SUPPLEMENTAL MATERIAL

Supplemental Table 1. Characteristics of the chromosome 11p11.2 regions sequenced in this study.

	Start postion (bp)	End position (bp)	Total region size (kb)	Total sequenced (kb)	$N_{Variants}$	Coverage (Read depth)	
						Mean (SD)	Range
ACP2	47217501	47227099	9.60	1.20	51	37.50 (18.31)	10 - 81
NR1H3	47227100	47247262	20.16	1.40	66	43.58 (20.08)	10 - 88
MADD	47246227	47309761	63.53	6.40	271	38.64 (35.00)	10 - 91
MYBPC3	47309354	47331966	22.61	2.20	67	35.58 (19.28)	10 - 79
SPI1	47332576	47379797	47.22	4.88	198	37.66 (18.50)	10 - 90
Total			163.13	16.08	653	38.44 (19.33)	10 - 91

Supplemental Table 2. Description of variation in the 5 genes at the MADD locus (ACP2, NR1H3, MADD, MYBPC3, SPI1) from RegulomeDB (PMID 22955989).

Prediction Scores	*ACP2*	*NR1H3*	*MADD*	*MYBPC3*	*SPI1*	Total
1a	-	-	0 (1)	-	-	0 (1)
1b	0 (1)	-	0 (2)	0 (1)	0 (2)	0 (6)
1c	-	-	-	-	-	-
1d	-	-	-	-	-	-
1e	-	-	-	-	-	-
1f	1 (2)	0 (2)	0 (12)	0 (7)	0 (16)	1 (39)
2a	-	2 (0)	1 (0)	-	-	3 (0)
2b	6 (1)	5 (1)	16 (2)	0 (1)	16 (1)	43 (6)
2c	-	-	-	-	-	-
3a	4 (0)	-	9 (2)	-	1 (0)	14 (2)
3b	-	-	-	-	-	-
Total (Prediction Scores 1-3) *	11 (4)	7 (3)	26 (19)	0 (9)	17 (19)	61 (54)
4	12 (0)	21 (5)	31 (3)	12 (1)	40 (2)	116 (11)
5	3 (1)	10 (0)	93 (9)	43 (0)	77 (7)	226 (55)
6	7 (3)	6 (4)	36 (13)	-	6 (6)	55 (26)
7	9 (1)	9 (1)	40 (1)	2 (0)	19 (5)	79 (8)
Total (All)	42 (9)	53 (13)	226 (45)	57 (10)	159 (39)	537 (116)

The number of common variants is indicated in parentheses

Annotation Prediction Score Definitions based on RegulomeDB (PMID 22955989)

1a = eQTL + TF binding + matched TF motif + matched DNase Footprint + DNase peak

1b = eQTL + TF binding + any motif + DNase Footprint + DNase peak

1c = eQTL + TF binding + matched TF motif + DNase peak

1d = eQTL + TF binding + any motif + DNase peak

1e = eQTL + TF binding + matched TF motif

1f = eQTL + TF binding / DNase peak

2a = TF binding + matched TF motif + matched DNase Footprint + DNase peak

2b = TF binding + any motif + DNase Footprint + DNase peak

2c = TF binding + matched TF motif + DNase peak

3a = TF binding + any motif + DNase peak

3b = TF binding + matched TF motif

4 = TF binding + DNase peak

5 = TF binding or DNase peak

6 = other

7 = N/A

* Prediction Scores 1-3 were used in secondary analysis

Supplemental Table 3. Contribution of signals from 53* rare variants in *NRIH3* to the overall SKAT test for association with fasting insulin

position (hg18)	Allele†	MAF	β	se	*p*-value ‡	Weighted Score §	rs	Annotation Prediction Score ||	% Test Contribution
chr11:47231478	C/T	0.00170	0.326	0.145	0.024	9.854		6	23.335
chr11:47227430	G/A	0.00068	0.766	0.235	0.001	8.673		2a#	20.537
chr11:47238495	T/C	0.00283	0.148	0.092	0.107	7.994	rs35378256	6	18.931
chr11:47237300	C/A	0.00144	0.334	0.164	0.042	4.985		4	11.806
chr11:47238607	G/A	0.00044	1.134	0.411	0.006	1.069		6	2.531
chr11:47243026	A/G	0.00026	1.609	0.612	0.009	0.968		7	2.293
chr11:47243029	T/A	0.00026	1.609	0.612	0.009	0.968		7	2.293
chr11:47235672	C/T	0.00174	-0.176	0.146	0.227	0.805	rs41275184	4	1.906
chr11:47242802	A/T	0.00025	-1.447	0.612	0.018	0.783		5	1.854
chr11:47242749	C/T	0.00025	-1.335	0.612	0.029	0.667		5	1.580
chr11:47238498	C/T	0.00044	0.724	0.411	0.078	0.436		6	1.033
chr11:47237171	G/A	0.00039	-0.563	0.325	0.084	0.419		7	0.993
chr11:47227397	G/A	0.00025	-1.000	0.612	0.103	0.374		4	0.885
chr11:47237296	C/T	0.00025	-0.995	0.612	0.104	0.370		4	0.877
chr11:47231637	G/A	0.00025	-0.985	0.612	0.108	0.363		5	0.860
chr11:47231692	G/A	0.00025	-0.985	0.612	0.108	0.363		5	0.860
chr11:47227354	C/A	0.00077	-0.367	0.325	0.259	0.356		4	0.842
chr11:47237380	C/T	0.00027	0.950	0.612	0.121	0.337		2b	0.799
chr11:47237267	G/A	0.00046	0.551	0.612	0.368	0.337		5	0.799
chr11:47235622	A/G	0.00029	0.924	0.612	0.131	0.319		2b	0.756
chr11:47237288	A/G	0.00030	0.300	0.287	0.296	0.305		4	0.722
chr11:47242919	C/T	0.00025	0.880	0.612	0.151	0.290		5	0.686
chr11:47231623	A/G	0.00025	0.878	0.612	0.152	0.288		5	0.683
chr11:47238688	G/A	0.00034	0.318	0.341	0.351	0.243		7	0.575
chr11:47227386	C/T	0.00025	0.610	0.612	0.319	0.139		4	0.329
chr11:47235352	G/C	0.00027	-0.529	0.612	0.388	0.105		2b	0.248
chr11:47238509	A/G	0.00044	0.347	0.411	0.398	0.100		7	0.237
chr11:47242705	C/T	0.00039	-0.181	0.325	0.578	0.043		5	0.103
chr11:47231581	G/T	0.00044	-0.225	0.411	0.585	0.042		7	0.099
chr11:47227243	G/A	0.00025	-0.318	0.612	0.603	0.038		2a	0.090
chr11:47235510	C/T	0.00039	-0.165	0.325	0.612	0.036		4	0.086
chr11:47233190	C/T	0.00025	0.294	0.612	0.632	0.032		2b	0.076
chr11:47238554	G/A	0.00039	-0.153	0.325	0.638	0.031		6	0.074
chr11:47231746	G/A	0.00025	0.217	0.612	0.723	0.018		4	0.042
chr11:47227493	C/A	0.00045	0.142	0.411	0.730	0.017		2b	0.040
chr11:47237388	T/A	0.00030	0.207	0.612	0.736	0.016		4	0.038
chr11:47237216	T/C	0.00025	0.159	0.612	0.795	0.009		7	0.022
chr11:47227412	G/A	0.00025	0.158	0.612	0.796	0.009		4	0.022
chr11:47231524	C/T	0.00025	0.138	0.612	0.822	0.007		6	0.017
chr11:47238699	C/T	0.00046	-0.079	0.411	0.847	0.005		7	0.012
chr11:47235669	C/T	0.00043	-0.056	0.325	0.862	0.004		4	0.010
chr11:47237290	C/T	0.00044	-0.063	0.411	0.878	0.003		4	0.008
chr11:47238524	T/C	0.00025	0.062	0.612	0.919	0.001		7	0.003
chr11:47231720	T/C	0.00025	0.051	0.612	0.933	0.001		5	0.002
chr11:47227423	A/C	0.00025	-0.050	0.612	0.935	0.001		4	0.002
chr11:47233300	C/T	0.00025	-0.044	0.612	0.943	0.001		4	0.002
chr11:47233378	C/T	0.00039	-0.015	0.325	0.963	0.000		4	0.001

* 6 variants were found to be monomorhic in the current sample

† The first one is the tested allele, and the second one is the other allele.

‡ *P*-value for single snp

§ Q statistic from meta SKAT analysis

|| RegulomeDB Score

chr11:47227430 is additionally predicted to lie in a FOXA1 transcription factor site binding motif

Annotation Prediction Score Definitions:

2a = TF binding + matched TF motif + matched DNase Footprint + DNase peak
2b = TF binding + any motif + DNase Footprint + DNase peak
4 = TF binding + DNase peak
5 = TF binding or DNase peak
6 = other
7 = N/A

Supplemental Table 4. Common variants meta-analysis results for ARIC, CHS and FHS. Results are shown for known associations with fasting glucose and fasting pro-insulin at independent SNPs identified by Dupuis *et al.*[1] (rs7944584) and Strawbridge *et al.*[4] (rs10838687).

Gene	rs #	Alleles *	MAF	Original Phenotype(s)	Fasting Insulin							Fasting Glucose							Reference
					Meta			Q	I^2	P_{het}	Direction (ARIC, CHS, FHS)	Meta			Q	I^2	P_{het}	Direction (ARIC, CHS, FHS)	
					β	se	p-value					β	se	p-value					
MADD	rs10838687	G/C	0.194	fasting proinsulin	-0.014	0.016	0.321	0.630	0.000	0.428	?+-	-0.005	0.022	0.714	0.467	0.000	0.494	?-+	PMID:21873549
	rs7944584	T/G	0.278	fasting glucose	-0.001	0.013	0.480	1.268	0.000	0.530	-+-	-0.038	0.014	0.054	0.022	0.000	0.989	---	PMID:20081858

The β's and se's are from the analysis that accounts for sampling weights; p-value is from the unweighted analysis.

* The first alelle is the risk allele, and the second is the other allele.

signifiance level = α = 0.05

Q = Cochrane's Q test (assessing whether a variant across studies is homogeneous).

I^2 = I squared Index

Phet = p-value of heterogeneity

Supplemental Table 5. Sequences of oligonucleotides used in functional studies.

Assay	Name	Forward strand	Reverse strand
EMSA	Non-specific oligonucleotide (NS)	5'-TTACTTCACACTTTAATAAA-3'	5'-TTTATTAAAGTGTGAAGTAA-3'
EMSA	chr11:47227430-G	5'GGTGCAGGACACAGTATGTAAACAACCCTTTGGAC-3'	5'-GTCCAAAGGGTGTTTACATACTGTGTCCTGCACC-3'
EMSA	chr11:47227430-A	5'-GGTGCAGGACACAGTATATAAACAACCCTTTGGAC-3'	5'-GTCCAAAGGGTTGTTTATATACTGTGTCCTGCACC-3'
EMSA and Luciferase assay	Consensus FoxA1 oligonucleotide	5'-GCTCCAGGGAATGTTTGTTCTTAAATACCATC-3'	5'-CGAGGTCCCTTACAAACAAGAATTTATGGTAG-3'
Luciferase assay	280mer-PCR	5'-AAAAACTCGAGGATCGGGTGCAGAATTGAGG-3'	5'-TTTTTGGATCCGTGGAGGGGAGGGAGGA-3'
Luciferase assay	Over-lapping-PCR	5'-GACACAGTATATAAACAACCCTTTG-3'	5'-CAAAGGGTTGTTTATATACTGTGTC-3'
Luciferase assay	40mer- chr11:47227430-G	5'/5Phos/AGCTTGGTGCAGGACACAGTATGTAAACAACCCTTTGGAC-3'	5'- /5Phos/GATCC GTCCAAAGGGTTGTTTACATACTGTGTCCTGCACC -3'
Luciferase assay	40mer- chr11:47227430-A	5'- /5Phos/AGCTTGGTGCAGGACACAGTATATAAACAACCCTTTGGAC -3'	5'- /5Phos/GATCC GTCCAAAGGGTTGTTTATATACTGTGTCCTGCACC -3'

Supplemental Figure 1: Regional plots for association of fasting glucose with 116 common variants at the chromosome 11p11.2 locus (*ACP2*, *NR1H3*, *MADD*, *MYBPC3* and *SPI1*). The -$\log_{10}$ *p*-value of variant associations are plotted on the upper y-axis versus chromosomal location on the x-axis (NCBI Genome Build 36). The two variants shown as blue circles are known from GWAS to be associated with fasting glucose (rs794584) [1] or fasting proinsulin (rs10838687) [2]. Green bars at the bottom of the graph represent the location of the five 11p11.2 locus genes in the region.