Supp. Table 1: The accession numbers of the KatG proteins used in the multiple sequence analysis

Mycobacterium	**UniProtKB**
M. tuberculosis	P9WIE5
M. avium paratuberculosis (K10)	Q73ZD5
M. marinum	B2HE73
M. smegmatis	A0QXX7
M. haemophilum	A0A0I9UM98

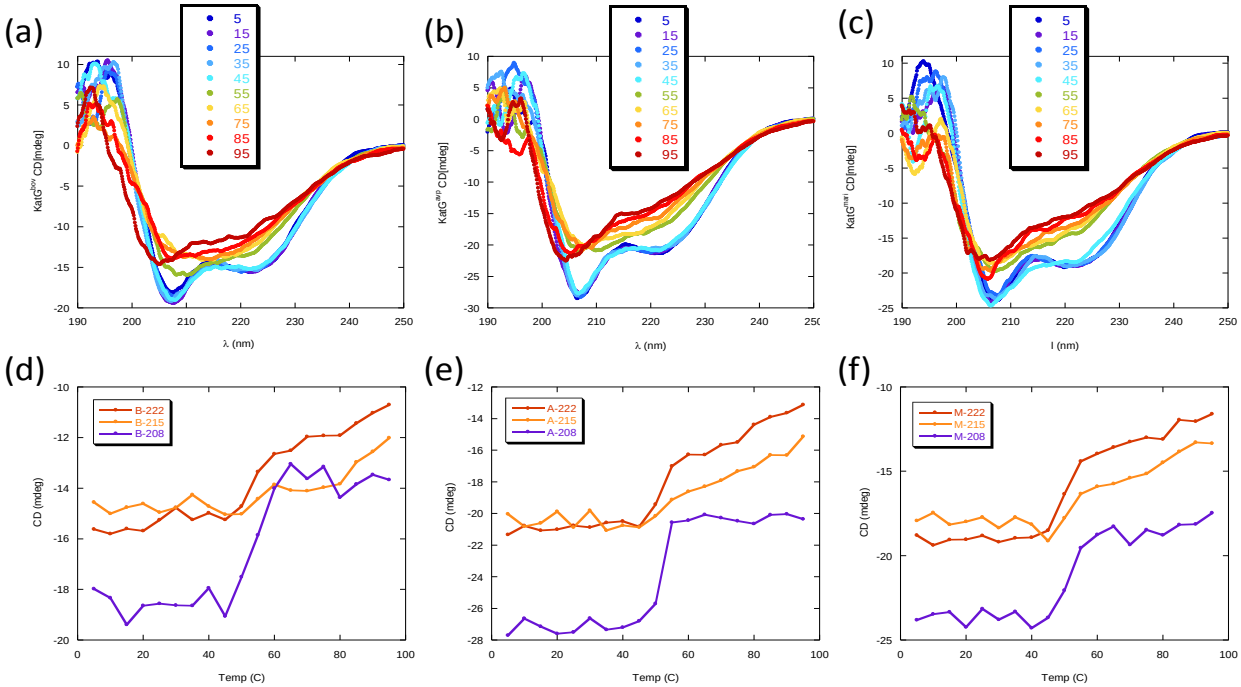
Supp. Table 2: Percent Identity Matrix - created by Clustal2.1

	M.tubeculosis	*M.haemophilum*	*M.smegmatis*	MAP	*M. marinum*
M.tubeculosis	100	86.47	66.26	68.56	68.7
M.haemophilum	86.47	100	65.49	67.93	68.2
M.smegmatis	66.26	65.49	100	84.22	81.29
M. avium paratuberculosis (K10)	68.56	67.93	84.22	100	85.73
M. marinum	68.7	68.2	81.29	85.73	100

	1. M. gilvum	2. M. fortuitum	3. M. smegmatis	4. M. marinum	5. M. ulcerans	6. M. asiaticum	7. M. gordonae	8. M. shigaense	9. M. szulgai	10. M. scrofulaceum	11. M. intracellulare	12. MAP	13. M. avium	14. M. kansasii	15. M. malmoense	16. M. vanbaalenii	17. Nocardia farcinica	18. M. abscessus	19. M. chelonae	20. M. haemophilum	21. M. microti	22. Mtb	23. M. canettii	24. M. africanum
M. gilvum	100	78.28	77.28	75.81	75.41	78.41	79.19	78.31	79.62	78.84	78.44	79.17	79.3	77.9	78.3	59.86	61.01	62.43	62.02	63.64	63.04	62.91	63.04	63.04
M. fortuitum	78.28	100	80.16	78.27	77.73	78.6	77.63	78.9	81.02	79.95	79.97	80.56	80.7	79.7	79.97	59.81	61.82	61.75	61.75	64.45	64.54	64.4	64.54	64.54
M. smegmatis	77.28	80.16	100	81.16	80.62	84.43	82.53	82.53	84.97	82.01	83.91	84.22	84.49	84.45	83.38	60.08	61.28	62.81	62.67	65.63	66.53	66.4	66.53	66.53
M. marinum	75.81	78.27	81.16	100	99.33	81.67	82.19	83.08	85.44	84.12	84.52	85.73	85.87	86.94	87.35	60.61	62.59	65.08	64.26	68.16	68.79	68.66	68.79	68.79
M. ulcerans	75.41	77.73	80.62	99.33	100	81.13	81.92	82.53	85.18	83.58	83.98	85.2	85.33	86.41	86.81	60.47	62.59	65.08	64.39	68.02	68.66	68.52	68.66	68.66
M. asiaticum	78.41	78.6	84.43	81.67	81.13	100	88.58	88.17	88.98	85.62	87.79	86.98	87.25	86.58	87.52	59.78	62.4	63.93	63.52	64.99	66.98	66.85	66.98	66.98
M. gordonae	79.19	77.63	82.53	82.19	81.92	88.58	100	89.39	89.52	85.73	86.83	87.1	87.23	86.29	86.69	59.86	62.07	64.3	64.02	66.03	67.35	67.21	67.35	67.35
M. shigaense	78.31	78.9	82.53	83.08	82.53	88.17	89.39	100	88.71	88.31	89.27	89.27	89.41	87.07	87.48	62.59	62.97	66.11	65.56	67.5	68.6	68.46	68.6	68.6
M. szulgai	79.62	81.02	84.97	85.44	85.18	88.98	89.52	88.71	100	89.11	90.07	89.93	90.2	89.66	89.26	61.71	62.67	64.62	65.03	66.89	68.34	68.21	68.34	68.34
M. scrofulaceum	78.84	79.95	82.01	84.12	83.58	85.62	85.73	88.31	89.11	100	90.2	90.6	90.87	89.13	89.66	61.62	62.04	64.94	64.26	66.94	67.71	67.57	67.71	67.71
M. intracellulare	78.44	79.97	83.91	84.52	83.98	87.79	86.83	89.27	90.07	90.2	100	92.63	93.03	90.21	90.88	61.62	64.08	65.48	64.8	67.62	68.79	68.66	68.79	68.79
MAP	79.17	80.56	84.22	85.73	85.2	86.98	87.1	89.27	89.93	90.6	92.63	100	99.6	90.08	90.88	61.45	63.99	66.21	65.67	67.93	68.7	68.56	68.7	68.7
M. avium	79.3	80.7	84.49	85.87	85.33	87.25	87.23	89.41	90.2	90.87	93.03	99.6	100	90.35	91.15	61.59	63.99	66.35	65.8	68.06	68.97	68.83	68.97	68.97
M. kansasii	77.9	79.7	84.45	86.94	86.41	86.58	86.29	87.07	89.66	89.13	90.21	90.08	90.35	100	90.88	62.04	63.95	65.89	65.21	68.16	69.34	69.2	69.34	69.34
M. malmoense	78.3	79.97	83.38	87.35	86.81	87.52	86.69	87.48	89.26	89.66	90.88	90.88	91.15	90.88	100	60.94	63.27	65.76	64.8	67.75	69.06	68.93	69.06	69.06
M. vanbaalenii	59.86	59.81	60.08	60.61	60.47	59.78	59.86	62.59	61.71	61.62	61.62	61.45	61.59	62.04	60.94	100	64.64	72.83	72.97	69.93	69.34	69.48	69.48	69.48
Nocardia farcinica	61.01	61.82	61.28	62.59	62.59	62.4	62.07	62.97	62.67	62.04	64.08	63.99	63.99	63.95	63.27	64.64	100	70.26	69.99	73.81	73.37	73.37	73.51	73.51
M. abscessus	62.43	61.75	62.81	65.08	65.08	63.93	64.3	66.11	64.62	64.94	65.48	66.21	66.35	65.89	65.76	72.83	70.26	100	94.72	75.48	73.26	73.26	73.4	73.4
M. chelonae	62.02	61.75	62.67	64.26	64.39	63.52	64.02	65.56	65.03	64.26	64.8	65.67	65.8	65.21	64.8	72.97	69.99	94.72	100	76.02	74.62	74.62	74.76	74.76
M. haemophilum	63.64	64.45	65.63	68.16	68.02	64.99	66.03	67.5	66.89	66.94	67.62	67.93	68.06	68.16	67.75	69.93	73.81	75.48	76.02	100	86.47	86.47	86.6	86.6
M. microti	63.04	64.54	66.53	68.79	68.66	66.98	67.35	68.6	68.34	67.71	68.79	68.7	68.97	69.34	69.06	69.34	73.37	73.26	74.62	86.47	100	99.73	99.86	99.86
Mtb	62.91	64.4	66.4	68.66	68.52	66.85	67.21	68.46	68.21	67.57	68.66	68.56	68.83	69.2	68.93	69.48	73.37	73.26	74.62	86.47	99.73	100	99.86	99.86
M. canettii	63.04	64.54	66.53	68.79	68.66	66.98	67.35	68.6	68.34	67.71	68.79	68.7	68.97	69.34	69.06	69.48	73.51	73.4	74.76	86.6	99.86	99.86	100	100
M. africanum	63.04	64.54	66.53	68.79	68.66	66.98	67.35	68.6	68.34	67.71	68.79	68.7	68.97	69.34	69.06	69.48	73.51	73.4	74.76	86.6	99.86	99.86	100	100

Supplementary Table 3: Comparison of identity between 23 different mycobacteria (and *N. farcinica*) in their KatG protein.

Supplementary figure 1:

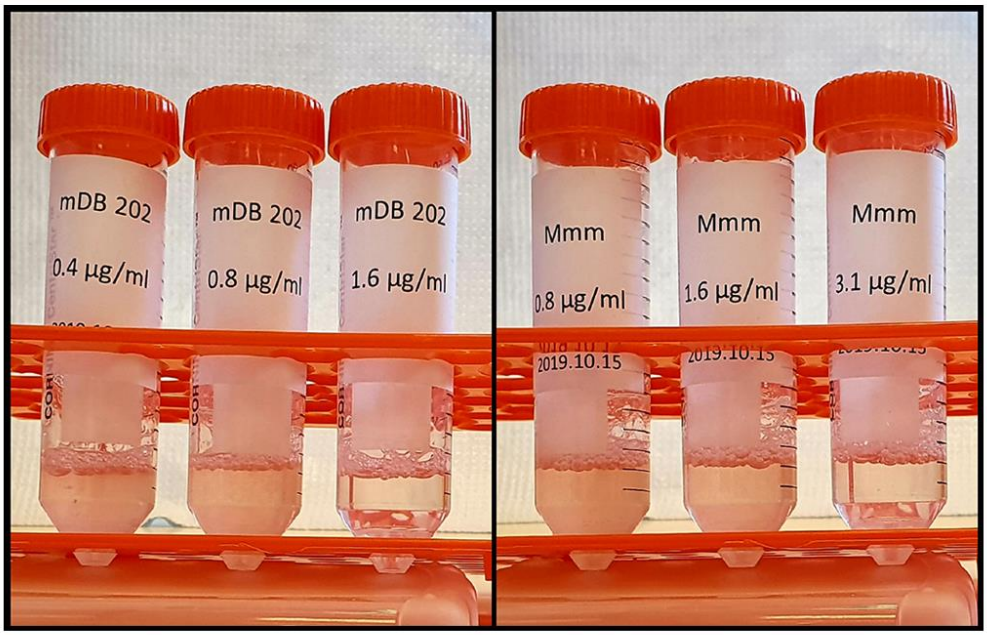


Supplementary Figure 1: Upper panel: Temperature dependence of the Far-UV CD spectrum of (A) KatG^{bov}, (B) KatG^{apv} and (C) KatG^{mari} in 25 mM phosphate buffer, pH 7.2, 25°C. Changes in the CD spectra were monitored as a function of temperature from 5 to 95 °C in 5 °C steps, spectra are shown only for every 10 °C change for clarity.

Lower panel: Singular wavelength changes of the signal at 222, 215 and 208 with temperature are presented for (D) KatG^{bov}, (E) KatG^{avp} and (F) KatG^{mari} .

Supplementary figure 2:

(a) (b)



<u>Supplementary Figure 2</u>: The MIC to isoniazid was compared between WT *M. marinum* (Mmm, right) and M.marinum$^{KatG\text{-}mar}$ (mutant mDB202, over-expressing its own KatG), on the left. Overexpression of KatG reduced the MIC X2, from ~3.1 µg/ml to ~1.6 µg/ml.