

Supplementary Table S1. Clinical characteristics of the study population

Characteristics	NFG (n = 1,281)	IFG (n = 247)	T2DM (n = 370)	F/ χ^2 /H	P
Age	52.45 ± 15.58	59.15 ± 12.57*	59.94 ± 12.06*	50.527	< 0.001
Gender, n (%)				6.173	0.046
Male	600 (46.84)	103 (41.70)	149 (40.27)		
Female	681 (53.16)	144 (58.30)	221 (57.03)		
BMI (kg/m ²)	24.76 ± 3.64	26.36 ± 3.72*	26.37 ± 3.61*	40.229	< 0.001
FBG (mmol/L)	4.74 ± 0.44	6.07 ± 0.35*	9.20 ± 3.29*#	1266.529	< 0.001
INS ^a	10.76 (7.99, 13.79)	13.06 (9.96, 17.68)*	13.19 (9.46, 19.04)*	46.640	< 0.001
TC (mmol/L)	4.45 ± 0.98	4.90 ± 0.98*	4.74 ± 1.09*	27.960	< 0.001
TG (mmol/L) ^a	1.23 (0.82, 1.90)	1.61 (1.10, 2.68)*	1.79 (1.15, 2.77)*	60.236	< 0.001
LDL-C (mmol/L)	2.52 ± 0.77	2.84 ± 0.79*	2.55 ± 0.82#	16.359	< 0.001
HDL-C (mmol/L)	1.25 ± 0.31	1.18 ± 0.31*	1.22 ± 0.29	5.649	0.004
HOMA-IR ^a	2.28 (1.66, 2.97)	3.46 (2.75, 4.67)*	5.09 (3.40, 8.04)*#	399.426	< 0.001
HOMA- β ^a	173.77 (123.20, 259.77)	104.64 (79.28, 138.42)*	54.91 (29.96, 93.24)*#	512.632	< 0.001
25(OH)D ₃ (ng/mL) ^b	20.05 (15.43, 29.38)	19.7 (15.70, 26.15)	18.73 (14.98, 27.45)	3.054	0.217
1,25(OH) ₂ D ₃ (ng/mL) ^b	22.83 (15.80, 47.52)	24.15 (19.01, 35.45)	20.67 (12.90, 31.46)*#	20.957	< 0.001
Hypertension, n (%)				68.183	< 0.001
No	808 (63.27)	118 (48.36)	149 (40.60)		
Yes	469 (36.73)	126 (51.64)	218 (59.40)		
Physical Activity, n (%)				20.565	< 0.001
Low	472 (36.93)	105 (42.86)	176 (47.70)		
Moderate	254 (19.87)	58 (23.67)	69 (18.70)		
High	552 (43.19)	82 (33.47)	124 (33.60)		
FAMTD, n (%)				19.972	< 0.001
No	228 (74.51)	214 (89.54)	297 (81.59)		
Yes	78 (25.49)	25 (10.46)	67 (18.41)		

Note. Data were given as means ± SD for normally distributed variables (age, BMI, FBG, TC, LDL-C, HDL-C), median (P_{25} , P_{75}) for non-normally distributed variables [INS, TG, HOMA-IR, HOMA- β , 25(OH)D₃, 1,25(OH)₂D₃], n (%) for categorical variables, and the significance of differences between groups evaluated using ANOVA, Kruskal Wallis H or χ^2 tests, respectively. *: $P < 0.05$ compared with NFG; #: $P < 0.05$ compared with IFG; ^a: Normally distributed variables after log transform; ^b: Kruskal Wallis H test. NFG, normal fasting blood glucose; IFG, impaired fasting blood glucose; T2DM, type 2 diabetes mellitus; BMI, body mass index; FBG, fasting blood glucose; INS, fasting serum insulin; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA- β , homeostasis model assessment of β -cell function; FAMTD, family history of T2DM.

Supplementary Table S2. Quantitative metabolic traits in non-T2DM subjects stratified according to genotype

SNP genotype	rs2189480			P	P ^a
	AA	CA	CC		
n (%)	804 (42.74)	828 (44.02)	249 (13.24)		
BMI (kg/m ²)	25.26 ± 3.74	25.37 ± 3.74	25.03 ± 3.55	0.518	
FBG (mmol/L)	5.83 ± 2.36	5.82 ± 2.30	5.61 ± 2.14	0.368	0.408
INS (mIU/L) ^b	11.38 (8.58, 15.70)	11.19 (8.26, 14.78)	11.74 (8.24, 15.53)	0.954	0.837
TC (mmol/L)	4.59 ± 1.00	4.57 ± 1.04	4.47 ± 1.01	0.489	0.538
TG (mmol/L) ^b	1.44 (0.93, 2.16)	1.34 (0.87, 2.09)	1.29 (0.89, 2.09)	0.144	0.129
LDL-C (mmol/L)	2.56 ± 0.78	2.50 ± 0.79	2.49 ± 0.71	0.413	0.397
HDL-C (mmol/L)	1.23 ± 0.29	1.24 ± 0.31	1.25 ± 0.33	0.704	0.653
HOMA-IR ^b	2.98 (1.98, 15.60)	2.91 (1.96, 14.84)	2.85 (1.83, 13.48)	0.591	0.673
HOMA-β ^b	130.20 (29.49, 211.88)	129.37 (34.66, 208.12)	137.09 (70.93, 215.94)	0.309	0.279
25(OH)D ₃ (ng/mL) ^c	15.33 (6.36, 23.28)	16.11 (6.44, 23.90)	15.73 (8.35, 25.00)	0.579	
1,25(OH) ₂ D ₃ (ng/mL) ^c	29.45 (19.19, 87.27)	33.78 (20.05, 89.62)	31.14 (17.00, 92.48)	0.298	

Note. Data were given as means ± SD for normally distributed variables (BMI, FBG, TC, LDL-C, HDL-C), median (P_{25} , P_{75}) for non-normally distributed variables [INS, TG, HOMA-IR, HOMA-β, 25(OH)D₃, 1,25(OH)₂D₃], n (%) for categorical variables. ^a: Adjusted for age, gender, BMI, drinking, smoking, physical activity, and family history of T2DM. P value for general liner model. ^b: Normally distributed variables after log transform; ^c: Kruskal Wallis H test. SNP, single nucleotide polymorphism; BMI, body mass index; FBG, fasting blood glucose; INS, fasting serum insulin; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of β-cell function.

Supplementary Table S3. Gene-environment interaction models using GMDR

Model	Training Bal.Acc.	Testing Bal.Acc.	CVC	P
Rs2189480 BMI	0.590	0.578	10/10	0.001
Rs2189480 Hypertension	0.597	0.598	10/10	0.001
Rs2189480 TC	0.554	0.553	10/10	0.001
Rs2189480 TG	0.598	0.599	10/10	0.001

Note. BMI, body mass index; TC, total cholesterol; TG, triglyceride; CVC, cross-validation consistency.