

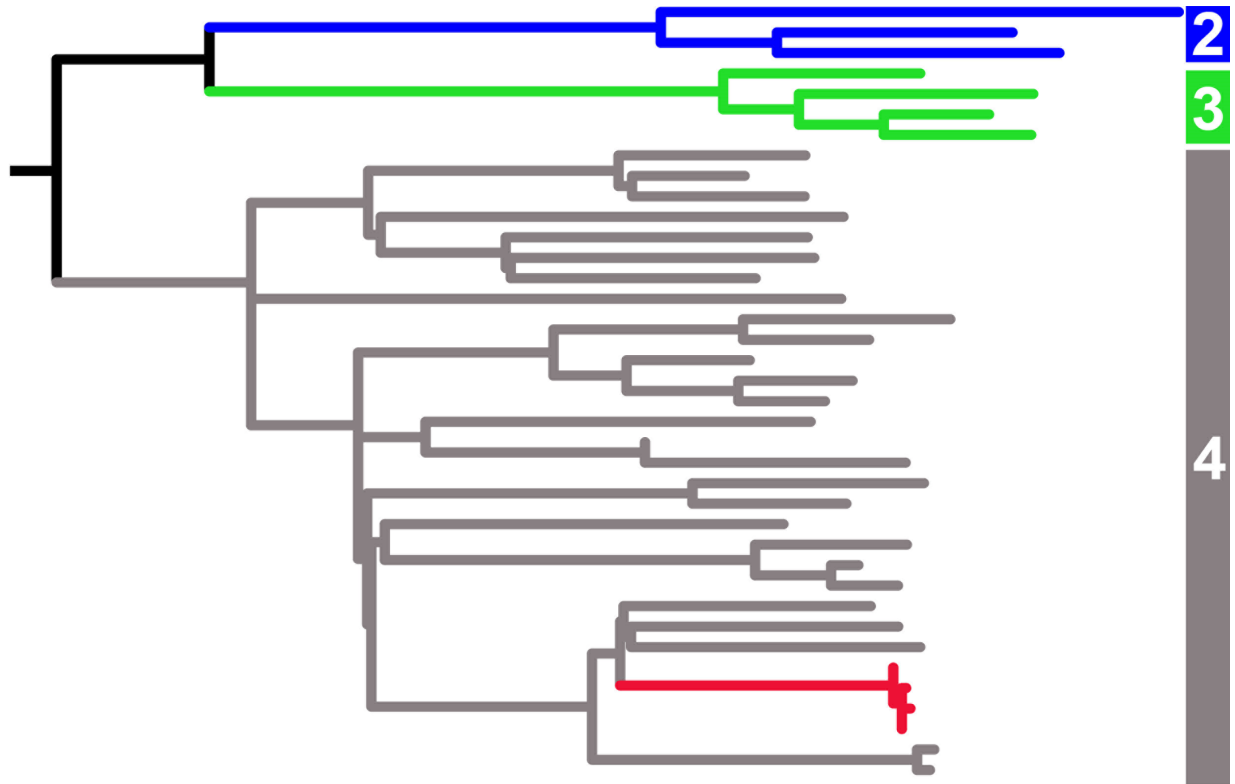
**Supplementary tables and figures.**

**Table S1. Cluster of orthologous groups of significantly up- and downregulated genes in isolates SF4-SF6 relative to SF1. Significantly enriched categories are highlighted in bold.**

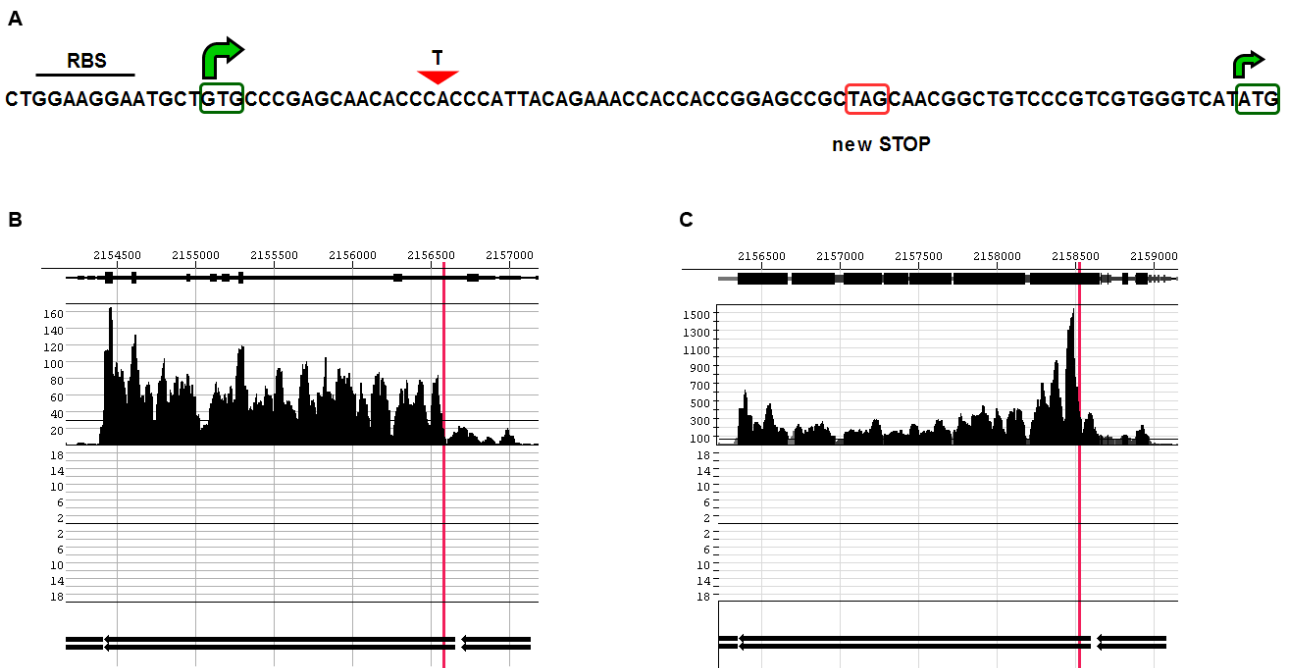
	COG term	Specified genes (n)	Genome (n)	specified genes (%)	Genome (%)	p value	corrected p value
<b>1&gt;4 down</b>	Secondary metabolites biosynthesis transport and catabolism	2	240	50	6	0.019	0.057
	Signal transduction mechanisms	1	103	25	2.58	0.095	0.286
	General function prediction only	1	441	25	11.03	0.311	0.933
<b>1&gt;4 up</b>	Cell motility	1	11	16.67	0.28	0.016	0.081
	Energy production and conversion	2	218	33.33	5.45	0.036	0.178
	Inorganic ion transport and metabolism	1	125	16.67	3.13	0.16	0.801
<b>1&gt;5 down</b>	<b>Secondary metabolites biosynthesis transport and catabolism</b>	4	240	36.36	6	0.003	<b>0.019</b>
	Signal transduction mechanisms	2	103	18.18	2.58	0.029	0.201
	Nucleotide transport and metabolism	1	64	9.09	1.6	0.15	1.051
<b>1&gt;5 up</b>	Carbohydrate transport and metabolism	2	114	10.53	2.85	0.085	0.934
	Translation ribosomal structure and biogenesis	2	121	10.53	3.03	0.093	1.021
	Inorganic ion transport and metabolism	2	125	10.53	3.13	0.097	1.071
<b>1&gt;6 down</b>	<b>Secondary metabolites biosynthesis transport and catabolism</b>	6	240	26.09	6	0.002	<b>0.016</b>
	Signal transduction mechanisms	3	103	13.04	2.58	0.018	0.177
	Lipid transport and metabolism	3	263	13.04	6.58	0.129	1.294
<b>1&gt;6 up</b>	Cell wall/membrane/envelope biogenesis	4	108	10	2.7	0.018	0.231
	General function prediction only	8	441	20	11.03	0.04	0.516
	Secondary metabolites biosynthesis transport and catabolism	5	240	12.5	6	0.058	0.76

**Table S2. Oligonucleotides listed by application**

Primer	Sequence	Application
gyrB_F	GGCACGAGAGTTGGTGCGGCG	
gyrB_S NPR1	CGGACTTGCGCGGATCCGTGA	
gyrB_S NPR2	CCGTGATGATCGCCTGAACTTCGT	
gyrB_W TR1	CGGACTTGCGCGGATCCGTGG	
gyrB_W TR2	CCGTGATGATCGCCTGAACTTCGG	
embB_F1	GTCGCGCAACCGGATGGCGTTC	SNP verification
embB_S NPR1	AGCTGGAGACATAACCACCAGCCGA	
embB_W TR1	AGCTGGAGACATAACCACCAGCCGT	
embB_F2	CTGCTGGACTGGGCGGTTCGGT	
embB_S NPR2	GCCGTCTTCCCACGTGTCGGTGTT	
embB_W TR2	GCCGTCTTCCCACGTGTCGGTGTC	
iniBF	CAAATCTCATCGGTGGCGGCCAATG	
iniBR	CGCAATCCGCTCATGGGGTCG	qPCR
rpoBF	GCCTGCGTACGGTCGGCGA	
rpoBR	GCCTCCACGTCCTGGGTGGTC	



**Figure S1.** Phylogenetic placement of patient isolates. Maximum likelihood tree based on 2801 synonymous SNPs. Numbers refer to the modern *M. tuberculosis* lineages 2,3 and 4.



**Figure S2. Expression of *katG*.** (A) Schematic overview of *katG* features. Ribosomal binding site (RBS) and start codon (GTG) are indicated. The insertion identified in isolates SF2-SF9 is indicated by a red triangle. The insertion results in a premature STOP codon which is followed by an alternative ATG start codon. (B) RNA-seq reads from isolate SF1 aligned to *katG*. (C) RNA-seq reads from isolates SF4-SF6 aligned to *katG*.