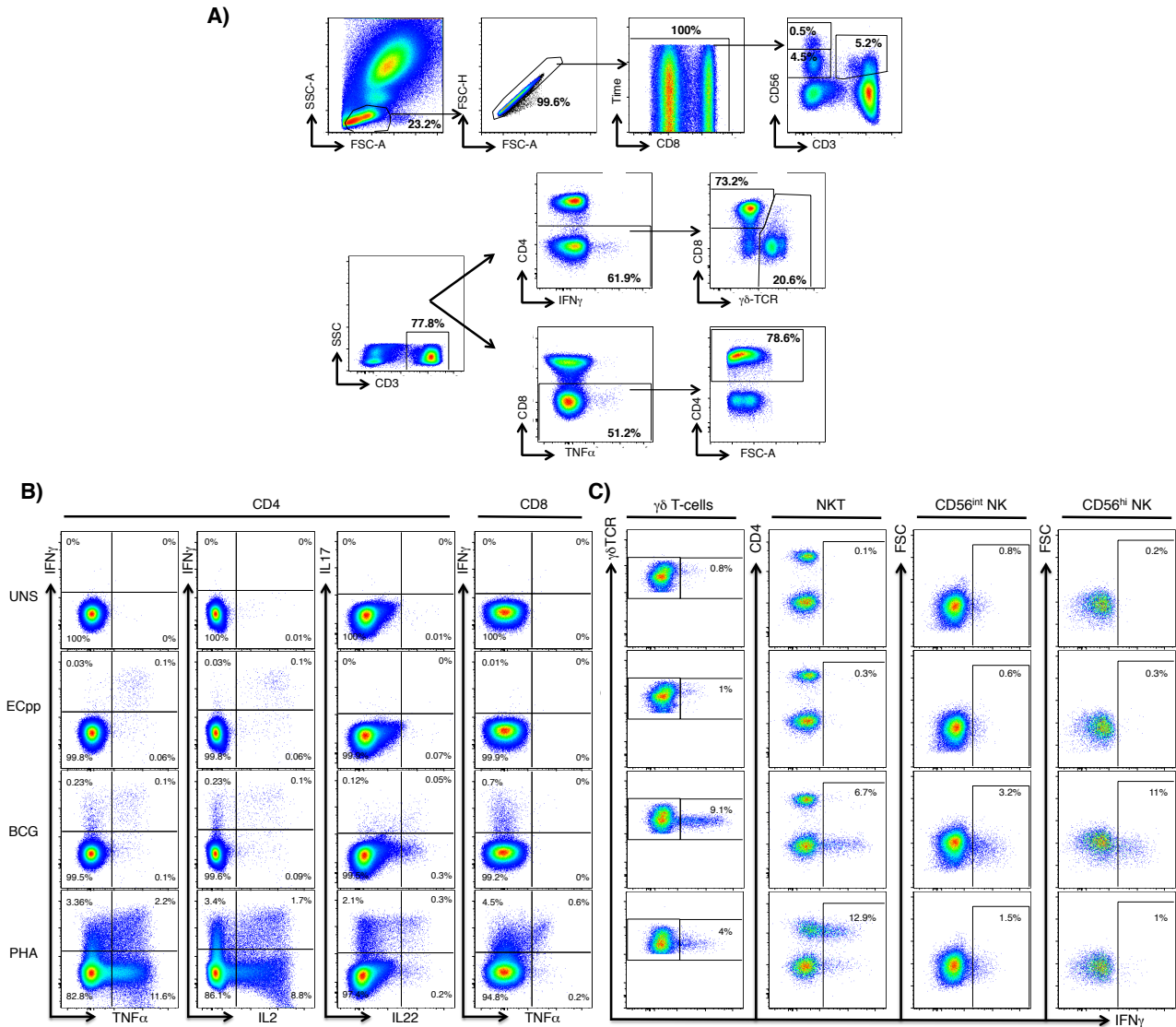


**S1 Table<sup>1</sup>: Antibody panels for flow cytometry**

Antigen	Conjugate	Clone	Supplier
<i>Panel 1</i>			
CD3	ECD	UCHT1	Beckman-Coulter
CD4	Qdot605	S3.5	Invitrogen
CD8	APC-H7	SK1	BD
TCR- $\gamma\delta$	Brilliant Violet 421	B1	BD
CD56	Brilliant Violet 711	HCD56	BioLegend
IFN $\gamma$	AlexaFluor700	B27	BD
TNF $\alpha$	PECy7	MAb11	eBioscience
IL-2	APC	MQ1-17H2	BD
IL-17	AlexaFluor488	N49-653	BD
IL-22	PE	IC7821P	R&D
<i>Panel 2</i>			
CD3	APC-H7	SK7	BD
CD8	Brilliant Violet 650	RPA-T8	BD
CD16	Brilliant Violet 510	3G8	BioLegend
CD26	APC	BA5b	BioLegend
CD56	Brilliant Violet 711	HCD56	BioLegend
CD57	Brilliant Violet 605	NK-1	BioLegend
CD66 (dump)	FITC	B1.1/CD66	BD
CD158b	PE	CH-L	BD
CD161	PECy5	DX12	BD
IFN $\gamma$	AlexaFluor700	B27	BD
TNF $\alpha$	PECy7	MAb11	eBioscience
Perforin	Brilliant Violet 421	B-D48	BioLegend

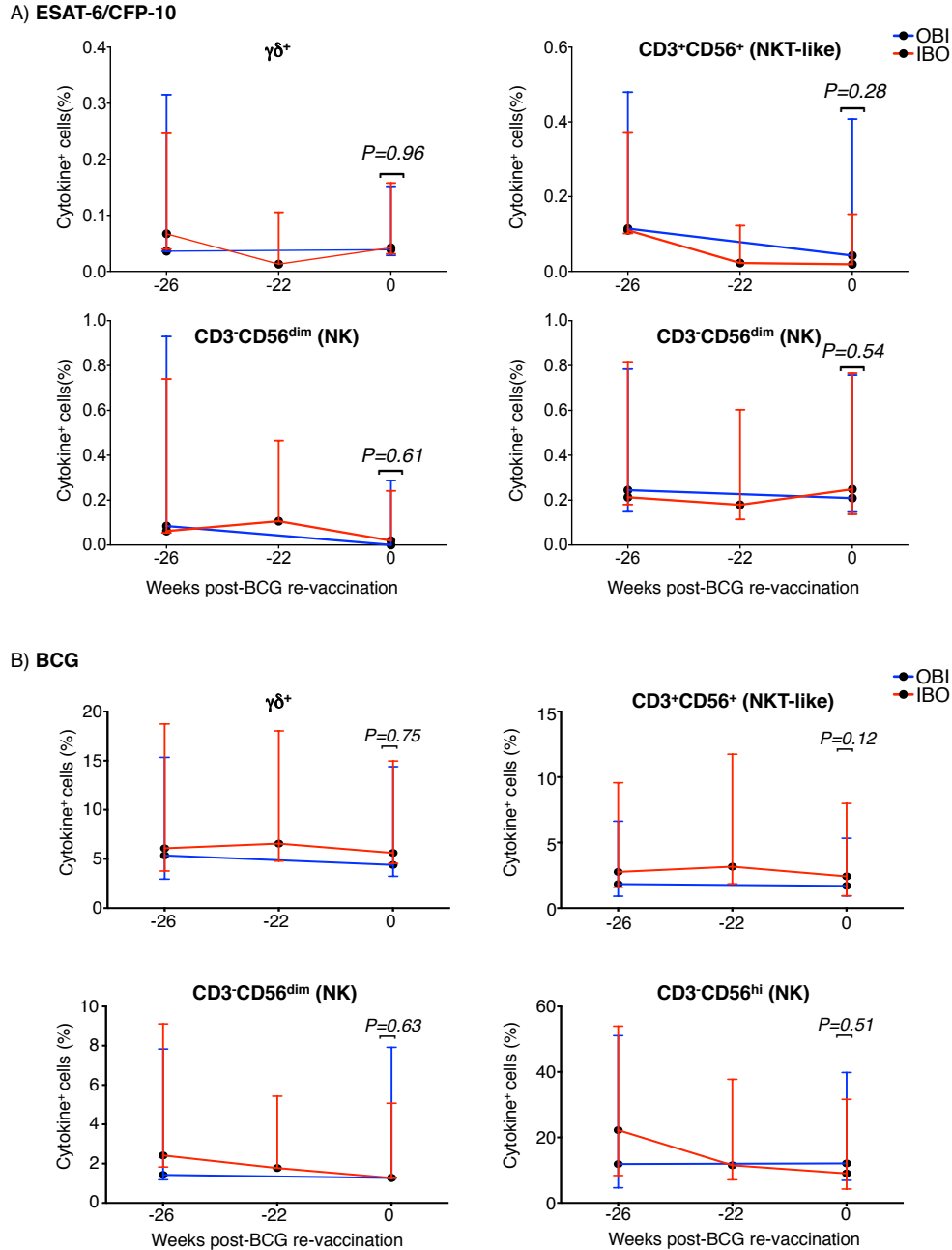
<sup>1</sup> **S1 Table.** Antibody cocktails used in flow cytometry analysis of whole blood assays.

**S1 Fig:**



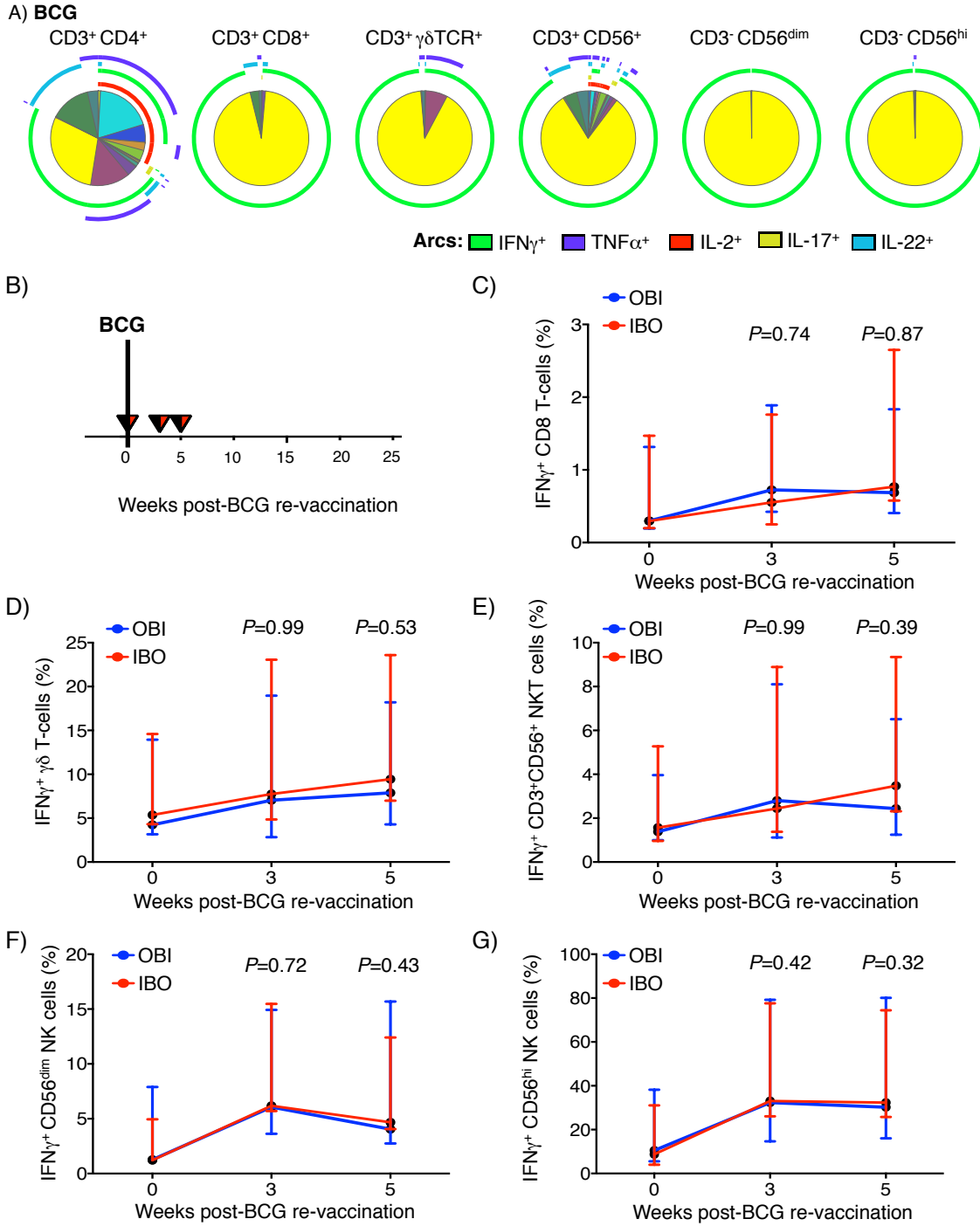
**S1 Fig. Flow cytometry gating strategy:** (A) Gating strategy applied to analyze stimulated whole blood samples. Small lymphocytes were gated based on forward (FSC) and side scatter (SSC), followed by doublet exclusion using FSC-area vs FSC-height. Then, to ensure uniform fluorescence during acquisition, a time gate was applied before identifying two CD3<sup>-</sup> natural killer (NK) cell subsets, defined as CD56<sup>hi</sup> and CD56<sup>dim</sup>. From the time gate, we also identified  $\gamma\delta$  T and CD8<sup>+</sup> T cells amongst CD3<sup>+</sup>CD4<sup>-</sup> cells (middle row) while CD4<sup>+</sup> T cells were identified amongst CD3<sup>+</sup>CD8<sup>-</sup> cells (bottom row). (B and C) Flow cytometric measurement of intracellular cytokine expression. (B) Representative plots illustrating cytokine expression in CD4<sup>+</sup> and CD8<sup>+</sup> T cells from a single whole blood sample. Rows correspond to the four stimulation conditions used in the assay. (C) IFN $\gamma$ -expression by  $\gamma\delta$  T cells, CD3<sup>+</sup>CD56<sup>+</sup> NKT-like cells, CD3<sup>-</sup>CD56<sup>dim</sup> NK and CD3<sup>-</sup>CD56<sup>hi</sup> NK cells.

S2 Fig:



**S2 Fig. Impact of INH treatment on antigen-specific responses to ESAT-6/CFP10 peptide pools (A) or BCG stimulation (B):** Frequencies of antigen-reactive cytokine<sup>+</sup>  $\gamma\delta$  (top left) T cells, CD3<sup>+</sup>CD56<sup>+</sup> NKT-like (top right), CD3<sup>+</sup>CD56<sup>dim</sup> NK (bottom left), and CD3<sup>+</sup>CD56<sup>hi</sup> NK (bottom right) cells. All frequencies were background subtracted. Red and blue lines correspond to group treated (IBO) or not treated (OBI) with INH for 6 months, respectively, in the time window preceding BCG re-vaccination. Unadjusted p-values were calculated with the Mann-Whitney *U*-test, comparing frequencies of cytokine-expressing cells between the two groups in each of the 6 immune subsets at the end of the 6-month INH Rx or observation. P-values below 0.025, correcting for testing in two groups using the Bonferroni method were considered statistically significant.

**S3 Fig:**



**S3 Fig. Impact of INH pre-treatment on frequency of BCG-specific IFN $\gamma$  production by non-CD4 T cells.** (A) Pie charts showing median proportions of BCG-specific CD4, CD8,  $\gamma\delta$  T, CD3<sup>+</sup>CD56<sup>+</sup> NKT-like, CD3<sup>-</sup>CD56<sup>dim</sup> NK, and CD3<sup>-</sup>CD56<sup>hi</sup> NK cells co-expressing IFN $\gamma$ , TNF $\alpha$ , IL-2, IL-17, and/or IL-22 at 3 weeks post-vaccination. (B) Schematic diagram of blood draws to assess short-term boosting of BCG-specific responses. Median frequencies (error bars denote IQR) of IFN $\gamma$ -expressing (C) CD8 T cells (defined as CD3<sup>+</sup>CD4<sup>-</sup>CD8<sup>+</sup> cells), (D)  $\gamma\delta$  T cells, (E) CD3<sup>+</sup>CD56<sup>+</sup> NKT-like cells, (F) CD3<sup>-</sup>CD56<sup>dim</sup> NK, and (G) CD3<sup>-</sup>CD56<sup>hi</sup> NK cells. Unadjusted p-values, calculated with Mann-Whitney *U*-tests, represent inter-group comparisons.