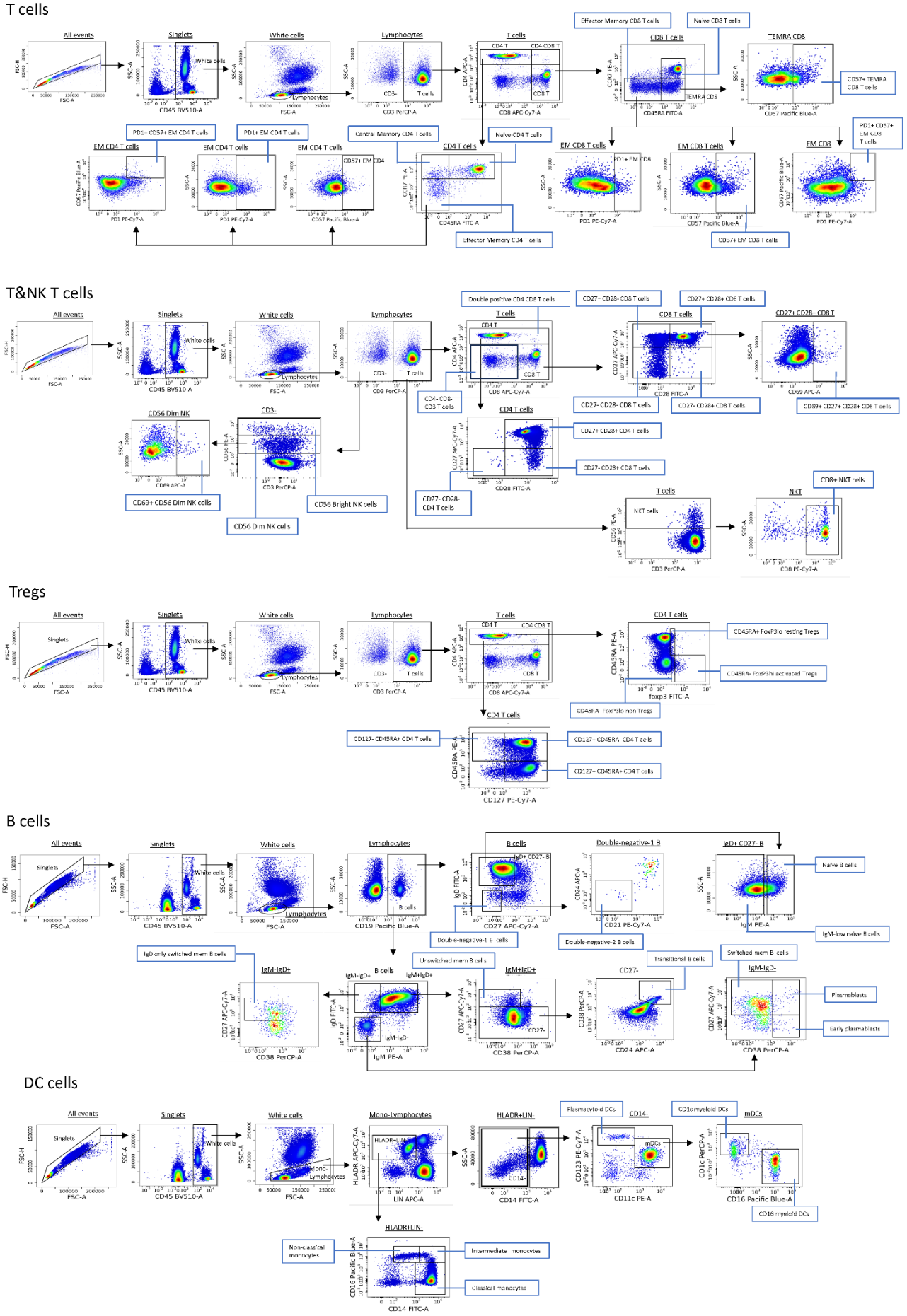
SUPPLEMENTARY MATERIAL

Marker	Fluorophore	µl/in 100 µl	Clone	Company	Cat. no.	Panel
CCR7	PE	2	G043H7	Biolegend	353204	T cell
CD3	PerCP	2	SK7	Biolegend	344814	T cell, T&NK cell, Treg
CD4	APC	2	SK3	Biolegend	344614	T cell
CD45	BrilliantViolet510	2	H130	Biolegend	304036	T cell, T&NK cell, Treg, B cell, DC cell
CD45RA	FITC	2	HI100	Biolegend	304148	T cell
CD57	Pacific Blue	2	HCD57	Biolegend	322315	T cell
CD8	APC/Cy7	2	SK1	Biolegend	344714	T cell
PD-1	PECy7	2	J105	eBioscience	25-2799-42	T cell
CD4	Pacific Blue	2	RPA-T4	Biolegend	300521	T&NK cell, Treg
CD69	APC	2	FN50	Biolegend	310918	T&NK cell
CD56	PE	2	HCD56	Biolegend	318305	T&NK cell
CD8	PECy7	2	RPA-T8	Biolegend	301012	T&NK cell
CD27	APC/Cy7	2	O323	Biolegend	302816	T&NK cell, B cell
CD28	AlexaFluor488	2	CD28.2	Biolegend	302916	T&NK cell
CD25	APC	2	2A3	BD	340907	Treg
CD127	PECy7	2	R34.34	Beckman	A64618	Treg
CD45RA	PE	2	HI100	Biolegend	304108	Treg
FoxP3	Alexa488	4	259D	Biolegend	320212	Treg
CD19	BrilliantViolet421	2	HIB19	Biolegend	302234	B cell
CD21	PECy7	2	Bu32	Biolegend	354911	B cell
CD24	APC	2	MLS	Biolegend	311117	B cell
CD38	PerCP	2	HIT2	Biolegend	303519	B cell
IgD	AlexaFluor488	2	IA6-2	Biolegend	348216	B cell
IgM	PE	2	MHM-88	Biolegend	314508	B cell
LIN	APC	2	UCHT1,HCD14, HIB19,2H7, HCD56	Biolegend	348703	DC cell
HLADR	APC-CY7	2	L243	Biolegend	307618	DC cell
CD14	AlexaFluor488	2	HCD14	Biolegend	325610	DC cell
CD1c	PerCP	2	L161	Biolegend	331511	DC cell
CD16	BrilliantViolet421	2	3G8	Biolegend	302038	DC cell
CD123	PECy7	2	6H6	Biolegend	306009	DC cell
CD11c	PE	2	Bu15	Biolegend	337205	DC cell

Supplementary Table 1. Antibodies used in the flow cytometry analysis.

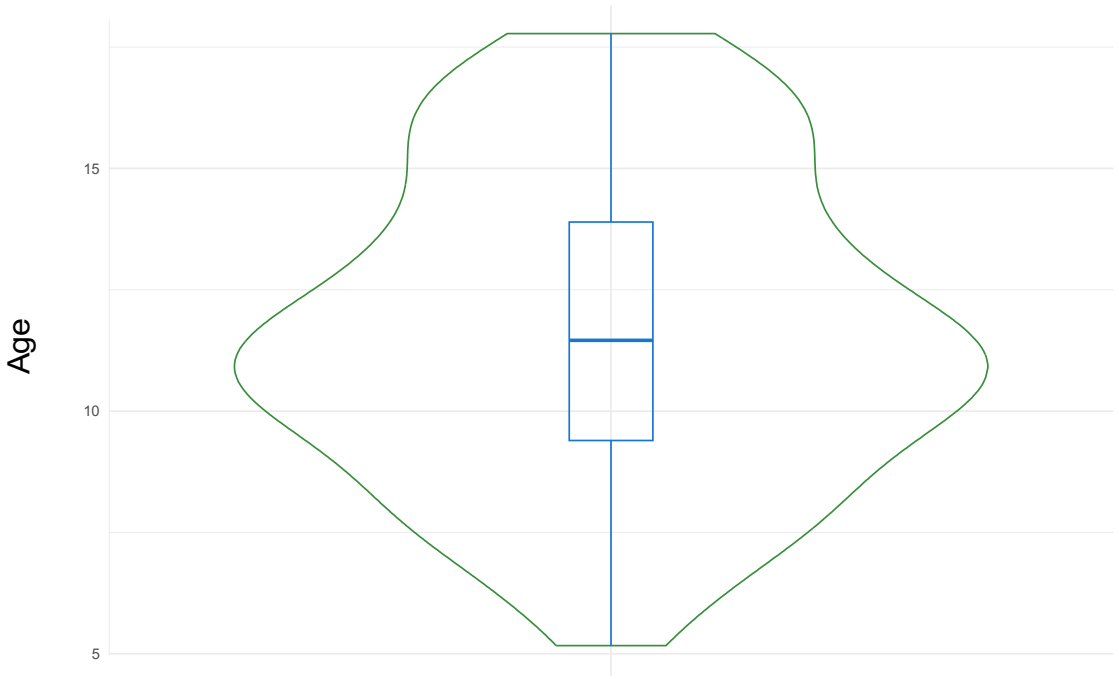
Population	N	Median	Interquartile range
IgM-low naive B cells	131	53.57	47.95-57.79
Naive B cells	131	25.03	21.76-30.39
Unswitched memory B cells	131	2.37	1.33-4.12
Transitional B cells	131	5.15	4.13-6.36
Early plasmablasts	131	0.17	0.07-0.33
Plasmablasts	131	0.63	0.28-1.18
Switched memory B cells	131	7.38	4.80-11.44
Double-negative-1 B cells	131	1.59	0.90-2.59
Double-negative-2 B cells	131	0.23	0.10-0.45
IgD only switched memory B cells	131	0.86	0.46-1.47
Plasmacytoid DCs	132	3.94	2.18-5.72
CD1c myeloid DCs	132	1.99	1.26-2.84
CD16 myeloid DCs	132	5.52	3.64-7.63
Classical monocytes	132	68.95	57.08-76.20
Intermediate monocytes	132	3.70	1.90-7.48
Non-classical monocytes	132	6.84	4.64-8.90
Double positive CD4 CD8 T cells	134	0.26	0.18-0.35
CD4- CD8- CD3 T cells	134	6.34	4.76-8.24
CD27+ CD28+ CD4 T cells	134	38.60	32.75-43.55
CD27- CD28+ CD4 T cells	134	1.44	0.98-2.00
CD27- CD28- CD4 T cells	134	0.02	0.01-0.16
Naive CD4 T cells	133	41.00	34.24-45.42
Effector memory CD4 T cells	133	11.25	9.39-14.10
Central memory CD4 T cells	133	6.53	5.24-8.25
PD1+ effector memory CD4 T cells	133	1.92	1.27-2.43
PD1+ CD57+ effector memory CD4 T cells	133	0.16	0.10-0.26
CD127+ CD45RA- CD4 T cells	128	26.31	21.23-32.88
CD127+ CD45RA+ CD4 T cells	128	68.36	62.13-74.04
CD127- CD45RA+ CD4 T cells	128	1.59	0.93-2.64
CD27+ CD28+ CD8 T cells	134	18.14	16.00-21.13
CD27- CD28+ CD8 T cells	134	0.33	0.14-0.64
CD27- CD28- CD8 T cells	134	0.66	0.29-2.89
CD27+ CD28- CD8 T cells	134	3.06	2.07-4.50
CD69+ CD27+ CD28+ CD8 T cells	134	0.71	0.40-1.34
Naive CD8 T cells	133	14.85	12.46-17.84
Effector memory CD8 T cells	133	5.78	4.43-7.09
CD57+ terminally differentiated effector memory CD8 T cells	133	0.93	0.53-2.31
CD57+ effector memory CD8 T cells	133	0.54	0.35-0.94
PD1+ CD57+ effector memory CD8 T cells	133	0.11	0.06-0.23
CD56dim NK cells	134	6.40	4.78-9.14
CD56bright NK cells	134	0.59	0.42-0.86
CD8+ NKT cells	134	1.04	0.56-1.57
CD69+ CD56dim NK cells	134	0.29	0.16-0.51
CD45RA+ FoxP3lo resting Tregs	128	3.23	2.01-4.12
CD45RA- FoxP3lo non Tregs	128	1.78	1.11-2.49
CD45RA- FoxP3hi activated Tregs	128	1.56	1.07-2.25

Supplementary Table 2. Immune cell subset frequencies in T1D patients.

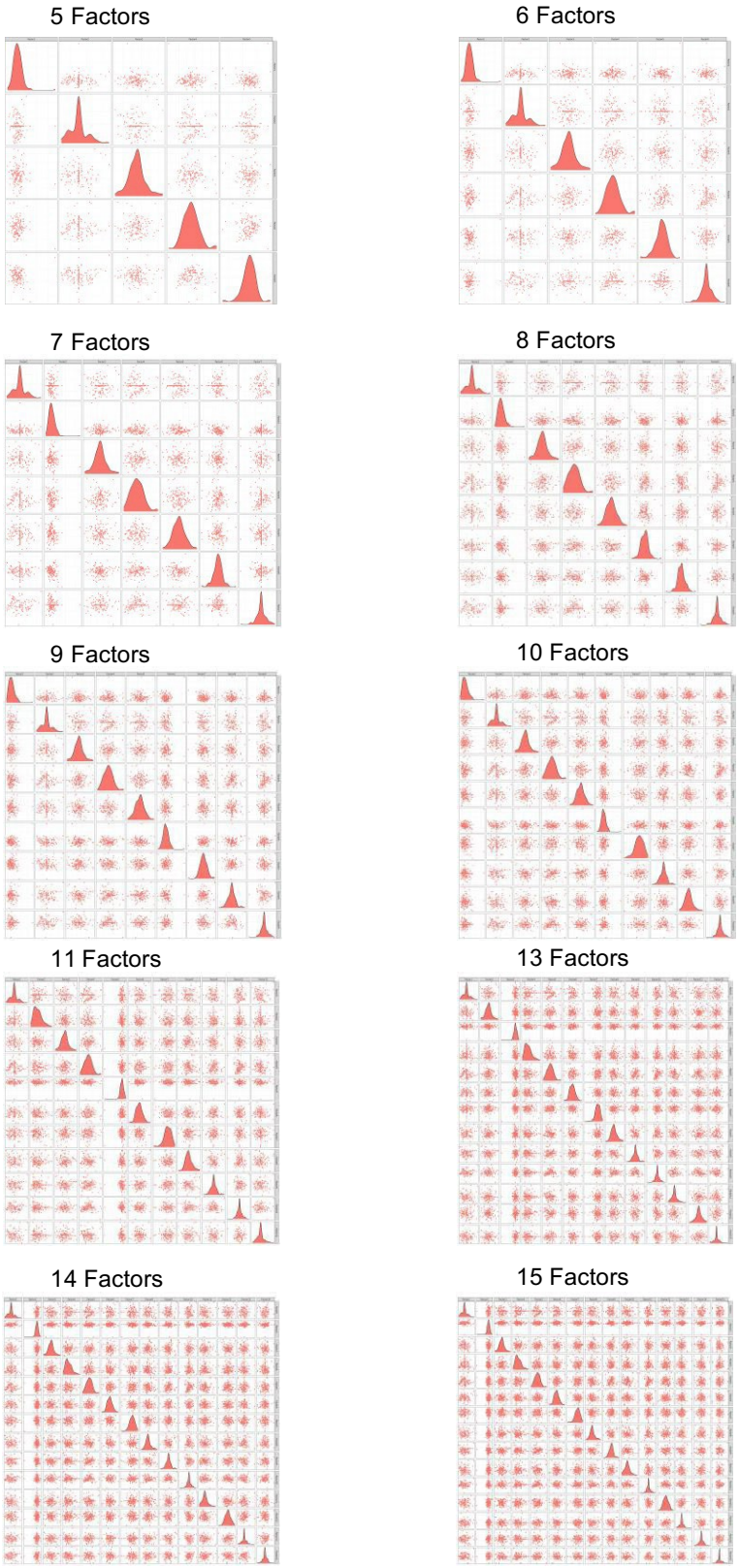


Supplementary Figure 1. Gating strategy for flow cytometry analysis. Five panels of antibodies (T cell, T&NK cell, Treg, B cell, DC cell) were used to identify 46 immune cell subsets through unsupervised clustering with the FlowSOM algorithm.

(Five antibody panels (T cell, T&NK cell, Treg, B cell, and DC cell) were used to profile immune cell populations. Unsupervised clustering was performed using the FlowSOM algorithm within the CyTOF/CATALYST pipeline, followed by manual merging of clusters with similar marker expression profiles, leading to the identification of 46 distinct immune cell subsets.)

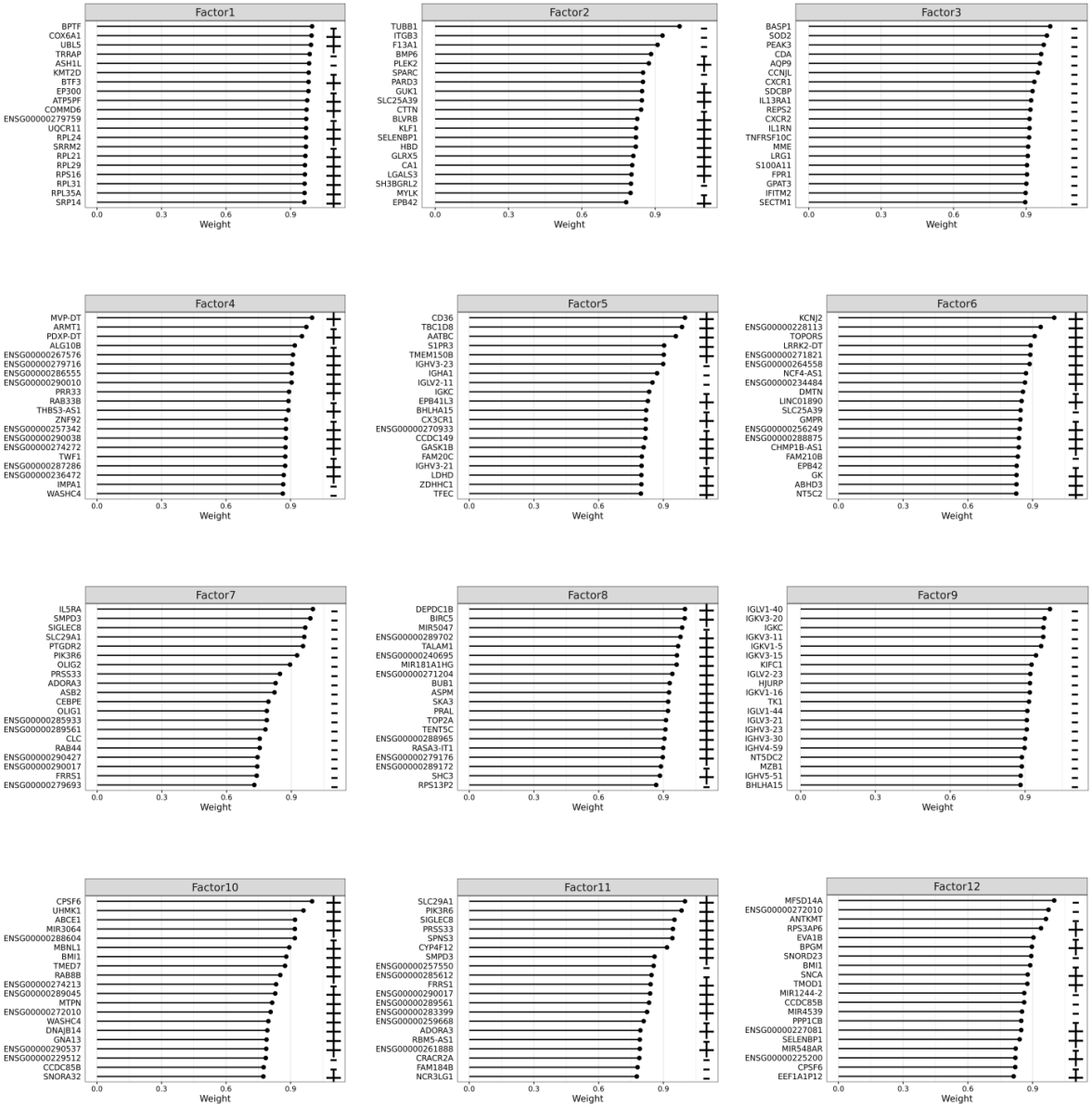


Supplementary Figure 2. Age distribution of the study cohort. The violin plot depicts the distribution of patient ages using density curves. The boxplot shows the median, lower and upper quartiles, and distribution extremes. Dots indicate the position of each data point representing patients.



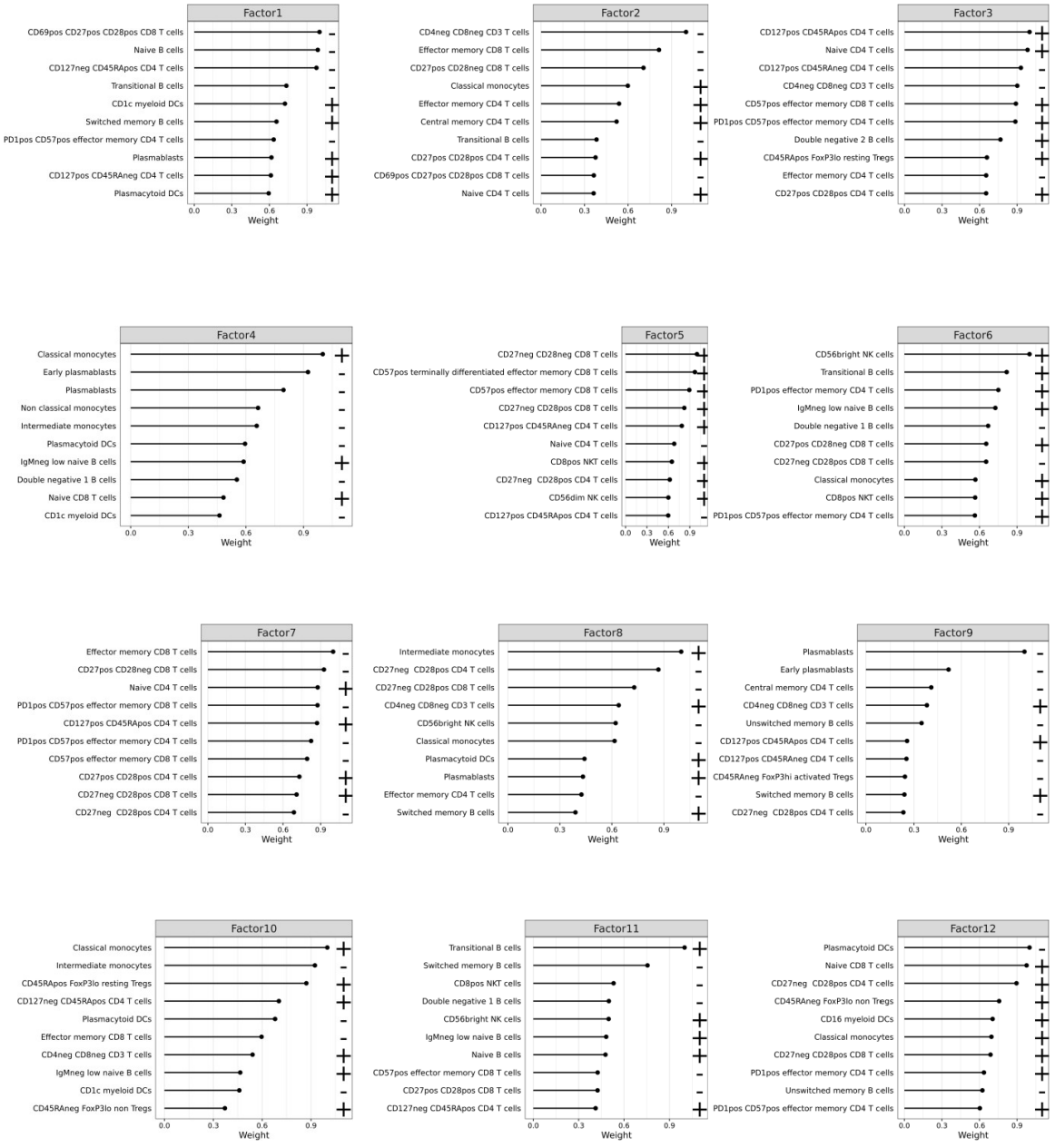
Supplementary Figure 3. Scatterplots of MOFA scores for different MOFA models. Each dot represents a patient, and patient coordinates are determined by the scores in the respective pair of factors. MOFA models ranged from 5 to 15 factors.

RNA



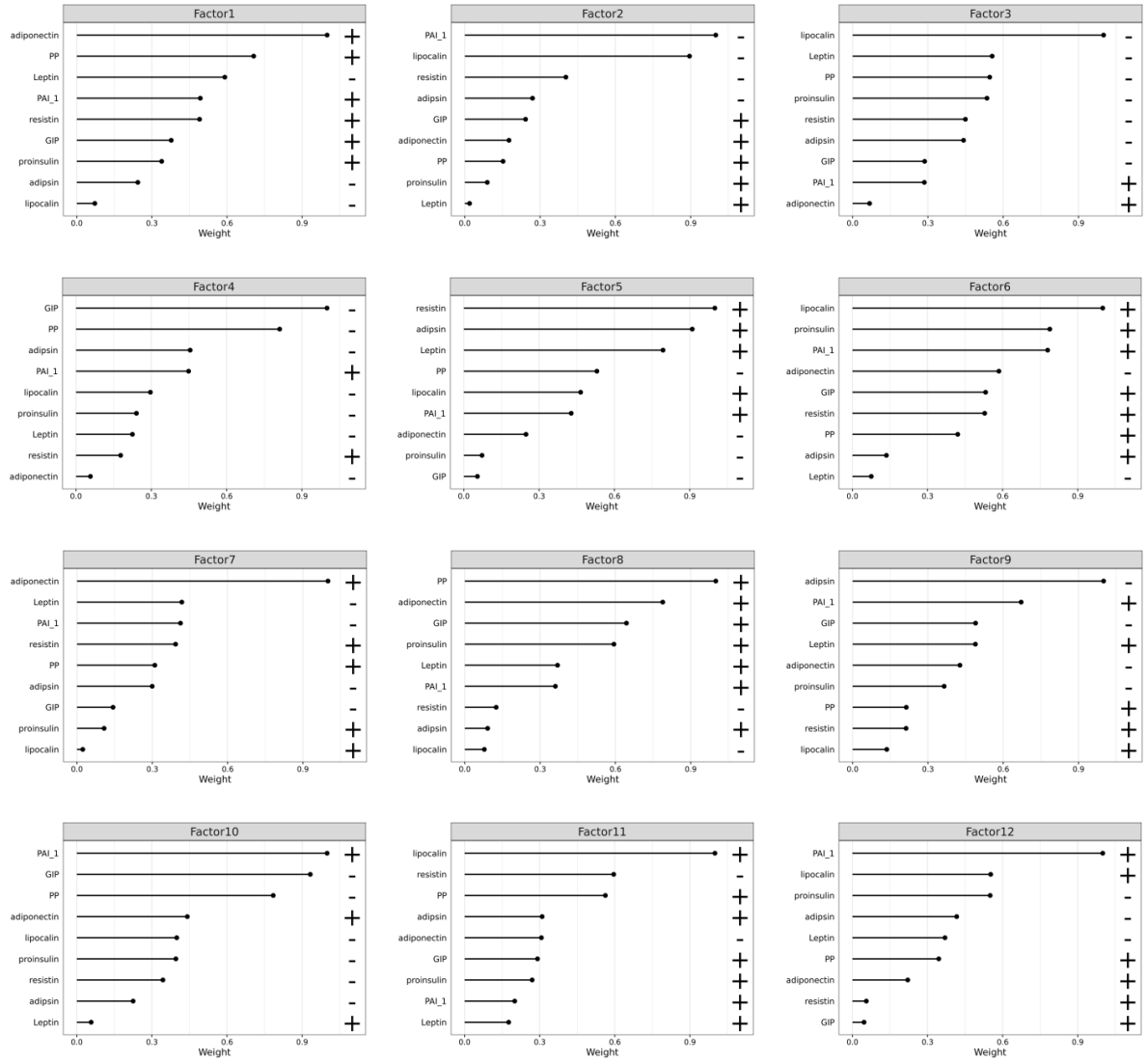
Supplementary Fig. 4. Weights of the top 20 RNA genes in each factor. Illustration of the top 20 genes for each factor that are accountable for the variability observed among factors. The x axis reported the weight of each gene on the factor while the sign (+ or -) indicates the direction of the association.

IMM

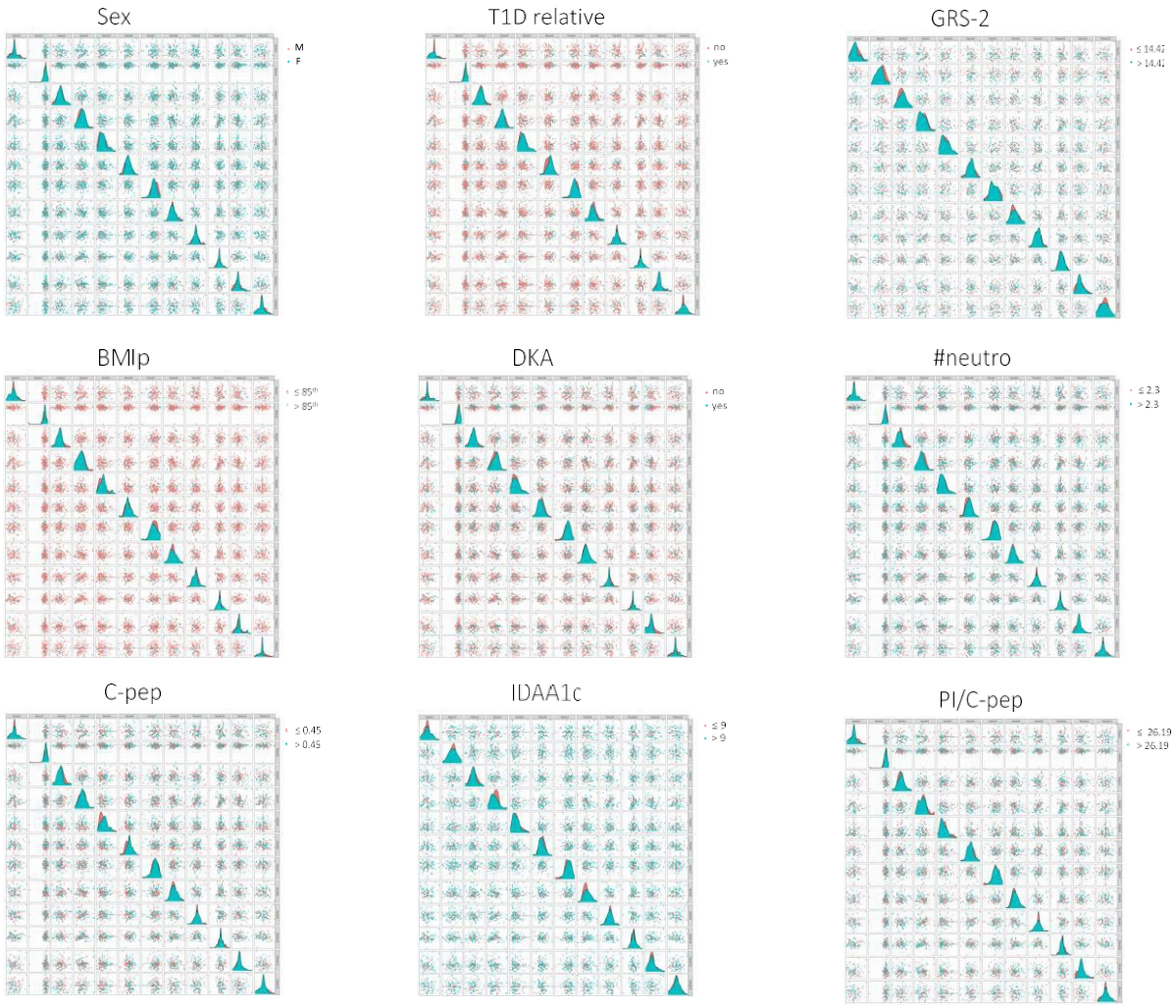


Supplementary Fig. 5. Weights of the top 10 immune cell subsets in each factor. Illustration of the top 10 immune cell subsets for each factor that are accountable for the variability observed among factors. The x axis reported the weight of each cell population on the factor while the sign (+ or -) indicates the direction of the association.

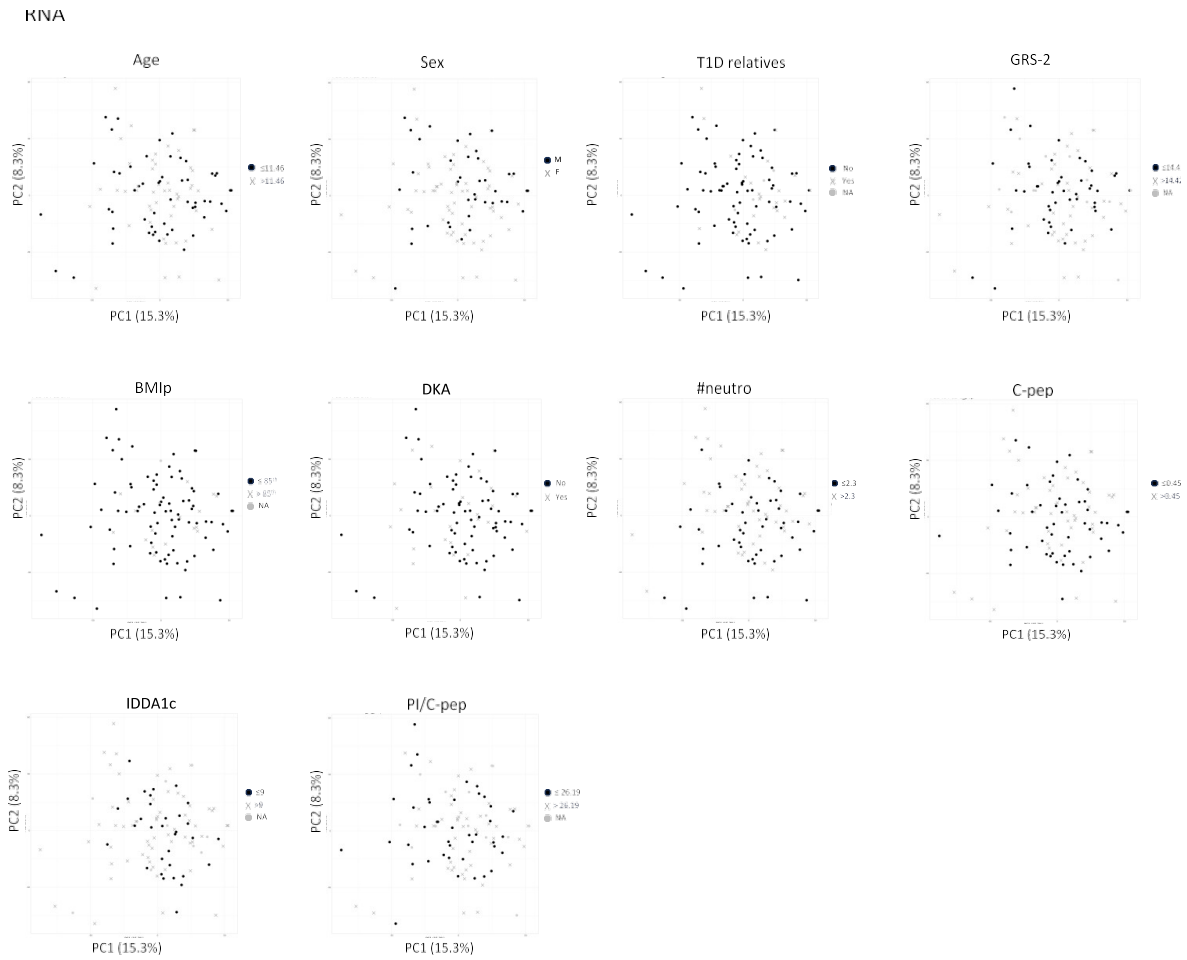
MetH



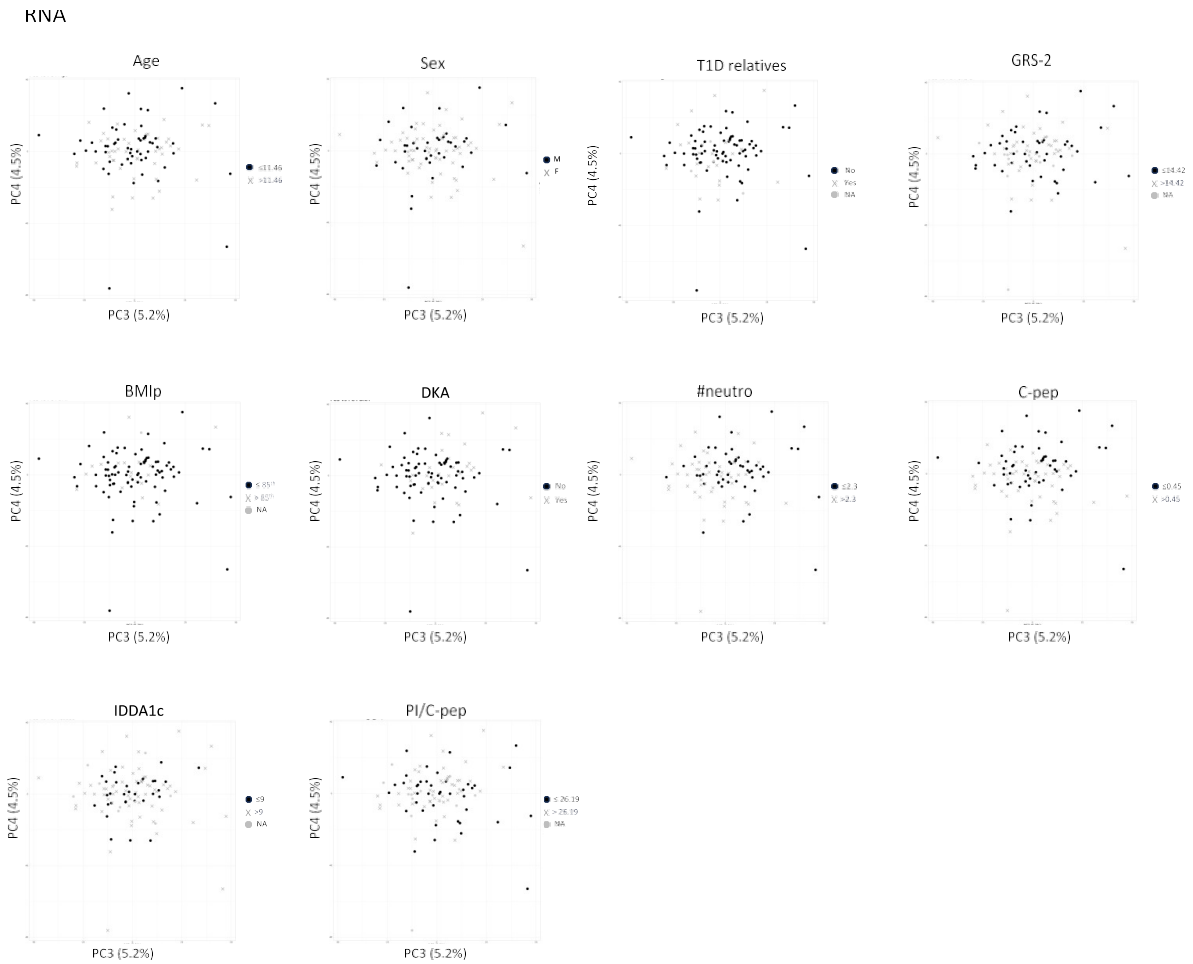
Supplementary Fig. 6. Weights of the metabolic hormones in each factor. Illustration of the 9 metabolic hormones weight for each factor. The x axis reported the weight of each cell population on the factor while the sign (+ or -) indicates the direction of the association.



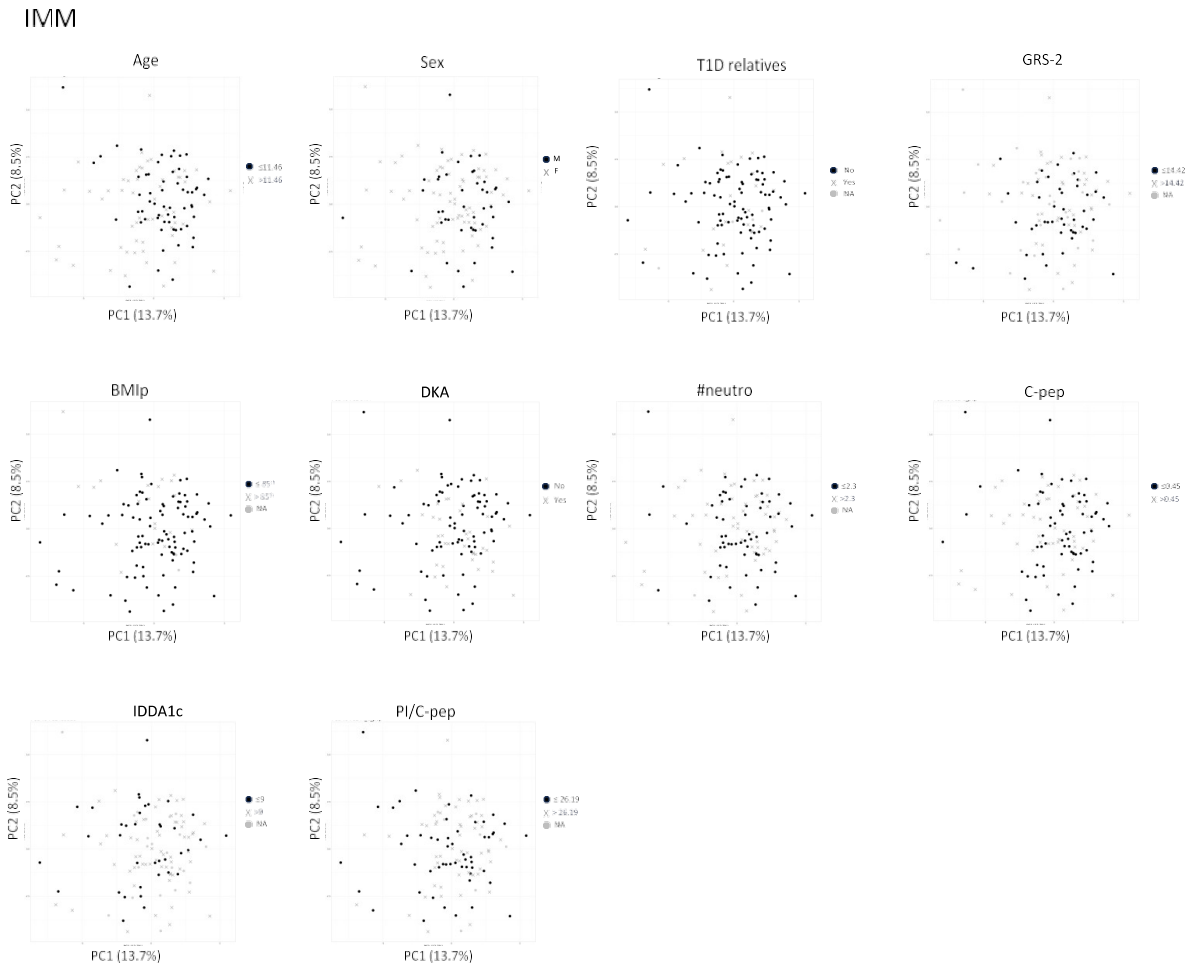
Supplementary Fig. 7. MOFA scoreplots of patient distribution for clinical phenotypes. MOFA scoreplots show patient distribution for clinical phenotypes including sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio and disease outcome (IDAA1c). Each dot represents a patient, and it is coloured according to the patient's clinical features.



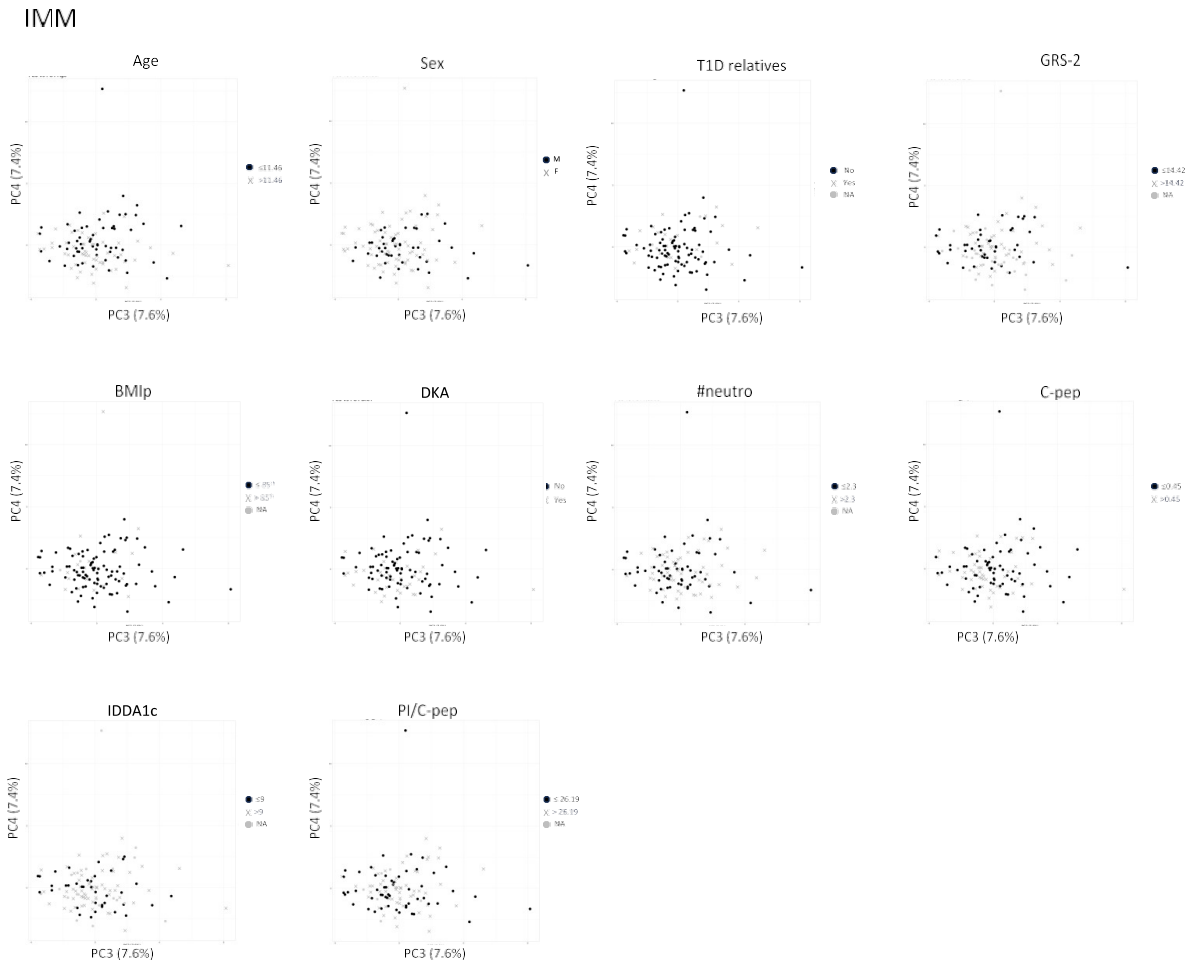
Supplementary Fig. 8. Principal component analysis 1 and 2 for RNA genes based on phenotypes. Transcriptome principal component analysis shows patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, disease outcome (IDAA1c) and batch effect.



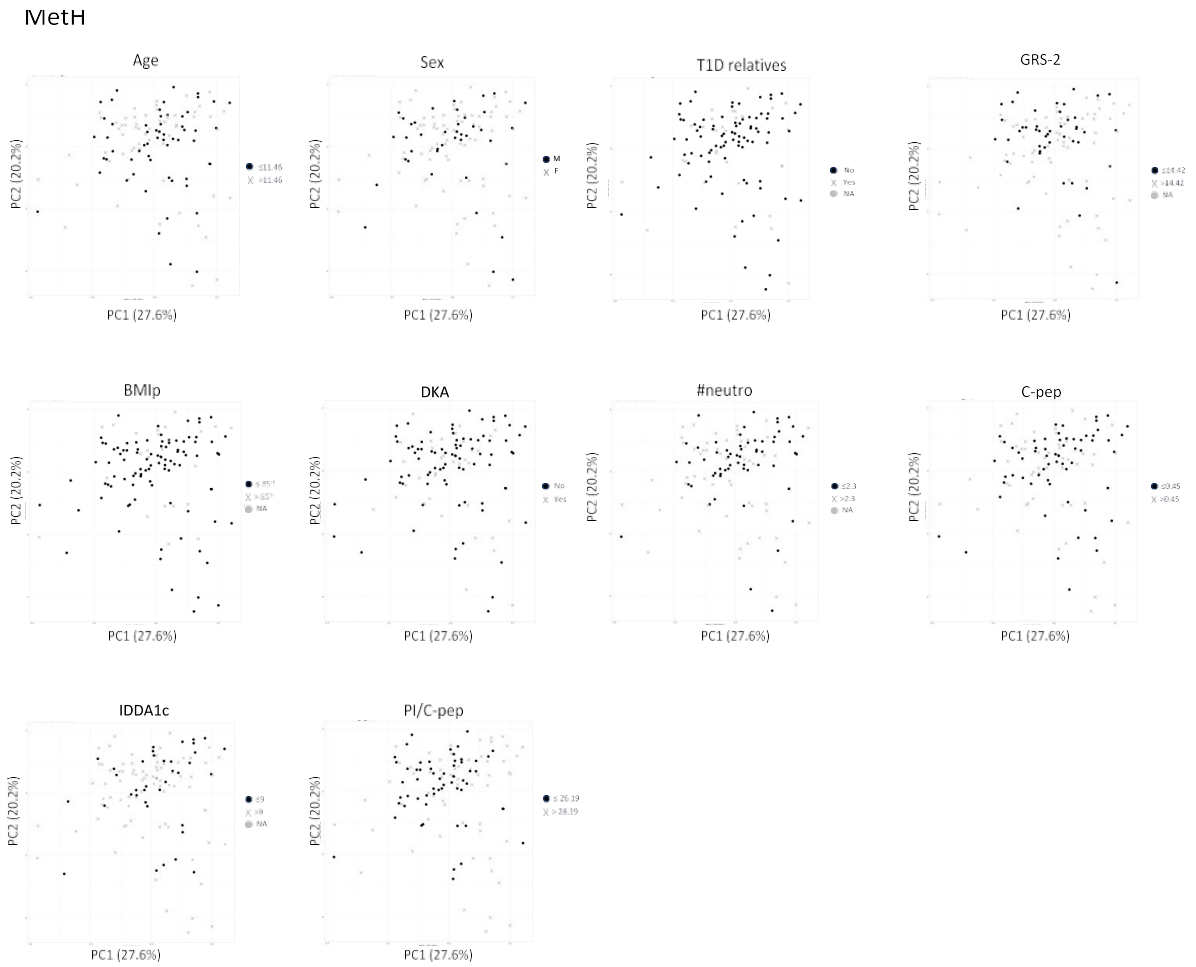
Supplementary Fig. 9. Principal component analysis 3 and 4 for RNA genes based on phenotypes. Transcriptome principal component analysis shows patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, disease outcome (IDAA1c) and batch effect.



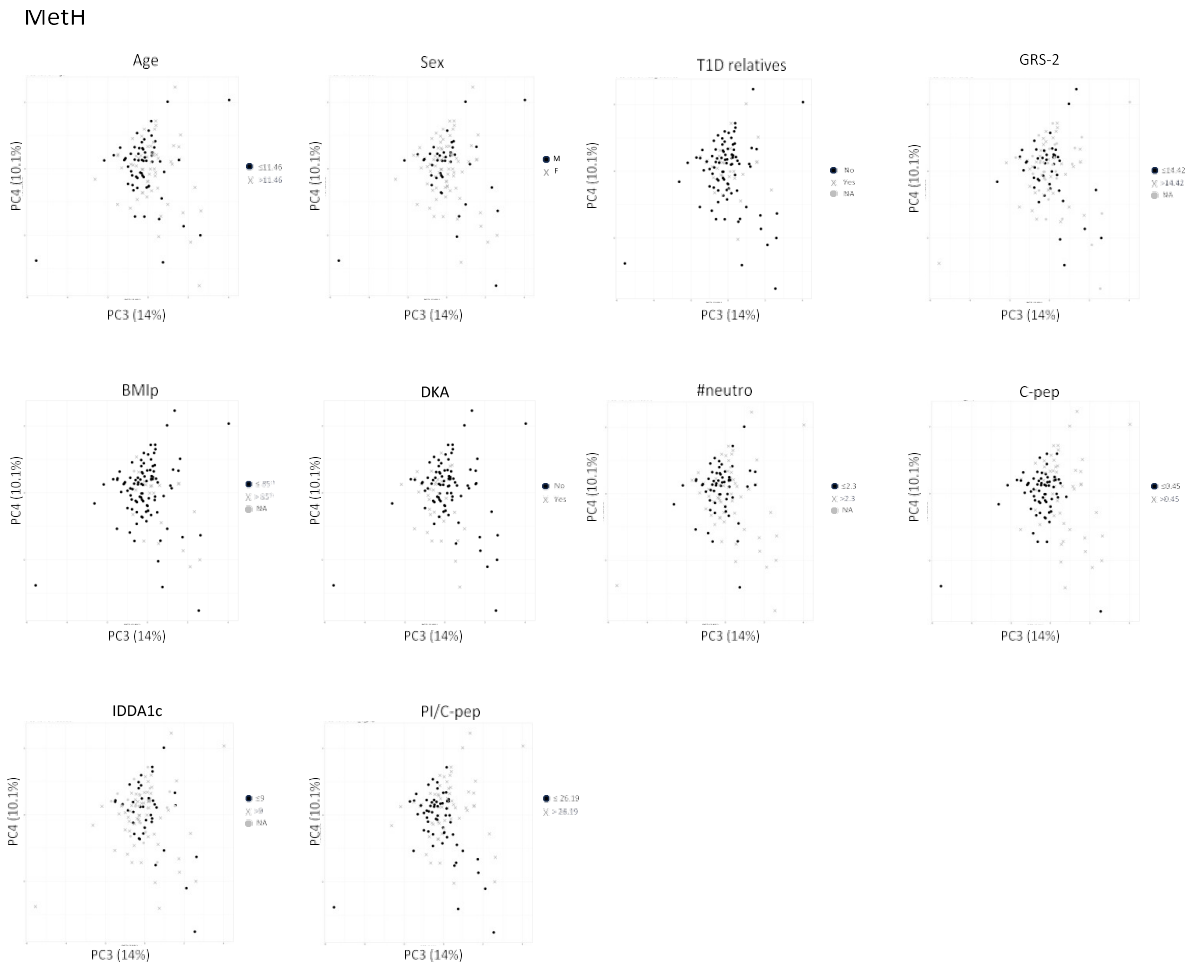
Supplementary Fig. 10. Principal component analysis 1 and 2 for immune cell populations based on phenotypes. Immunome principal component analysis shows patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, disease outcome (IDAA1c) and batch effect.



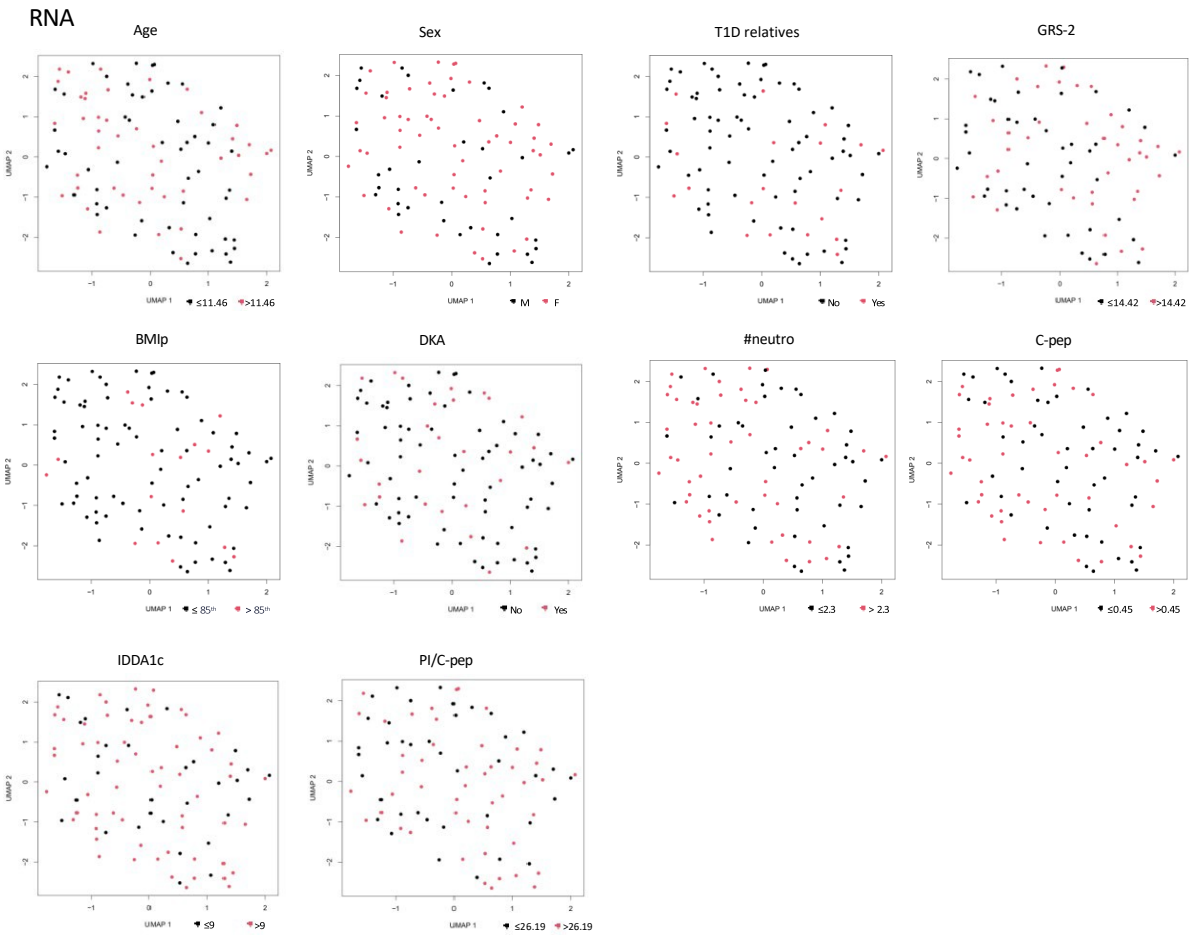
Supplementary Fig. 11. Principal component analysis 3 and 4 for immune cell populations based on phenotypes. Immunome principal component analysis shows patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, disease outcome (IDAA1c) and batch effect.



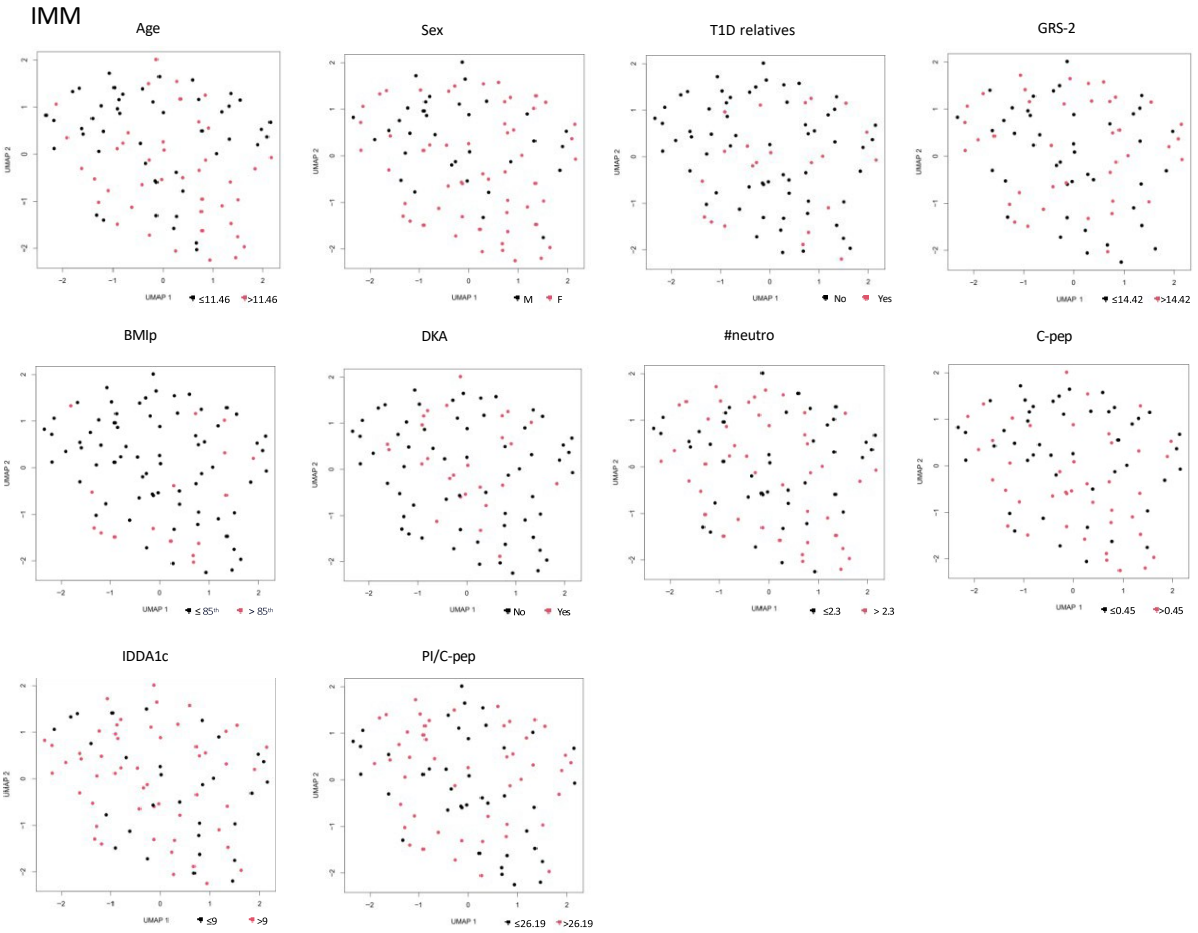
Supplementary Fig. 12. Principal component analysis 1 and 2 for metabolic hormones based on phenotypes. Metabolic hormones principal component analysis shows patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, disease outcome (IDAA1c) and batch effect.



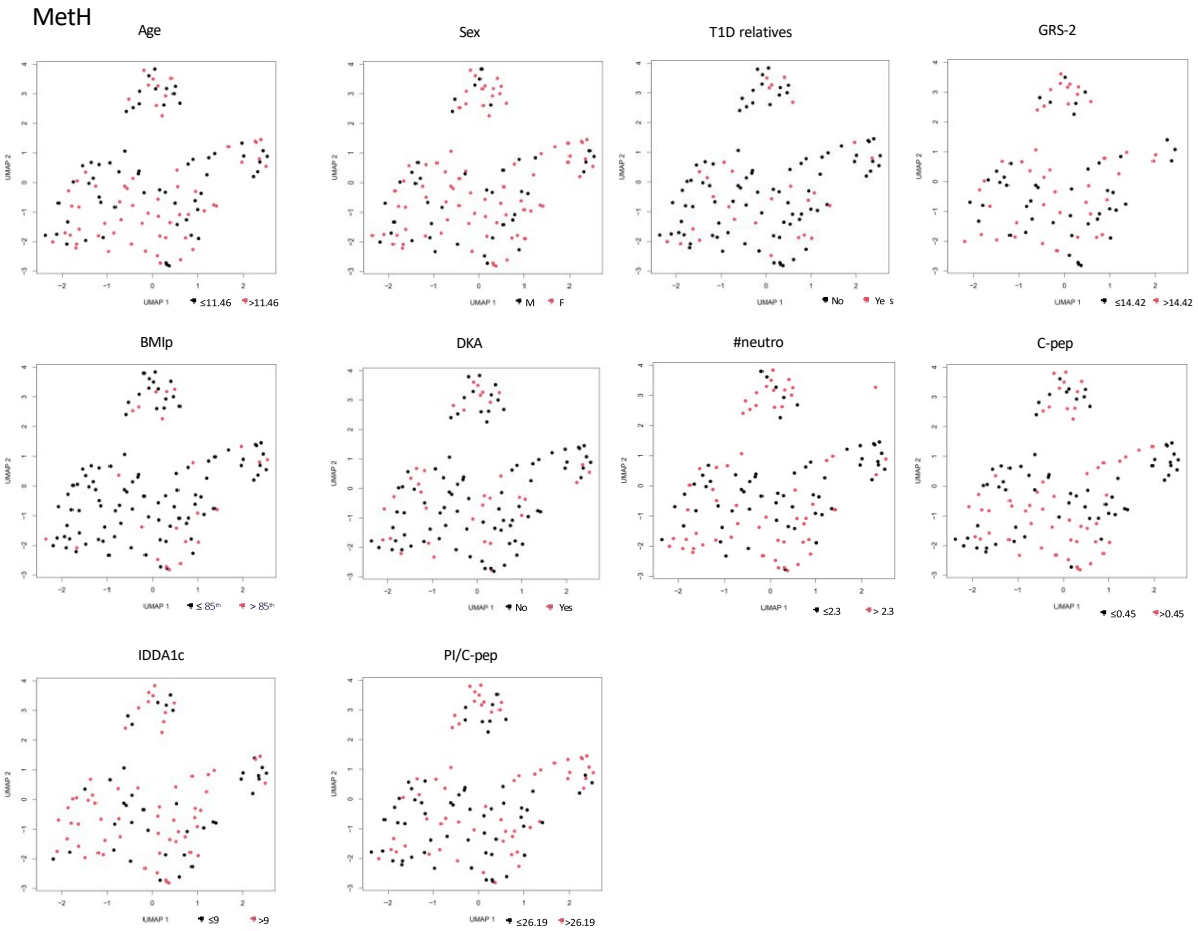
Supplementary Fig. 13. Principal component analysis 3 and 4 for metabolic hormones based on phenotypes. Metabolic hormones principal component analysis shows patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, disease outcome (IDAA1c) and batch effect.



Supplementary Fig. 14. UMAP for RNA genes based on phenotypes. The UMAP plots of the transcriptome data show patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, and disease outcome (IDAA1c).



Supplementary Fig. 15. UMAP for immune cell populations based on phenotypes. The UMAP plots of the immunome data show patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, and disease outcome (IDAA1c).



Supplementary Fig. 16. UMAP for metabolic hormones based on phenotypes. The UMAP plots of the metabolic hormone data show patient distribution based on age, sex, family history of T1D, genetic predisposition (GRS-2), percentile of body mass index (BMIp), presence of diabetic ketoacidosis (DKA), neutrophil count, C-peptide levels, PI/C-peptide ratio, and disease outcome (IDAA1c).