

Supplemental Table 1: Primer used in this study

hMLKL_for	CCCATGATCCCTCTGTGC
hMLKL_rev	GACTCCTTGGTTTAGATTTTGATACAC
hIRF1_for	ACA GCA CCA GTG ATC TGT ACA AC
hIRF1_rev	TTC CCT TCC TCA TCC TCA TCT
h28S_for	TTGAAAATCCGGGGGAGAG
h28S_rev	ACATTGTTCCAACATGCCAG
hRIPK1_for	GTGTACAAGGGGCCCAACT
hRIPK1_rev	CGGCTGTGTCTCAGTCTGTT
hRIPK3_for	GCCTCCACAGCCAGTGAC
hRIPK3_rev	TCGGTTGGCAACTCAACTT

Supplemental Table 2: gRNAs used in this study

IRF1 gRNA1	TTAATTCCAACCAAATCCCG
IRF1 gRNA2	TCTAGGCCGATACAAAGCAG
IRF1 gRNA3	GAACTCCCTGCCAGATATCG

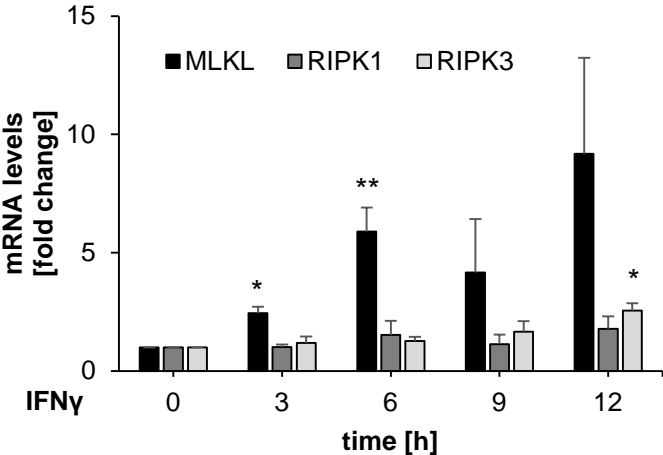
Supplemental Table 3: Results for upregulation of MLKL in DNA microarrays using platform Interferome

Dataset ID	Fold Change	Interferon Type	Treatment Time [h]	Probe ID	In Interferome deposited publication
147	3.199128	I	4	A_24_P185044	PMID: 25536401
315	2.4995701	II	6	A_24_P185044	no publication deposited
318	2.497687	II	6	A_24_P185044	PMID: 23801603
125	3.4278443	I	3	A_23_P61050	no publication deposited
147	3.194414	I	4	A_23_P61050	PMID: 25536401
174	2.0067785	II	20	A_23_P61050	PMID: 27233968
226	2.5212712	I	6	A_23_P61050	no publication deposited
293	16.121225	II	24	A_23_P61050	PMID: 27770554
294	3.5354736	I	72	A_23_P61050	PMID: 25414701
315	2.9219253	II	6	A_23_P61050	no publication deposited
318	2.9206066	II	6	A_23_P61050	PMID: 23801603
44	2.54955	I	6	238025_at	PMID: 20483728
67	5.379501	I	6	238025_at	PMID: 22875473
144	5.7262244	II	24	238025_at	PMID: 25168428
185	2.7878575	I	16	238025_at	PMID: 24569457
300	2.4528027	I	6	238025_at	PMID: 20805419
305	2.2880716	II	1.5	238025_at	PMID: 22610275
306	2.308728	I	1.5	238025_at	PMID: 22610275
75	2.02588	I	16	ILMN_1667825	PMID: 23626809
78	2.3977	I	12	ILMN_1667825	PMID: 23045702
81	2.18407	I	4	ILMN_1667825	PMID: 23045702
82	2.72911	II	12	ILMN_1667825	PMID: 23045702
83	2.69625	II	24	ILMN_1667825	PMID: 23045702
128	6.2672963	II	10	ILMN_1667825	PMID: 26424569
129	7.0557027	I	10	ILMN_1667825	PMID: 26424569
130	5.0771055	I	10	ILMN_1667825	PMID: 26424569
131	6.8568344	II	10	ILMN_1667825	PMID: 26424569
161	4.46232	I	6	ILMN_1667825	PMID: 24065129
162	4.98231	II	6	ILMN_1667825	PMID: 24065129
163	4.1562304	I	3	ILMN_1667825	PMID: 20956346
275	6.420122	I	8	ILMN_1667825	PMID: 22851595
276	5.1070356	I	2	ILMN_1667825	PMID: 22851595
277	5.8366957	I	8	ILMN_1667825	PMID: 22851595
278	4.5659633	I	2	ILMN_1667825	PMID: 22851595
280	2.1331036	I	48	ILMN_1667825	no publication deposited
281	2.233389	I	48	ILMN_1667825	no publication deposited
284	4.0358825	II	6	ILMN_1667825	PMID: 26030458
373	2.003676	I	24	ILMN_1667825	PMID: 23633948

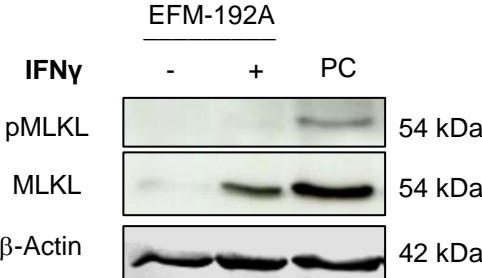
Supplemental Table 3 continued

<b>Dataset ID</b>	<b>Fold Change</b>	<b>Interferon Type</b>	<b>Treatment Time [h]</b>	<b>Probe ID</b>	<b>In Interferome deposited publication</b>
374	2.4460273	I	6	ILMN_1667825	PMID: 23633948
375	2.4212413	I	6	ILMN_1667825	PMID: 23633948
78	2.12785	I	12	ILMN_1715863	PMID: 23045702
82	2.19505	II	12	ILMN_1715863	PMID: 23045702
128	5.0299034	II	10	ILMN_1715863	PMID: 26424569
129	5.98513	I	10	ILMN_1715863	PMID: 26424569
130	4.0076976	I	10	ILMN_1715863	PMID: 26424569
131	5.810739	II	10	ILMN_1715863	PMID: 26424569
275	4.7557836	I	8	ILMN_1715863	PMID: 22851595
277	5.095506	I	8	ILMN_1715863	PMID: 22851595
278	3.021476	I	2	ILMN_1715863	PMID: 22851595
82	2.35299	II	12	ILMN_1737498	PMID: 23045702
83	2.37726	II	24	ILMN_1737498	PMID: 23045702
128	6.188601	II	10	ILMN_1737498	PMID: 26424569
129	7.521052	I	10	ILMN_1737498	PMID: 26424569
130	5.4541273	I	10	ILMN_1737498	PMID: 26424569
131	5.5040517	II	10	ILMN_1737498	PMID: 26424569
161	3.15909	I	6	ILMN_1737498	PMID: 24065129
162	3.31444	II	6	ILMN_1737498	PMID: 24065129
163	2.6113572	I	3	ILMN_1737498	PMID: 20956346
275	5.5661116	I	8	ILMN_1737498	PMID: 22851595
276	3.2793548	I	2	ILMN_1737498	PMID: 22851595
277	3.9632547	I	8	ILMN_1737498	PMID: 22851595
278	2.264143	I	2	ILMN_1737498	PMID: 22851595
143	4.3258543	I	6	8002778	PMID: 22005912
201	2.9556017	I	2	8002778	PMID: 24561305
202	2.20003	I	6	8002778	PMID: 24561305
301	3.5955815	I	6	8002778	PMID: 22677194
302	4.2909565	II	24	8002778	PMID: 22677194
303	2.6675231	I	24	8002778	PMID: 22677194
304	2.8380008	II	6	8002778	PMID: 22677194
307	5.3234553	II	48	8002778	PMID: 23150618
308	2.6459115	II	48	8002778	PMID: 23150618

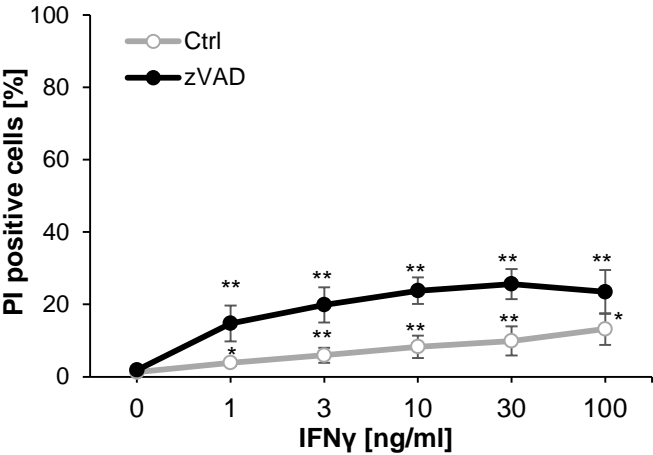
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



## Supplemental figure legends

### **Suppl. Fig. 1: Effect of IFN $\gamma$ on RIPK1 or RIPK3 expression.**

EFM-192A cells were treated for indicated time points with 1.5 ng/ml IFN $\gamma$ . mRNA levels of MLKL, RIPK1 and RIPK3 were quantified by qRT-PCR analysis and are shown as fold increase relative to untreated control cells with mean and SEM of at least three independent experiments performed in duplicate; \*P < 0.05; \*\*P < 0.01.

### **Suppl. Fig. 2: Effect of IFN $\gamma$ on MLKL phosphorylation.**

EFM-192A cells were treated with 1.5 ng/ml IFN $\gamma$  for 24 hours. Protein expression of phospho-MLKL (pMLKL), MLKL and  $\beta$ -Actin was analyzed by Western blotting. As positive control (PC) for pMLKL, HT-29 cells were treated with 1  $\mu$ M BV6 and 20  $\mu$ M zVAD.fmk for 24 hours.

### **Suppl. Fig. 3: IFN $\gamma$ induces cell death when caspases are inhibited.**

EFM-192A cells were treated with indicated concentrations of IFN $\gamma$  with or without 20  $\mu$ M zVAD.fmk for 72 hours. Cell death was determined by PI/HOECHST staining and ImageXpress Micro XLS system. Mean and SD of at least three independent experiments performed in duplicates are shown; \*P < 0.05; \*\*P < 0.01.