCR expression of *Ifnb1* **(b,f,j)**, *Cxcl10* **(c,g,k)**, *Irf7* **(d,h,l)**, and *Ifit1* **(e,i,m)**. (n=3) Mean \pm s.e.m.

Supplementary Fig. 10



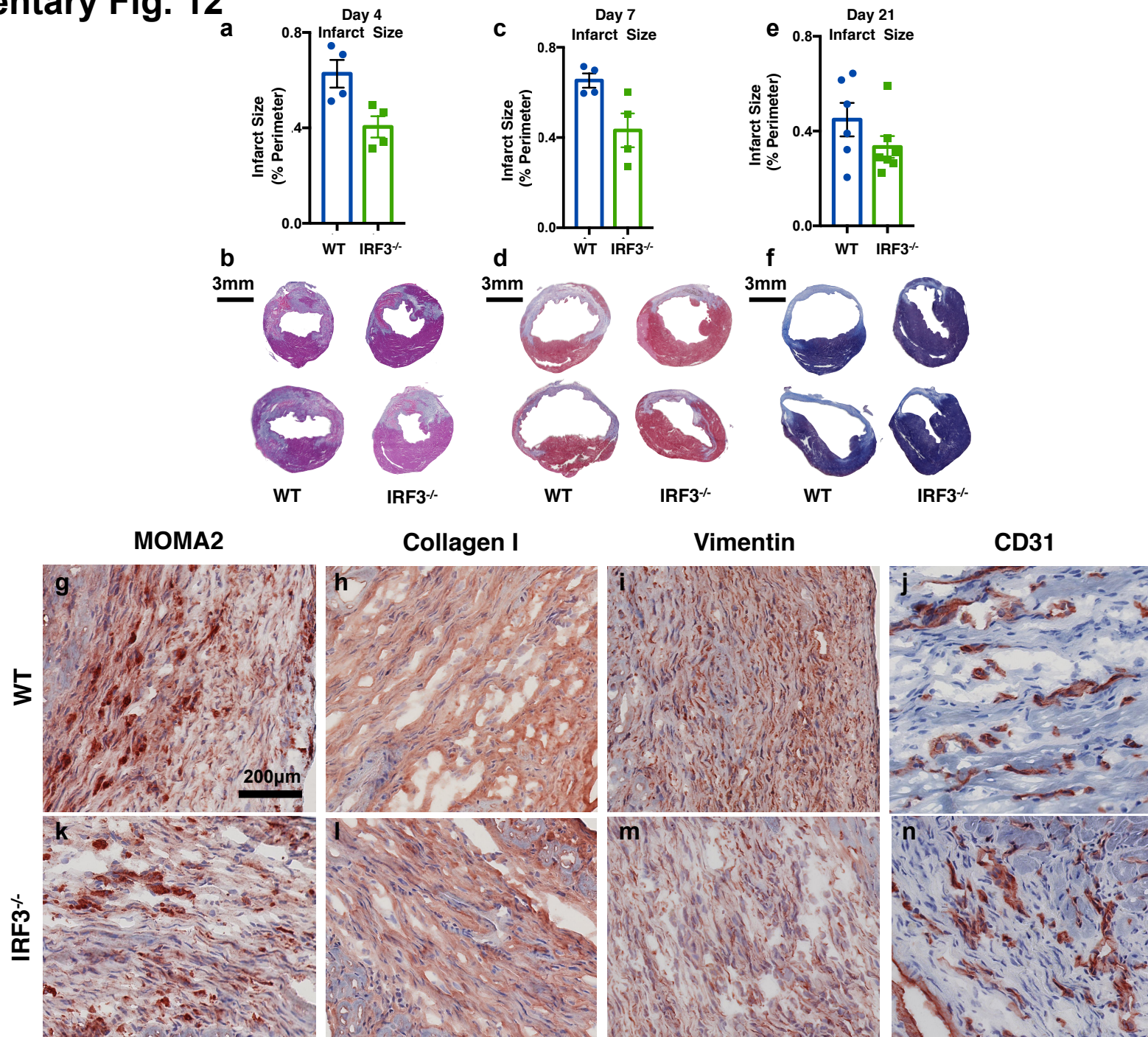
Supplementary Fig. 10. Echocardiographic, cardiac MRI, and fluorescence evaluation of baseline function, initial infarct size, coronary anatomy, and degree of spontaneous reperfusion. Baseline echocardiographic quantification of a) left ventricular end-diastolic dimensions (LVIDd), b) end-systolic dimensions (LVIDs), and c) fractional shortening (FS %) in *WT*, *cGas*^{-/-}, *Irf3*^{-/-}, and *Ifnar*^{-/-} mice. d) To evaluate infarct size on day 1 after MI, *WT* and *Irf3*^{-/-} mice were injected with gadolinium contrast and serial short axis sections were imaged by cardiac MRI. The area of enhancement was quantified, normalized to total myocardial mass, and reported as % Myocardium infarcted. e) *WT* and *Irf3*^{-/-} mice were injected with high molecular weight FITC dextran and the anterior wall was imaged on an Olympus OV110 small animal imaging system to examine coronary artery anatomy. Representative images of the anterior wall of *WT* and *Irf3*^{-/-} mice are shown. f) Red fluorescent microspheres were injected into the apex immediately following LAD ligation. At the time of harvest, green fluorescent microspheres were injected into the apex. On day 2, mice ventricles were collected and cut in short axis. Representative images of red microspheres (top), green microspheres (middle), and the overlay are shown.

Supplementary Fig. 11



Supplementary Fig. 11. STING^{gt/gt} mice response to MI. (a) 14-day survival compared to WT mice. (b) Left ventricular inner diameter at end-diastole (LVIDd) and (c) fractional shortening (FS %) measured by echocardiography on days 0, 4, and 21 after MI. Expression of (d) IRF3-dependent genes and (e) NFκB-dependent genes measured by qPCR before MI or on day 4 after MI. Mean ± s.e.m.

Supplementary Fig. 12



Supplementary Figure 12. Evaluation of infarct size from WT and IRF3^{-/-} mice (**a,b**) on day 4, (**c,d**) day 7, and (**e,f**) day 21 by percent circumference infarct measured from H&E and Masson's Trichrome stained short axis mid-ventricle sections. Immunohistochemical staining of (**g-j**) WT and (**k-n**) IRF3^{-/-} infarcts for (**g,k**) MOMA2, (**h,l**) Collagen I, (**i,m**) Vimentin, and (**j,n**) CD31. Scale bar in (g) applies to all immunohistochemical images (g-n).

Table T1. Markers Genes Discriminating Granulocytes vs All Other Clusters & Expression by ImmGen Datasets V1 and V2

	p_val	avg_diff	pct.1	pct.2	Index
<i>Il1b</i>	2.75E-233	2.2909851	0.972	0.44	1
<i>S100a9</i>	1.51E-220	3.8590683	0.768	0.055	2
<i>Cxcl2</i>	1.13E-200	2.0344236	0.956	0.633	3
<i>S100a8</i>	1.39E-190	3.6397535	0.693	0.04	4
<i>Nfkbia</i>	1.65E-173	1.6275374	0.96	0.792	5
<i>Srgn</i>	8.75E-131	1.6183156	0.925	0.622	6
<i>Tnf</i>	3.74E-126	2.4882106	0.677	0.236	7
<i>Il1r2</i>	2.08E-123	2.5301758	0.539	0.041	8
<i>Junb</i>	2.34E-123	1.2904801	0.941	0.73	9
<i>Zfp36</i>	6.85E-123	1.3811541	0.953	0.782	10
<i>Clec4e</i>	2.08E-113	2.5183319	0.614	0.16	11
<i>Nlrp3</i>	4.64E-111	2.1219958	0.574	0.135	12
<i>Cerl2</i>	1.85E-110	1.8771336	0.733	0.326	13
<i>Mmp9</i>	5.01E-110	2.4013915	0.473	0.027	14
<i>Csf3r</i>	5.49E-105	1.9583639	0.593	0.164	15
<i>Ccl3</i>	4.68E-101	2.0876752	0.621	0.283	16
<i>Gadd45b</i>	2.03E-100	1.6992927	0.726	0.312	17
<i>Cxcr2</i>	2.47E-94	2.6309711	0.44	0.052	18
<i>Trem1</i>	1.18E-88	2.2536066	0.429	0.035	19
<i>Tnfaip3</i>	1.61E-84	1.7407391	0.635	0.276	20
<i>Csf1</i>	5.32E-81	2.4198399	0.337	0.017	21
<i>Ptgs2</i>	2.22E-80	2.240447	0.525	0.164	22
<i>Acod1</i>	6.08E-80	2.5844952	0.342	0.021	23
<i>Mcl1</i>	4.35E-78	1.39455	0.794	0.547	24
<i>Tnfaip2</i>	3.65E-76	2.1701659	0.492	0.11	25
<i>Marcksl1</i>	8.82E-74	1.7999095	0.496	0.15	26
<i>Egr1</i>	4.33E-72	1.7659639	0.571	0.215	27
<i>Hdc</i>	2.44E-69	2.196161	0.347	0.029	28
<i>G0s2</i>	8.40E-68	3.0145106	0.304	0.021	29
<i>Nfkbiz</i>	1.35E-64	1.545699	0.581	0.242	30
<i>Btg2</i>	3.81E-64	1.6766973	0.541	0.189	31
<i>Hcar2</i>	1.89E-63	2.0091892	0.389	0.089	32
<i>Nfkbid</i>	3.10E-62	1.6848906	0.431	0.098	33
<i>Pim1</i>	2.16E-59	1.2451357	0.693	0.414	34
<i>Ppp1r15a</i>	3.07E-56	1.3571891	0.527	0.187	35
<i>Dusp2</i>	2.45E-54	1.5848908	0.473	0.155	36
<i>Plek</i>	8.79E-52	1.3674569	0.525	0.285	37
<i>Il1rn</i>	3.22E-50	1.6063409	0.499	0.213	38
<i>Gsr</i>	1.04E-47	1.6869301	0.356	0.072	39
<i>Ifitm1</i>	9.49E-47	1.1840327	0.433	0.108	40
<i>Socs3</i>	5.37E-46	1.2096628	0.637	0.41	41
<i>Irf1</i>	1.92E-45	1.7872454	0.323	0.08	42
<i>Ubc</i>	1.13E-44	0.8557603	0.813	0.653	43
<i>Cdk2ap2</i>	1.86E-43	1.5155735	0.389	0.129	44
<i>Lmnb1</i>	2.21E-43	1.47633	0.361	0.095	45
<i>Nr4a1</i>	8.36E-41	1.0215035	0.607	0.479	46
<i>Cd24a</i>	3.74E-39	1.7130572	0.262	0.041	47
<i>Vasp</i>	6.89E-39	1.2365953	0.361	0.133	48
<i>Bcl2a1b</i>	6.97E-39	1.1759828	0.438	0.226	49
<i>Icam1</i>	1.13E-37	1.5652636	0.286	0.073	50

V1

V2

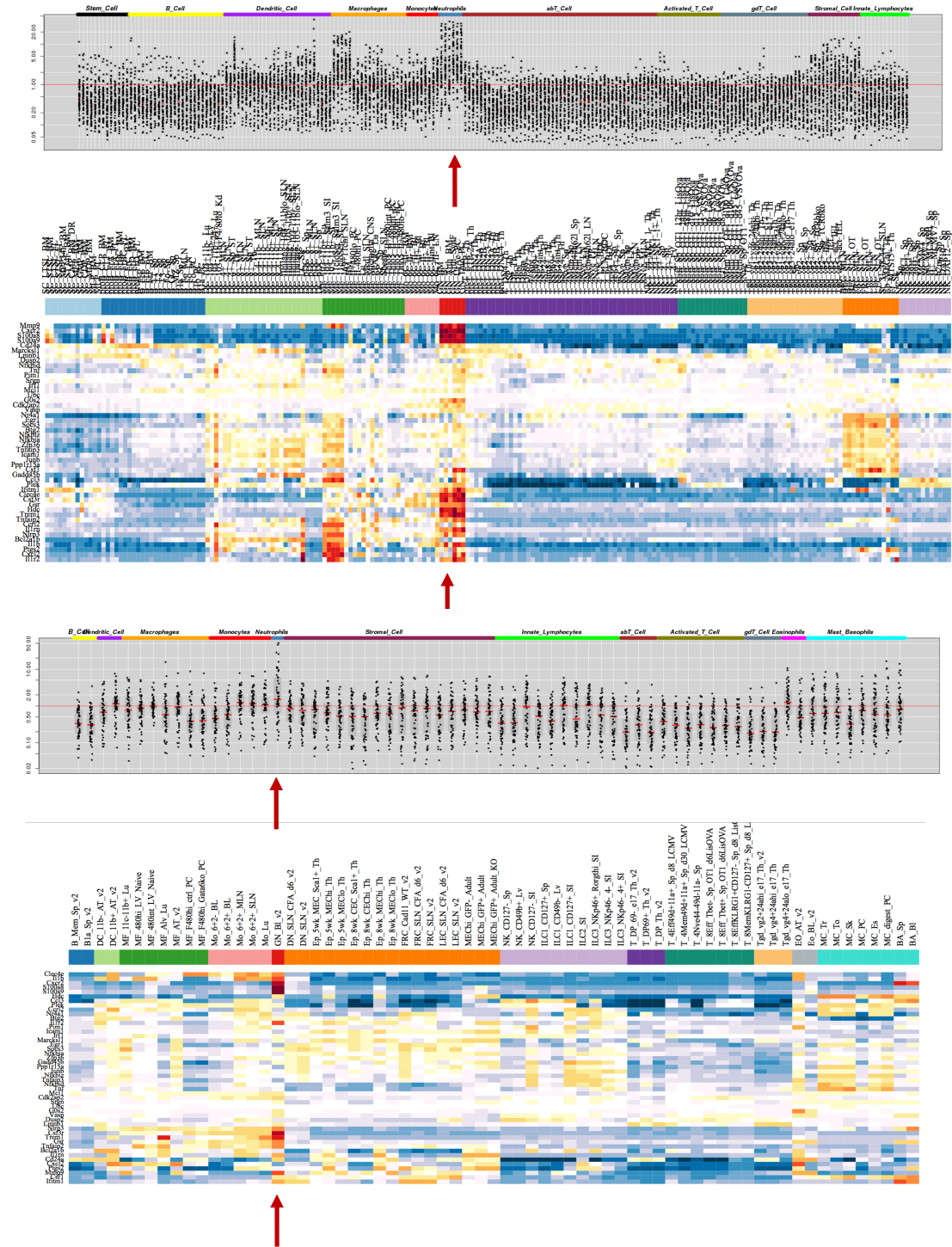
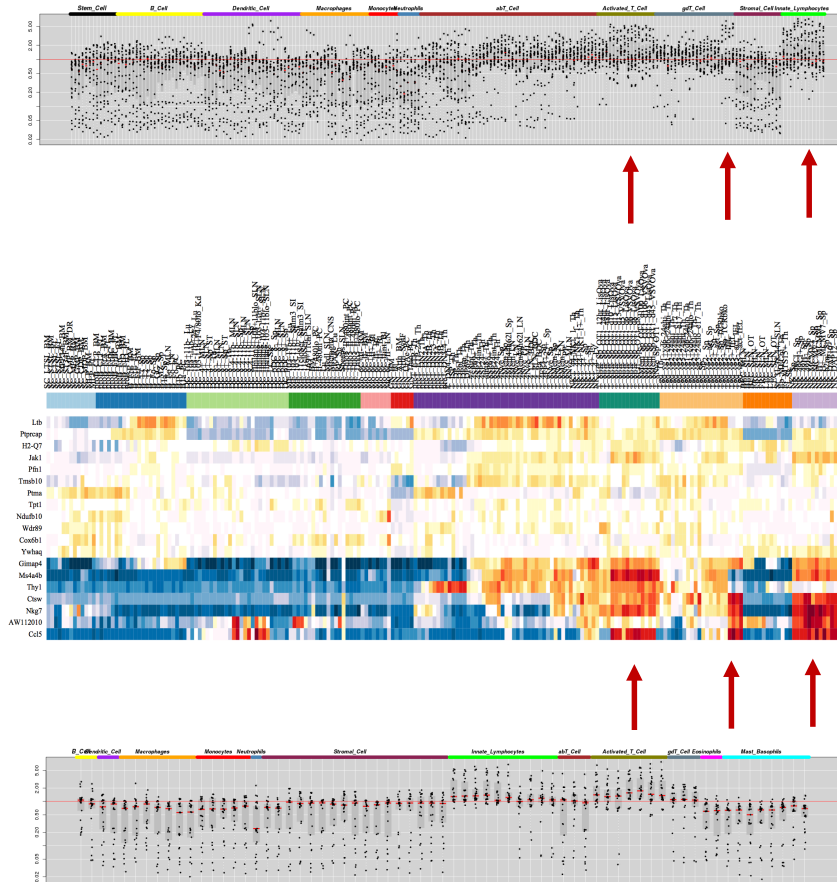


Table T2. Marker Genes Discriminating T Cells / NK Cells vs. All Other Clusters & Expression by ImmGen Datasets V1 and V2

	p_val	avg_diff	pct.1	pct.2	Index
	2.11E-30	3.201	0.571	0.001	1
Thy1	9.02E-28	2.585	0.536	0.001	2
Ms4a4b	5.91E-22	3.139	0.5	0.01	3
AW112010	5.37E-21	3.100	0.5	0.03	4
Ccl5	9.48E-15	3.383	0.429	0.013	5
Ctsw	6.60E-14	2.039	0.286	0.001	6
Ptpcap	2.51E-13	2.209	0.357	0.008	7
Gimap4	4.76E-13	2.022	0.286	0.001	8
Gm8624	1.18E-11	1.096	0.929	0.772	9
Ltb	1.83E-10	2.296	0.393	0.022	10
Gm9844	4.05E-10	1.352	0.75	0.399	11
H2.Q7	1.01E-08	1.960	0.393	0.048	12
Jak1	2.39E-08	1.797	0.393	0.232	13
Wdr89	8.77E-08	0.664	0.679	0.642	14
Ndufb10	2.54E-07	1.897	0.321	0.092	15
Ptma	5.96E-07	1.010	0.821	0.564	16
Tpt1	1.46E-06	0.688	1	0.899	17
Tmsb10	1.96E-06	1.250	0.5	0.262	18
Ywhaq	2.92E-06	1.383	0.286	0.119	19
Gm17541	3.37E-06	0.801	0.643	0.526	20
Cox6b1	4.46E-06	0.595	0.071	0.272	21
Pfn1	6.87E-06	0.931	0.607	0.503	22
NOTE:					
Marker genes not included if p < 1E-6					

V1



V2

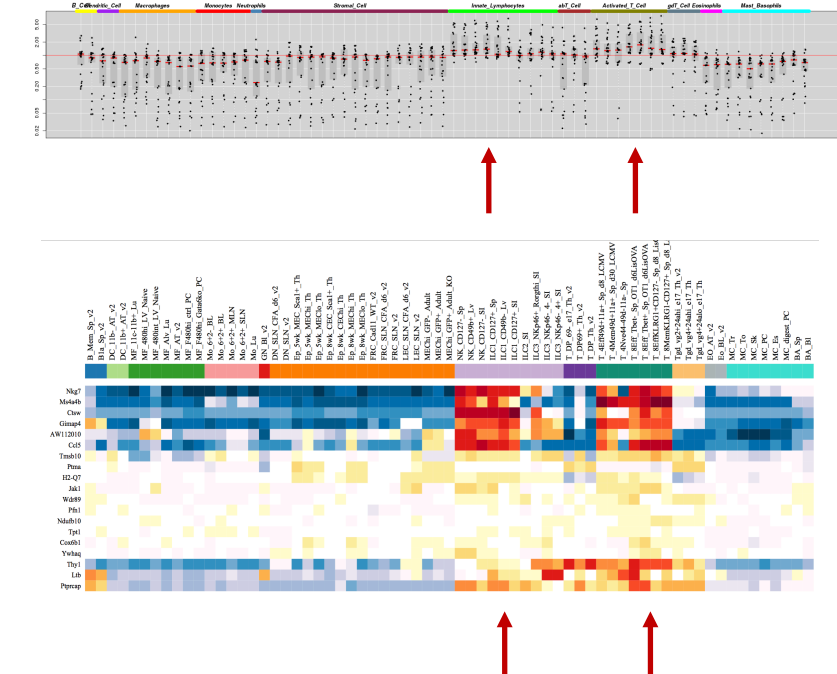


Table T3. Marker Genes Discriminating Monocytes vs. All Other Clusters & Expression by ImmGen Datasets V1 and V2

	p_val	avg_diff	pct.1	pct.2	Index
	3.03E-39	1.8878141	0.725	0.149	1
Lyz2	2.41E-35	1.2687296	0.99	0.711	2
Gm9844	9.60E-28	1.2664972	0.775	0.383	3
Ifitm6	8.44E-26	1.6556575	0.392	0.037	4
Actg1	2.47E-24	0.7137467	0.99	0.896	5
Ly6c2	1.48E-21	1.2193561	0.333	0.031	6
Ifitm3	3.38E-20	1.0655717	0.804	0.438	7
Tmsb10	4.36E-20	1.2128101	0.627	0.244	8
S100a4	6.84E-20	0.979081	0.824	0.387	9
Hp	9.86E-19	1.6577249	0.353	0.049	10
Ms4a6c	2.82E-14	0.982726	0.735	0.455	11
Ccr2	4.71E-14	1.099587	0.598	0.246	12
Chil3	1.29E-13	1.3852834	0.284	0.058	13
Vim	6.34E-13	0.7650885	0.882	0.618	14
C3	7.92E-13	1.1174667	0.284	0.048	15
Thbs1	1.20E-12	1.076147	0.549	0.228	16
Napsa	1.34E-12	1.1354792	0.373	0.09	17
Eef1a1	9.84E-12	0.5187097	0.99	0.891	18
Tpt1	1.02E-11	0.442213	1	0.895	19
Coro1a	1.57E-11	0.705812	0.735	0.465	20
Fn1	7.56E-11	0.8665351	0.716	0.423	21
S100a6	1.07E-10	0.6609656	0.784	0.534	22
Gm8624	1.79E-10	0.4686089	0.951	0.764	23
Emilin2	2.30E-10	1.1750277	0.422	0.177	24
Cybb	2.11E-09	0.9376377	0.559	0.341	25
Samhd1	1.12E-08	0.9602754	0.5	0.326	26
Srgn	1.39E-08	0.3066088	0.902	0.679	27
Ptpn1	1.40E-08	0.8968721	0.51	0.244	28
Ahnak	1.85E-08	0.9263587	0.529	0.285	29
Smpd13a	3.59E-08	1.087457	0.304	0.107	30
Msrb1	4.02E-08	0.8124817	0.52	0.271	31
Cytip	5.54E-08	0.9833889	0.324	0.106	32
Ifitm2	7.70E-08	0.6827715	0.627	0.356	33
Alox5ap	2.13E-07	0.6324217	0.716	0.511	34
Plbd1	2.84E-07	0.8345495	0.431	0.181	35
Il17ra	3.15E-07	1.2383521	0.275	0.103	36
Crip1	4.91E-07	0.8000464	0.539	0.318	37
Lgals3	9.64E-07	0.447887	0.735	0.503	38
Pld4	1.41E-06	0.79186	0.382	0.207	39
Ly6e	3.79E-06	0.5204468	0.725	0.473	40
Ccl9	5.18E-06	0.7466229	0.471	0.261	41
Flna	6.42E-06	0.7747612	0.5	0.288	42
F13a1	9.40E-06	0.9309539	0.324	0.149	43
NOTE:					
Marker genes not included if p < 1E-6					

V1

V2

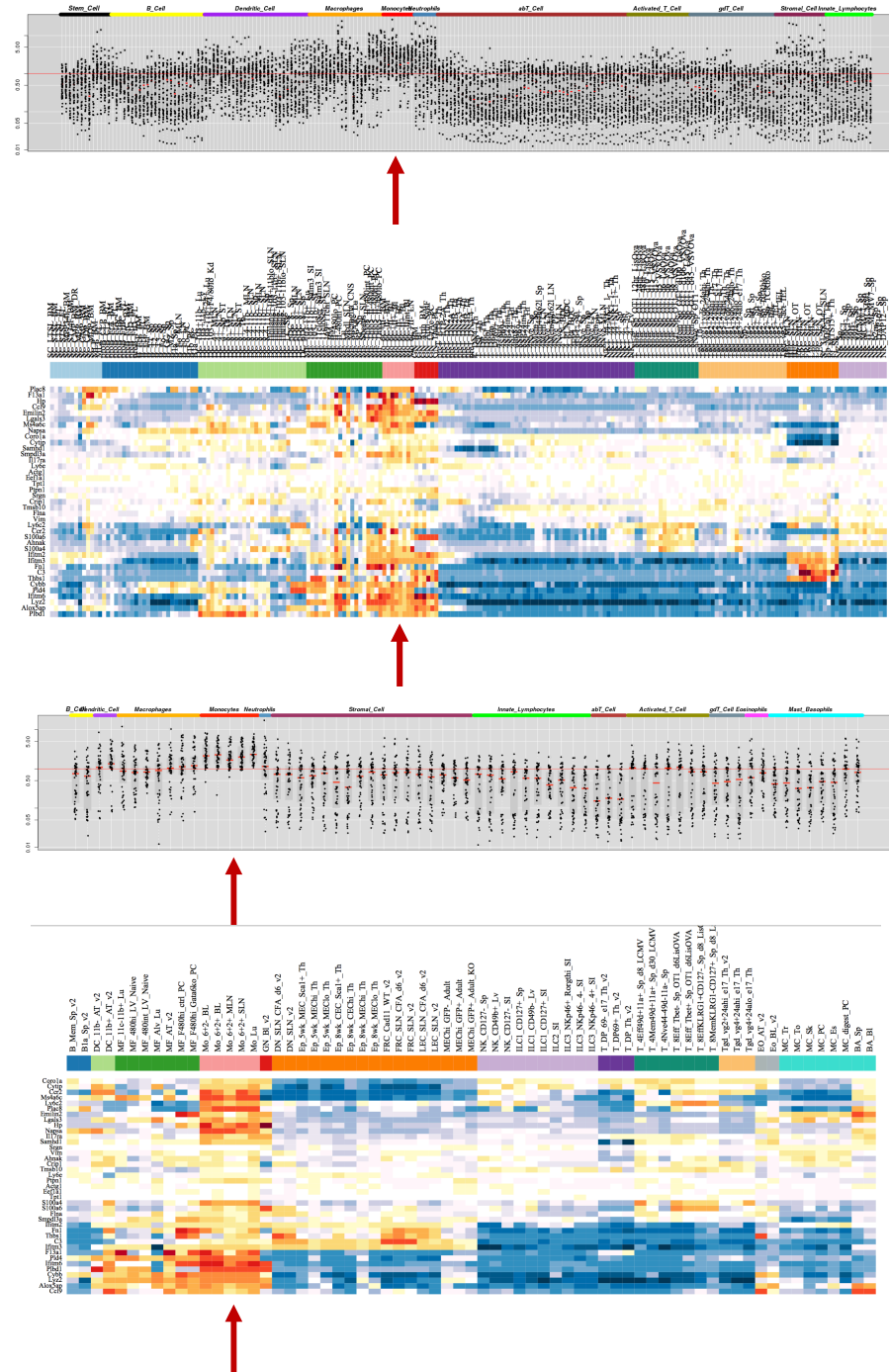
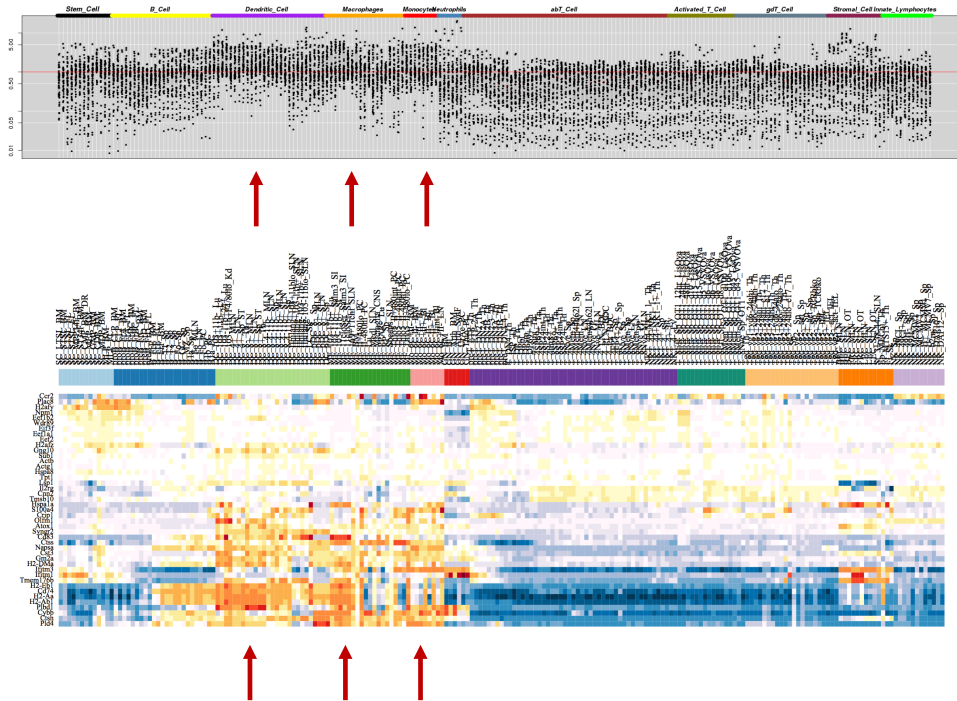


Table T4. Marker Genes Discriminating DCs and MHCII Macrophages vs All Other Clusters & Expression by ImmGen Datasets V1 and V2

	p_val	avg_diff	pct.1	pct.2	Index
	1.40E-243	2.8953498	0.964	0.264	1
H2.Eb1	3.83E-235	2.9838973	0.952	0.257	2
Cd74	7.45E-234	2.5191718	0.976	0.318	3
H2.Ab1	1.74E-212	2.6588799	0.919	0.135	4
H2.DMb1	4.47E-70	1.8297806	0.497	0.069	5
H2.DMa	1.28E-61	1.5305527	0.506	0.098	6
Tmem176b	3.87E-34	1.302146	0.401	0.103	7
Eef1a1	9.69E-33	0.4482603	0.994	0.875	8
Plbd1	4.82E-27	0.8231155	0.428	0.143	9
Rack1	3.42E-25	0.5179049	0.889	0.64	10
Hspa1b	4.20E-25	1.1437332	0.434	0.159	11
Napsa	5.83E-23	0.9680064	0.281	0.067	12
Tpt1	9.82E-23	0.3335181	0.979	0.884	13
Olfm1	8.12E-22	1.1609463	0.263	0.068	14
Gm8624	2.23E-21	0.438577	0.922	0.741	15
Gm2a	8.49E-21	0.7535648	0.599	0.329	16
Crip1	3.84E-19	0.791396	0.515	0.29	17
Cst3	6.34E-18	0.6352142	0.832	0.67	18
Gm17541	1.72E-17	0.4496434	0.731	0.483	19
Gng10	2.31E-16	0.9078513	0.32	0.121	20
Hspa1a	1.39E-15	0.8332575	0.446	0.22	21
Syng2	6.56E-15	0.8156688	0.29	0.118	22
Hspa8	6.59E-15	0.3736983	0.856	0.669	23
S100a4	1.54E-14	0.6766029	0.584	0.373	24
Eef1b2	2.84E-14	0.499485	0.599	0.358	25
Actg1	9.28E-14	0.250814	0.97	0.886	26
Cd83	2.01E-13	0.8340102	0.383	0.19	27
Cnn2	2.44E-13	0.7243477	0.281	0.106	28
Ifitm1	3.11E-13	1.0591874	0.323	0.152	29
Ccr2	5.83E-13	0.5874642	0.437	0.228	30
Ifitm3	8.31E-12	0.534256	0.614	0.424	31
Ctss	2.08E-11	0.342482	0.829	0.638	32
Sub1	2.10E-11	0.705828	0.35	0.173	33
Il2rg	4.17E-11	0.870753	0.269	0.127	34
Wdr89	5.16E-11	0.3765699	0.787	0.61	35
Actb	5.24E-11	0.2669947	0.979	0.906	36
Tmsb10	9.25E-11	0.5830557	0.416	0.232	37
Gm9844	1.77E-10	0.5090478	0.524	0.378	38
Plac8	2.67E-10	0.5605564	0.317	0.151	39
Eif3f	5.21E-10	0.6562466	0.317	0.155	40
Cybb	7.41E-10	0.453552	0.515	0.318	41
Eef2	3.42E-09	0.397018	0.629	0.442	42
H2afy	3.52E-09	0.7383702	0.365	0.199	43
Ctsh	4.78E-09	0.4856672	0.521	0.337	44
Npm1	4.79E-09	0.413198	0.389	0.218	45
X1700073E17Rik	1.10E-08	0.393853	0.485	0.311	46
H2afz	1.86E-08	0.4343918	0.434	0.259	47
Lsp1	1.93E-08	0.4149484	0.392	0.228	48
Pld4	2.75E-08	0.3298967	0.341	0.19	49
Atox1	7.83E-08	0.386581	0.449	0.282	50

V1



V2

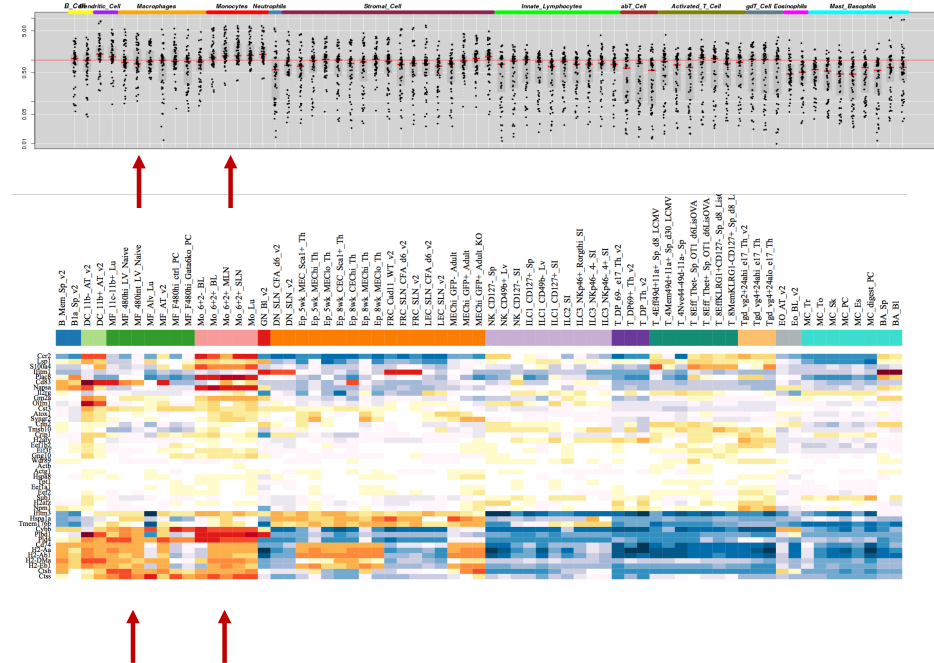
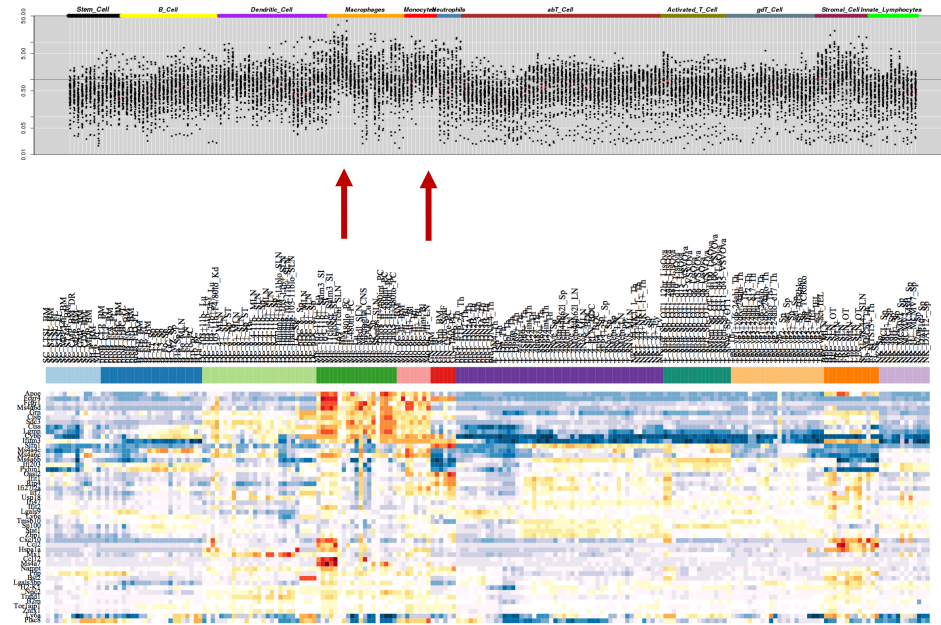


Table T5. Marker Genes Discriminating IFNIC Cardiac Macrophages vs All Other Clusters & Expression by ImmGen Datasets V1 and V2

	p_val	avg_diff	pct.1	pct.2	Index
Ifit2	9.20E-40	2.2497772	0.341	0.012	1
Irf7	8.95E-37	1.633694	0.543	0.087	2
Ifit1	1.20E-31	1.7309566	0.304	0.015	3
Mx1	6.33E-28	1.7234805	0.29	0.018	4
Ms4a4c	1.34E-27	1.6791356	0.486	0.098	5
Usp18	3.68E-26	1.6709251	0.304	0.025	6
Ifi47	5.29E-25	1.611792	0.333	0.039	7
Ifitm3	1.16E-24	0.8960768	0.633	0.428	8
Ly6a	5.64E-23	1.7662152	0.37	0.065	9
Bst2	5.35E-22	1.1259478	0.616	0.217	10
Cxcl10	7.13E-22	1.9792523	0.348	0.081	11
Fcgr1	7.69E-22	1.1204018	0.601	0.202	12
Znfx1	5.39E-20	1.1780485	0.348	0.059	13
Ifi203	1.25E-19	1.5970446	0.333	0.055	14
Pyhin1	1.55E-19	1.2952298	0.348	0.059	15
Lgals3bp	3.66E-19	1.0383473	0.594	0.222	16
Ccl12	1.24E-17	1.3153175	0.384	0.091	17
Ly6e	1.36E-17	0.7720473	0.604	0.461	18
Oasl2	1.67E-17	0.964558	0.333	0.062	19
Pnp	2.48E-17	1.191605	0.543	0.225	20
Stat1	1.54E-16	1.0485965	0.406	0.103	21
Sdc3	2.86E-16	0.9764329	0.58	0.242	22
Zbp1	1.72E-15	1.2092081	0.312	0.061	23
Lgals9	2.50E-13	0.9123917	0.5	0.193	24
Ms4a6c	6.52E-13	0.5775978	0.754	0.448	25
Ctsb	5.21E-12	0.3376105	0.942	0.759	26
Fcgr4	1.08E-10	0.9167507	0.312	0.088	27
Apoe	1.42E-10	0.4337064	0.506	0.666	28
Grn	2.17E-10	0.518762	0.662	0.647	29
Rtp4	2.65E-10	1.1326315	0.268	0.067	30
Ifi2712a	2.69E-10	0.9023308	0.384	0.144	31
Sp100	4.33E-10	0.8399678	0.37	0.128	32
Sifn1	5.71E-10	0.7848551	0.275	0.075	33
Plac8	6.99E-10	1.145184	0.399	0.163	34
B2m	7.32E-10	0.4687053	0.906	0.787	35
Ms4a6b	8.85E-10	0.961677	0.406	0.177	36
Ccl2	3.80E-09	0.9394994	0.449	0.202	37
Npc2	9.58E-09	0.6071815	0.717	0.474	38
Trafd1	1.60E-08	0.8169772	0.268	0.08	39
Nampt	2.06E-08	0.8239477	0.254	0.073	40
Ms4a6d	4.54E-08	0.527764	0.601	0.341	41
Hspa1a	6.67E-08	0.4658433	0.486	0.243	42
Cybb	1.22E-07	0.5927865	0.587	0.334	43
Ms4a7	1.37E-07	0.7091168	0.406	0.201	44
Lgmn	1.72E-07	0.4431669	0.775	0.542	45
Tor1aip1	1.95E-07	0.6572156	0.29	0.103	46
F630040K05Rik	2.30E-07	0.690849	0.254	0.087	47
Tmsb10	2.49E-07	0.428099	0.471	0.249	48
Ctss	2.66E-07	0.4280548	0.555	0.658	49
H2.K1	4.79E-07	0.485526	0.775	0.551	50

V1



V2

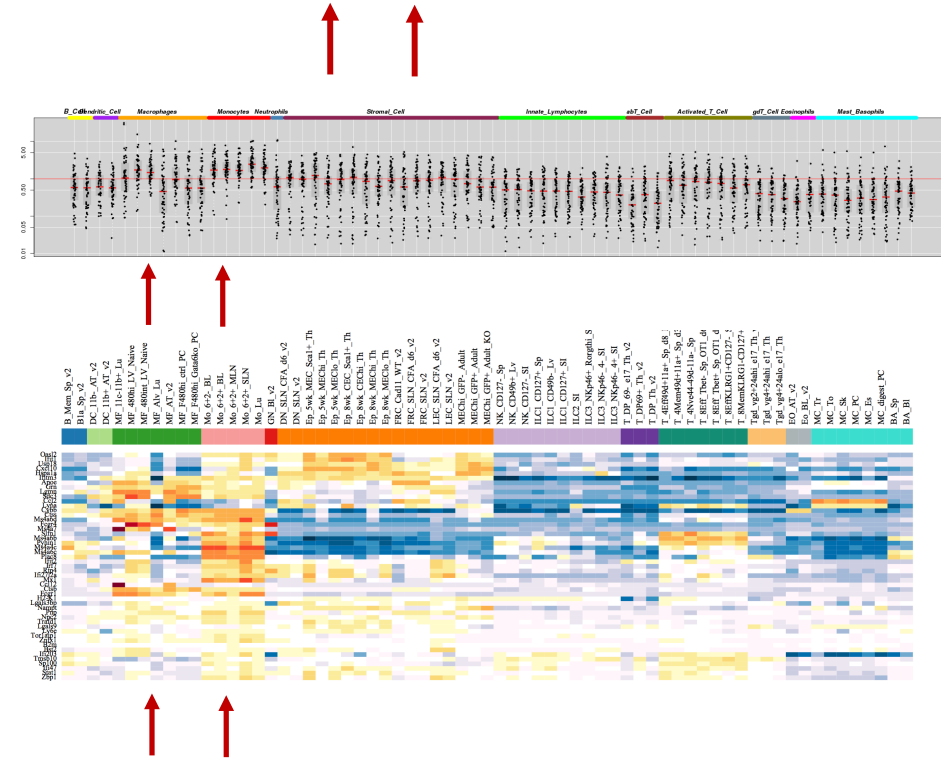


Table T7. Marker Genes Discriminating IFNIC Cardiac Macrophage vs. Nearest Macrophage Clusters

	p_val	avg_diff	pct.1	pct.2	Index	Known IRF3-	
Top 25 IFNIC Marker Genes	Isg15	7.25E-43	2.385147	0.761	0.1	1	1
	Ifit3	2.29E-30	2.137082	0.42	0.004	2	1
	Ifitm3	8.34E-29	1.357727	0.833	0.362	3	1
	Rsad2	1.70E-27	2.598378	0.457	0.029	4	1
	Irf7	2.65E-27	1.873448	0.543	0.057	5	1
	Ly6e	8.85E-26	1.288033	0.804	0.283	6	1
	Ms4a4c	1.05E-24	1.962114	0.486	0.043	7	
	Ifit2	2.99E-23	2.398901	0.341	0.004	8	1
	Plac8	6.95E-23	2.723074	0.399	0.029	9	
	Ifit1	3.83E-22	1.912645	0.304	0	10	1
	Ly6a	1.32E-19	2.175935	0.37	0.025	11	1
	Mx1	3.16E-19	1.922466	0.29	0.007	12	1
	Ifi47	1.62E-17	1.823248	0.333	0.025	13	1
	Ifi203	4.57E-17	1.93192	0.333	0.032	14	1
	Usp18	4.73E-16	1.787204	0.304	0.018	15	1
	Sifn1	2.22E-15	1.851305	0.275	0.018	16	1
	Stat1	6.60E-15	1.172177	0.406	0.068	17	1
	Znfx1	5.53E-14	1.272844	0.348	0.047	18	1
	Cxcl10	9.33E-14	2.163769	0.348	0.075	19	1
	Pyhin1	1.03E-13	1.507318	0.348	0.057	20	1
	Oasl2	4.94E-13	1.213093	0.333	0.05	21	1
	Zbp1	9.59E-13	1.423133	0.312	0.039	22	1
	Fgl2	1.20E-11	1.626506	0.297	0.043	23	
	Bst2	2.09E-11	0.856792	0.616	0.251	24	1
	Ifi2712a	3.84E-11	1.183773	0.384	0.09	25	1
	Lgals3bp	4.84E-11	0.838703	0.594	0.24	26	
	Cybb	7.47E-11	0.997945	0.587	0.258	27	
	Pnp	2.07E-10	1.018324	0.543	0.208	28	
	B2m	3.41E-10	0.542516	0.906	0.785	29	
	Cd52	4.07E-10	0.879583	0.674	0.333	30	
	Rtp4	8.23E-10	1.101674	0.268	0.043	31	
	Fcgr1	1.19E-09	0.745661	0.601	0.272	32	
	Fcgr4	4.65E-09	1.113389	0.312	0.068	33	
	Sp100	5.79E-09	1.039746	0.37	0.115	34	
	Ms4a6c	6.95E-09	0.546688	0.754	0.448	35	
	H2.K1	1.37E-08	0.760059	0.775	0.516	36	
	Cd74	2.06E-08	1.284161	0.514	0.29	37	
	H2.Aa	2.33E-08	1.671911	0.442	0.215	38	
	Ccl12	6.95E-08	1.018449	0.384	0.125	39	
	Lgals9	7.09E-08	0.851786	0.5	0.215	40	
	Ms4a6b	7.93E-08	1.087127	0.406	0.172	41	
	H2.T23	1.14E-07	0.604112	0.399	0.143	42	
	Cdkn1a	2.15E-07	0.780549	0.543	0.262	43	
	Psme1	5.02E-07	1.025067	0.333	0.115	44	
	Tmsb10	8.74E-07	0.666882	0.471	0.208	45	
	Ccl4	9.66E-07	0.924913	0.572	0.337	46	
	Ccdc62	1.15E-06	0.507871	0.29	0.093	47	
	H2.Eb1	2.20E-06	1.527816	0.37	0.222	48	
	Samhd1	3.04E-06	0.855966	0.493	0.247	49	
	Zfp36	8.84E-06	0.458738	0.862	0.688	50	