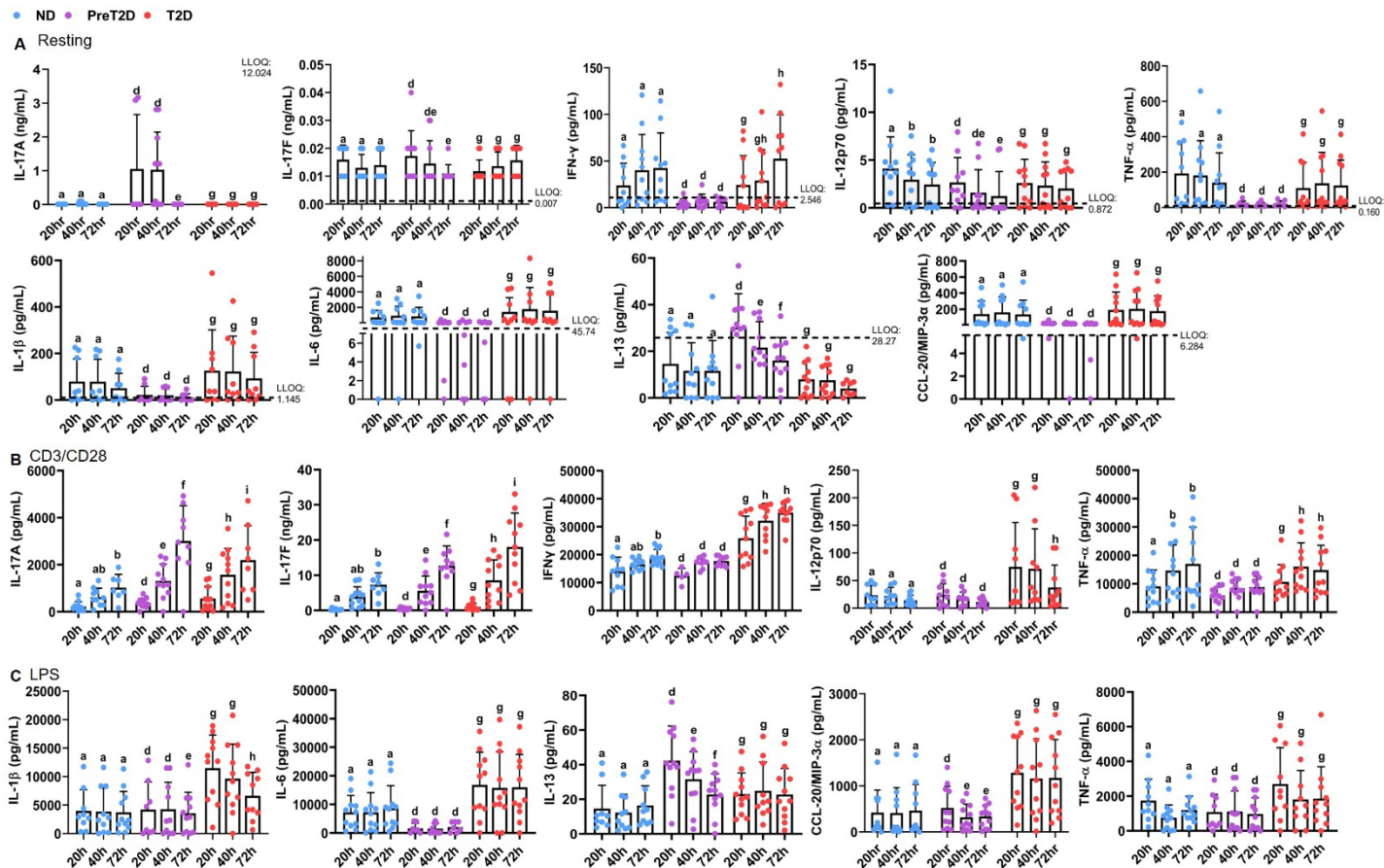**Fig. S1**: Cytokines produced by CD3/CD28- but not LPS- nor unstimulated PBMCs from cohorts indicated change over time as shown by PLSDA. **(A)** The second component that defines inflammation has more contribution from cytokines elicited by 40h CD3/CD28 stimulation (black bars), especially for samples from diabetes and non-diabetes (ND) subjects, than the first component (See Fig. 1). **(B)** Cytokine profiles produced by unstimulated PBMCs from the indicated cohort insignificantly change over time. N's are shown in Table S1.

Fig. S2: Cytokines produced by CD3/CD28- but not LPS- nor unstimulated PBMCs from cohorts indicated change over time. **(A)** Representative cytokines produced by PBMCs from each cohort without the presence of stimulation (resting). **(B)** Representative cytokines produced by PBMCs from each cohort stimulated with CD3/CD28 for 20-72h. **(C)** Representative cytokines produced by LPS stimulation (20-72hr) from each cohort. N's are shown in Table S1. Dashed lines represent the lower limit of quantification (LLOQ) to identify samples above or below this cut-off. Differences determined by a mixed-effects analysis and Tukey's multiple comparisons. Significance defined as *P* < 0.05 and represented as letters for each cohort (a-c for ND, d-f for PreT2D, and g-i for T2D). Bars assigned the same letter indicate no statistical difference amongst time points within the same cohort.
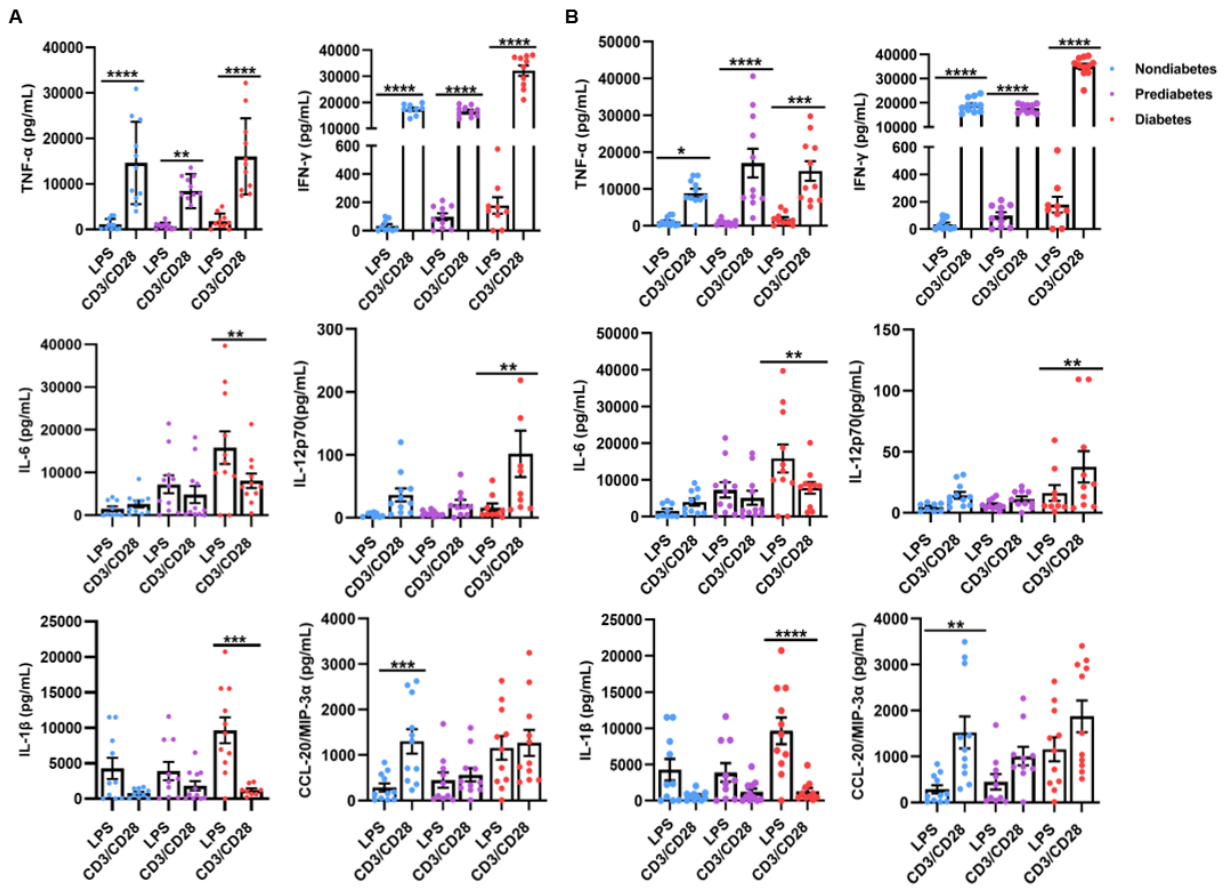
Fig. S3: T cell and myeloid cell stimulation elicits approximately equivalent TNFα production by PBMCs from all overweight/obese subjects. Direct comparison of cytokines elicited from PBMCs by 20 hr. LPS and **(A)** 40 hr CD3/CD28 or **(B)** 72 hrs CD/CD28 as measured in supernatants. PBMCs were from ND (blue), prediabetes (purple) or diabetes (red) subjects as indicated. Differences identified by 2-Way ANOVA are indicated. Bars show average and SD with Ns shown in Table S1.
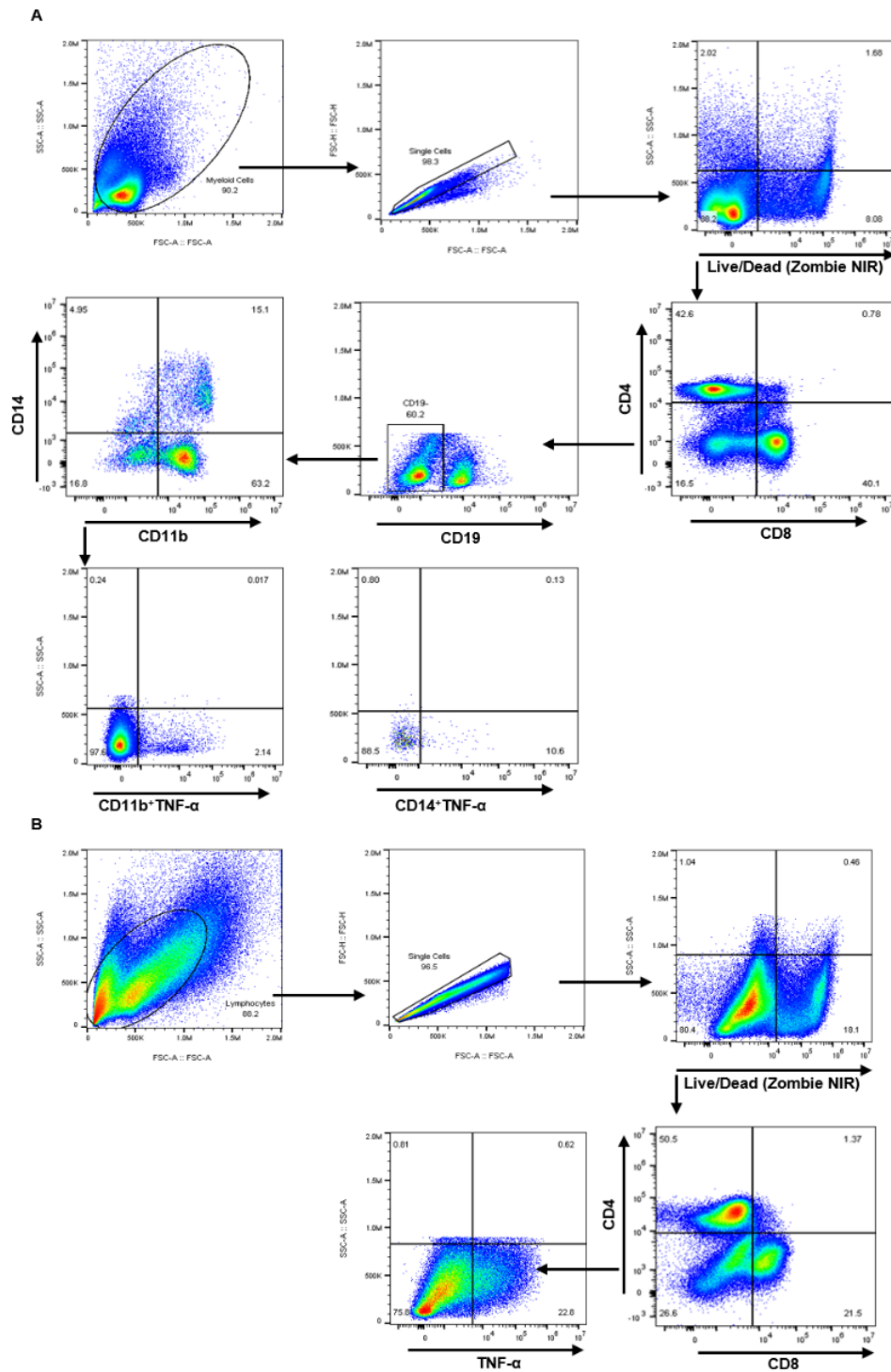
Fig. S4. Gating Strategy for Intracellular TNF-α Staining of Myeloid Cell and CD4$^+$ T cells. (A) Gating for CD11b$^+$ and CD14+ cells from LPS-stimulated PBMCS (20hrs) and intracellular TNF-α within these myeloid populations. **(B)** Gating for CD4+ T lymphocytes from α-CD3/α-CD28-stimulated PBMCs (40hrs) and intracellular TNF-α within the CD4+ population.
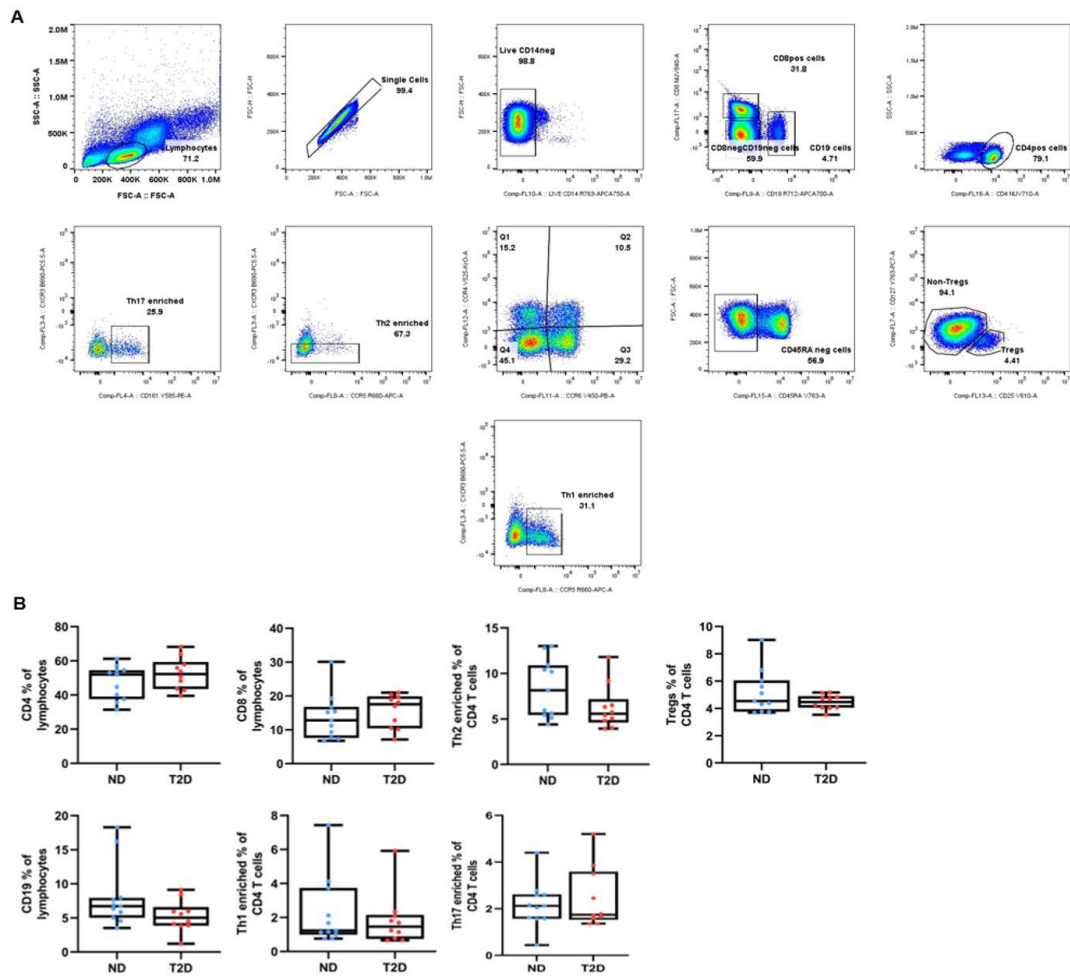
Fig. S5: T cell and myeloid subset frequencies in PBMCs are similar between resting PBMCs from ND and diabetes subjects, and TNF-α production by myeloid cells is low in response to CD3/CD28 stimulation. A. Flow cytometry gating strategy for quantification of immune cell subsets. **B.** Percentages of CD4+, CD8+, and CD19+ cells in resting PBMCs determined per gating in panel A. For all panels, samples are from ND (blue), prediabetes (purple), or diabetes (red) subjects. ND (n=11), T2D (n=10). Statistical difference was determined by **B.** Mann-Whitney U non-parametric t test

Table S1. Description of human donors

	Overweight/obesity + non-diabetes	Obesity + prediabetes	Overweight/obesity + type 2 diabetes
Age, years [median (range)]	56 (45-66)	56 (50-72)	60 (47-64)
BMI, kg m^2 [median (range)]	34.03 (27-40)	36.7 (31-38)	34.5 (26-38)
A1c, % [median (range)]*	5.4 (5.1-5.6)	5.4 (5.1-5.7)	7 (5.6-10.3)[†]
Fasting Blood Glucose [median (range)]	95 (88-107)	104.5 (98-110)[‡]	Not measured for T2D subjects
Total N	9	10	11
Females	6	8	6
Males	3	2	5
African American	1	1	3
White/non-Hispanic	8	9	8

*Clinical diagnosis of type 2 diabetes sufficient for subjects on glycemic control drugs; non-diabetes or prediabetes was confirmed in some subjects based on 2hr oral glucose tolerance test blood glucose measures (not shown).
†Indicates a significant difference between non-diabetes and type 2 diabetes subjects based on ANOVA ($P < 0.05$)
‡ Indicates a significant difference between non-diabetes and prediabetes subjects based on Student's t-test ($P < 0.05$)

Table S2. List of medications and smoker status

Medications	Overweight/obesity + non-diabetes	Obesity + prediabetes	Overweight/obesity + type 2 diabetes
Metformin (*N*)	0/9	0/10	9/11
TZDs (*N*)	0/9	0/10	1/11
DPP-4 Inhibitors (*N*)	0/9	0/10	3/11
Sulfonylurea (*N*)	0/9	0/10	2/11
Statins (*N*)	3/9	4/10	7/11
ACE Inhibitors (*N*)	2/9	2/10	3/11
Aspirin (*N*)	2/9	0/10	6/11
Smoker (*N*)	1/9	1/10	0/11

Table S3. MRMR prediction of non-diabetes, prediabetes, and type 2 diabetes donors.

Class	Precision	Recall	F1	AUC
ND	0.500	0.455	0.476	0.674
PreT2D	0.500	0.545	0.522	0.682
T2D	0.909	0.909	0.909	0.893
Micro Average	0.636	0.636	0.636	0.757