Supporting information

The sensor kinase MtrB of *Mycobacterium tuberculosis* regulates hypoxic survival and establishment of infection

Banerjee *et al*.

Three figures

Six tables

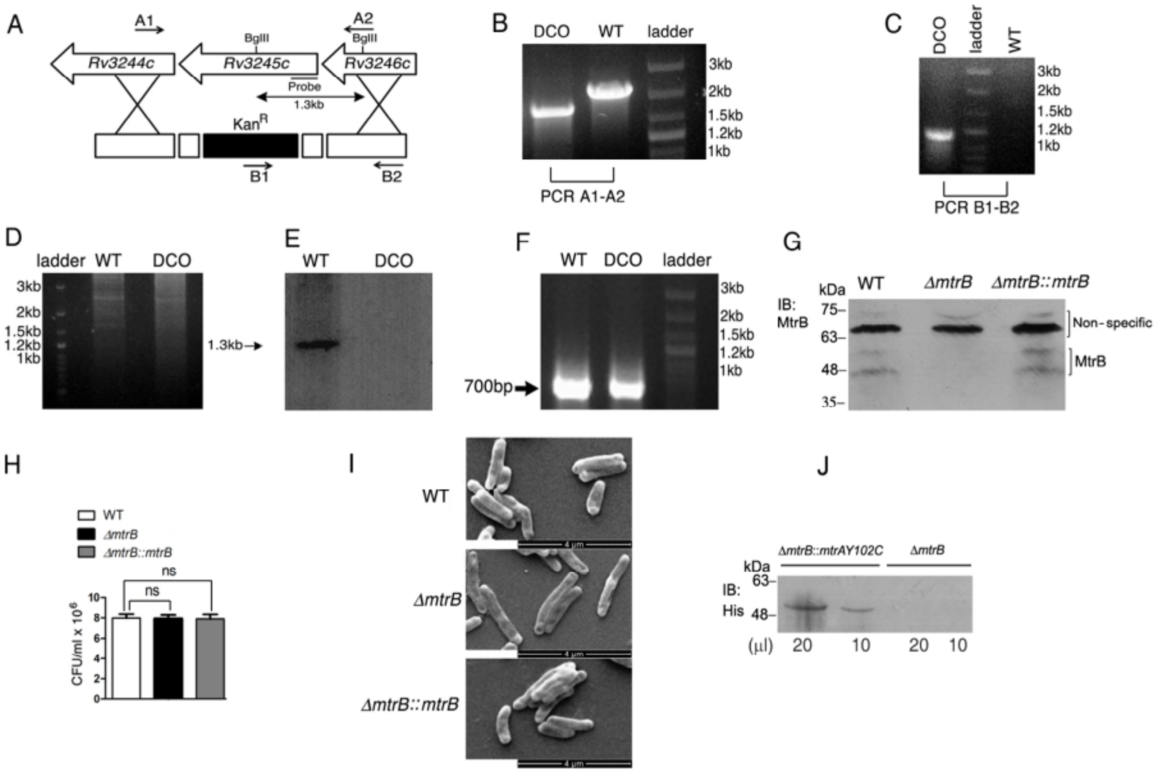

Fig. S1

Figure S1. Verification of inactivation of *mtrB*, scanning electron microscopy and crystal violet staining.

(A) Schematic representation of the *mtrB* (*Rv3245c*) locus on the *Mtb* H37Rv genome and strategy employed to replace *mtrB* with the kanamycin resistance gene (Kan^R). The BglII sites and the probe used for Southern blotting are indicated. (B) Verification of the inactivation of *mtrB* with primers A1 and A2 (see Table S5). The wild type (WT) *mtrB* gene product is ~2.1 kb while the deletion strain (DCO) gene product is ~1.5kb.(C) Verification of the inactivation of *mtrB* with primers B1 and B2 (see Table S5). The deletion strain (DCO) shows a product of ~1.2kb while there is no amplification in the case of the wild type (WT). (D,E) Southern Blotting to confirm deletion of *mtrB*. The agarose gel (D) corresponding to the blot (E) confirms the absence of probe binding in Δ*mtrB*.(F) PCR with primers P13 and P14 (see Table S5) confirms the presence of *mtrA* in the genomic DNA of Δ*mtrB*. The deletion strain (DCO) shows the same ~700bp amplicon as the wild type (WT).(G) Complemnetation of MtrB in Δ*mtrB* was confirmed by immunoblotting of bacterial lysates with MtrB antibody.(H) Bacteria was grown in the presence of 0.1% Tween 20 for the cell aggregation assay and CFUs were determined to confirm viability of bacteria. ns, non-significant. (I) Representative scanning electron micrographs of wild type (WT), Δ*mtrB* and Δ*mtrB::mtrB*. Images were acquired at 12000X magnification. Scale bar, 4 µm. Images are representative of three independent experiments.(J) The expression of MtrA(Y102C) in Δ*mtrB* was confirmed by immunoblotting. Equal numbers of bacteria [Δ*mtrB* alone or Δ*mtrB* complemented with plasmid overexpressing *mtrA(Y102C)*] were lysed and different amounts of bacterial lysates [indicated in µl] were immunoblotted with His antibody.

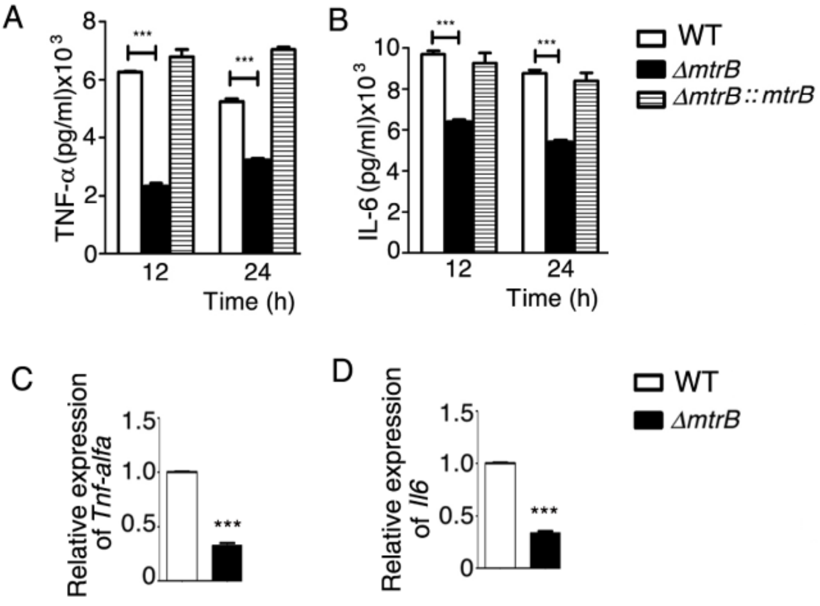

Fig. S2

Figure S2. MtrB is required to induce a pro-inflammatory response upon infection.

(A, B) Release of TNF-α (A) and IL-6 (B) was measured by ELISA from supernatants of BMDMs infected with wild type (WT), *ΔmtrB* or *ΔmtrB*::*mtrB* strains. Data represent means ± SD of three independent experiments. ***p ≤ 0.001.

(C, D) mRNA profiles in lungs of mice infected with WT or *ΔmtrB*. *Tnf-alfa* (C) or *Il-6* (D) was measured from RNA of lungs obtained after 4 weeks of infection, by qRT-PCR. *Gapdh* was used for normalization. Data represent means ± SD (4 mice per strain), ***p ≤ 0.001.

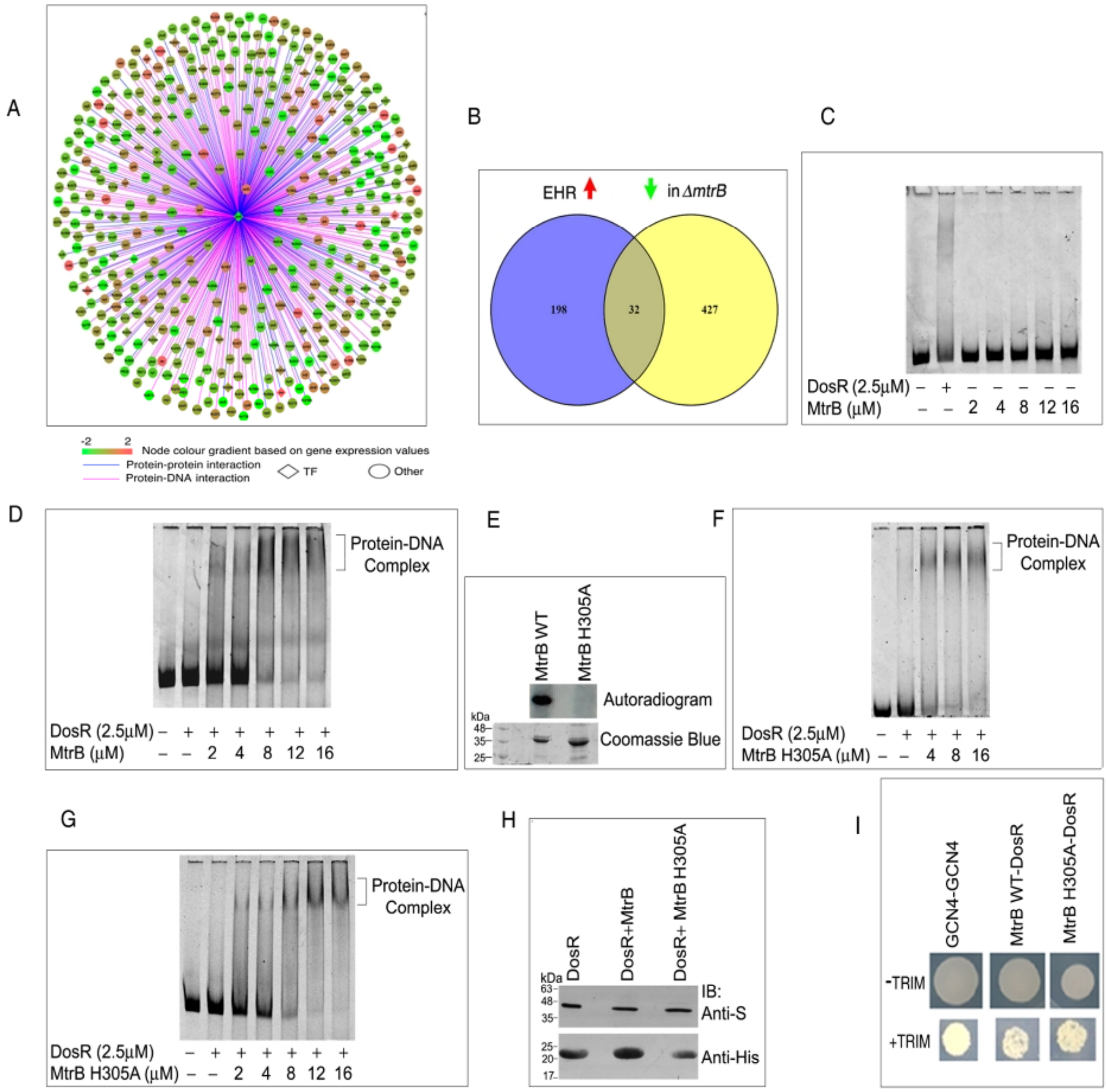

Fig. S3

Figure S3. The *dosR* interaction network, and phosphorylation independent interaction of MtrB with DosR

(A) The *dosR* protein-DNA and protein-protein interaction network of Δ*mtrB*. The color of each node represents its expression level in Δ*mtrB* compared to the wild type *M. tuberculosis*. Blue color edges show protein-protein interactions. Pink color edges show protein-DNA interactions. Rectangular nodes show transcription factors (TF) while circular nodes show other proteins. (B) Venn diagram representing the overlap between genes associated with long-term hypoxia (EHR), and genes downregulated in Δ*mtrB*. Red arrow shows upregulated genes. Green arrow shows downregulated genes. (C) Binding of MtrB to the *hspX* promoter was analysed by EMSA. EMSA was performed by incubating the PCR fragment derived from the *hspX* promoter with DosR (2.5 µM) alone or varying concentrations of MtrB. The reaction mixture was separated by PAGE and the DNA-protein complex was visualised on a Typhoon biomolecular imager. (D) EMSA was performed by incubating the PCR fragment derived from the *dosR* promoter with DosR (2.5 µM) in the presence of varying concentrations of MtrB. (E)Autophosphorylation of MtrB (or its mutant) was evaluated by incubation of MtrB with γ-^{32}P-ATP followed by SDS-PAGE and autoradiography. (F, G) Binding of MtrB (H305A) to the *hspX* (F) or *dosR* (G) promoter was analysed by EMSA. (H) Pull down assays to analyze interaction between MtrB and DosR. S-MtrB (cytosolic domain) expressing *E. coli* lysate (or S-MtrB (H305A) (cytosolic domain)-expressing *E. coli* lysate) was incubated with His-DosR (expressed in *E. coli*) immobilized on Ni^{2+}-NTA agarose. After washing the protein-bound resin, bound proteins were analyzed by immunoblotting with S-antibody, and reprobed with His antibody. (I) M-PFC assay to determine association of DosR with MtrB (H305A). *M. smegmatis* expressing DosR fused to one half of mDHFR and MtrB (H305A) (cytosolic domain) fused to another half of mDHFR, was grown in the absence (-) or in the presence (+) of TRIM (20 µg/ml). Plates were incubated at 37°C for 7 days. Growth on TRIM indicated reconstitution of DHFR, which occurs when there is interaction between the protein pair. GCN4-GCN-4 served as positive control.

Table S1. 101 genes that are reported to be upregulated in *M. tuberculosis* after 2-24 h infection of macrophages but were downregulated in *ΔmtrB* compared to the wild type

Gene	Rv number	Fold change	Function (TubercuList)
acg	Rv2032	-4.10	conserved hypotheticals
arsC	Rv2643	-1.05	cell wall and cell processes
bfrB	Rv3841	-3.30	intermediary metabolism and respiration
ctpF	Rv1997	-4.94	cell wall and cell processes
cyp125	Rv3545c	-1.23	intermediary metabolism and respiration
cysN	Rv1286	-1.59	intermediary metabolism and respiration
desA1	Rv0824c	-1.52	lipid metabolism
desA2	Rv1094	-1.20	lipid metabolism
devR	Rv3133c	-5.03	regulatory proteins
devS	Rv3132c	-4.47	regulatory proteins
dxs2	Rv3379c	-1.15	intermediary metabolism and respiration
fadA6	Rv3556c	-1.02	lipid metabolism
fadD9	Rv2590	-1.24	lipid metabolism
fdxA	Rv2007c	-2.81	intermediary metabolism and respiration
fprB	Rv0886	-1.32	intermediary metabolism and respiration
frdA	Rv1552	-1.18	intermediary metabolism and respiration
gltA1	Rv1131	-2.03	intermediary metabolism and respiration
grpE	Rv0351	-1.06	virulence, detoxification, adaptation
hycD	Rv0084	-1.52	intermediary metabolism and respiration
lat	Rv3290c	-1.46	intermediary metabolism and respiration
lhr	Rv3296	-0.95	information pathways
lppN	Rv2270	-1.37	cell wall and cell processes
mbtG	Rv2378c	-1.33	lipid metabolism
mce3C	Rv1968	-0.95	virulence, detoxification, adaptation
mpt70	Rv2875	-1.49	cell wall and cell processes
narK2	Rv1737c	-4.75	cell wall and cell processes
nrp	Rv0101	-1.20	lipid metabolism
otsB1	Rv2006	-3.41	virulence, detoxification, adaptation
pdhA	Rv2497c	-1.28	intermediary metabolism and respiration
PE34	Rv3746c	-0.92	PE/PPE
PE4	Rv0160c	-0.93	PE/PPE
pfkB	Rv2029c	-6.53	intermediary metabolism and respiration
pks2	Rv3825c	-0.92	lipid metabolism
PPE24	Rv1753c	-0.88	PE/PPE
rocA	Rv1187	-1.22	intermediary metabolism and respiration
Rv0079	Rv0079	-2.39	conserved hypotheticals
Rv0080	Rv0080	-4.02	conserved hypotheticals
Rv0081	Rv0081	-4.35	regulatory proteins
Rv0082	Rv0082	-3.50	intermediary metabolism and respiration
Rv0083	Rv0083	-1.37	intermediary metabolism and respiration
Rv0569	Rv0569	-3.59	conserved hypotheticals
Rv0571c	Rv0571c	-4.61	conserved hypotheticals
Rv0572c	Rv0572c	-3.53	conserved hypotheticals
Rv0574c	Rv0574c	-3.31	conserved hypotheticals
Rv0575c	Rv0575c	-1.26	intermediary metabolism and respiration
Rv0823c	Rv0823c	-1.22	regulatory proteins
Rv0843	Rv0843	-1.00	intermediary metabolism and respiration
Rv0885	Rv0885	-1.16	conserved hypotheticals
Rv1129c	Rv1129c	-1.19	regulatory proteins
Rv1130	Rv1130	-2.63	conserved hypotheticals
Rv1190	Rv1190	-1.41	conserved hypotheticals
Rv1222	Rv1222	-0.99	conserved hypotheticals
Rv1375	Rv1375	-0.97	conserved hypotheticals
Rv1405c	Rv1405c	-0.96	intermediary metabolism and respiration
Rv1733c	Rv1733c	-3.62	cell wall and cell processes
Rv1734c	Rv1734c	-1.55	conserved hypotheticals
Rv1735c	Rv1735c	-2.17	cell wall and cell processes
Rv1738	Rv1738	-4.00	conserved hypotheticals
Rv1739c	Rv1739c	-1.91	cell wall and cell processes
Rv1813c	Rv1813c	-4.64	conserved hypotheticals

Rv1989c	Rv1989c	-1.46	conserved hypotheticals
Rv1996	Rv1996	-3.40	conserved hypotheticals
Rv1999c	Rv1999c	-4.20	cell wall and cell processes
Rv2003c	Rv2003c	-4.50	conserved hypotheticals
Rv2005c	Rv2005c	-5.53	conserved hypotheticals
Rv2008c	Rv2008c	-1.10	conserved hypotheticals
Rv2012	Rv2012	-1.02	conserved hypotheticals
Rv2028c	Rv2028c	-6.72	conserved hypotheticals
Rv2030c	Rv2030c	-6.74	conserved hypotheticals
Rv2059	Rv2059	-1.31	conserved hypotheticals
Rv2557	Rv2557	-1.37	conserved hypotheticals
Rv2619c	Rv2619c	-0.87	conserved hypotheticals
Rv2620c	Rv2620c	-1.08	cell wall and cell processes
Rv2624c	Rv2624c	-5.32	conserved hypotheticals
Rv2625c	Rv2625c	-4.98	cell wall and cell processes
Rv2626c	Rv2626c	-5.50	conserved hypotheticals
Rv2627c	Rv2627c	-4.47	conserved hypotheticals
Rv2628	Rv2628	-4.69	conserved hypotheticals
Rv2629	Rv2629	-3.47	conserved hypotheticals
Rv2630	Rv2630	-3.30	conserved hypotheticals
Rv2650c	Rv2650c	-1.08	insertion seqs and phages
Rv2666	Rv2666	-1.35	insertion seqs and phages
Rv2897c	Rv2897c	-1.12	conserved hypotheticals
Rv2990c	Rv2990c	-1.28	conserved hypotheticals
Rv3115	Rv3115	-2.15	insertion seqs and phages
Rv3126c	Rv3126c	-0.97	conserved hypotheticals
Rv3127	Rv3127	-4.64	conserved hypotheticals
Rv3128c	Rv3128c	-2.29	conserved hypotheticals
Rv3129	Rv3129	-4.52	conserved hypotheticals
Rv3131	Rv3131	-3.16	conserved hypotheticals
Rv3134c	Rv3134c	-4.79	conserved hypotheticals
Rv3174	Rv3174	-1.06	intermediary metabolism and respiration
Rv3289c	Rv3289c	-1.74	cell wall and cell processes
Rv3428c	Rv3428c	-1.49	insertion seqs and phages
Rv3541c	Rv3541c	-0.88	conserved hypotheticals
Rv3660c	Rv3660c	-1.12	virulence, detoxification, adaptation
Rv3698	Rv3698	-1.06	conserved hypotheticals
Rv3839	Rv3839	-1.26	conserved hypotheticals
TB31.7	Rv2623	-4.17	conserved hypotheticals
usfY	Rv3288c	-1.84	conserved hypotheticals
yrbE3B	Rv1965	-1.05	virulence, detoxification, adaptation

Table S2. 32 genes reported to be acid-responsive but downregulated in *ΔmtrB* compared to the wild type

Gene	**Rv number**	**Fold change**	**Function (TubercuList)**
apt	Rv2584c	-0.99	intermediary metabolism and respiration
fadD15	Rv2187	-1.53	lipid metabolism
fadD9	Rv2590	-1.24	lipid metabolism
gltA1	Rv1131	-2.03	intermediary metabolism and respiration
hpx	Rv3171c	-1.80	virulence, detoxification, adaptation
lat	Rv3290c	-1.46	intermediary metabolism and respiration
lipU	Rv1076	-2.40	intermediary metabolism and respiration
lprE	Rv1252c	-1.33	cell wall and cell processes
mtrA	Rv3246c	-1.54	regulatory proteins
pdhA	Rv2497c	-1.28	intermediary metabolism and respiration
pdhB	Rv2496c	-0.98	intermediary metabolism and respiration
phoH2	Rv1095	-1.51	intermediary metabolism and respiration
pks2	Rv3825c	-0.92	lipid metabolism
regX3	Rv0491	-4.02	regulatory proteins
rocA	Rv1187	-1.22	intermediary metabolism and respiration
Rv0079	Rv0079	-2.39	conserved hypotheticals
Rv0083	Rv0083	-1.37	conserved hypotheticals
Rv0197	Rv0197	-0.98	intermediary metabolism and respiration
Rv0678	Rv0678	-0.99	conserved hypotheticals
Rv1130	Rv1130	-2.63	conserved hypotheticals
Rv1435c	Rv1435c	-1.32	cell wall and cell processes
Rv2159c	Rv2159c	-1.89	conserved hypotheticals
Rv2160c	Rv2160c	-1.95	regulatory proteins
Rv2161c	Rv2161c	-1.56	intermediary metabolism and respiration
Rv2256c	Rv2256c	-1.35	conserved hypotheticals
Rv2484c	Rv2484c	-0.94	conserved hypotheticals
Rv2557	Rv2557	-1.37	conserved hypotheticals
Rv2558	Rv2558	-1.90	conserved hypotheticals
Rv2638	Rv2638	-0.89	conserved hypotheticals
Rv2867c	Rv2867c	-1.43	conserved hypotheticals
Rv3079c	Rv3079c	-1.08	conserved hypotheticals
Rv3258c	Rv3258c	-0.96	conserved hypotheticals
Rv3289c	Rv3289c	-1.74	cell wall and cell processes
Rv3675	Rv3675	-1.03	cell wall and cell processes
Rv3848	Rv3848	-1.55	cell wall and cell processes

Table S3. 71 genes that were proposed to be essential for optimal *M. tuberculosis* growth but were found to be downregulated in *ΔmtrB* compared to the wild type.

Gene	Rv number	Fold change	Function (TubercuList)
accA2	Rv0973c	-1.10	lipid metabolism
accD6	Rv2247	-1.01	lipid metabolism
acpM	Rv2244	-1.35	lipid metabolism
clpC1	Rv3596c	-0.98	intermediary metabolism and respiration
cobQ2	Rv3713	-1.52	intermediary metabolism and respiration
cspA	Rv3648c	-1.55	virulence, detoxification, adaptation
cydB	Rv1622c	-0.99	intermediary metabolism and respiration
cysN	Rv1286	-1.59	intermediary metabolism and respiration
desA1	Rv0824c	-1.52	lipid metabolism
desA2	Rv1094	-1.20	lipid metabolism
devS	Rv3132c	-4.47	regulatory proteins
dnaB	Rv0058	-1.87	information pathways
dnaJ1	Rv0352	-1.08	virulence, detoxification, adaptation
dxs1	Rv2682c	-1.07	intermediary metabolism and respiration
ftsK	Rv2748c	-1.42	cell wall and cell processes
ftsQ	Rv2151c	-1.98	cell wall and cell processes
ftsW	Rv2154c	-1.19	cell wall and cell processes
ftsZ	Rv2150c	-1.39	cell wall and cell processes
gltB	Rv3859c	-1.26	intermediary metabolism and respiration
grpE	Rv0351	-1.06	virulence, detoxification, adaptation
hemL	Rv0524	-1.33	intermediary metabolism and respiration
hupB	Rv2986c	-1.78	information pathways
hycP	Rv0085	-2.41	intermediary metabolism and respiration
hycQ	Rv0086	-1.70	intermediary metabolism and respiration
ilvE	Rv2210c	-1.31	intermediary metabolism and respiration
kasA	Rv2245	-0.99	lipid metabolism
lpqB	Rv3244c	-1.71	cell wall and cell processes
lsr2	Rv3597c	-1.45	conserved hypotheticals
mbtG	Rv2378c	-1.33	lipid metabolism
murC	Rv2152c	-2.00	cell wall and cell processes
murD	Rv2155c	-0.88	cell wall and cell processes
murF	Rv2157c	-1.46	cell wall and cell processes
murG	Rv2153c	-1.44	cell wall and cell processes
murX	Rv2156c	-1.82	cell wall and cell processes
pks7	Rv1661	-1.23	lipid metabolism
pks8	Rv1662	-1.50	lipid metabolism
PPE24	Rv1753c	-0.88	PE/PPE
PPE50	Rv3135	-1.61	PE/PPE
ppnK	Rv1695	-1.03	intermediary metabolism and respiration
pros	Rv2845c	-1.00	information pathways
pyrB	Rv1380	-1.13	intermediary metabolism and respiration
qcrA	Rv2195	-1.14	intermediary metabolism and respiration
ripA	Rv1477	-1.98	virulence, detoxification, adaptation
rocA	Rv1187	-1.22	intermediary metabolism and respiration
rplL	Rv0652	-0.96	information pathways
rpmC	Rv0709	-1.15	information pathways
rpoC	Rv0668	-1.56	information pathways
rpsE	Rv0721	-1.13	information pathways
rpsQ	Rv0710	-1.23	information pathways
Rv0208c	Rv0208c	-1.89	intermediary metabolism and respiration
Rv0236c	Rv0236c	-1.86	cell wall and cell processes
Rv0289	Rv0289	-1.04	conserved hypotheticals
Rv0290	Rv0290	-0.94	cell wall and cell processes
Rv0312	Rv0312	-1.01	conserved hypotheticals
Rv0697	Rv0697	-1.02	intermediary metabolism and respiration
Rv1456c	Rv1456c	-1.01	cell wall and cell processes
Rv1738	Rv1738	-4.00	conserved hypotheticals
Rv2164c	Rv2164c	-1.79	cell wall and cell processes
Rv2166c	Rv2166c	-1.25	conserved hypotheticals
Rv2897c	Rv2897c	-1.12	conserved hypotheticals

Rv2926c	Rv2926c	-0.99	conserved hypotheticals
Rv2927c	Rv2927c	-1.52	conserved hypotheticals
Rv3131	Rv3131	-3.16	conserved hypotheticals
Rv3267	Rv3267	-1.94	conserved hypotheticals
Rv3559c	Rv3559c	-0.98	intermediary metabolism and respiration
Rv3660c	Rv3660c	-1.12	virulence, detoxification, adaptation
Rv3752c	Rv3752c	-1.26	intermediary metabolism and respiration
TB31.7	Rv2623	-4.17	conserved hypotheticals
thrS	Rv2614c	-1.07	information pathways
uvrD2	Rv3198c	-1.59	information pathways
wag31	Rv2145c	-0.97	cell wall and cell processes

Table S4. 32 Genes that are upregulated during the Enduring Hypoxic Response (EHR) but are downregulated in *ΔmtrB* compared to the wild type.

Gene	**Rv number**	**Fold change**	**Function (TubercuList)**
hycD	Rv0084	-1.52	intermediary metabolism and respiration
nrdB	Rv0233	-1.02	information pathways
Rv0349	Rv0349	-1.30	conserved hypotheticals
dnaJ1	Rv0352	-1.08	virulence, detoxification, adaptation
Rv0575c	Rv0575c	-1.26	intermediary metabolism and respiration
end	Rv0670	-1.09	information pathways
Rv0827c	Rv0827c	-1.74	regulatory proteins
PE_PGRS14	Rv0834c	-0.91	PE/PPE
Rv1375	Rv1375	-0.97	conserved hypotheticals
Rv1405c	Rv1405c	-0.96	intermediary metabolism and respiration
cydA	Rv1623c	-1.87	intermediary metabolism and respiration
Rv1733c	Rv1733c	-3.62	cell wall and cell processes
Rv1744c	Rv1744c	-0.94	cell wall and cell processes
Rv1760	Rv1760	-1.27	conserved hypotheticals
Rv1989c	Rv1989c	-1.46	conserved hypotheticals
cmtR	Rv1994c	-1.41	Transcriptional regulator(MerR Family)
Rv2012	Rv2012	-1.02	conserved hypotheticals
pdhA	Rv2497c	-1.28	intermediary metabolism and respiration
Rv2557	Rv2557	-1.37	conserved hypotheticals
Rv2558	Rv2558	-1.90	conserved hypotheticals
Rv2626c	Rv2626c	-5.50	conserved hypotheticals
Rv2627c	Rv2627c	-4.47	conserved hypotheticals
Rv2628	Rv2628	-4.69	conserved hypotheticals
arsC	Rv2643	-1.05	cell wall and cell processes
Rv3174	Rv3174	-1.06	intermediary metabolism and respiration
Rv3175	Rv3175	-1.14	intermediary metabolism and respiration
lat	Rv3290c	-1.46	intermediary metabolism and respiration
cyp125	Rv3545c	-1.23	intermediary metabolism and respiration
lsr2	Rv3597c	-1.45	conserved hypotheticals
Rv3848	Rv3848	-1.55	cell wall and cell processes
whiB6	Rv3862c	-1.04	regulatory proteins
Rv3864	Rv3864	-1.14	conserved hypotheticals

Table S5. Primers for genetic manipulations and qRT-PCR.

Primers for genetic manipulations

Sl. No.	**Primer sequence (5’- 3’)**	**Purpose**
P1	AGATATCCGCGGCCGTGCCCAGCGTGACC	Cloning
P2	CGTCTAGAGCCCCGTGTCATCGGGC	Cloning
P3	ATAAAGCTTCCGGAATACAAGGAACGTCAG	Cloning
P4	ATAACTAGTGTGACTCGCTGTGCGTCCAT	Cloning
P5	ATGAATTCGGTGTTTACTCGTGATGTGCTGCT	KO verification
P6	AAAAAGCTTCGATTCGGTGAGGAACTGAC	KO verification
P7	CAGGATGAGGATCGTTTCGC	KO verification
P8	AGCGGCCATCGTGCCTCCCC	KO verification
P9	GTCACCAATCGTGTCCTCGACATC	Southern Blot
P10	GCGTACTGGTAGGCGGCCTG	Southern Blot
P11	AGAATTCATGATCTTCGGCTCGCGCCGACGCAT	Cloning
P12	AAAAAGCTTTCAACCGCTCCACTCCGCGTGCTC	Cloning
P13	AGGTACCCATATGGACACCATGAGGCA	mtrA check
P14	AAAAAGCTTCGGAGGTCCGGCCTTG	mtrA check
P15	AAGAATTCATGTCGCGTCAGGTGGTG	Cloning
P16	AAAAAGCTTCAACCGCTCCACTCCG	Cloning
P17	AAGGATCCGTGGTAAAGGTCTTCTTGGT	Cloning
P18	AAGGTACCATCGATTGGTCCATCACCGGGTGGCC	Cloning
P19	AAGGTACCCAATTGTGTCGCGTCAGGTGGTG	Cloning
P20	AGAATTCATCGATACCGCTCCACTCCGCGTGCT	Cloning

Primers for qRT-PCR

Primer	Sequence (5’- 3’)
pfkBtbF[a]	CCAAGCAGTATCGTTTCGTG
pfkBtbR[b]	GATAGTAGTCGGCAGCCACA
fdxAtbF	GTCCTGTGTGCAGGAGTGTC
fdxAtbR	GGTAGATCGCCTTCCCAGTA
Rv0080tbF	GTCCAGTCAATCACCTCGTG
Rv0080tbR	ATCAAGGTCGTCGGCTTC
Rv0081tbF	GTCGGTGAGTTGCTGTCCT
Rv0081tbR	GCAATCGAATAGATCATCGC
fadA6tbF	GTGCAGAACATGAGCCAGAT
fadA6tbR	AAATCTCCTGGTCGCCATAC
murGtbF	GACGGTCGCCGAAGTATC
murGtbR	CATTCAGCCGCTGTTCAC
ilvEtbF	CGCCGCTATATCGAAGAGAT
ilvEtbR	AATAGCCAACTGCAACAACG
ftsZtbF	ACAACTACCTGGCCGTCATC
ftsZtbR	ATGAATTCCACGCCTTTGA
ftsWtbF	CGTTCATCAACATCGGCTAT

ftsWtbR	GATGATGCCTATCAGCGAAA
ftsQtbF	TTGCCTTATTTCGATGTGGA
ftsQtbR	GGCTTGCAACTTCAGGATG
esxGtbF	CGGCTCAGGCGTTTCAC
esxGtbR	CCGCCGCCACAAACC
esxHtbF	CAGGCCGCGTTGCA
esxHtbR	CTGCCACGCCTGATACGT
dosRtbF	CCGATCTGCGCTGTCTGATC
dosRtbR	GTCCAGCGCCCACATCTTT
dosStbF	TTCGGCACTCTGTACCTGAC
dosStbR	CCTTAGCCTGCTGGTAGAGC
tgs1tbF	GCTAGCTGGGCTCTCCGATGAA
tgs1tbR	AACGCCTCGCTTGGATTGACA
narXtbF	TCCACACACGGGGTGAATTG
narXtbR	ATAGTCGGTCTCCTGCGTCT
narK2tbF	GTGACCTGGGAGATGTCGTTT
narK2tbR	ACCGTGGAGAACCCGTAGAT

[a] F stands for Forward; [b] R stands for Reverse.

Table S6. Primers for EMSA

Primer	Sequence (5’- 3’)
hspX EMSA F[a]	TCTGAACGGCGGTTGGCAGACAAC
Cy5 *hspX* EMSA R[b]	CGGGAAGGGTGGTGGCCATTTGATG
dosR EMSA F	GTCAGCGCGGTTGTCGCGGAG
Cy5 *dosR* EMSA R	GACCTTTACCACCAGGGCACC

[a] F stands for Forward; [b] R stands for Reverse.