

**Interleukin-17 limits Hypoxia-inducible factor 1 $\alpha$  and development of hypoxic granulomas during tuberculosis**

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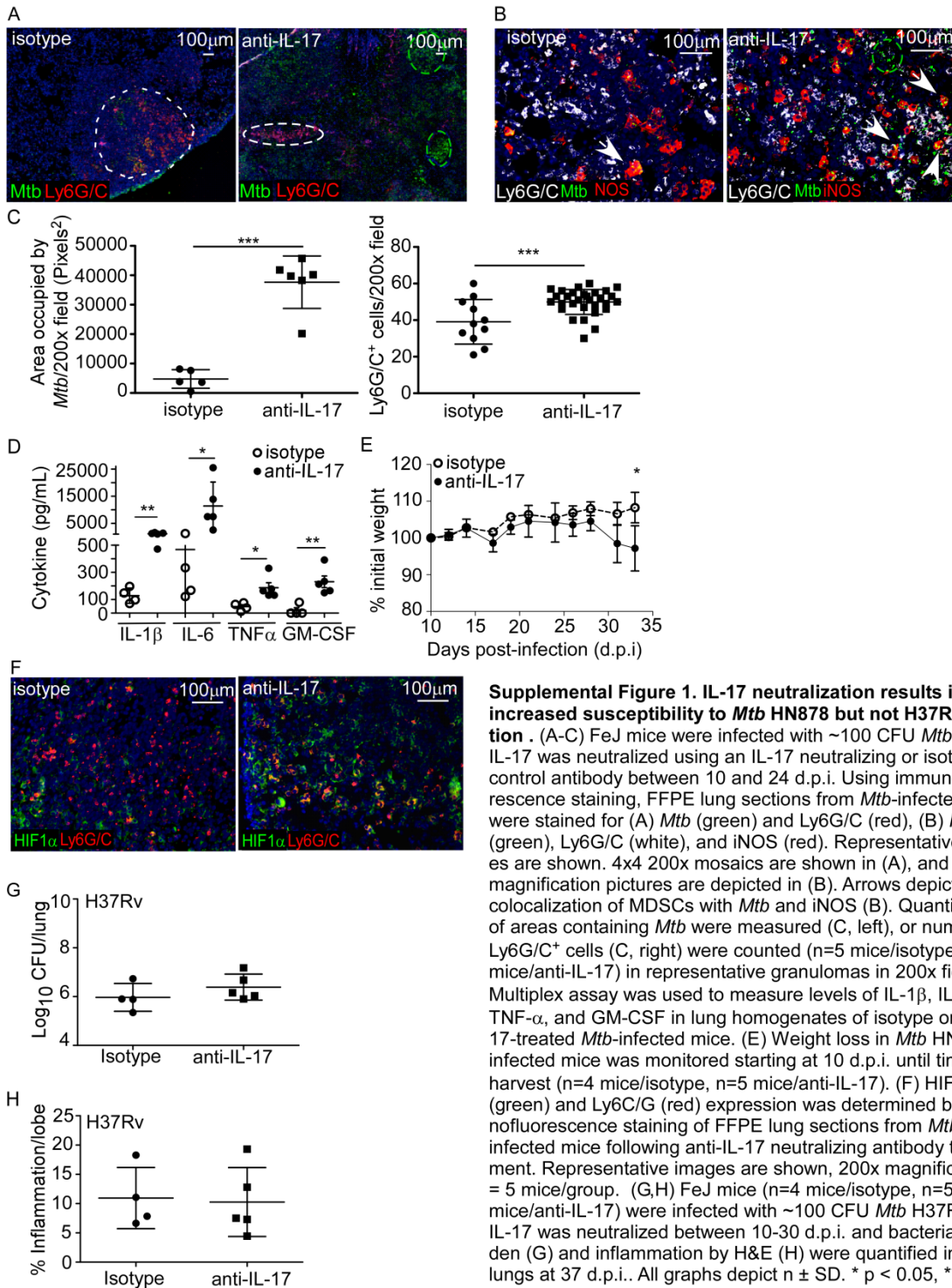
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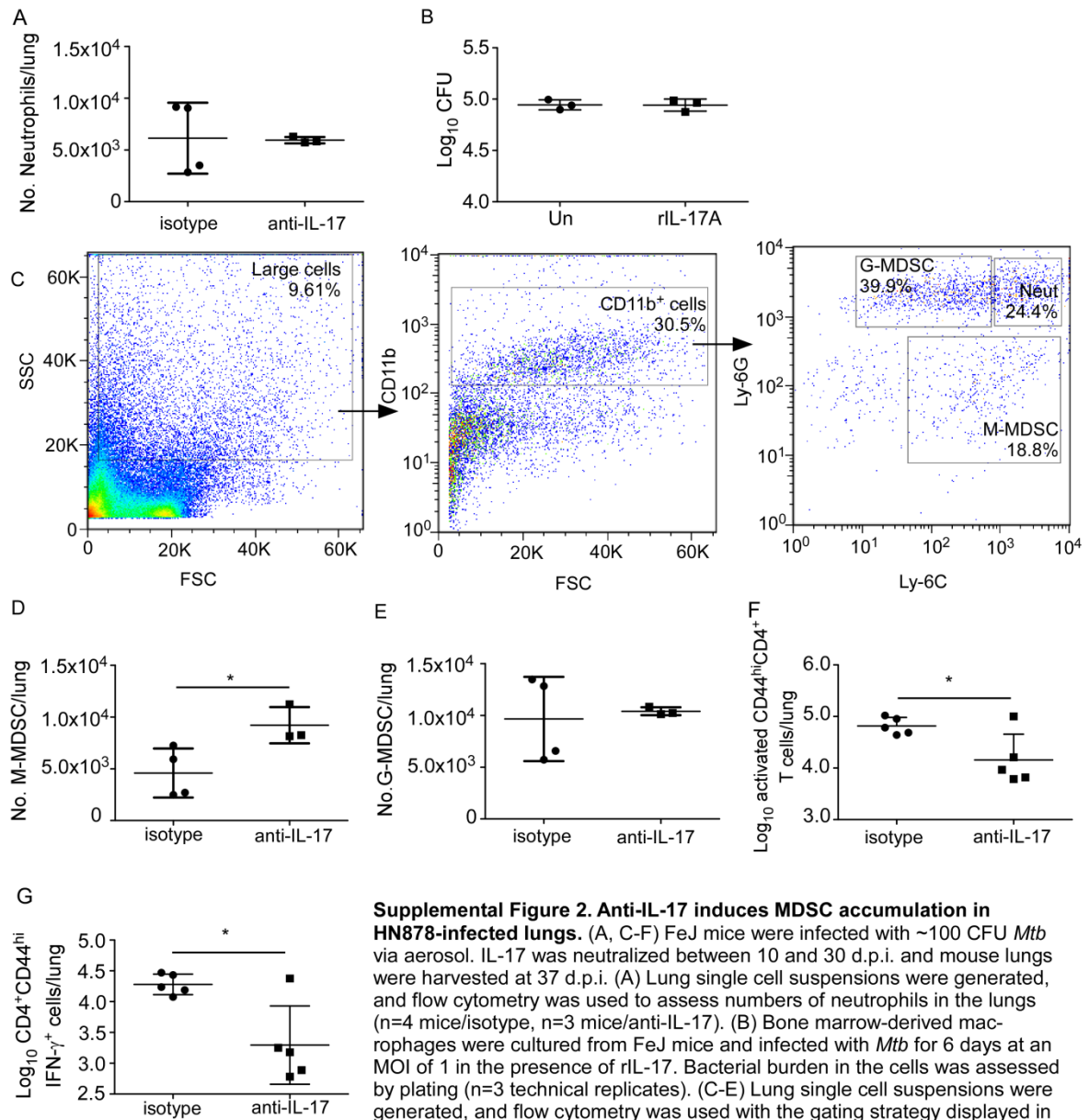
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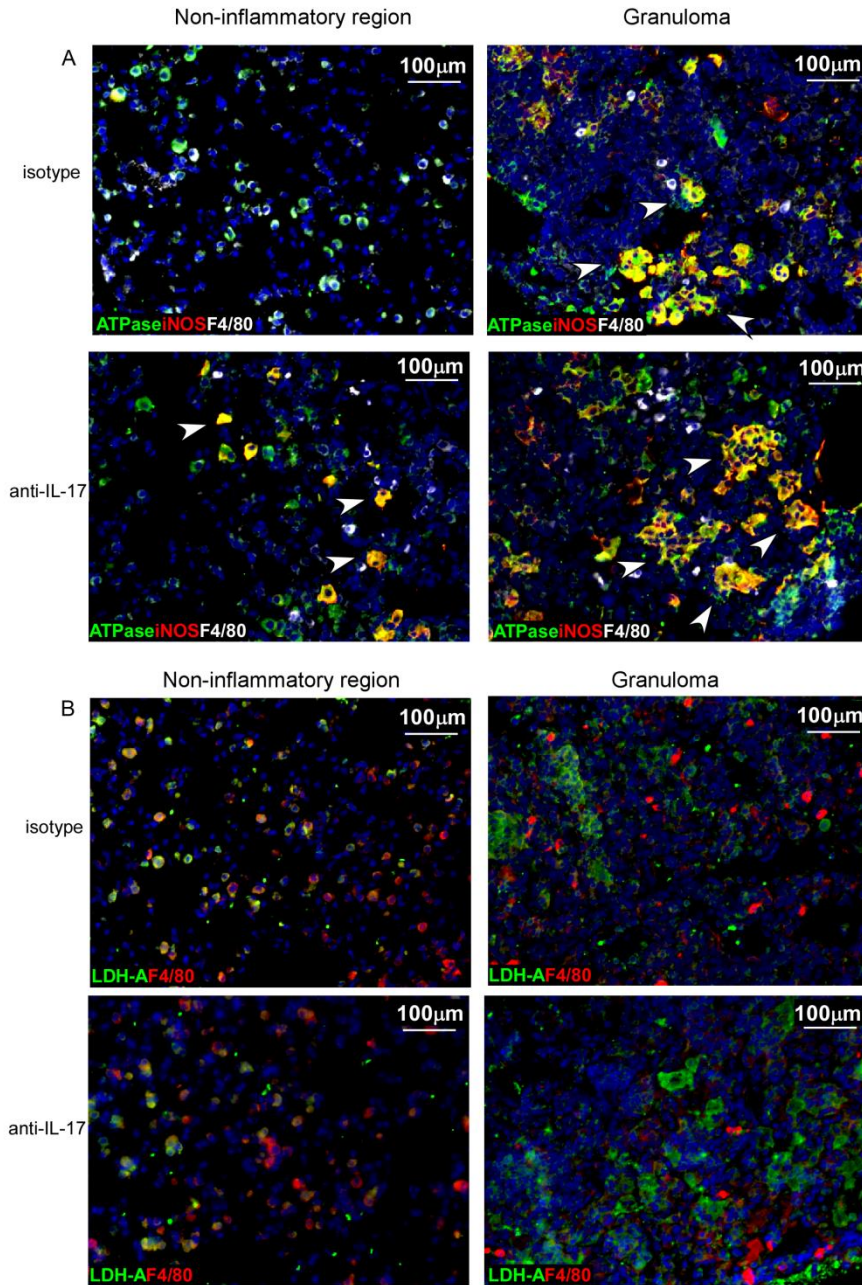
Supplemental Figures and Figure legends



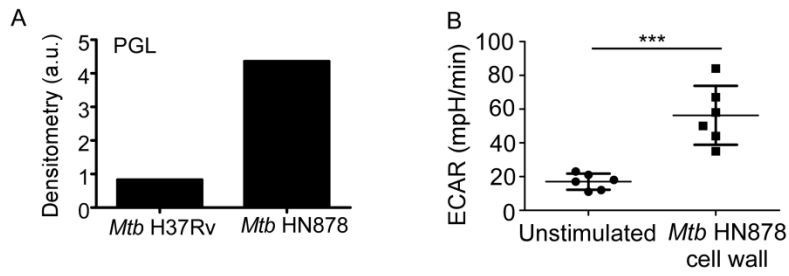
**Supplemental Figure 1. IL-17 neutralization results in increased susceptibility to *Mtb* HN878 but not H37Rv infection .** (A-C) FeJ mice were infected with ~100 CFU *Mtb* HN878. IL-17 was neutralized using an IL-17 neutralizing or isotype control antibody between 10 and 24 d.p.i. Using immunofluorescence staining, FFPE lung sections from *Mtb*-infected mice were stained for (A) *Mtb* (green) and Ly6G/C (red), (B) *Mtb* (green), Ly6G/C (white), and iNOS (red). Representative images are shown. 4x4 200x mosaics are shown in (A), and 200x magnification pictures are depicted in (B). Arrows depict colocalization of MDSCs with *Mtb* and iNOS (B). Quantification of areas containing *Mtb* were measured (C, left), or number of Ly6G/C+ cells (C, right) were counted (n=5 mice/isotype, n=6 mice/anti-IL-17) in representative granulomas in 200x field. (D) Multiplex assay was used to measure levels of IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and GM-CSF in lung homogenates of isotype or anti-IL-17-treated *Mtb*-infected mice. (E) Weight loss in *Mtb* HN878-infected mice was monitored starting at 10 d.p.i. until time of harvest (n=4 mice/isotype, n=5 mice/anti-IL-17). (F) HIF1 $\alpha$  (green) and Ly6C/G (red) expression was determined by immunofluorescence staining of FFPE lung sections from *Mtb*-infected mice following anti-IL-17 neutralizing antibody treatment. Representative images are shown, 200x magnification. n = 5 mice/group. (G,H) FeJ mice (n=4 mice/isotype, n=5 mice/anti-IL-17) were infected with ~100 CFU *Mtb* H37Rv and IL-17 was neutralized between 10-30 d.p.i. and bacterial burden (G) and inflammation by H&E (H) were quantified in the lungs at 37 d.p.i.. All graphs depict n  $\pm$  SD. \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001 by student's *t*-test (C-E,G,H).



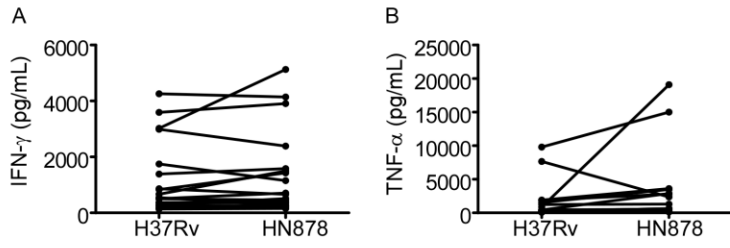
**Supplemental Figure 2. Anti-IL-17 induces MDSC accumulation in HN878-infected lungs.** (A, C-F) FeJ mice were infected with ~100 CFU *Mtb* via aerosol. IL-17 was neutralized between 10 and 30 d.p.i. and mouse lungs were harvested at 37 d.p.i. (A) Lung single cell suspensions were generated, and flow cytometry was used to assess numbers of neutrophils in the lungs (n=4 mice/isotype, n=3 mice/anti-IL-17). (B) Bone marrow-derived macrophages were cultured from FeJ mice and infected with *Mtb* for 6 days at an MOI of 1 in the presence of rIL-17. Bacterial burden in the cells was assessed by plating (n=3 technical replicates). (C-E) Lung single cell suspensions were generated, and flow cytometry was used with the gating strategy displayed in (C) to assess numbers of (D) M-MDSCs (CD11b<sup>+</sup>Ly-6C<sup>hi</sup>Ly-6G<sup>lo</sup>) (n=4 mice/isotype, n=4 mice/anti-IL-17), (E) G-MDSCs (CD11b<sup>+</sup>Ly-6C<sup>lo</sup>Ly-6G<sup>hi</sup>) (n=4 mice/isotype, n=4 mice/anti-IL-17) in the lungs. (F, G) Lung single cell suspensions were generated and stimulated for 5 hours with PMA and ionomycin in the presence of GolgiStop, and flow cytometry was used to determine numbers of (F) activated CD44<sup>hi</sup>CD4<sup>+</sup> T cells (n=5 mice/group), and (G) activated CD44<sup>hi</sup>CD4<sup>+</sup> IFN- $\gamma$ -producing T cells in the lungs (n=5 mice/group). All graphs depict n  $\pm$  SD. \* p < 0.05, by student's *t*-test (A,B,D-G).



**Supplemental Figure 3. Glycolytic markers are expressed by recruited macrophages within granulomas.** Using immunofluorescence staining, FFPE lung sections from *Mtb*-infected mice following treatment with isotype or anti-IL-17 neutralizing antibody (10-24 d.p.i.) were stained for (A) ATPase (green), iNOS (red), F4/80 (white), and (B) LDH-A (green) and F4/80 (red) in both non-inflammatory regions and granuloma. Representative images are shown, 200x magnification. Arrows depict areas of increased glycolysis (A,B).



**Supplemental Figure 4. *Mtb* HN878 cell wall components drive glycolysis.** (A) Densitometry of PGL presence in total lipid extracts from *Mtb* H37Rv and HN878. Total lipid extracts were analyzed by two dimensional thin layer chromatography and the solvent system as a 1st-D: chloroform:methanol (96:4, v/v) and as the 2nd-D: toluene:acetone (80:20, v/v). Plates were developed by 10% sulfuric acid in ethanol and 5% phosphomolybdate acid in ethanol. Spots were identified as PGL when positive using all developers. Presence of PGL was confirmed by a 2D-TLC comparison with PGL content from strain *M. bovis* BCG (data not shown). (B) Quantification of ECAR values in unstimulated macrophages or macrophages stimulated with HN878 cell wall fractions (20  $\mu$ g/mL) following 24 h stimulation (n=6 technical replicates). \*\*\*p<0.001 as analyzed by student's *t*-test (B).



**Supplemental Figure 5. *Mtb* HN878 does not drive differential IFN- $\gamma$  or TNF- $\alpha$  production in human PBMCs from TB patients.** PBMCs were isolated from TB patients. (A) IFN- $\gamma$  (n=20 patients) and (B) TNF- $\alpha$  (n=18 patients) production by PBMCs isolated from TB patients following stimulation with 10  $\mu$ g/mL either *Mtb* H37Rv or HN878 cell wall extract was assessed by multiplex assay. Statistical significance was determined by Two-way ANOVA.

**Supplemental Table 1. Differential expression of genes by RNAseq following anti-IL-17 neutralization.** FeJ mice were infected with *Mtb* and received control or anti-IL-17 treatment. On day 30, lung RNA was isolated and RNAseq analysis was carried out to determine fold change in mRNA expression in anti-IL-17 treated lungs compared to control FeJ *Mtb*-infected lungs. Top 100 upregulated and 100 downregulated genes are shown; n=4 mice/isotype and n=3 mice/anti-IL-17 groups.

Gene I.D.	Gene	Description	Fold change (anti-IL-17A vs isotype)	q value
213742	Xist	inactive X specific transcripts	11.0456	0.049548
11846	Arg1	arginase, liver	4.18188	0.002183
20862	Stfa2	stefin A2	3.91602	0.025186
11657	Alb	albumin	3.66186	0.002183
18788	Serpib2	serine (or cysteine) peptidase inhibitor, clade B, member 2	3.33733	0.002183
18054	Ngp	neutrophilic granule protein	3.26001	0.002183
229927	Clca4	chloride channel calcium activated 4	3.17649	0.002183
668727	Mrgpra2a	MAS-related GPR, member A2A	2.92601	0.048997
433016	Gm5483	predicted gene 5483	2.74658	0.002183
12985	Csf3	colony stimulating factor 3 (granulocyte)	2.70691	0.002183
16171	Il17a	interleukin 17A	2.69092	0.002183
20310	Cxcl2	chemokine (C-X-C motif) ligand 2	2.58466	0.002183
245195	Retnlg	resistin like gamma	2.44249	0.002183
16156	Il11	interleukin 11	2.36714	0.002183
20714	Serpina3k	serine (or cysteine) peptidase inhibitor, clade A, member 3K	2.28437	0.026846
76459	Car12	carbonic anhydrase 12	2.28119	0.002183
235712	Mrgpra2b	MAS-related GPR, member A2B	2.25182	0.002183
268885	Stfa2l1	stefin A2 like 1	2.25029	0.002183
20202	S100a9	S100 calcium binding protein A9 (calgranulin B)	2.23397	0.002183
67855	Asprv1	aspartic peptidase, retroviral-like 1	2.16465	0.002183
20201	S100a8	S100 calcium binding protein A8 (calgranulin A)	2.1364	0.002183
23844	Clca3	chloride channel calcium activated 3	2.10008	0.002183



<b>215257</b>	Il1f9	interleukin 1 family, member 9	2.0168	0.002183
<b>213002</b>	Ifitm6	interferon induced transmembrane protein 6	1.9867	0.002183
<b>20302</b>	Ccl3	chemokine (C-C motif) ligand 3	1.97135	0.002183
<b>13874</b>	Ereg	epiregulin	1.92969	0.002183
<b>67133</b>	Gp2	glycoprotein 2 (zymogen granule membrane)	1.90274	0.002183
<b>257630</b>	Il17f	interleukin 17F	1.88939	0.047605
<b>232345</b>	A2m	alpha-2-macroglobulin	1.7695	0.002183
<b>244233</b>	Cd163l1	CD163 molecule-like 1	1.70188	0.002183
<b>20303</b>	Ccl4	chemokine (C-C motif) ligand 4	1.70168	0.002183
<b>12945</b>	Dmbt1	deleted in malignant brain tumors 1	1.64371	0.002183
<b>12904</b>	Crabp2	cellular retinoic acid binding protein II	1.62727	0.023395
<b>13076</b>	Cyp1a1	cytochrome P450, family 1, subfamily a, polypeptide 1	1.61305	0.002183
<b>12796</b>	Camp	cathelicidin antimicrobial peptide	1.5906	0.008254
<b>78354</b>	2210407C18Rik	RIKEN cDNA 2210407C18 gene	1.58018	0.002183
<b>21785</b>	Tff2	trefoil factor 2 (spasmolytic protein 1)	1.57519	0.002183
<b>74002</b>	Psd2	pleckstrin and Sec7 domain containing 2	1.55507	0.002183
<b>21943</b>	Tnfsf11	tumor necrosis factor (ligand) superfamily, member 11	1.49329	0.002183
<b>385643</b>	Kng2	kininogen 2	1.46632	0.014886
<b>26366</b>	Ceacam10	carcinoembryonic antigen-related cell adhesion molecule 10	1.41942	0.026846
<b>17384</b>	Mmp10	matrix metalloproteinase 10	1.41887	0.002183
<b>18413</b>	Osm	oncostatin M	1.41054	0.002183
<b>19695</b>	Reg3g	regenerating islet-derived 3 gamma	1.36915	0.002183
<b>104307</b>	Rnu12	RNA U12, small nuclear	1.35832	0.002183
<b>245126</b>	Tarm1	T cell-interacting, activating receptor on myeloid cells 1	1.35234	0.002183
<b>16176</b>	Il1b	interleukin 1 beta	1.35216	0.002183
<b>17394</b>	Mmp8	matrix metalloproteinase 8	1.31245	0.002183
<b>22409</b>	Wnt10a	wingless related MMTV integration site 10a	1.29647	0.005545
<b>16664</b>	Krt14	keratin 14	1.28463	0.01168
<b>319707</b>	C430002N11Rik	RIKEN cDNA C430002N11 gene	1.2618	0.027734
<b>23892</b>	Grem1	gremlin 1	1.25209	0.002183
<b>240913</b>	Adamts4	a disintegrin-like and metalloproteinase (reprolysin type) with thrombospondin	1.25107	0.002183

type 1 motif, 4				
<b>19275</b>	Ptprn	protein tyrosine phosphatase, receptor type, N	1.2479	0.002183
<b>226841</b>	Vash2	vasohibin 2	1.24072	0.006945
<b>12143</b>	Blk	B lymphoid kinase	1.2381	0.002183
<b>80976</b>	Syt13	synaptotagmin XIII	1.22512	0.006945
<b>11687</b>	Alox15	arachidonate 15-lipoxygenase	1.18884	0.002183
<b>53867</b>	Col5a3	collagen, type V, alpha 3	1.17634	0.002183
<b>74614</b>	Ocstamp	osteoclast stimulatory transmembrane protein	1.17144	0.008254
<b>16178</b>	Il1r2	interleukin 1 receptor, type II	1.17136	0.002183
<b>20209</b>	Saa2	serum amyloid A 2	1.16041	0.031173
<b>21941</b>	Tnfrsf8	tumor necrosis factor receptor superfamily, member 8	1.15553	0.040356
<b>58217</b>	Trem1	triggering receptor expressed on myeloid cells 1	1.14956	0.002183
<b>380924</b>	Olfm4	olfactomedin 4	1.14143	0.002183
<b>67038</b>	2010109I03Rik	RIKEN cDNA 2010109I03 gene	1.13374	0.026026
<b>214058</b>	Megf11	multiple EGF-like-domains 11	1.13094	0.002183
<b>80982</b>	9930013L23Rik	RIKEN cDNA 9930013L23 gene	1.12616	0.002183
<b>11994</b>	Pcdh15	protocadherin 15	1.12504	0.002183
<b>14472</b>	Gbx2	gastrulation brain homeobox 2	1.1071	0.037413
<b>11489</b>	Adam12	a disintegrin and metallopeptidase domain 12 (meltrin alpha)	1.10349	0.002183
<b>17395</b>	Mmp9	matrix metallopeptidase 9	1.09862	0.002183
<b>18787</b>	Serpine1	serine (or cysteine) peptidase inhibitor, clade E, member 1	1.09065	0.002183
<b>17167</b>	Marco	macrophage receptor with collagenous structure	1.08494	0.002183
<b>16181</b>	Il1rn	interleukin 1 receptor antagonist	1.08048	0.002183
<b>16365</b>	Irg1	immunoresponsive gene 1	1.08046	0.002183
<b>17967</b>	Ncam1	neural cell adhesion molecule 1	1.0681	0.002183
<b>14603</b>	Gif	gastric intrinsic factor	1.05711	0.024287
<b>18612</b>	Etv4	ets variant gene 4 (E1A enhancer binding protein, E1AF)	1.04397	0.009406
<b>74180</b>	Muc5b	mucin 5, subtype B, tracheobronchial	1.03649	0.002183
<b>20344</b>	Selp	selectin, platelet	1.03295	0.028519
<b>15117</b>	Has2	hyaluronan synthase 2	1.02999	0.002183
<b>112407</b>	Egln3	EGL nine homolog 3 ( <i>C. elegans</i> )	1.02532	0.002183
<b>433638</b>	I830077J02Rik	RIKEN cDNA I830077J02 gene	1.01414	0.016911

<b>23795</b>	Agr2	anterior gradient 2	1.00783	0.013928
<b>20558</b>	Slfn4	schlafen 4	1.00429	0.002183
<b>14313</b>	Fst	follistatin	1.00397	0.002183
<b>58185</b>	Rsad2	radical S-adenosyl methionine domain containing 2	1.00294	0.002183
<b>14940</b>	Gzmc	granzyme C	0.998492	0.003959
<b>226245</b>	Plekhs1	pleckstrin homology domain containing, family S member 1	0.998168	0.002183
<b>17386</b>	Mmp13	matrix metalloproteinase 13	0.97445	0.002183
<b>11828</b>	Aqp3	aquaporin 3	0.97088	0.01168
<b>16323</b>	Inhba	inhibin beta-A	0.963175	0.002183
<b>67313</b>	5730559C18Rik	RIKEN cDNA 5730559C18 gene	0.950793	0.041581
<b>14115</b>	Fbln2	fibulin 2	0.946032	0.002183
<b>20856</b>	Stc2	stanniocalcin 2	0.931361	0.002183
<b>21826</b>	Thbs2	thrombospondin 2	0.927537	0.002183
<b>12475</b>	Cd14	CD14 antigen	0.92404	0.002183
<b>13003</b>	Vcan	versican	0.922183	0.002183
<b>108115</b>	Slco4a1	solute carrier organic anion transporter family, member 4a1	0.922043	0.003959
<b>57277</b>	Slurp1	secreted Ly6/Plaur domain containing 1	-0.79203	0.006945
<b>12373</b>	Casq2	calsequestrin 2	-0.79657	0.003959
<b>22437</b>	Xirp1	xin actin-binding repeat containing 1	-0.79766	0.041581
<b>69066</b>	1810010H24Rik	RIKEN cDNA 1810010H24 gene	-0.80207	0.002183
<b>117158</b>	Scgb3a2	secretoglobin, family 3A, member 2	-0.80262	0.002183
<b>20269</b>	Scn3a	sodium channel, voltage-gated, type III, alpha	-0.80608	0.002183
<b>233335</b>	Synm	synemin, intermediate filament protein	-0.80839	0.002183
<b>18133</b>	Nov	nephroblastoma overexpressed gene	-0.81594	0.002183
<b>56363</b>	Tmeff2	transmembrane protein with EGF-like and two follistatin-like domains 2	-0.81728	0.003959
<b>67298</b>	Gprasp1	G protein-coupled receptor associated sorting protein 1	-0.81742	0.002183
<b>21924</b>	Tnnc1	troponin C, cardiac/slow skeletal	-0.81837	0.002183
<b>70337</b>	Iyd	iodotyrosine deiodinase	-0.81919	0.023395
<b>21954</b>	Tnni3	troponin I, cardiac 3	-0.82163	0.002183
<b>17896</b>	Myl4	myosin, light polypeptide 4	-0.8217	0.002183
<b>13009</b>	Csrp3	cysteine and glycine-rich protein 3	-0.82606	0.002183
<b>15505</b>	Hsph1	heat shock 105kDa/110kDa protein 1	-0.82786	0.002183
<b>14652</b>	Glp1r	glucagon-like peptide 1 receptor	-0.82964	0.002183

<b>66277</b>	Klf15	Kruppel-like factor 15	-0.83337	0.002183
<b>12869</b>	Cox8b	cytochrome c oxidase subunit VIIIb	-0.84322	0.039699
<b>216974</b>	Proca1	protein interacting with cyclin A1	-0.85208	0.021609
<b>53896</b>	Slc7a10	solute carrier family 7 (cationic amino acid transporter, y+ system), member 10	-0.85763	0.041039
<b>241877</b>	Slc10a5	solute carrier family 10 (sodium/bile acid cotransporter family), member 5	-0.85783	0.021609
<b>15129</b>	Hbb-b1	hemoglobin, beta adult major chain	-0.85836	0.002183
<b>66797</b>	Cntnap2	contactin associated protein-like 2	-0.86281	0.029391
<b>76477</b>	Pcolce2	procollagen C-endopeptidase enhancer 2	-0.8661	0.002183
<b>69327</b>	1700007K13Rik	RIKEN cDNA 1700007K13 gene	-0.86904	0.002183
<b>218038</b>	Amph	amphiphysin	-0.86983	0.002183
<b>246133</b>	Kcne2	potassium voltage-gated channel, Isk-related subfamily, gene 2	-0.87412	0.002183
<b>228003</b>	Klhl41	kelch-like 41	-0.87699	0.008254
<b>17898</b>	Myl7	myosin, light polypeptide 7, regulatory	-0.87716	0.002183
<b>14799</b>	Gria1	glutamate receptor, ionotropic, AMPA1 (alpha 1)	-0.87797	0.002183
<b>15122</b>	Hba-a1	hemoglobin alpha, adult chain 1	-0.87913	0.002183
<b>22693</b>	Zfp30	zinc finger protein 30	-0.88159	0.032717
<b>11464</b>	Actc1	actin, alpha, cardiac muscle 1	-0.88685	0.002183
<b>246278</b>	Cd207	CD207 antigen	-0.89381	0.002183
<b>66106</b>	Smpx	small muscle protein, X-linked	-0.90198	0.002183
<b>241431</b>	Xirp2	xin actin-binding repeat containing 2	-0.91186	0.002183
<b>208595</b>	Gm9897	predicted gene 9897	-0.9255	0.026026
<b>20391</b>	Sgca	sarcoglycan, alpha (dystrophin-associated glycoprotein)	-0.92766	0.04356
<b>73713</b>	Rbm20	RNA binding motif protein 20	-0.93078	0.009406
<b>76722</b>	Ckmt2	creatine kinase, mitochondrial 2	-0.93213	0.002183
<b>13897</b>	Ces1e	carboxylesterase 1E	-0.93838	0.002183
<b>68460</b>	Dhrs7c	dehydrogenase/reductase (SDR family) member 7C	-0.94712	0.042878
<b>1E+08</b>	C130080G10Rik	RIKEN cDNA C130080G10 gene	-0.95311	0.017898
<b>76757</b>	Trdn	triadin	-0.95502	0.006945
<b>228432</b>	Ano3	anoctamin 3	-0.95715	0.012784
<b>70893</b>	Glb1l3	galactosidase, beta 1 like 3	-0.95972	0.039031
<b>239318</b>	Plcx3	phosphatidylinositol-specific phospholipase C, X domain containing	-0.97536	0.04707

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15507	Hspb1	heat shock protein 1	-0.97805	0.002183
15130	Hbb-b2	hemoglobin, beta adult minor chain	-0.97979	0.002183
53315	Sult1d1	sulfotransferase family 1D, member 1	-0.98184	0.002183
20739	Spta1	spectrin alpha, erythrocytic 1	-0.98306	0.002183
14077	Fabp3	fatty acid binding protein 3, muscle and heart	-0.98434	0.002183
13983	Esr2	estrogen receptor 2 (beta)	-1.00726	0.044958
21743	Inmt	indolethylamine N-methyltransferase	-1.02672	0.002183
245631	Mum111	melanoma associated antigen (mutated) 1-like 1	-1.03076	0.002183
12715	Ckm	creatine kinase, muscle	-1.03329	0.002183
20533	Slc4a1	solute carrier family 4 (anion exchanger), member 1	-1.04303	0.005545
50874	Tmod4	tropomodulin 4	-1.04555	0.005545
69142	Cd209f	CD209f antigen	-1.05778	0.01587
320026	A330076H08Rik	RIKEN cDNA A330076H08 gene	-1.07489	0.047605
14859	Gsta3	glutathione S-transferase, alpha 3	-1.08451	0.002183
18162	Npr3	natriuretic peptide receptor 3	-1.09809	0.002183
18946	Pnliprp1	pancreatic lipase related protein 1	-1.10666	0.009406
18843	Bpifa1	BPI fold containing family A, member 1	-1.13948	0.002183
14080	Fabp1	fatty acid binding protein 1, liver	-1.14715	0.002183
18979	Pon1	paraoxonase 1	-1.14861	0.002183
170786	Cd209a	CD209a antigen	-1.16595	0.002183
16519	Kcnj3	potassium inwardly-rectifying channel, subfamily J, member 3	-1.16882	0.013928
75497	Fabp12	fatty acid binding protein 12	-1.16937	0.01168
11529	Adh7	alcohol dehydrogenase 7 (class IV), mu or sigma polypeptide	-1.1694	0.002183
226040	Tmem252	transmembrane protein 252	-1.18235	0.010528
26549	Itgb1bp2	integrin beta 1 binding protein 2	-1.18391	0.002183
14560	Gdf10	growth differentiation factor 10	-1.19687	0.003959
66183	Sptssb	serine palmitoyltransferase, small subunit B	-1.1983	0.012784
223272	Itgb1	integrin, beta-like 1	-1.20632	0.002183
21955	Tnnt1	troponin T1, skeletal, slow	-1.22664	0.002183
77705	9230104L09Rik	RIKEN cDNA 9230104L09 gene	-1.22856	0.002183
24117	Wif1	Wnt inhibitory factor 1	-1.26099	0.002183
63954	Rbp7	retinol binding protein 7, cellular	-1.2907	0.002183
17901	Myl1	myosin, light polypeptide 1	-1.29877	0.002183

<b>18205</b>	Ntf3	neurotrophin 3	-1.32325	0.009406
<b>320981</b>	Enpp6	ectonucleotide pyrophosphatase/phosphodiesterase 6	-1.33195	0.002183
<b>319893</b>	A230057D06Rik	RIKEN cDNA A230057D06 gene	-1.35713	0.002183
<b>241041</b>	Gm4956	predicted gene 4956	-1.36308	0.01168
<b>14858</b>	Gsta2	glutathione S-transferase, alpha 2 (Yc2)	-1.41723	0.023395
<b>234564</b>	Ces1f	carboxylesterase 1F	-1.41956	0.002183
<b>12623</b>	Ces1g	carboxylesterase 1G	-1.42668	0.002183
<b>193740</b>	Hspa1a	heat shock protein 1A	-1.48489	0.002183
<b>338417</b>	Scgb1c1	secretoglobin, family 1C, member 1	-1.48617	0.044273
<b>22290</b>	Uty	ubiquitously transcribed tetratricopeptide repeat gene, Y chromosome	-1.49399	0.002183
<b>75581</b>	Yipf7	Yip1 domain family, member 7	-1.50661	0.047605
<b>26908</b>	Eif2s3y	eukaryotic translation initiation factor 2, subunit 3, structural gene Y-linked	-1.53431	0.002183
<b>20592</b>	Kdm5d	lysine (K)-specific demethylase 5D	-1.56097	0.002183
<b>26900</b>	Ddx3y	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, Y-linked	-1.63542	0.002183
<b>70192</b>	Cd209g	CD209g antigen	-1.63616	0.046407
<b>244723</b>	Olfm2	olfactomedin 2	-1.67152	0.002183
<b>223513</b>	Abra	actin-binding Rho activating protein	-1.71371	0.002183
<b>209268</b>	Igsf1	immunoglobulin superfamily, member 1	-1.75089	0.003959
<b>15511</b>	Hspa1b	heat shock protein 1B	-2.21837	0.002183

**Supplemental Table 2. Differential protein profiles in *Mtb* HN878 vs. H37Rv.**

MALDI-TOF with proteins annotated by blasting on Tuberculist and top list of proteins expressed in HN878 when compared to H37Rv is shown.

<b>Identified Proteins (2369)</b>	<b>Accession Number</b>	<b>Molecular Weight</b>	<b>Fold change HN878:H37Rv</b>
<b>pks1</b>	Rv2946c	167 kDa	34
<b>aceAb</b>	Rv1916	45 kDa	23
<b>espE</b>	Rv3864	42 kDa	21
<b>Rv0958</b>	Rv0958	50 kDa	15
<b>prpD</b>	Rv1130	58 kDa	15
<b>aceAa</b>	Rv1915	40 kDa	14
<b>aspC</b>	Rv0337c	47 kDa	14
<b>Rv0648</b>	Rv0648	130 kDa	14
<b>Rv3627c</b>	Rv3627c	47 kDa	11
<b>Rv0799c</b>	Rv0799c	36 kDa	11
<b>Rv1883c</b>	Rv1883c	17 kDa	11
<b>prpC</b>	Rv1131	43 kDa	11
<b>Rv3829c</b>	Rv3829c	57 kDa	9.7
<b>ctpl</b>	Rv0107c	170 kDa	9.4
<b>recG</b>	Rv2973c	80 kDa	9.3
<b>fadD24</b>	Rv1529	63 kDa	9.3
<b>iniA</b>	Rv0342	70 kDa	9.2
<b>gnd1</b>	Rv1844c	52 kDa	8.9
<b>regX3</b>	Rv0491	25 kDa	8.9
<b>lat</b>	Rv3290c	49 kDa	8.9
<b>cfp29</b>	Rv0798c	29 kDa	8.8
<b>espF</b>	Rv3865	11 kDa	8.8
<b>bcp</b>	Rv2521	17 kDa	8.5
<b>Rv2731</b>	Rv2731	50 kDa	8.3
<b>Rv3077</b>	Rv3077	67 kDa	8.2
<b>Rv1680</b>	Rv1680	30 kDa	8.0
<b>Rv1676</b>	Rv1676	26 kDa	7.7
<b>tgs3</b>	Rv3234c	30 kDa	7.7
<b>echA9</b>	Rv1071c	36 kDa	7.7
<b>Rv1109c</b>	Rv1109c	23 kDa	7.4
<b>Rv3233c</b>	Rv3233c	20 kDa	7.3

<b>Rv3479</b>	Rv3479	109 kDa	6.9
<b>Rv2024c</b>	Rv2024c	57 kDa	6.9
<b>Rv1995</b>	Rv1995	28 kDa	6.9
<b>iniC</b>	Rv0343	53 kDa	6.7
<b>accA2</b>	Rv0973c	71 kDa	6.5
<b>Rv2957</b>	Rv2957	31 kDa	6.5
<b>Rv1667c</b>	Rv1667c	24 kDa	6.5
<b>Rv1461</b>	Rv1461	94 kDa	6.1
<b>tesB1</b>	Rv1618	33 kDa	6.0
<b>Rv2484c</b>	Rv2484c	52 kDa	6.0
<b>atsD</b>	Rv0663	86 kDa	6.0
<b>Rv2277c</b>	Rv2277c	32 kDa	6.0
<b>cyp139</b>	Rv1666c	48 kDa	6.0
<b>TB27.3</b>	Rv0577	27 kDa	6.0
<b>ligA</b>	Rv3014c	75 kDa	5.9
<b>lldD1</b>	Rv0694	42 kDa	5.2
<b>fdhF</b>	Rv2900c	85 kDa	5.2
<b>rip</b>	Rv2869c	43 kDa	5.2
<b>tgs4</b>	Rv3088	51 kDa	5.2
<b>ptrBb</b>	Rv0782	61 kDa	5.2
<b>ltp4</b>	Rv3522	38 kDa	5.2
<b>thiD</b>	Rv0422c	28 kDa	5.2
<b>PPE68</b>	Rv3873	37 kDa	5.2
<b>Rv0756c</b>	Rv0756c	25 kDa	5.2
<b>fadE26</b>	Rv3504	44 kDa	5.2
<b>ispD</b>	Rv3582c	24 kDa	5.1
<b>glgE</b>	Rv1327c	79 kDa	5.0
<b>mutA</b>	Rv1492	65 kDa	4.8
<b>accD2</b>	Rv0974c	56 kDa	4.8
<b>Rv0443</b>	Rv0443	19 kDa	4.8
<b>fbpD</b>	Rv3803c	31 kDa	4.8
<b>Rv2522c</b>	Rv2522c	49 kDa	4.8
<b>yrbE1A</b>	Rv0167	28 kDa	4.8
<b>pafB</b>	Rv2096c	35 kDa	4.8
<b>Rv0200</b>	Rv0200	24 kDa	4.8
<b>PE13</b>	Rv1195	10 kDa	4.8
<b>gpdA1</b>	Rv0564c	36 kDa	4.6
<b>Rv1509</b>	Rv1509	33 kDa	4.6
<b>ppgK</b>	Rv2702	27 kDa	4.6



<b>Rv2468c</b>	Rv2468c	17 kDa	4.4
<b>hsaD</b>	Rv3569c	32 kDa	4.4
<b>Rv3725</b>	Rv3725	33 kDa	4.4
<b>Rv3327</b>	Rv3327	63 kDa	4.4
<b>Rv2670c</b>	Rv2670c	40 kDa	4.4
<b>Rv2958c</b>	Rv2958c	47 kDa	4.4
<b>Rv2714</b>	Rv2714	36 kDa	4.4
<b>vapC1</b>	Rv0065	14 kDa	4.4
<b>aac</b>	Rv0262c	20 kDa	4.4
<b>suhB</b>	Rv2701c	30 kDa	4.4
<b>phoR</b>	Rv0758	52 kDa	4.3
<b>plcB</b>	Rv2350c	56 kDa	4.3
<b>Rv1708</b>	Rv1708	34 kDa	4.3
<b>mtrB</b>	Rv3245c	62 kDa	4.3
<b>Rv0177</b>	Rv0177	20 kDa	4.3
<b>Rv1476</b>	Rv1476	20 kDa	4.3
<b>ribH</b>	Rv1416	16 kDa	4.3
<b>Rv2073c</b>	Rv2073c	26 kDa	4.3
<b>Rv0634c</b>	Rv0634c	26 kDa	4.3
<b>ftsZ</b>	Rv2150c	39 kDa	4.2
<b>cyp138</b>	Rv0136	49 kDa	4.1
<b>Rv3091</b>	Rv3091	62 kDa	4.1
<b>Rv0347</b>	Rv0347	37 kDa	4.1
<b>fadD29</b>	Rv2950c	67 kDa	4.1
<b>gabD1</b>	Rv0234c	54 kDa	4.1

**Supplemental Table 3. MGIT assay to determine MIC of acriflavine on *Mtb* HN878.** *Mtb* HN878 7H9 liquid cultures were inoculated with varying concentration of acriflavine or untreated (n=6/no drug; n=3/acriflavine concentration). SD denotes standard deviation.

	<b>Growth MGIT</b>	<b>Average hours to growth detection (<math>\pm</math>SD)</b>
<b>No drug</b>	YES	10
<b>0.25 <math>\mu</math>g/ml</b>	YES	10
<b>0.75 <math>\mu</math>g/ml</b>	YES	10.67 ( $\pm$ .58)
<b>1.5 <math>\mu</math>g/ml</b>	YES	11.67 ( $\pm$ .58)
<b>3 <math>\mu</math>g/ml</b>	YES	16.33 ( $\pm$ .58)
<b>25 <math>\mu</math>g/ml</b>	NO	No growth

**Supplemental Table 4. SNPs screened with Sequenom.** DNA from PTB and LTBI patients were screened for known immune-related SNPs listed below using the Sequenom i-PLEX Gold MassARRAY system. Highlighted SNPs were statistically significant by Chi Sq.

<b>Gene</b>	<b>Reference SNP</b>
<b>Bcl6</b>	rs1056936
<b>Bcl6</b>	rs112650365
<b>Bcl6</b>	rs139857005
<b>Bcl6</b>	rs142387697
<b>Bcl6</b>	rs143522266
<b>Bcl6</b>	rs144416315
<b>Bcl6</b>	rs147478441
<b>Bcl6</b>	rs147650939
<b>Bcl6</b>	rs147671000
<b>Bcl6</b>	rs147914986
<b>Bcl6</b>	rs148348997
<b>Bcl6</b>	rs150319050
<b>Bcl6</b>	rs151194132
<b>Bcl6</b>	rs2229362
<b>Bcl6</b>	rs34463990
<b>Bcl6</b>	rs36011786
<b>Bcl6</b>	rs61752081
<b>Bcl6</b>	rs66557861
<b>Bcl6</b>	rs67973148
<b>Bcl6</b>	rs77274617
<b>CD209</b>	rs11465360
<b>CXCL13</b>	rs114867987
<b>CXCL13</b>	rs115525661
<b>CXCL13</b>	rs149195141
<b>CXCL13</b>	rs150188610
<b>CXCL13</b>	rs187741836
<b>PDCD1</b>	rs137861407
<b>PDCD1</b>	rs138016578

<b>PDCD1</b>	rs138031190
<b>PDCD1</b>	rs141718335
<b>PDCD1</b>	rs142434414
<b>PDCD1</b>	rs142544044
<b>PDCD1</b>	rs143359677
<b>PDCD1</b>	rs144217487
<b>PDCD1</b>	rs146642159
<b>PDCD1</b>	rs147213978
<b>PDCD1</b>	rs147586902
<b>PDCD1</b>	rs2227982
<b>PDCD1</b>	rs28615468
<b>PDCD1</b>	rs55993679
<b>PDCD1</b>	rs56124337
<b>ICOS</b>	rs10183087
<b>ICOS</b>	rs1365828
<b>ICOS</b>	rs144520938
<b>ICOS</b>	rs1559931
<b>ICOS</b>	rs4270326
<b>ICOS</b>	rs4404254
<b>ICOS</b>	rs6726035
<b>ICOS</b>	rs76778263
<b>ICOS</b>	rs77411896
<b>IDO1</b>	rs115833371
<b>IDO1</b>	rs12545877
<b>IDO1</b>	rs34155785
<b>IDO1</b>	rs35059413
<b>IDO1</b>	rs35099072
<b>IDO1</b>	rs61753677
<b>IFNg</b>	rs1327473
<b>IFNg</b>	rs1327474
<b>IFNg</b>	rs150875052
<b>IFNg</b>	rs2430561
<b>IFNg</b>	rs76012457
<b>IL-12RB2</b>	rs3762317
<b>IL-17A</b>	rs138238811
<b>IL-17A</b>	rs139620979
<b>IL-17A</b>	rs144233360

IL-17A	rs148704956
<b>IL-17A</b>	<b>rs2275913</b>
IL-17A	rs3748067
IL-17A	rs3819024
IL-17A	rs3819025
IL-17F	rs117796773
IL-17F	rs12203582
IL-17F	rs1266828
IL-17F	rs144854652
IL-17F	rs145598353
IL-17F	rs148584839
<b>IL-17F</b>	<b>rs2397084</b>
IL-17F	rs763780
IL-17F	rs7771511
IL-17F	rs9382084
IL-17RA	rs112267700
IL-17RA	rs138404135
IL-17RA	rs140221307
IL-17RA	rs140367455
IL-17RA	rs140868574
IL-17RA	rs142092933
IL-17RA	rs142199303
IL-17RA	rs143008696
IL-17RA	rs143198423
IL-17RA	rs143897670
IL-17RA	rs144085995
IL-17RA	rs145378071
IL-17RA	rs145526959
IL-17RA	rs146002484
IL-17RA	rs146478431
IL-17RA	rs147495146
IL-17RA	rs147554210
IL-17RA	rs149220878
IL-17RA	rs149717999
IL-17RA	rs149771513
IL-17RA	rs150290858
IL-17RA	rs150618101

IL-17RA	rs151166583
IL-17RA	rs151220068
IL-17RA	rs28376631
IL-17RA	rs34545718
IL-17RA	rs41358047
IL-17RA	rs41432148
IL-17RA	rs74827998
IL-1B	rs1143627
IL-1R1	rs2871448
IL-21	rs137963779
IL-21	rs141748932
IL-21	rs143807041
IL-21	rs145809792
IL-21	rs148990483
IL-21	rs2221903
IL-21	rs907715
IL-21R	rs12934152
IL-21R	rs137946070
IL-21R	rs140808008
IL-21R	rs142403771
IL-21R	rs143921988
IL-21R	rs144751116
IL-21R	rs144923802
IL-21R	rs145338579
IL-21R	rs147673485
IL-21R	rs147984317
IL-21R	rs148782015
IL-21R	rs149800707
IL-21R	rs179760
IL-21R	rs3093310
IL-21R	rs3093319
IL-21R	rs3093359
IL-21R	rs3093363
IL-21R	rs3093364
IL-21R	rs3093375
IL-21R	rs3093379
IL-21R	rs36031126

IL-21R	rs52822694
IL-21R	rs56148525
IL-21R	rs8057464
IL-21R	rs963154
IL-22	rs138190698
IL-22	rs141801221
IL-22	rs144734266
IL-22	rs149366319
IL-22	rs2227472
IL-22	rs2227473
IL-22	rs2227483
IL-22	rs2227485
IL-22	rs2227513
IL-23R	rs111257711
IL-23R	rs111876012
IL-23R	rs112114661
IL-23R	rs113281071
IL-23R	rs113943721
IL-23R	rs11465797
IL-23R	rs139858085
IL-23R	rs141095761
IL-23R	rs143130647
IL-23R	rs144070297
IL-23R	rs144606217
IL-23R	rs146440064
IL-23R	rs35700985
IL-23R	rs41313262
IL-23R	rs76418789
IL-27	rs144603375
IL-27	rs144797498
IL-27	rs147722011
IL-27	rs150815897
IL-27	rs153109
IL-27	rs186366663
IL-6	rs11544633
IL-6	rs13306435
IL-6	rs13447445

IL-6	rs13447446
IL-6	rs142164099
IL-6	rs142759801
IL-6	rs1800796
IL-6	rs2069830
<b>IL-6</b>	<b>rs2069837</b>
IL-6	rs2069842
IL-6	rs2069860
IL-6	rs3087226
IL-6	rs34012176
IL-6	rs34709428
IL-6	rs55719549
IL-6	rs56383910
<b>NOS2</b>	rs1799765
<b>SLC22A5</b>	rs274553
<b>SLC22A5</b>	rs274559
<b>TBX21</b>	rs148984713
<b>TBX21</b>	rs17244544
<b>TBX21</b>	rs2240017
<b>TBX21</b>	rs71141929
<b>TBX21</b>	rs71141930
<b>TEX12</b>	rs1293344
<b>TLR4</b>	rs11536861
<b>TLR4</b>	rs1927914
<b>PTPN22</b>	rs3789612
<b>VDR</b>	rs11574004
<b>VDR</b>	rs11574005

**Supplemental Table 5. Human TB patient cohort clinical data.** Genomic DNA was isolated from PBMCs collected from 30 PTB patients, and PCR was used to



determine their rs2275913 genotype (-197 A/A, G/G, G/A). Clinical data, including smear positivity, TB treatment history, lung damage score as calculated by chest X-ray, as well as the drug sensitivity of the infecting *Mtb* strain were also collected.

<b>GG</b>							
Patient No.	Gender	Age	Sample	Smear	Previous TB txt	Drug Resistance	Lung damage score
1	Male	31	sputum	3	No	No	8
2	Male	20	sputum	3	No	No	8
3	Male	52	BAL	0	No	No	1
4	Female	32	BAL	3	No	No	10
5	Male	49	sputum	1	No	Yes	8
6	Male	49	sputum	3	Yes	Yes	7
7	Male	25	BAL/Biopsy	0	No	No	8
8	Female	28	sputum	0	No	No	2
9	Male	39	sputum	3	Yes	No	4
10	Male	41	sputum	3	Yes	Yes	3
11	Female	20	sputum	3	Yes	No	6
12	Female	28	sputum	3	No	No	5
13	Female	21	sputum	3	No	No	8
14	Male	56	sputum	3	Yes	No	9
15	Male	41	BAL	0	No	No	4
16	Male	37	sputum	3	Yes	Yes	14
17	Female	31	sputum	3	Yes	No	5
18	Female	41	sputum	3	No	No	7
19	Female	55	sputum	3	No	No	6
20	Male	23	sputum	2	No	No	4
21	Male	57	BAL	2	No	No	10
<b>AA/GA</b>							
22	Male	23	sputum	3	No	No	11
23	Male	39	sputum	3	No	No	9
24	Male	58	sputum	3	Yes	No	4
25	Male	66	sputum	1	Yes	Yes	6
26	Male	37	BAL	0	No	No	5
27	Male	55	sputum	3	Yes	No	0
28	Female	45	sputum	1	No	No	1

29	Female	23	sputum	3	No	No	12
30	Male	39	sputum	3	Yes	No	6