

SUPPLEMENTARY DATA

Supplementary Table 1. Spearman correlations between plasma GIP and metabolic phenotypes in the PPP-Botnia study.

		Fasting GIP	GIP 120 min
Fasting GIP (pg/ml)	<i>r</i>	-	0.363
	<i>P</i>	-	2.8×10^{-136}
	<i>N</i>		4373
BMI (kg/m ²)	<i>r</i>	0.054	-0.034
	<i>P</i>	0.0003	0.021
	<i>N</i>	4468	4517
Fat%	<i>r</i>	0.038	0.171
	<i>P</i>	0.045	2.6×10^{-20}
	<i>N</i>	2826	2870
Lean body mass	<i>r</i>	0.043	-0.266
	<i>P</i>	0.023	1.6×10^{-47}
	<i>N</i>	2826	2870
ISI	<i>r</i>	-0.096	-0.016
	<i>P</i>	3.8×10^{-10}	0.30
	<i>N</i>	4232	4341

Supplementary Table 2. Spearman correlations between *GIPR* mRNA in adipose tissue and metabolic phenotypes in non-diabetic participants of the EUGENE2 (Kuopio) and Danish-twins studies

		<i>GIPR</i> mRNA (EUGENE2-Kuopio) N=110	<i>GIPR</i> mRNA (Danish-Twins) N=187
BMI (kg/m ²)	<i>r</i>	-0.361	-0.303
	<i>P</i>	0.0001	3×10^{-5}
Waist (cm)	<i>r</i>	-0.472	-0.271
	<i>P</i>	1×10^{-6}	0.0002
Subcutaneous fat in CT (cm ²)	<i>r</i>	-0.112	-
	<i>P</i>	0.26	-
Intraabdominal fat in CT (cm ²)	<i>r</i>	-0.533	-
	<i>P</i>	1×10^{-6}	-
		Whole body glucose uptake (umol/kg/min)	ISI
Insulin sensitivity	<i>r</i>	0.385	0.168
	<i>P</i>	3×10^{-5}	0.023
Glucose oxidation (μmol/kg/min)	<i>r</i>	0.376	-
	<i>P</i>	7×10^{-5}	-
Lipid oxidation (mg/kg/min)	<i>r</i>	-0.257	
	<i>P</i>	0.008	
Adiponectin (μg/ml)	<i>r</i>	0.434	-
	<i>P</i>	2×10^{-5}	-

SUPPLEMENTARY DATA

Supplementary Table 3. Effect of the *GIPR* rs10423928 on body composition measured by DEXA in the Danish low birth weight cohort.

Phenotype	Genotypes		P value
	TT	TA/AA	
Risk (A) allele frequency, %	20.3		
Number	74	44	
Anthropometrics			
Height (cm)	182.0 ± 7.0	182.2 ± 7.1	0.881
Weight (kg)	79.9 ± 11.1	75.3 ± 8.6	0.016
BMI (kg/m ²)	24.1 ± 3.0	22.8 ± 2.9	0.024
Birth weight (g)	3265 ± 656	3401 ± 651	0.302
Fasting P-glucose (mmol/l)	5.36 ± 0.50	5.42 ± 0.52	0.466
Fasting P-insulin (pmol/l)	34.2 ± 18.0	30.9 ± 15.8	0.338
HbA1c (%)	5.15 ± 0.25	5.17 ± 0.33	0.376
HOMA- IR	8.32 ± 4.90	7.51 ± 3.94	0.374
DEXA			
Fat percentage (%)	20.9 ± 7.1	19.3 ± 6.9	0.306
Bone mass trunk (g)	1043 ± 221	1002 ± 148	0.332
Fat mass trunk (g)	8213 ± 4201	7854 ± 3640	0.642
Lean mass trunk (g)	27627 ± 3018	26368 ± 2757	0.014
Bone mass total (g)	3273 ± 458	3211 ± 367	0.510
Fat mass total (g)	16238 ± 7736	15282 ± 6721	0.473
Lean mass total (g)	59836 ± 6525	56953 ± 5698	0.006

Data are means ± SD. P values are adjusted for birth weight and sampling period.

SUPPLEMENTARY DATA

Supplementary Table 4. Effect of the *GIPR* rs10423928 on substrate oxidation in the Danish overfeeding study.

	Control diet			P value	Overfeeding			P value	P value (Interdiet)
GIP (ng/ml)									
TT (n:27)	47.0	±	17.1	0.25	90.7	±	63.3	0.14	0.003
TA or AA (n:17)	54.0	±	22.5		65.7	±	28.0		0.12
F-p-glucose (mmol/l)									
TT (n:25)	4.67	±	0.50	0.283	5.12	±	0.41	0.823	<0.001
TA or AA (n:17)	4.85	±	0.49		5.10	±	0.34		0.010
F-p-insulin (pmol/l)									
TT (n:25)	34.2	±	14.3	0.508	45.7	±	29.1	0.625	0.030
TA or AA (n:17)	37.1	±	16.9		41.5	±	22.4		0.131
HOMA									
TT (n:25)	3698	±	1968	0.551	5384	±	3818	0.770	0.019
TA or AA (n:17)	4026	±	1771		4677	±	2284		0.094
Basal FOX (mg/min/FFM)									
TT (n:26)	1.15		0.44	0.027	1.05		0.33	0.66	0.34
TA or AA (n:16)	0.84		0.40		1.11		0.36		0.014
Ins.stim. FOX (mg/min/FFM)									
TT (n:22)	0.05		0.32	0.69	0.22		0.35	0.60	6.0×10 ⁻¹³
TA or AA (n:16)	0.10		0.400		0.30		0.30		5.2×10 ⁻⁷
Basal GOX (mg/min/FFM)									
TT (n:26)	1.98		0.64	0.018	2.33		0.71	0.50	0.063
TA or AA (n:16)	2.55		0.97		2.45		0.69		0.740
Ins.stim. GOX (mg/min/FFM)									
TT (n:22)	5.02		0.83	0.83	4.89		0.92	0.80	0.51
TA or AA (n:16)	5.07		0.93		4.92		0.83		0.555
Respiratory quotient									
TT (n:26)	<u>2.39</u>	±	<u>2.19</u>	0.025	<u>2.62</u>		<u>1.57</u>	0.83	0.12
TA or AA (n:16)	<u>4.52</u>	±	<u>5.00</u>		<u>2.81</u>		<u>2.24</u>		0.25
M-value									

SUPPLEMENTARY DATA

TT (n:25)	13.8	±	2.7	0.371	12.0	±	3.3	0.432	0.021
TA or AA (n:17)	13.1	±	2.4		12.7	±	2.8		0.187
AUCins0-10									
TT (n:25)	2176	±	1293	0.405	2967	±	1759	0.728	<0.001
TA or AA (n:17)	2532	±	1508		3170	±	1990		0.020
AUCins0-30									
TT (n:25)	5053	±	2717	0.303	7094	±	3891	0.998	<0.001
TA or AA (n:17)	5967	±	3073		7091	±	3909		0.03

Data are mean ± SD. Interdiet P values are from paired T-test.

SUPPLEMENTARY DATA

Supplementary Table 5A. Effect of the *GIPR* rs10423928 on metabolic phenotypes in Danish twin study.

Phenotype	Number	Genotypes			Additive model (dominant)		
		TT	TA	AA	BETA	SE	P Value
Risk (A) allele frequency, %		27.7					
Number	287	148	119	20			
IGT/T2D (N)	121	64	47	10	-	-	0.72
Age (yrs)	287	74.1 ± 4.8	73.1 ± 5.4	74.2 ± 5.8	-0.463	0.490	0.35
Height (cm)	286	166 ± 8	167 ± 10	163 ± 9	-0.383	0.612	0.53
Weight (kg)	285	73.4 ± 13.8	72.9 ± 12.4	65.7 ± 13.2	-1.351	1.283	0.29
Waist (cm)	239	91.9 ± 11.4	91.6 ± 10.5	86.7 ± 13.7	-1.428	1.095	0.19
BMI (kg/m ²)	285	26.5 ± 4.7	26.0 ± 3.6	25.0 ± 4.6	-0.356	0.455	0.44
Fasting P-glucose (mmol/l)	239	5.68 ± 0.58	5.52 ± 0.47	5.53 ± 0.42	-0.099	0.053	0.063
Fasting P-OPN (pg/ml)	118	54 ± 24	50 ± 30	50 ± 9	-0.099	0.094	0.29
Fasting P-GIP (pg/ml)	248	44 ± 19	46 ± 22	37 ± 24	-0.033	0.044	0.45
<i>GIPR</i> mRNA							
Monozygous	86	0.16 ± 0.09	0.21 ± 0.15	0.19 ± 0.08	0.118	0.09	0.21
Heterozygous	133	0.18 ± 0.10	0.16 ± 0.09	0.23 ± 0.18	0.064	0.08	0.45
<i>OPN</i> mRNA							
Monozygous	81	0.18 ± 0.32	0.045 ± 0.07	0.055 ± 0.05	-0.458 (-0.880)	0.03 (0.03)	0.09 (0.009)
Heterozygous	117	0.05 ± 0.06	0.04 ± 0.05	0.04 ± 0.03	-0.072	0.18	0.69

Data are mean ± SD. *P* values are adjusted for age, sex and BMI.

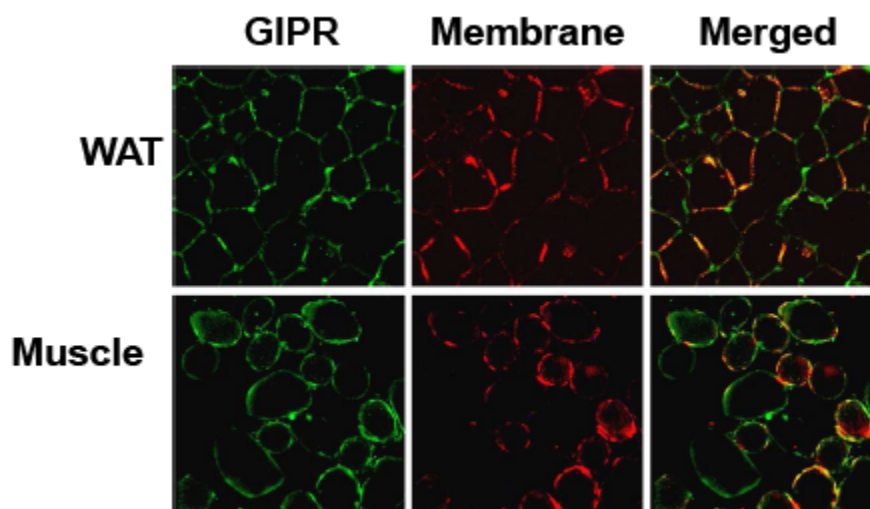
SUPPLEMENTARY DATA

Supplementary Table 5B. Effect of the *GIPR* rs10423928 on metabolic phenotypes in EUGENE study.

Phenotype	Number	Genotypes			Additive model
		TT	TA	AA	<i>P</i> Value
Risk (A) allele frequency, %			21.1		
Number	277	175	87	15	
IGT/T2D (N)	33/0	18/0	13/0	2/0	
Age (yrs)	277	35.2 ± 6.2	35.1 ± 6.6	38.6 ± 5.1	0.12
Height (cm)	277	172.3 ± 9.3	173.0 ± 8.3	170.5 ± 8.5	0.57
Weight (kg)	277	77.7 ± 16.8	79.1 ± 16.5	76.7 ± 15.1	0.76
BMI (kg/m ²)	273	26.2 ± 5.1	26.3 ± 4.9	26.2 ± 5.0	0.99
Fasting P-glucose (mmol/l)	277	5.20 ± 0.45	5.20 ± 0.46	5.15 ± 0.33	0.89
<i>GIPR</i> mRNA	110	1.22 ± 0.61	1.35 ± 0.79	1.30 ± 0.56	0.44
<i>OPN</i> mRNA	115	1.14 ± 1.23	1.09 ± 1.13	0.51 ± 0.46	0.45

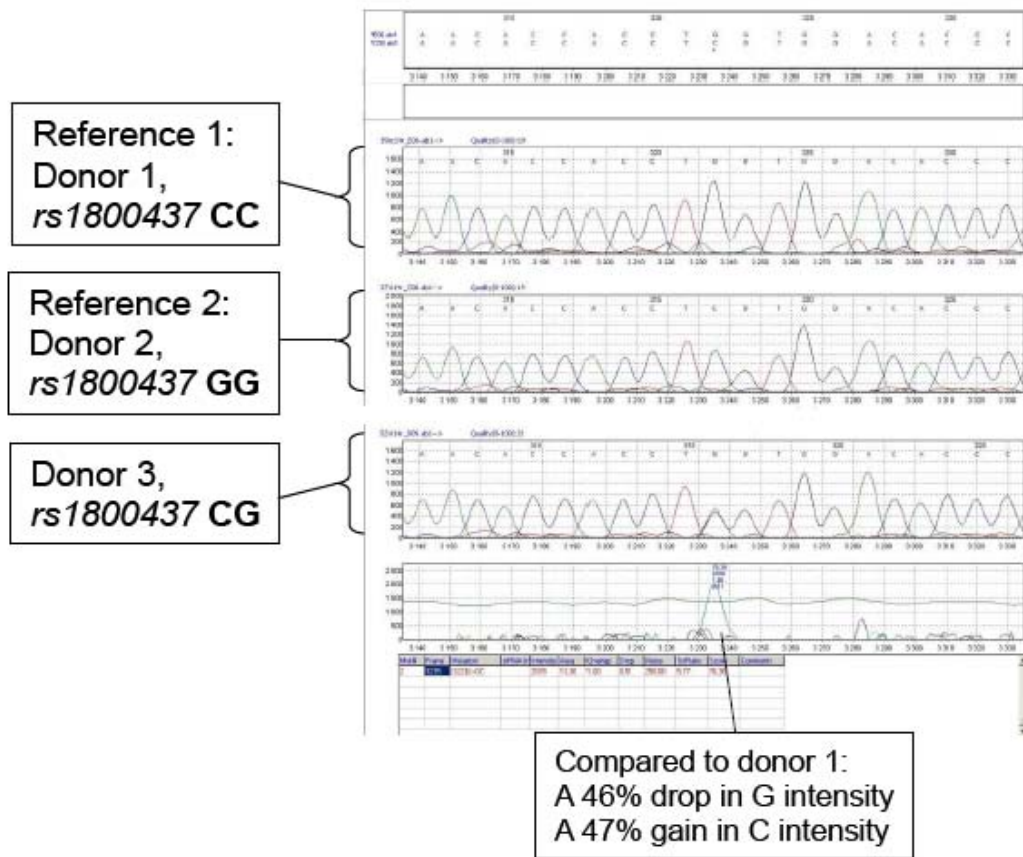
Data are mean ± SD. *P* values are adjusted for age and BMI.

Supplementary Figure 1. Expression of the *GIPR* in cell membrane from adipose and muscle tissues.



SUPPLEMENTARY DATA

Supplementary Figure 2. GIPR allele-specific expression analysis in adipose tissue.



Average drop in G / gain in C for all CG donors: 46.1 ± 4 %