SUPPLEMENTAL INFORMATION

Figure S1

Log(2) ratios and Log(10) P-values of d45 wildtype mouse output libraries compared with inoculum libraries are plotted, each dot representing one gene. Red dots represent: A.) genes required for growth *in vivo* at d45 and B.) genes required for growth *in vivo* at d10. C.) Distributions of Log(2) ratios for genes tagged as essential for *in vivo* growth at both time points, essential only at day 10, and non-essential at both time points.

Figure S2

A.) Gene Set Enrichment Analysis (GSEA) using genes required in vivo in Sassetti et al. as a comparison gene set. For each time point, a list ranked by p-values and ratios was used to perform GSEA, and enrichment Family Wise Error Rate P-values were calculated. Enrichment plots represent running score determined by enrichment of the gene set in the ranked list. B.) Distributions of Log(2) ratios for genes tagged as essential in both studies, only in Sassetti et al., and non-essential in both studies.

Figure S3

Wild type, tryptophan auxotroph, and complemented strains were used to infect macrophages. One day after infection, macrophages were either stimulated with IFN-γ and TNF-α or remained unstimulated. The tryptophan auxotroph grew poorly in unstimulated macrophages and were hypersuscpetible to the effects of IFN-γ and TNF-α (B).

Figure S4

trpE KO Mtb strains were infected into mouse peritoneal macrophages with and without IFN-γ and TNF-α. To determine if the cytokine effect was tryptophan dependent, 100 μM tryptophan was supplemented in the media.

Figure S5

Wildtype Mtb and the trpE deletion strain were grown in the presence and absence of 1-MT, demonstrating that 1-MT does not restore growth of the auxotrophic strain.

Figure S6

Mycobacterium smegmatis was grown in various concentrations of 5-FABA and 6-FABA to determine the MICs of the compounds.

Figure S7

Mouse peritoneal macrophages were treated with increasing doses of 6-FABA or staurosporine, and viability was calculated using an assay for LDH release.

Figure S8

A.) Human monocyte-derived macrophages were infected with Mtb and treated with IFN-γ (with vitamin D in human macrophages and with TNF-α in mouse macrophages) and/or 6-FABA on day 1. Doses were titrated such that the effect of a single treatment would decrease CFU compared to the untreated macrophage control. CFU ratios of the experimental conditions to the untreated controls were calculated (B). Using these ratios, the predicted non-synergistic value was determined and compared to the actual combined effect of IFN-γ and 6-FABA.

Figure S9

A single dose of 5-FABA, 6-FABA and the corresponding esters was administered intraperitoneally or orally at 25mg/kg to female CD-1 mice. Blood samples were collected in heparinized tubes at 6 to 8 serial timepoints between 0 and 24h post-dosing. Plasma levels of 5-FABA, 6-FABA and the corresponding esters were quantified by high pressure liquid chromatography coupled to tandem mass spectrometry (LC/MS/MS).

Table S1

Differential read counts for each gene were compared between mouse output libraries and the *in vitro* input controls. For each gene, we report a p-value (Mann Whitney U test), a false discovery rate (Benjamini-Hochberg) and read count ratio.

Table S2

Read count comparison analysis between output libraries from MHCII$^{-/-}$ mice and wildtype mice.

Table S3

Read count comparison analysis between libraries subjected to various *in vitro* stresses: acid, nitric oxide, carbon starvation and tryptophan starvation.

Table S4

Read counts for each TA position in the genome. All conditions and all replicates are shown in this table, including wildtype mice, MHCII$^{-/-}$ mice, CD4-depleted mice, acid stress, nitric oxide stress, carbon starvation, iron depletion and rescue, and tryptophan and full amino acid rescue.