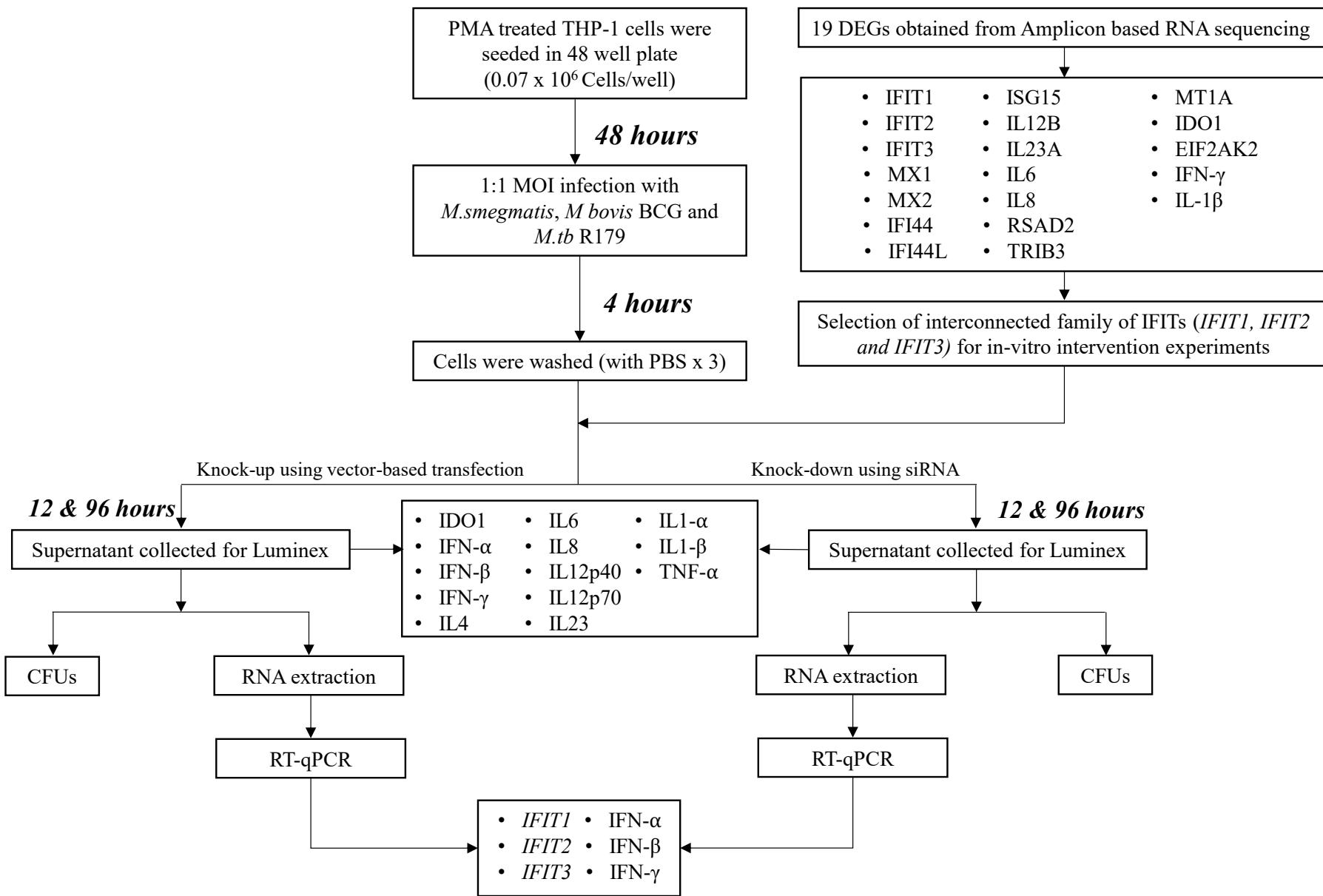


Supplementary data

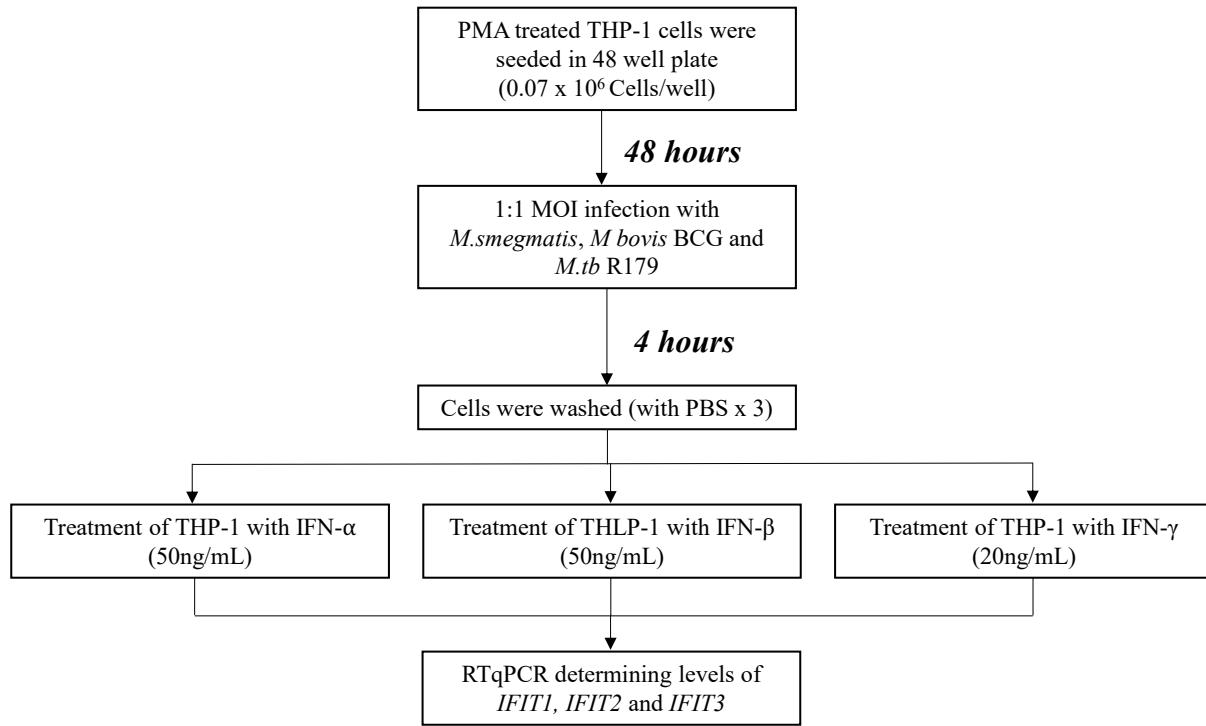
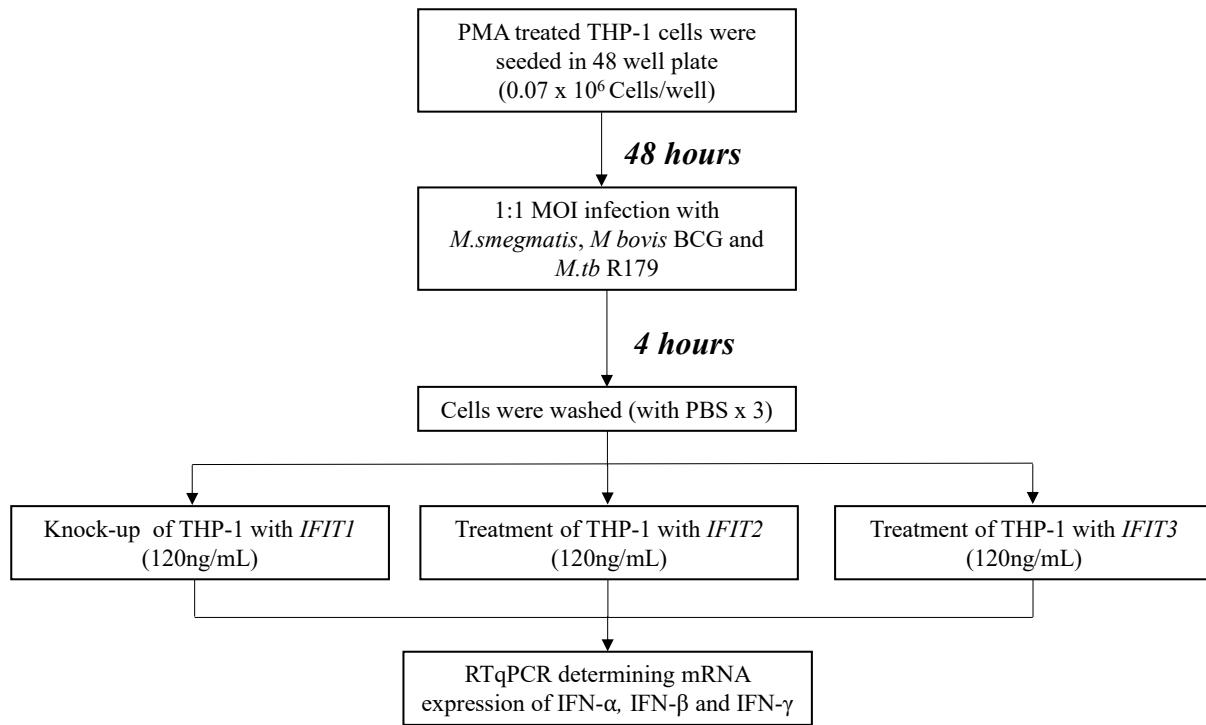
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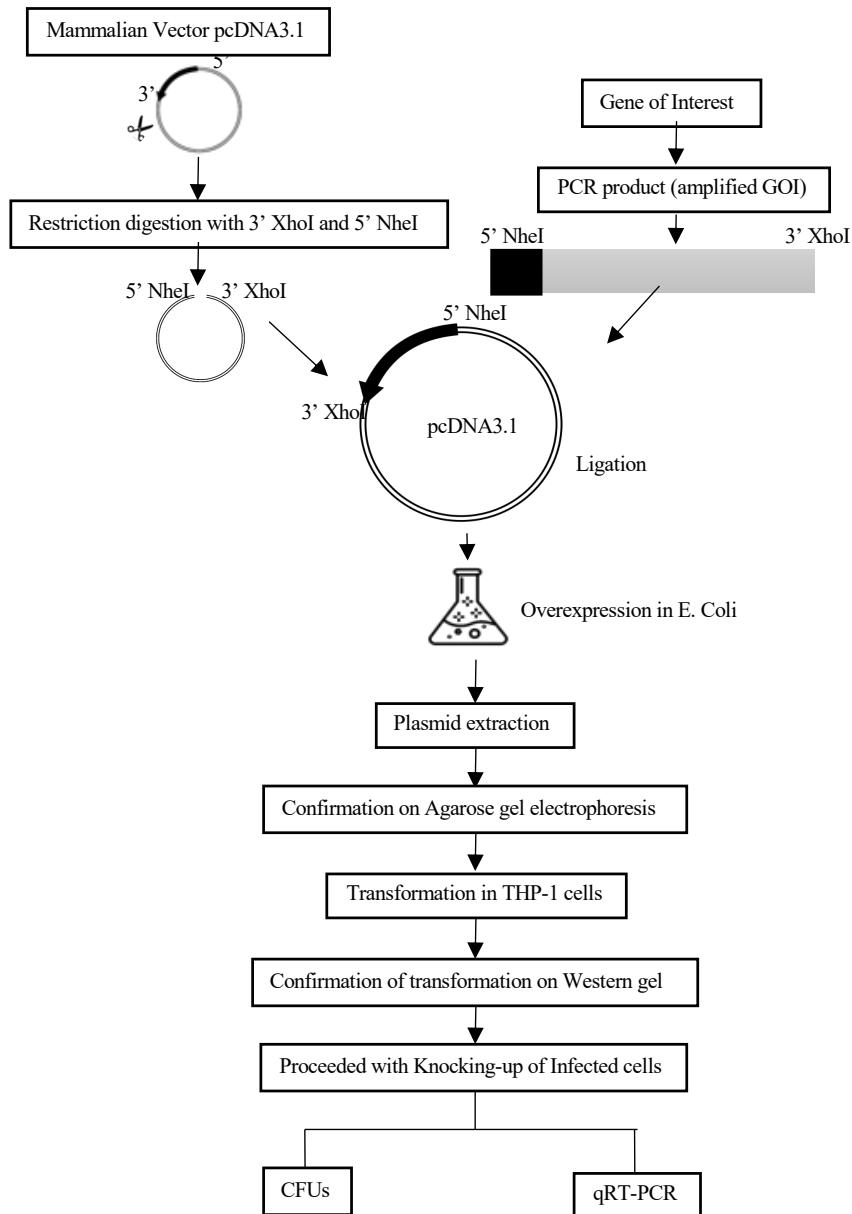
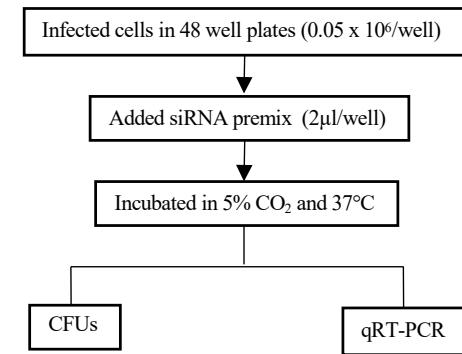
Supplementary Figure 1: Flow of methodology adopted for the knock-up and knock-down experiments.

Abbreviations: CFUs= colony forming units, BCG=Bacillus Calmette–Guerin, DEGs= Differentially expressed genes, EIF2AK2=eukaryotic translation initiation factor 2 alpha kinase 2, FDR=false discovery rate, IDO=indoleamine 2,3-dioxygenase, hMDMs=human monocyte-derived macrophages, IFI=interferon-induced protein, IFIT=interferon-induced protein with tetratricopeptide, IFN=interferon gamma, IL=interleukin, ISG=interferon-stimulated gene, MOI= multiplicity of infection, MTA=metastasis-associated protein, MX=interferon-induced GTP binding protein, PMA= Phorbol 12-myristate 13-acetate, RSAD=radical S-adenosyl methionine domain-containing protein 2, qRT-PCR=Quantitative reverse transcription polymerase chain reaction, TRIB= trible homolog, UBC=polyubiquitin-C.

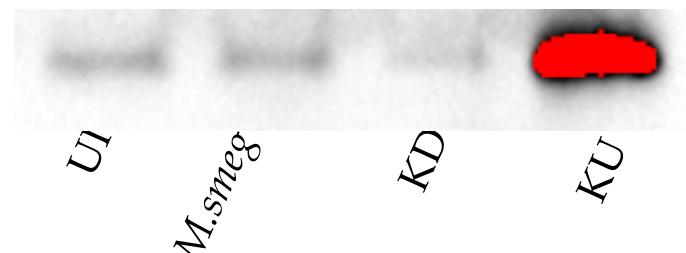
A**B**

Supplementary Figure 2: Flow diagram depicting the effect of co-stimulation with IFN- α , IFN- β and IFN- γ on expression of IFITs determined by qRT-PCR (A) and the effect of knock-up of IFITs on the mRNA expression of IFN- α , IFN- β and IFN- γ (B).

Abbreviations: PMA= Phorbol Myristate Acetate, MOI= Multiplicity of infection, BCG= Bacillus Calmette-Guérin, PBS= Phosphate-buffered saline, THP-1 cells= human monocyte derived macrophages, IFN= Interferon, IFIT= Interferon-induced protein with tetratricopeptide repeats

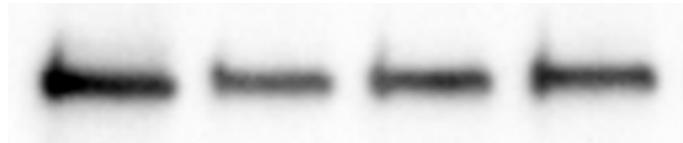
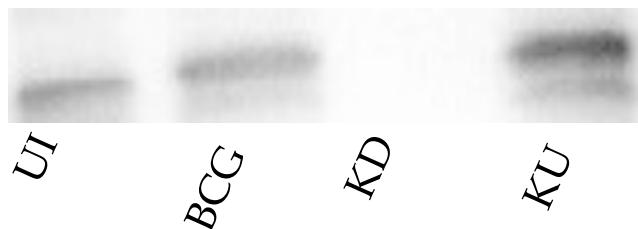
A**B**

Supplementary Figure 3: Flow diagram describing knock-up and knock-down of IFITs. Flow depicts (A) cloning and vector (*E. Coli*) derived overexpression of *IFITs* (knock-up) and (B) siRNA targeting *IFITs* (knock-down) in THP-1 cells.

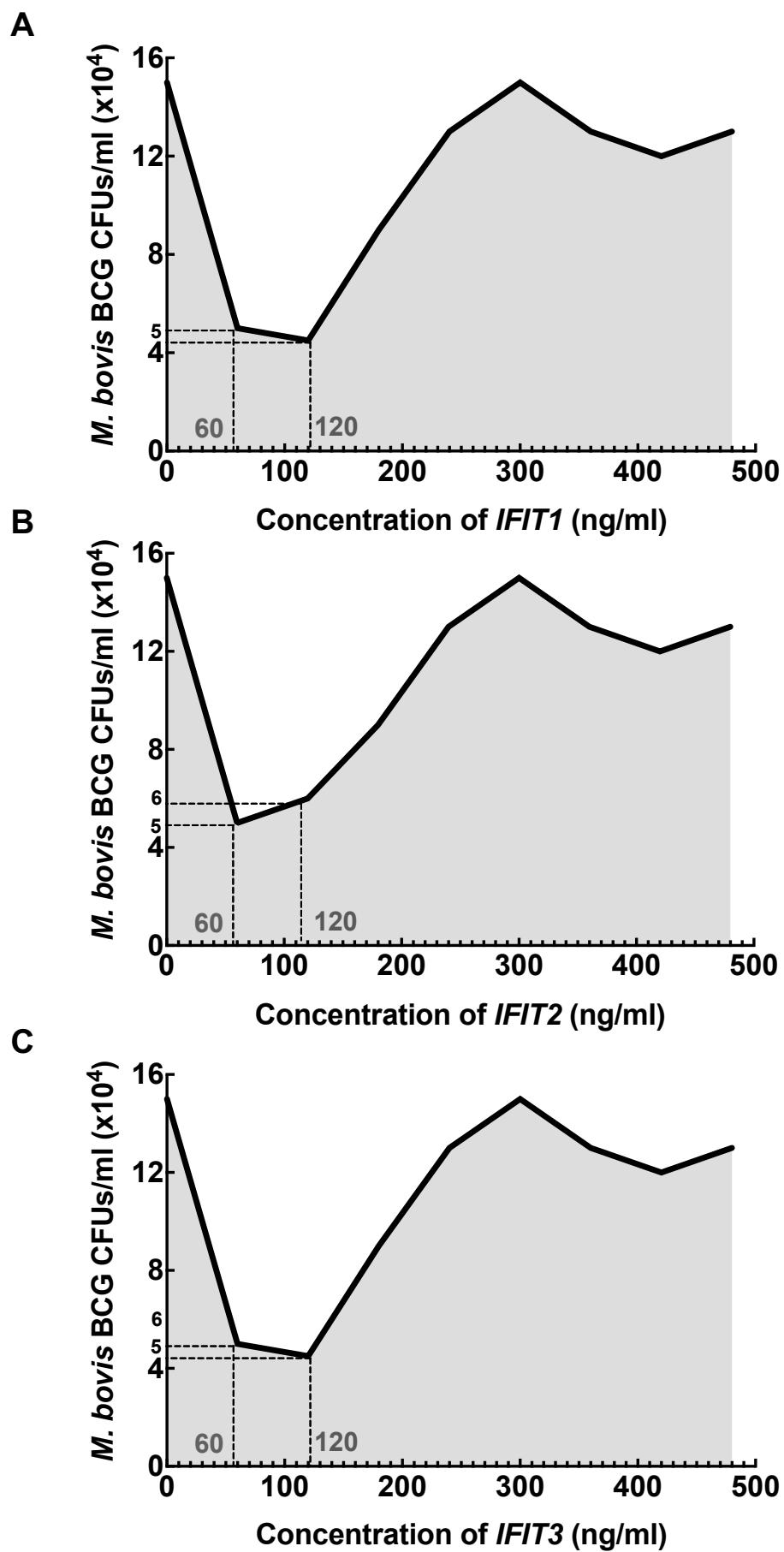


Supplementary Figure 4:
Representative Western Blot confirming knock-down and knock-up (vector based overexpression) of IFIT1 in THP-1 infected with *M.smegmatis*, *M bovis BCG*, and *R179* at 12-hours post infection (IFIT1-55KDa, GAPDH-37KDa)

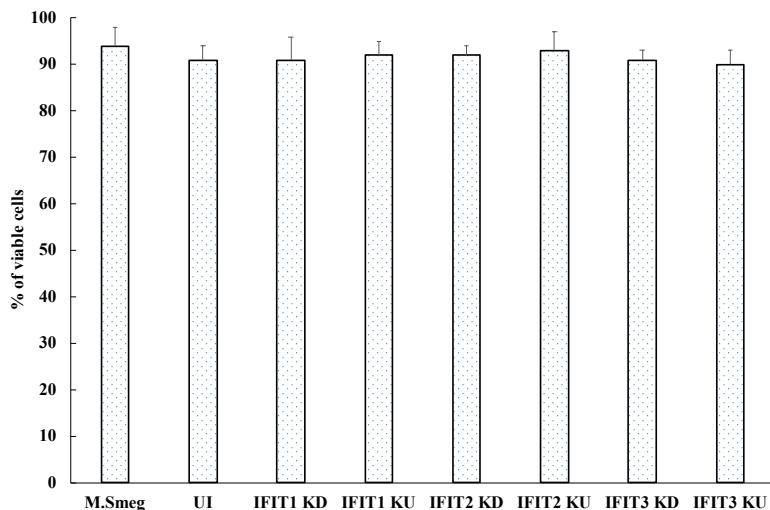
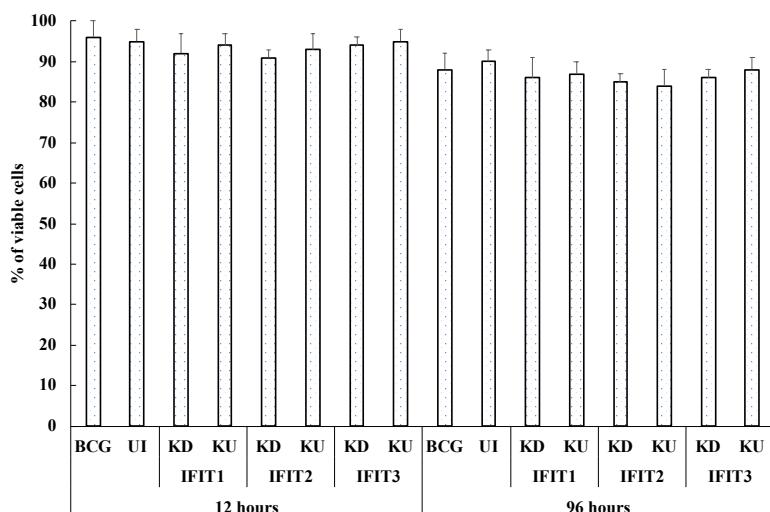
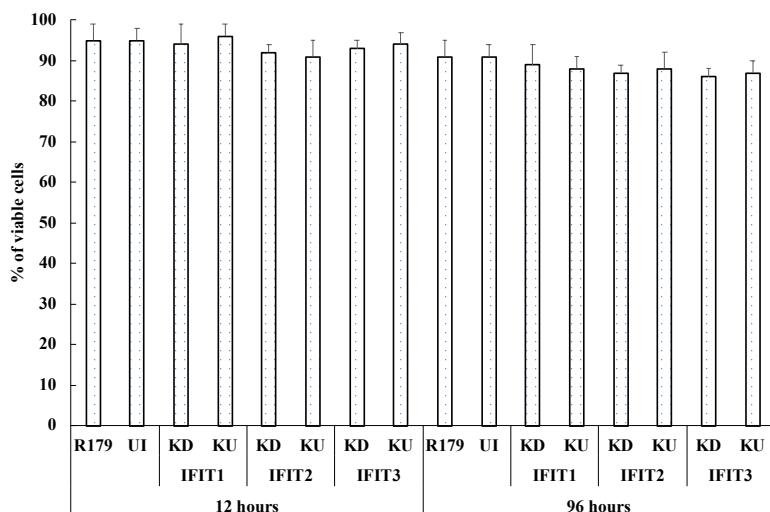
Abbreviations: KD=Knock-down, KU=Knock-up, UI=Uninfected



GAPDH

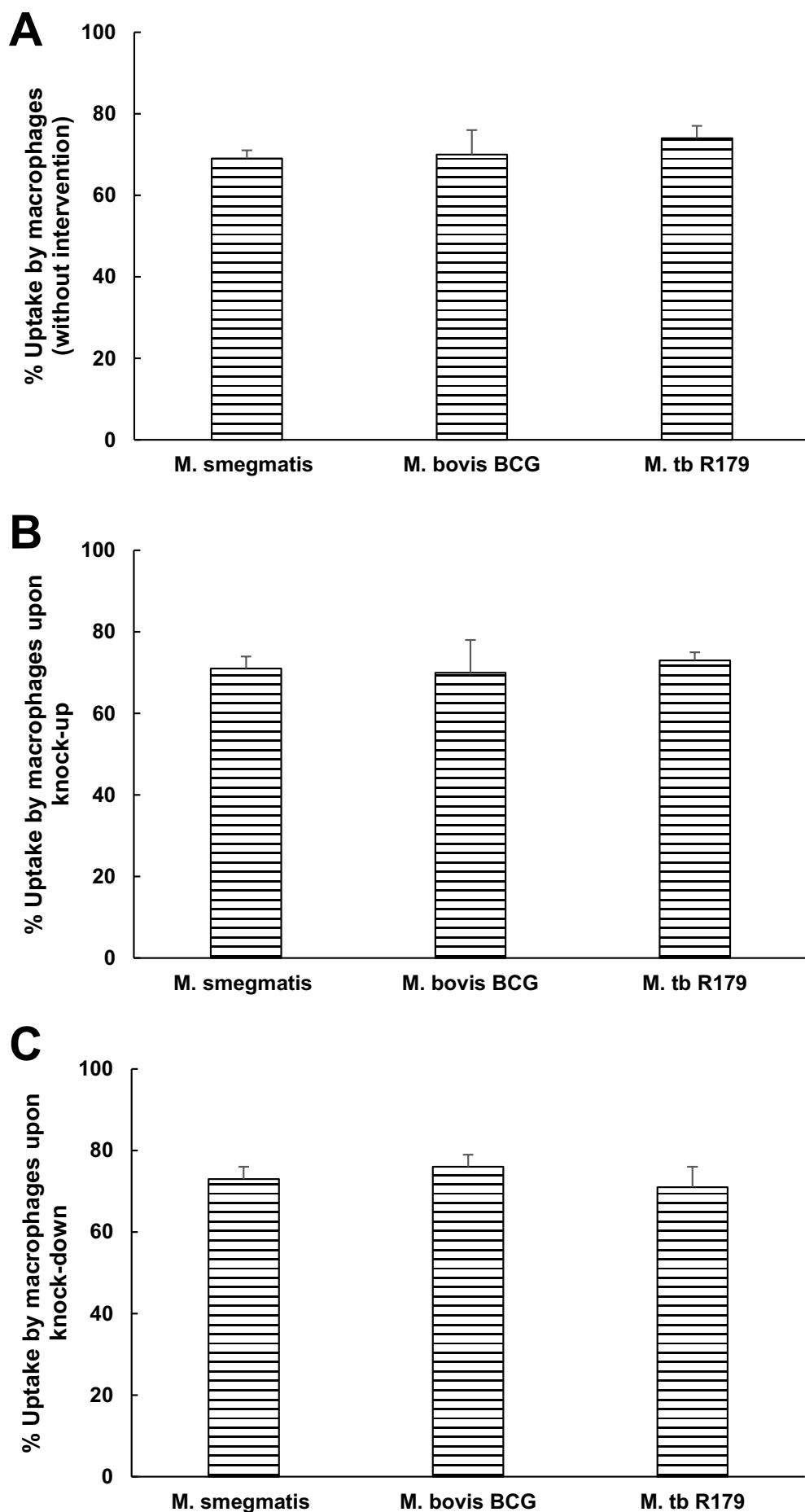


Supplementary Figure 5: Titration of IFITs for knock-up at different concentrations. Panel shows (A) *IFIT1*, (B) *IFIT2* and (C) *IFIT3* at different concentrations for knock-up in colony forming units of *M. bovis* BCG. We found concentration of 120 ng/ml to be most effective in reducing *in vitro* CFUs of BCG. Abbreviation: BCG= Bacillus Calmette–Guerin, IFIT= interiferon-induced protein with tetratricopeptide.

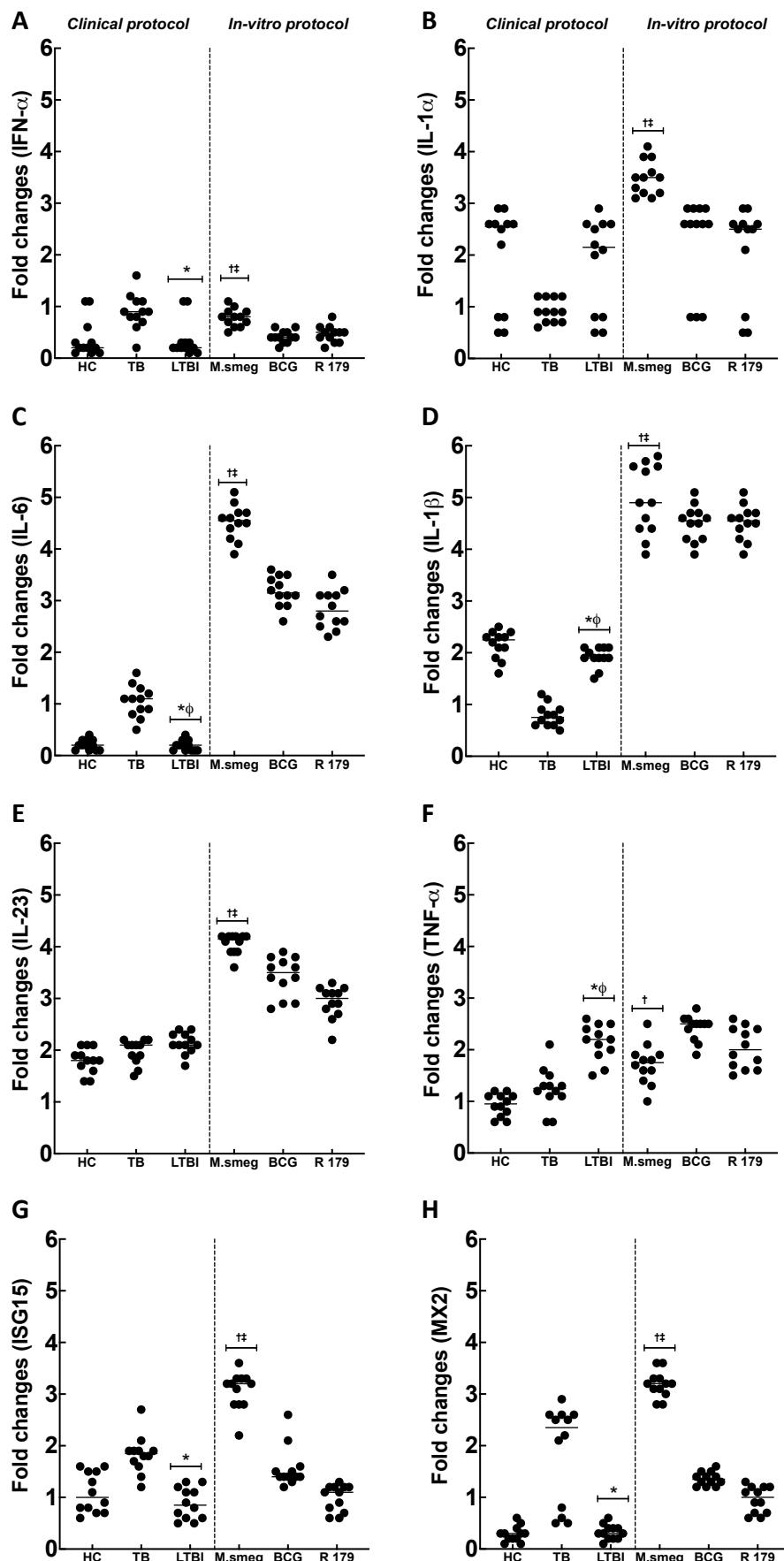
A**B****C**

Supplementary Figure 6: Viability of THP-1 cells after knock-down and knock-up of *IFITs* infected with A) *M. smegmatis*, B) *M. bovis* BCG and C) *M. tb* R179. The viability of the cells was found to be >85%, which was consistent and similar across the three species and knock-up and knock-down.

Abbreviations: KD= Knock-down, KU= Knock-up, UI= Uninfected

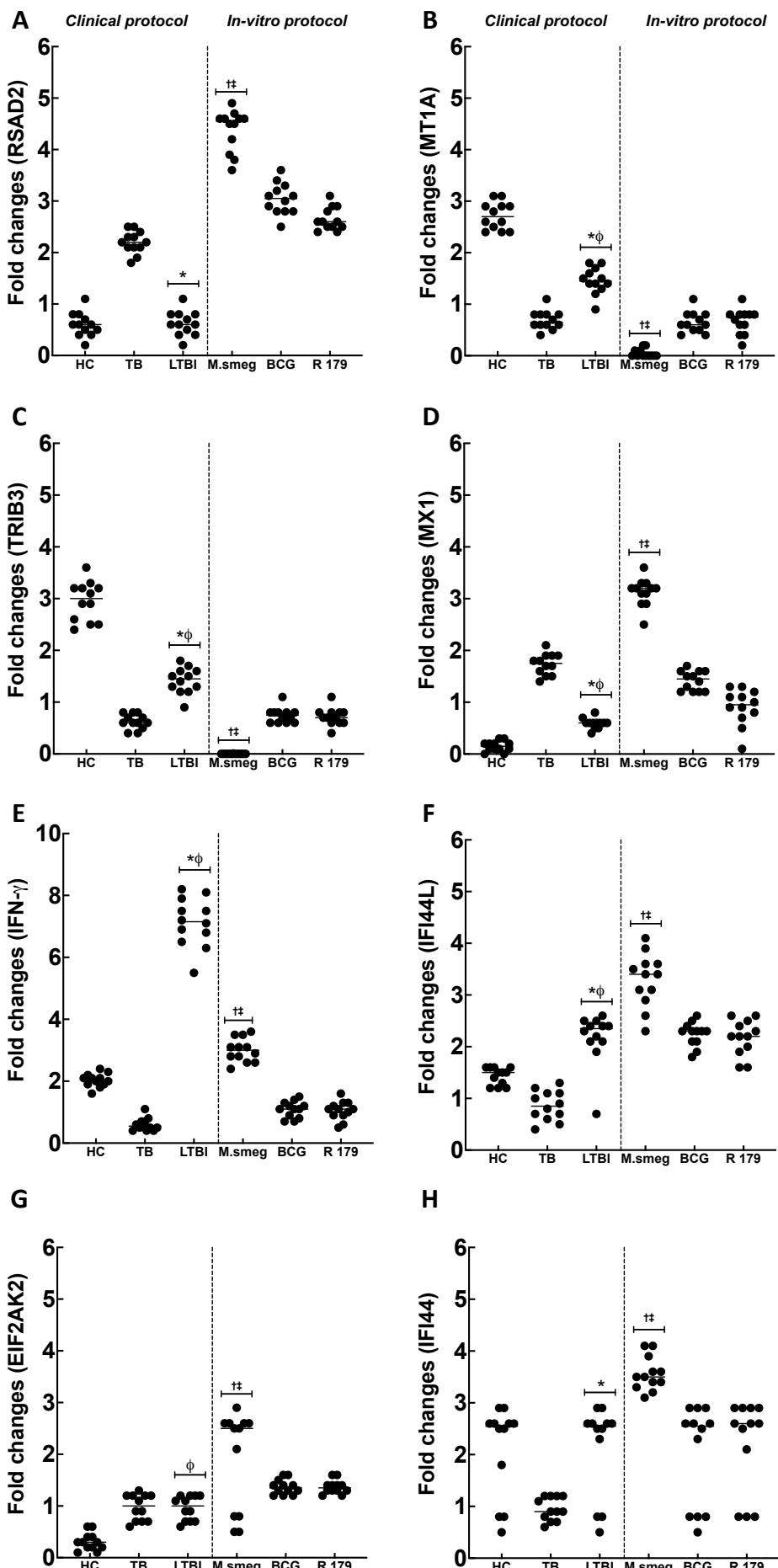


Supplementary Figure 7: Comparison of bacterial uptake by THP-1 cells across different mycobacterial species without intervention (A), after knock-up (B) and knock-down (C) of IFITs. The bacterial uptakes were found to be similar across different



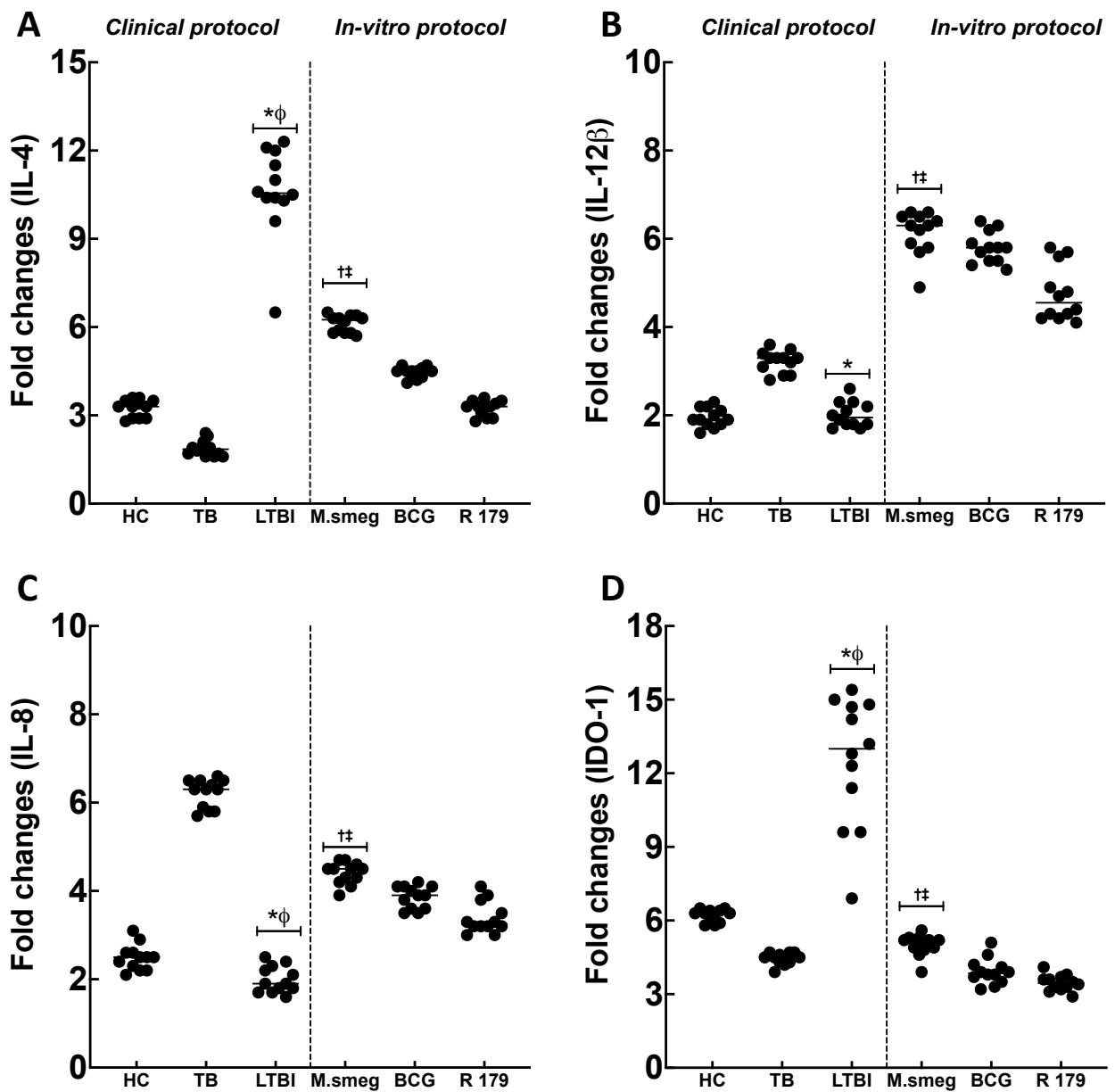
Supplementary Figure 8a: Fold changes of different mRNA detected by qRT-PCR for clinical and *in vitro* protocol. Compared to TB cases IFN- α , IL-6, ISG15 and MX2 were found to be lower, while TNF- α and IL-1 β found to be higher in LTBI cases. For *in vitro* protocol, fold changes for *M. smegmatis* were found to be higher than *M. bovis* BCG and *M. tb* R179.

* = vs. TB, † = vs. HC, ‡ = vs. BCG, and § = vs. R179



Supplementary Figure 8b: Fold changes of different mRNA detected by qRT-PCR for clinical and *in vitro* protocol. Compared to TB cases IFN- γ , TRIB3, MT1A, IFI44 and IFI44L were found to be lower, while RSAD2 and MX1 found to be higher in LTBI cases. For *in vitro* protocol, fold changes of RSAD2, MX1, IFN- γ , IFI44, IFI44L and EIF2AK2 were found to be higher, while TRIB3 and MT1A were lower for *M. smegmatis* compared to *M. bovis* BCG and *M. tb* R179.

*= vs. TB, †= vs. HC, ‡= vs. BCG, and †‡= vs. R179



Supplementary Figure 8c: Fold changes of different mRNA detected by qRT-PCR for clinical and *in vitro* protocol. Compared to TB cases IL-4 and IDO-1 were found to be lower, while IL-8 and IL-12 β found to be higher in LTBI cases. For *in vitro* protocol, fold changes were found to be higher in *M. smegmatis* compared to *M. bovis* BCG and *M. tb* R179.

1 **Supplementary Table 1:** Demographic and clinical information of study participants. Data
 2 presented as mean \pm S.D, median (IQR), and n/N (%).

	<i>In vitro</i> protocol	Clinical protocol (n=24)	
	Healthy controls (n=12)	LTBI cases (n=12)	Active TB cases (n=12)
Age (Years) Median (IQR)	27 (26-28.5)	37.2 (30.8-56.7)	49.5 (36.5-57) p=0.406
Gender (%)			
Female	6/12 (50)	9/12 (75)	6/12 (33)
Male	6/12 (50)	3/12 (25)	6/12 (67) p=0.206
BMI (kg/m²)	23.59 \pm 2.3	27.44 \pm 9.1	26.36 \pm 5.2 p=0.725

3 Abbreviations: BMI= body mass index, LTBI= latent tuberculosis infection, TB= Tuberculosis

Supplementary Table 2: Effect of in vitro knock-up and knock-down of IFITs on CFUs of *M. smegmatis*, *M. bovis BCG* and *M. tb R179*. Compared to untreated CFUs, we observed significant reduction in CFUs after knock-up of individual *IFIT1*, *IFIT2* and *IFIT3*. Also, higher CFUs observed after knock-down of individual *IFITs*. Combined effect of *IFITs* during knock-up and knock-down found to increase the survivability of *in vitro* CFUs. Results represented as increase (+%) or decrease (-%) in CFUs compared to untreated wells. Data represented as n and n/N (%).

Untreated CFUs	CFUs after Knock-up ($\times 10^4$)				CFUs after Knock-down ($\times 10^4$)			
	<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>	<i>Average effect of knock-up</i>	<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>	<i>Average effect of knock-down</i>
<i>M. smegmatis</i>								
At 12 hours	41	30	29	26	-31%	85	89	90
% Change from untreated CFUs	-11/41 (-27%)	-12/41 (-29%)	-15/41 (-37%)			+44/41 (+107%)	+48/41 (+117%)	+49/41 (+120%)
		p<0.0001*	p<0.0001* p=0.806 [†]	p<0.0001* p=0.343 [†] p=0.481 [‡]		p<0.0001*	p<0.0001* p=0.232 [†]	p<0.0001* p=0.156 [†] p=0.812 [‡]
At 24 hours	15	8	7	6	-53%	26	26	28
% Change from untreated CFUs	-7/15 (-47%)	-8/15 (-53%)	-9/15 (-60%)			+11/15 (+73%)	+11/15 (+73%)	+13/15 (+87%)
		p=0.001*	p=0.003* p=0.715 [†]	p=0.006* p=0.464 [†] p=0.713 [‡]		p=0.003*	p=0.003* p>0.999 [†]	p=0.002* p=0.761 [†] p=0.761 [‡]
<i>M. bovis BCG</i>								
At 12 hours	60	39	39	40	-34%	86	88	87
% Change from untreated CFUs	-21/60 (-35%)	-21/60 (-35%)	-20/60 (-33%)			+26/60 (+43%)	+28/60 (+47%)	+27/60 (+45%)
		p<0.0001*	p<0.0001* p>0.999 [†]	p<0.0001* p=0.847 [†] p=0.847 [‡]		p<0.0001*	p<0.0001* p=0.821 [†]	p<0.0001* p=0.909 [†] p=0.911 [‡]

Continue...

<i>At 96 hours</i>	71	49	49	51	-30%	97	101	102	+41%
<i>% Change from untreated CFUs</i>	-22/71 (-31%)	-22/71 (-31%)	-20/71 (-29%)			+26/71 (+37%)	+30/71 (+42%)	+31/71 (+44%)	
	p<0.0001*	p<0.0001* p>0.999†	p<0.0001* p=0.713† p=0.713‡			p<0.0001*	p<0.0001* p=0.651†	p<0.0001* p=0.576† p=0.915‡	
<i>M. tb R179</i>									
<i>At 12 hours</i>	51	39	39	38	-24%	84	89	89	+69%
<i>% Change from untreated CFUs</i>	-12/51 (-24%)	-12/51 (-24%)	-13/51 (-25%)			+33/51 (+65%)	+36/51 (+71%)	+36/51 (+71%)	
	p<0.0001*	p<0.0001* p>0.999†	p<0.0001* p=0.818† p=0.818‡			p<0.0001*	p<0.0001* p=0.649†	p<0.0001* p=0.649† p>0.999‡	
<i>At 96 hours</i>	74	43	42	41	-43%	99	100	99	+34%
<i>% Change from untreated CFUs</i>	-31/74 (-42%)	-32/74 (-43%)	-33/74 (-45%)			+25/74 (+34%)	+26/74 (+35%)	+25/74 (+34%)	
	p<0.0001*	p<0.0001* p=0.868†	p<0.0001* p=0.740† p=0.868‡			p<0.0001*	p<0.0001* p=0.904†	p<0.0001* p<0.999† p=0.904‡	
<i>Overall (across all three species)</i>	-32.5% (-30% to 43%)					+57% (+41% to +78%)			

*=vs. Untreated CFUs, †=vs. *IFIT1*, ‡=vs. *IFIT2*, §=vs. *IFIT3*

Abbreviations: BCG= Bacillus Calmette–Guérin, CFUs= colony forming units, *IFITs*= interferon-induced protein with tetratricopeptide repeats

Supplementary Table 3: Mycobacterial species and plasmids used for the *in vitro* knock-up and knock-down of *IFITs* in the study.

Description		Source/Reference
<i>M. tb</i> species		
<i>M. smegmatis</i>	<i>M. smegmatis</i> MC155	Laboratory collection (Harper <i>et al.</i> , 2010)
<i>M. bovis</i> BCG	<i>M. bovis</i> BCG strain Pasteur 1743P2	Laboratory collection (Viljoen <i>et al.</i> , 2013)
<i>M. tb</i> R179	Beijing genotype strain R220	Clinical isolate (Johnson <i>et al.</i> , 2006)
<i>E. coli</i> DH5 α	ATCC53868	Laboratory collection
Plasmid for overexpression (knock-up)		
pcDNA3.1 3xFlag <i>IFIT1</i>	Mammalian expression vector with human <i>IFIT1</i> as an insert and without mutations	(Katibah <i>et al.</i> , 2013)
pcDNA3.1 3xFlag <i>IFIT2</i>	Mammalian expression vector with human <i>IFIT2</i> as an insert without mutations	(Katibah <i>et al.</i> , 2013)
pcDNA3.1 3xFlag <i>IFIT3</i>	Mammalian expression vector with human <i>IFIT3</i> as an insert without mutations	(Katibah <i>et al.</i> , 2013)
siRNA pre-mix of <i>IFITs</i> (knock-down)		
siRNA Premix	Target Sequence (5' to 3')	Catalogue Number (length)
<i>Hs-IFIT1</i>	CAGGCTGTCCGCTTAAATCCA	Catalogue no. S100445879 (4396 bp)
<i>Hs-IFIT1</i>	TACATGGGAGTTATCCATTGA	Catalogue no. S103224284 (4396 bp)
<i>Hs-IFIT2</i>	AAAGAAAAGTTACTGGAACCAA	Catalogue no. S104145372 (3505 bp)
<i>Hs-IFIT2</i>	CCCATAGAGGTTAGTCCTGCA	Catalogue no. S104259010 (3505 bp)
<i>Hs-IFIT3</i>	ATGCTATGGACTATTGAAATA	Catalogue no. S103152737 (2467 bp)
<i>Hs-IFIT3</i>	AGAGATGATTGAAGCACTAAA	Catalogue no. S104197788 (2467 bp)

Abbreviations: BCG= Bacillus Calmette–Guérin, *E. coli*= Escherichia coli, *IFIT*= interferon-induced protein with tetratricopeptide.

Supplementary Table 4: Cytokines expression (pg/ml) 12 hours post *M. smegmatis* infection†. Compared to *M. smegmatis* infected THP-1 cells without intervention, we observed significantly lower level of cytokines after knock-down and higher level after knock-up of *IFITs*. For knock-down, levels of IFN- α , IFN- β , IL-1 α , IL-4 and IL-12p70 were found to be similar. Also, for knock-up, levels of IL-1 α , IL-1 β and TNF- α were found to be similar. Data presented as mean \pm S.D.

Cytokines	Uninfected	<i>M. smegmatis</i>	Knock-down (siRNA)			Knock-up (vector-based over-expression)		
			<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>	<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>
<i>at 12 hours</i>								
IDO-1	971 \pm 13.4	1550.3 \pm 16.4 p=0.047*	0.3 \pm 0.5 p<0.001* p<0.001†	8.6 \pm 1.5 p<0.001* p<0.001†	9 \pm 1 p<0.001* p<0.001†	1864.3 \pm 5.8 p=0.001* p=0.708†	2343 \pm 7.5 p<0.001* p=0.001†	2865 \pm 9.8 p<0.001* p<0.001†
IFN- α	29 \pm 1	82 \pm 6.2 p>0.999*	0.3 \pm 0.5 p>0.999* p>0.999†	6 \pm 1 p>0.999* p>0.999†	12.5 \pm 2 p>0.999* p>0.999†	1085 \pm 9.8 p=0.001* p=0.003†	1255.6 \pm 9.4 p=0.044* p=0.001†	984.6 \pm 15.6 p<0.001* p<0.001†
IFN- β	0	0 p>0.999*	0 p>0.999* p>0.999†	0 p>0.999* p>0.999†	0 p>0.999* p>0.999†	635 \pm 12.5 p<0.001* p<0.001†	414.6 \pm 8.5 p<0.001* p<0.001†	488.3 \pm 8 p<0.001* p<0.001†
IFN- γ	527.3 \pm 12	1361 \pm 7.5 p=0.0004*	0 p=0.101* p<0.001†	0 p=0.101* p<0.001†	0 p=0.101* p<0.001†	7599 \pm 946.8 p<0.001* p<0.001†	7405.3 \pm 1029.2 p<0.001* p<0.001†	7670 \pm 908.8 p<0.001* p<0.001†
IL-4	7.6 \pm 4.7	487.3 \pm 9.6 p<0.001*	0 p>0.999* p=0.016†	0.3 \pm 0.5 p>0.999* p=0.017†	2.3 \pm 2.5 p>0.999* p=0.017†	5164.3 \pm 179.8 p<0.001* p<0.001†	5134.3 \pm 305.1 p<0.001* p<0.001†	4954.6 \pm 492.2 p<0.001* p<0.001†

*vs. Uninfected, †vs. *M. smegmatis*

IL-6	239.3 ± 19.8	1983.6 ± 4 p<0.001*	0.6 ± 0.5 p=909 * p<0.001†	9 ± 8.1 p=0.924 * p<0.001†	0.6 ± 1.1 p=0.909 * p<0.001†	3530.6 ± 467.3 p<0.001* p<0.001†	3567.3 ± 216.7 p<0.001* p<0.001†	2921 ± 84.1 p<0.001* p<0.001†
IL-8	657 ± 19.6	9442.6 ± 489.8 p<0.001 *	1300.6 ± 3 p= 0.016* p<0.002†	676.3 ± 19.8 p=0.999 * p=0.001†	991.6 ± 38.2 p=0.635 * p<0.001†	8680.6 ± 84.5 p<0.001* p= 0.002†	8932.6 ± 52.5 p<0.001* p=0.125 †	7451.6 ± 797.8 p<0.001* p<0.001†
IL-12p40	94.6 ± 6.6	753.6 ± 9.7 p=0.013 *	3.6 ± 3.2 p=0.999 * p= 0.002†	9.3 ± 4.5 p=0.924 * p=0.003†	0 p=0.999 * p=0.002†	3421.6 ± 477.3 p<0.001* p<0.001†	2591 ± 360.2 p<0.001* p<0.001†	3828 ± 164.8 p<0.001* p<0.001†
IL-12p70	16.6 ± 4.1	406.3 ± 14.7 p=0.437 *	0.3 ± 0.5 p>0.999 * p=0.038 †	0 p>0.999 * p=0.038 †	0 p>0.999 * p=0.038 †	561.6 ± 8.7 p=0.078 * p= 0.991†	844.6 ± 32 p=0.001 * p= 0.283†	767.6 ± 32.6 p=0.002 * p=0.539 †
IL-23	1245 ± 52.7	2069.6 ± 122.9 p=0.001 *	0.6 ± 1.1 p<0.001 * p<0.001†	0 p<0.001 * p<0.001†	2 ± 3.4 p<0.001 * p<0.001†	4599.3 ± 510.1 p<0.001 * p<0.001†	4547.3 ± 253.6 p<0.001 * p<0.001†	3207.3 ± 179.4 p<0.001 * p<0.001†

*vs. Uninfected, †vs. *M. smegmatis*

IL-1α	243.3 \pm 9.4	254.3 \pm 40.5 p<0.999 *	67.3 \pm 3 p= 0.982 * p= 0.975 †	74.6 \pm 10.9 p=0.986 * p= 0.980 †	75 \pm 8.7 p=0.986 * p= 0.980 †	6932.3 \pm 79 p<0.001 *	5453 \pm 380.7 p<0.001 * p<0.001 †	4562.6 \pm 312.5 p<0.001 * p<0.001 †
IL-1β	22 \pm 4.3	131 \pm 13.1 p=0.0002 *	8.6 \pm 3.2 p=0.982 * p=0.998 †	7 \pm 2.6 p=0.986 * p=0.998 †	1 \pm 1 p=0.986 * p=0.997 †	1278 \pm 151.6 p<0.001 *	1484.6 \pm 41.7 p<0.001 * p<0.001 †	1160.6 \pm 165.7 p<0.001 * p<0.001 †
TNF-α	30 \pm 5.5	634.3 \pm 33.8 p=0.032 *	139.3 \pm 23.1 p= 0.999 * p= 0.151 †	264.6 \pm 20.6 p= 0.916 * p= 0.508 †	113.6 \pm 9.5 p<0.999 * p= 0.109 †	4456.6 \pm 318.1 p<0.001 *	6202 \pm 168.3 p<0.001 * p<0.001 †	4154.6 \pm 123.1 p<0.001 * p<0.001 †

*vs. Uninfected, † vs. *M. smegmatis*

Abbreviations: IDO, indoleamine 2,3-dioxygenase; IFI, interferon-induced protein; IFIT, interferon-induced protein with tetratricopeptide; IFN, interferon gamma; IL, interleukin; ISG, interferon-stimulated gene

Supplementary Table 5: Cytokine expression (pg/ml) after 12 and 96 hours of *M. bovis* BCG infection. Compared to BCG infected THP-1 cells without intervention, we observed higher levels of cytokines for knock-down and knock-up of *IFITs*. The level of most of the cytokines increases significantly after knock-up of *IFITs*. For knock-down, levels of IFN- α , IFN- β , IL-4 and IL-12p70 were found to be similar. Also, for knock-up, levels of IL-1 α , IL-1 β and TNF- α were found to be similar. Data presented as mean \pm S.D

Cytokines	Uninfected	<i>M. bovis</i> BCG	Knock-down (siRNA)			Knock-up (vector-based over-expression)		
			<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>	<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>
<i>at 12 hours</i>								
IDO-1	971 \pm 13.4	1489.3 \pm 112.2 p = 0.073*	0.3 \pm 0.5 p < 0.001* p < 0.001†	8.6 \pm 1.5 p < 0.001* p < 0.001†	9 \pm 1 p < 0.001* p < 0.001†	3201.3 \pm 86.6 p < 0.001* p < 0.001†	3198 \pm 171.4 p < 0.001* p < 0.001†	4069.3 \pm 141.9 p < 0.001* p < 0.001†
IFN- α	29 \pm 1	83.6 \pm 9 p > 0.999*	0.3 \pm 0.5 p > 0.999* p > 0.999†	6 \pm 1 p > 0.999* p > 0.999†	12.6 \pm 2 p > 0.999* p > 0.999†	769.6 \pm 28.5 p = 0.001* p = 0.003†	579.6 \pm 36.1 p = 0.044* p = 0.101†	872 \pm 103.7 p < 0.001* p = 0.0004†
IFN- β	0	0 p > 0.999*	0 p > 0.999* p > 0.999†	0 p > 0.999* p > 0.999†	0 p > 0.999* p > 0.999†	8225.6 \pm 413.2 p < 0.001* p < 0.001†	5366.3 \pm 304 p < 0.001* p < 0.001†	6498.6 \pm 160.9 p < 0.001* p < 0.001†
IFN- γ	527.3 \pm 12	1691 \pm 84.7 p < 0.001* p < 0.001†	0 p = 0.064* p < 0.001†	0 p = 0.064* p < 0.001†	0 p = 0.064* p < 0.001†	6937.3 \pm 369.8 p < 0.001* p < 0.001†	8228.3 \pm 404.2 p < 0.001* p < 0.001†	6273.3 \pm 370.5 p < 0.001* p < 0.001†
IL-4	7.6 \pm 4.7	829 \pm 31.9 p = 0.0002* p < 0.001†	0 p > 0.999* p < 0.001†	0.3 \pm 0.5 p > 0.999* p < 0.001†	2.3 \pm 2.5 p > 0.999* p < 0.001†	5797.6 \pm 810.4 p < 0.001* p < 0.001†	5019.6 \pm 290.5 p < 0.001* p < 0.001†	4559.6 \pm 252.1 p < 0.001* p < 0.001†

*vs. Uninfected, †vs. *M. bovis* BCG

IL-6	239.3 ± 19.8	2376 ± 319 p<0.001*	0.6 ± 0.5 p=0.880* p<0.001†	9 ± 8.1 p=0.898* p<0.001†	0.6 ± 1.1 p=0.880* p<0.001†	9253.3 ± 378.3 p<0.001* p<0.001†	6491 ± 157.4 p<0.001* p<0.001†	8353.6 ± 225.3 p<0.001* p<0.001†
IL-8	657 ± 19.6	9113 ± 572 p<0.001*	1854.6 ± 127.1 p<0.001* p<0.001†	1106.6 ± 72.5 p=0.186* p<0.001†	1799.3 ± 56.5 p<0.001* p<0.001†	8328 ± 616.3 p<0.001* p<0.001†	8526 ± 677.8 p<0.001* p=0.024†	7928 ± 54.5 p<0.001* p<0.001†
IL-12p40	94.6 ± 6.6	493.6 ± 60 p=0.327*	3.6 ± 3.2 p<0.999* p=0.110†	9.3 ± 4.5 p<0.999* p=0.110†	0 p<0.999* p=0.110†	3241.3 ± 652.6 p<0.001* p<0.001†	2480 ± 419.2 p<0.001* p<0.001†	1080.6 ± 61.2 p<0.001* p=0.024†
IL-12p70	16.6 ± 4.1	375.3 ± 59.9 p=0.469*	0.3 ± 0.5 p<0.999* p=0.409†	0 p<0.999* p=0.408†	0 p<0.999* p=0.408†	1538.6 ± 26.6 p<0.001* p<0.001†	1087 ± 17.6 p<0.001* p<0.001†	1968 ± 195 p<0.001* p<0.001†
IL-23	1245 ± 52.7	2205 ± 213.6 p<0.001*	528 ± 102.8 p=0.002* p<0.001†	147.3 ± 25.5 p<0.001* p<0.001†	376.3 ± 39.4 p<0.001* p<0.001†	6530 ± 453.2 p<0.001* p<0.001†	6558 ± 258.9 p<0.001* p<0.001†	4408.6 ± 495.2 p<0.001* p<0.001†
IL-1α	243.3 ± 9.4	254.6 ± 40.5 p>0.999*	72.6 ± 11.7 p=0.979* p=0.970†	67.6 ± 21.1 p=0.974* p=0.965†	57.3 ± 26.3 p=0.966* p=0.953†	786.3 ± 71.2 p=0.050* p=0.060†	621.6 ± 95 p=0.390* p=0.438†	1139.6 ± 122.5 p<0.001* p<0.001†
IL-1β	22 ± 4.3	127 ± 15.6 p=0.998*	12.3 ± 8.7 p>0.999* p=0.998†	12 ± 7.2 p>0.999* p=0.998†	2.3 ± 1.5 p>0.999* p=0.996†	752.3 ± 33.2 p=0.001* p=0.012†	743.3 ± 26.8 p=0.002* p=0.014†	597.3 ± 65.2 p=0.029* p=0.144†
TNF-α	30 ± 5.5	679.3 ± 103.3 p=0.007*	104 ± 11 p>0.999* p=0.029†	56.3 ± 16.6 p>0.999* p=0.012†	14 ± 2 p>0.999* p=0.005†	8295 ± 303.9 p<0.001* p<0.001†	8200.6 ± 608.7 p<0.001* p<0.001†	6406 ± 168 p<0.001* p<0.001†

*vs. Uninfected, †vs. *M. bovis* BCG

Cytokines	Uninfected	<i>M. bovis</i> BCG	Knock-down (siRNA)			Knock-up (vector-based over-expression)		
			<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>	<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>
<i>at 96 hours</i>								
IDO-1	971 ± 13.4	1504.3 ± 86.5 p=0.112*	0.3 ± 0.5 p<0.001* p<0.001†	8.6 ± 1.5 p<0.001* p<0.001†	9 ± 1 p<0.001* p<0.001†	2525.3 ± 346.7 p<0.001* p<0.001†	1236.6 ± 185.1 p=0.869* p=0.864†	2724 ± 249 p<0.001* p<0.001†
IFN- α	29 ± 1	74 ± 7.9 p>0.999 *	0.3 ± 0.5 p>0.999 * p>0.999 †	6 ± 1 p>0.999 * p>0.999†	12.6 ± 2 p>0.999* p>0.999†	534 ± 74 p=0.158* p=0.258†	131.6 ± 9 p=0.995* p>0.999 †	664.6 ± 34 p=0.026* p=0.052†
IFN- β	0	0 p>0.999*	0 p>0.999 * p>0.999 †	0 p>0.999* p>0.999†	0 p>0.999* p>0.999†	6310.3 ± 248.4 p<0.001* p<0.001†	5512.6 ± 101 p<0.001* p<0.001†	4534 ± 365.8 p<0.001* p<0.001†
IFN- γ	527.3 ± 12	964.3 ± 30 p=0.322*	0 p=0.121* p<0.001†	0 p=0.121* p<0.001†	0 p=0.121* p<0.001†	5936.3 ± 635.3 p<0.001* p<0.001†	8237.3 ± 459.7 p<0.001* p<0.001†	7457.6 ± 298.2 p<0.001* p<0.001†
IL-4	7.6 ± 4.7	492 ± 13.4 p=0.200*	0 p>0.999 * p=0.184†	0.3 ± 0.5 p>0.999* p=0.184†	2.3 ± 2.5 p>0.999* p=0.188†	4410.3 ± 177.9 p<0.001* p<0.001†	4216 ± 102.8 p<0.001* p<0.001†	3453.6 ± 366.5 p<0.001* p<0.001†

*vs. Uninfected, †vs. *M. bovis* BCG

IL-6	239.3 ± 19.8	2347.6 ± 315.4 p<0.001*	0.6 ± 0.5 p=0.921* p<0.001†	9 ± 8.1 p=0.934* p<0.001†	0.6 ± 1.1 p=0.921* p<0.001†	6586 ± 492.9 p<0.001* p<0.001†	7373.3 ± 163.5 p<0.001* p<0.001†	4651 ± 385.9 p<0.001* p<0.001†
IL-8	657 ± 19.6	9296.6 ± 445.6 p<0.001*	1208.3 ± 160.5 p=0.089* p<0.001†	1479.3 ± 153.8 p<0.001* p<0.001†	979.6 ± 20.9 p=0.708* p<0.001†	3270.6 ± 1025.6 p<0.001* p<0.001†	2677 ± 417.2 p<0.001* p<0.001†	2662.3 ± 263.8 p<0.001* p<0.001†
IL-12p40	94.6 ± 6.6	589.6 ± 59 p=0.178*	3.6 ± 3.2 p>0.999 * p=0.055†	9.3 ± 4.5 p>0.999* p=0.059†	0 p>0.999* p=0.052†	1355 ± 527.6 p<0.001* p=0.003†	2553.3 ± 370.2 p<0.001* p<0.001†	2358.3 ± 433.3 p<0.001* p<0.001†
IL-12p70	16.6 ± 4.1	23.6 ± 1.1 p>0.999*	0 p>0.999 * p>0.999†	0.3 ± 0.5 p>0.999* p>0.999†	0 p>0.999* p>0.999†	1448 ± 264.7 p<0.001* p<0.001†	1873.6 ± 126.1 p<0.001* p<0.001†	2923 ± 346.1 p<0.001* p<0.001†
IL-23	1245 ± 52.7	1077.6 ± 49.6 p=0.989*	407.3 ± 12 p=0.001* p=0.015†	410.3 ± 13.5 p=0.001* p=0.016†	231.6 ± 46.1 p<0.001* p=0.001†	5143 ± 409.8 p<0.001* p<0.001†	4478 ± 251.8 p<0.001* p<0.001†	4507 ± 319.5 p<0.001* p<0.001†
IL-1α	243.3 ± 9.4	262.6 ± 42.8 p>0.999*	14.6 ± 3 p=0.936* p=0.904†	14.3 ± 3 p=0.936* p=0.904†	38.3 ± 3 p=0.964* p=0.942†	732.6 ± 112.4 p=0.189* p=0.233†	551.6 ± 112.3 p=0.754* p=0.810†	469.3 ± 45.4 p=0.940* p=0.963†

*vs. Uninfected, †vs. *M. bovis* BCG

IL-1β	22 ± 4.3	125.3 ± 17.3 p>0.999*	8.6 ± 3.2 p=0.998†	7 ± 2.6 p>0.999*	1 ± 1 p=0.998†	456 ± 16 p=0.331*	504.3 ± 32.1 p=0.204*	833 ± 96.3 p=0.001* p=0.010†
TNF-α	30 ± 5.5	352.6 ± 40.7 p=0.708*	54.3 ± 11.5 p=0.784†	52.3 ± 18.7 p>0.999*	21 ± 6.2 p=0.778†	4875.6 ± 969.5 p<0.001*	5929 ± 477.6 p<0.001*	3955.6 ± 312.9 p<0.001* p<0.001†

*vs. Uninfected, †vs. *M. bovis* BCG

Supplemental Table 6. Cytokines expression (pg/ml) after 12 and 96 hours of *M. tb* R179 infection of THP-1 cells. The levels of IDO-1, INF- γ , IL-6, IL-8, IL-10, IL-12p40, IL-12p70, IL-23 and TNF- α were found to be significantly higher after knock-up of IFITs. Although, the levels of IL-1 α , IL-1 β and IFN- α were found to be similar after knock-up of IFITs. After knock-down of IFITs, levels of IDO-1, INF- γ , IL-6, IL-8, IL-12p70, IL-23 and TNF- α were found to be significantly reduced. The levels of IL-1 α , IL-1 β , IL-4, IL-12p40, IFN- α and INF- β were found to be similar before and after knock-down of IFITs. Data presented as mean \pm S.D.

Cytokines	Uninfected	<i>M. tb</i> R179	Knock-down (siRNA)			Knock-up (vector-based over-expression)		
			<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>	<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT3</i>
<i>at 12 hours</i>								
IDO-1	971 \pm 13.4	1338.8 \pm 30 p=0.902*	0.3 \pm 0.5 p=0.017* p<0.001†	8.6 \pm 1.5 p=0.019* p<0.001†	9 \pm 1 p=0.019* p<0.001†	2849.3 \pm 562.2 p<0.001* p<0.001†	3148.6 \pm 87.6 p<0.001* p<0.001†	3693.6 \pm 511.2 p<0.001* p<0.001†
IFN-α	29 \pm 1	77.3 \pm 2.5 p>0.999*	0.3 \pm 0.5 p>0.999* p>0.999†	6 \pm 1 p>0.999* p>0.999†	12.6 \pm 2 p>0.999* p>0.999†	739.3 \pm 64.6 p=0.206* p=0.287†	574.3 \pm 40.5 p=0.544* p=0.659†	836.3 \pm 114.3 p=0.093* p=0.141†
IFN-β	0	0 p>0.999*	0 p>0.999* p>0.999†	0 p>0.999* p>0.999†	0 p>0.999* p>0.999†	8143.6 \pm 271.5 p<0.001* p<0.001†	5759.6 \pm 781.3 p<0.001* p<0.001†	6483.6 \pm 158.5 p<0.001* p<0.001†
IFN-γ	527.3 \pm 12	927.3 \pm 84 p=0.855*	0 p=0.587* p=0.028†	0 p=0.587* p=0.028†	0 p=0.587* p=0.028†	7077.3 \pm 583 p<0.001* p<0.001†	7868.3 \pm 221.9 p<0.001* p<0.001†	7563.3 \pm 1206.4 p<0.001* p<0.001†
IL-4	7.6 \pm 4.7	800 \pm 50.8 p=0.106*	0 p>0.999* p=0.099†	0.3 \pm 0.5 p>0.999* p=0.099†	2.3 \pm 2.5 p>0.999* p=0.102†	5379.6 \pm 143.6 p<0.001* p<0.001†	8436.3 \pm 453.5 p<0.001* p<0.001†	4521.3 \pm 285.2 p<0.001* p<0.001†
IL-6	239.3 \pm 19.8	918 \pm 19.6 p=0.257*	0.6 \pm 0.5 p=0.990* p=0.032†	9 \pm 8.1 p=0.992* p=0.032†	0.6 \pm 1.1 p=0.992* p=0.035†	6532.6 \pm 470.2 p<0.001* p<0.001†	5303.3 \pm 329.7 p<0.001* p<0.001†	7818.3 \pm 291.9 p<0.001* p<0.001†
IL-8	657 \pm 19.6	8822.3 \pm 972.2 p<0.001*	794 \pm 32 p>0.999* p<0.001†	1066.3 \pm 74.1 p=0.804* p<0.001†	1664.6 \pm 187.3 p=0.012* p<0.001†	6573.6 \pm 204.5 p<0.001* p<0.001†	6886.6 \pm 50.6 p<0.001* p<0.001†	2778.6 \pm 2096.4 p<0.001* p<0.001†

*vs. Uninfected, †vs. *M. tb* R179

IL-12p40	94.6 ± 6.6	245 ± 13.5 p>0.999*	3.6 ± 3.2 p>0.999* p=0.990†	9.3 ± 4.5 p>0.999* p=0.992†	0 p>0.999* p=0.989†	3463.6 ± 458 p<0.001* p<0.001†	3054.3 ± 858 p<0.001* p<0.001†	4108 ± 35.5 p<0.001* p<0.001†
IL-12p70	16.6 ± 4.1	302.6 ± 17.7 p=0.974*	0 p>0.999* p=0.001†	3.3 ± 5.7 p>0.999* p=0.001†	0 p>0.999* p=0.001†	4589.6 ± 54 p<0.001* p<0.001†	4112 ± 61.7 p<0.001* p<0.001†	2766.6 ± 201.6 p<0.001* p<0.001†
IL-23	1245 ± 52.7	2009.3 ± 94.4 p=0.135*	332.3 ± 27.7 p=0.034* p<0.001†	350.6 ± 12.6 p=0.041* p<0.001†	346.3 ± 43 p=0.039* p<0.001†	6610.3 ± 521.1 p<0.001* p<0.001†	7477.6 ± 848.2 p<0.001* p<0.001†	7405 ± 489 p<0.001* p<0.001†
IL-1α	243.3 ± 9.4	249.3 ± 41.4 p>0.999*	71.3 ± 9.4 p=0.998* p=0.998†	68 ± 20.6 p=0.999* p=0.998†	77 ± 11.1 p>0.999* p=0.945†	702.3 ± 156.7 p=0.744* p=0.757†	601.3 ± 90.1 p=0.914* p=0.921†	438.6 ± 24.1 p=0.997* p=0.998†
IL-1β	22 ± 4.3	337.6 ± 23.4 p=0.954*	39 ± 7.9 p>0.999* p=0.966†	66 ± 12 p>0.999* p=0.980†	10.3 ± 7.3 p>0.999* p=0.945†	757.6 ± 38.2 p=0.169* p=0.821†	697 ± 53.8 p=0.264* p=0.912†	647 ± 24 p=0.362* p=0.959†
TNF-α	30 ± 5.5	1222.3 ± 30.7 p=0.001*	30.3 ± 4.5 p>0.999* p=0.001†	61 ± 17.5 p>0.999* p=0.002†	17 ± 7 p>0.999* p=0.001†	5956 ± 281.6 p<0.001* p<0.001†	8084 ± 411.6 p<0.001* p<0.001†	9036.6 ± 839.7 p<0.001* p<0.001†

*vs. Uninfected, †vs. *M. tb* R179

Cytokines	Uninfected	<i>M. tb</i> R179	Knock-down (siRNA)			Knock-up (vector-based over-expression)		
			<i>IFIT1</i>	<i>IFIT1</i>	<i>IFIT2</i>	<i>IFIT1</i>	<i>IFIT1</i>	<i>IFIT2</i>
<i>at 96 hours</i>								
IDO-1	971 ± 13.4	1798 ± 63.6	0.3 ± 0.5 p=0.008*	8.6 ± 1.5 p=0.001*	9 ± 1 p=0.001*	2445.3 ± 368.3 p<0.001*	2313.6 ± 52.2 p<0.001*	2680.6 ± 324.5 p<0.001*
IFN-α	29 ± 1	71.3 ± 12.5	0.3 ± 0.5 p>0.999*	6 ± 1 p>0.999*	12.6 ± 2 p>0.999*	127.3 ± 26 p>0.999*	275.6 ± 44.2 p>0.999*	262.6 ± 37 p>0.999*
IFN-β	0	6 ± 3.4 p>0.999*	0 p>0.999*	12 p>0.999*	6 p>0.999*	6347 ± 302 p<0.001*	5513.3 ± 100.8 p<0.001*	4776 ± 112.2 p<0.001*
IFN-γ	527.3 ± 12	1014.6 ± 62.6	0 p=0.389*	0 p=0.287*	0 p<0.001†	5772 ± 899.6 p<0.001*	4627.7 ± 522.8 p<0.001*	4709 ± 138.1 p<0.001†
IL-4	7.6 ± 4.7	517.6 ± 54.8	0 p=0.329*	0.3 ± 0.5 p>0.999*	2.3 ± 2.5 p=0.310†	4120.6 ± 390.4 p<0.001*	4591 ± 715.7 p<0.001*	5585 ± 542.5 p<0.001†

*vs. Uninfected, †vs. *M. tb* R179

IL-6	239.3 ± 19.8	2347.6 ± 315.4 p<0.001*	0.6 ± 0.5 p=0.965* p<0.001†	9 ± 8.1 p=0.970* p<0.001†	0.6 ± 1.1 p=0.965* p<0.001†	6645.6 ± 538.5 p<0.001* p<0.001†	7180.3 ± 480.4 p<0.001* p<0.001†	3915.3 ± 1243 p<0.001* p<0.001†
IL-8	657 ± 19.6	9531.7 ± 572.8 p<0.001*	889 ± 161 p=0.970* p<0.001†	548 ± 91.5 p>0.999* p<0.001†	991.7 ± 38.2 p=0.821* p<0.001†	4049 ± 643.8 p<0.001* p<0.001†	4932.7 ± 52.5 p<0.001* p<0.001†	4684.3 ± 226.6 p<0.001* p<0.001†
IL-12p40	94.7 ± 6.6	254.7 ± 11.6 p=0.997*	3.7 ± 3.2 p>0.999* p=0.963†	9.3 ± 4.5 p>0.999* p=0.963†	0 p>0.999* p=0.963†	2475.7 ± 454.5 p<0.001* p<0.001†	2732 ± 421.9 p<0.001* p<0.001†	2837.7 ± 820 p<0.001* p<0.001†
IL-12p70	16.7 ± 4.1	95.3 ± 7.5 p>0.999*	0 p>0.999* p>0.999†	0.3 ± 0.5 p>0.999* p>0.999†	0 p>0.999* p>0.999†	3419 ± 153.5 p<0.001* p<0.001†	3627.7 ± 185.2 p<0.001* p<0.001†	3172.7 ± 725.4 p<0.001* p<0.001†
IL-23	1245 ± 52.7	267.7 ± 36.6 p=0.993*	49 ± 54.5 p<0.001* p<0.001†	34 ± 7 p<0.001* p<0.001†	38.7 ± 40 p<0.001* p<0.001†	724 ± 295.7 p<0.001* p<0.001†	536.3 ± 329.8 p<0.001* p<0.001†	528.3 ± 376.6 p<0.001* p<0.001†
IL-1α	243.3 ± 9.4	267.7 ± 46.4 p>0.999*	49 ± 4.5 p=0.989* p=0.979†	34 ± 4.3 p=0.983* p=0.969†	38.7 ± 9 p=0.985* p=0.972†	724 ± 12.5 p=0.408* p=0.478†	536.3 ± 86.6 p=0.900* p=0.936†	4541 ± 147.1 p=0.910* p=0.945†
IL-1β	22 ± 4.3	118.3 ± 27 p>0.999*	32.3 ± 2.5 p>0.999* p>0.999†	23.3 ± 2.5 p>0.999* p>0.999†	52.7 ± 4.7 p>0.999* p>0.999†	456.7 ± 15.3 p=0.543* p=0.812†	553 ± 96.2 p=0.278* p=0.543†	372.3 ± 54.8 p=0.783* p=0.952†
TNF-α	30 ± 5.5	352.7 ± 40.7 p=0.847*	49.3 ± 13.5 p>0.999* p=0.884†	21 ± 9.5 p>0.999* p=0.827†	24.3 ± 11 p>0.999* p=0.835†	6098.7 ± 532 p<0.001* p<0.001†	6119 ± 204.4 p<0.001* p<0.001†	5411.3 ± 509.1 p<0.001* p<0.001†

*vs. Uninfected, †vs. *M. tb* R179

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