ONLINE APPENDIX

Power Calculation

We used Quanto for power calculations.[1] For the study of individual SNPs, assuming an additive model and allele frequency of 40%, we had 80% power to detect a per-allele effect on FG of 0.058, 0.067, and 0.067mmol/L or higher for non-Hispanic whites, non-Hispanic blacks, and Mexican Americans, respectively. For IFG risk, assuming an allele frequency of 20%, we had 80% power to detect a per-allele odds ratio (OR) of at least 1.33, 1.42, and 1.36 for the 3 racial/ethnic groups, respectively. For the GRS with the same assumptions, we had 80% power to detect a per-allele effect on FG of 0.016, 0.019, and 0.019mmol/L. For IFG risk, the corresponding ORs were 1.09, 1.11, and 1.11, respectively.

References

1. Gauderman WJ. Sample size requirements for association studies of gene-gene interaction. *Am J Epidemiol.* 2002;155(5):478-484.

Online-Appendix Table 1. Weighted Allele and Genotype Frequencies of 16 Fasting Glucose-associated Single Nucleotide Polymorphisms by Race/ethnicity, Third National Health and Nutrition Examination Survey DNA Bank (NHANES III 1991-1994)

				Non-Hispanic white					Non-Hispanic black					Mexican American				
SNP	Chromosome	Nearest gene	Risk allele (+/-)†	Risk allele frequency	HapMap CEU risk allele frequency	Non-carrier	Heterozygous	Homozygous	Risk allele frequency	HapMap ASW risk allele frequency	Non-carrier	Heterozygous	Homozygous	Risk allele frequency	HapMap MEX risk allele frequency	Non-carrier	Heterozygous	Homozygous
rs340874	1	*PROX1*	C/T	52.4 (48.9-55.9)	56.2	22.8 (18.7-27.6)	49.5 (45.8-53.3)	27.6 (24.4-31.1)	21.9 (19.2-24.8)	16.0	60.5 (55.6-65.2)	35.2 (31.2-39.5)	4.3 (3.2-5.8)	41.2 (38.2-44.2)	43.0	35.9 (32.5-39.5)	45.9 (43.8-48.0)	18.2 (15.6-21.2)
rs573225	2	*G6PC2*	A/G	69.9 (67.7-72.1)	65.5	8.7 (6.7-11.2)	42.8 (38.7-47.0)	48.6 (44.9-52.2)	92.6 (90.9-93.9)	94.3	n/a	14.0 (11.6-16.6)	86.0) (82.6-89.6	82.6 (79.8-85.1)	83.0	3.3 (2.4-4.4)	28.2 (23.5-33.4)	68.5 (63.3-73.3)
rs780094	2	*GCKR*	C/T	58.3 (55.9-60.6)	60.6	15.4 (12.9-18.3)	52.7 (49.3-56.0)	31.9 (28.9-35.1)	80.8 (78.7-82.7)	85.8	4.0 (2.8-5.7)	30.4 (27.0-34.0)	65.6 (62.0-69.0)	65.1 (62.1-67.9)	71.4	12.3 (9.8-15.3)	45.4 (41.4-49.4)	42.4 (38.2-46.6)
rs11708067	3	*ADCY5*	A/G	77.8 (75.4-80.0)	77.4	4.0 (2.8-5.9)	36.3 (32.7-40.0)	59.7 (55.7-63.5)	85.3 (83.2-87.2)	81.1	1.9 (1.1-3.0)	25.7 (22.8-28.9)	72.4 (68.8-75.8)	72.4 (69.8-75.0)	65.0	9.0 (7.0-11.5)	37.2 (33.3-41.2)	53.9 (49.8-57.9)
rs11920090	3	*SLC2A2*	T/A	85.4 (83.8-86.8)	85.3	2.7 (1.6-4.6)	23.8 (21.2-26.6)	73.5 (70.9-75.9)	66.0 (63.8-68.1)	66.7[1]	12.2 (10.5-14.2)	43.6 (39.9-47.4)	44.2 (40.6-47.8)	86.5 (84.0-88.7)	n/a	2.0 (1.3-2.9)	23.0 (19.8-26.7)	75.0 (70.8-78.8)
rs2191349	7	*DGKB*	T/G	54.7 (52.7-56.6)	53.3	19.5 (17.1-22.2)	51.6 (48.8-54.4)	28.8 (26.6-31.1)	57.9 (55.8-59.9)	40.7*	17.6 (14.9-20.6)	49.1 (44.9-53.4)	33.3 (30.3-36.4)	41.9 (38.2-45.7)	n/a	34.5 (30.4-38.7)	47.3 (43.6-51.0)	18.3 (14.5-22.8)
rs4607517	7	*GCK*	A/G	17.1 (15.3-18.9)	19.5	69.4 (66.5-72.2)	27.1 (24.5-29.9)	3.5 (2.4-5.2)	9.4 (7.6-11.7)	10.4	82.6 (78.9-85.8)	15.9 (13.2-19.0)	1.5 (0.9-2.5)	21.8 (19.8-23.8)	14.0	61.5 (58.0-64.9)	33.5 (29.7-37.5)	5.0 (3.4-7.3)
rs11558471	8	*SLC30A8*	A/G	69.0 (65.6-72.2)	74.8	10.0 (7.6-13.0)	42.1 (38.9-45.2)	48.0 (43.6-52.4)	88.7 (86.9-90.3)	81.1	2.4 (1.5-3.7)	17.9 (15.1-21.2)	79.7 (76.5-82.6)	72.9 (70.7-75.0)	81.0	8.0 (6.2-10.2)	38.1 (34.4-42.0)	53.9 (50.3-57.4)
rs7034200	9	*GLIS3*	A/C	51.3 (48.9-53.7)	52.5	24.2 (21.2-27.4)	49.0 (46.2-51.9)	26.8 (24.4-29.4)	62.6 (60.3-64.8)	58.5*	13.6 (11.5-16.0)	47.6 (44.3-51.0)	38.8 (35.5-42.1)	52.3 (50.4-54.2)	n/a	21.4 (19.1-23.9)	52.6 (50.4-54.8)	26.0 (24.0-28.0)
rs10885122	10	*ADRA2A*	G/T	86.1 (84.7-87.4)	90.0	2.2 (1.2-4.1)	23.4 (20.4-26.6)	74.4 (71.8-76.9)	34.9 (32.6-37.2)	21.7*	44.0 (40.4-47.5)	42.3 (38.7-46.0)	13.7 (11.8-16.0)	82.9 (80.8-84.9)	n/a	2.9 (2.1-4.0)	28.3 (24.8-32.2)	68.8 (64.9-72.4)
rs7903146	10	*TCF7L2*	T/C	29.1 (26.8-31.6)	27.9	51.8 (49.0-54.6)	38.1 (35.3-41.1)	10.0 (7.6-13.3)	26.7 (25.3-28.2)	33.7	53.9 (51.3-56.5)	38.8 (35.7-42.1)	7.3 (5.8-9.1)	18.0 (16.3-19.8)	25.0	66.0 (63.0-69.0)	32.0 (29.2-34.9)	2.0 (1.2-3.3)
rs10830963	11	*MTNR1B*	G/C	28.0 (25.8-30.3)	30.0	51.6 (48.0-55.2)	40.8 (37.7-44.0)	7.6 (6.2-9.3)	7.9 (6.4-9.8)	3.8*	85.3 (81.8-88.2)	13.6 (10.5-17.3)	1.2 (0.5-2.7)	21.1 (18.5-24.0)	25.0	62.6 (58.5-66.5)	32.6 (29.2-36.1)	4.8 (3.0-7.6)
rs174550	11	*FADS1*	T/C	66.5 (63.9-69.0)	63.3	11.4 (10.2-12.8)	44.2 (40.0-48.5)	44.4 (40.0-48.9)	89.8 (87.6-91.6)	98.3*	1.8 (0.9-3.6)	16.8 (14.2-19.8)	81.4 (77.9-84.4)	39.2 (34.5-44.1)	n/a	39.3 (32.9-46.0)	43.0 (37.5-48.7)	17.7 (13.8-22.5)
rs11605924	11	*CRY2*	A/C	48.3 (45.5-51.2)	54.2	26.9 (23.5-30.5)	49.7 (46.8-52.5)	23.5 (20.8-26.4)	85.4 (83.3-87.3)	88.2	2.7 (1.6-4.4)	23.8 (20.8-27.0)	73.6 (70.1-76.7)	50.0 (46.5-53.6)	n/a	24.8 (21.7-28.2)	50.2 (48.0-52.5)	24.9 (21.0-29.3)
rs7944584	11	*MADD*	A/T	71.4 (68.9-73.8)	71.2	8.6 (7.0-10.4)	40.0 (36.7-43.4)	51.4 (47.5-55.2)	93.7 (91.7-95.3)	92.5	0.8 (0.3-2.4)	10.8 (8.1-14.4)	88.3 (84.7-91.2)	84.3 (82.0-86.3)	78.0	3.6 (1.9-6.6)	24.3 (21.3-27.7)	72.1 (68.9-75.1)
rs11071657	15	*C2CD4B*	A/G	64.2 (62.0-66.4)	59.2	11.8 (9.7-14.1)	48.0 (43.2-52.8)	40.2 (36.3-44.3)	86.4 (83.7-88.6)	94.2*	1.7 (0.7-3.7)	24.0 (20.6-27.7)	74.4 (70.1-78.2)	49.2 (46.1-52.3)	n/a	27.3 (24.4-30.5)	47.0 (43.7-50.2)	25.7 (21.9-29.8)

Abbreviations: CEU, Utah residents with Northern and Western European ancestry from the CEPH collection; ASW, African ancestry in Southwest USA; MEX, Mexican ancestry in Los Angeles, California; n/a: not available; NHANES, Third National Health and Nutrition Examination Survey DNA Bank. Data and 95% confidence intervals are in parentheses.

*HapMap estimate for Yoruba in Ibadan, Nigeria.
† FG rising allele (+) is denoted first.

Online-Appendix Table 2. Regression Coefficients of 16 Fasting Glucose-associated Single Nucleotide Polymorphisms on Fasting Glucose Levels and Homeostasis Model Assessed Beta-cell Function by Race/ethnicity, Third National Health and Nutrition Examination Survey DNA Bank (NHANES III 1991-1994)

	Non-Hispanic white		Non-Hispanic black		Mexican American		
SNPs	β-coefficient*	***P*-value**†	β-coefficient *	***P*-value**†	β-coefficient *	***P*-value**†	***P*-value for heterogeneity**‡
rs340874 (nr. ***PROX1***)							
Fasting glucose (mmol/L)	0.006 (-0.052, 0.063)	0.842	-0.001 (-0.057, 0.055)	0.971	0.014 (-0.046, 0.073)	0.642	0.918
HOMA-B	1.86 (-4.67, 8.39)	0.561	3.96 (-9.19, 17.10)	0.539	-1.19 (-18.54, 16.16)	0.889	0.916
rs573225 (nr. ***G6PC2***)							
Fasting glucose (mmol/L)	0.078 (0.038, 0.119)	<0.001	0.030 (-0.091, 0.151)	0.610	0.095 (0.012, 0.178)	0.026	0.592
HOMA_B	-11.14 (-21.79, -0.49)	0.041	-4.20 (-28.87, 20.47)	0.728	-7.96 (-25.02, 9.11)	0.345	0.906
rs780094 (nr. *GCKR*)							
Fasting glucose (mmol/L)	0.063 (0.013, 0.114)	0.016	0.012 (-0.055, 0.080)	0.705	0.036 (-0.019, 0.092)	0.189	0.411
HOMA_B	-4.02 (-11.57, 3.54)	0.283	-1.31 (-16.97, 14.35)	0.864	-1.23 (-14.16, 11.70)	0.846	0.583
rs11708067 (nr. *ADCY5*)							
Fasting glucose (mmol/L)	0.039 (-0.020, 0.098)	0.181	0.063 (-0.035, 0.161)	0.199	0.028 (-0.020, 0.076)	0.242	0.804
HOMA_B	1.67 (-6.60, 9.94)	0.680	-16.25 (-31.00, -1.49)	0.032	-14.59 (-26.23, -2.94)	0.016	0.016
rs11920090 (nr. *SLC2A2*)							
Fasting glucose (mmol/L)	0.037 (-0.029, 0.102)	0.259	0.050 (-0.020, 0.121)	0.149	0.048 (-0.079, 0.176)	0.442	0.931
HOMA_B	-16.40 (-34.44, 1.64)	0.073	-2.62 (-13.25, 8.01)	0.615	-13.23 (-29.41, 2.95)	0.104	0.246
rs2191349 (nr. *DGKB*)							
Fasting glucose (mmol/L)	-0.009 (-0.046, 0.027)	0.601	0.062 (-0.001, 0.125)	0.054	-0.001 (-0.050, 0.048)	0.960	0.130
HOMA_B	5.70 (-1.95, 13.35)	0.137	-11.19 (-20.12, -2.26)	0.016	-9.53 (-21.28, 2.22)	0.107	0.007

rs4607517 (nr. *GCK*)							
Fasting glucose (mmol/L)	0.017 (-0.051, 0.085)	0.615	0.011 (-0.069, 0.090)	0.779	0.088 (0.032, 0.145)	0.004	0.268
HOMA_B	-5.80 (-20.70, 9.11)	0.429	0.17 (-18.47, 18.82)	0.985	-7.07 (-24.64, 10.49)	0.413	0.907
rs11558471 (nr. *SLC30A8*)							
Fasting glucose (mmol/L)	0.065 (0.019, 0.111)	0.008	0.071 (-0.020, 0.163)	0.121	-0.035 (-0.092, 0.022)	0.211	0.093
HOMA_B	-11.01 (-26.75, 4.73)	0.161	0.19 (-21.30, 21.67)	0.986	-0.02 (-10.60, 10.56)	0.997	0.377
rs7034200 (nr. *GLIS3*)							
Fasting glucose (mmol/L)	-0.005 (-0.045, 0.036)	0.811	-0.006 (-0.067, 0.055)	0.847	0.044 (-0.006, 0.095)	0.082	0.434
HOMA_B	-1.80 (-9.97, 6.36)	0.653	-3.67 (-17.44, 10.11)	0.587	16.57 (3.57, 29.58)	0.015	0.204
rs10885122 (nr. *ADRA2A*)							
Fasting glucose (mmol/L)	-0.060 (-0.122, 0.002)	0.056	0.058 (-0.003, 0.118)	0.061	0.044 (-0.030, 0.117)	0.233	0.009
HOMA_B	0.38 (-11.51, 12.26)	0.948	-2.51 (-14.92, 9.89)	0.679	-12.35 (-31.52, 6.81)	0.195	0.539
rs7903146 (nr. *TCF7L2)*							
Fasting glucose (mmol/L)	0.007 (-0.039, 0.053)	0.752	0.032 (-0.028, 0.093)	0.278	0.025 (-0.033, 0.083)	0.380	0.637
HOMA_B	-1.68 (-14.00, 10.64)	0.780	-2.21 (-16.88, 12.45)	0.758	-14.43 (-32.19, 3.34)	0.106	0.658
rs10830963 (nr. *MTNR1B*)							
Fasting glucose (mmol/L)	0.035 (-0.031, 0.102)	0.285	0.111 (0.039, 0.184)	0.004	0.068 (0.008, 0.127)	0.027	0.228
HOMA_B	-10.08 (-22.58, 2.42)	0.109	-7.76 (-32.70, 17.17)	0.526	-5.08 (-16.64, 6.49)	0.373	0.953
rs174550 (nr. *FADS1*)							
Fasting glucose (mmol/L)	-0.024 (-0.057, 0.009)	0.139	0.055 (-0.023, 0.133)	0.158	-0.005 (-0.063, 0.053)	0.855	0.106
HOMA_B	4.52 (-4.10, 13.14)	0.290	-22.19 (-42.16, -2.22)	0.031	1.40 (-8.02, 10.83)	0.761	0.046
rs11605924 (nr. *CRY2*)							
Fasting glucose (mmol/L)	0.019 (-0.034, 0.072)	0.472	0.032 (-0.024, 0.089)	0.249	0.049 (-0.001, 0.100)	0.053	0.601
HOMA_B	-2.21 (-9.42, 5.00)	0.532	-2.14 (-16.74, 12.46)	0.765	-2.83 (-14.45, 8.78)	0.618	0.967
rs7944584 (nr. *MADD*)							
Fasting glucose (mmol/L)	0.017 (-0.036, 0.070)	0.516	-0.040 (-0.118, 0.038)	0.304	0.072 (-0.060, 0.204)	0.271	0.426
HOMA_B	0.84 (-9.34, 11.02)	0.866	-9.22 (-41.91, 23.46)	0.565	-17.02 (-51.86, 17.82)	0.323	0.489
rs11071657 (nr. *C2CD4B*)							
Fasting glucose (mmol/L)	0.004 (-0.048, 0.056)	0.884	-0.015 (-0.111, 0.081)	0.754	-0.002 (-0.047, 0.042)	0.910	0.927
HOMA_B	-4.53 (-13.58, 4.52)	0.311	-1.05 (-20.35, 18.25)	0.911	12.03 (-1.16, 25.23)	0.072	0.117

Abbreviations: HOMA B, homeostasis model-assessed beta-cell functionfunction; NHANES III, Third National Health

and Nutrition Examination Survey DNA Bank. Data and 95% confidence intervals are in parentheses.

* β-coefficients (95% confidence intervals) of linear regression models adjusted for age and sex.
† *P*-values for β-coefficients are based on Satterthwaite adjusted-F test.
‡ *P*-values for testing differences in effect of each single nucleotide polymorphism on fasting glucose levels and HOMA-B across race/ethnicity groups are based on Satterthwaite adjusted-F statistics.

Online-Appendix Table 3. Adjusted Mean (95% confidence interval) of Fasting Glucose Levels and Homeostasis Model-assessed Beta-cell Function of 16 Fasting Glucose-associated Single Nucleotide Polymorphisms by Genotype and Race/ethnicity, Third National Health and Nutrition Examination Survey DNA Bank (NHANES III 1991-1994)

	Non-Hispanic white				Non-Hispanic black				Mexican American			
SNP	Non carrier	Heterozygous	Homozygous	*P*-value*	Non carrier	Heterozygous	Homozygous	*P*-value*	Non carrier	Heterozygous	Homozygous	*P*-value*
rs340874												
FG (mmol/L)	5.20 (5.12-5.27)	5.15 (5.12-5.19)	5.20 (5.13-5.28)	0.9036	5.11 (5.04-5.18)	5.13 (5.09-5.18)	5.04 (4.93-5.15)	0.1536	5.22 (5.14-5.30)	5.23 (5.17-5.29)	5.25 (5.15-5.36)	0.6375
HOMA_B	120.2 (110.0-130.4)	120.3 (106.1-134.6)	123.8 (109.1-138.4)	0.5810	157.0 (144.1-169.9)	157.0 (144.0-170.1)	176.6 (127.0-226.3)	0.4663	154.3 (137.8-170.9)	139.2 (131.8-146.5)	157.3 (122.4-192.2)	0.8740
rs573225												
FG (mmol/L)	5.04 (4.99-5.09)	5.16 (5.12-5.19)	5.22 (5.17-5.26)	<0.0001*	5.25 (4.50-6.00)	5.07 (4.97-5.18)	5.12 (5.07-5.17)	0.7273	5.12 (4.91-5.32)	5.16 (5.07-5.25)	5.27 (5.21-5.32)	0.1371
HOMA_B	135.9 (107.4-164.4)	126.0 (109.9-142.1)	114.3 (104.9-123.8)	0.0877	281.1 (154.6-407.6)	154.3 (134.8-173.7)	158.0 (145.0-171.1)	0.0547	150.1 (122.7-177.5)	156.1 (137.3-175.0)	145.0 (130.1-159.9)	0.6826
rs780094												
FG (mmol/L)	5.10 (5.02-5.18)	5.17 (5.12-5.22)	5.23 (5.17-5.28)	0.0151*	5.16 (5.00-5.32)	5.09 (5.01-5.17)	5.12 (5.07-5.18)	0.6656	5.25 (5.12-5.39)	5.18 (5.13-5.23)	5.28 (5.20-5.36)	0.7510
HOMA_B	123.3 (104.5-142.0)	123.5 (109.2-137.8)	116.6 (105.6-127.7)	0.4751	156.3 (139.3-173.4)	159.8 (140.6-179.1)	157.3 (144.6-170.0)	0.9259	163.9 (127.2-200.5)	141.2 (131.5-150.8)	151.5 (139.0-164.1)	0.4873
rs11708067												
FG (mmol/L)	5.10 (4.99-5.22)	5.16 (5.11-5.21)	5.19 (5.16-5.23)	0.1366	5.16 (4.88-5.44)	5.05 (4.96-5.14)	5.14 (5.08-5.19)	0.8651	5.18 (5.04-5.32)	5.22 (5.16-5.28)	5.24 (5.17-5.32)	0.3711
HOMA_B	117.6 (91.8-143.3)	120.5 (107.4-133.6)	121.9 (109.7-134.1)	0.7034	161.3 (105.3-217.3)	173.0 (152.9-193.2)	152.6 (144.1-161.2)	0.7406	177.9 (156.1-199.6)	150.9 (134.4-167.4)	141.7 (129.8-153.6)	0.0014*
rs11920090												
FG (mmol/L)	5.13 (4.88-5.37)	5.15 (5.08-5.22)	5.19 (5.15-5.22)	0.6118	5.10 (4.98-5.23)	5.07 (5.01-5.12)	5.16 (5.08-5.24)	0.3964	5.13 (4.90-5.35)	5.20 (5.04-5.35)	5.24 (5.19-5.29)	0.3354
HOMA_B	131.3 (104.1-158.6)	136.8 (110.7-162.9)	115.8 (105.5-126.1)	0.2285	176.0 (148.8-203.3)	150.7 (137.4-164.0)	160.3 (146.5-174.0)	0.2017	164.7 (126.9-202.5)	159.1 (135.3-182.9)	144.6 (133.5-155.7)	0.2591
rs2191349												
FG (mmol/L)	5.20 (5.15-5.26)	5.17 (5.13-5.20)	5.18 (5.11-5.25)	0.4860	4.99 (4.88-5.09)	5.14 (5.08-5.21)	5.14 (5.08-5.20)	0.0180*	5.25 (5.17-5.33)	5.20 (5.13-5.26)	5.27 (5.18-5.36)	0.7319
HOMA_B	115.1 (99.5-130.8)	120.6 (108.9-132.2)	126.5 (110.3-142.7)	0.1186	161.8 (143.2-180.5)	166.3 (150.6-182.1)	143.8 (135.8-151.8)	0.0583	159.0 (140.5-177.6)	143.1 (132.3-154.0)	142.2 (127.3-157.1)	0.1391
rs4607517												
FG (mmol/L)	5.17 (5.13-5.21)	5.21 (5.15-5.27)	5.14 (5.02-5.27)	0.6812	5.11 (5.07-5.16)	5.11 (5.01-5.20)	5.21 (5.00-5.42)	0.3671	5.20 (5.12-5.27)	5.28 (5.22-5.34)	5.39 (5.20-5.58)	0.0515
HOMA_B	125.4 (112.8-137.9)	109.7 (96.5-123.0)	144.5 (82.0-207.1)	0.5039	158.0 (148.4-167.6)	161.1 (134.6-187.7)	144.2 (115.9-172.5)	0.3853	153.9 (140.0-167.9)	131.0 (121.0-141.0)	178.2 (91.1-265.4)	0.5668

SNP	Non-Hispanic white				Non-Hispanic black				Mexican American			
	Non carrier	Heterozygous	Homozygous	*P*-value*	Non carrier	Heterozygous	Homozygous	*P*-value*	Non carrier	Heterozygous	Homozygous	*P*-value*
rs11558471												
FG (mmol/L)	5.06 (4.98-5.15)	5.17 (5.13-5.21)	5.21 (5.16-5.27)	0.0044*	4.97 (4.74-5.20)	5.06 (4.96-5.16)	5.13 (5.08-5.18)	0.1856	5.26 (5.19-5.33)	5.26 (5.19-5.34)	5.21 (5.14-5.29)	0.3448
HOMA_B	144.1 (89.6-198.7)	122.9 (110.4-135.4)	116.6 (106.9-126.2)	0.2795	138.4 (115.2-161.5)	164.1 (136.9-191.3)	158.4 (146.8-169.9)	0.1276	143.1 (117.2-169.1)	149.5 (133.1-165.9)	146.9 (135.0-158.9)	0.7439
rs7034200												
FG (mmol/L)	5.19 (5.14-5.24)	5.17 (5.13-5.21)	5.18 (5.11-5.25)	0.7923	5.11 (5.04-5.18)	5.12 (5.07-5.17)	5.11 (5.01-5.20)	0.9259	5.21 (5.13-5.28)	5.21 (5.12-5.29)	5.29 (5.20-5.38)	0.0991
HOMA_B	125.7 (106.6-144.8)	118.8 (107.6-130.0)	121.8 (105.7-138.0)	0.6291	163.6 (130.8-196.5)	158.6 (147.7-169.5)	155.7 (142.8-168.6)	0.6387	129.4 (117.9-140.8)	149.2 (139.4-159.0)	162.8 (141.3-184.3)	0.0121*
rs10885122												
FG (mmol/L)	5.26 (5.14-5.38)	5.22 (5.15-5.30)	5.16 (5.12-5.20)	0.0414*	5.08 (5.00-5.16)	5.11 (5.06-5.17)	5.21 (5.12-5.30)	0.0334*	5.17 (5.01-5.33)	5.20 (5.10-5.30)	5.24 (5.19-5.30)	0.2783
HOMA_B	120.3 (107.0-133.6)	121.0 (104.5-137.5)	121.3 (108.9-133.8)	0.9021	158.2 (141.1-175.4)	160.2 (145.8-174.7)	149.9 (138.0-161.9)	0.3498	163.1 (113.5-212.6)	157.7 (136.6-178.7)	143.9 (132.1-155.7)	0.3718
rs7903146												
FG (mmol/L)	5.17 (5.13-5.22)	5.18 (5.15-5.21)	5.18 (5.07-5.29)	0.8621	5.09 (5.04-5.15)	5.14 (5.06-5.21)	5.14 (4.99-5.29)	0.5235	5.22 (5.16-5.28)	5.26 (5.18-5.33)	5.20 (5.03-5.38)	0.8381
HOMA_B	122.7 (109.8-135.6)	119.9 (102.4-137.3)	120.7 (100.9-140.6)	0.8614	161.8 (146.9-176.6)	149.6 (140.0-159.2)	174.2 (127.5-220.8)	0.5913	153.4 (139.1-167.7)	140.4 (127.1-153.6)	115.9 (94.5-137.2)	0.0067*
rs10830963												
FG (mmol/L)	5.16 (5.11-5.22)	5.18 (5.12-5.23)	5.26 (5.18-5.35)	0.0980	5.10 (5.05-5.15)	5.20 (5.10-5.29)	5.39 (5.17-5.61)	0.0184*	5.21 (5.15-5.27)	5.25 (5.17-5.33)	5.41 (5.22-5.59)	0.0336*
HOMA_B	127.2 (109.4-144.9)	116.4 (106.0-126.7)	108.2 (95.3-121.2)	0.0803	159.3 (148.5-170.2)	149.6 (115.6-183.7)	154.1 (118.1-190.2)	0.7858	150.9 (137.6-164.2)	143.6 (131.2-156.0)	146.2 (119.9-172.5)	0.7723
rs174550												
FG (mmol/L)	5.23 (5.17-5.30)	5.17 (5.13-5.21)	5.17 (5.12-5.21)	0.0611	5.07 (4.74-5.40)	5.06 (4.98-5.13)	5.12 (5.08-5.17)	0.7232	5.25 (5.17-5.34)	5.19 (5.13-5.25)	5.27 (5.15-5.39)	0.7999
HOMA_B	120.9 (100.3-141.6)	116.8 (106.0-127.5)	125.7 (111.3-140.2)	0.5564	163.9 (129.1-198.7)	182.8 (151.3-214.4)	152.6 (144.0-161.3)	0.5413	145.8 (136.0-155.7)	151.3 (137.7-164.8)	146.9 (123.4-170.4)	0.9169
rs11605924												
FG (mmol/L)	5.15 (5.10-5.20)	5.19 (5.15-5.23)	5.18 (5.10-5.27)	0.4987	5.11 (4.89-5.32)	5.08 (5.01-5.15)	5.12 (5.07-5.18)	0.8759	5.21 (5.14-5.27)	5.20 (5.14-5.27)	5.30 (5.20-5.41)	0.0508
HOMA_B	125.3 (105.6-145.0)	119.2 (108.5-130.0)	121.1 (104.4-137.8)	0.5449	175.1 (138.7-211.5)	156.4 142.9-169.9)	157.8 (144.1-171.6)	0.3499	151.1 (123.7-178.4)	148.3 (131.7-164.9)	145.4 (131.5-159.3)	0.6190
rs7944584												
FG (mmol/L)	5.13 (5.01-5.25)	5.18 (5.14-5.22)	5.18 (5.14-5.23)	0.4205	5.35 (5.06-5.65)	5.12 (5.03-5.22)	5.11 (5.06-5.16)	0.0799	5.19 (4.83-5.54)	5.16 (5.04-5.27)	5.25 (5.20-5.31)	0.6780
HOMA_B	133.2 (107.2-159.1)	115.2 (103.2-127.3)	123.9 (110.5-137.3)	0.3868	148.5 (112.1-184.8)	170.3 (131.6-209.1)	156.6 (146.2-167.1)	0.6148	194.1 (57.7-330.5)	155.0 (132.5-177.4)	143.8 (132.6-155.0)	0.4525
rs11071657												
FG (mmol/L)	5.13 (5.06-5.21)	5.20 (5.14-5.25)	5.17 (5.11-5.22)	0.4256	4.99 (4.70-5.27)	5.15 (5.06-5.24)	5.11 (5.05-5.16)	0.4409	5.24 (5.15-5.33)	5.22 (5.16-5.28)	5.24 (5.16-5.31)	0.9186
HOMA_B	123.8 (107.4-140.2)	124.1 (110.3-138.0)	117.0 (104.2-129.8)	0.4886	182.3 (141.9-222.6)	155.7 (137.1-174.3)	158.2 (144.3-172.2)	0.2066	135.7 (125.2-146.3)	149.4 (136.2-162.6)	159.8 (134.4-185.1)	0.0765

Abbreviations: FG, fasting glucose; HOMA-B, homeostasis model assessed beta-cell function; NHANES, Third National Health and Nutrition Examination Survey DNA Bank; SNP, single nucleotide polymorphisms. Data and 95% confidence intervals are in parentheses.

* *P*-values for testing difference in fasting glucose levels or HOMA-B across genotype are based on Satterthwaite adjusted-F statistics.

Online-Appendix Table 4. Adjusted Mean Fasting Glucose Levels and Homeostasis Model Assessed Beta-cell Function by Quintiles of Unweighted Genetic Risk Score and Race/ethnicity, Third National Health and Nutrition Examination Survey DNA Bank (NHANES III 1991-1994)

Characteristics	β (SE)*	*P*-value†	Quintiles of the 16 SNP Unweighted Genetic Risk Score					*P*-value‡	R^{2}§	
			Q1	Q2	Q3	Q4	Q5		Without Score	With Score
Non-Hispanic white‖										
n			238	144	371	137	264			
GRS range			10 - 16	17	18 - 19	20	21			
Fasting glucose (mmol/L)	0.020 (0.010)	0.052	5.10(5.04-5.15)	5.14(5.06-5.22)	5.20(5.15-5.25)	5.21(5.15-5.28)	5.22(5.13-5.32)	0.058	0.208	0.2217
HOMA_B	-3.0 (1.48)	0.054	139.7(110.8-168.6)	111.9(101.5-122.3)	122.7(110.8-134.7)	109.6(98.0-121.1)	117.3(103.0-131.7)	0.091	0.013	0.0253
Non-Hispanic black‖										
n			213	143	154	148	163			
GRS range			12 - 18	19	20	21	22			
Fasting glucose (mmol/L)	0.034 (0.009)	0.001	5.02(4.94-5.09)	5.04(4.94-5.14)	5.16(5.04-5.28)	5.13(5.06-5.19)	5.23(5.15-5.32)	0.001	0.115	0.1432
HOMA_B	-5.5 (1.55)	0.002	166.2(150.6-181.8)	187.3(143.6-230.9)	150.0(131.7-168.3)	147.4(133.6-161.3)	145.9(130.4-161.5)	0.004	0.064	0.0806
Mexican American‖										
n			155	114	277	106	193			
GRS range			10 - 15	16	17 - 18	19	20			
Fasting glucose (mmol/L)	0.032 (0.007)	0.001	5.15(5.05-5.24)	5.16(5.08-5.25)	5.23(5.16-5.30)	5.27(5.11-5.43)	5.35(5.26-5.44)	<0.001	0.135	0.156
HOMA_B	-3.5 (1.70)	0.052	155.0(132.5-177.4)	161.1(140.5-181.8)	154.0(134.9-173.2)	136.7(125.3-148.0)	128.8(116.4-141.1)	0.017	0.043	0.053

Abbreviations: FG, fasting glucose; GRS, genetic risk score; HOMA-B, homeostasis model assessed beta-cell function; n = number of participants; NHANES, Third National Health and Nutrition Examination Survey DNA Bank; SE, standard error; SNP, single nucleotide polymorphisms. Data and 95% confidence intervals are in parentheses.

* β-coefficients of linear regression models adjusted for age and sex.
† *P*-values for β-coefficients based on Satterthwaite adjusted-F test.
‡ *P*-values for testing difference in FG levels or HOMA-B across quintiles of genetic risk score based on Satterthwaite adjusted-F statistics.
§ Adjusted R^2 for regression models with and without genetic risk score.
‖ $P = 0.333$ and $P = 0.534$ for testing heterogeneity of genetic risk score on FG levels and HOMA-B across race/ethnicity groups based on Satterthwaite adjusted-F statistics respectively.

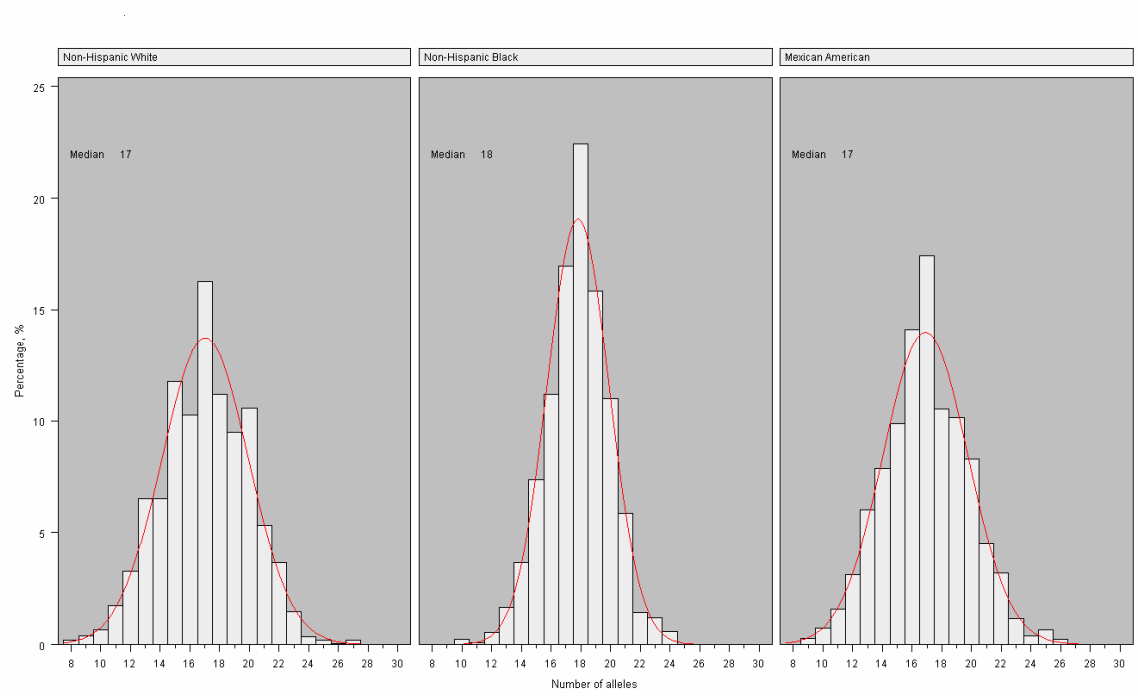
Online-Appendix Table 5. Adjusted Prevalence and Odds Ratio for Impaired Fasting Glucose by Quintiles of Unweighted Genetic Risk Score and Race/ethnicity, Third National Health and Nutrition Examination Survey DNA Bank (NHANES III 1991-1994)

Characteristics	GRS as Continuous Variable	*P*-value*	Quintiles of the Unweighted Genetic Risk Score				
			Q1	Q2	Q3	Q4	Q5
Non-Hispanic white							
Number of cases	289		43	40	97	37	72
Score range	10 - 27		10 - 16	17	18 - 19	20	21
IFG prevalence adjusted for age and sex	20.4 (16.8-24.0)		16.4 (9.9-22.8)	21.2 (13.1-29.3)	22.9 (17.0-28.7)	21.6 (13.21-30.02)	20.9 (13.2-28.6)
OR adjusted for age and sex	1.05 (0.94-1.18)	0.362	1	1.43 (0.62-3.26)	1.59 (1.03-2.48)	1.47 (0.61-3.55)	1.40 (0.56-3.51)
Non-Hispanic black							
Number of cases	145		27	24	30	22	42
GRS range	12 - 26		12 - 18	19	20	21	22
IFG prevalence adjusted for age and sex	18.2 (15.4-21.0)		12.5 (6.8-18.2)	15.0 (8.8-21.2)	20.3 (13.0-27.6)	18.1 (12.1-24.1)	25.9 (20.3-31.4)
OR adjusted for age and sex	1.16 (1.03-1.30)	0.017	1	1.26 (0.60-2.66)	1.89 (0.82-4.35)	1.61 (0.79-3.26)	2.67 (1.25-5.71)
Mexican American							
Number of cases	227		32	31	66	31	67
GRS range	10 - 26		10 - 15	16	17 - 18	19	20
IFG prevalence adjusted for age and sex	24.6 (20.1-29.1)		20.0 (12.5-27.6)	25.2 (19.1-31.2)	23.2 (16.6-29.8)	27.2 (14.9-39.4)	31.4 (24.1-38.6)
OR adjusted for age and sex	1.09 (1.01-1.19)	0.029	1	1.39 (0.71-2.69)	1.23 (0.79-1.92)	1.55 (0.80-3.02)	1.95 (0.98-3.86)

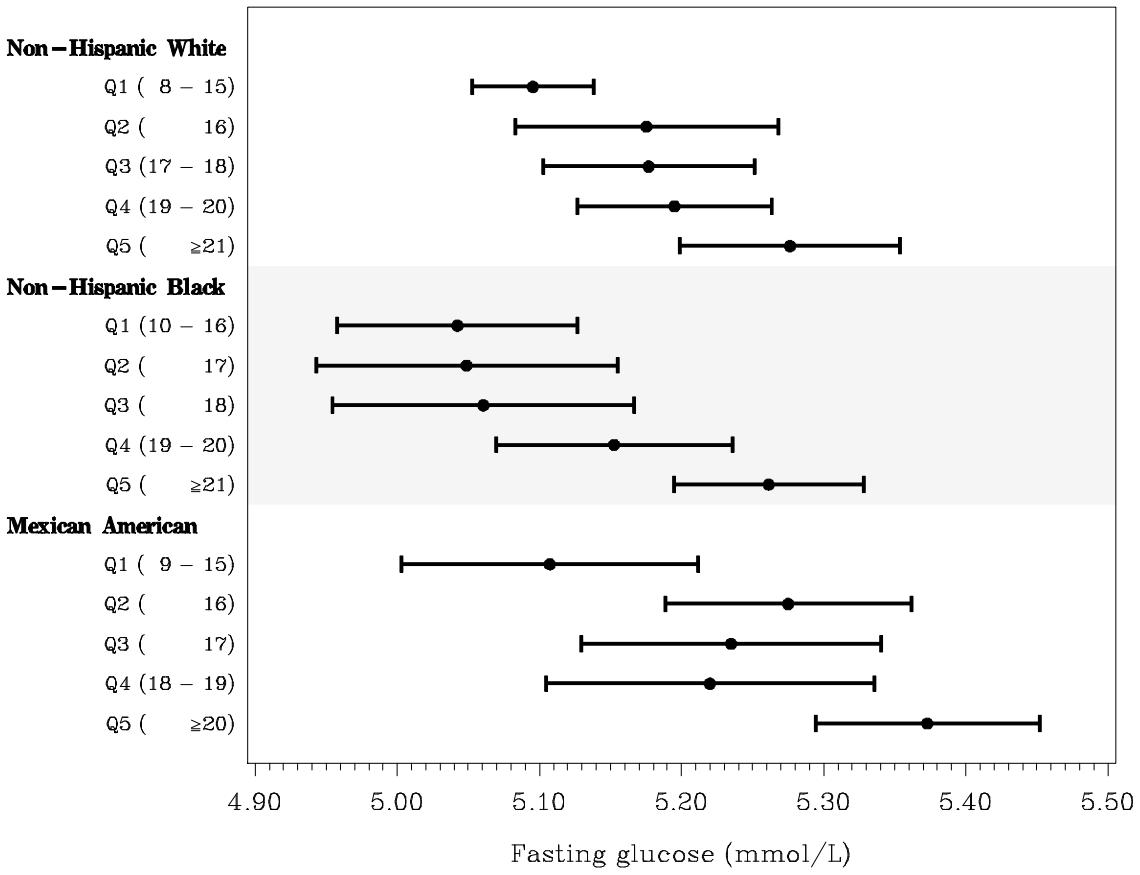
Abbreviations: GRS, genetic risk score; IFG, impaired fasting glucose; NHANES, Third National Health and Nutrition Examination Survey DNA Bank OR, odds ratio. Data are and 95% confidence intervals are in parentheses.

* For prevalence of IFG, adjusted OR, *P*-values for trend test across quintiles of genetic risk score, and *P*-value for using genetic risk score as a continuous variable in logistic regression models are based on Satterthwaite adjusted-F test. $P = 0.393$ for testing heterogeneity of genetic risk score as a continuous variable on risk for IFG across race/ethnicity groups on the basis of Satterthwaite's adjusted-F statistics.

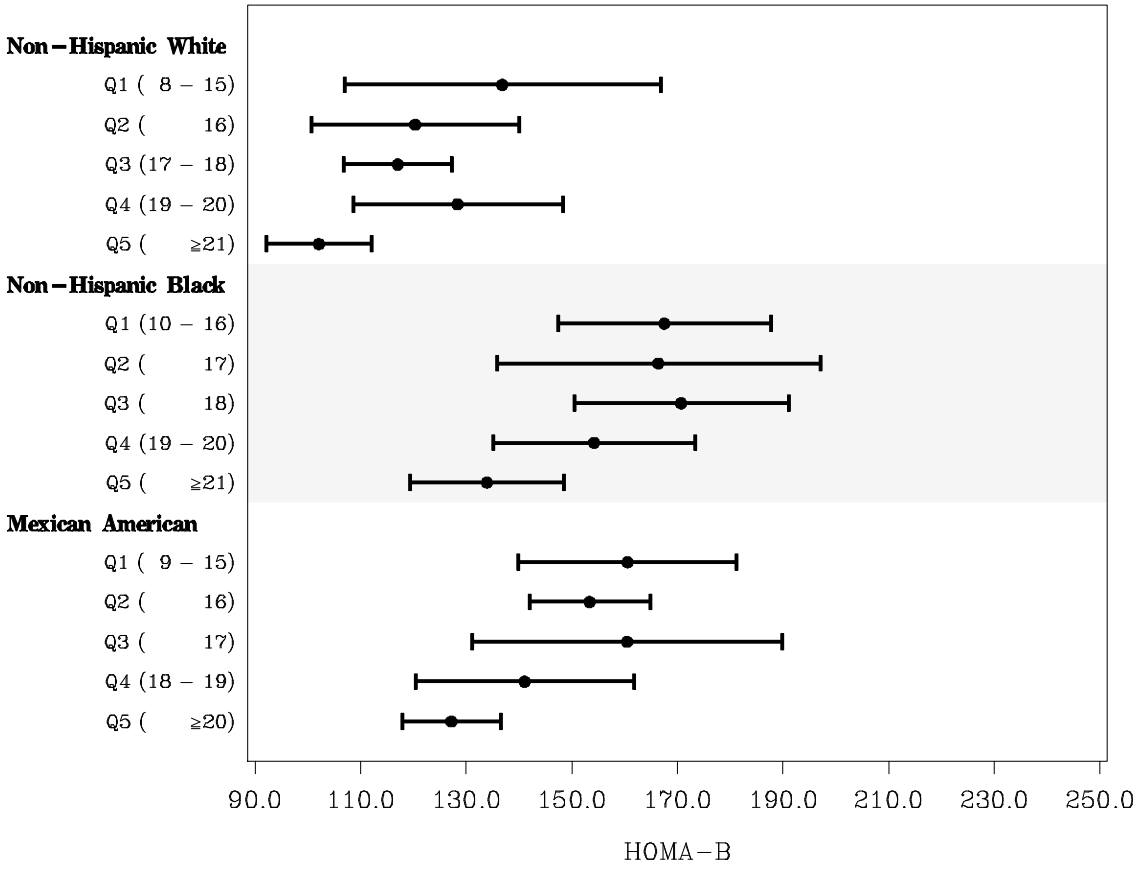
Online-Appendix Figure 1. Distribution of weighted genetic risk score by race/ethnicity, Third National Health and Nutrition Examination Survey DNA Bank (NHANES III 1991-1994).



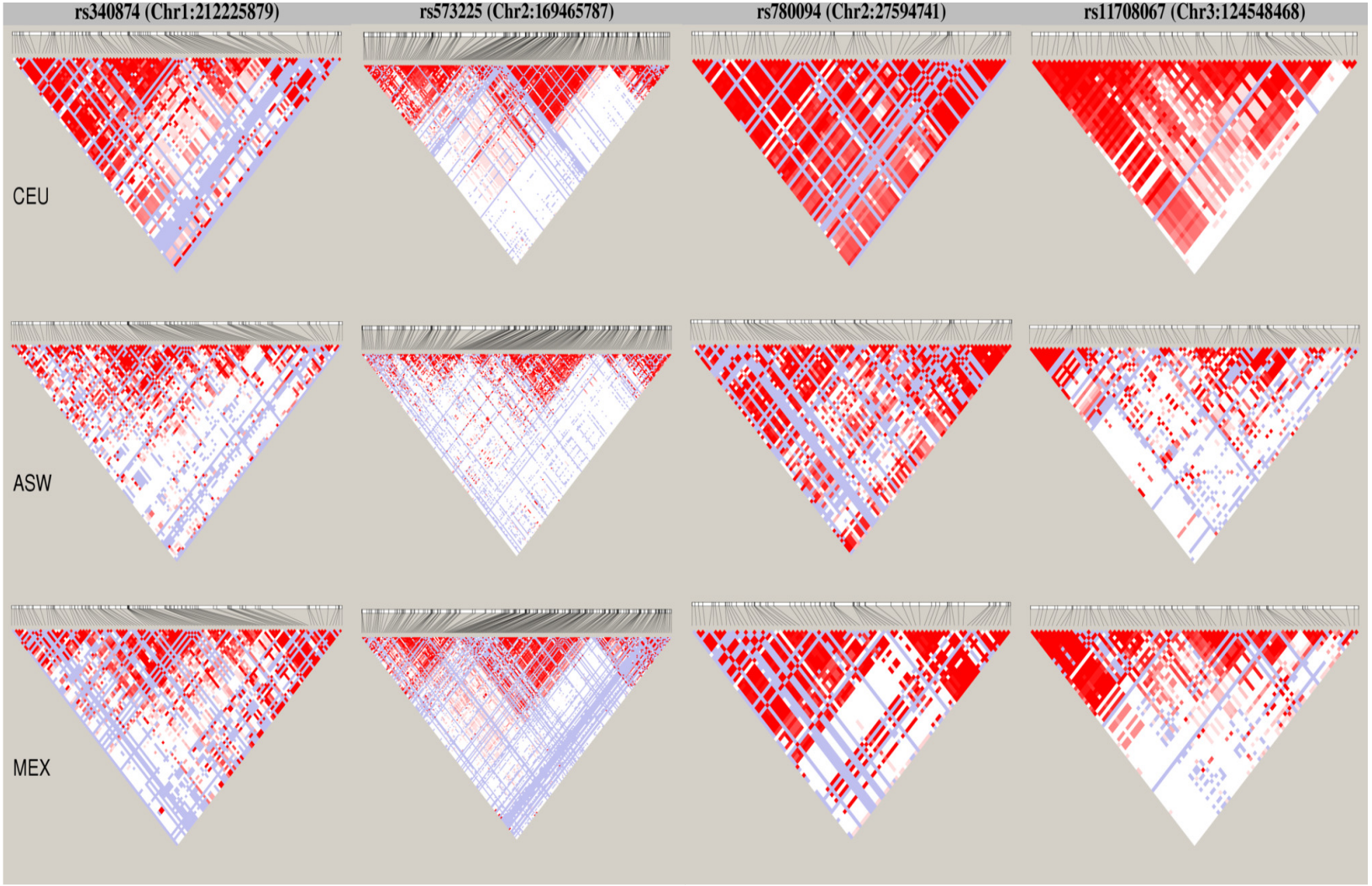
Online-Appendix Figure 2. Adjusted mean fasting glucose levels (2a) and HOMA-B (2b) by quintiles of weighted genetic risk score and race/ethnicity, Third National Health and Nutritional Examination Survey DNA Bank (NHANES III 1991-1994)
2a

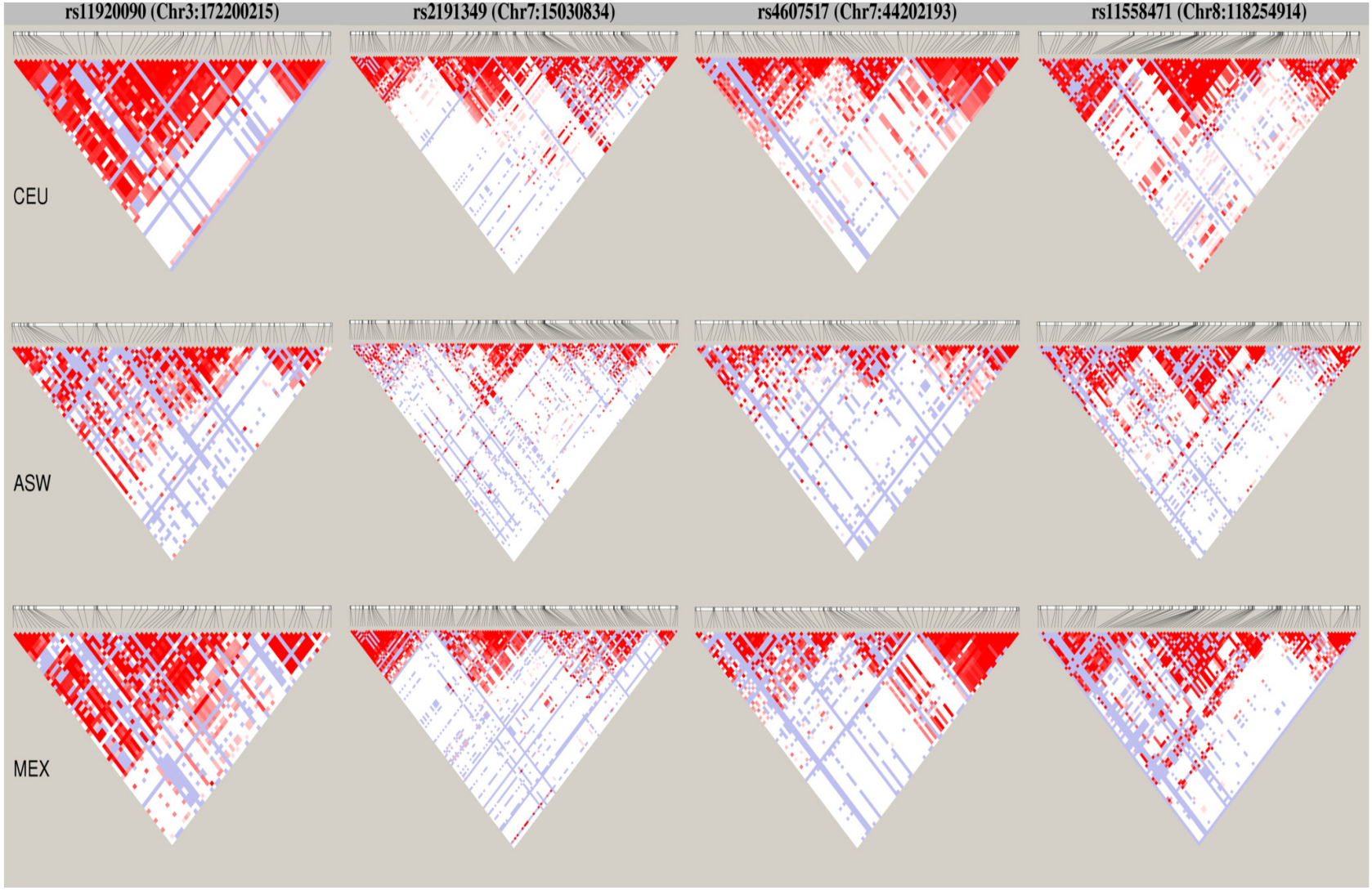


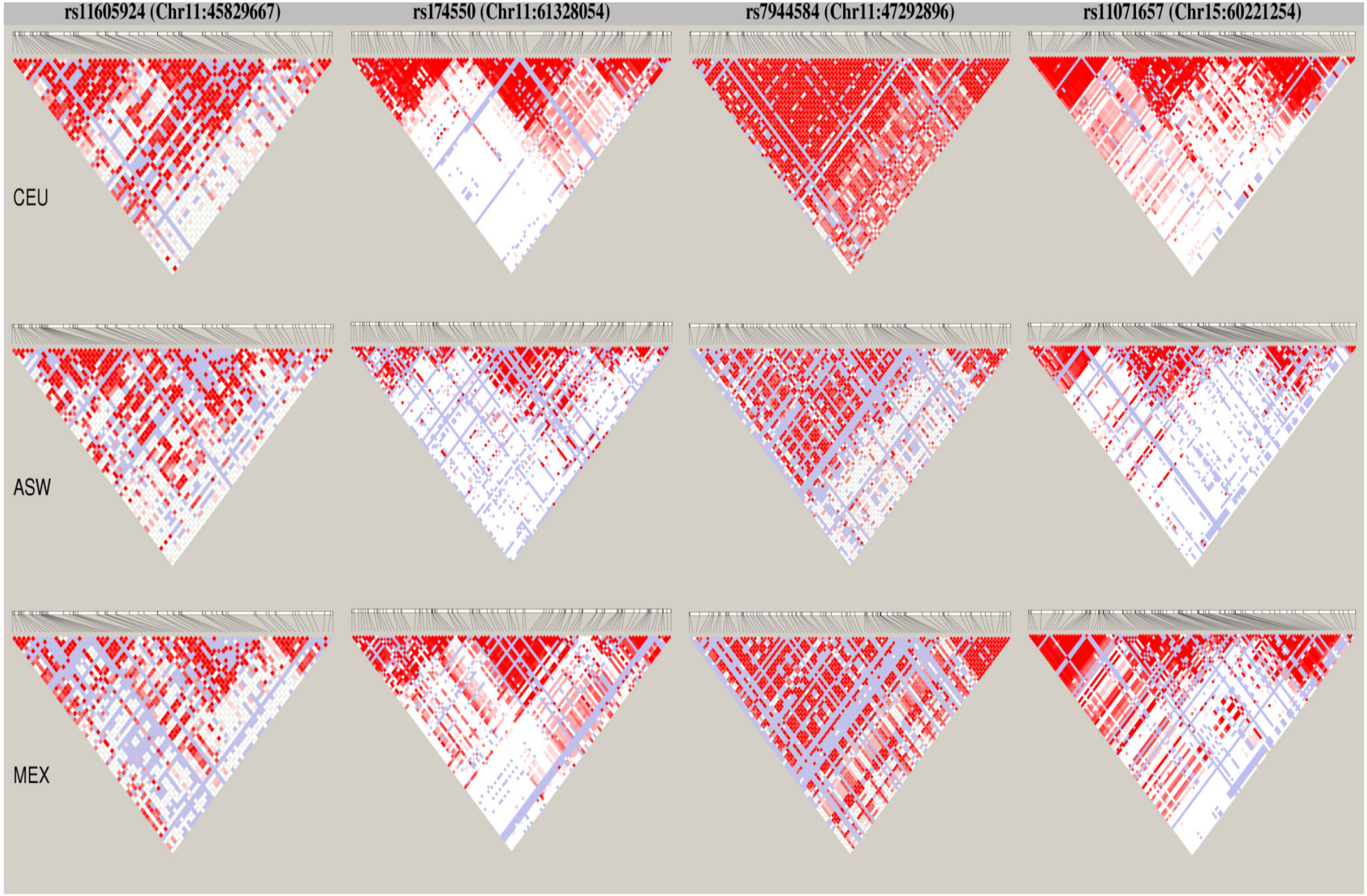
2b



Online-Appendix Figure 3. Heatmap representations of LD measured as D' created using Haploview 4.2 for the 16 FG-associated SNPs and surrounding region (+/- 100 kb) among the CEU (first row), ASW (2nd row), and MEX (3rd row) populations from HapMap release 2.7







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