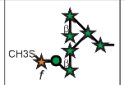
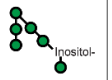
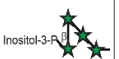
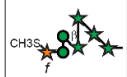
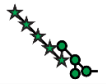
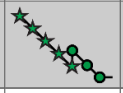
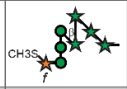
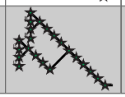
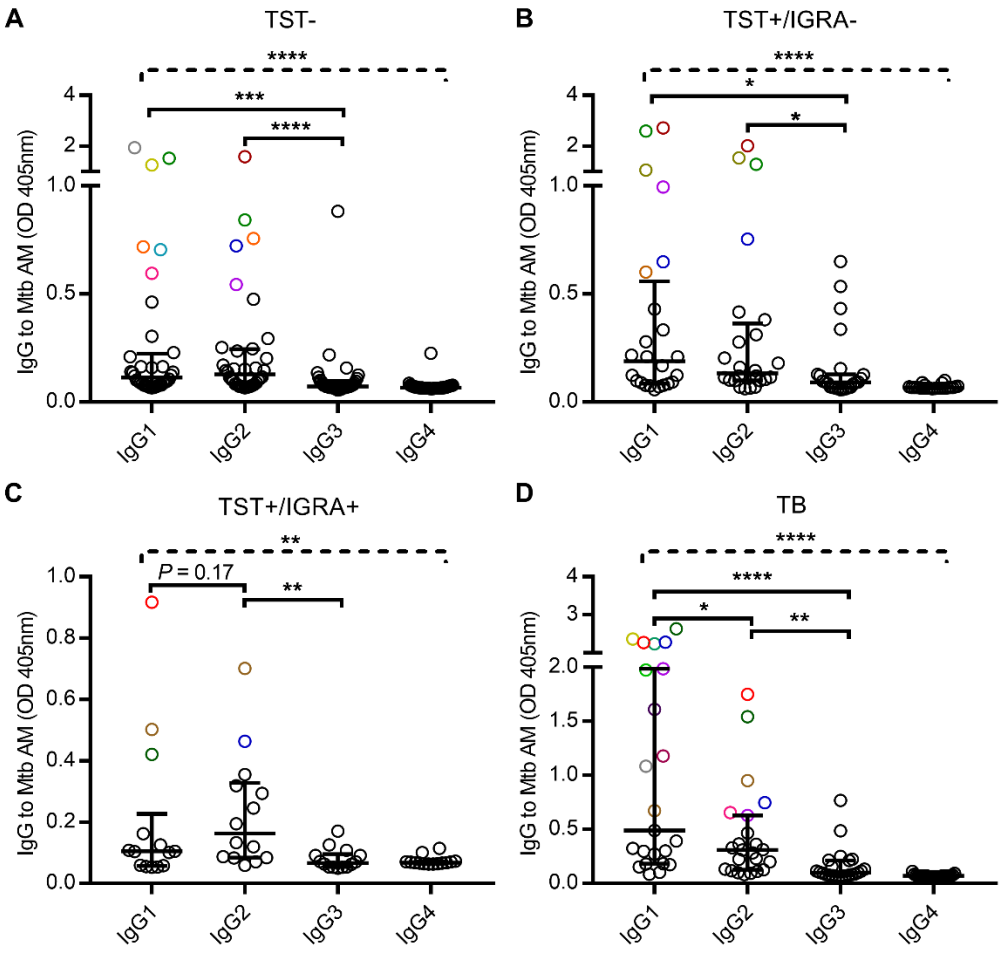
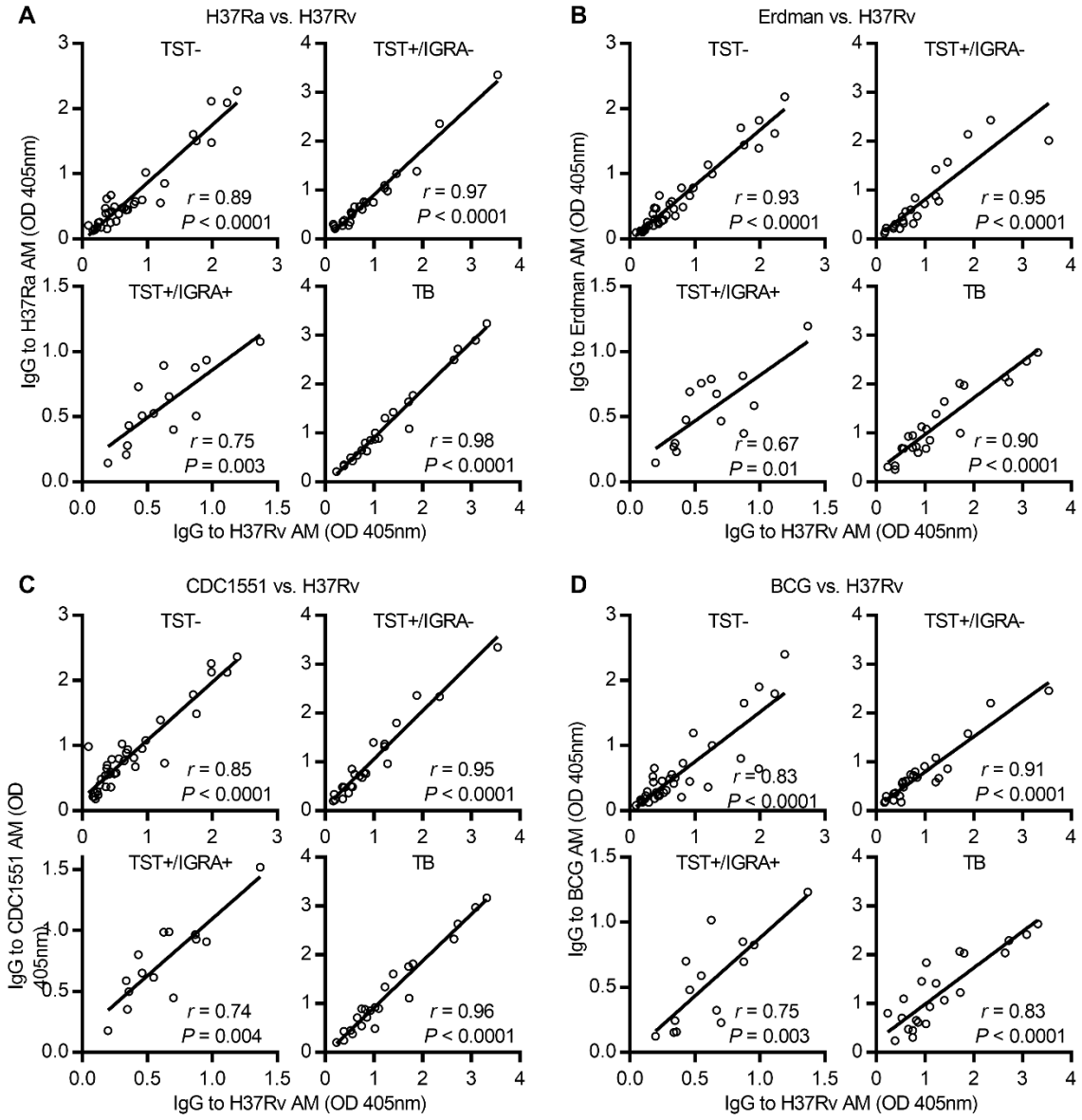
Supplemental Table 1. AM oligosaccharide structures and correlations between serum IgG reactivity to each AM OS and Mtb macrophage phagocytosis in TST+/IGRA+ and TB subject groups

		TST+/IGRA+		TB				TST+/IGRA+		TB				TST+/IGRA+		TB	
		r	p	r	p			r	p	r	p			r	p	r	p
S#1		0.39	0.26	0.40	0.18	**S#11**		0.18	0.63	0.26	0.39	**S#23**		0.21	0.56	0.22	0.47
S#2		0.61	0.07	0.35	0.24	**S#12**		0.20	0.58	-0.27	0.37	**S#25**		0.28	0.43	-0.25	0.40
S#3		**0.70**	**0.03**	0.38	0.20	**S#15**		0.38	0.28	0.24	0.42	**S#44**		0.13	0.73	-0.09	0.77
S#4		0.36	0.31	-0.22	0.46	**S#16**		0.33	0.35	0.43	0.14	**S#46**		-0.18	0.63	0.11	0.71
S#5		0.05	0.89	-0.02	0.95	**S#17**		0.16	0.66	-0.69	0.01	**S#49**		**0.68**	**0.03**	0.29	0.33
S#6		0.14	0.70	0.04	0.91	**S#18**		0.45	0.19	0.21	0.48	**S#50**		-0.17	0.64	-0.34	0.26
S#7		**0.68**	**0.03**	0.27	0.38	**S#19**		0.56	0.10	0.03	0.92	**S#56**		0.58	0.09	0.26	0.40
S#8		**0.77**	**0.01**	0.47	0.10	**S#20**		0.43	0.22	0.43	0.14	**S#57**		0.55	0.10	0.16	0.61
S#9		**0.76**	**0.01**	0.03	0.92	**S#21**		0.55	0.10	0.14	0.64	**S#58**		-0.43	0.21	-0.46	0.11
S#10		-0.02	0.97	-0.02	0.96	**S#22**		0.47	0.18	0.24	0.43	**S#59**		0.01	> 0.99	-0.04	0.90

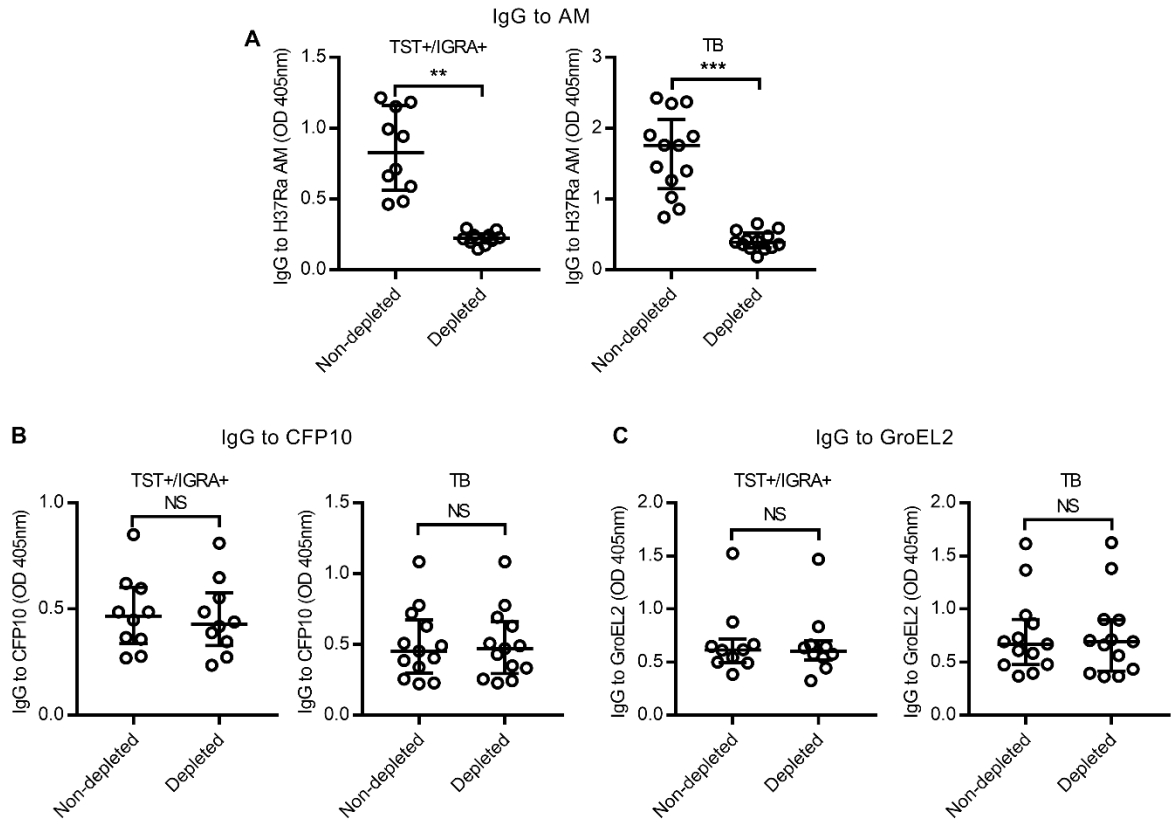
Green star: Ara*f* residue; green circle: mannose; orange star: xylose residue. Spearman rank correlation. Compound S#46 is an OS motif of the mycobacterial capsular PS alpha-glucan, which served as a control. TST+/IGRA+: Tuberculin skin-test positive, interferon-gamma release assay positive asymptomatic subjects; TB: subjects with active tuberculosis.



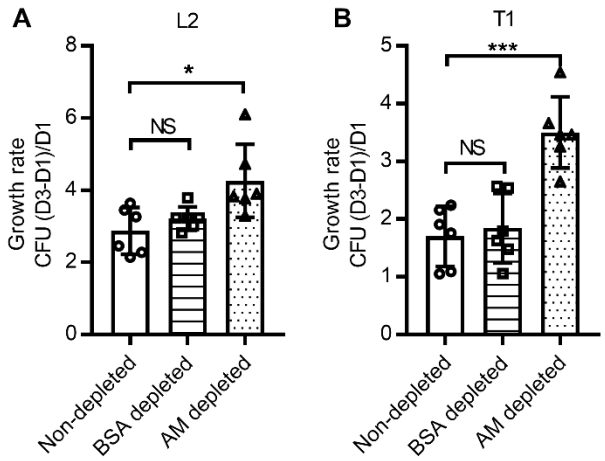
Supplemental Figure 1. Comparison of IgG1-4 subclass responses to Mtb (H37Rv) capsular AM among subjects at various Mtb infection states. (**A**–**D**) Sera (1:50) from (**A**) asymptomatic TST- subjects, *n* = 36; (**B**) Asymptomatic TST+/IGRA- subjects, *n* = 24; (**C**) Asymptomatic TST+/IGRA+ subjects, *n* = 14; and (**D**) TB patients, *n* = 23. Subjects with an anti-IgG subclass titer > 0.4 in TST+/IGRA+ group, and > 0.5 in other groups have been assigned individual different colors. TST: Tuberculin skin-test; IGRA: Interferon-gamma release assay; TB: active tuberculosis. Dashed lines represent Friedman test for comparison of paired values of multiple groups. Solid lines represent Wilcoxon matched-pairs signed rank test. Lines and error bars represent medians with interquartile ranges. *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$, and ****: $P < 0.0001$.



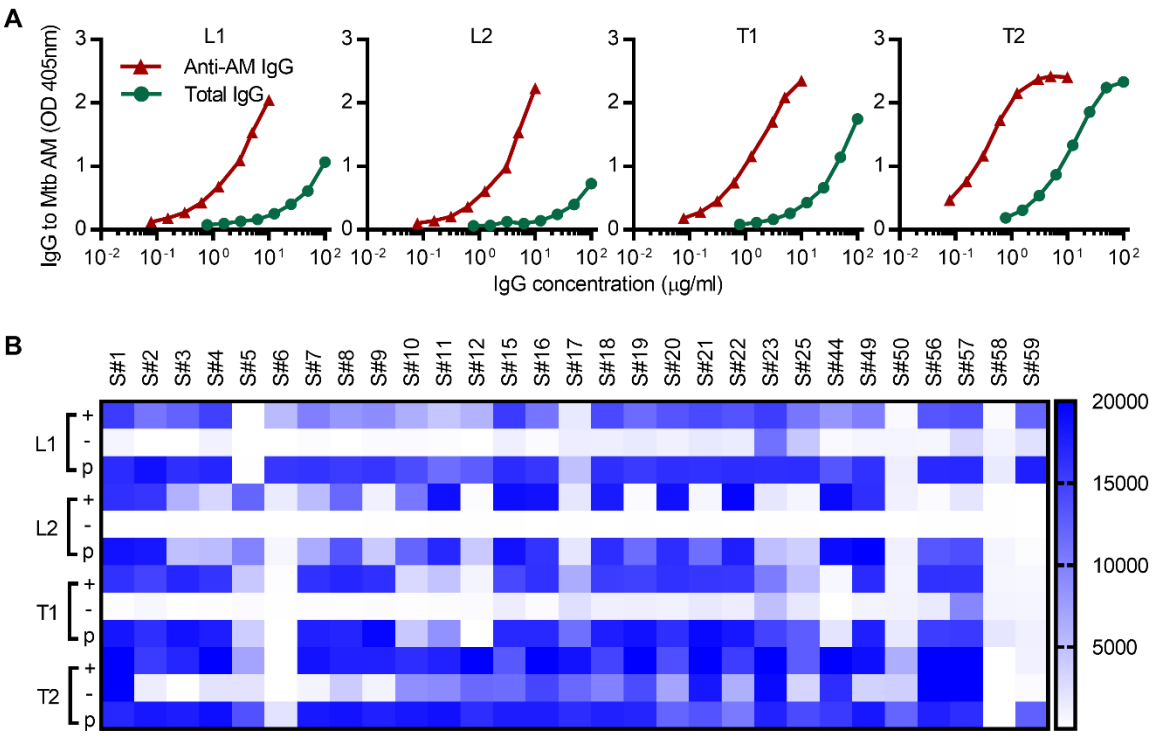
Supplemental Figure 2. Cross-reactivity of IgG to capsular AM isolated from different strains of the Mtb complex group irrespective of Mtb infection state. (**A**–**D**) Scatter plots show correlations between serum (1:50) IgG responses to AM isolated from Mtb H37Rv versus (**A**) the avirulent Mtb strain H37Ra; (**B**) the lab Mtb strain Erdman; (**C**) the clinical Mtb strain CDC1551; and (**D**) the M. *bovis* BCG vaccine stain (Pasteur) for each subject group. TST-: Asymptomatic TST negative subjects, *n* = 36; TST+/IGRA-: Asymptomatic TST positive IGRA negative subjects, *n* = 24; TST+/IGRA+: Asymptomatic TST positive IGRA positive subjects, *n* = 14; and TB: patients with active tuberculosis, *n* = 23. TST: Tuberculin skin-test; and IGRA: Interferon-gamma release assay. Spearman rank.



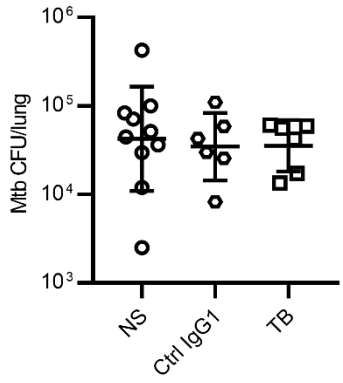
Supplemental Figure 3. Significant reduction of IgG reactivity to AM but not to other Mtb antigens in heat-inactivated sera depleted of anti-AM antibodies. (**A**) IgG responses to capsular AM isolated from Mtb H37Ra in non-depleted compared to anti-AM Ab depleted sera (1:100) by AM-coupled beads. (**B**–**C**) IgG responses in non-depleted compared to anti-AM Ab depleted sera to (**B**) the secreted Mtb protein CFP10, and (**C**) the surface protein GroEL2. Lines and error bars represent medians with interquartile ranges. TST+/IGRA+: Tuberculin skin-test positive, interferon-gamma release assay positive asymptomatic subjects, n = 10; and TB: subjects with active tuberculosis, n = 13. Wilcoxon matched-pairs signed rank test. **: $P < 0.01$, ***: $P < 0.001$, and NS: not significant ($P \geq 0.05$).



Supplemental Figure 4. Depletion of sera with AM-coupled beads enhanced Mtb intracellular growth compared to non-depleted sera or sera depleted with BSA-coupled beads. Columns and error bars represent mean and SD. Unpaired t test. *: $P < 0.05$, ***: $P < 0.001$, and NS: not significant ($P \geq 0.05$).



Supplemental Figure 5. Purification of anti-AM polyclonal IgG from human sera. (**A**) Anti-AM polyclonal IgG purified from two TST+/IGRA+ (L1 & L2) and two TST+/IGRA- sera (T1 & T2) showed higher binding capacity to capsular AM than the corresponding total IgG used at the same concentrations. (**B**) Reactivity of serum IgG to AM OS motifs before (+) and after AM-specific Ab depletion (-), and for purified AM-specific IgG (p). Color features represent the median fluorescent reactivity (MFI) to each of the OS motifs.



Supplemental Figure 6. Passive transfer of purified human anti-AM polyclonal IgG from a TB patient showed no effect on mycobacterial burden in Mtb-infected mice. Lung CFU (mean and SD) 2 weeks after low-dose infection (Erdman; mean lung CFU 35±3 one day post infection) in mice receiving i.p. normal saline (NS; *n* = 10), irrelevant IgG1 control mAb (Ctrl IgG1; *n* = 6) or anti-AM IgG (8 µg i.p. one day pre-infection, 4 µg at one day and 4 µg at one week post-infection) from one high-titer pulmonary TB patient (*n* = 6). One-way ANOVA *P* = 0.9.