

SUPPLEMENTAL MATERIAL

Table S3. RNA-seq mapping results. Total number of reads (in millions) and percentages of total paired reads.

Sample	Total paired reads	Sense reads: CDS and ncRNA	Sense reads: only ncRNA	Anti-sense reads
DE	51.2	38.6 (75.4 %)	6.4 (12.5 %)	2.1 (4.2 %)
DE	49.5	36.9 (74.5 %)	5.8 (11.6 %)	2.0 (4.1 %)
DS	51.4	36.0 (70.0 %)	12.1 (23.5 %)	4.4 (8.5 %)
DS	62.7	45.1 (72.0 %)	14.3 (22.8 %)	5.9 (9.4 %)
DNRP1	61.8	43.6 (70.7 %)	7.9 (12.8 %)	3.6 (5.8 %)
DNRP1	31.0	23.4 (75.6 %)	6.7 (21.5 %)	1.3 (4.3 %)
LE	58.5	47.2 (80.6 %)	8.8 (15.1 %)	1.8 (3.0 %)
LE	53.2	42.4 (79.6 %)	9.6 (18.1 %)	1.5 (2.7 %)
LS	57.5	46.1 (80.1 %)	18.9 (32.9 %)	0.87 (1.5 %)
LS	51.7	40.6 (78.5 %)	16.3 (31.4 %)	0.94 (1.8 %)
LNRP1	65.8	51.1 (77.6 %)	13.2 (20.0 %)	2.6 (4.0 %)
LNRP1	63.7	51.4 (80.6 %)	15.7 (24.6 %)	1.6 (2.6 %)

Table S4. Differential expression analysis of functional categories. Dextrose conditions were used as control group and Lipid as treatment (general D vs L), growth stages were used as a batch effect.

Increased expression in the presence of lipids:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>Intermediary metabolism and respiration</i>	3.2549851	0.000577347	0.005773469	920
<i>Lipid metabolism</i>	2.63201945	0.004369886	0.021849431	268
<i>Regulatory proteins</i>	0.938987183	0.174168298	0.580560994	195
<i>Virulence, detoxification and adaptation</i>	0.654360315	0.256602683	0.641506708	236
<i>Cell wall and cell processes</i>	0.382127259	0.351210219	0.702420439	761
<i>Conserved hypothetical</i>	0.160041507	0.436432065	0.727386776	1027
<i>Information pathways</i>	-0.260140305	0.602561252	0.860801789	241
<i>Stable RNA</i>	-0.797625025	0.785588402	0.981985503	29
<i>PE/PPE</i>	-2.414969445	0.991853302	0.99886261	162
<i>Insertion seqs and phages</i>	-3.098665085	0.99886261	0.99886261	87
Diminished expression in the presence of lipids:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>Insertion seqs and phages</i>	-3.098665085	0.00113739	0.011373897	87
<i>PE/PPE</i>	-2.414969445	0.008146698	0.040733489	162
<i>Stable RNA</i>	-0.797625025	0.214411598	0.714705326	29
<i>Information pathways</i>	-0.260140305	0.397438748	0.99359687	241
<i>Conserved hypothetical</i>	0.160041507	0.563567935	0.999422653	1027
<i>Cell wall and cell processes</i>	0.382127259	0.648789781	0.999422653	761
<i>Virulence, detoxification and adaptation</i>	0.654360315	0.743397317	0.999422653	236
<i>Regulatory proteins</i>	0.938987183	0.825831702	0.999422653	195
<i>Lipid metabolism</i>	2.63201945	0.995630114	0.999422653	268
<i>Intermediary metabolism and respiration</i>	3.2549851	0.999422653	0.999422653	920

Table S5. Differential expression analysis of KEGG pathways. Differential pathways analysis with Dextrose as control group and Lipid as treatment, growth stages were used as a batch effect.

Significant up-regulated pathways	FDR	Set size
mtu01120 Microbial metabolism in diverse environments	0.002487853	216
mtu00984 Steroid degradation	0.002487853	13
mtu02020 Two-component system	0.03991373	54
mtu00620 Pyruvate metabolism	0.044056934	47
mtu01200 Carbon metabolism	0.044056934	111
mtu00071 Fatty acid degradation	0.044056934	50
mtu00310 Lysine degradation	0.044056934	38
mtu00280 Valine, leucine and isoleucine degradation	0.044056934	56
mtu00380 Tryptophan metabolism	0.044056934	42
mtu00650 Butanoate metabolism	0.044056934	55
mtu00190 Oxidative phosphorylation	0.044056934	46

Table S6. Differential expression analysis of functional categories for exponential stage. Dextrose exponential condition was used as control and lipid exponential as treatment (DE vs LE).

Increased expression in LE:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>PE/PPE</i>	1.351029443	0.088830099	0.79256419	160
<i>Stable RNA</i>	0.58858318	0.279661374	0.79256419	22
<i>Regulatory proteins</i>	0.492998416	0.311147797	0.79256419	195
<i>Conserved hypothetical</i>	0.476105649	0.317025676	0.79256419	998
<i>Intermediary metabolism and respiration</i>	-0.139092353	0.555303673	0.999254255	917
<i>Insertion seqs and phages</i>	-0.550710317	0.708708303	0.999254255	83
<i>Virulence, detoxification and adaptation</i>	-0.614619739	0.730442291	0.999254255	232
<i>Lipid metabolism</i>	-0.856270429	0.803878397	0.999254255	268
<i>Cell wall and cell processes</i>	-1.725681159	0.957695104	0.999254255	755
<i>Information pathways</i>	-3.196667552	0.999254255	0.999254255	241
Diminished expression in LE:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>Information pathways</i>	-3.196667552	0.000745745	0.007457445	241
<i>Cell wall and cell processes</i>	-1.725681159	0.042304896	0.211524482	755
<i>Lipid metabolism</i>	-0.856270429	0.196121603	0.582583394	268
<i>Virulence, detoxification and adaptation</i>	-0.614619739	0.269557709	0.582583394	232
<i>Insertion seqs and phages</i>	-0.550710317	0.291291697	0.582583394	83
<i>Intermediary metabolism and respiration</i>	-0.139092353	0.444696327	0.741160544	917
<i>Conserved hypothetical</i>	0.476105649	0.682974324	0.800376251	998
<i>Regulatory proteins</i>	0.492998416	0.688852203	0.800376251	195
<i>Stable RNA</i>	0.58858318	0.720338626	0.800376251	22
<i>PE/PPE</i>	1.351029443	0.911169901	0.911169901	160

Table S7. Differential expression analysis of functional categories for stationary stage. Dextrose stationary condition was used as control and lipid stationary as treatment (DS vs LS).

Increased expression in LS:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>Intermediary metabolism and respiration</i>	3.168922275	0.000777753	0.007777532	920
<i>Cell wall and cell processes</i>	2.610061912	0.004571528	0.019282174	756
<i>Information pathways</i>	2.51481911	0.006131746	0.019282174	241
<i>Lipid metabolism</i>	2.430551828	0.00771287	0.019282174	267
<i>Conserved hypothetical</i>	-0.411979103	0.659800886	0.999974615	1017
<i>Stable RNA</i>	-1.091112442	0.859640497	0.999974615	26
<i>Virulence, detoxification and adaptation</i>	-1.29289663	0.901653686	0.999974615	233
<i>Regulatory proteins</i>	-1.843877562	0.967013669	0.999974615	195
<i>PE/PPE</i>	-2.691080125	0.996251728	0.999974615	161
<i>Insertion seqs and phages</i>	-4.164218156	0.999974615	0.999974615	87
Diminished expression in LS:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>Insertion seqs and phages</i>	-4.164218156	2.54E-05	0.000253852	87
<i>PE/PPE</i>	-2.691080125	0.003748272	0.018741361	161
<i>Regulatory proteins</i>	-1.843877562	0.032986331	0.109954437	195
<i>Virulence, detoxification and adaptation</i>	-1.29289663	0.098346314	0.245865784	233
<i>Stable RNA</i>	-1.091112442	0.140359503	0.280719007	26
<i>Conserved hypothetical</i>	-0.411979103	0.340199114	0.566998524	1017
<i>Lipid metabolism</i>	2.430551828	0.99228713	0.999222247	267
<i>Information pathways</i>	2.51481911	0.993868254	0.999222247	241
<i>Cell wall and cell processes</i>	2.610061912	0.995428472	0.999222247	756
<i>Intermediary metabolism and respiration</i>	3.168922275	0.999222247	0.999222247	920

Table S8. Differential expression analysis of functional categories for NRP1 stage. Dextrose NRP1 condition was used as control and lipid NRP1 as treatment (DNRP1 vs LNRP1).

Increased expression in LNRP1:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>Virulence, detoxification and adaptation</i>	4.273008619	1.18E-05	0.000117511	233
<i>Regulatory proteins</i>	3.925030603	5.17E-05	0.000258685	195
<i>Lipid metabolism</i>	2.820063698	0.00249043	0.008301433	267
<i>Intermediary metabolism and respiration</i>	2.309445168	0.010514734	0.026286835	920
<i>Conserved hypothetical</i>	0.368607862	0.35622953	0.712459059	1002
<i>Insertion seqs and phages</i>	-0.101260223	0.540264856	0.900441427	84
<i>Stable RNA</i>	-0.399475572	0.654342281	0.934774687	25
<i>Information pathways</i>	-1.44441487	0.925312568	0.998612354	240
<i>Cell wall and cell processes</i>	-1.642080768	0.949606567	0.998612354	756
<i>PE/PPE</i>	-3.015187087	0.998612354	0.998612354	162
Diminished expression in LNRP1:				
Functional category	Mean log₂ fold change	p value	FDR	Set size
<i>PE/PPE</i>	-3.015187087	0.001387646	0.013876457	162
<i>Cell wall and cell processes</i>	-1.642080768	0.050393433	0.248958105	756
<i>Information pathways</i>	-1.44441487	0.074687432	0.248958105	240
<i>Stable RNA</i>	-0.399475572	0.345657719	0.864144298	25
<i>Insertion seqs and phages</i>	-0.101260223	0.459735144	0.919470288	84
<i>Conserved hypothetical</i>	0.368607862	0.64377047	0.999988249	1002
<i>Intermediary metabolism and respiration</i>	2.309445168	0.989485266	0.999988249	920
<i>Lipid metabolism</i>	2.820063698	0.99750957	0.999988249	267
<i>Regulatory proteins</i>	3.925030603	0.999948263	0.999988249	195
<i>Virulence, detoxification and adaptation</i>	4.273008619	0.999988249	0.999988249	233

Table S9. Quantification and statistical analysis of gene expression determined by qRT-PCR.

GENE	STAGE	Dextrose conditions			Lipid conditions			STATISTIC ANALYSIS Two Way-ANOVA between: dextrose vs lipids				Relative expression. Fold change*
		Mean	Std Dev	N	Mean	Std Dev	N	DF	Mean Square	F Ratio	P value	
<i>rv3160c</i>	Exponential	1.6E+05	3.6E+04	6	1.5E+06	5.9E+05	8	1	5.9E+12	2.8E+01	<0.001	9.4↑
	Stationary	2.1E+05	1.3E+05	7	1.1E+06	3.0E+05	3	1	1.5E+12	4.5E+01	<0.001	5.1↑
	NRP1	7.8E+04	3.3E+03	4	2.5E+07	2.0E+07	7	1	1.6E+15	6.4E+00	0.033	326.8↑
<i>rv3161c</i>	Exponential	1.3E+03	1.6E+02	3	1.1E+05	1.3E+04	4	1	2.0E+10	1.9E+02	<0.001	82.7↑
	Stationary	6.7E+04	4.7E+04	7	4.8E+05	1.3E+05	3	1	3.5E+11	5.9E+01	<0.001	7.1↑
	NRP1	1.5E+04	6.6E+03	7	5.6E+06	5.1E+06	7	1	1.1E+14	8.4E+00	0.013	372.2↑
<i>PPE53</i>	Exponential	2.1E+05	6.7E+04	7	5.1E+05	1.1E+05	6	1	2.9E+11	3.4E+01	<0.001	2.4↑
	Stationary	5.3E+04	8.0E+03	3	5.8E+04	1.0E+04	3	1	3.5E+07	4.2E-01	0.553	1.1
	NRP1	2.9E+05	2.1E+05	6	5.6E+06	4.3E+06	6	1	2.9E+11	3.4E+01	<0.001	19.1↑
<i>che1</i>	Exponential	6.0E+05	7.7E+04	6	9.6E+05	4.7E+05	7	1	4.4E+11	3.5E+00	0.089	1.6↑
	Stationary	5.0E+04	1.9E+04	6	9.0E+05	1.3E+05	3	1	1.4E+12	2.6E+02	<0.001	17.9↑
	NRP1	1.3E+05	2.7E+04	3	2.7E+05	2.4E+04	4	1	3.5E+10	5.6E+01	<0.001	2.1↑
<i>mmpS5</i>	Exponential	1.4E+05	5.4E+04	8	5.9E+06	1.9E+06	6	1	1.1E+14	7.6E+01	<0.001	41.4↑
	Stationary	7.4E+04	8.9E+03	4	1.6E+06	3.3E+04	4	1	4.9E+12	8.5E+03	<0.001	22.0↑
	NRP1	1.9E+06	8.0E+05	8	1.5E+07	1.3E+07	6	1	5.7E+14	7.6E+00	0.017	7.9↑
<i>hsd4A</i>	Exponential	4.8E+03	6.9E+02	3	2.0E+04	9.1E+03	4	1	3.9E+08	7.7E+00	0.039	4.2↑
	Stationary	3.4E+04	7.5E+03	6	4.6E+05	1.1E+05	3	1	3.6E+11	1.0E+02	<0.001	13.4↑
	NRP1	1.5E+05	4.3E+04	6	1.1E+06	9.8E+05	6	1	2.6E+12	5.4E+00	0.043	7.0↑
<i>usfY</i>	Exponential	9.1E+04	2.6E+04	6	1.1E+06	4.2E+05	6	1	2.9E+12	3.3E+01	<0.001	11.9↑
	Stationary	1.1E+05	5.3E+03	3	2.9E+06	2.9E+05	3	1	1.2E+13	2.8E+02	<0.001	26.7↑
	NRP1	1.5E+06	9.2E+05	6	2.5E+07	2.4E+07	7	1	1.9E+15	6.1E+00	0.031	16.8↑
<i>hrp1</i>	Exponential	3.4E+05	8.5E+04	6	2.6E+07	1.7E+07	7	1	2.1E+15	1.4E+01	0.003	76.4↑
	Stationary	4.0E+05	1.2E+05	6	3.1E+06	4.0E+05	3	1	1.4E+13	2.5E+02	<0.001	7.6↑
	NRP1	2.1E+07	9.8E+06	7	1.7E+07	2.6E+07	6	1	1.1E+15	5.2E+00	0.051	-1.2
<i>Rv1639c</i>	Exponential	4.0E+05	1.8E+05	7	3.1E+05	7.4E+04	6	1	2.7E+10	1.3E+00	0.274	-1.3↓
	Stationary	1.1E+04	2.8E+03	6	7.2E+04	1.4E+04	3	1	7.5E+09	1.2E+02	<0.001	6.4↑
	NRP1	5.0E+05	2.7E+05	6	4.6E+04	1.1E+04	7	1	6.6E+11	2.0E+01	0.001	-10.8
<i>Rv0560</i>	Exponential	9.2E+04	1.7E+04	7	5.9E+04	9.2E+03	7	1	3.7E+09	2.0E+01	<0.001	0.6↑
	Stationary	1.6E+05	1.5E+05	7	4.9E+04	6.2E+03	4	1	3.4E+10	2.1E+00	0.177	-3.4↓
	NRP1	6.2E+04	4.7E+04	7	9.2E+06	6.0E+06	7	1	2.9E+14	1.6E+01	0.002	148.3↑

*Ratio of gene expression in lipid/dextrose conditions. Increased (↑) and diminished (↓) expression in lipids.

Table S10. Primers used for qPCR

Gen / Rv number	Primers	Product name	Design reference
<i>rpsL</i> / <i>rv0682</i>	Fw: 5'-CCTTCAGAGCCGCGGTCT- 3' Rev: 5'-CCAACCATCCAGCAGCTGG- 3'	Ribosomal protein S12	1
<i>rrs</i> / <i>MTB000019</i>	Fw: ATGACGGCCTTCGGGTTGTAA Rev: CGGCTGCTGGCACGTAGTTG	Ribosomal RNA 16S	1
<i>rv3160c</i>	Fw: CTGGACCACCTGCATGCTTC Rev: CCATCTCCGCGACTAGCTCC	Possible transcriptional regulatory protein (probably TetR-family)	2
<i>Rv3161c</i>	Fw: CAGGGTTCCCTTCACCGTTC Rev: GCGGAATAAAGCCGAACCAC	Possible dioxygenase	2
<i>PPE53</i> / <i>rv3159c</i>	Fw: CAATGCCACCAAGTTGTGCG Rev: ACATCGGCTCCTCCAACATC	PPE family protein PPE53	This study
<i>che1</i> / <i>rv2393</i>	Fw: 5' -GATCGGCTCATCGCATCCC- 3' Rev: 5' -CTCCGGTCGGGTGATGAAAG- 3'	Ferrochelatase Che1	This study
<i>mmpS5</i> / <i>Rv0677c</i>	Fw: GCCGGAAACTTCGTACTIONCA Rev: CCGCACTTTCTTTGGTTCCG	Possible conserved membrane protein MmpS5	This study
<i>hsd4A</i> / <i>rv3502c</i>	Fw: 5' -TTGCGGGTGAGCAGAAAATG- 3' Rev: 5' -CATCGTGGTGAACAATGCCG- 3'	Possible 17-beta-hydroxysteroid dehydrogenase	This study
<i>usfY</i> / <i>rv3288c</i>	Fw: 5' -ACAGATACCCAGGCCAATGC- 3' Rev: 5' -CGGAATAGGACGGAAACGGA- 3'	Putative protein UsfY	This study
<i>hrp1</i> / <i>rv2626c</i>	Fw: GCGGACCTGATGTTCTTCCA Rev: CTAGACCCGAATACCGCCAC	Hypoxic response protein 1 Hrp1	This study
<i>rv1639c</i>	Fw: ATCCACGAATACCACGACGG Rev: GTCAATTCAACACACCCGCC	Conserved hypothetical membrane protein	This study
<i>rv0560</i>	Fw: CGATTGCAGATAGCCCTCCC Rev: TTTACCGGCTATGACGGCAG	Possible benzoquinone methyltransferase (methylase)	This study

REFERENCES:

1. Badillo-López, C. *et al.* Differential expression of *dnaA* and *dosR* genes among members of the *Mycobacterium tuberculosis* complex under oxic and hypoxic conditions. *Int. Microbiol.* **13**, 9–13 (2010).
2. Betts, J. C. *et al.* Signature gene expression profiles discriminate between isoniazid- thiolactomycin-, and triclosan-treated *Mycobacterium tuberculosis* . *Antimicrob. Agents Chemother.* **47**, 2903–2913 (2003).