

Figure S1: Pearson correlation result for the proteomics data corresponding to Fig. 1(C).

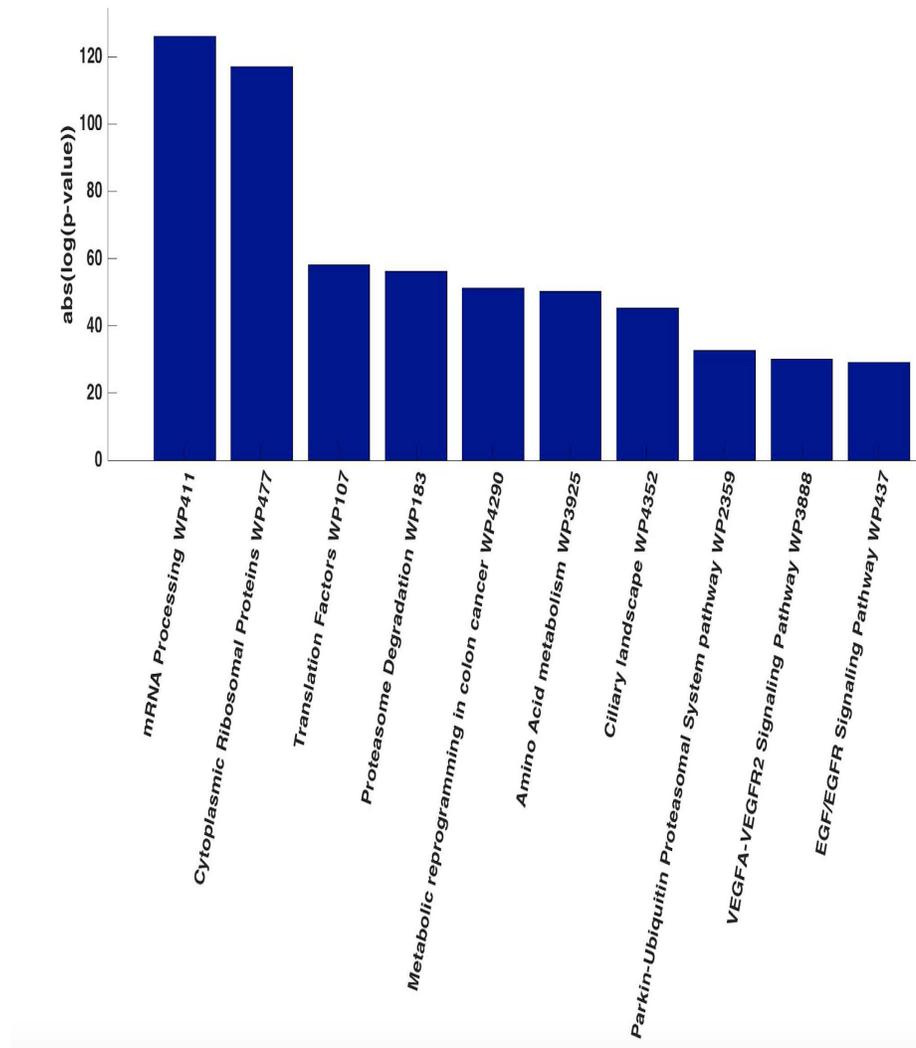
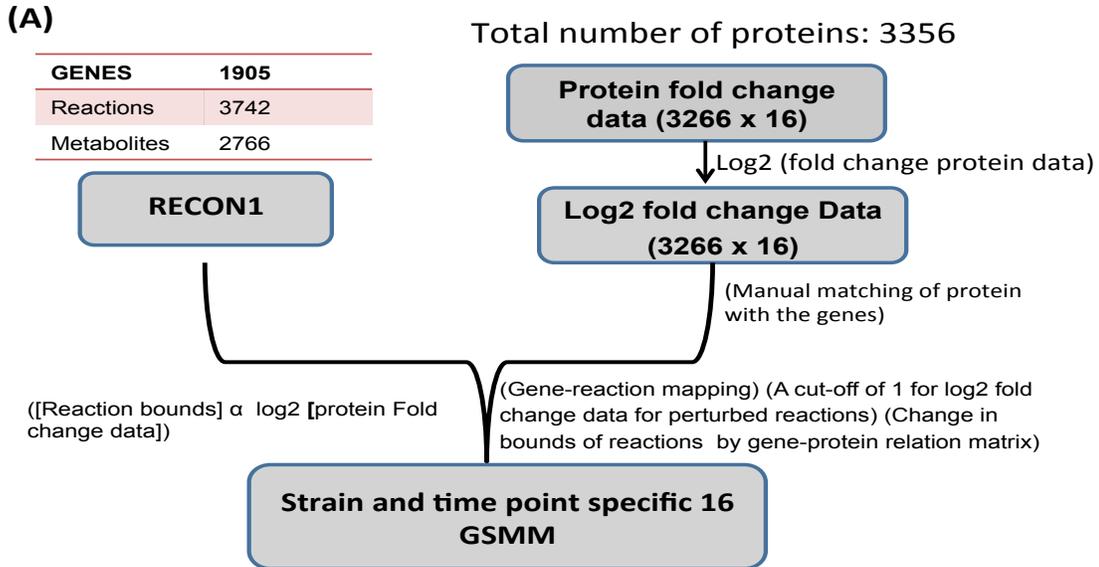


Figure S2: **Whole proteome Pathway analysis.** Shows the pathway analysis of the union of perturbed proteins in all the proteomics profile.



**(B)**

S.No	Model name	Perturbed Reactions (reaction-upper bound)>10
1	Ra6	218
2	Rv6	222
3	Bnd6	219
4	Jal6	126
5	Ra18	218
6	Rv18	28
7	Bnd18	170
8	Jal18	351
9	Ra30	188
10	Rv30	168
11	Bnd30	198
12	Jal30	146
13	Ra42	249
14	Rv42	75
15	Bnd42	116
16	jal42	137

Total Perturbed reactions all the strains and time points	841
Common to all strains	none

Figure S3: **Biological Process network and finding perturbed paths.** (A) A workflow diagram of the genome scale metabolic models reconstruction. (B) The bounds were changed by mapping of proteomics data were analyzed across the 16 GSMM. The table shows the high bound metabolic reactions (reaction bounds >10) in the 16 models and the reactions which were common to all the infection (avirulent and virulent) across all time point and all the metabolic reactions perturbed during the infection of both avirulent and virulent strain time independent. or strain dependent cluster across the 16 models.

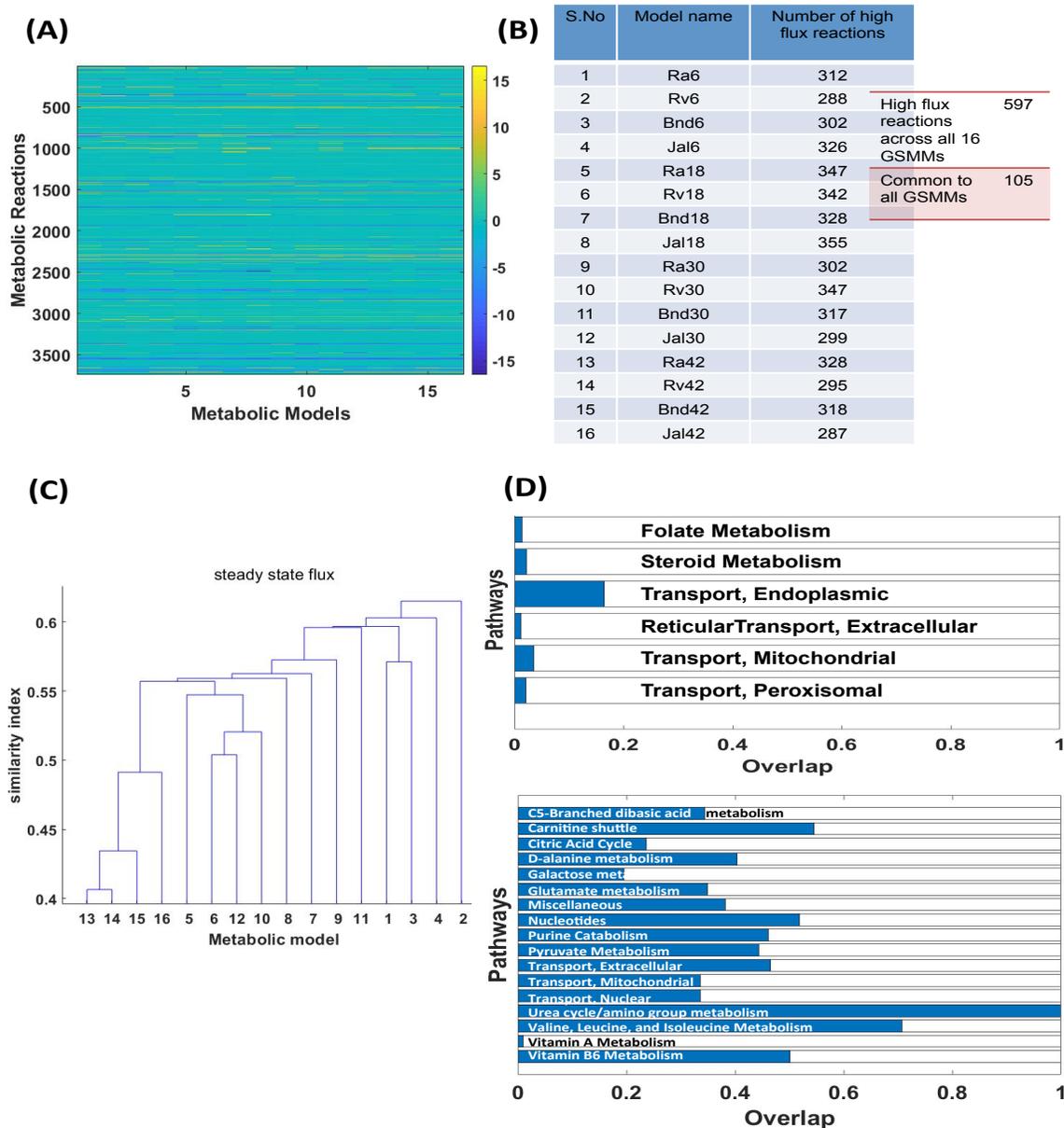


Figure S4: **Flux balance analysis of GSMMs.** (A) A heat map of the steady state fluxes of the 3742 recon reactions across the 16 GSMM. (B) The table shows the Union of the all the reactions having a high flux a cutoff of (fluxes>5) and the reactions perturbed during Mtb infection independent of time and strain. (C) Show the hierarchy clustering of the 16 GSMM to elucidate of the obtained metabolic steady states of different strains at different time points. (D) A metabolic pathway analysis of the common to all reactions and union of all reactions with high fluxes.

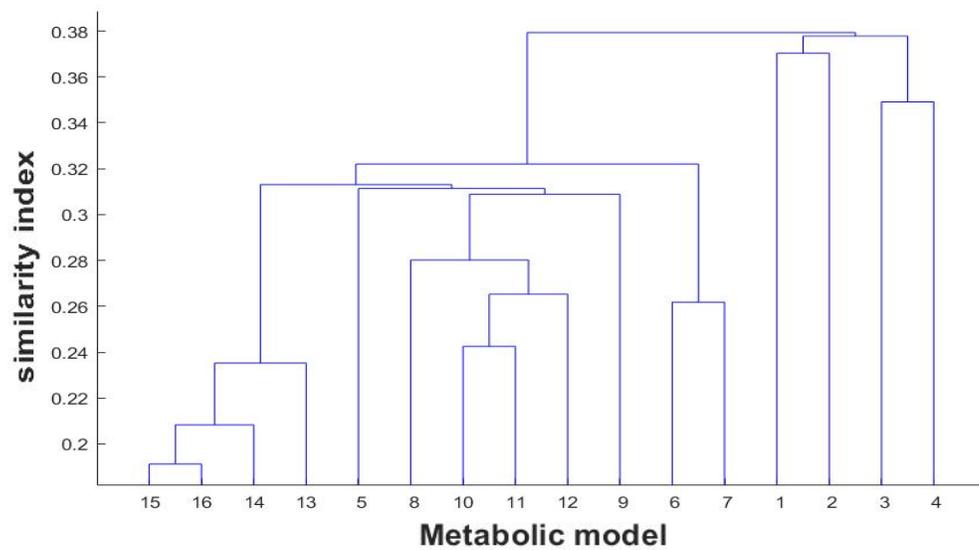


Figure S5: Pearson correlation result for the metabolic flux corresponding to Fig. S4(C).

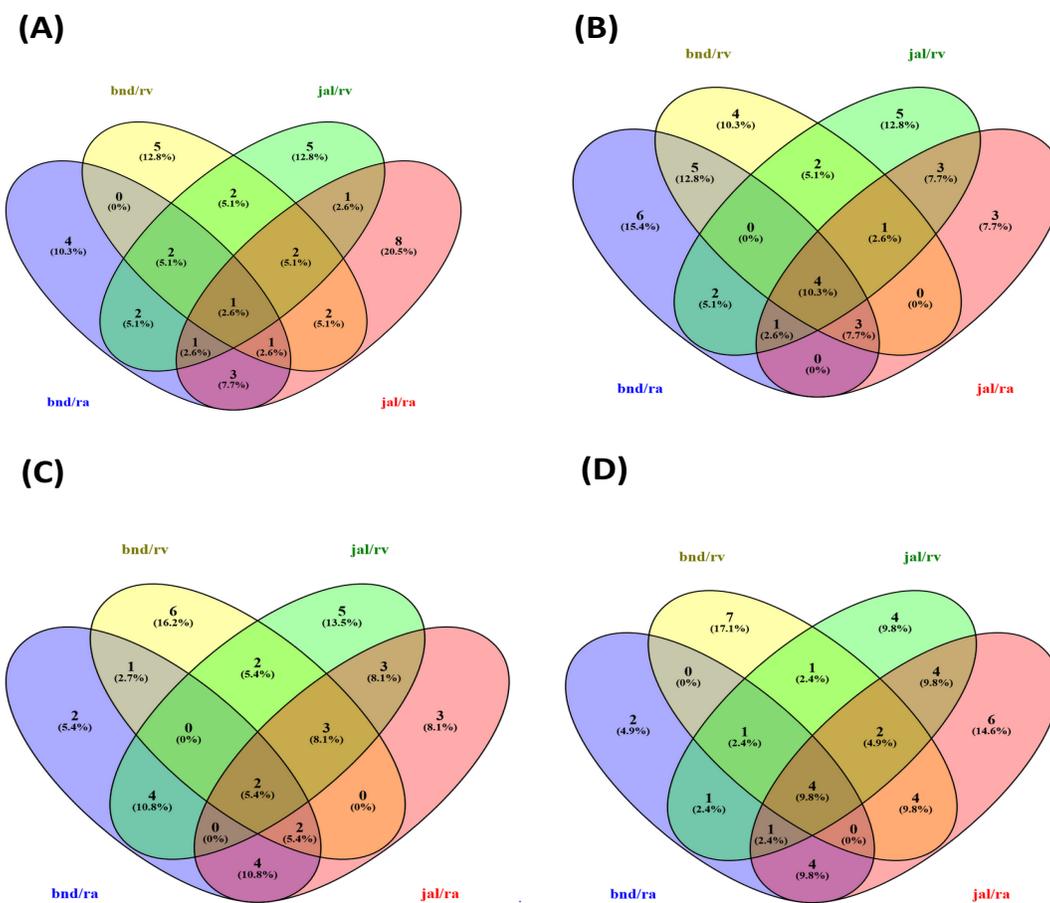


Figure S6: Differences in host response between reference strains and clinical isolates at (A) 6 hours, (B) 18 hours, (C) 30 hours and (D) 42 hours.

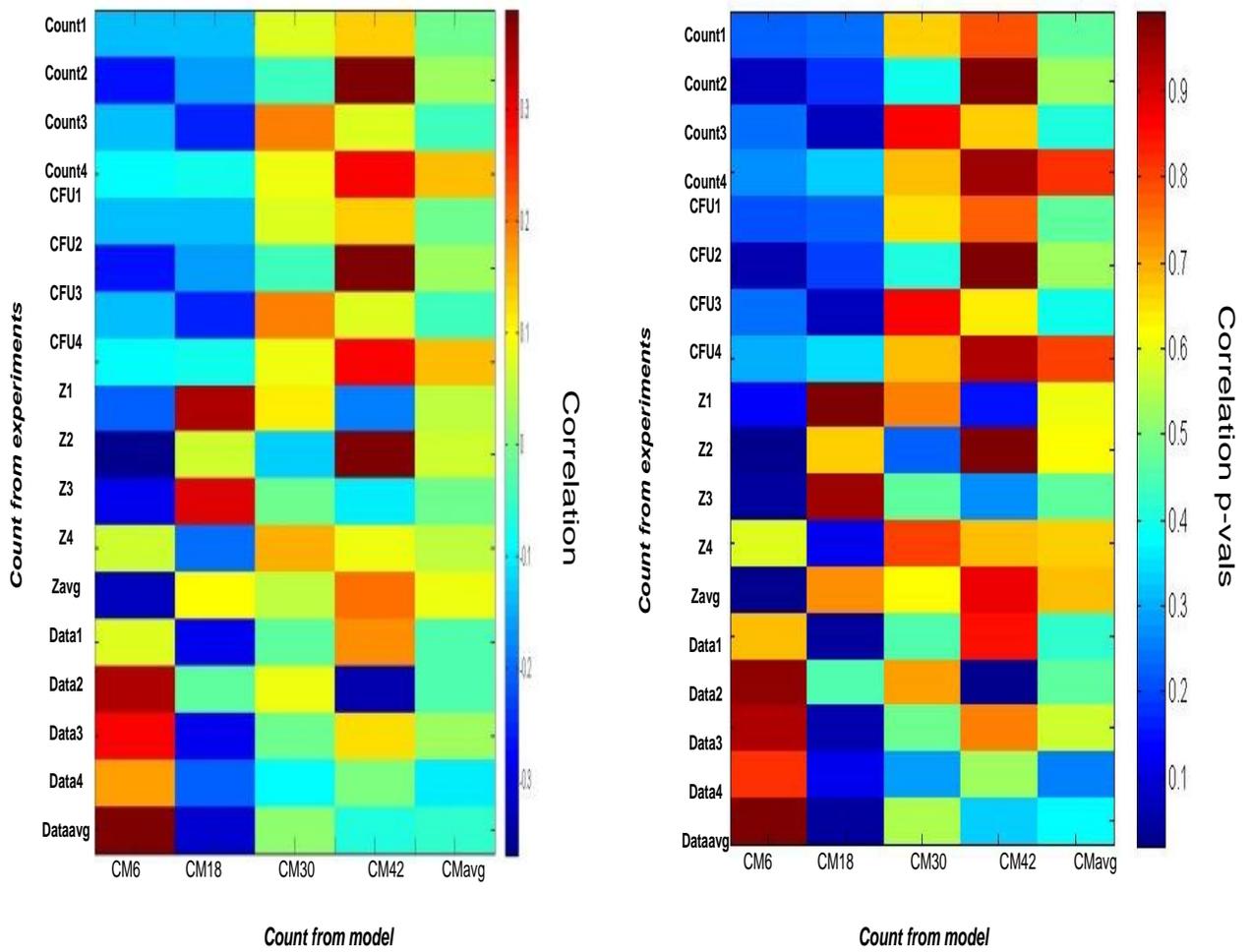


Figure S7: **Gene knock out Results**. Shows the correlation values of RV models at the four time points and with the all the experimental counts (Left panel) and the corresponding (p-values).