

Table S1 - Biomarkers in the OLINK Inflammation panel and assay characteristics in the German Diabetes Study

Assay ID	Biomarker	Full name	UniProt No	Gene symbol	Intra-assay CV (%)	Inter-assay CV (%)
101_IL-8	IL-8	Interleukin-8	P10145	<i>CXCL8</i>	1.1	1.6
102_VEGF-A	VEGF-A	Vascular endothelial growth factor A	P15692	<i>VEGFA</i>	0.8	1.1
103_BDNF*	BDNF	Brain-derived neurotrophic factor	P23560	<i>BDNF</i>	n/a	n/a
105_MCP-3	MCP-3	Monocyte chemoattractant protein 3 (CCL7)	P80098	<i>CCL7</i>	4.7	8.2
106_GDNF	GDNF	Glial cell line-derived neurotrophic factor	P39905	<i>GDNF</i>	9.6	8.3
107_CDCP1	CDCP1	CUB domain-containing protein 1	Q9H5V8	<i>CDCP1</i>	3.3	5.1
108_CD244	CD244	Natural killer cell receptor 2B4	Q9BZW8	<i>CD244</i>	1.2	2.2
109_IL-7	IL-7	Interleukin-7	P13232	<i>IL7</i>	1.2	2.5
110_OPG	OPG	Osteoprotegerin	O00300	<i>TNFRSF11B</i>	0.5	1.0
111_LAP TGF-beta-1	LAP TGFβ1	Latency-associated peptide transforming growth factor beta-1	P01137	<i>TGFB1</i>	0.8	1.6
112_uPA	uPA	Urokinase-type plasminogen activator	P00749	<i>PLAU</i>	0.6	1.4
113_IL-6	IL-6	Interleukin-6	P05231	<i>IL6</i>	1.9	4.0

114_IL-17C	IL-17C	Interleukin-17C	Q9P0M4	<i>IL17C</i>	7.0	6.0
115_MCP-1	MCP-1	Monocyte chemotactic protein 1 (CCL2)	P13500	<i>CCL2</i>	0.8	1.9
116_IL-17A	IL-17A	Interleukin-17A	Q16552	<i>IL17A</i>	12.5	11.5
117_CXCL11	CXCL11	C-X-C motif chemokine 11	O14625	<i>CXCL11</i>	0.8	2.5
118_AXIN1	Axin-1	Axin-1	O15169	<i>AXIN1</i>	5.1	10.4
120_TRAIL	TRAIL	TNF-related apoptosis-inducing ligand (TNFSF10)	P50591	<i>TNFSF10</i>	0.7	1.6
121_IL-20RA**	IL-20RA	Interleukin-20 receptor subunit alpha	Q9UHF4	<i>IL20RA</i>	n/a	n/a
122_CXCL9	CXCL9	C-X-C motif chemokine 9	Q07325	<i>CXCL9</i>	0.9	2.6
123_CST5	CST5	Cystatin D	P28325	<i>CST5</i>	0.9	2.1
124_IL-2RB**	IL-2RB	Interleukin-2 receptor subunit beta	P14784	<i>IL2RB</i>	n/a	n/a
125_IL-1 alpha**	IL-1 α	Interleukin-1 alpha	P01583	<i>IL1A</i>	n/a	n/a
126_OSM	OSM	Oncostatin-M	P13725	<i>OSM</i>	1.4	3.7
127_IL-2**	IL-2	Interleukin-2	P60568	<i>IL2</i>	n/a	n/a
128_CXCL1	CXCL1	C-X-C motif chemokine 1	P09341	<i>CXCL1</i>	0.7	1.4
129_TSLP**	TSLP	Thymic stromal lymphopoietin	Q969D9	<i>TSLP</i>	n/a	n/a

130_CCL4	CCL4	C-C motif chemokine 4	P13236	<i>CCL4</i>	0.9	1.6
131_CD6	CD6	T cell surface glycoprotein CD6 isoform	Q8WWJ7	<i>CD6</i>	1.5	3.6
132_SCF	SCF	Stem cell factor (c-Kit-ligand)	P21583	<i>KITLG</i>	0.4	1.0
133_IL-18	IL-18	Interleukin-18	Q14116	<i>IL18</i>	0.9	2.9
134_SLAMF1	SLAMF1	Signaling lymphocytic activation molecule (SLAM)	Q13291	<i>SLAMF1</i>	11.6	11.5
135_TGF-alpha	TGF α	Transforming growth factor alpha	P01135	<i>TGFA</i>	2.2	3.6
136_MCP-4	MCP-4	Monocyte chemotactic protein 4 (CCL13)	Q99616	<i>CCL13</i>	1.9	3.9
137_CCL11	Eotaxin	Eotaxin (CCL11)	P51671	<i>CCL11</i>	0.8	1.8
138_TNFSF14	TNFSF14	Tumor necrosis factor ligand superfamily member 14 (LIGHT)	O43557	<i>TNFSF14</i>	1.0	2.7
139_FGF-23	FGF-23	Fibroblast growth factor 23	Q9GZV9	<i>FGF23</i>	8.7	11.4
140_IL-10RA	IL-10RA	Interleukin-10 receptor subunit alpha	Q13651	<i>IL10RA</i>	7.5	9.8
141_FGF-5	FGF-5	Fibroblast growth factor 5	Q8NF90	<i>FGF5</i>	11.7	9.3
142_MMP-1	MMP-1	Matrix metalloproteinase-1	P03956	<i>MMP1</i>	0.4	0.9
143_LIF-R	LIF-R	Leukemia inhibitory factor receptor	P42702	<i>LIFR</i>	1.4	4.6
144_FGF-21	FGF-21	Fibroblast growth factor 21	Q9NSA1	<i>FGF21</i>	1.2	7.8

145_CCL19	CCL19	C-C motif chemokine 19	Q99731	<i>CCL19</i>	0.8	2.5
148_IL-15RA	IL-15RA	Interleukin-15 receptor subunit alpha	Q13261	<i>IL15RA</i>	11.7	9.6
149_IL-10RB	IL-10RB	Interleukin-10 receptor subunit beta	Q08334	<i>IL10RB</i>	1.1	1.2
150_IL-22 RA1**	IL-22RA1	Interleukin-22 receptor subunit alpha-1	Q8N6P7	<i>IL22RA1</i>	n/a	n/a
151_IL-18R1	IL-18R1	Interleukin-18 receptor 1	Q13478	<i>IL18R1</i>	1.0	2.1
152_PD-L1	PD-L1	Programmed cell death 1 ligand 1	Q9NZQ7	<i>CD274</i>	1.7	2.7
153_Beta-NGF	Beta-NGF	Beta-nerve growth factor	P01138	<i>NGF</i>	3.2	5.6
154_CXCL5	CXCL5	C-X-C motif chemokine 5	P42830	<i>CXCL5</i>	0.6	1.4
155_TRANCE	TRANCE	TNF-related activation-induced cytokine (TRANCE, TNFSF11, RANKL, OPGL)	O14788	<i>TNFSF11</i>	2.0	5.4
156_HGF	HGF	Hepatocyte growth factor	P14210	<i>HGF</i>	0.7	1.6
157_IL-12B	IL-12B	Interleukin-12 subunit beta	P29460	<i>IL12B</i>	1.9	4.1
158_IL-24**	IL-24	Interleukin-24	Q13007	<i>IL24</i>	n/a	n/a
159_IL-13**	IL-13	Interleukin-13	P35225	<i>IL13</i>	n/a	n/a
160_ARTN**	Artemin	Artemin	Q5T4W7	<i>ARTN</i>	n/a	n/a
161_MMP-10	MMP-10	Matrix metalloproteinase-10 (SL-2)	P09238	<i>MMP10</i>	0.8	1.7

162_IL-10	IL-10	Interleukin-10	P22301	<i>IL10</i>	3.9	5.0
163_TNF**	TNF α	Tumor necrosis factor-alpha	P01375	<i>TNF</i>	n/a	n/a
164_CCL23	CCL23	C-C motif chemokine 23	P55773	<i>CCL23</i>	0.7	2.7
165_CD5	CD5	T-cell surface glycoprotein CD5	P06127	<i>CD5</i>	1.7	2.7
166_MIP-1 alpha	MIP-1 α	Macrophage inflammatory protein-1alpha (C-C motif chemokine 3/CCL3)	P10147	<i>CCL3</i>	1.6	2.9
167_Flt3L	Flt3L	Fms-related tyrosine kinase 3 ligand	P49771	<i>FLT3LG</i>	1.0	2.1
168_CXCL6	CXCL6	C-X-C motif chemokine 6	P80162	<i>CXCL6</i>	0.8	2.4
169_CXCL10	CXCL10	C-X-C motif chemokine 10 (IP-10)	P02778	<i>CXCL10</i>	0.9	2.9
170_4E-BP1	EIF4EBP1	Eukaryotic translation initiation factor 4E-binding protein 1	Q13541	<i>EIF4EBP1</i>	1.4	5.0
171_IL-20**	IL-20	Interleukin-20	Q9NYY1	<i>IL20</i>	n/a	n/a
172_SIRT2	SIRT2	SIR2-like protein 2	Q8IXJ6	<i>SIRT2</i>	5.7	6.0
173_CCL28	CCL28	C-C motif chemokine 28	Q9NRJ3	<i>CCL28</i>	7.4	7.0
174_DNER	DNER	Delta and Notch-like epidermal growth factor-related receptor	Q8NFT8	<i>DNER</i>	0.6	1.7
175_EN-RAGE	EN-RAGE	Protein S100-A12 (EN-RAGE)	P80511	<i>S100A12</i>	1.9	8.5
176_CD40	CD40	CD40L receptor	P25942	<i>CD40</i>	0.8	1.8

177_IL-33**	IL-33	Interleukin-33	O95760	<i>IL33</i>	n/a	n/a
178_IFN-gamma**	IFN γ	Interferon-gamma	P01579	<i>IFNG</i>	n/a	n/a
179_FGF-19	FGF-19	Fibroblast growth factor 19	O95750	<i>FGF19</i>	1.1	3.3
180_IL-4**	IL-4	Interleukin-4	P05112	<i>IL4</i>	n/a	n/a
181_LIF**	LIF	Leukemia inhibitory factor	P15018	<i>LIF</i>	n/a	n/a
182_NRTN**	Neurturin	Neurturin	Q99748	<i>NRTN</i>	n/a	n/a
183_MCP-2	MCP-2	Monocyte chemoattractant protein 2 (MCP-2, CCL8)	P80075	<i>CCL8</i>	0.7	1.5
184_CASP-8	Caspase-8	Caspase-8	Q14790	<i>CASP8</i>	4.8	8.7
185_CCL25	CCL25	C-C motif chemokine 25	O15444	<i>CCL25</i>	1.2	2.3
186_CX3CL1	CX3CL1	Fractalkine	P78423	<i>CX3CL1</i>	1.9	2.9
187_TNFRSF9	TNFRSF9	Tumor necrosis factor receptor superfamily member 9	Q07011	<i>TNFRSF9</i>	1.2	2.0
188_NT-3	NT-3	Neurotrophin-3	P20783	<i>NTF3</i>	5.9	7.6
189_TWEAK	TWEAK	Tumor necrosis factor (Ligand) superfamily, member 12 (TWEAK)	O43508	<i>TNFSF12</i>	0.8	1.9
190_CCL20	CCL20	C-C motif chemokine 20	P78556	<i>CCL20</i>	1.7	3.5
191_ST1A1	ST1A1	Sulfotransferase 1A1	P50225	<i>SULT1A1</i>	3.3	5.3

192_STAMPB	STAMPB	STAM-binding protein	O95630	<i>STAMPB</i>	2.5	3.8
193_IL-5**	IL-5	Interleukin-5	P05113	<i>IL5</i>	n/a	n/a
194_ADA	ADA	Adenosine deaminase	P00813	<i>ADA</i>	2.9	4.2
195_TNFB	TNF β	Tumor necrosis factor-beta (lymphotoxin-alpha/LT-alpha)	P01374	<i>LTA</i>	1.8	3.3
196_CSF-1	CSF-1	Macrophage colony-stimulating factor 1	P09603	<i>CSF1</i>	0.9	1.7

LOD, limit of detection; n/a, not applicable (NPX of control measurements below LOD); NPX, normalised protein expression values.

*No data reported owing to technical problems with the assay.

**Excluded from analysis because missing data for >25%.

Table S2 - Biomarkers of inflammation in the study population according to diabetes subgroups

Biomarker	Full name	SAID n=87	SIDD n=12	SIRD n=39	MOD n=133	MARD n=143	P
IL-8	Interleukin-8	6.74 (6.38; 7.08)	6.68 (6.31; 7.27)	6.99 (6.82; 7.54)	6.87 (6.60; 7.23)	6.98 (6.72; 7.28)	<0.0001*
VEGF-A	Vascular endothelial growth factor A	10.11 (9.83; 10.54)	9.97 (9.57; 10.53)	10.32 (10.13; 10.81)	10.22 (9.88; 10.6)	10.20 (9.84; 10.61)	0.1335
MCP-3	Monocyte chemotactic protein 3 (CCL7)	2.13 (1.86; 2.58)	2.21 (2.16; 2.70)	2.59 (2.28; 3.37)	2.43 (2.13; 2.74)	2.31 (2.14; 2.61)	<0.0001*
GDNF	Glial cell line-derived neurotrophic factor	1.71 (1.55; 1.94)	1.69 (1.53; 1.90)	1.90 (1.74; 2.06)	1.81 (1.60; 2.07)	1.78 (1.63; 2.02)	0.082
CDCP1	CUB domain-containing protein 1	2.60 (2.23; 3.07)	3.04 (2.21; 3.31)	3.34 (2.94; 3.69)	3.10 (2.76; 3.52)	3.15 (2.85; 3.54)	<0.0001*
CD244	Natural killer cell receptor 2B4	5.89 (5.69; 6.09)	5.61 (5.48; 5.81)	5.91 (5.68; 6.13)	5.84 (5.70; 5.99)	5.75 (5.53; 5.91)	0.0005*
IL-7	Interleukin-7	4.88 (4.59; 5.27)	5.11 (4.62; 5.47)	4.97 (4.60; 5.25)	5.14 (4.75; 5.47)	5.05 (4.72; 5.42)	0.0833
OPG	Osteoprotegerin	10.37 (10.14; 10.56)	10.28 (10.07; 10.51)	10.73 (10.39; 10.95)	10.51 (10.21; 10.82)	10.50 (10.25; 10.74)	<0.0001*
LAP TGFβ1	Latency-associated peptide transforming growth factor beta-1	8.66 (8.38; 9.00)	8.66 (8.26; 8.92)	8.85 (8.58; 9.11)	8.87 (8.58; 9.09)	8.76 (8.42; 8.95)	0.0127
uPA	Urokinase-type plasminogen activator	10.14 (9.90; 10.31)	9.87 (9.76; 10.07)	10.23 (10.03; 10.41)	10.09 (9.91; 10.26)	10.11 (9.87; 10.31)	0.0039
IL-6	Interleukin-6	3.15 (2.78; 3.61)	3.51 (2.66; 3.77)	4.20 (3.85; 4.87)	3.90 (3.47; 4.46)	3.65 (3.19; 4.10)	<0.0001*
IL-17C	Interleukin-17C	1.53 (1.25; 1.88)	1.46 (1.14; 1.51)	1.65 (1.26; 1.96)	1.58 (1.26; 1.90)	1.39 (1.21; 1.74)	0.0430
MCP-1	Monocyte chemotactic protein 1 (CCL2)	11.01 (10.76; 11.42)	11.13 (10.80; 11.28)	11.44 (11.12; 11.76)	11.17 (10.90; 11.44)	11.15 (10.89; 11.44)	0.0061
IL-17A	Interleukin-17A	1.04 (0.92; 01.2)	0.75 (0.71; 1.09)	1.05 (0.91; 1.28)	0.99 (0.79; 1.28)	0.99 (0.78; 1.20)	0.1924
CXCL11	C-X-C motif chemokine 11	7.78 (7.42; 8.21)	7.48 (7.13; 8.22)	7.96 (7.57; 08.4)	7.78 (7.37; 8.17)	7.80 (7.39; 8.20)	0.5630
Axin-1	Axin-1	1.96 (1.73; 2.28)	1.66 (1.46; 2.11)	1.99 (1.62; 2.46)	1.99 (1.57; 2.33)	1.84 (1.53; 2.10)	0.0455
TRAIL	TNF-related apoptosis-inducing ligand (TNFSF10)	8.44 (8.22; 8.63)	8.28 (8.10; 8.76)	8.41 (8.22; 8.73)	8.45 (8.22; 8.63)	8.41 (8.19; 8.63)	0.9023

CXCL9	C-X-C motif chemokine 9	7.13 (6.64; 7.59)	6.91 (6.76; 7.24)	7.33 (6.83; 8.20)	7.02 (6.68; 7.38)	7.34 (6.93; 7.89)	0.0001*
CST5	Cystatin D	5.81 (5.53; 6.16)	5.68 (5.38; 5.83)	5.94 (5.59; 6.32)	5.62 (5.34; 6.01)	5.88 (5.54; 6.29)	0.0005*
OSM	Oncostatin-M	4.34 (3.81; 4.94)	4.68 (3.78; 5.02)	4.83 (4.20; 5.35)	4.67 (4.33; 5.24)	4.26 (3.87; 4.77)	<0.0001*
CXCL1	C-X-C motif chemokine 1	9.03 (8.54; 9.31)	8.76 (8.39; 9.13)	9.02 (8.77; 9.55)	8.98 (8.66; 9.24)	8.90 (8.63; 9.22)	0.1737
CCL4	C-C motif chemokine 4	7.29 (6.84; 7.62)	7.4 (6.77; 7.60)	7.37 (7.04; 7.88)	7.33 (7.02; 7.75)	7.43 (7.03; 7.77)	0.1056
CD6	T cell surface glycoprotein CD6 isoform	4.56 (4.26; 4.81)	4.36 (4.08; 4.44)	4.41 (4.19; 4.70)	4.47 (4.19; 4.73)	4.42 (4.15; 4.71)	0.2836
SCF	Stem cell factor (c-Kit-ligand)	9.91 (9.70; 10.12)	10.00 (9.32; 10.11)	9.58 (9.32; 9.91)	9.58 (9.27; 9.82)	9.81 (9.57; 10.08)	<0.0001*
IL-18	Interleukin-18	7.84 (7.37; 8.12)	7.88 (7.37; 8.03)	8.17 (7.83; 8.65)	8.02 (7.71; 8.35)	7.86 (7.59; 8.16)	0.0001*
SLAMF1	Signaling lymphocytic activation molecule (SLAM)	1.83 (1.54; 2.04)	1.81 (1.54; 2.21)	2.06 (1.75; 2.39)	1.89 (1.67; 2.15)	1.83 (1.54; 2.09)	0.0166
TGF α	Transforming growth factor alpha	4.08 (3.62; 4.41)	3.93 (3.51; 4.22)	4.2 (3.56; 4.62)	4.16 (3.77; 4.51)	3.94 (3.63; 4.33)	0.0577
MCP-4	Monocyte chemoattractant protein 4 (CCL13)	4.53 (4.21; 4.93)	4.84 (3.96; 5.22)	5.09 (4.37; 5.37)	4.63 (4.28; 5.10)	4.80 (4.49; 5.19)	0.0024
Eotaxin	Eotaxin (CCL11)	8.02 (7.65; 8.30)	8.10 (7.89; 8.33)	8.24 (7.94; 8.51)	7.98 (7.64; 8.30)	8.21 (8.00; 8.43)	<0.0001*
TNFSF14	Tumor necrosis factor ligand superfamily member 14 (LIGHT)	5.78 (5.23; 6.22)	5.68 (5.32; 5.81)	5.72 (5.40; 6.36)	5.81 (5.39; 6.18)	5.58 (5.08; 6.03)	0.0078
FGF-23	Fibroblast growth factor 23	1.38 (1.22; 1.58)	1.16 (0.92; 1.40)	1.65 (1.25; 1.86)	1.31 (1.09; 1.57)	1.31 (1.13; 1.52)	0.0006*
IL-10RA	Interleukin-10 receptor subunit alpha	1.06 (0.85; 1.30)	0.90 (0.67; 1.09)	1.09 (0.89; 1.47)	1.04 (0.88; 1.36)	0.98 (0.80; 1.30)	0.1179
FGF-5	Fibroblast growth factor 5	1.07 (0.90; 1.29)	1.10 (1.00; 1.24)	1.12 (1.01; 1.25)	1.06 (0.96; 1.20)	1.10 (0.94; 1.26)	0.5468
MMP-1	Matrix metalloproteinase-1	14.10 (13.38; 14.57)	14.00 (12.98; 14.34)	14.20 (13.65; 14.53)	14.19 (13.53; 14.54)	14.12 (13.41; 14.56)	0.6553
LIF-R	Leukemia inhibitory factor receptor	2.88 (2.72; 3.09)	2.79 (2.67; 3.11)	3.04 (2.76; 3.14)	2.89 (2.74; 3.03)	2.87 (2.71; 3.02)	0.0768
FGF-21	Fibroblast growth factor 21	4.98 (3.95; 6.07)	5.50 (3.75; 6.17)	6.92 (6.40; 8.14)	6.47 (5.52; 7.56)	6.34 (5.61; 7.18)	<0.0001*
CCL19	C-C motif chemokine 19	9.02 (8.53; 9.48)	8.94 (8.28; 9.15)	9.45 (8.96; 9.96)	9.22 (8.89; 9.68)	8.98 (8.51; 9.51)	<0.0001*

IL-15RA	Interleukin-15 receptor subunit alpha	0.98 (0.86; 1.09)	0.96 (0.80; 1.09)	1.03 (0.96; 1.23)	0.96 (0.86; 1.07)	0.99 (0.87; 1.12)	0.0565
IL-10RB	Interleukin-10 receptor subunit beta	6.76 (6.60; 6.97)	6.67 (6.42; 6.86)	7.02 (6.77; 7.25)	6.86 (6.68; 7.06)	6.73 (6.53; 6.93)	<0.0001*
IL-18R1	Interleukin-18 receptor 1	7.05 (6.76; 7.37)	7.46 (6.80; 7.63)	7.32 (7.02; 7.55)	7.31 (7.02; 7.71)	7.07 (6.75; 7.31)	<0.0001*
PD-L1	Programmed cell death 1 ligand 1	4.03 (3.82; 4.22)	3.77 (3.54; 4.12)	4.02 (3.80; 4.36)	3.93 (3.75; 4.16)	3.90 (3.67; 4.08)	0.0049
Beta-NGF	Beta-nerve growth factor	1.79 (1.63; 1.98)	1.66 (1.53; 1.74)	1.86 (1.65; 2.05)	1.77 (1.63; 1.94)	1.70 (1.58; 1.88)	0.0047
CXCL5	C-X-C motif chemokine 5	12.02 (11.48; 12.49)	12.06 (11.30; 12.43)	11.94 (11.49; 12.58)	12.11 (11.58; 12.58)	12.06 (11.48; 12.45)	0.8775
TRANCE	TNF-related activation-induced cytokine (TRANCE, TNFSF11, RANKL, OPGL)	4.95 (4.36; 5.48)	4.77 (4.52; 5.17)	4.69 (4.15; 5.07)	4.69 (4.32; 5.13)	4.61 (4.21; 5.09)	0.0322
HGF	Hepatocyte growth factor	8.62 (8.36; 8.96)	8.63 (8.32; 9.01)	9.18 (8.86; 9.33)	9.01 (8.74; 9.32)	8.78 (8.55; 9.06)	<0.0001*
IL-12B	Interleukin-12 subunit beta	4.21 (3.87; 4.75)	3.82 (3.46; 4.13)	4.52 (4.08; 5.20)	4.25 (3.88; 4.78)	4.04 (3.61; 4.39)	<0.0001*
MMP-10	Matrix metalloproteinase-10 (SL-2)	6.02 (5.61; 6.38)	6.03 (5.59; 6.54)	6.09 (5.79; 6.47)	5.90 (5.59; 6.26)	5.97 (5.63; 6.36)	0.3347
IL-10	Interleukin-10	2.75 (2.45; 3.02)	2.70 (2.58; 2.94)	2.92 (2.68; 3.22)	2.76 (2.50; 3.06)	2.72 (2.46; 3.00)	0.1646
CCL23	C-C motif chemokine 23	9.72 (9.44; 10.09)	9.32 (9.02; 9.67)	9.92 (9.48; 10.17)	9.71 (9.49; 10.04)	9.79 (9.53; 10.08)	0.0224
CD5	T-cell surface glycoprotein CD5	4.87 (4.63; 5.10)	4.56 (4.48; 4.71)	5.00 (4.74; 5.22)	4.85 (4.70; 5.01)	4.72 (4.44; 4.93)	<0.0001*
MIP-1 α	Macrophage inflammatory protein-1alpha (C-C motif chemokine 3/CCL3)	5.20 (4.80; 5.57)	5.48 (5.08; 5.67)	5.61 (5.17; 6.05)	5.40 (5.19; 5.71)	5.43 (5.06; 5.74)	0.0035
Flt3L	Fms-related tyrosine kinase 3 ligand	8.70 (8.39; 9.02)	8.65 (8.54; 8.92)	9.22 (8.63; 9.38)	8.82 (8.48; 9.13)	8.88 (8.59; 9.18)	0.0002*
CXCL6	C-X-C motif chemokine 6	8.56 (8.16; 8.96)	8.29 (8.02; 8.71)	8.94 (8.27; 9.41)	8.65 (8.33; 9.01)	8.48 (8.09; 8.87)	0.0031
CXCL10	C-X-C motif chemokine 10 (IP-10)	8.24 (7.85; 8.71)	7.85 (7.40; 8.29)	8.57 (8.14; 8.88)	8.38 (7.82; 8.74)	8.23 (7.90; 8.73)	0.0470
EIF4EBP1	Eukaryotic translation initiation factor 4E-binding protein 1	7.14 (6.69; 7.66)	7.02 (6.58; 7.68)	7.45 (7.01; 7.85)	7.28 (6.83; 7.85)	7.13 (6.76; 7.62)	0.0889
SIRT2	SIR2-like protein 2	2.09 (1.86; 2.47)	2.1 (1.62; 2.38)	2.29 (1.95; 2.68)	2.21 (1.90; 2.49)	1.99 (1.83; 2.28)	0.0156

CCL28	C-C motif chemokine 28	1.42 (1.24; 1.70)	1.24 (0.97; 1.54)	1.44 (1.22; 1.68)	1.33 (1.16; 1.52)	1.46 (1.29; 1.75)	0.0012
DNER	Delta and Notch-like epidermal growth factor-related receptor	8.20 (7.98; 8.37)	8.18 (7.98; 8.31)	8.04 (7.90; 8.20)	8.09 (7.86; 8.25)	8.10 (7.92; 8.25)	0.0217
EN-RAGE	Protein S100-A12 (EN-RAGE)	5.04 (4.30; 5.74)	4.15 (3.90; 4.80)	5.15 (4.85; 5.68)	5.19 (4.44; 5.62)	4.85 (4.26; 5.46)	0.0116
CD40	CD40L receptor	9.73 (9.46; 9.99)	9.57 (9.45; 9.90)	9.93 (9.62; 10.22)	9.80 (9.61; 10.05)	9.77 (9.53; 10.01)	0.0076
FGF-19	Fibroblast growth factor 19	8.00 (7.34; 8.57)	8.32 (6.83; 8.93)	8.01 (7.18; 8.53)	7.85 (7.07; 8.43)	8.03 (7.21; 8.60)	0.4946
MCP-2	Monocyte chemoattractant protein 2 (MCP-2, CCL8)	8.77 (8.39; 9.18)	8.75 (8.05; 9.21)	8.83 (8.52; 9.33)	8.93 (8.59; 9.39)	8.86 (8.55; 9.33)	0.0887
Caspase-8	Caspase-8	2.08 (1.80; 2.40)	1.68 (1.49; 1.85)	2.27 (1.93; 2.79)	2.16 (1.83; 2.52)	1.99 (1.80; 2.36)	0.0005*
CCL25	C-C motif chemokine 25	6.22 (5.75; 6.59)	6.44 (6.13; 6.84)	6.48 (6.27; 6.81)	6.22 (5.75; 6.63)	6.34 (6.08; 6.65)	0.0046
CX3CL1	Fractalkine	5.80 (5.57; 6.07)	5.68 (5.27; 6.02)	5.73 (5.52; 5.97)	5.64 (5.41; 5.91)	5.69 (5.48; 5.94)	0.0975
TNFRSF9	Tumor necrosis factor receptor superfamily member 9	6.35 (6.06; 6.60)	5.90 (5.62; 6.21)	6.38 (6.14; 6.76)	6.14 (5.95; 6.34)	6.15 (5.87; 6.35)	<0.0001*
NT-3	Neurotrophin-3	1.65 (1.47; 1.92)	1.38 (1.25; 1.90)	1.70 (1.52; 1.84)	1.61 (1.40; 1.79)	1.58 (1.38; 1.81)	0.1324
TWEAK	Tumor necrosis factor (Ligand) superfamily, member 12 (TWEAK)	9.68 (9.48; 9.84)	9.36 (9.18; 9.62)	9.44 (9.19; 9.60)	9.44 (9.23; 9.67)	9.54 (9.28; 9.74)	<0.0001*
CCL20	C-C motif chemokine 20	4.83 (4.29; 5.32)	4.53 (4.24; 5.33)	5.47 (4.74; 6.86)	5.13 (4.53; 5.73)	4.76 (4.28; 5.35)	0.0004*
ST1A1	Sulfotransferase 1A1	2.25 (1.73; 2.82)	2.05 (1.58; 2.64)	2.17 (1.80; 3.21)	2.17 (1.69; 2.71)	2.06 (1.68; 2.73)	0.5197
STAMPB	STAM-binding protein	3.66 (3.44; 3.92)	3.62 (3.40; 3.84)	3.78 (3.55; 4.24)	3.76 (3.49; 4.02)	3.60 (3.40; 3.91)	0.0583
ADA	Adenosine deaminase	3.61 (3.41; 3.85)	3.54 (3.19; 3.69)	3.60 (3.40; 3.78)	3.60 (3.38; 3.83)	3.55 (3.32; 3.84)	0.5811
TNF β	Tumor necrosis factor-beta (lymphotoxin-alpha/LT-alpha)	4.17 (3.89; 4.46)	3.87 (3.68; 4.07)	3.96 (3.71; 4.27)	4.00 (3.71; 4.20)	3.94 (3.66; 4.15)	<0.0001*
CSF-1	Macrophage colony-stimulating factor 1	7.95 (7.71; 8.11)	7.80 (7.67; 7.97)	8.15 (8.01; 8.28)	8.03 (7.91; 8.18)	7.93 (7.78; 8.06)	<0.0001*

Data are presented as median (25th percentile; 75th percentile). Differences between diabetes subgroups were analyzed with the Kruskal-Wallis Test.

MARD, moderate age-related diabetes; MOD, moderate obesity-related diabetes; SAID, severe autoimmune diabetes; SIDD, severe insulin-deficient diabetes; SIRD, severe insulin-resistant diabetes.

*Significant Tukey-Kramer *P* values after correction for multiple testing with the Bonferroni method ($0.05/74=0.0007$).

Table S3 - Unadjusted and adjusted pairwise comparisons of biomarkers of inflammation between diabetes subgroups

Biomarker	Cluster pairs		Model 1 (unadjusted)			Model 2 (adjusted)		
			β	SE	$P_{\text{Tukey-Kramer}}$	β	SE	$P_{\text{Tukey-Kramer}}$
CASP-8	SAID	SIDD	0.4	0.1	0.00065*	0.6	0.1	0.0002*
CASP-8	SAID	SIRD	-0.2	0.1	0.2074	-0.1	0.2	0.8812
CASP-8	SAID	MOD	-0.1	0.1	0.7797	-0.02	0.1	0.9994
CASP-8	SAID	MARD	0.02	0.1	0.9959	0.05	0.1	0.9896
CASP-8	SIDD	SIRD	-0.6	0.1	<0.0001*	-0.7	0.2	0.0005*
CASP-8	SIDD	MOD	-0.5	0.1	<0.0001*	-0.6	0.1	0.0001*
CASP-8	SIDD	MARD	-0.4	0.1	0.0006*	-0.5	0.1	0.0005*
CASP-8	SIRD	MOD	0.1	0.1	0.6035	0.1	0.1	0.8514
CASP-8	SIRD	MARD	0.2	0.1	0.0805	0.2	0.1	0.5680
CASP-8	MOD	MARD	0.1	0.1	0.3737	0.07	0.08	0.9199
CCL11	SAID	SIDD	-0.1	0.2	0.9959	0.1	0.1	0.9644
CCL11	SAID	SIRD	-0.3	0.1	0.0323	-0.2	0.1	0.5733
CCL11	SAID	MOD	0.01	0.1	0.9989	-0.03	0.09	0.9983
CCL11	SAID	MARD	-0.2	0.1	0.0044	-0.09	0.09	0.8280
CCL11	SIDD	SIRD	-0.2	0.2	0.7877	-0.3	0.2	0.4520
CCL11	SIDD	MOD	0.1	0.2	0.9877	-0.1	0.1	0.9150
CCL11	SIDD	MARD	-0.2	0.2	0.8489	-0.2	0.1	0.6891
CCL11	SIRD	MOD	0.3	0.1	0.0064	0.2	0.1	0.4433
CCL11	SIRD	MARD	0.03	0.1	0.9933	0.1	0.1	0.8562
CCL11	MOD	MARD	-0.2	0.1	<0.0001*	-0.07	0.07	0.8875
CCL20	SAID	SIDD	0.2	0.2	0.8355	0.3	0.3	0.8270
CCL20	SAID	SIRD	-0.8	0.2	0.0042	-0.7	0.3	0.1862
CCL20	SAID	MOD	-0.3	0.1	0.1121	-0.4	0.2	0.3233

CCL20	SAID	MARD	-0.1	0.1	0.9623			-0.5	0.2	0.1337	
CCL20	SIDD	SIRD	-1	0.3	0.0039			-1.0	0.4	0.0789	
CCL20	SIDD	MOD	-0.6	0.2	0.0950			-0.7	0.3	0.1675	
CCL20	SIDD	MARD	-0.3	0.2	0.6058			-0.8	0.3	0.0834	
CCL20	SIRD	MOD	0.5	0.2	0.2606			0.4	0.3	0.6749	
CCL20	SIRD	MARD	0.7	0.2	0.0203			0.3	0.3	0.8896	
CCL20	MOD	MARD	0.2	0.1	0.4616			-0.1	0.2	0.9854	
CD5	SAID	SIDD	0.2	0.1	0.1396			0.2	0.1	0.2530	
CD5	SAID	SIRD	-0.1	0.1	0.2334			-0.2	0.1	0.3363	
CD5	SAID	MOD	-0.004	0.04	1.0000			-0.04	0.06	0.9717	
CD5	SAID	MARD	0.1	0.04	0.0678			-0.02	0.07	0.9990	
CD5	SIDD	SIRD	-0.3	0.1	0.0045			-0.4	0.1	0.0148	
CD5	SIDD	MOD	-0.2	0.1	0.0966			-0.2	0.1	0.0928	
CD5	SIDD	MARD	-0.1	0.1	0.8348			-0.2	0.1	0.1680	
CD5	SIRD	MOD	0.1	0.1	0.1696			0.1	0.08	0.3020	
CD5	SIRD	MARD	0.3	0.1	0.0002*			0.2	0.08	0.2277	
CD5	MOD	MARD	0.1	0.01	0.0065			0.02	0.05	0.9932	
CDCP1	SAID	SIDD	-0.2	0.2	0.8718			0.3	0.1	0.1609	
CDCP1	SAID	SIRD	-0.7	0.1	<0.0001*			0.03	0.2	0.9997	
CDCP1	SAID	MOD	-0.5	0.1	<0.0001*			-0.06	0.1	0.9792	
CDCP1	SAID	MARD	-0.6	0.1	<0.0001*			-0.1	0.1	0.8711	
CDCP1	SIDD	SIRD	-0.5	0.2	0.1380			-0.3	0.2	0.5294	
CDCP1	SIDD	MOD	-0.3	0.2	0.7301			-0.4	0.1	0.0624	
CDCP1	SIDD	MARD	-0.4	0.2	0.4545			-0.4	0.1	0.0329	
CDCP1	SIRD	MOD	0.3	0.1	0.1490			-0.09	0.1	0.9632	
CDCP1	SIRD	MARD	0.2	0.1	0.5046			-0.1	0.1	0.8831	
CDCP1	MOD	MARD	-0.1	0.1	0.7367			-0.04	0.09	0.9872	
CSF-1	SAID	SIDD	0.1	0.1	0.3773			0.2	0.09	0.2555	

CSF-1	SAID	SIRD	-0.2	0.04	<0.0001*			-0.1	0.07	0.2886	
CSF-1	SAID	MOD	-0.1	0.02	0.0050			-0.07	0.05	0.6300	
CSF-1	SAID	MARD	0.0001	0.03	1.0000			-0.04	0.05	0.9409	
CSF-1	SIDD	SIRD	-0.4	0.1	0.0001*			-0.3	0.1	0.0109	
CSF-1	SIDD	MOD	-0.3	0.1	0.0035			-0.2	0.08	0.0262	
CSF-1	SIDD	MARD	-0.1	0.1	0.3252			-0.2	0.08	0.0771	
CSF-1	SIRD	MOD	0.1	0.04	0.2060			0.07	0.05	0.6435	
CSF-1	SIRD	MARD	0.2	0.04	<0.0001*			0.1	0.06	0.3340	
CSF-1	MOD	MARD	0.1	0.04	<0.0001*			0.03	0.04	0.9330	
CST5	SAID	SIDD	0.2	0.1	0.6746			0.2	0.1	0.7605	
CST5	SAID	SIRD	-0.1	0.1	0.7797			-0.2	0.15	0.5814	
CST5	SAID	MOD	0.2	0.1	0.0791			0.1	0.09	0.6914	
CST5	SAID	MARD	-0.1	0.1	0.8100			0.005	0.1	1.0000	
CST5	SIDD	SIRD	-0.3	0.2	0.2999			-0.4	0.2	0.2134	
CST5	SIDD	MOD	0	0.1	0.9999			-0.06	0.2	0.9935	
CST5	SIDD	MARD	-0.3	0.1	0.3178			-0.2	0.2	0.7742	
CST5	SIRD	MOD	0.3	0.1	0.0294			0.3	0.1	0.0316	
CST5	SIRD	MARD	0.04	0.1	0.9902			0.2	0.1	0.3721	
CST5	MOD	MARD	-0.2	0.1	0.0002*			-0.1	0.08	0.5909	
CXCL9	SAID	SIDD	0.3	0.2	0.6490			0.4	0.2	0.5931	
CXCL9	SAID	SIRD	-0.3	0.2	0.4362			-0.2	0.2	0.8664	
CXCL9	SAID	MOD	0.2	0.1	0.3794			0.1	0.1	0.8937	
CXCL9	SAID	MARD	-0.2	0.1	0.4334			0.05	0.2	0.9974	
CXCL9	SIDD	SIRD	-0.6	0.3	0.1453			-0.6	0.3	0.2683	
CXCL9	SIDD	MOD	-0.1	0.2	0.9685			-0.2	0.2	0.8653	
CXCL9	SIDD	MARD	-0.5	0.2	0.1789			-0.3	0.2	0.6981	
CXCL9	SIRD	MOD	0.5	0.1	0.0147			0.3	0.2	0.2333	
CXCL9	SIRD	MARD	0.1	0.1	0.9756			0.3	0.2	0.5680	
CXCL9	MOD	MARD	-0.4	0.1	0.0001*			-0.08	0.1	0.9556	

EN-RAGE	SAID	SIDD	0.6	0.2	0.0143	0.7	0.2	0.0143
EN-RAGE	SAID	SIRD	-0.1	0.2	0.9417	-0.3	0.3	0.7567
EN-RAGE	SAID	MOD	0.1	0.1	0.9982	-0.2	0.1	0.8716
EN-RAGE	SAID	MARD	0.2	0.1	0.6270	-0.1	0.2	0.9458
EN-RAGE	SIDD	SIRD	-0.8	0.2	0.0067	-1.0	0.3	0.0049
EN-RAGE	SIDD	MOD	-0.7	0.2	0.0044	-0.9	0.2	0.0005*
EN-RAGE	SIDD	MARD	-0.5	0.2	0.0946	-0.8	0.2	0.0010
EN-RAGE	SIRD	MOD	0.1	0.2	0.9777	0.1	0.2	0.9497
EN-RAGE	SIRD	MARD	0.3	0.2	0.3242	0.2	0.2	0.9074
EN-RAGE	MOD	MARD	0.2	0.1	0.2648	0.04	0.1	0.9990
FGF-21	SAID	SIDD	-0.1	0.5	0.9999	0.9	0.6	0.5317
FGF-21	SAID	SIRD	-2.1	0.3	<0.0001	-0.09	0.4	0.9996
FGF-21	SAID	MOD	-1.4	0.2	<0.0001*	-0.2	0.3	0.9235
FGF-21	SAID	MARD	-1.4	0.2	<0.0001*	-0.3	0.3	0.8145
FGF-21	SIDD	SIRD	-2.1	0.5	0.0006*	-0.9	0.6	0.5569
FGF-21	SIDD	MOD	-1.3	0.5	0.0614	-1.1	0.6	0.2777
FGF-21	SIDD	MARD	-1.3	0.5	0.0535	-1.2	0.6	0.2160
FGF-21	SIRD	MOD	0.8	0.2	0.0116	-0.1	0.3	0.9915
FGF-21	SIRD	MARD	0.7	0.2	0.0073	-0.2	0.3	0.9613
FGF-21	MOD	MARD	-0.009	0.2	1.0000	-0.08	0.2	0.9966
FGF-23	SAID	SIDD	0.2	0.1	0.1238	0.2	0.1	0.4951
FGF-23	SAID	SIRD	-0.3	0.1	0.0297	-0.1	0.1	0.8394
FGF-23	SAID	MOD	0.02	0.1	0.9898	0.09	0.07	0.7488
FGF-23	SAID	MARD	0.1	0.04	0.7723	0.06	0.07	0.8984
FGF-23	SIDD	SIRD	-0.5	0.1	0.0006*	-0.3	0.2	0.2820
FGF-23	SIDD	MOD	-0.2	0.1	0.2241	-0.09	0.1	0.9368
FGF-23	SIDD	MARD	-0.2	0.1	0.3612	-0.1	0.1	0.8557
FGF-23	SIRD	MOD	0.3	0.1	0.0147	0.2	0.1	0.2944

FGF-23	SIRD	MARD	0.3	0.1	0.0040		0.2	0.1	0.4405	
FGF-23	MOD	MARD	0.03	0.04	0.9707		-0.02	0.07	0.9965	
Flt3L	SAID	SIDD	-0.01	0.2	1		0.2	0.1	0.5266	
Flt3L	SAID	SIRD	-0.4	0.1	0.0005*		-0.01	0.1	1.0000	
Flt3L	SAID	MOD	-0.1	0.1	0.2505		0.03	0.09	0.9972	
Flt3L	SAID	MARD	-0.2	0.06	0.0026		0.06	0.09	0.9671	
Flt3L	SIDD	SIRD	-0.4	0.2	0.1148		-0.2	0.2	0.6684	
Flt3L	SIDD	MOD	-0.1	0.1	0.9021		-0.2	0.1	0.6387	
Flt3L	SIDD	MARD	-0.2	0.1	0.5005		-0.2	0.1	0.7695	
Flt3L	SIRD	MOD	0.3	0.1	0.0354		0.04	0.1	0.9954	
Flt3L	SIRD	MARD	0.2	0.1	0.3761		0.07	0.1	0.9714	
Flt3L	MOD	MARD	-0.1	0.1	0.3359		0.03	0.08	0.9947	
HGF	SAID	SIDD	0.1	0.1	0.9941		0.2	0.1	0.4593	
HGF	SAID	SIRD	-0.5	0.1	<0.0001*		0.03	0.1	0.9996	
HGF	SAID	MOD	-0.4	0.1	<0.0001*		-0.06	0.08	0.9261	
HGF	SAID	MARD	-0.1	0.1	0.1169		-0.07	0.08	0.9130	
HGF	SIDD	SIRD	-0.5	0.1	0.0011		-0.2	0.2	0.7373	
HGF	SIDD	MOD	-0.4	0.1	0.0090		-0.3	0.1	0.1839	
HGF	SIDD	MARD	-0.2	0.1	0.5284		-0.3	0.1	0.1727	
HGF	SIRD	MOD	0.1	0.1	0.5542		-0.09	0.09	0.8625	
HGF	SIRD	MARD	0.3	0.1	<0.0001*		-0.09	0.1	0.8627	
HGF	MOD	MARD	0.2	0.04	<0.0001*		0.003	0.07	1.0000	
IL-6	SAID	SIDD	0.04	0.2	0.9998		0.6	0.2	0.0181	
IL-6	SAID	SIRD	-1.1	0.1	<0.0001*		-0.4	0.2	0.2805	
IL-6	SAID	MOD	-0.7	0.1	<0.0001*		-0.2	0.1	0.5610	
IL-6	SAID	MARD	-0.5	0.1	<0.0001*		-0.3	0.1	0.1295	
IL-6	SIDD	SIRD	-1.1	0.2	<0.0001*		-0.9	0.2	0.0008	
IL-6	SIDD	MOD	-0.7	0.2	0.0140		-0.8	0.2	0.0008	

IL-6	SIDD	MARD	-0.5	0.2	0.1696			-0.9	0.2	0.0001*	
IL-6	SIRD	MOD	0.4	0.1	0.0097			0.2	0.1	0.6858	
IL-6	SIRD	MARD	0.6	0.1	<0.0001*			0.09	0.1	0.9814	
IL-6	MOD	MARD	0.2	0.1	0.116			-0.1	0.1	0.8598	
IL_10RB	SAID	SIDD	0.1	0.1	0.5045			0.2	0.1	0.3976	
IL_10RB	SAID	SIRD	-0.2	0.1	0.0002*			-0.04	0.09	0.9893	
IL_10RB	SAID	MOD	-0.1	0.04	0.247			0.01	0.06	0.9997	
IL_10RB	SAID	MARD	0.02	0.03	0.9796			0.02	0.06	0.9987	
IL_10RB	SIDD	SIRD	-0.4	0.1	0.0006*			-0.2	0.1	0.3677	
IL_10RB	SIDD	MOD	-0.2	0.1	0.0738			-0.2	0.1	0.4603	
IL_10RB	SIDD	MARD	-0.1	0.1	0.6401			-0.2	0.1	0.4945	
IL_10RB	SIRD	MOD	0.2	0.1	0.0266			0.05	0.07	0.9376	
IL_10RB	SIRD	MARD	0.3	0.1	<0.0001*			0.06	0.07	0.9276	
IL_10RB	MOD	MARD	0.1	0.02	0.0229			0.005	0.05	1.0000	
IL_12B	SAID	SIDD	0.5	0.1	0.0055			0.4	0.2	0.1687	
IL_12B	SAID	SIRD	-0.3	0.1	0.2206			-0.3	0.2	0.4858	
IL_12B	SAID	MOD	0.009	0.1	1.0000			0.06	0.1	0.9886	
IL_12B	SAID	MARD	0.3	0.1	0.0181			0.2	0.1	0.6559	
IL_12B	SIDD	SIRD	-0.8	0.2	<0.0001*			-0.7	0.2	0.0212	
IL_12B	SIDD	MOD	-0.5	0.1	0.0047			-0.3	0.2	0.3056	
IL_12B	SIDD	MARD	-0.3	0.1	0.3611			-0.2	0.2	0.6996	
IL_12B	SIRD	MOD	0.3	0.1	0.1610			0.4	0.2	0.1241	
IL_12B	SIRD	MARD	0.5	0.1	0.0005*			0.5	0.2	0.0323	
IL_12B	MOD	MARD	0.2	0.1	0.0084			0.1	0.1	0.8350	
IL_17C	SAID	SIDD	0.2	0.1	0.1642			0.3	0.1	0.0624	
IL_17C	SAID	SIRD	-0.1	0.1	0.8673			-0.2	0.2	0.8481	
IL_17C	SAID	MOD	-0.04	0.1	0.9575			-0.05	0.1	0.9903	
IL_17C	SAID	MARD	0.04	0.1	0.975			-0.2	0.1	0.4189	

IL_17C	SIDD	SIRD	-0.3	0.1	0.0488			-0.4	0.2	0.0546	
IL_17C	SIDD	MOD	-0.3	0.1	0.0387			-0.3	0.1	0.0285	
IL_17C	SIDD	MARD	-0.2	0.1	0.4123			-0.5	0.1	0.0008	
IL_17C	SIRD	MOD	0.04	0.1	0.9915			0.1	0.1	0.8957	
IL_17C	SIRD	MARD	0.1	0.1	0.6042			-0.02	0.1	0.9999	
IL_17C	MOD	MARD	0.1	0.1	0.6940			-0.1	0.1	0.6421	
IL_18R1	SAID	SIDD	-0.2	0.2	0.8690			0.06	0.2	0.9977	
IL_18R1	SAID	SIRD	-0.3	0.1	0.0117			-0.1	0.1	0.7529	
IL_18R1	SAID	MOD	-0.3	0.1	<0.0001*			-0.2	0.08	0.0907	
IL_18R1	SAID	MARD	0.01	0.1	0.9980			-0.08	0.08	0.8667	
IL_18R1	SIDD	SIRD	-0.1	0.2	0.9950			-0.2	0.2	0.8392	
IL_18R1	SIDD	MOD	-0.1	0.2	0.9879			-0.3	0.2	0.5793	
IL_18R1	SIDD	MARD	0.2	0.2	0.8163			-0.1	0.2	0.9368	
IL_18R1	SIRD	MOD	-0.01	0.1	0.9995			-0.06	0.1	0.9796	
IL_18R1	SIRD	MARD	0.3	0.1	0.0017			0.07	0.1	0.9583	
IL_18R1	MOD	MARD	0.3	0.1	<0.0001*			0.1	0.07	0.3791	
MCP_3	SAID	SIDD	-0.1	0.1	0.9104			0.07	0.1	0.9864	
MCP_3	SAID	SIRD	-0.5	0.1	<0.0001*			-0.1	0.2	0.8723	
MCP_3	SAID	MOD	-0.3	0.1	0.0058			-0.07	0.1	0.9539	
MCP_3	SAID	MARD	-0.2	0.1	0.1182			-0.1	0.1	0.8608	
MCP_3	SIDD	SIRD	-0.4	0.2	0.1400			-0.2	0.2	0.7216	
MCP_3	SIDD	MOD	-0.1	0.1	0.8605			-0.1	0.1	0.8072	
MCP_3	SIDD	MARD	-0.04	0.1	0.9975			-0.2	0.1	0.6727	
MCP_3	SIRD	MOD	0.2	0.1	0.1602			0.08	0.1	0.9671	
MCP_3	SIRD	MARD	0.3	0.1	0.0097			0.05	0.1	0.9940	
MCP_3	MOD	MARD	0.1	0.1	0.5319			-0.03	0.08	0.9974	
OPG	SAID	SIDD	0.1	0.1	0.9558			0.3	0.1	0.0790	
OPG	SAID	SIRD	-0.4	0.1	<0.0001*			-0.06	0.1	0.9908	

OPG	SAID	MOD	-0.2	0.1	0.0125			-0.02	0.08	0.9984	
OPG	SAID	MARD	-0.2	0.1	0.0123			0.08	0.08	0.8283	
OPG	SIDD	SIRD	-0.5	0.1	0.0053			-0.4	0.1	0.1243	
OPG	SIDD	MOD	-0.3	0.1	0.165			-0.3	0.1	0.0469	
OPG	SIDD	MARD	-0.3	0.1	0.1925			-0.2	0.1	0.3294	
OPG	SIRD	MOD	0.2	0.1	0.1159			0.03	0.1	0.9967	
OPG	SIRD	MARD	0.2	0.1	0.0624			0.1	0.1	0.6546	
OPG	MOD	MARD	0.01	0.04	0.9989			0.1	0.07	0.5158	
OSM	SAID	SIDD	-0.1	0.2	0.9995			0.3	0.2	0.7437	
OSM	SAID	SIRD	-0.4	0.2	0.0777			-0.3	0.2	0.7604	
OSM	SAID	MOD	-0.4	0.1	0.0076			-0.1	0.1	0.8439	
OSM	SAID	MARD	0.1	0.1	0.8790			-0.1	0.1	0.8982	
OSM	SIDD	SIRD	-0.4	0.3	0.6510			-0.6	0.3	0.2945	
OSM	SIDD	MOD	-0.3	0.2	0.6804			-0.4	0.2	0.3070	
OSM	SIDD	MARD	0.1	0.2	0.9689			-0.4	0.2	0.3513	
OSM	SIRD	MOD	0.05	0.1	0.9975			0.1	0.2	0.9593	
OSM	SIRD	MARD	0.5	0.1	0.0052			0.1	0.2	0.9458	
OSM	MOD	MARD	0.5	0.1	<0.0001*			0.02	0.1	0.9999	
SCF	SAID	SIDD	0.1	0.1	0.8974			-0.1	0.1	0.9482	
SCF	SAID	SIRD	0.3	0.1	0.0032			-0.2	0.1	0.5579	
SCF	SAID	MOD	0.4	0.1	<0.0001*			0.1	0.07	0.4192	
SCF	SAID	MARD	0.1	0.04	0.1193			0.04	0.07	0.9678	
SCF	SIDD	SIRD	0.1	0.1	0.8548			-0.09	0.1	0.9827	
SCF	SIDD	MOD	0.2	0.1	0.3394			0.2	0.1	0.4614	
SCF	SIDD	MARD	-0.004	0.1	1.0000			0.1	0.1	0.8302	
SCF	SIRD	MOD	0.1	0.1	0.6342			0.3	0.1	0.0187	
SCF	SIRD	MARD	-0.1	0.1	0.2559			0.2	0.1	0.1811	
SCF	MOD	MARD	-0.3	0.1	<0.0001*			-0.08	0.07	0.7821	

TNFB	SAID	SIDD	0.3	0.1	0.0157		0.2	0.1	0.4563	
TNFB	SAID	SIRD	0.2	0.1	0.1536		0.1	0.1	0.7571	
TNFB	SAID	MOD	0.2	0.1	0.0078		0.1	0.08	0.3918	
TNFB	SAID	MARD	0.3	0.1	<0.0001*		0.1	0.08	0.3659	
TNFB	SIDD	SIRD	-0.1	0.1	0.9086		-0.02	0.1	0.9999	
TNFB	SIDD	MOD	-0.1	0.1	0.7033		-0.04	0.1	0.9964	
TNFB	SIDD	MARD	-0.033	0.1	0.9959		-0.03	0.1	0.9986	
TNFB	SIRD	MOD	-0.01	0.1	0.9996		-0.02	0.1	0.9998	
TNFB	SIRD	MARD	0.1	0.1	0.9336		-0.01	0.1	1.0000	
TNFB	MOD	MARD	0.1	0.04	0.3621		0.01	0.06	1.0000	
TNFRSF9	SAID	SIDD	0.4	0.1	0.0018		0.4	0.1	0.0142	
TNFRSF9	SAID	SIRD	-0.1	0.1	0.5317		-0.1	0.1	0.8280	
TNFRSF9	SAID	MOD	0.2	0.1	0.0307		0.1	0.08	0.3989	
TNFRSF9	SAID	MARD	0.2	0.1	0.0260		0.1	0.08	0.4157	
TNFRSF9	SIDD	SIRD	-0.5	0.1	<0.0001*		-0.5	0.1	0.0054	
TNFRSF9	SIDD	MOD	-0.2	0.1	0.1405		-0.2	0.1	0.2240	
TNFRSF9	SIDD	MARD	-0.2	0.1	0.1803		-0.2	0.1	0.2599	
TNFRSF9	SIRD	MOD	0.3	0.1	0.0004*		0.3	0.09	0.0261	
TNFRSF9	SIRD	MARD	0.3	0.1	0.0004*		0.3	0.09	0.0385	
TNFRSF9	MOD	MARD	0.008	0.04	0.9997		0.005	0.06	1.0000	
TWEAK	SAID	SIDD	0.3	0.1	0.0241		0.1	0.1	0.4930	
TWEAK	SAID	SIRD	0.2	0.1	0.0012		-0.2	0.1	0.4189	
TWEAK	SAID	MOD	0.2	0.04	<0.0001*		0.004	0.06	1.0000	
TWEAK	SAID	MARD	0.2	0.04	0.0022		-0.02	0.06	0.9980	
TWEAK	SIDD	SIRD	-0.1	0.1	0.9821		-0.3	0.1	0.0669	
TWEAK	SIDD	MOD	-0.1	0.1	0.9387		-0.1	0.1	0.5328	
TWEAK	SIDD	MARD	-0.1	0.1	0.6215		-0.2	0.1	0.3850	
TWEAK	SIRD	MOD	-0.01	0.1	0.9986		0.2	0.08	0.1648	
TWEAK	SIRD	MARD	-0.1	0.1	0.6701		0.1	0.08	0.3439	

TWEAK	MOD	MARD	-0.06	0.04		0.5787			-0.02	0.05	0.9930	
uPA	SAID	SIDD	0.2	0.1		0.0091			0.2	0.1	0.0288	
uPA	SAID	SIRD	-0.1	0.1		0.1524			0.005	0.1	1.0000	
uPA	SAID	MOD	0.03	0.04		0.976			0.07	0.06	0.7939	
uPA	SAID	MARD	0.01	0.04		0.9989			0.04	0.06	0.9621	
uPA	SIDD	SIRD	-0.4	0.1		<0.0001*			-0.25	0.1	0.1375	
uPA	SIDD	MOD	-0.2	0.1		0.0167			-0.2	0.08	0.1754	
uPA	SIDD	MARD	-0.2	0.1		0.0069			-0.2	0.08	0.0876	
uPA	SIRD	MOD	0.2	0.1		0.0211			0.06	0.07	0.8728	
uPA	SIRD	MARD	0.1	0.04		0.0424			0.04	0.07	0.9837	
uPA	MOD	MARD	-0.01	0.03		0.9939			-0.03	0.05	0.9836	

Only biomarkers with at least one significant pairwise comparison are reported.

Model 2: adjustment for age at diagnosis, BMI, HbA1c, HOMA2-IR, HOMA2-B and glutamic acid decarboxylase antibodies.

Beta coefficients estimate the mean difference between cluster 1 and cluster 2 within each cluster pair (in NPX as biomarker unit).

Bold print indicates significant differences at $P < 0.05$ after correction for pairwise multiple comparisons using the Tukey-Kramer test.

* indicates significant differences at $P < 0.0007$ after additional Bonferroni correction ($0.05/74 = 0.0007$).

CASP-8, caspase-8; CCL11, eotaxin; CCL20/C-C motif chemokine 20; CD5, T-cell surface glycoprotein CD5; CDCP1, CUB domain-containing protein 1; CSF-1, macrophage colony-stimulating factor 1; CST5, cystatin D; CXCL9, C-X-C motif chemokine 9; EN-RAGE, protein S100-A12; FGF21, fibroblast growth factor 21; FGF-23, fibroblast growth factor 23; Flt3L, Fms-related tyrosine kinase 3 ligand; HGF, hepatocyte growth factor; IL-6, interleukin-6; IL-10RB, interleukin-10 receptor subunit beta; IL-12B, interleukin-12 subunit beta; IL-17C, interleukin-17C; IL-18R1,

interleukin-18 receptor 1; MARD, mild age-related diabetes ; MCP-3, monocyte chemotactic protein 3; MOD, mild obesity-related diabetes; OPG, osteoprotegerin; OSM, oncostatin-M; SAID, severe autoimmune diabetes; SCF, stem cell factor; SE, standard error; SIDDD, severe insulin-deficient diabetes; SIRD, severe insulin resistant diabetes; TNFB, tumor necrosis factor-beta; TNFRSF9, tumor necrosis factor receptor superfamily member 9; TWEAK, tumor necrosis factor (Ligand) superfamily, member 12; uPA, urokinase-type plasminogen activator.

Table S4 - Spearman correlations between biomarkers of inflammation and variables used in the definition of diabetes subgroups

Biomarker	Age		BMI		HbA1c		HOMA2-B		HOMA2-IR		GADA	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
CASP-8	0.004	0.941	0.119	0.016	0.032	0.515	0.154	0.002	0.073	0.135	-0.039	0.434
CCL11	0.310	<0.0001	0.035	0.475	0.040	0.411	0.060	0.221	0.044	0.371	-0.089	0.067
CCL20	-0.045	0.353	0.201	<0.0001	0.111	0.022	0.160	0.001	0.211	<0.0001	-0.060	0.219
CD5	-0.169	0.001	0.041	0.406	0.023	0.635	0.092	0.063	0.071	0.152	0.006	0.899
CDCP1	0.504	<0.0001	0.399	<0.0001	0.136	0.006	0.201	<0.0001	0.419	<0.0001	-0.331	<0.0001
CSF-1	-0.029	0.558	0.295	<0.0001	0.035	0.479	0.214	<0.0001	0.274	<0.0001	-0.124	0.011
CST5	0.145	0.003	-0.096	0.051	-0.020	0.69	-0.037	0.455	-0.059	0.234	0.032	0.514
CXCL9	0.340	<0.0001	0.055	0.267	-0.038	0.441	0.098	0.047	0.028	0.575	-0.034	0.488
EN-RAGE	-0.100	0.041	0.069	0.157	0.010	0.839	0.073	0.141	0.017	0.731	0.014	0.762
FGF-21	0.354	<0.0001	0.419	<0.0001	0.038	0.446	0.289	<0.0001	0.485	<0.0001	-0.354	<0.0001
FGF-23	0.004	0.929	0.078	0.115	-0.062	0.206	0.183	0.0002	0.109	0.027	0.010	0.839
Flt3L	0.390	<0.0001	0.223	<0.0001	0.081	0.100	0.133	0.007	0.284	<0.0001	-0.165	0.001
HGF	0.110	0.025	0.461	<0.0001	0.070	0.157	0.329	<0.0001	0.467	<0.0001	-0.235	<0.0001
IL-6	0.260	<0.0001	0.544	<0.0001	0.133	0.007	0.353	<0.0001	0.480	<0.0001	-0.319	<0.0001
IL-10RB	0.017	0.736	0.230	<0.0001	0.082	0.096	0.172	0.0004	0.313	<0.0001	-0.100	0.042
IL-12B	-0.061	0.215	0.151	0.002	-0.025	0.611	0.115	0.020	0.101	0.039	0.047	0.339
IL-17C	-0.138	0.004	0.100	0.041	0.090	0.064	0.078	0.113	0.073	0.137	0.038	0.439
IL-18R1	-0.029	0.559	0.285	<0.0001	0.250	<0.0001	0.030	0.539	0.332	<0.0001	-0.144	0.003
MCP-3	0.191	<0.0001	0.356	<0.0001	0.065	0.184	0.228	<0.0001	0.325	<0.0001	-0.223	<0.0001
OPG	0.340	<0.0001	0.253	<0.0001	0.080	0.104	0.186	0.0001	0.281	<0.0001	-0.208	<0.0001
OSM	-0.126	0.010	0.251	<0.0001	0.173	<0.0001	0.101	0.040	0.207	<0.0001	-0.093	0.057
SCF	-0.009	0.856	-0.333	<0.0001	-0.145	0.003	-0.171	0.0005	-0.370	<0.0001	0.180	<0.0001
TNFB	-0.217	<0.0001	-0.119	0.016	-0.034	0.495	-0.045	0.366	-0.132	0.007	0.197	<0.0001
TNFRSF9	0.011	0.831	0.012	0.805	-0.013	0.799	0.098	0.046	-0.001	0.981	0.110	0.025
TWEAK	-0.153	0.002	-0.266	<0.0001	-0.040	0.420	-0.137	0.005	-0.344	<0.0001	0.199	<0.0001
uPA	0.136	0.006	0.110	0.026	-0.026	0.593	0.141	0.004	0.125	0.011	-0.029	0.55

The table shows only the 26 biomarkers of inflammation with at least one significant pairwise cluster difference after adjustment for multiple testing with both Tukey-Kramer and Bonferroni corrections in either the unadjusted or in the adjusted model.

BMI, body mass index; CASP-8, caspase-8; CCL11, eotaxin; CCL20/C-C motif chemokine 20; CD5, T-cell surface glycoprotein CD5; CDCP1, CUB domain-containing protein 1; CSF-1, macrophage colony-stimulating factor 1; CST5, cystatin D; CXCL9, C-X-C motif chemokine 9; EN-RAGE, protein S100-A12; FGF21, fibroblast growth factor 21; FGF-23, fibroblast growth factor 23; Flt3L, Fms-related tyrosine kinase 3 ligand; GADA, glutamic acid decarboxylase antibodies; HGF, hepatocyte growth factor; HOMA-B, homeostasis model assessment of β -cell function; HOMA-IR, homeostasis model assessment of insulin resistance. IL-6, interleukin-6; IL-10RB, interleukin-10 receptor subunit beta; IL-12B, interleukin-12 subunit beta; IL-17C, interleukin-17C; IL-18R1, interleukin-18 receptor 1; MCP-3, monocyte chemotactic protein 3; OPG, osteoprotegerin; OSM, oncostatin-M; SCF, stem cell factor; TNFB, tumor necrosis factor-beta; TNFRSF9, tumor necrosis factor receptor superfamily member 9; TWEAK, tumor necrosis factor (ligand) superfamily, member 12; uPA, urokinase-type plasminogen activator.

Table S5 - Mendelian randomization results based on EN-RAGE (S100-A12) as exposure and diabetes and diabetes-related complications as outcomes

Outcome	IVW β (SE)	IVW <i>P</i> value	IV (SNP)
Type 2 diabetes	0.030 (0.027)	0.276	rs3014874 rs62143206
Type 2 diabetes with diabetic angiopathy	0.240 (0.216)	0.267	rs3014874 rs62143206
Type 2 diabetes with renal complications	0.279 (0.131)	0.033	rs3014874 rs62143206
Type 2 diabetes with diabetic retinopathy	-0.010 (0.091)	0.905	rs3014874 rs62143206
Type 2 diabetes with diabetic neuropathy	0.150 (0.148)	0.310	rs3014874 rs62143206
Type 1 diabetes	0.054 (0.058)	0.353	rs3014874 rs62143206
Type 1 diabetes with diabetic angiopathy	-0.073 (0.287)	0.797	rs3014874 rs62143206
Type 1 diabetes with renal complications	0.151 (0.159)	0.343	rs3014874 rs62143206
Type 1 diabetes with diabetic retinopathy	0.019 (0.112)	0.865	rs3014874 rs62143206
Type 1 diabetes with diabetic neuropathy	-0.136 (0.266)	0.607	rs62143206 rs62143206

IV, instrumental variable; IVW, inverse variance weighted random effects model; SE, standard error; SNP, single nucleotide polymorphism.

Definition of the diabetic complications in the FinnGen Biobank (<https://risteys.finnngen.fi/>):

-Diabetic angiopathy: peripheral circulatory complications; vascular diseases that are associated with diabetes mellitus.

-Renal complications: no further definition available.

-Diabetic retinopathy: ophthalmic complications; a chronic, pathological complication associated with diabetes mellitus, where retinal damages are incurred due to microaneurysms in the vasculature of the retina, progressively leading to abnormal blood vessel growth, and swelling and leaking of fluid from blood vessels, resulting in vision loss or blindness.

-Diabetic neuropathy: neurological complications; a chronic, pathological complication associated with diabetes mellitus, where nerve damages are incurred due to diabetic microvascular injury involving small blood vessels that supply these nerves, resulting in peripheral and/or autonomic nerve dysfunction.

Table S6 - Mendelian randomization results based on IL-6 as exposure and diabetes and diabetes-related complications as outcomes

Outcome	IVW β (SE)	IVW <i>P</i> value	IV (SNP)
Type 2 diabetes	0.097(0.089)	0.273	rs11872808 rs75892156
Type 2 diabetes with diabetic angiopathy	0.776 (0.810)	0.338	rs11872808 rs75892156
Type 2 diabetes with renal complications	0.330 (0.383)	0.388	rs11872808 rs75892156
Type 2 diabetes with diabetic retinopathy	0.533 (0.311)	0.087	rs11872808 rs75892156
Type 2 diabetes with diabetic neuropathy	0.544 (0.405)	0.179	rs11872808 rs75892156
Type 1 diabetes	0.076 (0.161)	0.633	rs11872808 rs75892156
Type 1 diabetes with diabetic angiopathy	-0.222 (0.633)	0.725	rs11872808 rs75892156
Type 1 diabetes with renal complications	-0.269 (0.415)	0.516	rs11872808 rs75892156
Type 1 diabetes with diabetic retinopathy	0.170 (0.261)	0.513	rs11872808 rs75892156
Type 1 diabetes with diabetic neuropathy	0.172 (0.485)	0.722	rs11872808 rs75892156

IV, instrumental variable ; IVW, inverse variance weighted random effects model; SE, standard error; SNP, single nucleotide polymorphism.

Definition of the diabetic complications in the FinnGen Biobank (<https://risteys.finnngen.fi/>):

-Diabetic angiopathy: peripheral circulatory complications; vascular diseases that are associated with diabetes mellitus.

-Renal complications: no further definition available.

-Diabetic retinopathy: ophthalmic complications; a chronic, pathological complication associated with diabetes mellitus, where retinal damages are incurred due to microaneurysms

in the vasculature of the retina, progressively leading to abnormal blood vessel growth, and swelling and leaking of fluid from blood vessels, resulting in vision loss or blindness.

-Diabetic neuropathy: neurological complications; a chronic, pathological complication associated with diabetes mellitus, where nerve damages are incurred due to diabetic microvascular injury involving small blood vessels that supply these nerves, resulting in peripheral and/or autonomic nerve dysfunction.

Table S7 - Mendelian randomization results based on diabetes and diabetes-related complications as exposures and EN-RAGE (S100-A12) as outcome

Exposure	Method	β (SE)	<i>P</i>	Number of SNPs (IV)	Pleiotropy test *
Type 2 diabetes	IVW	0.036 (0.089)	0.684	7	0.727
Type 2 diabetes with diabetic retinopathy	Wald	0.014 (0.090)	0.870	1	NA
Type 1 diabetes	IVW	0.001 (0.033)	0.972	7	0.703
Type 1 diabetes with diabetic angiopathy	Wald	-0.002 (0.026)	0.916	1	NA
Type 1 diabetes with renal complications	IVW	0.010 (0.021)	0.630	2	NA
Type 1 diabetes with diabetic retinopathy	IVW	-0.004 (0.030)	0.886	5	0.944
Type 1 diabetes with diabetic neuropathy	IVW	-0.015 (0.011)	0.161	4	0.947

* Pleiotropy *P* value represents the *P* value of the intercept of Egger's regression.

IV, instrumental variable; IVW, inverse variance weighted random effects model; NA, not applicable; SE, standard error; SNP, single nucleotide polymorphism.

Definition of the diabetic complications in the FinnGen Biobank (<https://risteys.finnngen.fi/>):

-Diabetic angiopathy: peripheral circulatory complications; vascular diseases that are associated with diabetes mellitus.

-Renal complications: no further definition available.

-Diabetic retinopathy: ophthalmic complications; a chronic, pathological complication associated with diabetes mellitus, where retinal damages are incurred due to microaneurysms in the vasculature of the retina, progressively leading to abnormal blood vessel growth, and swelling and leaking of fluid from blood vessels, resulting in vision loss or blindness.

-Diabetic neuropathy: neurological complications; a chronic, pathological complication associated with diabetes mellitus, where nerve damages are incurred due to diabetic microvascular injury involving small blood vessels that supply these nerves, resulting in peripheral and/or autonomic nerve dysfunction.

Table S8 - Mendelian randomization results based on diabetes and diabetes-related complications as exposures and IL-6 as outcome

Exposure	Method	β (SE)	<i>P</i>	Numbr of SNPs (IV)	Pleiotropy test *
Type 2 diabetes	IVW	0.047 (0.071)	0.510	7	0.406
Type 2 diabetes with diabetic retinopathy	Wald	-0.059 (0.090)	0.509	1	NA
Type 1 diabetes	IVW	-0.025 (0.033)	0.445	7	0.897
Type 1 diabetes with diabetic angiopathy	Wald	0.009 (0.026)	0.727	1	NA
Type 1 diabetes with renal complications	IVW	-0.020 (0.021)	0.333	2	NA
Type 1 diabetes with diabetic retinopathy	IVW	-0.046 (0.029)	0.119	5	0.267
Type 1 diabetes with diabetic neuropathy	IVW	0.006 (0.011)	0.565	4	0.329

* Pleiotropy *P* value represents the *P* value of the intercept of Egger's regression.

IV, instrumental variable; IVW, inverse variance weighted random effects model; NA, not applicable; SE, standard error; SNP, single nucleotide polymorphism.

Definition of the diabetic complications in the FinnGen Biobank (<https://risteys.finnngen.fi/>):

-Diabetic angiopathy: peripheral circulatory complications; vascular diseases that are associated with diabetes mellitus.

-Renal complications: no further definition available.

-Diabetic retinopathy: ophthalmic complications; a chronic, pathological complication associated with diabetes mellitus, where retinal damages are incurred due to microaneurysms in the vasculature of the retina, progressively leading to abnormal blood vessel growth, and swelling and leaking of fluid from blood vessels, resulting in vision loss or blindness.

-Diabetic neuropathy: neurological complications; a chronic, pathological complication associated with diabetes mellitus, where nerve damages are incurred due to diabetic microvascular injury involving small blood vessels that supply these nerves, resulting in peripheral and/or autonomic nerve dysfunction.

Fig. S1 – Study population

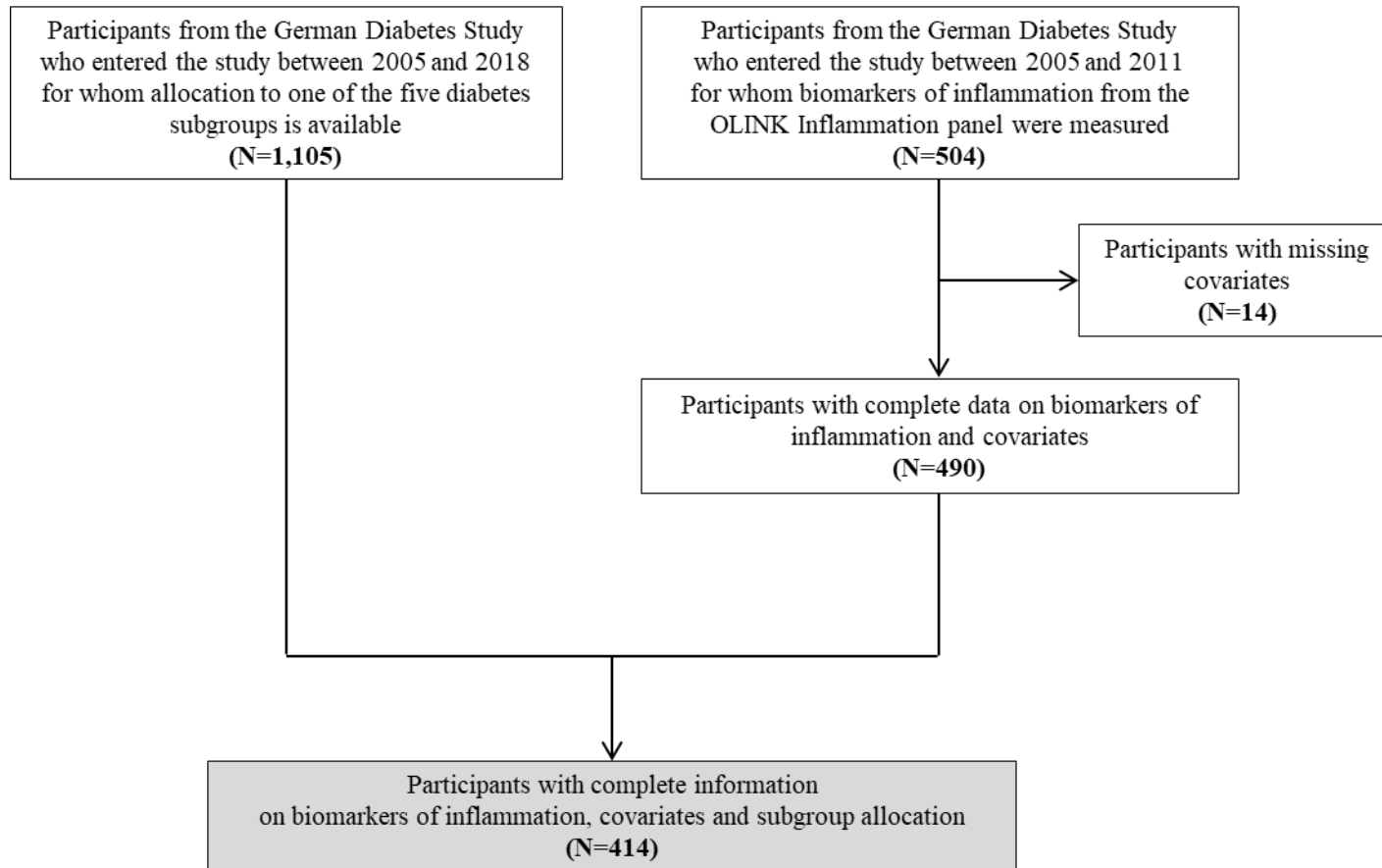
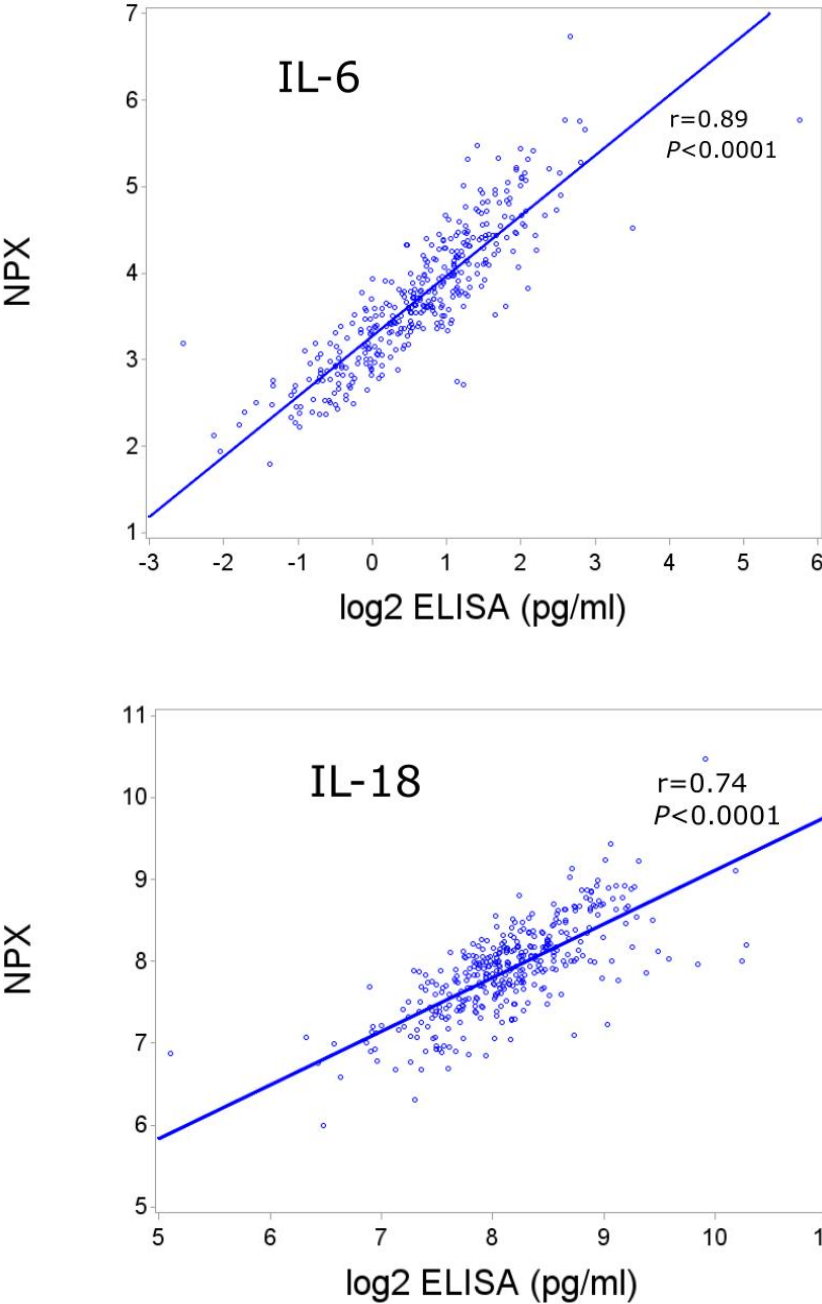


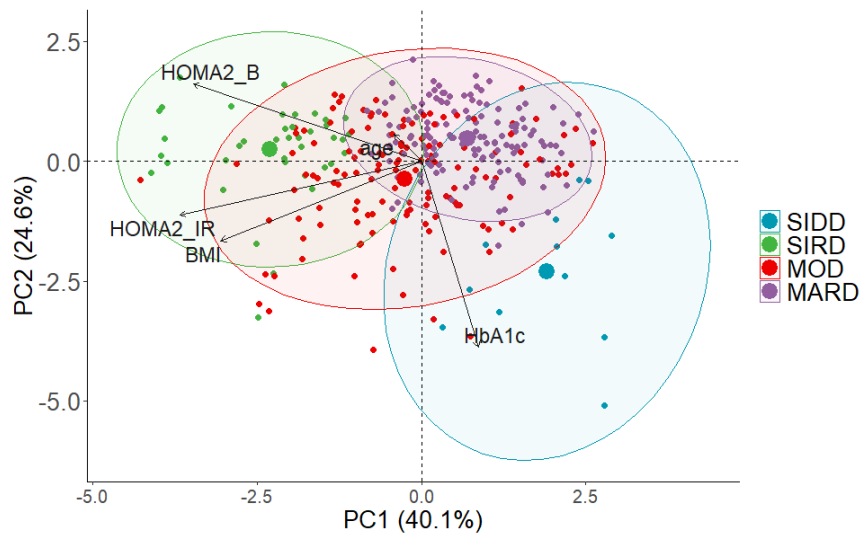
Fig. S2 – Correlation of IL-6 and IL-18 levels measured with ELISA and primer extension assay (PEA) technology in the German Diabetes Study



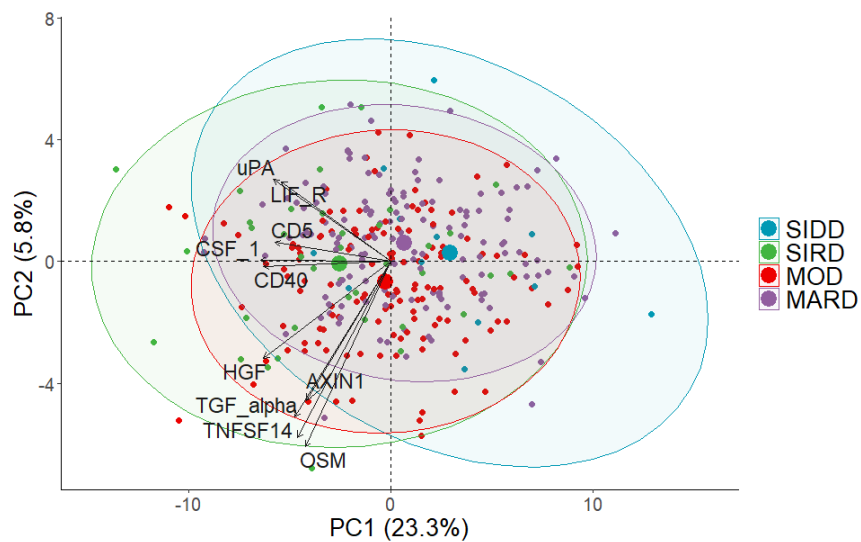
Correlations are estimated using Spearman correlation coefficients (r) and corresponding P values.

Fig. S3 - Principle component analysis based on clustering variables and biomarkers of inflammation

A



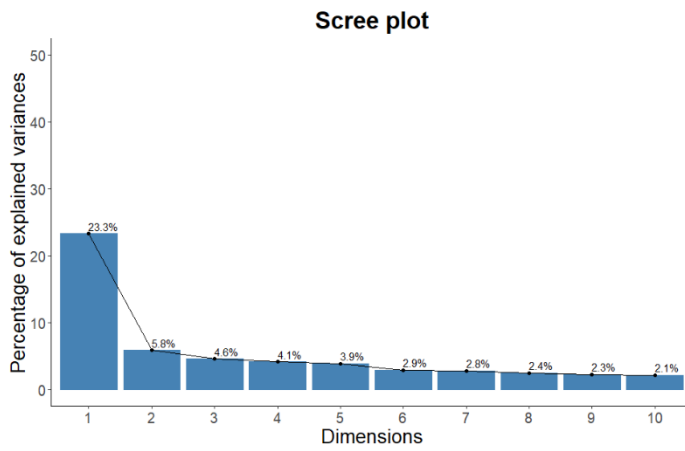
B



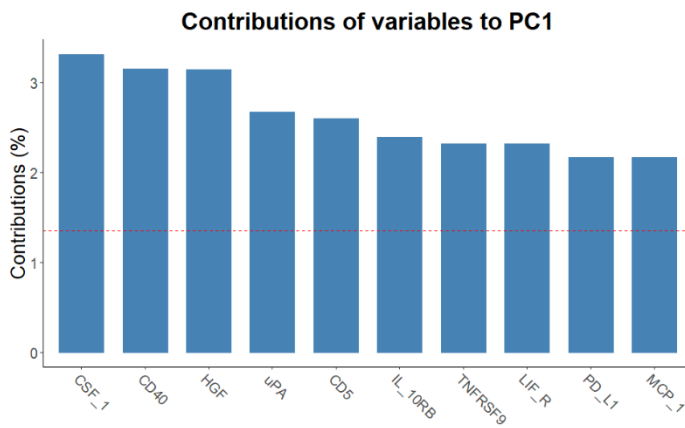
Principal component analysis (PCA) plot of the first two principal components (PC1 and PC2) based on clustering variables except GADA (A) or based on biomarkers of inflammation (B). Arrows indicate the variables with the most important contribution (highest values of \cos^2) to PC1 and PC2.

Fig. S4 - Contributions of biomarkers of inflammation to principal components

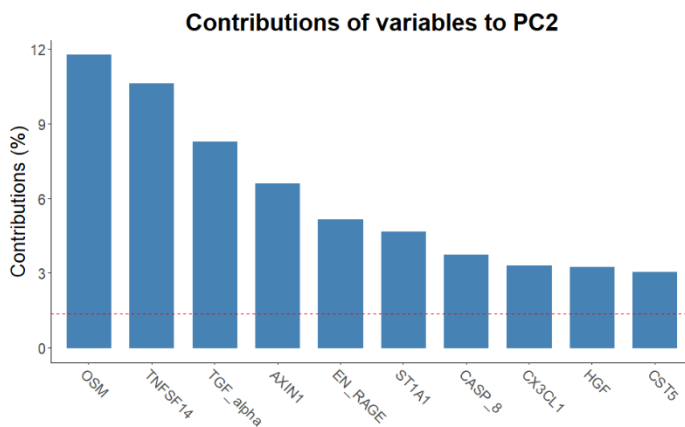
A



B



C



A. Scree plot of eigenvalues indicating the contributions of the first ten principal components to the explained variance of the PCA based on biomarkers of inflammation (see Fig. 3B). B, C. Plots showing the contributions of different biomarkers of inflammation to PC1 (B) and

PC2 (C). Red dashed lines indicate the expected value if contributions were uniform across biomarkers.