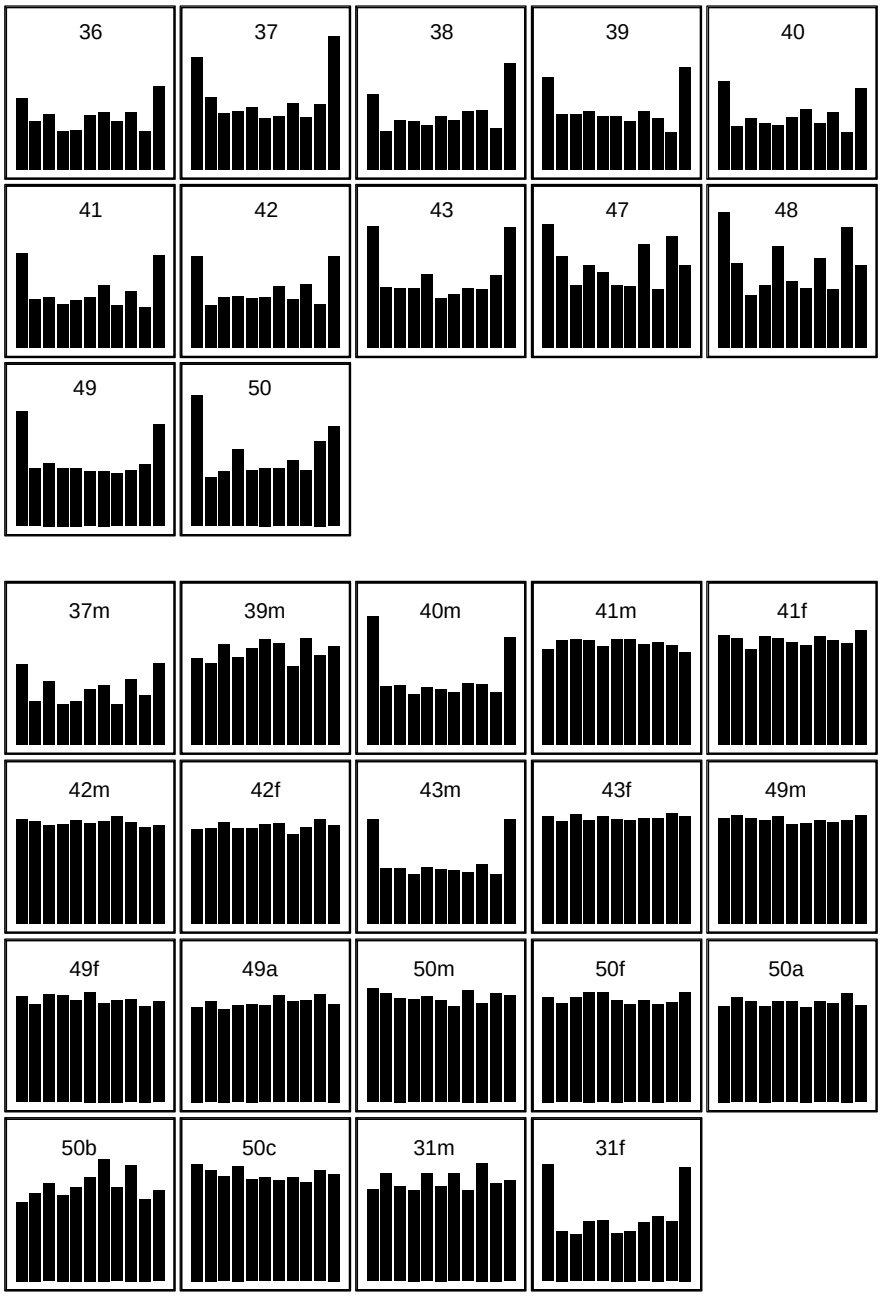
A novel highly-penetrant form of obesity due to microdeletions on chromosome 16p11.2

Supplementary online material

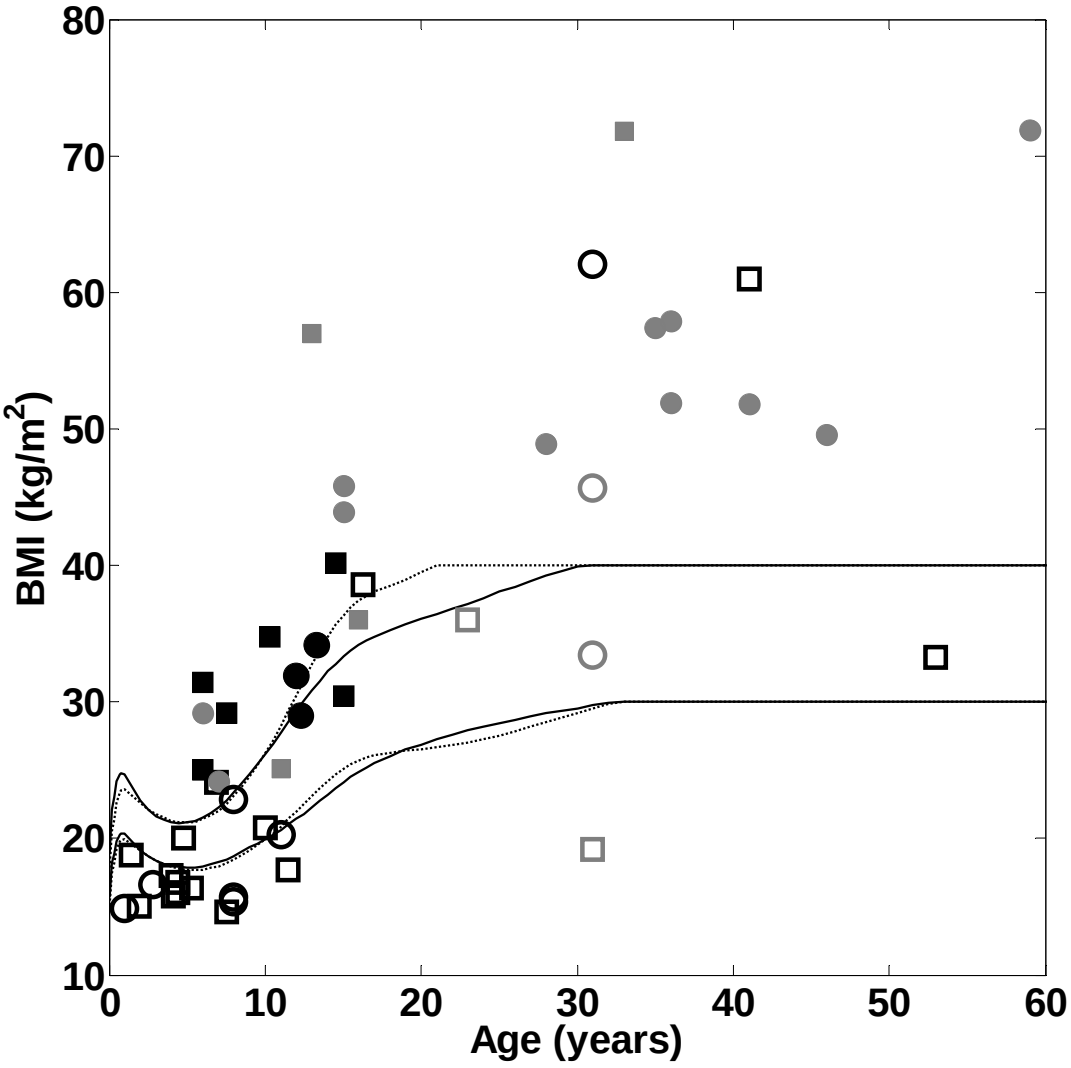
Supplementary Figure S1

Validation of 16p11.2 deletions by MLPA and determination of their modes of inheritance. MLPA was carried out using 9 probe pairs within and 2 lying outside the deletion (one to each side), as shown in Figure 1, together with 9 control (nominally copy number invariant) probe pairs. Panels show the relative magnitude of the normalised, integrated signal at each probe location in order of chromosomal location. Where DNA was available, samples were analysed if they were identified from GWAS data as carrying a deletion at 16p11.2 (top) or if they were a first degree relative of a proband (bottom). Labels correspond to the case ID of the proband as shown in Table S2; f = father; m = mother; a-c = siblings.



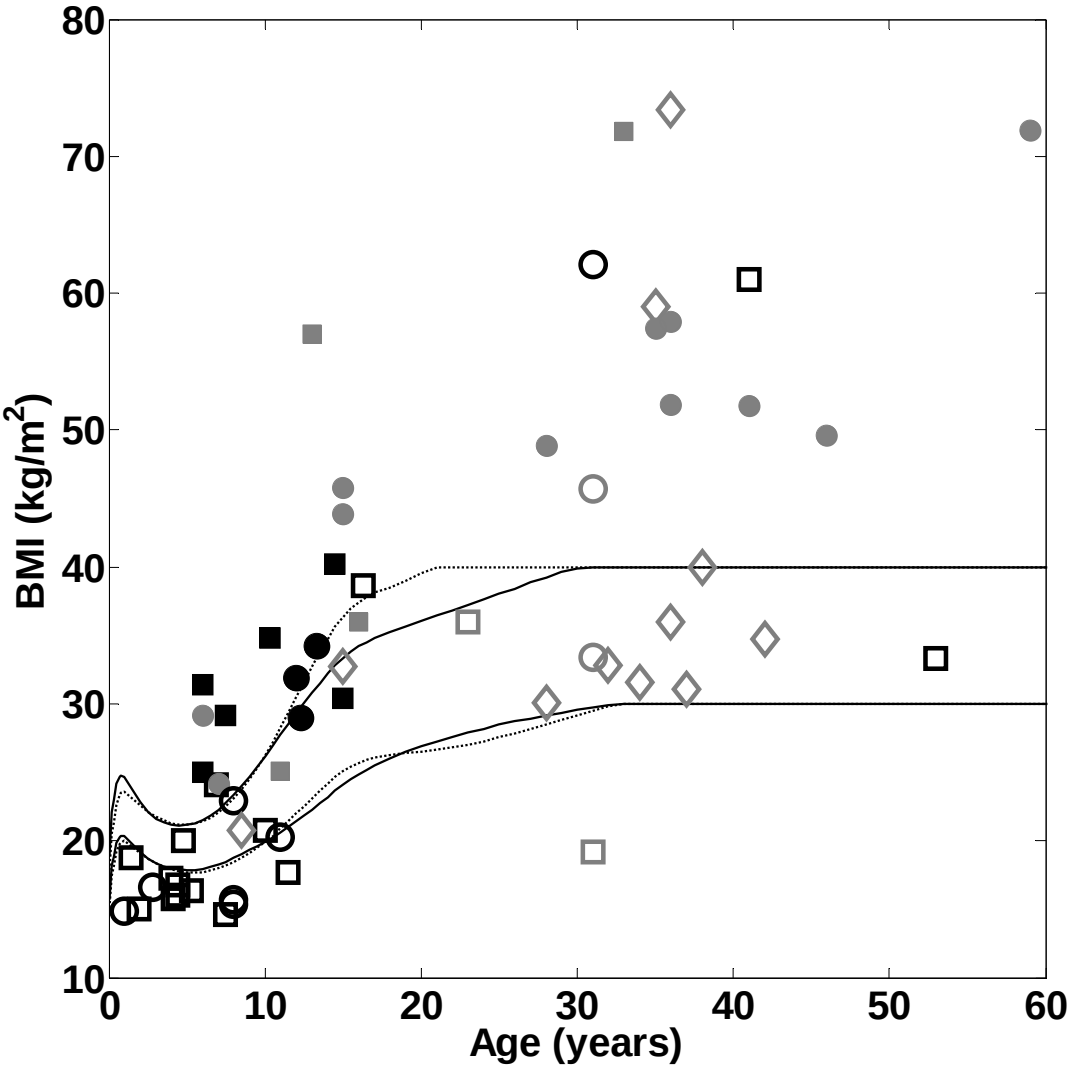
Supplementary Figure S2

Dependence of BMI on age in subjects having a deletion at 16p11.2. Data are shown for all probands identified in this study as having a deletion at 16p11.2, for whom phenotypic information is available. Lines denote the age- and gender-corrected thresholds (solid/broken – male/female) for obesity (adults – BMI ≥ 30 $kg.m^{-2}$, children ≥ 97^{th} percentile) and morbid obesity (adults – BMI ≥ 40 $kg.m^{-2}$, children Z-BMI ≥ 4). Symbols are as follows: Square/circle – male/female; black/grey – ascertained/not ascertained for developmental delay; filled/open – ascertained/not ascertained for obesity. Thus, individuals from general population are shown as open grey circles or squares.



Supplementary Figure S3

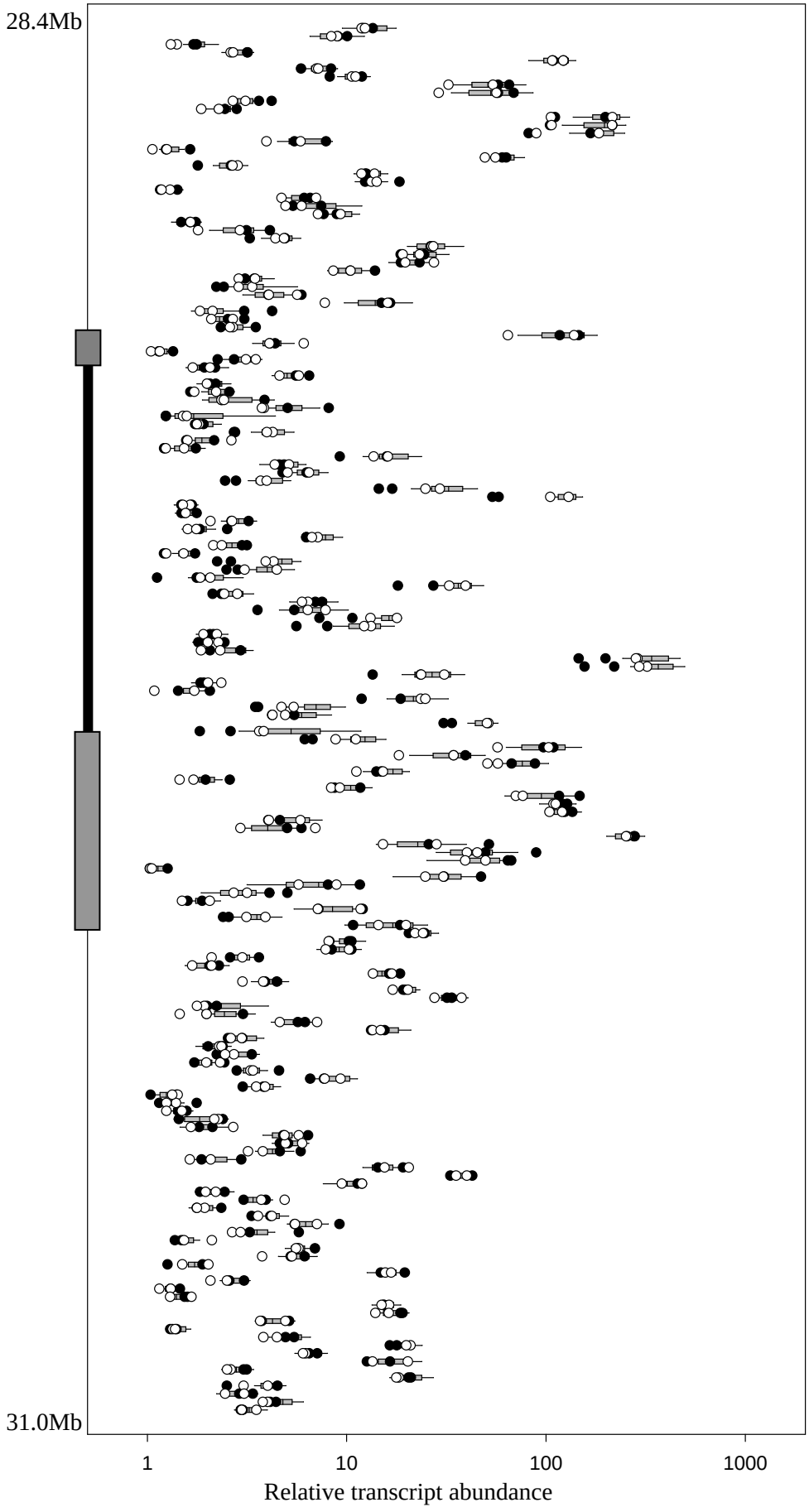
Dependence of BMI on age in probands having a deletion at 16p11.2. Data are shown for all individuals identified in this study as having a deletion at 16p11.2, for whom phenotypic information is available. Lines denote the age- and gender-corrected thresholds (solid/broken – male/female) for obesity (adults – BMI ≥ 30 $kg.m^{-2}$, children ≥ 97^{th} percentile) and morbid obesity (adults – BMI ≥ 40 $kg.m^{-2}$, children Z-BMI ≥ 4). Symbols are as follows: Square/circle – male/female; black/grey – ascertained/not ascertained for developmental delay; filled/open – ascertained/not ascertained for obesity; grey diamond – first-degree relative of a proband. Thus, individuals from general population are shown as open grey circles or squares.



Supplementary Figure S4

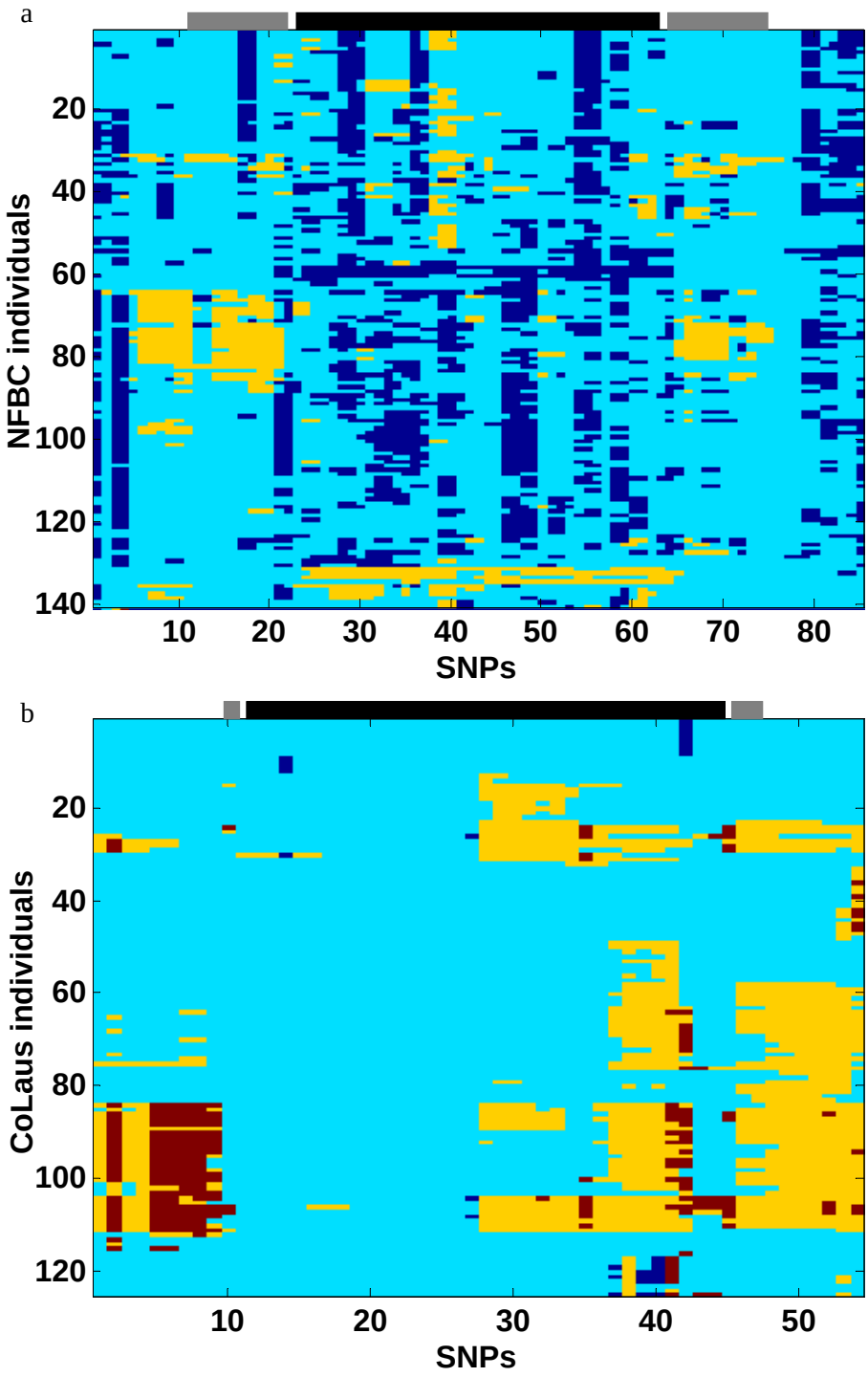
Transcript levels for genes within and nearby 16p11.2 deletions. Expression data for adipose tissue from the SOS Sib Pair cohort were analysed for probes detecting transcripts for genes lying within the interval chr16:28.4–31.0Mb (see Supplementary Table S4 for details). Transcript levels in the two individuals carrying a deletion of 16p11.2 (black symbols) are plotted alongside those for their non-obese siblings (white). Also shown are box plots summarising the data for the other 157 obese subjects from this study, indicating the 10^{th}, 25^{th}, 50^{th}, 75^{th} and 90^{th} percentiles for each transcript. The positions of the the 16p11.2 deletion and the flanking segmental duplications relative to the transcripts are indicated by a solid line and grey bars at the left axis.

Within the deleted region, there is a consistent reduction in expression in the subjects carrying a deletion, relative to both their siblings and to other obese subjects. In contrast, although CNVs have been shown to have the potential to affect expression of neighbouring genes up to 0.5Mb distant[42,43], no such clear and consistent differences in transcript levels are observed for the genes lying nearby, outside the region of the 16p11.2 deletion.


28.4Mb
31.0Mb
1
10
100
1000
Relative transcript abundance

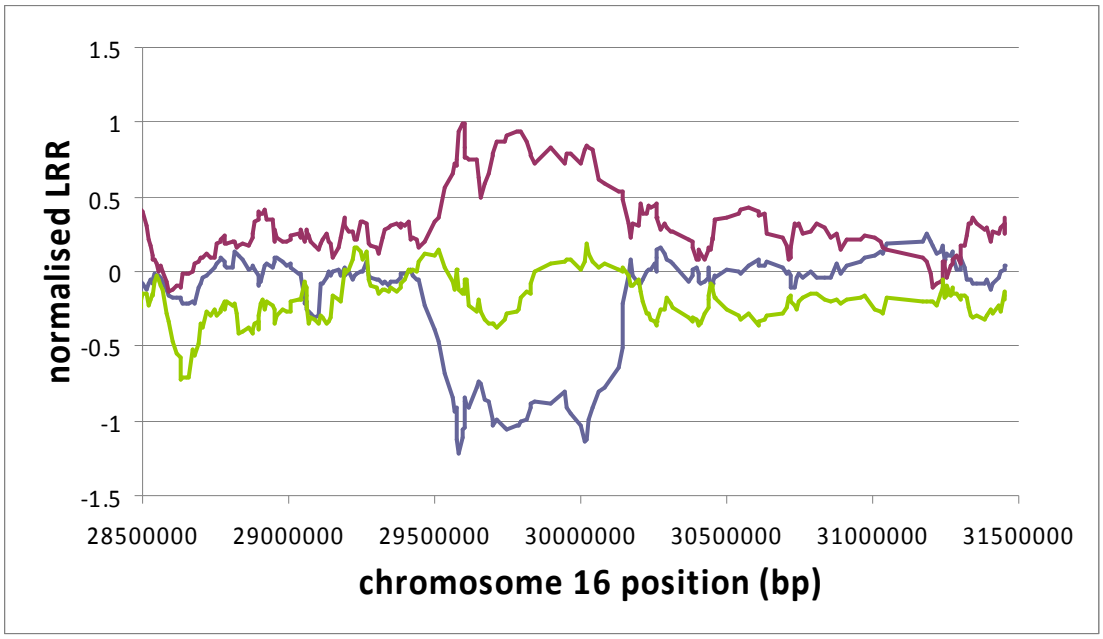
Supplementary Figure S5

Graphical representation of the output of CNV discovery algorithms. Copy number calls at SNPs within and surrounding the deleted region (black bar) and its flanking segmental duplications (grey bars) are shown as follows: blue – 1 copy; cyan – 2 copies (i.e. no aberration); yellow – 3 copies; red – 4 copies. (a) cnvHap output for the NFBC cohort, showing all individuals with at least 10 aberrant probes within the deletion; (b) Gaussian Mixture Model output for the CoLaus cohort, showing all individuals with at least 1 aberrant probeset. The different patterns for the two methods reflect the locations interrogated by the respective platforms, and also the respective sensitivities of the platforms and algorithms to copy number variation.



Supplementary Figure S6

Validation of deletion calls from Illumina genotyping data. LogR ratio (LRR) data exported from Illumina BeadStudio was normalised with respect to the median and variance for each probe, and smoothed by averaging over a 9-point moving window. Example data are shown for samples from the NFBC cohort that had normal copy number (green) and which carried a deletion (blue) or duplication (purple).



Supplementary Table S1

Cognitive/behavioral symptoms observed in carriers of 16p11.2 deletions. Data are shown for patients ascertained for developmental delay, and for affected relatives if available. 'No data' indicates that this phenotype was not assessed. NA – not applicable due to age of the patient.

case ID	Age	Mental retardation	Language	Hyperphagia	ASD	Other Behavioral symptoms
1	4.1	Borderline-mild	Language delay	yes	no	no data
2	16.3	Executive function deficits	Language deficit	yes	no, social cognition deficit	Shyness, obsessive compulsive disorder
3	5.3	No	Echolalia	no data	yes	Stereotypes, hyperactivity
4	31	no	no data	yes	no data	no data
5	8	No	Dysphasia	fluctuating	no	Hyperactivity
6	41	Mild	Language delay	severe	no data	no data
7	10	Mild-modeate	Language delay	mild	no data	no data
8	11	Mild, IQ 72-49	mild language delay	yes	no	anxiety
9	11.5	Mild	Language delay	no	yes	Oppositional, aggressivity, stereotypes
10	1.4	NA	NA	no	no	no
11	2.8	Mild to moderate, global delay	Language delay	yes	no data	Hyperactivity
12	53	Mild to moderate	no data	no	no	no data
13	1	Developmental age: 5 months	NA	no	NA	NA
14	4.4	Borderline, IQ 73	Language delay	no	no	Hyperactivity
15	4.8	Mild	Language delay	no	yes	no data
16	6.9	Mild	Language delay	yes	no	Oppositional, aggressivity
17	7.5	No, IQ 77-89	Language delay	no	no	Anxiety, hyperactivity
18	1.9	moderate	Language delay	no	NA	none / NA
19	4.4	Moderate, IQ 57	Severe language delay	no	yes	Repetitive, restricted behavior
20	8	Borderline, VIQ: 78, PIQ: 96	Language delay	no	no	Attention deficit
21	4	Moderate	Severe language delay	no	no	Hyperactivity, temper tantrums, oppositional
22	8	no data	no data	no	no	Attention deficit, mutism
63	15	Mild, VIQ: 67, PIQ: 61	no data	yes	no	Hyperactivity, aggressivity, anxiety
64	36	Borderline	no data	yes	no	no data

Supplementary Table S2

Obesity characteristics of carriers of 16p11.2 deletions. The basis for ascertainment and all available data for gender, age and BMI are shown for each subject identified as carrying a deletion at 16p11.2. Also shown are the methods used to identify the deletion and for its validation, and the inheritance of the deletion as inferred from the results of analysis of parental DNAs where these were available. n.d. – not determined

Ascertainment	case ID	gender	location	Age (years)	BMI	inheritance	CNV detection platform	
							detection	validation
Developmental Delay	1	M	Estonia	4.1	15.8	de novo	Illumina Human CNV370-Duo	qPCR
	2	M	Lausanne	16.3	38.6	inherited (mother)	aCGH Agilent 244k	none
	3	M	Lille	5.3	16.4	inherited (mother)	aCGH Agilent 44K	qPCR
	4	F	Lille	31	62.1	probably inherited[a]	aCGH Agilent 44K	qPCR
	5	F	Lille	8	22.9	de novo	aCGH Agilent 44K	qPCR
	6	M	Lille	41	61	n.d.	aCGH Agilent 44K	qPCR
	7	M	Lille	10	20.8	inherited (father)	aCGH Agilent 44K	qPCR
	8	F	Lille	11	20.3	inherited (mother)	aCGH Agilent 44K	qPCR
	9	M	Lille	11.5	17.7	n.d.	aCGH Agilent 44K	qPCR
	10	M	Lille	1.4	18.8	inherited (father)	aCGH Agilent 44K	qPCR
	11	F	Lyon	2.8	16.6	inherited (father)	aCGH Agilent 105K	qPCR
	12	M	Lyon	53	33.3	n.d.	aCGH Agilent 105K	qPCR
	13	F	Nancy	1	14.9	de novo	aCGH Agilent 105K	qPCR
	14	M	Nancy	4.4	16.8	de novo	aCGH Agilent 105K	qPCR
	15	M	Nancy	4.8	20.0	inherited (mother)	aCGH Agilent 105K	qPCR
	16	M	Nantes	6.9	24.1	inherited (mother)	aCGH Agilent 44K	FISH
	17	M	Nantes	7.5	14.6	inherited (mother)	aCGH Agilent 44K	FISH
	18	M	Nantes	1.9	15.0	inherited (mother)	aCGH Agilent 44K	FISH
	19	M	Paris	4.4	16.0	de novo	FISH	none
	20	F	Rouen	8	15.4	n.d.	QMPSF	FISH
	21	M	Rouen	4	17.3	de novo	QMPSF	FISH
	22	F	Rouen	8	15.7	inherited (mother)	QMPSF	FISH

Obesity & Developmental Delay	23	M	Lille	6	31.4	n.d.	qPCR	aCGH Agilent 44K
	24	M	Lille	10.3	34.8	n.d.	qPCR	aCGH Agilent 44K
	25	F	Lille	12	31.9	n.d.	qPCR	aCGH Agilent 44K
	26	M	Lille	14.5	40.2	n.d.	qPCR	aCGH Agilent 44K
	27	F	Lille	13.3	34.2	n.d.	qPCR	aCGH Agilent 44K
	28	M	Lille	15	30.5	n.d.	qPCR	aCGH Agilent 44K
	29	M	Lille	6	25.0	n.d.	qPCR	aCGH Agilent 44K
	30	F	Nîmes	12.3	29.0	n.d.	qPCR	aCGH Agilent 44K
	31	M	London	7.5	29.2	inherited (father)	aCGH Agilent 185K	none
General Population	32	M	Estonia	23	36	n.d.	Illumina Human CNV370-Duo	qPCR
	33	F	Finland	31	33.4	n.d.	Illumina Human CNV370-Duo	multiple algorithms
	34	F	Finland	31	45.7	n.d.	Illumina Human CNV370-Duo	multiple algorithms
	35	M	Finland	31	19.2	n.d.	Illumina Human CNV370-Duo	multiple algorithms
Adult Obesity	36	F	Lille	28	48.9	n.d.	Illumina Human CNV370-Duo	MLPA
	37	M	Lille	33	71.8	inherited (mother)	Illumina Human CNV370-Duo	MLPA
	38	F	Lille	41	51.8	n.d.	Illumina Human CNV370-Duo	MLPA
	39	F	Lille	36	57.9	n.d.	Illumina Human CNV370-Duo	MLPA
Childhood Obesity	40	M	Lille	16	36.0	inherited (mother)	Illumina Human CNV370-Duo	MLPA
	41	F	Lille	7	24.2	de novo	Illumina Human CNV370-Duo	MLPA
	42	F	Lille	6	29.2	de novo	Illumina Human CNV370-Duo	MLPA
	43	M	Lille	11	25.1	inherited (mother)	Illumina Human CNV370-Duo	MLPA
	44	F	Cambridge	15	43.9	n.d.	Affymetrix 6.0	MLPA
	45	M	Cambridge	13	57.0	n.d.	Affymetrix 6.0	MLPA
	46	F	Cambridge	15	45.8	n.d.	Affymetrix 6.0	MLPA
Obesity Bariatric Surgery	47	F	Lille	46	49.6	n.d.	Illumina Human 1M-Duo	MLPA
	48	F	Lille	59	71.9	n.d.	Illumina Human 1M-Duo	MLPA

Obesity Discordant Siblings	49	F	Gothenburg	36	51.9	de novo	Illumina Human 610K-Quad	MLPA
	50	F	Gothenburg	35	57.4	de novo	Illumina Human 610K-Quad	MLPA
Proband Relative	51	F	Lausanne	36	73.4	Mother of 2	aCGH Agilent 244K	none
	52	F	Lille			Mother of 3	MLPA	none
	53	M	Lille	35	59	Brother of 4[a]	aCGH Agilent 44K	qPCR
	54	M	Lille			Father of 7	qPCR	none
	55	F	Lille	42	34.7	Mother of 8	aCGH Agilent 44K	qPCR
	56	F	Lille	8.5	20.8	Sister of 8	aCGH Agilent 44K	qPCR
	57	M	Lille			Father of 10	MLPA	none
	58	M	Lyon	37	31.1	Father of 11	qPCR, 3 primer pairs	none
	59	F	Nancy	28	30.1	Mother of 15	qPCR	none
	60	F	Nantes	32	32.8	Mother of 16	FISH	none
	61	F	Nantes	34	31.6	Mother of 17	FISH	none
	62	F	Nantes			Mother of 18	FISH	none
	63	M	Rouen	15	32.7	Brother of 22	QMPSF	FISH
	64	F	Rouen	36	36	Mother of 22	QMPSF	FISH
	65	M	London	38	40	Father of 31	aCGH Agilent 244K	MLPA
	66	F	Lille			Mother of 37	MLPA	none
	67	F	Lille			Mother of 40	MLPA	none
	68	F	Lille			Mother of 43	MLPA	none

[a]The proband's brother has the deletion, but both parents are deceased so inheritance cannot be confirmed. One instance has been reported[4] of presumed germ-line mosaicism in which a deletion was found in two siblings but neither parent.

Supplementary Table S3

Obesity phenotype of carriers of 16p11.2 deletions from other publications, as included in Figure 2.

Publication	Patient ID	gender	Age (years)	BMI
Bijlsma *et al*.[11]	Case 1	M	44.0	28.7
	Case 2	M	17.2	40.1
	Case 3	F	8.2	26.6
	Case 6	F	7.0	16.8
	Case 8	F	11.0	20.1
	Case 10	F	8.0	14.7
	Case 11	M	4.0	14.6
	Case 13	M	4.8	16.7
Fernandez *et al*.[14]	Proband 2	M	13.0	42.5
	Proband 3	M	4.5	16.7
	Patient 3b	M	3.5	14.6
	Patient 3c	F	35.5	34.7
Ghebranious *et al*.[13]	Twin1	M	28.0	31.3
	Twin2	M	28.0	34.0
McCarthy *et al*.[12]	CHOP1	F	3.0	16.8
	CHOP4	M	14.8	23.5
	03C18520	M	23.0	31.4
	AU041905	M	8.0	15.9
Shimojima *et al.*[15]	-	M	3.2	16.5
Weiss *et al*.[10]	Pt1	M	6.5	16.3
	Pt3	M	1.4	16.3
	Pt4	M	9.2	31.8
	Pt5	M	9.2	32.0
	Aut1	F	5.2	16.0
	Aut2	M	10.5	29.9

Supplementary Table S4

Expression analysis transcript probeset details. The details of probes analysed in the course of expression analysis (Supplementary Figure S4), listing the Affymetrix probeset identification code, the gene whose transcript is listed as being detected by the probe, and the chromosomal coordinate (build hg18) for the start of that gene.

Probe ID	Gene	Coordinate
209275_s_at	*CLN3*	28396101
210859_x_at	*CLN3*	28396101
220023_at	*AC138894.3*	28413494
1552995_at	*IL27*	28418184
209230_s_at	*NUPR1*	28456107
221822_at	*CCDC101*	28472748
48117_at	*CCDC101*	28472748
207122_x_at	*SULT1A2*	28510765
211385_x_at	*SULT1A1*	28524404
238995_at	*SULT1A1*	28524404
217314_at	*AC145285.2*	28618998
200647_x_at	*EIF3S8*	28630283
210949_s_at	*EIF3S8*	28630283
215230_x_at	*EIF3S8*	28630283
201806_s_at	*ATXN2L*	28741821
207798_s_at	*ATXN2L*	28741821
201113_at	*TUFM*	28761233
238190_at	*TUFM*	28761233
209322_s_at	*SH2B1*	28782579
40149_at	*SH2B1*	28782579
205444_at	*ATP2A1*	28797305
219057_at	*RABEP2*	28823244
74694_s_at	*RABEP2*	28823244
77508_r_at	*RABEP2*	28823244
206398_s_at	*CD19*	28850761
212808_at	*NFATC2IP*	28869814
212809_at	*NFATC2IP*	28869814
217526_at	*NFATC2IP*	28869814
217527_s_at	*NFATC2IP*	28869814
229235_at	*NFATC2IP*	28869814
223173_at	*SPNS1*	28893597
209881_s_at	*LAT*	28903648
211005_at	*LAT*	28903648
216902_s_at	*AC009093.1*	28993664
216908_x_at	*AC009093.1*	28993664
243124_at	*AC009093.1*	28993664
221184_at	*AC009093.2*	29167674
241644_at	*BOLA2*	29365833
215299_x_at	*SULT1A4*	29374628
1558044_s_at	*AC009086.2*	29471943
1558534_at	*AC009086.2*	29471943
237464_at	*AC009086.2*	29471943
1568964_x_at	*SPN*	29581801
206056_x_at	*SPN*	29581801
206057_x_at	*SPN*	29581801
216981_x_at	*SPN*	29581801
204044_at	*QPRT*	29582101
242414_at	*QPRT*	29582101
1559584_a_at	*C16orf54*	29661285
214142_at	*ZG16*	29697091
202183_s_at	*KIF22*	29709542
216969_s_at	*KIF22*	29709542
207824_s_at	*MAZ*	29725356
212064_x_at	*MAZ*	29725356
228798_x_at	*AC009133.1*	29729246
218300_at	*C16orf53*	29734786
227192_at	*C16orf53*	29734786
202180_s_at	*MVP*	29739230
201253_s_at	*CDIPT*	29777179
240537_s_at	*AC120114.2*	29782656
218720_x_at	*SEZ6L2*	29789981
223458_at	*SEZ6L2*	29789981
233337_s_at	*SEZ6L2*	29789981
238406_x_at	*SEZ6L2*	29789981
1553997_a_at	*ASPHD1*	29819201
214993_at	*ASPHD1*	29819201
221889_at	*KCTD13*	29825158
45653_at	*KCTD13*	29825158
238142_at	*KCTD13*	29825158
224981_at	*TMEM219*	29880852
204877_s_at	*TAOK2*	29892723
204878_s_at	*TAOK2*	29892723
204986_s_at	*TAOK2*	29892723
204504_s_at	*HIRIP3*	29911812
227286_at	*INO80E*	29914532
205744_at	*DOC2A*	29924336
1557162_at	*C16orf92*	29942156
227781_x_at	*FAM57B*	29943249
200966_x_at	*ALDOA*	29971945
214687_x_at	*ALDOA*	29971945
208932_at	*PPP4C*	29994812
207684_at	*TBX6*	30004583
215122_at	*TBX6*	30004583
223179_at	*YPEL3*	30011136
232077_s_at	*YPEL3*	30011136
219722_s_at	*GDPD3*	30023632
212046_x_at	*MAPK3*	30032927
209083_at	*CORO1A*	30102393
209836_x_at	*BOLA2B*	30111740
203615_x_at	*SULT1A3*	30113244
209607_x_at	*SULT1A3*	30113244
210580_x_at	*SULT1A3*	30113244
218317_x_at	*SULT1A3*	30113244
222094_at	*SULT1A3*	30113244

Probe ID	Gene	Coordinate
233334_x_at	*SULT1A3*	30113244
211996_s_at	*AC106782.7*	30141697
214035_x_at	*AC106782.7*	30141697
214870_x_at	*AC106782.7*	30141697
215920_s_at	*AC106782.7*	30141697
215921_at	*AC106782.7*	30141697
221501_x_at	*AC106782.7*	30141697
238449_at	*AC106782.7*	30141697
1557987_at	*AC106782.7*	30141697
215123_at	*AC106782.7*	30141697
215002_at	*AC106782.7*	30141697
235060_at	*AC106782.7*	30141697
235167_at	*AC106782.7*	30141697
238341_at	*AC106782.7*	30141697
242114_at	*AC106782.7*	30141697
231989_s_at	*AC106782.4*	30186315
244766_at	*AC106782.4*	30186315
210396_s_at	*AC106782.8*	30204010
202257_s_at	*CD2BP2*	30269588
202256_at	*CD2BP2*	30269588
220947_s_at	*TBC1D10B*	30275923
205163_at	*MYLPF*	30293613
227552_at	*37135*	30296955
227470_at	*ZNF48*	30313934
219781_s_at	*ZNF771*	30326236
218069_at	*DCTPP1*	30342520
200961_at	*SEPHS2*	30362453
1554240_a_at	*ITGAL*	30391484
213475_s_at	*ITGAL*	30391484
218916_at	*ZNF768*	30442826
206180_x_at	*ZNF747*	30449189
228856_at	*ZNF747*	30449189
238606_at	*ZNF747*	30449189
239774_at	*ZNF747*	30449189
57516_at	*ZNF764*	30472586
222120_at	*ZNF764*	30472586
213527_s_at	*ZNF688*	30488529
213529_at	*ZNF688*	30488529
235951_s_at	*ZNF688*	30488529
235950_at	*ZNF688*	30488529
213525_at	*AC002310.1*	30491072
1554769_at	*ZNF785*	30497795
1554770_x_at	*ZNF785*	30497795
242272_at	*ZNF785*	30497795
227294_at	*ZNF689*	30521380
227445_at	*ZNF689*	30521380
1559397_s_at	*PRR14*	30569724
218714_at	*PRR14*	30569724
45687_at	*PRR14*	30569724
218255_s_at	*FBRS*	30577790
242217_s_at	*FBRS*	30577790
238771_at	*FBRS*	30577790
1552630_a_at	*SRCAP*	30617031
1569138_a_at	*SRCAP*	30617031
212275_s_at	*SRCAP*	30617031
213667_at	*SRCAP*	30617031
215053_at	*SRCAP*	30617031
38766_at	*SRCAP*	30617031
203709_at	*PHKG2*	30667092
231300_at	*C16orf93*	30676254
206845_s_at	*RNF40*	30681100
239801_at	*RNF40*	30681100
1556368_at	*RNF40*	30681100
1556369_a_at	*RNF40*	30681100
213196_at	*ZNF629*	30697271
219072_at	*BCL7C*	30752874
206813_at	*CTF1*	30811875
1553586_at	*NCRNA00095*	30841418
228277_at	*FBXL19*	30841893
221864_at	*ORAI3*	30867888
213202_at	*SETD1A*	30876116
222817_at	*HSD3B7*	30904020
230691_at	*STX1B*	30908078
203530_s_at	*STX4*	30951820
229395_at	*STX4*	30951820
219047_s_at	*ZNF668*	30979672
204876_at	*ZNF646*	30993265
214226_at	*AC135050.2*	31002259

Supplementary Table S5

Details of genes lying within the deleted region at 16p11.2. Gene name, coordinates and strand of protein coding region are according to genome build hg18. Protein function descriptions are based on GeneCards entries (http://www.genecards.org/) or from the indicated references. Change in expression is given as the mean transcript level (all probes) in the 2 deletion carriers relative to obese (normal/lean) subjects (data as in Supplementary Figure S4). Possible functional relevance to obesity (bold type) or developmental delay/ cognitive deficit (italics) is as indicated. The first three pairs of genes lie within the segmental duplications.

Gene name	CDS start	CDS end	Strand	Change in Expr^n	Protein function	Refs
BOLA2 *BOLA2B*	29365833 30111796	29373786 30112615	- -	0.6 (0.8)	**Possibly involved in cell proliferation or cell-cycle regulation**	
GIYD1 *GIYD2*	29373376 30112906	29377041 30116288	+ +	-	GIY-YIG domain containing	
SULT1A4 *SULT1A3*	29373902 30119550	29383801 30122742	+ +	1.0 (1.5)	**Induced in response to fasting or as a result of a defect in leptin signalling** *Catalyzes the sulfate conjugation of phenolic monoamine neurotransmitters*	44
SPN	29582550	29583753	+	1.1 (1.1)	**Sialophorin, CD43. Activator of JNK1 and MAPK3 signalling**	45-47
QPRT	29598019	29616233	+	1.2 (1.3)	*Catabolism of quinolinate, a neural excitotoxin and NMDA receptor agonist*	48
C16orf54	29663098	29663773	-	0.5 (0.8)		
MAZ	29725523	29728564	+	0.7 (0.8)	***Interacts with SP1 in regulating transcription of serotonin receptor gene HTR1A***	49
PRRT2	29731876	29733460	+		Proline-rich transmembrane protein	
C16orf53	29735347	29738576	+	0.8 (0.8)		
MVP	29749371	29766811	+	0.5 (0.8)	**Regulates cytoplasmic localisation of PTEN**	50
CDIPT	29778010	29781679	-	0.4 (0.5)	Phosphatidylinositol synthesis	
SEZ6L2	29790520	29817841	-	0.9 (0.9)	*Seizure-related. May contribute to specialized ER function in neurons*	
ASPHD1	29819793	29824719	+	1.0 (1.1)	Aspartate beta-hydroxylase domain containing	
KCTD13	29825693	29844855	-	0.6 (0.6)	**Similar to TNFAIP1, a mediator of insulin resistance in rodent obesity models**	
TMEM219	29881965	29890367	+	0.6 (0.7)	Transmembrane protein	
TAOK2	29896594	29906802	+	0.8 (0.8)	**Activates JNK1 and MAPK3 pathways via the upstream MKK3 and MKK6 kinases**	
HIRIP3	29912028	29914427	-	0.6 (0.5)	Possibly functions in some aspects of chromatin and histone metabolism	
INO80E	29915132	29924264	+	0.5 (0.5)	INO80 complex subunit E	
DOC2A	29925007	29929044	-	1.0 (1.0)	*Possibly involved in Ca^{2+}-dependent neurotransmitter release*	
C16orf92	29942176	29943049	+	1.1 (1.1)		
FAM57B	29944004	29949349	-	0.9 (0.8)		
ALDOA	29986076	29989034	+	0.5 (0.6)	Fructose-bisphosphate aldolase A	
PPP4C	29995199	30003884	+	0.7 (0.8)	**Regulates JNK1 signalling**	
TBX6	30005046	30010015	-	1.0 (1.0)	Transcription factor involved in regulation of early developmental processes	
YPEL3	30011531	30014190	-	0.6 (0.6)	Possibly involved in proliferation and apoptosis in myeloid precursor cells	
GDPD3	30023693	30032300	-	0.8 (0.9)	**Glycerophosphodiesterase domain**	
MAPK3	30035658	30042031	-	0.7 (0.7)	**ERK1. Multiple roles in proliferation and differentiation of preadipocytes**	51
CORO1A	30104031	30107786	+	0.3 (0.5)	Coronin. Actin binding protein	

Supplementary references

42. Merla *et al.* Submicroscopic deletion in patients with Williams-Beuren syndrome influences expression levels of the nonhemizygous flanking genes. *Am. J. Hum. Genet.* **79**, 332-341 (2006).
43. Henrichsen, C.N. *et al.* Segmental copy number variation shapes tissue transcriptomes. *Nat. Genet.* **41**, 424-429 (2009).
44. Li, J.-Y. *et al.* Food Deprivation-induced Expression of Minoxidil Sulfotransferase in the Hypothalamus Uncovered by Microarray Analysis. *J. Biol. Chem*. **277**, 9069-9076 (2002).
45. Cho, J.Y., Chain, B.M., Vives, J., Horejsi, V., Katz, D.R. Regulation of CD43-induced U937 homotypic aggregation. *Exp. Cell Res.* **290**, 155-167 (2003).
46. Mattioli, I., Dittrich-Breiholz, O., Livingstone, M., Kracht, M., Schmitz, M.L. Comparative analysis of T-cell costimulation and CD43 activation reveals novel signaling pathways and target genes. *Blood* **104**, 3302-3304 (2004).
47. Fierro, N.A., Pedraza-Alva, G., Rosenstein, Y. TCR-Dependent Cell Response Is Modulated by the Timing of CD43 Engagement. *J . Immunol.* **176**, 7346-7353 (2006).
48. Guillemin, G.J., Brew, B.J. Implications of the kynurenine pathway and quinolinic acid in Alzheimer's disease. *Redox Rep.* **7**, 199-206 (2002)
49. Parks, C.L., Shenk, T. The serotonin 1a receptor gene contains a TATA-less promoter that responds to MAZ and Sp1. *J. Biol. Chem.* **271**, 4417-4430 (1996).
50. Minaguchi, T., Waite, K.A., Eng, C. Nuclear Localization of PTEN Is Regulated by Ca^{2+} through a Tyrosil Phosphorylation–Independent Conformational Modification in Major Vault Protein. *Cancer Res.* **66**, 11677-11682
51. Bost, F., Aouadi, M., Caron, L., Binetruy, B. The role of MAPKs in adipocyte differentiation and obesity. *Biochimie* **87**, 51-56 (2005).