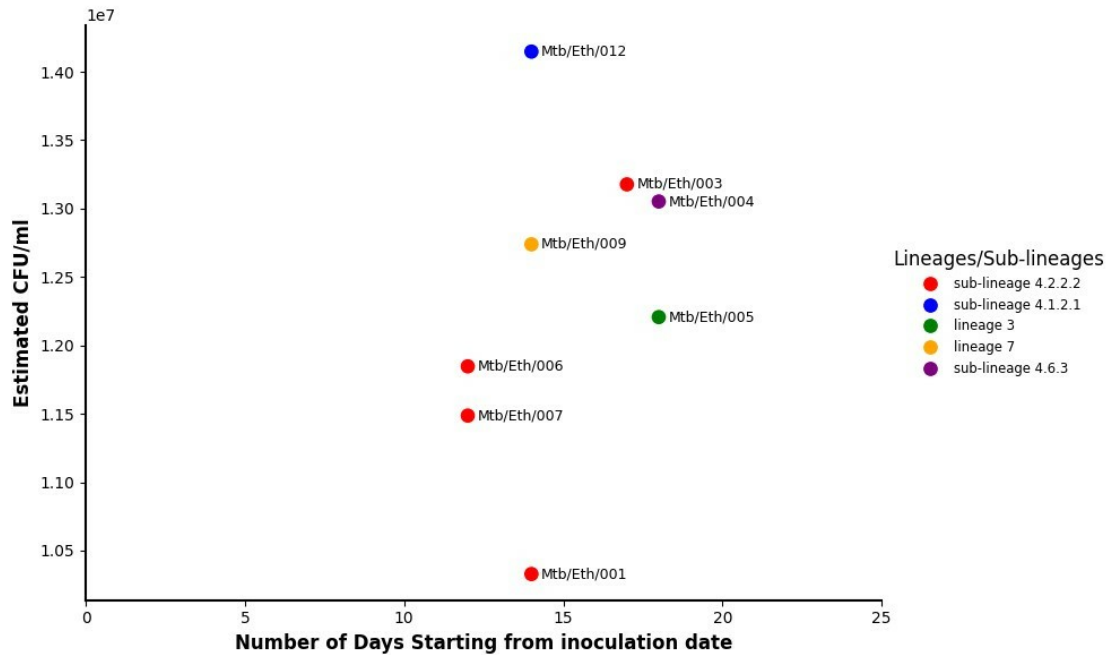
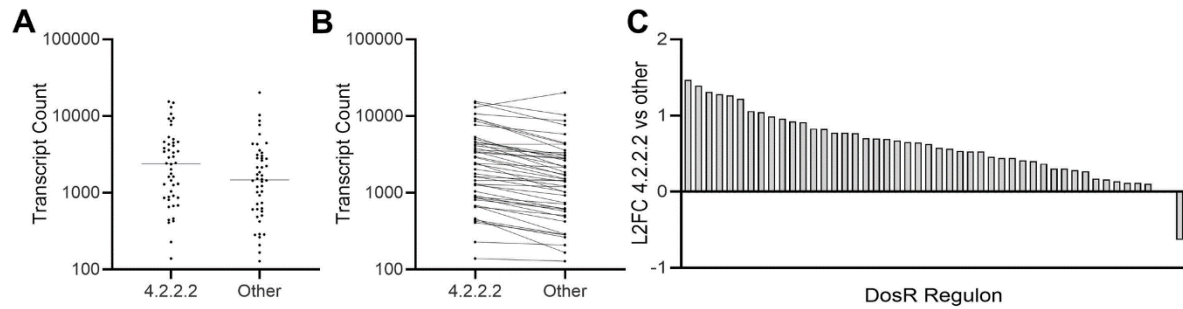


Supplementary Figures and Tables

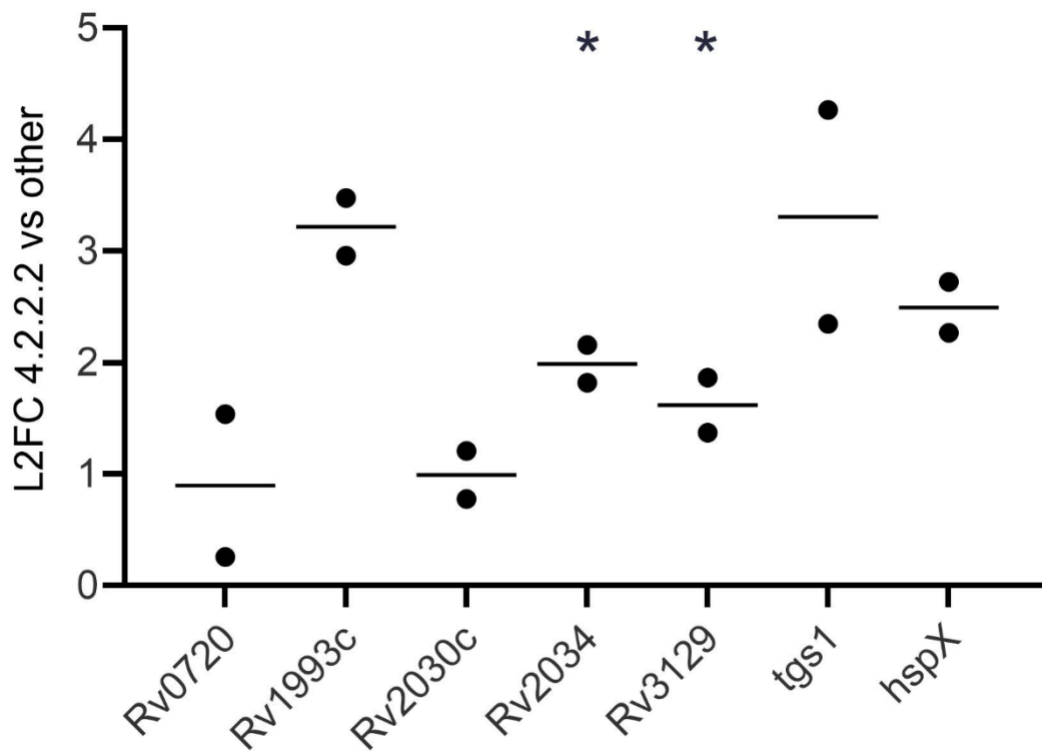
Supplementary Figure 1: Scatter plot illustrating the determined colony-forming units/mL for the respective eight *Mycobacterium tuberculosis* clinical isolates, with values ranging from 1.0×10^7 to 1.4×10^7 CFU/ml.



Supplementary Figure 2: The expression of the DosR regulon [53] in sub-lineage 4.2.2.2 compared to other lineage/sub-lineage *Mycobacterium tuberculosis* clinical isolates, showing a trend of DosR regulon induction in lineage 4.2.2.2. (A/B) Plotting transcript count after normalization using DEseq2. (C) Plotting the log2 fold change of each DosR-regulated gene in sub-lineage 4.2.2.2 compared to other lineage/sub-lineage Ethiopian *Mtb* isolates.



Supplementary Figure 3: The upregulation of genes in sub-lineage 4.2.2.2 by RT-qPCR (Figure 3B), plotting the two technical replicates independently, and showing the average log₂ fold change from the four sub-lineage 4.2.2.2 isolates relative to the four other genotypes. Also including the DosR-regulated genes, *tgsI* and *hspX*. Asterisks mark significance by Mann-Whitney U test ($p < 0.05$).



Supplementary Table 4: *Mycobacterium tuberculosis* DosR regulon genes as defined by Park, et al, 2003. <https://doi.org/10.1046/j.1365-2958.2003.03474.x>

No.	Gene Name	H37Rv Locus Tag
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1	Rv0079	Rv0079
2	Rv0080	Rv0080
3	Rv0081	Rv0081
4	Rv0082	Rv0082
5	Rv0083	Rv0083
6	Rv0084	Rv0084
7	Rv0085	Rv0085
8	Rv0086	Rv0086
9	Rv0087	Rv0087
10	Rv0088	Rv0088
11	Rv0089	Rv0089
12	Rv0090	Rv0090
13	Rv0569	Rv0569
14	Rv0570	Rv0570
15	Rv0571c	Rv0571c
16	Rv0572c	Rv0572c
17	Rv0573c	Rv0573c
18	Rv0574c	Rv0574c
19	Rv0575c	Rv0575c
20	Rv1733c	Rv1733c
21	Rv1734c	Rv1734c
22	Rv1735c	Rv1735c
23	Rv1736c	Rv1736c
24	Rv1737c	Rv1737c
25	Rv1738	Rv1738
26	Rv1739c	Rv1739c

27	Rv1740	Rv1740	
28	Rv1996	Rv1996	
29	Rv2028c	Rv2028c	
30	Rv2029c	Rv2029c (pfkB)	
31	Rv2030c	Rv2030c	
32	Rv2031c	Rv2031c (hspX)	
33	Rv2032	Rv2032	
34	Rv2033c	Rv2033c	
35	Rv2623	Rv2623	
36	Rv2624c	Rv2624c	
37	Rv2625c	Rv2625c	
38	Rv2626c	Rv2626c	
39	Rv2627c	Rv2627c	
40	Rv2628	Rv2628	
41	Rv2629	Rv2629	
42	Rv3130c	Rv3130c (acg)	
43	Rv3131	Rv3131	
44	Rv3132c	Rv3132c	
45	Rv3133c	Rv3133c (dosR)	
46	Rv3134c	Rv3134c	
47	Rv3135	Rv3135	
48	Rv3136	Rv3136	

Supplementary Table 6: Primer sequences for RT-qPCR confirmation of upregulated differentially expressed genes identified by RNAseq (plus *tgsl* and *hspX*).

Rv Number	Primer forward (5'-3')	Primer reverse (5'-3')
Rv0720	<i>GCAATCAGTTTCCGCGACTC</i>	<i>CGTTGAGGTCGTTACCAAGT</i>
Rv1993c	<i>CCCCTCCATCACGGTCAC</i>	<i>GAGCTATTGGTTAAGGCGGC</i>
Rv2030c	<i>CGGTAGATAAACGACGCCGA</i>	<i>AGGAGCTCTTCCACCAGACT</i>
Rv2034	<i>CTCAAAGTGCTCAAGACCGC</i>	<i>GTGTCCAGAACCGGTTCGAG</i>
Rv3129	<i>TCGACGATTCCGTTACCGTG</i>	<i>TCCCAGGCTCATCAGCAAAG</i>
Rv2031c	<i>CTGACCATCGCGGACCATAA</i>	<i>CGGCTGGAAGACGAGATGAA</i>
Rv3130c	<i>GCCAAGATCGAAGTCGGGAT</i>	<i>CCTTCTTATCGTCGCTCGCT</i>
Rv0298	<i>GCGATCGACGCGGAC</i>	<i>GCCGGTACGGTTTTAGCC</i>

Supplementary Table 7: Summary of metadata for *Mycobacterium tuberculosis* clinical isolates obtained from Ethiopia patients and used for the study.

Sample ID	SRA RunID for WGS	SRA RunID for RNA-seq data	WGS based resistance classification	Lineage/sublineage	Estimated CFU/ml at time of RNA extraction	No. of RNA reads
Mtb/Eth/001	SRR33015696	SRR34092685	Resistant	4.2.2.2	10329000	14,914,364
Mtb/Eth/003	SRR33015695	SRR34092684	Resistant	4.2.2.2	13177300	13,516,960
Mtb/Eth/004	SRR33015694	SRR34092683	Sensitive	4.6.3	13052100	13,689,414
Mtb/Eth/005	SRR33015693	SRR34092682	Sensitive	3	12207000	15,265,857
Mtb/Eth/006	SRR33015692	SRR34092681	Sensitive	4.2.2.2	11847050	13,088,502
Mtb/Eth/007	SRR33015691	SRR34092680	Sensitive	4.2.2.2	11487100	12,976,451
Mtb/Eth/009	SRR33015690	SRR34092679	Sensitive	7	12739100	12,112,976
Mtb/Eth/012	SRR33015689	SRR34092678	Sensitive	4.1.2.1	14147600	14,940,153