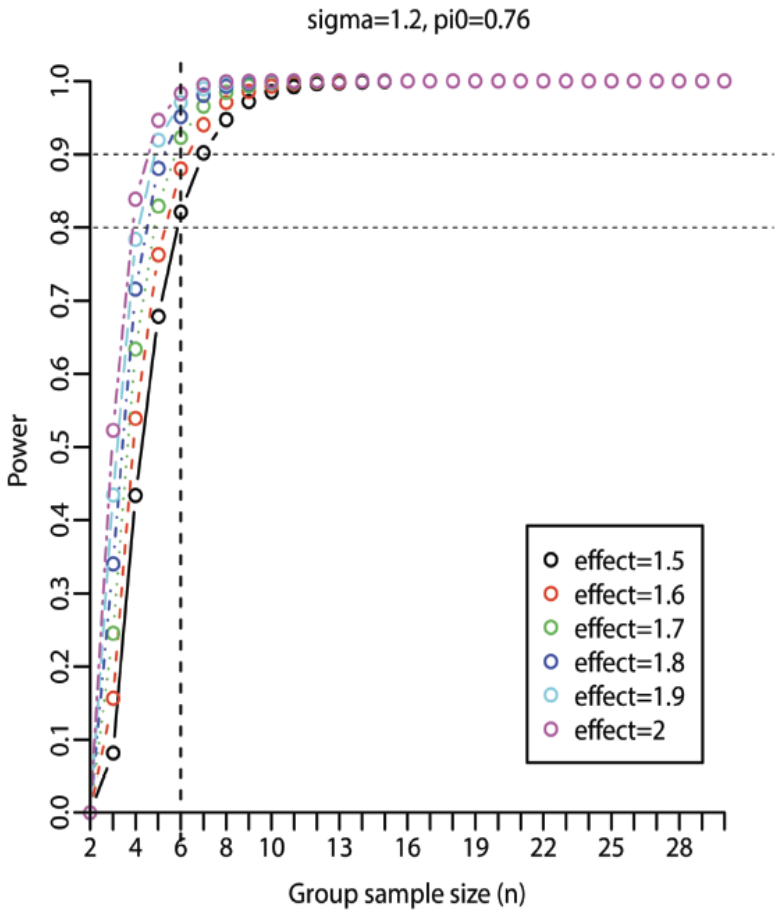
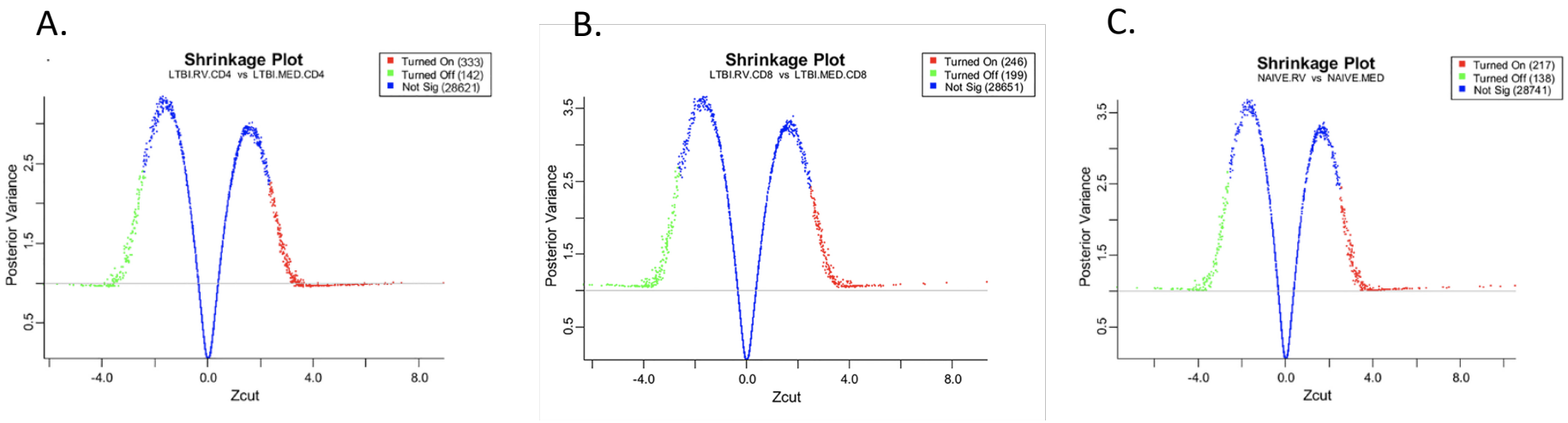


Supplemental Figure 1: Scree plot of power analyses and sample size calculations.

The figure displays the predictive power of various sample sizes based on the variability of the data (s) and the treatment effect size. As indicated, the samples size of our smallest study group, n=6, is associated with an 80-98% power of detecting a fold-change (Fc) effect in the 1.5-2.0 range.

Calculations are based on a Completely Randomized Design with Repeated Measures of a single Treatment Factor (Uninfected /*Mtb* infection of unsorted BAL cells /*Mtb* infection of CD4-depleted) on independent Experimental Units (subject-specific cell cultures). The *a priori* power analysis was based on calculation of the group sample size *n* required to detect a minimum effect in the Treatment Factor as a function of power, while controlling for an appropriate error rate that is consistent with the large number of simultaneous inferences associated with this type of high-dimensional dataset. This type of data requires application of methology that gives a sample size that would control the False Discovery Rate (denoted FDR or α) [30] and simultaneously guarantee a certain power (denoted 1-β). We utilized methodology described in Liu, et al [31] with a less conservative extension of the FDR called positive FDR (denoted pFDR) [34-35]. After variance stabilization and normalization of the data [34-35], the usual distributional assumptions of test statistics become applicable [31]. Calculations utilized the experimental group sample size n, and the common standard deviation of all variables (i.e. genes) by σ and the effect size by Δ/σ. We calculated the group sample size n required to detect e.g a minimum fold change *Fc* (effect size $\Delta/\sigma = \log_2(Fc)/\sigma$) in the treatment factor effect as a function of power 1-β, the parameter π_o (interpreted as the probability of non-differentially expressed variables), the common standard deviation σ, and a fixed level α of *pFDR*. Using Bayes Rule, for any estimate of π_o and α level of *pFDR* that we wish to control, we find the rejection region and the corresponding critical values for each sample size n [31]. Based on a pilot study in our hands, estimates of the parameters π_o and of the common standard deviation σ of the variables across experiments were $\pi_o = 0.41\text{-}0.98$ and and $\sigma = 0.72\text{-}1.19$, which is consistent with estimates found in other platforms in high-dimensional data [31]. Under the above assumption and most conservative estimations (for fixed $\pi_o = 0.98$ and $\sigma = 1.19$), while controlling the *FDR* at 5% ($FDR \leq 0.05$), a group sample size of n $n \geq 6$ is can detect a Fold-Change effect within the $1.5 \leq Fc \leq 2.0$ range, with at least 80% power, as illustrated..



Supplemental Figure 2: Shrinkage plots of differential *Mtb*-induced BAL cells gene expression.

The determination of differentially-expressed genes in unsorted BAL cells from LTBI subjects in the CD4-depletion and CD8-depletion studies (A and B) and in *Mtb*-naïve subjects (C) are represented. Differential expression was determined after initial preprocessing using implementations and algorithms (including our own) available from the R project, which is a open-access programming language and platform for statistical computing and visualization of the Comprehensive R Archive Network (CRAN) consortium (http://cran.r-project.org/). A single pre-filtering was performed on the initial 33,297 features of the Affymetrix Human Genome U133 plus 2.0 arrays: After filtering the 4,201 Affymetrix control probesets out, the dataset was left with 29,096 mRNA probesets. There were no missing values. The dataset of measured intensities was corrected for global normalization, variance-stabilization and normality using our recently developed '*Joint Adaptive Mean-Variance Regularization*' procedure as previously described [34-35] on the variables (genes or mRNA probesets). The entire procedure, including plot-generating functions, are implemented in our R package 'MVR' [36].

Analysis of differential expression of our variables (genes or mRNA probesets) between contrasts of interest was assessed in the context variable selection in a regression setting using our recent Bayesian hierarchical model and termed "Bayesian ANOVA". The Bayesian hierarchical model produces so-called Spike & Slab shrunken regression estimates [38-40], that are advantageous in that they allow to build a parsimonious model. These estimates work by borrowing information across variables in a way that optimally balances false positive and false negative detection rates, and hence minimize the total misclassification errors. This approach eliminates the huge problem of specifying an arbitrarily *FDR* cutoff value of significance, and the drawback of excessive conservativeness [41]. In addition, it does not ignore the correlation structure or dependency between the variables, which is very frequently present within large datasets of observational data. Finally, minimal assumptions about the data are made, which makes this approach applicable to a wide range of settings. Overall, this methodology has practical and important applications in high-dimensional, noisy and correlated data, as often occur with "omics" datasets. It is currently implemented as a R package 'spikeslab', and as a stand-alone Java-based software, freely available to academic users: Bayesian Analysis of Microarray (BAM) (www.bamarray.com) [42]. Our further analysis was based on an absolute Z-cut value of 2.5 for each data set.

Supplemental Table II:

Functions of genes comprising the signature of the role of CD4+ T cells in BAL cell recall responses to *Mtb* in healthy LTBI subjects

Functions of genes comprising the signature of the role of CD4+ T-cells in BAL cell recall responses to *Mtb* in healthy LTBI subjects

*highlighting = 9/47 genes (19%) involved in antiviral/anti-influenza response

Symbol	Entrez Gene Name	Function
AICDA	activation induced cytidine deaminase	Creates mutations in DNA, master regulator of secondary antibody diversification
CCL5	C-C motif chemokine ligand 5 (aka RANTES)	Chemotactic to T cells, eosinophils and basophils
CD226	CD226 molecule (aka PTA1, DNAM-1)	Mediates cellular adhesion via ligands CD112 and CD155
CD274	CD274 molecule (aka PD-L1, B7H1)	Expressed on APCs, binds to T-cell PD-1 inhibiting T-cell proliferation and reducing apoptosis of Treg
CD40	CD40 molecule	Expressed on APCs, provides for co-stimulation of CD4 cells via binding to CD154 (CD40L), also increases IFNγ-induced phagoycte activation
CD80	CD80 molecule 9aka B7-1)	Expressed on APCs, provides T-cell co-stimulation by binding to CD28 or CTLA-4
CSF2RB	colony stimulating factor 2 receptor beta common subunit	Common subunit to type 1 cytokine receptors GM-CSF receptor, IL-3R, IL-5R
CXCL10	C-X-C motif chemokine ligand 10 (aka IP-10)	Interferon-inducible, chemotactic to monocytes/macrophages, T cells, NK cells, dendritic cells
CXCL11	C-X-C motif chemokine ligand 11 (aka I-TAC)	Induced strongly by IFNγ and IFNβ, weakly by IFNα, higher affinity for CXCR3 than CXCL9 or CXCL 10, chemotactic for activated T cells
CXCL9	C-X-C motif chemokine ligand 9 (aka MIG)	Induced by IFNγ, chemotactic via CXCR3
DNAJC7	DnaJ heat shock protein family (Hsp40) member C7	Interacts with checkpoint protein RAD9A
FAS	Fas cell surface death receptor (aka CD95, APO-1)	Mediates apoptosis
GZMB	granzyme B	Serine protease within cytotoxic granules of NK cells and cytotoxic T cells
HLA-F	major histocompatibility complex, class I, F	Expressed on activated memory T cells, signals Treg to initiate production of inhibitory cytokines, serves a chaparone brining HLA Class I to cell surface, ligand for KIR
ICOS	inducible T cell costimulator (aka CD278)	Expressed on activated T cells, suggested to be more important for Th2 than Th1 activation
IFI35	interferon induced protein 35	Interacts with N-myc interactor (NMI) which augments STAT mediated transcription responses to IL-2 and IFNg, also with Basic leucine zipper transcription factor, ATF-like (BATF) associated with Th17 responses
IFIT3	interferon induced protein with tetratricopeptide repeats 3	Role in host anitviral response by modeulating immune signaling and apoptosis
IFITM3	interferon induced transmembrane protein 3	Important role in immunity to H1N1 influenza ("swine flu")
IFNG	interferon gamma	Numerous activities in macrophage activation, antiviral response, immunogregulation, anti-tumor responses
IL10RA	interleukin 10 receptor subunit alpha	Mediates immunosuppressive signal of IL-10
IL15	interleukin 15	Structural similarity to IL-2, secreted by mononuclear phagocytes in response to viral infection, induces proliferation of NK cells
IL15RA	interleukin 15 receptor subunit alpha (aka CD122)	High affinity binding of IL-15, enhances cell proliferation, increases expression of apoptosis inhibitor BCL2l/BCL2-XL and BCL2, also a component of IL-2R
IL27	interleukin 27	Member of IL-12 family, expressed by APCs, via IL-27R activates JAK-STAT and p38 MAPK pathways for inflammatory or anti-inflammatory effect
IRF1	interferon regulatory factor 1	Transcription factor, regulates expression of target genes by binding interferon stimulated response element (ISRE), role in TLR antiviral responses and provides link between TLR9 and IFNγ responses
JAK2	Janus kinase 2	Non-receptor tyrosine kinase, involved in signaling of IFN receptors as well as GM-CSF receptor family
KL	klotho	Roles in sensiitivity to insulin, protection from arteriosclerosis and aging
LTA	lymphotoxin alpha (aka TNF-β)	Varying roles in membrane-bound vs soluble form, can support cell proliferation, differentation, and apoptosis--important in development of Peyer's patches
MAP2K1	mitogen-activated protein kinase kinase 1 (aka MEK1)	Integration point for multiple biologic signals mediating celular proliferation, differentiation, and transcriptional regulation
MX1	MX dynamin like GTPase 1 (aka IFN-induced GTP binding protein Mx1)	Antiviral state specifically against influenza virus
NECTIN2	nectin cell adhesion molecule 2 (aka PVRL2, CD112)	Component of adherens junctions, serves as entry point for certain mutant strains of HSV and pseudorabies virus
NLRC5	NLR family CARD domain containing 5	PRR implicated in innate immunity to viruses, potentially by regulating IFN activity, may increase MHCI expression
PARP14	poly(ADP-ribose) polymerase family member 14	Control of antimicrobial resposnes via impact on accumulation of multiple IFN-stimulated genes to the nucleus
PARP9	poly(ADP-ribose) polymerase family member 9	Facilitates STAT1 phosphorylation in M1 phagocytes
PNPLA3	patatin like phospholipase domain containing 3	Triacyglycerol lipase and acylglycerol-O-transferase activities; involved in triacylglycerol hydrolysis in adipocytes, possible role in energy metabolism
PSMB8	proteasome subunit beta 8	Contributes to assembly to the 20S proteasome complex forming proteolytic chamber for substrate degradation
PSMB9	proteasome subunit beta 9	Contributes to assembly to the 20S proteasome complex forming proteolytic chamber for substrate degradation
PSME1	proteasome activator subunit 1	Component of the 26S proteosome, cleave peptides in ATP/ubiquitin dependent, non-lysosomal pathway; modified "immunoproteasome" processes class I MHC peptids
PSME2	proteasome activator subunit 2	Component of the 26S proteosome, cleave peptides in ATP/ubiquitin dependent, non-lysosomal pathway; modified "immunoproteasome" processes class I MHC peptids
RARRES3	retinoic acid receptor responder 3	Nucelear receptor protein of steroid/thyroid hormone receptor family of transcriptional regulators
RFX5	regulatory factor X5	A nuclear protein complex that binds to Xbox of MHC-II promoters
SOCS2	suppressor of cytokine signaling 2	Inducible by EPO, GM-CSF, IL10 and IFNγ, negative regulator of cytokine signalling, also interactions with insulin-like growth factor 1 receptor
STAT2	signal transducer and activator of transcription 2	In response to IFN, forms complex with STAT1 and IRF9 to act as transactivator
TAP1	transporter 1, ATP binding cassette subfamily B member	Role in transport of intracellular peptide antigens to ER to facilitate MMHC Class I antigen presentation
TAP2	transporter 2, ATP binding cassette subfamily B member	Role in transport of intracellular peptide antigens to ER to facilitate MMHC Class I antigen presentation
TNFSF10	TNF superfamily member 10 (aka TRAIL, CD253)	Cytokine that promotes apoptosis (particularly of tumor cells) by biding to specific death receptors
UBD	ubiquitin D	Through covalent bonding targets other proteins for 26S degradation; implicated in caspase-dependent apoptosis, mitotic regulation, and dendrictic cell maturation
USP53	ubiquitin specific peptidase 53	Classified as deubiquinating enzyme based on structure but likely catalytically inactive