

SUPPLEMENTARY DATA

**Supplementary Table 1.** Main clinical characteristics of the pediatric cohort evaluating  $\beta$ -cell function assessed from OGTT by the Oral C-peptide Minimal Model

	<b>Total Cohort</b>	<b>NGT Obese Youth</b>	<b>IGT Obese Youth</b>
<b>Number</b> †	714	530	184
<b>Gender (M/F)</b>	290/424	224/306	66/118
<b>Race (C/AA/H)</b>	316/188/210	240/144/146	76/44/64
<b>GT (NGT/IGT)</b>	530/184	530/0	0/184
<b>Age</b>	13.6±3.1	13.7±3.1	13.1±2.9
<b>BMI (kg/m<sup>2</sup>)</b>	33.4±7.4	33.2±7.3	34.2±7.4
<b>BMI-Z</b>	2.2±0.4	2.2±0.4	2.2±0.4
<b>Fasting Glucose (mg/dl)</b>	92±8	91±7	97±10
<b>2-h Glucose (mg/dl)</b>	122±25	111±16	155±14
<b>Fasting Insulin (<math>\mu</math>U/ml)</b>	33.9±21.3	31.7±20.4	40.3±22.5
<b>Phi total *</b>	84.8 (60.6-112.8)	89.3 (64.8-125.6)	72.5 (55.9-97.0)
<b>SI *</b>	19.4 (10.6-32.6)	22.8 (14.1-36.6)	10.7 (6.1-20.1)
<b>DI total *</b>	2512 (1401-4274)	3121 (1909-5543)	1294 (727-2217)

Data are means±SD or \*median (interquartile range).

†Number of participants. M: Male; F: Female; C: Caucasians; AA: African Americans; H: Hispanics; NGT: Normal Glucose Tolerance; IGT: Impaired Glucose Tolerance; BMI: Body Mass Index; BMI-Z: Body Mass Index Zeta Score; SI: Insulin Sensitivity; DI: Disposition Index

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**Supplementary Table 2.** Minor allele frequencies (MAF) genotype distribution (101, 102 and 202) and Hardy Weinberg Equilibrium for each of the studied SNPs

Caucasians						
Gene	rs	MAF	<b>101</b>	<b>102</b>	<b>202</b>	HWE p-value
<i>TCF7L2</i> (C/T)	rs7903146	0.31	150	135	31	0.94
<i>HHEX</i> (C/T)	rs1111875	0.37	126	144	46	0.64
<i>IGF2BP2</i> (G/T)	rs4402960	0.32	143	143	30	0.50
<i>CDKALI</i> (G/C)	rs7754840	0.41	113	147	56	0.49
<i>HNF1A</i> (A/C)	rs1169288	0.35	138	138	40	0.54
African Americans						
<i>TCF7L2</i> (C/T)	rs7903146	0.29	93	78	17	0.92
<i>HHEX</i> (C/T)	rs1111875	0.28	104	64	20	0.04
<i>IGF2BP2</i> (G/T)	rs4402960	0.51	42	99	47	0.45
<i>CDKALI</i> (G/C)	rs7754840	0.52	45	91	52	0.67
<i>HNF1A</i> (A/C)	rs1169288	0.14	139	45	4	0.87
Hispanics						
<i>TCF7L2</i> (C/T)	rs7903146	0.27	113	79	18	0.43
<i>HHEX</i> (C/T)	rs1111875	0.33	89	102	19	0.18
<i>IGF2BP2</i> (G/T)	rs4402960	0.32	98	91	21	0.98
<i>CDKALI</i> (G/C)	rs7754840	0.43	77	86	47	0.02
<i>HNF1A</i> (A/C)	rs1169288	0.37	80	104	26	0.37

**Supplementary Table 3.** Prevalence of Family History (FH) of type 2 diabetes according to the genetic risk score

	Number of Risk Alleles								
	0	1	2	3	4	5	6	7	8
Negative FH (%)	92	83	76	77	72	71	41	67	50
Positive FH (%)	8	17	24	23	28	29	59	33	50

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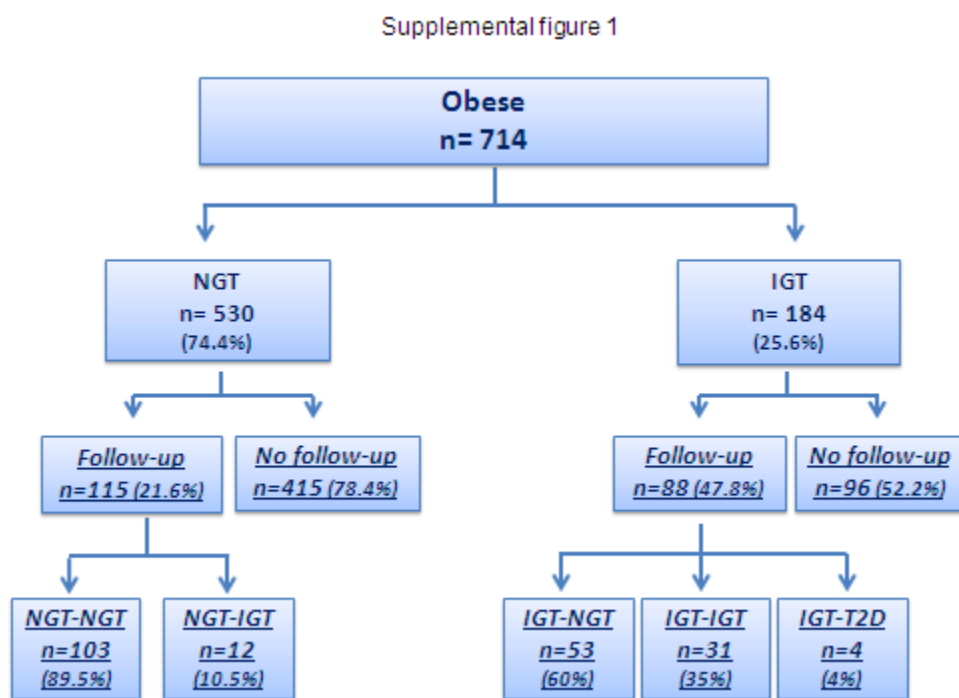
**Supplementary Table 4.** Linear regression analysis evaluating the association between 2h-glucose, Insulin Sensitivity (S<sub>I</sub>) or Disposition Index (DI) total and the gene risk score adjusted for Age, Gender, BMI-Z and Glucose Tolerance, divided by ethnicity

Dependent Variables	Independent variables	Ethnic Group					
		Caucasians		African Americans		Hispanics	
		Beta	P	Beta	P	Beta	P
<b>Log 2h glucose</b>	<b>Age</b>	-.139	.013	-.068	.346	.022	.755
	<b>Gender</b>	.094	.088	.080	.258	.090	.195
	<b>BMI-Z</b>	.174	.002	.102	.159	.040	.571
	<b>Gene score</b>	.221	<b>.000</b>	.327	<b>.000</b>	.307	<b>.000</b>
<b>Log S<sub>I</sub></b>	<b>Age</b>	-.116	.022	-.111	.079	-.236	.001
	<b>Gender</b>	-.059	.240	-.159	.011	-.136	.044
	<b>BMI-Z</b>	-.460	.000	-.374	.000	-.219	.001
	<b>GT</b>	-.360	.000	-.469	.000	-.364	.000
	<b>Gene score</b>	.041	.423	.101	.113	.024	.722
<b>Log DI Total</b>	<b>Age</b>	-.136	.009	-.106	.088	-.171	.009
	<b>Gender</b>	-.049	.333	-.053	.387	-.134	.037
	<b>BMI-Z</b>	-.378	.000	-.306	.000	-.186	.005
	<b>GT</b>	-.415	.000	-.489	.000	-.387	.000
	<b>Gene score</b>	-.120	<b>.025</b>	-.157	<b>.014</b>	-.254	<b>.000</b>

BMI-Z: Body Mass Index Zeta Score; GT: Glucose Tolerance.

SUPPLEMENTARY DATA

Supplementary Figure 1.



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**Supplementary Figure 2.** Association between the allele score and Clamp derived measures of beta cell secretion (first and second phase for c-peptide, respectively)

