Supplementary Table 1—Clinical characteristics, autoantibodies, medication, and defecation in the studied sample

Variable	Healthy controls (n = 29)	Type 2 diabetes patients (n = 31)	LADA patients (n = 30)	Classic type 1 diabetes patients (n = 29)	P
RBC ($\times 10^{12}$/L)	4.70 (4.30–4.98)	4.72 (4.46–4.98)	4.56 (4.35–4.90)	4.42 (4.21–4.85)	0.28
Hemoglobin (g/L)	144.00 (127.50–152.50)	144.00 (132.00–149.00)	136.50 (126.00–149.00)	135.00 (124.50–146.50)	0.547
WBC ($\times 10^9$/L）	5.70 (4.68–6.40)[a,c]	7.00 (5.47–7.85)[b]	5.01 (4.41–6.47)[a]	6.36 (5.24–7.59)[b,c]	0.004
ALT (U/L)	16.80 (12.80–21.60)	19.00 (14.10–30.10)	17.00 (13.25–20.55)	15.85 (12.33–21.73)	0.300
AST (U/L)	21.15 (17.28–23.55)	19.20 (15.50–22.70)	17.80 (15.25–22.40)	18.60 (15.20–24.30)	0.469
GGT (U/L)	17.05 (13.03–21.00)[a]	23.40 (15.30–39.70)[b]	15.70 (12.30–21.40)[a]	15.20 (10.63–21.80)[a]	0.009
Creatinine (μmol/L)	60.00 (52.00–69.50)[a]	56.00 (44.00–60.00)[b]	54.00 (44.88–61.25)[b]	49.00 (42.00–59.50)[b]	0.007
Uric acid (μmol/L)	306.50 (263.50–385.75)[a]	279.00 (224.00–370.00)[a,c]	221.00 (175.00–7–272.50)[b]	263.00 (203.50–315.00)[b,c]	0.001
Autoantibodies					
GADA positive (%)	0 (0)[a]	0 (0)[a]	30 (100)[b]	18 (62.07)[c]	<0.001
IA-2A positive (%)	0 (0)[a]	0 (0)[a]	13 (43.33)[b]	7 (24.14)[b]	<0.001
Zn-T8 positive (%)	0 (0)[a]	0 (0)[a]	5 (16.67)[b]	5 (17.24)[b]	0.003
Medication					
1. Insulin (%)	0 (0)[a]	26 (83.87)[b]	27 (90.00)[b,c]	29 (100)[c]	<0.001
2. Acarbose (%)	0 (0)	6 (19.35)	3（10.00)	3 (10.34）	0.080
3. Metformin (%)	0 (0)[a]	5 (16.13)[a]	10 (33.33)[b]	1 (3.45)[a,b]	<0.001
4. DDP4 inhibitors (%)	0(0)[a]	5 (16.13)[b]	5 (16.67)[b]	0(0)[a]	0.033
5. Aspirin (%)	0 (0)	0 (0)	0 (0)	1 (3.45)	0.487
6. Lipid-lowering agents (%)	0 (0)	4 (12.90)	2 (6.67)	2 (6.90)	0.267
7. Hypotensor (%)	0 (0)	5 (16.13)	2 (6.67)	2 (6.90)	0.132
8. Levothyroxine (Euthyrox) (%)	0 (0)	0 (0)	3 (10.00)	0 (0)	0.041
Defecation consistency (the Bristol stool form scale)					
Type 1–Separate, hard lumps (%)	0 (0)	2 (6.45)	1 (3.33)	2 (6.90)	0.717
Type 2–Lumpy, sausage-shaped (%)	1 (3.45)	6 (19.35)	2 (6.67)	3 (10.34)	0.271

Type 3–Sausage-shaped with cracks (%)	2 (6.90)	2 (6.45)	7 (23.33)	3 (10.34)	0.253
Type 4–Smooth and soft (%)	19 (65.52)	15 (48.39)	13 (43.33)	16 (55.17)	0.073
Type 5–Soft and edges (%)	2 (6.90)	4 (12.90)	4 (13.33)	1 (3.45)	0.579
Type 6–Mushy with ragged edges (%)	0 (0)	0 (0)	2 (6.67)	1 (3.45)	0.504
Type 7–Liquid (%)	0 (0)	0 (0)	0 (0)	1 (3.45)	0.468

LADA, latent autoimmune diabetes in adults; RBC, red blood cells; WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; GADA, GAD antibody; IA-2A, insulinoma-associated protein-2 antibody; Zn-T8, zinc transporter-8; DDP4 inhibitors, dipeptidyl peptidase 4 inhibitors. Data are % (n) and median (25th–75th percentile). Superscript symbols ([a], [b], [c]) next to values in a row indicate that the medians of the different groups are significantly different ($P<0.05$)

Supplementary Table 2—Clinical characteristics, autoantibodies, medication, and defecation

Variable	LADA patients (n = 30)	T1D-A patients (n = 18)	T1D-B patients (n = 11)	P
Male/Female	10/20	10/8	8/3	
Age (years)	36.5 (30.5–45)	34 (30–46.25)	39 (31–49)	0.637
Duration of diabetes (months)	24 (2.5–36)[a]	36 (15.5-84)[b]	84 (1–120)[b]	0.026
BMI (kg/m^2)	20.48 (18.31–22.29)[a]	21.24 (19.93–22.39)[a,b]	22.67 (22.43–23.43)[b]	0.025
WHR	0.88 (0.82–0.94)	0.88 (0.84–0.94)	0.90 (0.86–0.93)	0.879
SBP (mmHg)	110.5 (106–125.25)	116 (108.75–127)	121 (116–133)	0.237
DBP (mmHg)	73 (64–80.5)	76.5 (69.5–81)	80 (70–84)	0.396
HbA1c (%)	9.10 (7.08–11.80)	8.85 (6.80–9.78)	7.60 (6.50–8.90)	0.176
HbA1c (mmol/mol)	76 (54–105)	73 (51–83)	60 (48–74)	0.176
FPG (mmol/L)	6.90 (6.00–8.15)	6.40 (4.80–8.20)	11.20 (6.90–11.42)	0.115
OGTT-2h PG (mmol/L)	19.65 (16.68–23.42)	22.30 (18.70–24.70)	21.40 (19.18–25.79)	0.289
FCP (ng/mL)	0.375 (0.255–0.496)[a]	0 (0–0.11)[b]	0 (0–0.01)[b]	<0.001
OGTT-2h PC (ng/mL)	1.12 (0.62–1.46)[a]	0.21 (0–0.34)[b]	0 (0–0.01)[b]	<0.001
AUC Glucose	50.59 (37.25–58.35)	55.70 (49.66–69.90)	52.97 (45.21–71.78)	0.240
AUC C-Peptide	173.20 (109.20–220.80)[a]	35.31 (0–48.83)[b]	0 (0–1.05)[b]	<0.001
TC (mg/dL)	4.34 (3.87–5.27)	4.59 (4.09–5.57)	4.37 (3.98–5.20)	0.762
TG (mg/dL)	0.91 (0.62–1.43)	0.89 (0.62–1.32)	1.20 (0.87–1.66)	0.222
HDL-c (mg/dL)	1.33 (1.10–1.62)	1.43 (1.06–1.78)	1.18 (1.06–1.35)	0.430
LDL-c (mg/dL)	2.33 (1.85–3.04)	2.40 (1.98–2.82)	2.33 (2.07–2.92)	0.899

Inflammatory markers

TNF-α (pg/mL)	5.44 (4.60–9.74)	5.01 (4.30–6.48)	6.05 (4.16–6.74)	0.628
IL-6 (pg/mL)	1.61 (1.25–2.74)	1.43 (1.16–2.81)	2.08 (1.25–3.78)	0.715
IL-10 (pg/mL)	1.26 (1.11-2.05)	1.32 (1.24–1.66)	1.53 (1.23-1.76)	0.682
IL-1β (pg/mL)	2.67 (2.03–2.97)	2.48 (2.03–3.18)	2.47 (2.08–3.28)	0.914
LBP (ng/mL)	34.73 (29.48–39.89)[a]	31.73 (27.81–35.87)[a,b]	27.36 (25.89–31.01)[b]	0.009
Other biochemical tests				
RBC ($\times 10^{12}$/L)	4.56 (4.35–4.90)	4.48 (4.36–4.93)	4.36 (4.12–4.80)	0.276
Hemoglobin (g/L)	136.50 (126.00–149.00)	137.50 (129.00–147.00)	128.00 (118.00–147.00)	0.444
WBC ($\times 10^9$/L)	5.01 (4.41–6.47)[a]	6.43 (5.20–7.69)[b]	5.56 (5.19–7.70)[a,b]	0.038
ALT (U/L)	17.00 (13.25–20.55)	14.45 (12.57–21.00)	17.60 (10.35–25.17)	0.64
AST (U/L)	17.85 (15.60–22.80)	19.25 (15.42–24.55)	17.00 (14.80–24.20)	0.885
GGT (U/L)	15.70 (12.30–21.40)	14.90 (10.68–19.55)	16.15 (9.95–34.88）	0.708
Creatinine (mmol/L)	54.00 (44.88–61.25)	48.00 (41.50–56.25)	49.00 (42.00–66.00)	0.647
Uric acid (μmol/L)	221.00 (175.00–272.50)[a]	224.50 (193.50–275.25)[a]	311.00 (263.00–326.00)[b]	0.027
Autoantibodies				
GADA positive (%)	30 (100)[a]	18 (100)[a]	0 (0)[b]	<0.001
IA-2A positive (%)	13 (43.33)[a]	7 (38.89)[a]	0 (0)[b]	0.032
Zn-T8 positive (%)	5 (16.67)	5 (27.78)	0 (0)	0.159
Medication				
1. Insulin (%)	27 (90.00)	18 (100)	11 (100)	0.399
2. Acarbose (%)	3 (10.00)	2 (11.11)	1 (9.09)	0.896

3. Metformin (%)	10 (33.33)	1 (5.56)	0 (0)	0.081
4. DDP4 inhibitors (%)	5 (16.67)	1 (5.56)	0 (0)	0.22
5. Aspirin (%)	0 (0)	1 (5.56)	0 (0)	
6. Lipid-lowering agents (%)	2 (6.67)	2 (11.11)	0 (0)	
7. Hypotensor (%)	2 (6.67)	2 (11.11)	0 (0)	
8. Levothyroxine (Euthyrox) (%)	3 (10.00)	0 (0)	0 (0)	

Defecation consistency (the Bristol stool form scale)

Type 1 Separate, hard lumps (%)	1 (3.33)	1 (5.56)	1 (9.09)	0.476
Type 2 Lumpy, sausage-shaped (%)	2 (6.67)	3 (16.67)	0 (0)	0.279
Type 3 Sausage-shaped with cracks (%)	7 (23.33)	3 (16.67)	0 (0)	0.107
Type 4 Smooth and soft (%)	13 (43.33)	9 (50)	7 (63.64)	0.208
Type 5 Soft and edges (%)	4 (13.33)	1 (5.56)	0 (0)	0.279
Type 6 Mushy with ragged edges (%)	2 (6.67)	0 (0)	1 (9.09)	0.476
Type 7 Liquid (%)	0 (0)	0 (0)	1 (9.09)	0.032

LADA, latent autoimmune diabetes in adults; T1D-A, type 1 diabetes-A (GADA positive); T1DB, type 1 diabetes-B (GADA negative). WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; OGTT, oral glucose tolerance test; OGTT 2h PG, OGTT 2h postprandial glucose; FCP, fasting C-peptide; OGTT 2h CP, OGTT 2h postprandial c-peptide; AUC $_{Glucose}$, areas under the receiver operating characteristic curves for glucose during OGTT; AUC $_{C-peptide}$, areas under the receiver operating characteristic curves for C-peptide during

OGTT; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein; LDL-c, low-density lipoprotein; IL, interleukin; TNF-α, tumor necrosis factor-α; LBP, lipopolysaccharide-binding protein; RBC, red blood cells; WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; GADA, GAD antibodies; IA-2A, insulinoma-associated protein-2 antibody; Zn-T8, zinc transporter-8; DDP4 inhibitors, dipeptidyl peptidase 4 inhibitors. Data are % (n) and median (25th–75th percentile). Different superscript symbols ([a], [b]) next to values in a row indicate that the means of the different groups are significantly different (P<0.05).

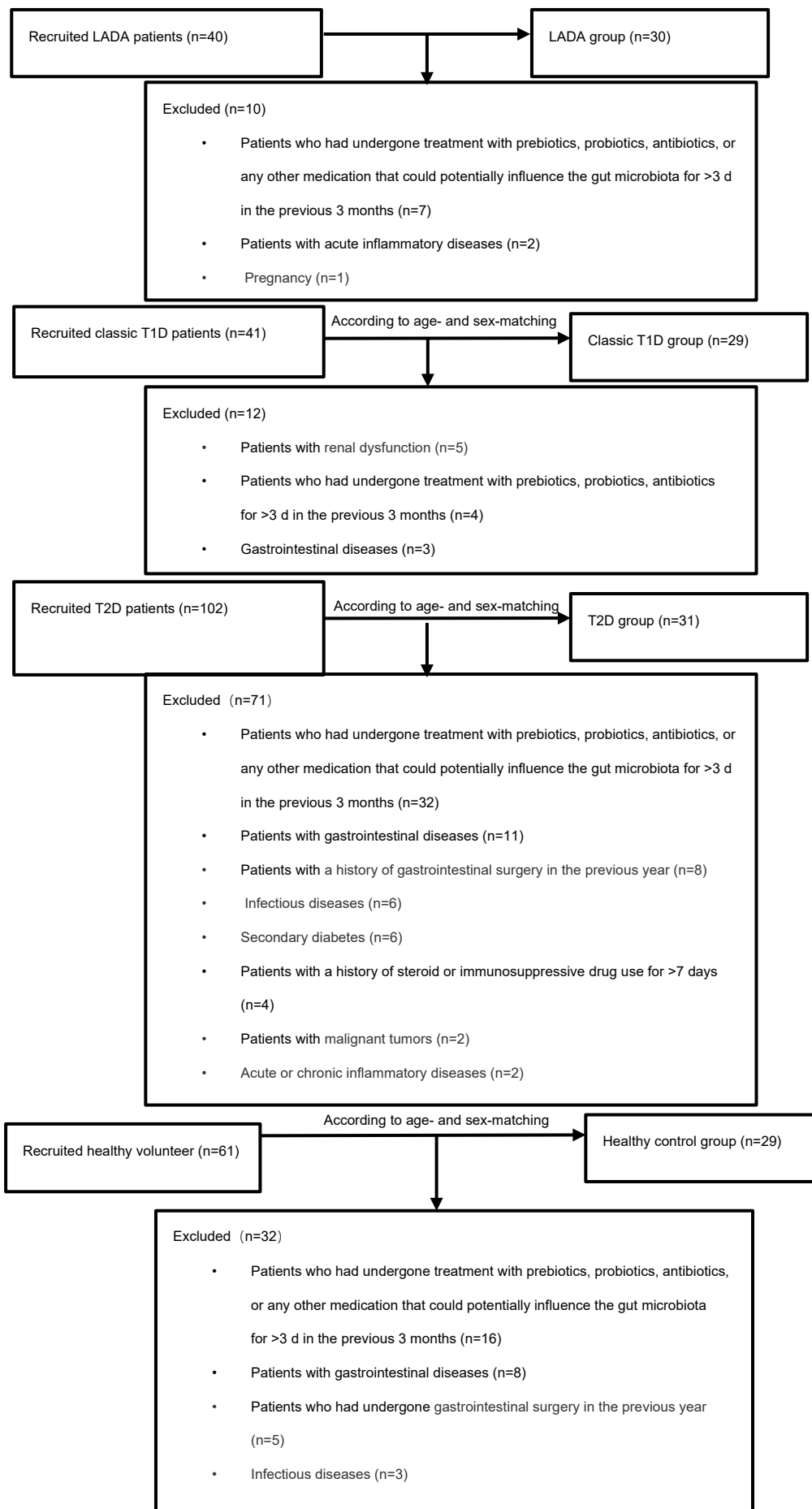**Supplementary Table 3—Clinical characteristics, autoantibodies, medication, and defecation**

Variable	GAD-P patients (n=48)	GAD-N patients (n=11)	T2D patients (n=31)	Healthy controls (n=29)	P
Male/Female	20/28	8/3	11/20	11/18	
Age (years)	35 (31-45)	39 (31-49)	39 (31-48)	34 (28.5-52.5)	0.897
Duration of diabetes (months)	24 (4.5-48)	84 (1-120)	36 (12-84)		0.18
BMI (kg/m²)	20.74 (18.38-22.20)[a]	22.67 (22.43-23.43)[a,b]	23.51 (21.22-25.40)[b]	22.14 (19.99-24.41)[a,b]	<0.001
WHR	0.88 (0.83-0.93)	0.90 (0.86-0.93)	0.92 (0.87-0.94)	0.86 (0.83-0.92)	0.235
SBP (mmHg)	114 (106-125.75)	121 (116-133)	120 (110-130)	112 (106-120.5)	0.122
DBP (mmHg)	75 (66.25-80)	80 (70-84)	76 (72-80)	71 (65-77)	0.105
HbA1c (%)	8.95 (7.03-10.78)[a]	7.60 (6.50-8.90)[a]	9.00 (7.00-10.06)[a]	5.30 (5.20-5.50)[b]	<0.001
HbA1c (mmol/mol)	74 (53-94)[a]	60 (48-74)[a]	75 (53-86)[a]	34 (33-37)[b]	<0.001
FPG (mmol/L)	6.80 (5.70-8.15)[a]	11.20 (6.90-11.42)[a]	7.15 (6.28-10.25)[a]	4.85 (4.43-5.28)[b]	<0.001
OGTT-2h PG (mmol/L)	21.56 (16.90-23.70)[a]	21.40 (19.18-25.79)[a]	17.10 (13.75-19.33)[a]	6.15 (5.50-6.90)[b]	<0.001
FCP (ng/mL)	0.25 (0.08-0.47)[a]	0 (0-0.01)[a]	0.78 (0.50-1.26)[b]	1.08 (0.86-1.36)[b]	<0.001
OGTT-2h PC (ng/mL)	0.64 (0.32-1.32)[a]	0 (0-0.01)[a]	2.99 (2.10-4.70)[b]	5.58 (4.11-7.73)[b]	<0.001
AUC Glucose	52.93 (43.70-59.00)[a]	52.97 (45.21-71.78)[a]	44.82 (40.79-49.76)[a]	20.68 (19.60-21.91)[b]	<0.001

AUC C-Peptide	105 (41.33-199.28)[a]	0 (0-1.05)[a]	426.85 (287.28-597.63)[b]	875.90 (743.70-1112.50)[c]	<0.001
TC (mg/dL)	4.46 (4.04-5.40)	4.37 (3.98-5.20)	4.90 (3.68-5.33)	4.57 (4.12-4.89)	0.723
TG (mg/dL)	0.89 (0.62-1.39)[a]	1.20 (0.87-1.66)[a,b]	1.35 (0.97-2.12)[b]	1.08 (0.89-1.21)[a,b]	0.015
HDL-c (mg/dL)	1.38 (1.09-1.65)[a]	1.18 (1.06-1.35)[a,b]	1.15 (0.94-1.27)[b]	1.36 (1.26-1.56)[a]	0.002
LDL-c (mg/dL)	2.37 (1.94-2.86)	2.33 (2.07-2.92)	2.99 (2.16-3.27)	2.56 (2.38-2.78)	0.185
Inflammatory markers					
TNF-α (pg/mL)	5.41 (4.48-6.49)[a]	6.05 (4.16-6.74)[a,b]	5.60 (5.16-6.28)[a]	4.49 (4.06-5.09)[b]	0.002
IL-6 (pg/mL)	1.55 (1.19-2.69)[a]	2.08 (1.25-3.78)[a]	2.69 (1.55-5.68)[a]	1.09 (0.92-1.27)[b]	<0.001
IL-10 (pg/mL)	1.26 (1.11-2.05)[a]	1.32 (1.03-1.48)[a,b]	1.44 (1.21-1.66)[a,b]	1.63 (1.24-1.84)[b]	0.007
IL-1β (pg/mL)	2.64 (2.03-2.97)[a,b]	2.47 (2.08-3.28)[a,b]	3.03 (2.47-3.77)[a]	2.19 (2.03-2.64)[b]	<0.001
LBP (ng/mL)	33.41 (28.73-38.02)[a]	27.36 (25.89-31.01)[a,b]	32.91 (29.41-36.50)[a]	26.35 (23.58-29.24)[b]	<0.001
Other biochemical markers					
RBC (×10^{12}/L)	4.52 (4.37-4.89)	4.36 (4.12-4.80)	4.72 (4.46-4.98)	4.70 (4.30-4.98)	0.207
Hemoglobin (g/L)	136.50 (127.25-149)	128 (118-147)	144 (132-149)	144 (127.5-152.5)	0.356
WBC (×10^{9}/L）	5.60 (4.64-6.82)	5.56 (5.19-7.70)	7.00 (5.47-7.85)	5.70 (4.68-6.40)	0.053
ALT (U/L)	16.70 (12.70-20.10)	17.60 (10.35-25.17)	19.00 (14.10-30.01)	16.8 (12.8-21.6)	0.320
AST (U/L)	18.25 (15.48-23.15)	17.00 (14.80-24.20)	19.20 (15.50-22.70)	21.15 (17.28-23.55)	0.449
GGT (U/L)	15.40 (11.10-21.20)[a]	16.15 (9.95-34.88)[a,b]	23.40 (15.30-39.70)[b]	17.05 (13.03-21.00)[a,b]	0.007
Creatinine (mmol/L)	51 (44.12-60.75)[a]	49 (42-66)[a,b]	56 (44-58)[a,b]	60 (52-69.5)[b]	0.009

Uric Acid (μmol/L)	224 (177-275)[a]	311 (263-326)[a,b]	279 (224-370)[a,b]	306.5 (263.5-385.75)[b]	<0.001
Autoantibodies					
GADA positive (%)	48 (100)[a]	0 (0)[b]	0 (0)[b]	0 (0)[b]	<0.001
IA-2A positive (%)	20 (41.67)	0 (0)	0 (0)	0 (0)	
Zn-T8 positive (%)	10 (20.83)	0 (0)	0 (0)	0 (0)	
Medication					
1. Insulin (%)	45 (93.75)	11 (100)	26 (83.87)	0 (0)	
2. Acarbose (%)	5 (10.42)	1 (9.09)	6 (19.35)	0 (0)	
3. Metformin (%)	11 (22.92)	0 (0)	5 (16.13)	0 (0)	
4. DDP4 inhibitors (%)	6 (12.50)	0 (0)	5 (16.13)	0 (0)	
5. Aspirin (%)	1 (2.08)	0 (0)	0 (0)	0 (0)	
6. Lipid-lowering agents (%)	4 (8.33)	0 (0)	4 (12.90)	0 (0)	
7. Hypotensor (%)	4 (8.33)	0 (0)	5 (16.13)	0 (0)	
8. Levothyroxine (Euthyrox) (%)	3 (6.25)	0 (0)	0 (0)	0 (0)	
Defecation consistency (The Bristol Stool Form Scale)					
Type 1 Separate, hard lumps (%)	2 (4.16)	1 (9.09)	2 (6.45)	0 (0)	
Type 2 Lumpy, sausage-shaped (%)	5 (10.42)	0 (0)	6 (19.35)	1 (3.45)	/
Type 3 Sausage-shaped with crack (%)	10 (20.83)	0 (0)	2 (6.45)	2 (6.90)	/

|			
Type 4 Smooth and soft (%)	22 (45.83)	7 (63.64)	15 (48.39)	19 (65.52)
Type 5 Soft and edges (%)	5 (10.42)	0 (0)	4 (12.90)	2 (6.90)
Type 6 Mushy with ragged edges (%)	2 (4.16)	1 (9.09)	0 (0)	0 (0)
Type 7 Liquid (%)	0 (0)	1 (9.09)	0 (0)	0 (0)

LADA, latent autoimmune diabetes in adults; T1D-A, GADA-P (GADA-positive); GADA-P (GADA-negative); T2D, type 2 diabetes; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; OGTT, oral glucose tolerance test; OGTT 2h PG, OGTT 2h postprandial glucose; FCP, fasting C-peptide; OGTT 2h CP, OGTT 2h postprandial c-peptide; AUC $_{Glucose}$, areas under the receiver operating characteristic curves for glucose during OGTT; AUC $_{C-peptide}$, areas under the receiver operating characteristic curves for C-peptide during OGTT; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein; LDL-c, low-density lipoprotein; IL, interleukin; TNF-α, tumor necrosis factor-α; LBP, lipopolysaccharide-binding protein; RBC, red blood cells; WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; GADA, GAD antibodies; IA-2A, insulinoma-associated protein-2 antibody; Zn-T8, zinc transporter-8; DDP4 inhibitors, dipeptidyl peptidase 4 inhibitors. Data are % (n) and median (25th–75th percentile). Different superscript symbols (^{a}, ^{b}, ^{c}) next to values in a row indicate that the means of the different groups are significantly different (P<0.05).

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Recruited LADA patients (n=40) ──────────────────────────→ LADA group (n=30)
                                              │
                                              ▼
        Excluded (n=10)

            • Patients who had undergone treatment with prebiotics, probiotics, antibiotics, or
              any other medication that could potentially influence the gut microbiota for >3 d
              in the previous 3 months (n=7)

            • Patients with acute inflammatory diseases (n=2)

            • Pregnancy (n=1)

Recruited classic T1D patients (n=41) ──According to age- and sex-matching──→ Classic T1D group (n=29)
                                              │
                                              ▼
        Excluded (n=12)

            • Patients with renal dysfunction (n=5)

            • Patients who had undergone treatment with prebiotics, probiotics, antibiotics
              for >3 d in the previous 3 months (n=4)

            • Gastrointestinal diseases (n=3)

Recruited T2D patients (n=102) ──According to age- and sex-matching──→ T2D group (n=31)
                                              │
                                              ▼
        Excluded （n=71）

            • Patients who had undergone treatment with prebiotics, probiotics, antibiotics, or
              any other medication that could potentially influence the gut microbiota for >3 d
              in the previous 3 months (n=32)

            • Patients with gastrointestinal diseases (n=11)

            • Patients with a history of gastrointestinal surgery in the previous year (n=8)

            • Infectious diseases (n=6)

            • Secondary diabetes (n=6)

            • Patients with a history of steroid or immunosuppressive drug use for >7 days
              (n=4)

            • Patients with malignant tumors (n=2)

            • Acute or chronic inflammatory diseases (n=2)

Recruited healthy volunteer (n=61) ──According to age- and sex-matching──→ Healthy control group (n=29)
                                              │
                                              ▼
        Excluded （n=32）

            • Patients who had undergone treatment with prebiotics, probiotics, antibiotics,
              or any other medication that could potentially influence the gut microbiota
              for >3 d in the previous 3 months (n=16)

            • Patients with gastrointestinal diseases (n=8)

            • Patients who had undergone gastrointestinal surgery in the previous year
              (n=5)

            • Infectious diseases (n=3)
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Supplementary Diagram 1—Schematic diagram of patients included and excluded. LALA, latent autoimmune diabetes in adults; T1D, type 1 diabetes; T2D, type 2 diabetes.
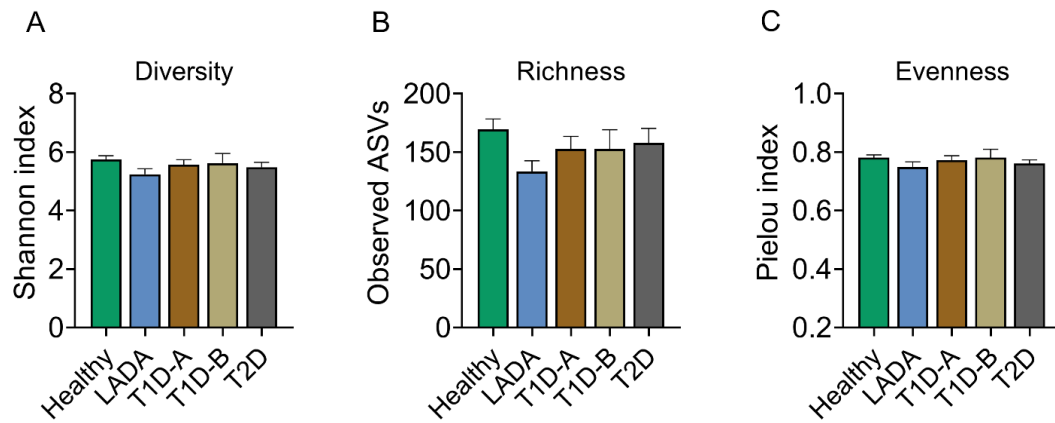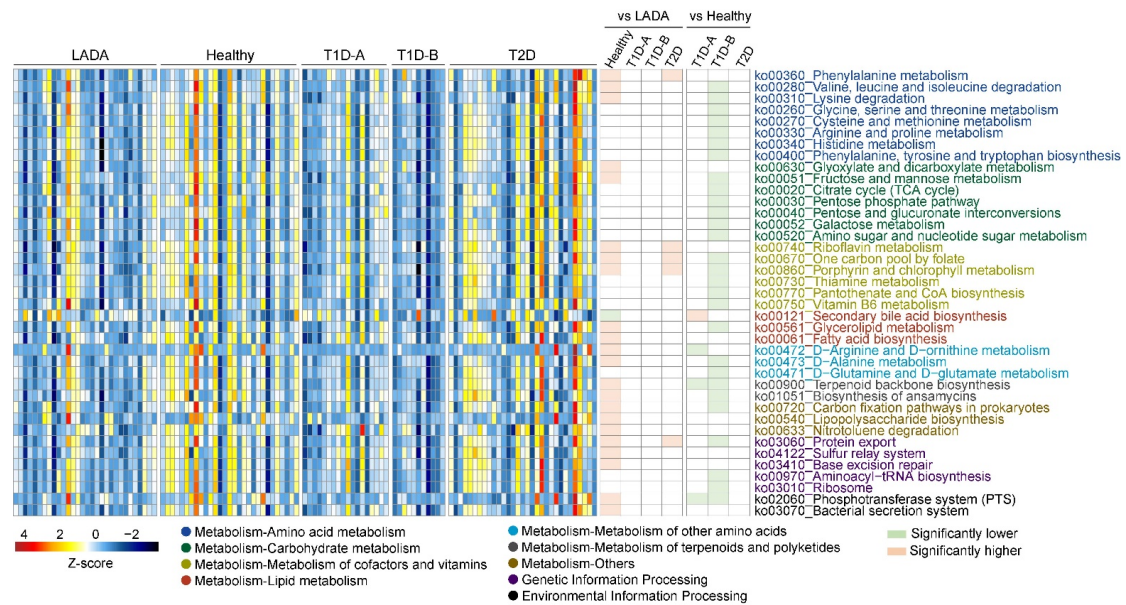

Supplementary Figure 1—Comparison of α-diversity (A, Diversity; B, Richness and C, Evenness) between the healthy subjects, latent autoimmune diabetes in adults (LADA), type 1 diabetes-A (T1D-A; GADA-positive), type 1 diabetes-B (T1D-B; GADA-negative) and type 2 diabetes (T2D) groups. Comparisons were performed using the Kruskal-Wallis test with Dunn's post-hoc analysis, for significant differences, the *P*-value was controlled at 0.05.
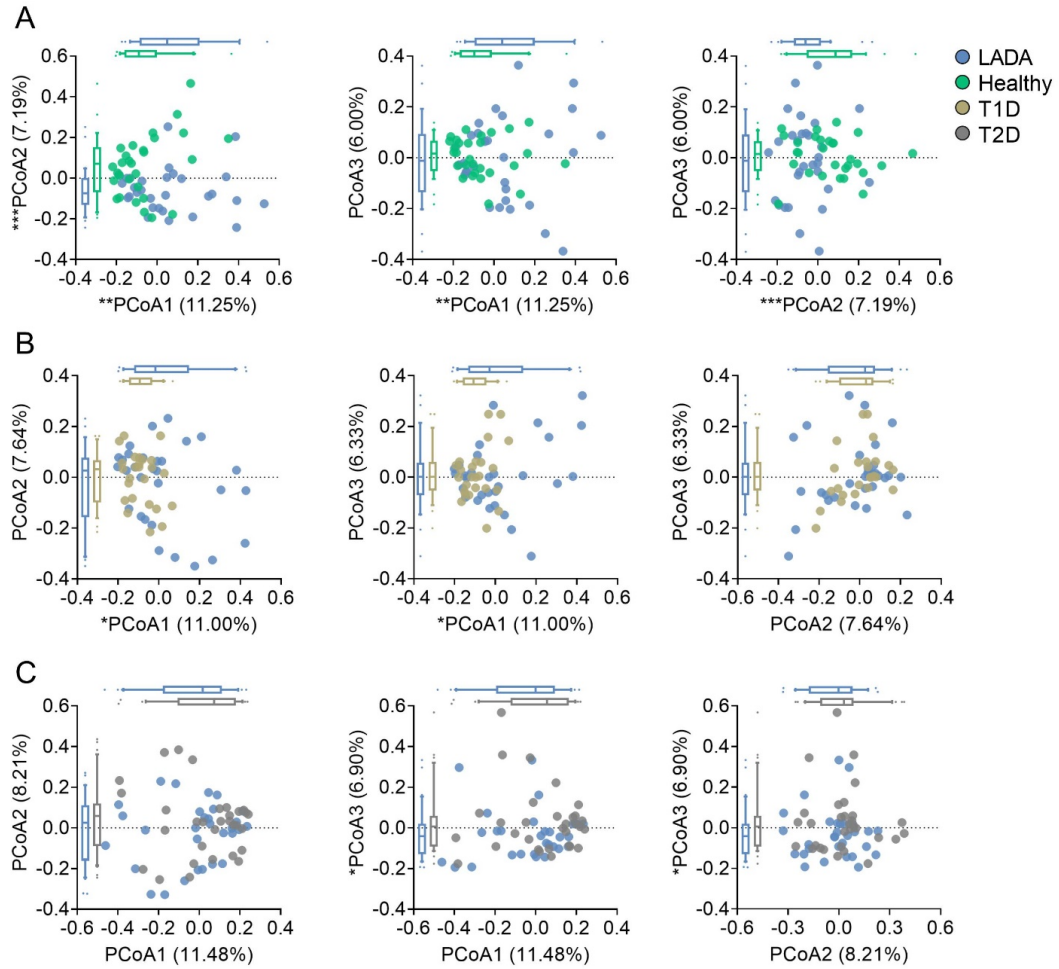
Supplementary Figure 2—Comparison of the gut microbiota between patients with latent autoimmune diabetes in adults (LADA) and healthy subjects and patients with classic type 1 diabetes (T1D) and type 2 diabetes (T2D) patients. Principal coordinates analysis (PCoA) of the LADA and healthy groups (A), LADA and T1D groups (B), LADA and T2D groups (C) on the first three principle coordinates performed based on the Bray Curtis distance. The PCoA scores of the gut microbiota between the LADA and healthy groups, LADA and T1D groups, LADA and T2D groups on the PCoA1, PCoA2, and PCoA3 were tested using the Mann-Whitney U; for significant differences, the *P*-value was controlled at 0.05.
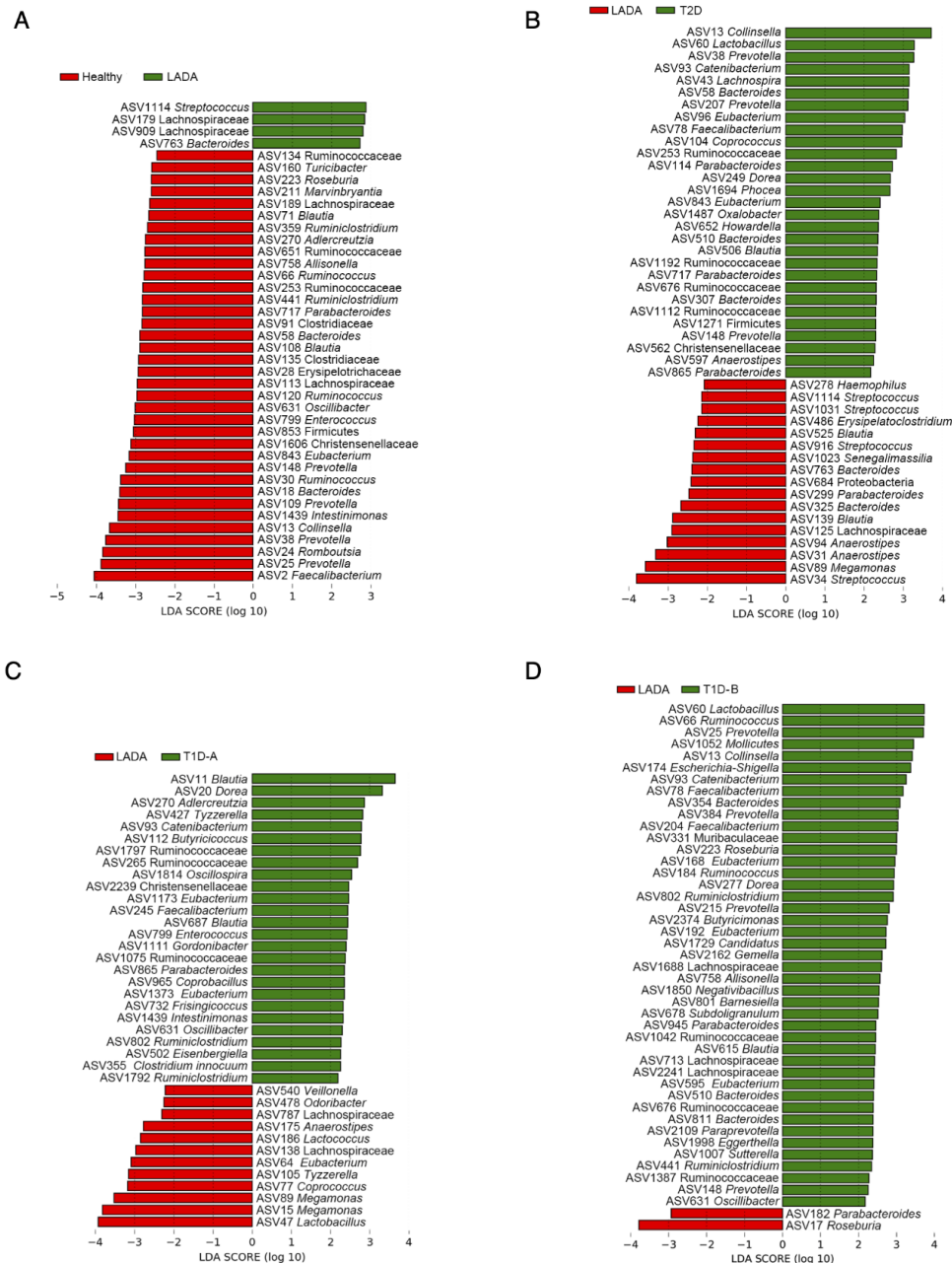
Supplementary Figure 3—Identification of major amplicon sequence variants (ASVs) contributing to the differences in the gut microbiota of patients with latent autoimmune diabetes in adults (LADA) with other cohorts using LEfSe. (A) ASVs contributing to the differences between the LADA and healthy groups. (B) ASVs contributing to the differences between the LADA and type 2 diabetes (T2D) groups. (C) ASVs contributing to the differences between the LADA and type 1 diabetes-A (T1D-A; GADA-positive) groups. (D) ASVs contributing to the differences between the LADA and type 1 diabetes-B (T1D-B; GADA-negative) groups.

Supplementary Figure 4—Distribution of 139 amplicon sequence variants (ASVs) contributing to the differences in the gut microbiota of patients with latent autoimmune diabetes in adults (LADA) with cohorts among the four other groups, i.e., healthy; T1D-A, type 1 diabetes-A (GADA-positive); T1D-B, type 1 diabetes-B (GADA-negative); and T2D, type 2 diabetes. The color bar (left hand side) represents the 12 co-abundance groups (CAGs) clustered among the 139 ASVs based on their Spearman correlations.

Supplementary Figure 5—Heatmap of the different predicted KEGG metabolic pathways of gut microbiota between latent autoimmune diabetes in adults (LADA), healthy, type 1 diabetes-A (T1D-A, GADA-positive), type 1 diabetes-B (T1D-B, GADA-negative), and type 2 diabetes (T2D) groups. Comparisons of the abundance of each pathway between LADA, healthy, T1D-A, T1D-B, and T2D groups were performed using the Wilcoxon rank-sum test; significant differences had *P*-value that was controlled at 0.05.
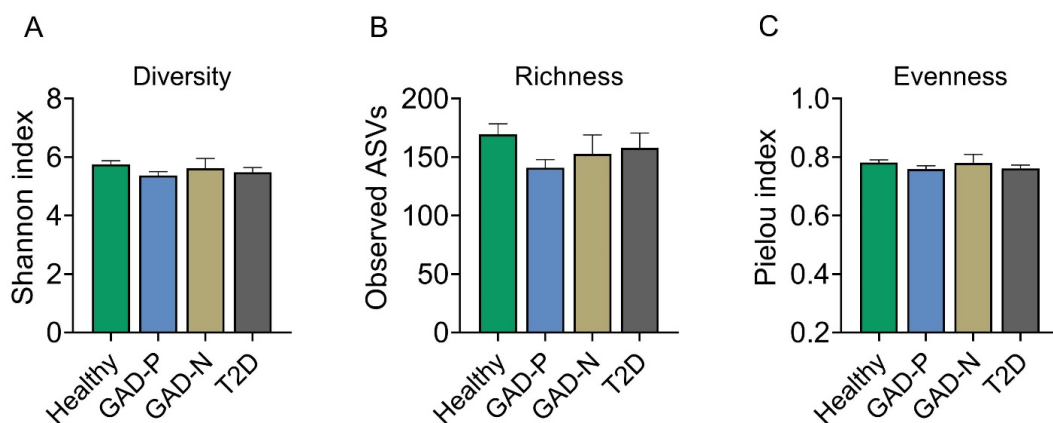
Supplementary Figure 6—Comparison of α-diversity (A, Diversity; B, Richness and C, Evenness) between the healthy subjects, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. Comparisons were performed using the Kruskal-Wallis test with Dunn's post-hoc analysis, for significant differences, the *P*-value was controlled at 0.05.
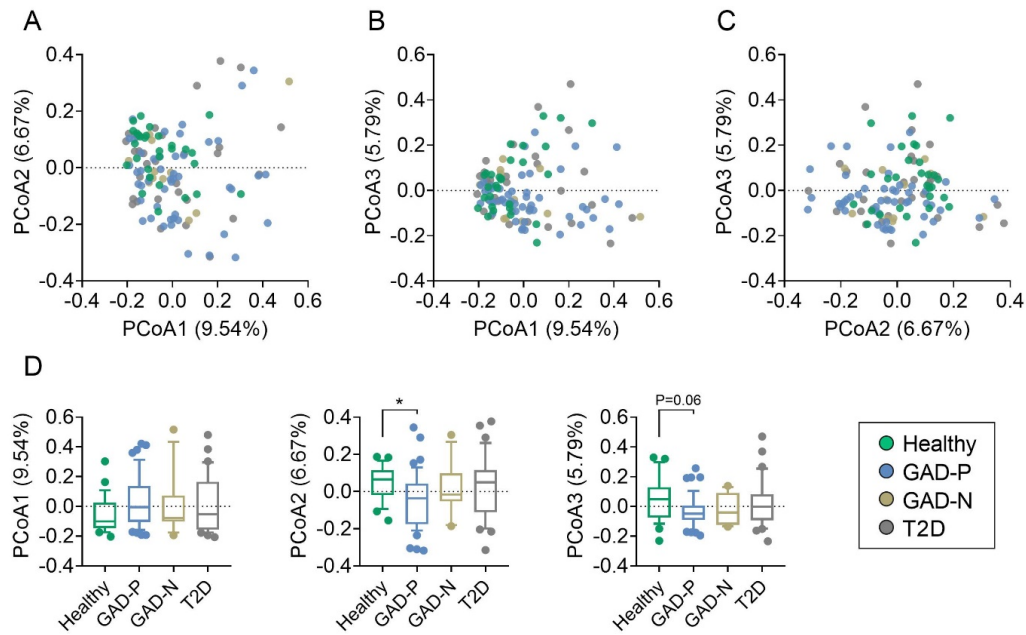
Supplementary Figure 7—Comparison of the gut microbiota between healthy, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. Principal coordinates analysis (PCoA) of the four groups on the first three principle coordinates was performed based on the Bray Curtis distance. Comparisons were performed using the Kruskal-Wallis test with Dunn's post-hoc analysis, for significant differences, the *$P<0.05$.
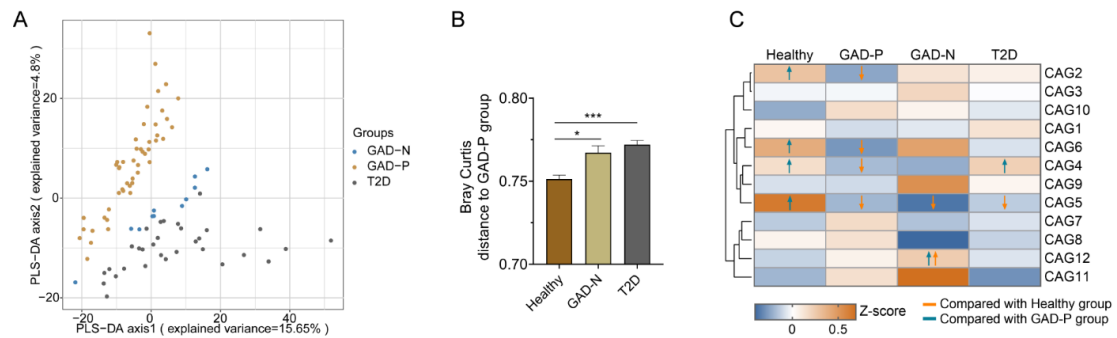
Supplementary Figure 8—Comparison of the gut microbiota between healthy, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. A, PLS-DA of the gut microbiota composition of GADA-P, GADA-N, and T2D groups. B, Comparison of the between-sample Bray Curtis distances of the gut microbiota of healthy, GADA-N, T2D groups to the GADA-P group. C, Relative abundance of 12 CAGs across different groups. The abundance profiles were transformed of into Z scores by subtracting the average abundance and dividing the standard deviations of all the samples. The Z score was negative (shown in blue) when the row abundance was lower than the mean. Comparisons among the relative abundance of each CAG among 5 groups were performed using the Kruskal-Wallis test with Dunn's multiple comparisons test, the significant differences (*P*-value controlled

at 0.05) were marked with arrows, upward-facing arrow represents significantly higher values compared to those in the corresponding group, and downward-facing arrow represents significantly lower values compared to those in the corresponding group.
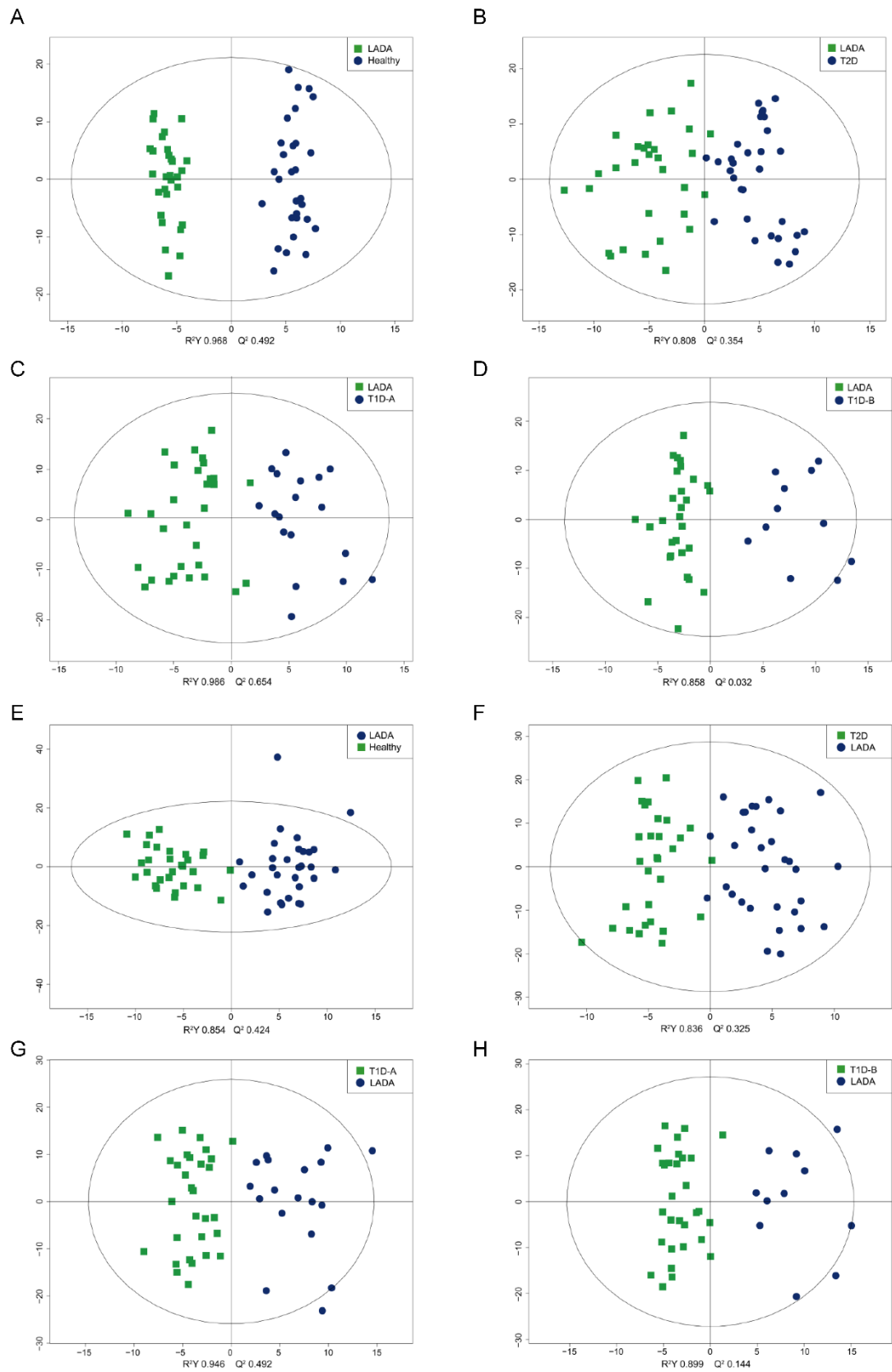
Supplementary Figure 9—Orthogonal projection to latent structure-discriminant analysis (OPLS-DA) score plots of fecal metabolites. (A–D) Comparisons in the
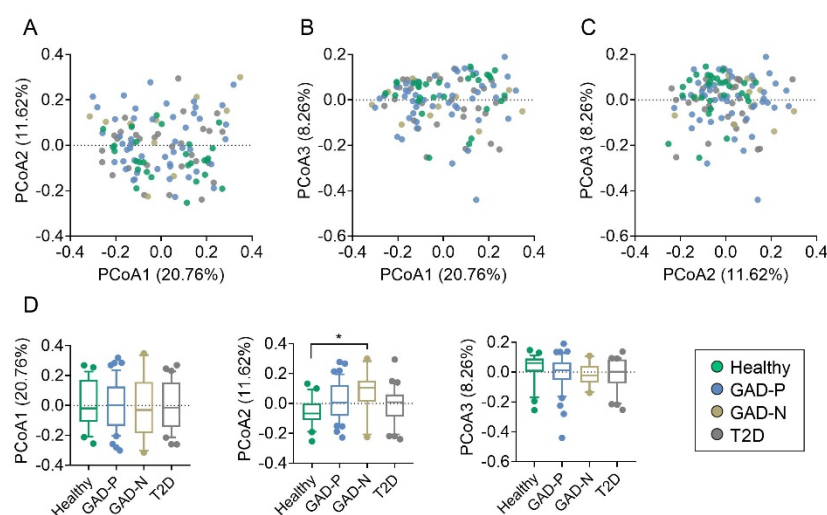
negative ion mode. (E–H) Comparisons under the positive ionic mode. Abbreviations: LADA, latent autoimmune diabetes in adults; T1D-A, type 1 diabetes-A (GADA-positive); T1D-B, type 1 diabetes-B (GADA-negative); T2D, type 2 diabetes.
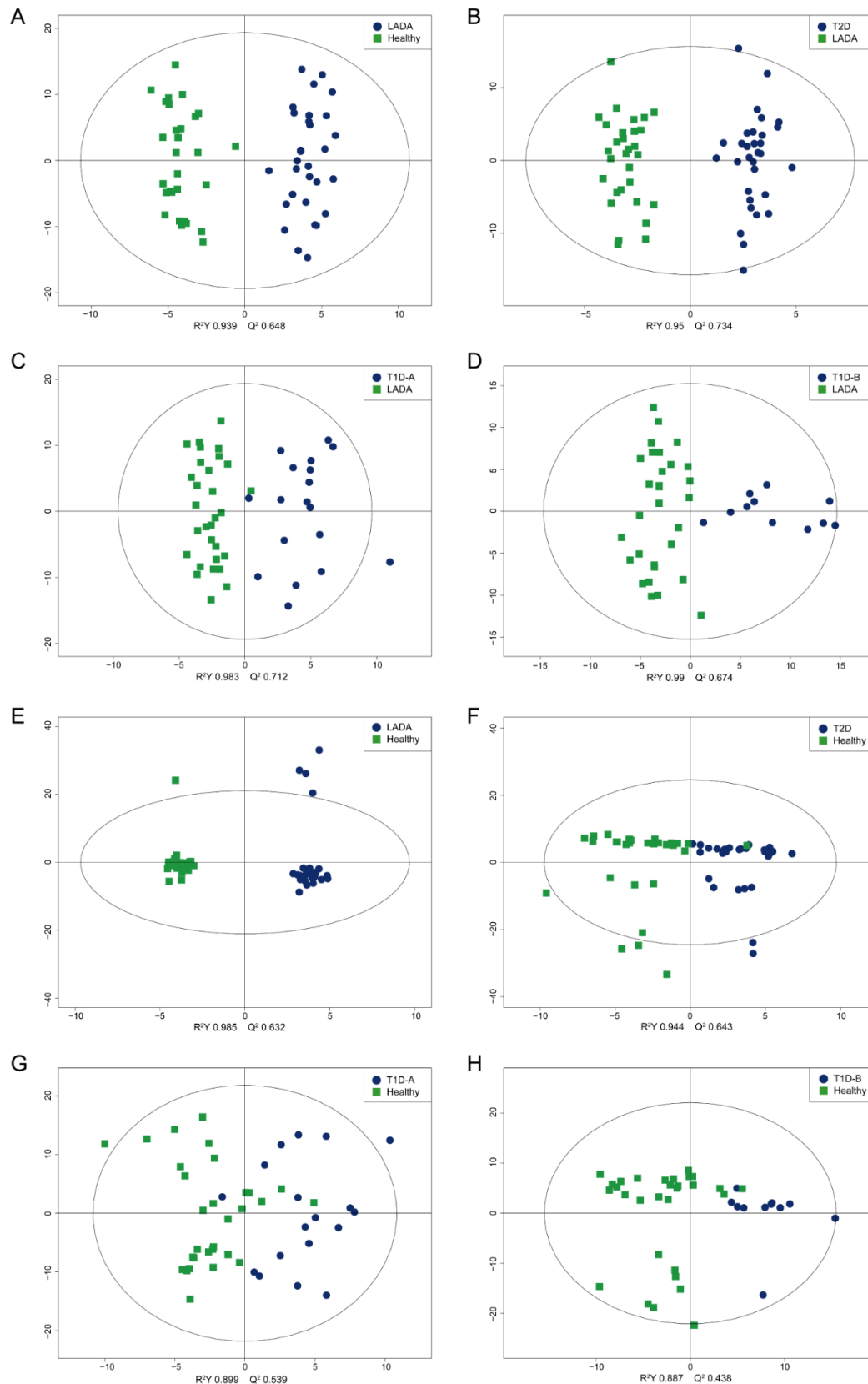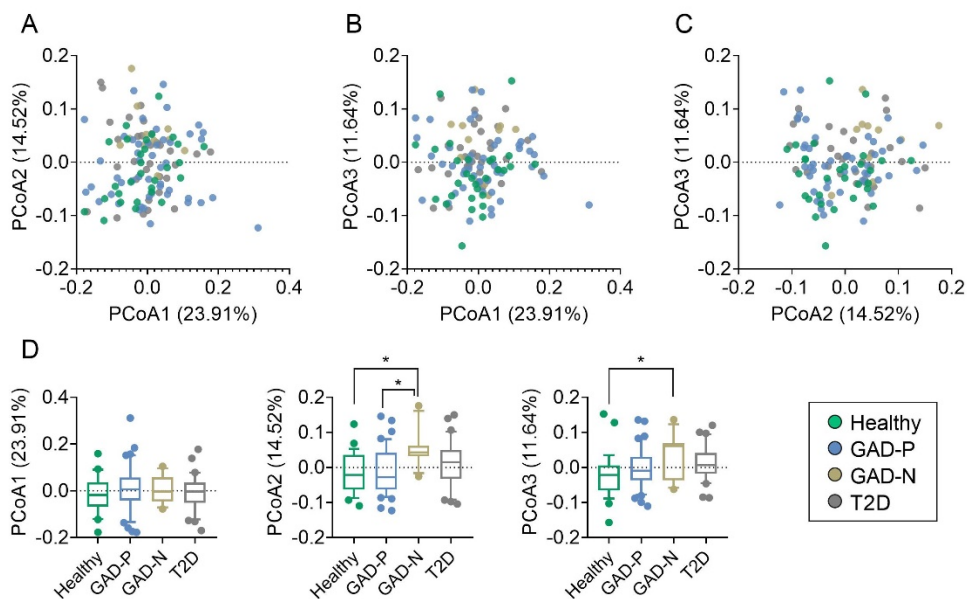
Supplementary Figure 10—Orthogonal projection to latent structure-discriminant analysis (OPLS-DA) score plots of serum metabolites. (A–D) Comparisons in the negative ion mode. (E–H) Comparisons in the positive ion mode. Abbreviations: LADA, latent autoimmune diabetes in adults; T1D-A, type 1 diabetes-A (GADA-positive); T1D-B, type 1 diabetes-B (GADA-negative); T2D, type 2 diabetes.
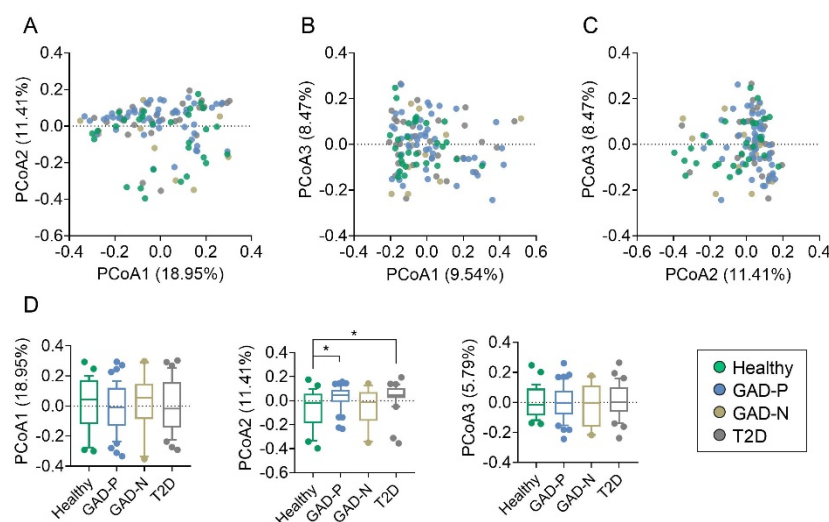
Supplementary Figure 11—Comparison of the fecal metabolites detected in the negative ion mode between healthy, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. Comarisons were performed using the Kruskal-Wallis test with Dunn's multiple comparions test; significant differences had a *P*-value that was controlled at 0.05.
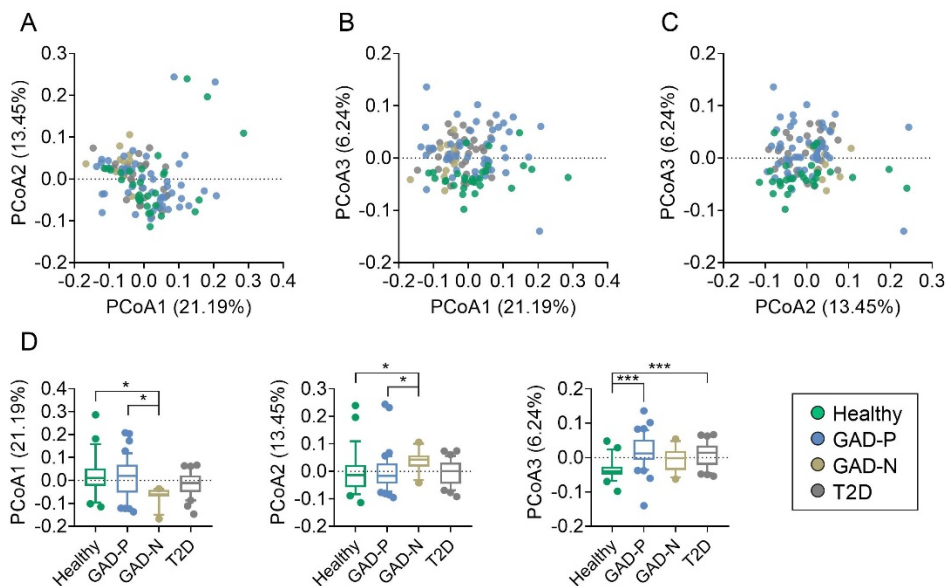

Supplementary Figure 12—Comparison of the fecal metabolites detected in the positive ion mode between healthy, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. Comarisons were performed using the Kruskal-Wallis test with Dunn's multiple comparions test; for significant differences,

Supplementary Figure 13—Comparison of the serum metabolites detected in the negative ion mode between healthy, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. Comarisons were performed using the Kruskal-Wallis test with Dunn's multiple comparions test; for significant differences, the *P*-value was controlled at 0.05.
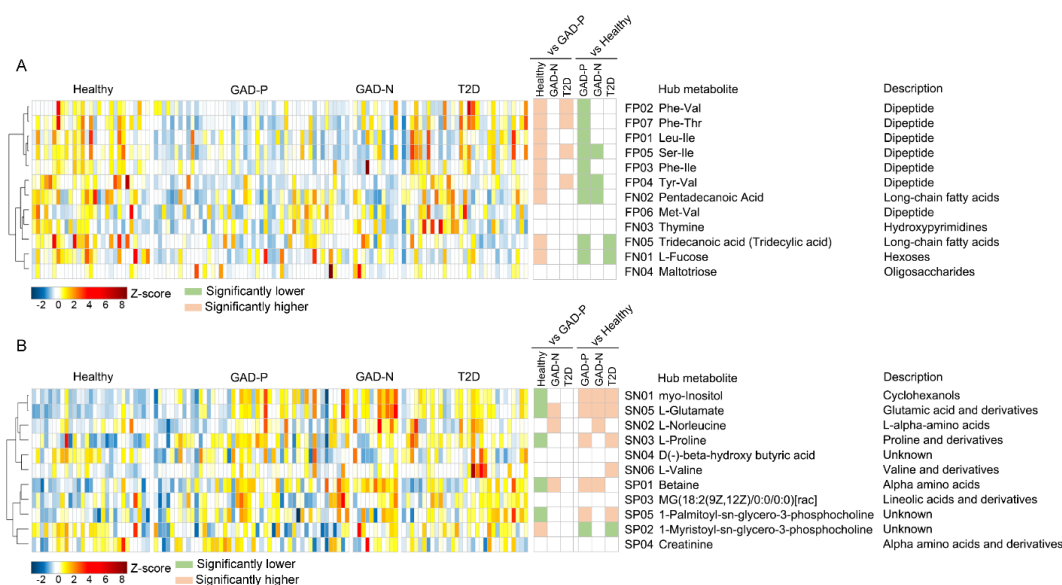

Supplementary Figure 14—Comparison of the serum metabolites detected in the negative ion mode between healthy, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. Comarisons were performed using the Kruskal-Wallis test with Dunn's multiple comparions test; for significant differences,

Supplementary Figure 15—Comparison of the major fecal and serun modules among healthy, GADA-positive (GADA-P), GADA-negative (GADA-N), and type 2 diabetes (T2D) groups. A, Distribution of the 12 fecal metabolite modules among the five groups. The abundance profiles were transformed into Z scores by subtracting the average abundance anding dividing the standard deviations of all the samples. The Z score was negative (shown in blue) when the row abundance was lower than tne mean. Comarisons among the abundance of each module among 5 groups were performed using the Kruskal-Wallis test with Dunn's multiple comparions test; significant differences had a *P*-value was controlled at 0.05. B, Distribution of the 11 serum metabolite modules among the five groups. The abundance profiles were transformed into Z scores by subtracting the average abundance anding dividing the standard deviations of all the samples. The Z score was negative (shown in blue) when the row abundance was lower than tne mean. Comarisons among the abundance of each module among 5 groups were performed using the Kruskal-Wallis test with Dunn's multiple comparions test; significant differences had a *P*-value was controlled at 0.05.