Table S1

Inclusion criteria	Exclusion criteria
1. Male and female gender 2. Age 18-79 years 3. Clinical diagnosis of type 2 diabetes mellitus according to American Diabetes Association guidelines* 4. HbA_{1c} ≥ 7.0% on current therapy	1. Patients with chronic inflammatory diseases (e.g. RA, IBD, COPD) 2. Patients with latent autoimmune diabetes in adults 3. Patients taking anti-inflammatory or immunosuppressive drugs (e.g. corticosteroids) 4. Patients with advanced liver disease (clinically evident signs of liver cirrhosis or LSM >12 kPa) 5. Patients with chronic kidney disease of stages G3b** and worse, defined as estimated glomerular filtration rate <45 ml/min per 1.73m^2 6. Patients with acute infection/vaccinated in the past month 7. Patients with C reactive protein >10 mg/l 8. Patients with recurrent urinary tract infection 9. Patients with active malignant disease 10. Patients with diseases that impact the HPA-axis (e.g. Addison's disease, Cushing syndrome, etc.) 11. Patients taking insulin or more than two oral antidiabetic drugs

*American Diabetes Association Professional Practice C. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes care. 2024;47:S20-S42.
** KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements. 2013;3(1):1–150. doi:10.1038/kisup.2012.73.

Table S2

Antibody (clone)	Source	Identifier
Anti-human CD3 monoclonal antibody Alexa Fluor 700 (OKT3)	eBioScience, Inc., San Diego, California, United States	56-0037-42
Fixable Viability Dye eFluor 506	eBioScience, Inc., San Diego, California, United States	65-0866-14
Anti-human CD45RA monoclonal antibody SB645 (HI100)	eBioScience, Inc., San Diego, California, United States	64-0458-42
Anti-human CD45RO monoclonal antibody PE-eFluor 610 (UCHL1)	eBioScience, Inc., San Diego, California, United States	61-0457-42
Anti-human CD27 monoclonal antibody FITC (LG.7F9)	eBioScience, Inc., San Diego, California, United States	11-0271-82
Anti-human CD28 monoclonal antibody PE (CD28.2)	eBioScience, Inc., San Diego, California, United States	12-0289-42
Anti-human IFN-γ monoclonal antibody FITC (4S.B3)	eBioScience, Inc., San Diego, California, United States	11-7319-82
Anti-human TNF-α monoclonal antibody PE-Cyanine7 (MAb11)	eBioScience, Inc., San Diego, California, United States	25-7349-82
Anti-human IL-2 monoclonal antibody APC (MQ1-17H12)	eBioScience, Inc., San Diego, California, United States	17-7029-82
Anti-human Granzyme B monoclonal antibody PE (N4TL33)	eBioScience, Inc., San Diego, California, United States	12-8896-42
Anti-human Granzyme B monoclonal antibody eFluor 450 (N4TL33)	eBioScience, Inc., San Diego, California, United States	48-8896-42
Anti-human CD16 monoclonal antibody APC-eFluor 780 (CB16)	eBioScience, Inc., San Diego, California, United States	47-0168-42
Anti-human CD56 monoclonal antibody PE (NCAM)	eBioScience, Inc., San Diego, California, United States	12-0567-42
Anti-human CD337 monoclonal antibody eFluor 450 (AF29-4D12)	eBioScience, Inc., San Diego, California, United States	48-3379-42
Anti-human CD314 monoclonal antibody PerCP-eFluor 710 (1D11)	eBioScience, Inc., San Diego, California, United States	46-5878-42
Anti-human Perforin monoclonal antibody APC (dG9)	eBioScience, Inc., San Diego, California, United States	17-9994-42
Anti-human CD69 monoclonal antibody SB780 (FN50)	eBioScience, Inc., San Diego, California, United States	78-0699-42
Anti-human TCRα/β monoclonal antibody PE-eFluor 610 (IP26)	eBioScience, Inc., San Diego, California, United States	61-9986-42
Anti-human CX3CR1 monoclonal antibody APC (2A9-1)	eBioScience, Inc., San Diego, California, United States	17-6099-42
Anti-human IL-17A monoclonal antibody APC (eBio64DEC17)	eBioScience, Inc., San Diego, California, United States	17-7179-42
Anti-human KIR2D monoclonal antibody FITC (NKVFS1)	Miltenyi Biotec, Bergisch Gladbach, Germany	130-092-687
Anti-human NKG2A monoclonal antibody APC (REA110)	Miltenyi Biotec, Bergisch Gladbach, Germany	130-113-563
Anti-human NKG2C monoclonal antibody PE-Vio 615 (REA205)	Miltenyi Biotec, Bergisch Gladbach, Germany	130-123-037
Anti-human TCR Vδ1 monoclonal antibody PerCP-Vio 770 (REA173)	Miltenyi Biotec, Bergisch Gladbach, Germany	130-120-440
Anti-human TCR Vδ2 monoclonal antibody PE (REA771)	Miltenyi Biotec, Bergisch Gladbach, Germany	130-111-010
Anti-human CD197 monoclonal antibody Brilliant Violet 421 (G043H7)	BioLegend, San Diego, California, United States	353208

Clones indicated in parentheses. APC, allophycocyanin; CX3CR1, CX3C motif chemokine receptor 1; FITC, fluorescein isothiocyanate; IFN, interferon; IL, interleukin; KIR, killer-cell immunoglobulin-like receptor; NKG2A, natural killer group 2 member A; NKG2C, natural killer cell group 2 isoform C; PE, phycoerythrin; PerCP, peridinin chlorophyll-A protein; SB, super bright; TCR, T cell receptor; TNF, tumor necrosis factor.

Table S3

	Control (n=30)	Diabetes (n=25)	p value
Age, years	58±13 (53–68)	60±8 (44-74)	0.362
Female sex, n (%)	12 (40)	10 (40)	0.999
Glycated haemoglobin A_{1c}, %	5.4±0.4	8.3.±1.1	
Fasting plasma glucose, mmol/l	5.6±0.6	9.3±2.1	<0.001
HOMA-insulin resistance	3.00±1.88	7.9±4.5	<0.001
HOMA-beta cell function	11.65±5.26	7.52±4.1	0.003
Quantitative insulin sensitivity check index	0.34±0.03	0.29±0.02	<0.001
Body mass index, kg/m^2	27.1±4.0	30.7±3.7	0.001
Body fat, %	28.1±8.4	29.8±8.7	0.093
Skeletal muscle index, kg/m^2	8.0±1.0	8.8±1.3	0.014
Waist-hip ratio	0.90±0.09	0.97±0.07	0.021
Leukocyte count, $\times 10^9$ per litre	6.4±1.7	7. 7±2.2	0.013
C reactive protein, mg/l	2.5±2.5	2.9±2.4	0.542
Triglycerides, mmol/l	1.2±0.6	1.8±1.2	0.021
HDL cholesterol, mmol/l	1.6±0.5	1.2±0.4	0.001
LDL cholesterol, mmol/l	3.1±1.2	2.8±1.0	0.299
Total cholesterol, mmol/l	5.1±1.5	4.6±1.3	0.212
Statin use, n (%)	10 (33.33)	13 (52)	0.168
Aspartate aminotransferase, U/l	26.6±6.0	29.2±13.5	<0.001
Alanine aminotransferase, U/l	27.4±7.3	38.2±22.4	0.015
Hepatic steatosis index	38.1±5.1	44.1±6.1	0.008
Triglyceride-glucose index	4.59±0.25	9.3±0.6	<0.001
NAFLD-liver fat score	1.1±1.0	2.5±1.8	0.002

Table S4

	SGLT2i **Baseline (*n*=15)**	**SGLT2i/GLP1ra** **Baseline (*n*=10)**	***p* value**	**SGLT2i** **Baseline (*n*=15)**	**SGLT2i/GLP1ra** **Baseline (*n*=10)**	***p* value**
Age, Years	63.7±7 (48-74)	53.4±15 (44-68)				
Female sex, n (%)	6 (40)	4 (40)				
Glycated haemoglobin A_{1c}, %	8.1±1.0	7.9±2.2	0.252	6.7±0.3	6.0±1.7	0.055
Fasting plasma glucose, mmol/l	8.6±1.2	9.5±3.4	**0.038**	7.0±0.9	6.5±1.8	0.419
HOMA-insulin resistance	7.9±5.1	8.3±3.3	0.975	4.2±3.2	5.3±3.6	0.631
HOMA-beta cell function	8.1±3.6	6.6±4.1	0.424	7.2±4.0	9.1±5.0	0.235
Quantitative insulin sensitivity check index	0.29±0.02	0.27±0.07	0.526	0.33±0.04	0.29±0.08	0.633
Body mass index, kg/m^2	29.3±8.4	30.2±8.4	**0.017**	27.5±3.2	27.6±7.4	0.091
Body fat, %	28.5±7.9	29.6±10.3	0.355	28.9±8.7	29.1±9.0	0.698
Skeletal muscle index, kg/m^2	8.8±1.4	8.2±2.3	0.993	8.0±1.3	7.9±2.0	0.446
Waist-hip ratio	0.96±0.06	0.91±0.27	0.517	0.96±0.05	0.91±0.25	0.806
Leukocyte count, $\times 10^9$ per litre	7.6±1.6	7.5±3.0	0.672	7.9±1.6	8.3±3.0	0.263
C reactive protein, mg/l	2.3±1.8	3.6±2.6	0.111	1.9±2.1	1.9±1.4	0.957
Triglycerides, mmol/l	1.8±1.3	2.1±1.3	0.995	1.6±1.0	1.8±1.0	0.999
HDL cholesterol, mmol/l	1.2±0.4	1.2±0.3	0.946	1.4±0.3	1.3±0.4	0.934
LDL cholesterol, mmol/l	2.7±1.0	2.8±0.9	0.527	2.1±1.0	2.1±1.2	0.822
Total cholesterol, mmol/l	4.5±1.4	4.6±1.4	0.636	8.1±1.0	8.1±1.0	0.911
Statin use, *n* (%)	9 (60)	7 (70)		14 (93)	9 (90)	
Aspartate aminotransferase, U/l	29.7±14.5	30.6±15.3	0.823	27.3±9.9	25.3±11.6	0.577
Alanine aminotransferase, U/l	36.7±22.6	42.0±21.8	0.674	29.7±11.2	26.6±13.0	0.306
Hepatic steatosis index	41.6±4.6	43.6±12.6	**0.011**	39.2±4.3	38.2±10.8	0.360
Triglyceride-glucose index	9.2±0.7	8.9±2.4	0.262	8.9±0.6	8.4±2.3	0.916
NAFLD-liver fat score	2.6±1.9	2.6±1.6	0.795	1.3±1.5	1.8±1.7	0.745
Urea, mmol/l	6.3±1.3	5.2±1.5	0.100	7.1±1.8	5.6±2.0	0.066
Creatinine, µmol/l	77.5±10.6	70.1±22.6	0.546	79.2±15.9	67.5±23.4	0.158
eGFR, ml/min/1.73m^2	78.6±12.2	83.1±25.8	0.063	81.5±13.6	86.0±28.0	0.054

Figure S1

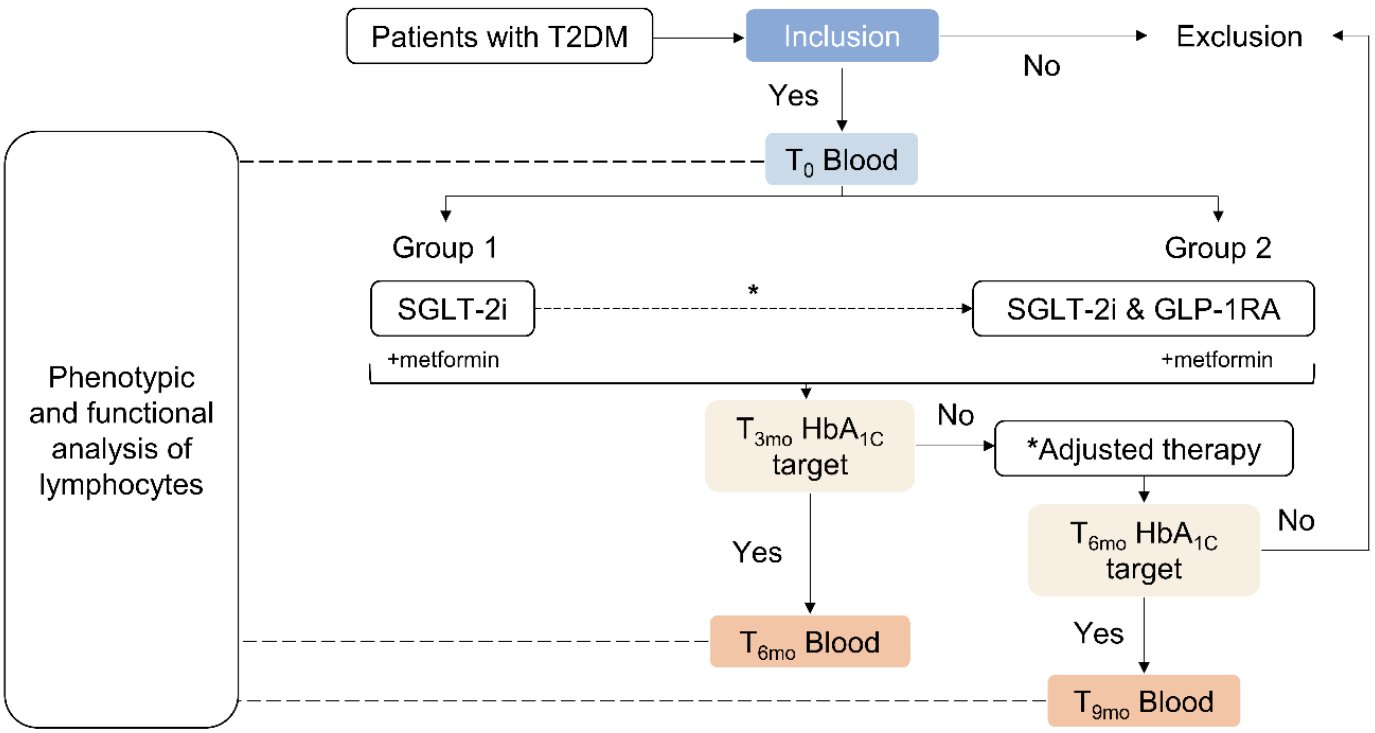

Patients with T2DM
Inclusion
Exclusion
No
Yes
T_0 Blood
Group 1
Group 2
SGLT-2i
*
SGLT-2i & GLP-1RA
+metformin
+metformin
Phenotypic and functional analysis of lymphocytes
T_{3mo} HbA_{1C} target
No
*Adjusted therapy
T_{6mo} HbA_{1C} target
No
Yes
Yes
T_{6mo} Blood
T_{9mo} Blood

Figure S2

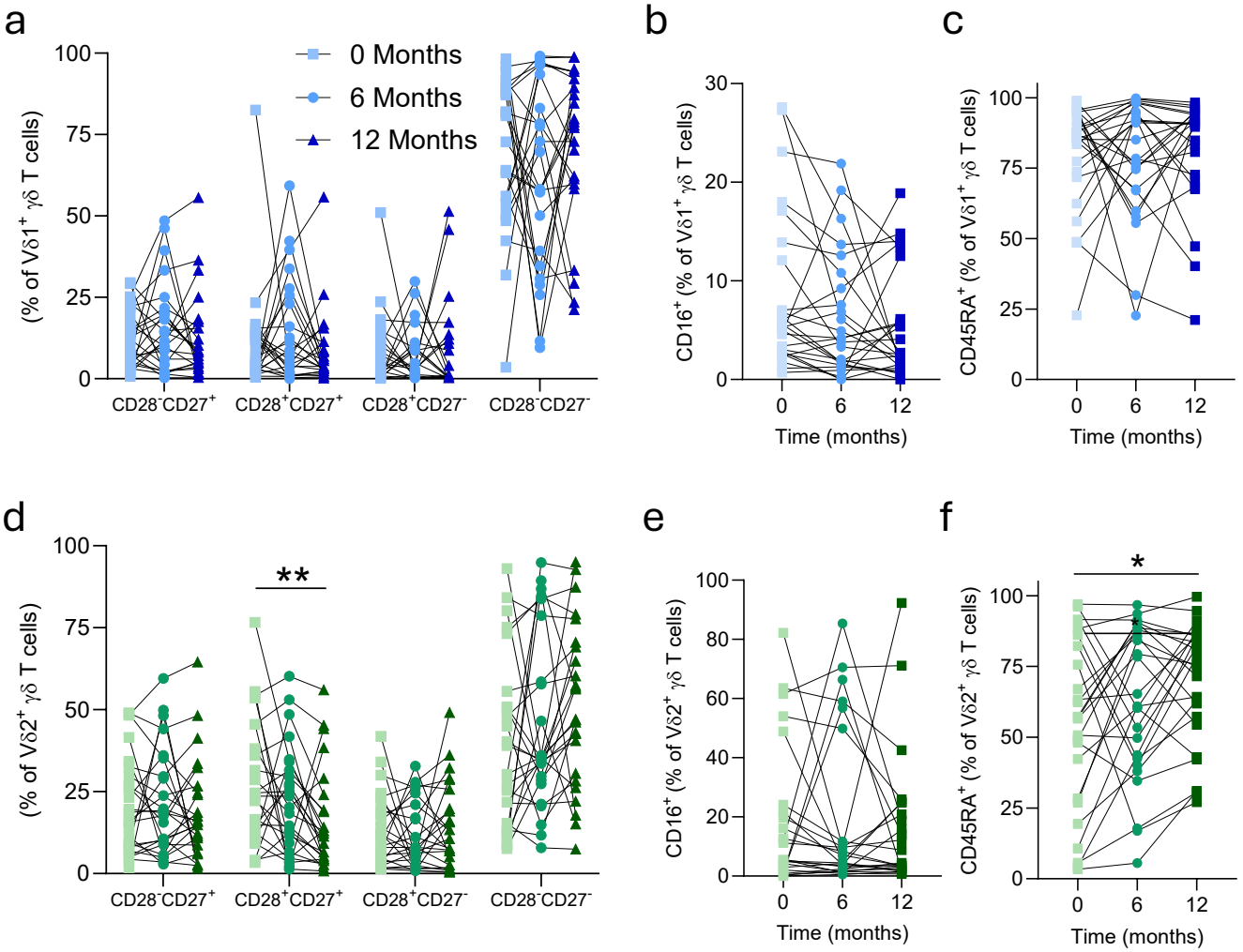

a
b
c
d
e
f
0 Months
6 Months
12 Months
(% of Vδ1+ γδ T cells)
CD16+ (% of Vδ1+ γδ T cells)
CD45RA+ (% of Vδ1+ γδ T cells)
(% of Vδ2+ γδ T cells)
CD16+ (% of Vδ2+ γδ T cells)
CD45RA+ (% of Vδ2+ γδ T cells)
CD28-CD27+
CD28+CD27+
CD28+CD27-
CD28-CD27-
Time (months)
**
*

Figure S3

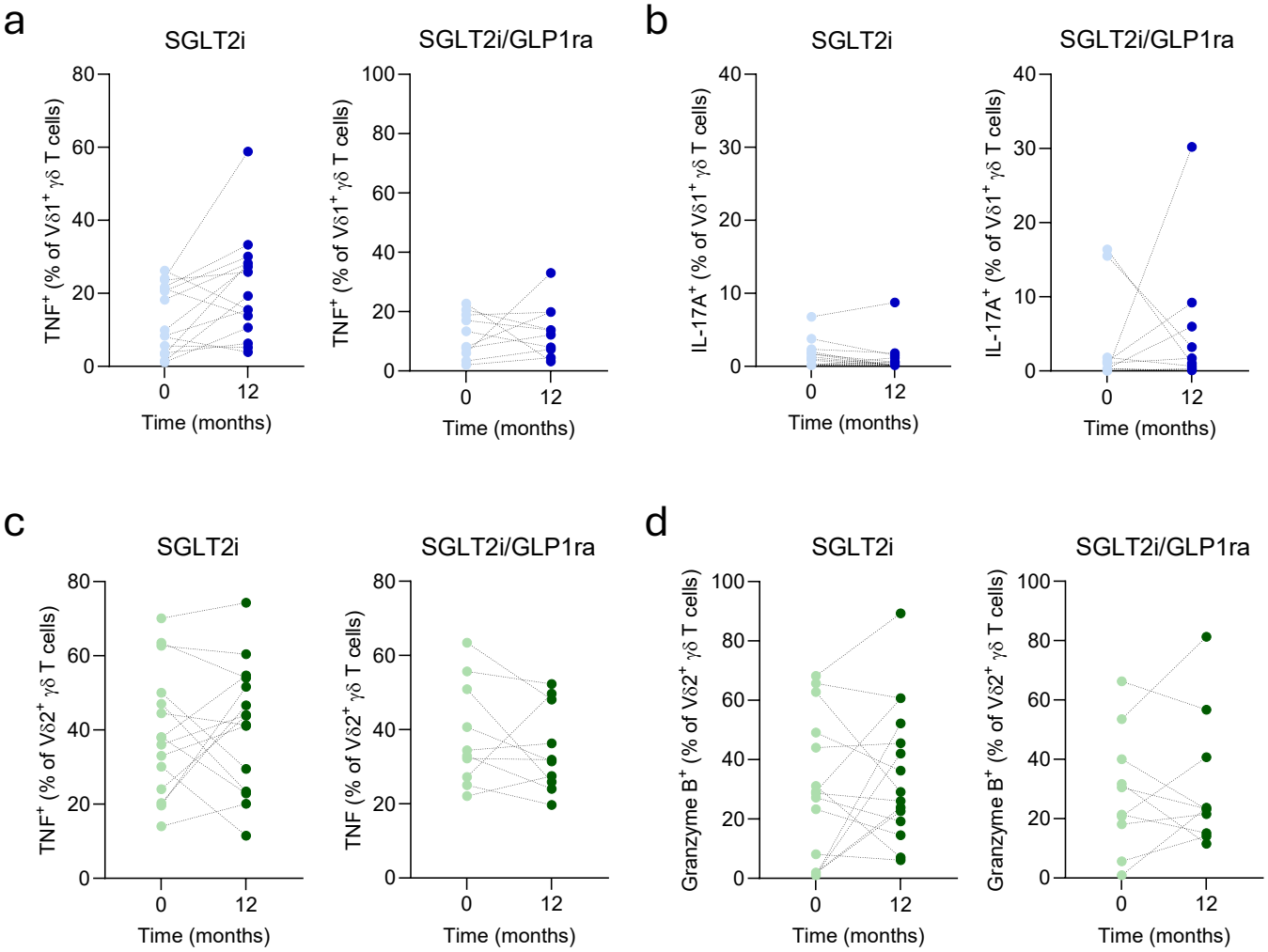
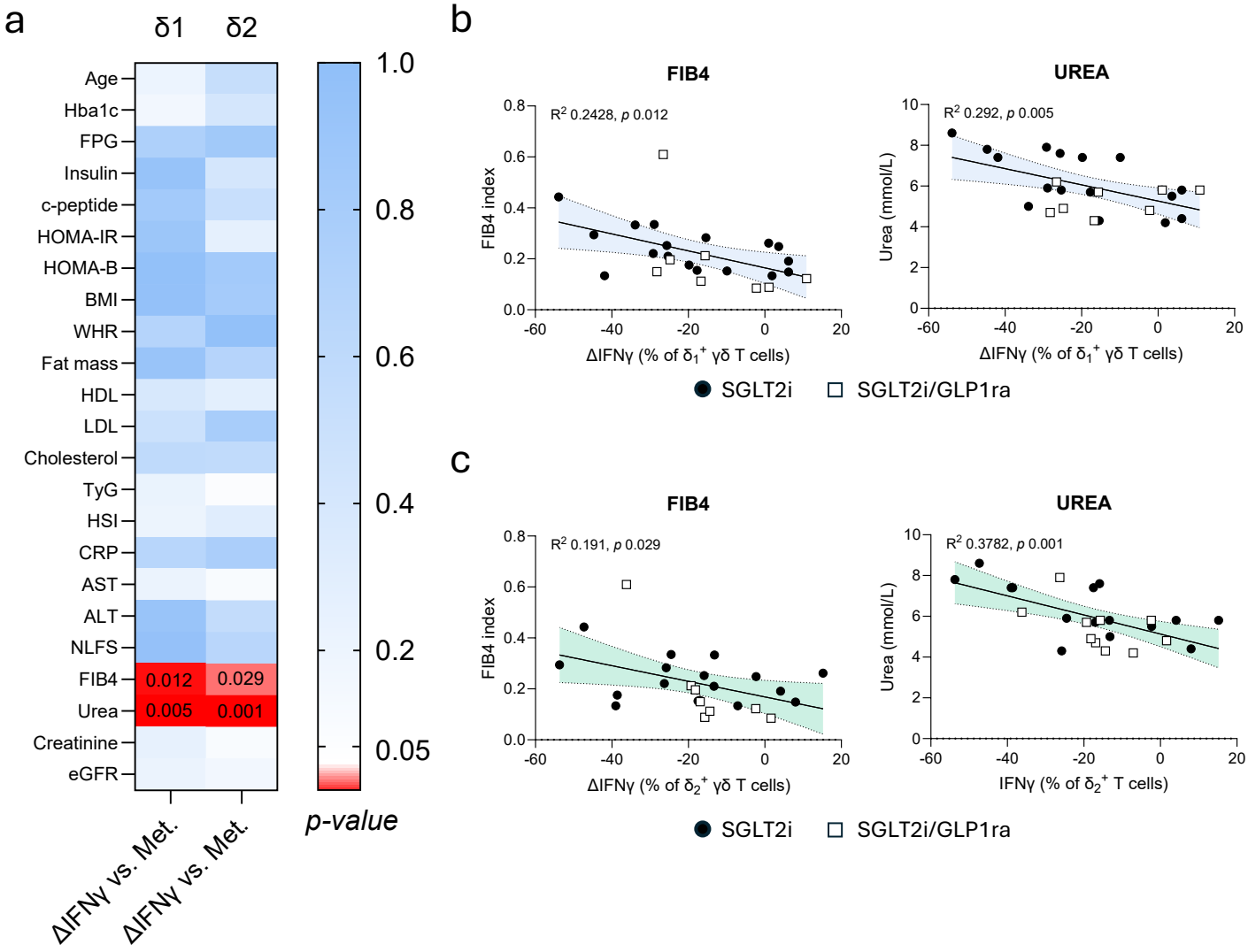

a
SGLT2i
SGLT2i/GLP1ra
TNF+ (% of Vδ1+ γδ T cells)
b
IL-17A+ (% of Vδ1+ γδ T cells)
c
TNF+ (% of Vδ2+ γδ T cells)
TNF (% of Vδ2+ γδ T cells)
d
Granzyme B+ (% of Vδ2+ γδ T cells)
Time (months)
0
12

Figure S4


a
δ1
δ2
Age
Hba1c
FPG
Insulin
c-peptide
HOMA-IR
HOMA-B
BMI
WHR
Fat mass
HDL
LDL
Cholesterol
TyG
HSI
CRP
AST
ALT
NLFS
FIB4
Urea
Creatinine
eGFR
0.012
0.029
0.005
0.001
1.0
0.8
0.6
0.4
0.2
0.05
p-value
ΔIFNγ vs. Met.
ΔIFNγ vs. Met.
b
FIB4
UREA
R² 0.2428, p 0.012
R² 0.292, p 0.005
FIB4 index
Urea (mmol/L)
ΔIFNγ (% of δ1+ γδ T cells)
ΔIFNγ (% of δ1+ γδ T cells)
SGLT2i
SGLT2i/GLP1ra
c
FIB4
UREA
R² 0.191, p 0.029
R² 0.3782, p 0.001
FIB4 index
Urea (mmol/L)
ΔIFNγ (% of δ2+ γδ T cells)
IFNγ (% of δ2+ T cells)
SGLT2i
SGLT2i/GLP1ra