Moderate to vigorous physical activity interactions with genetic variants and body mass index in a large US ethnically diverse cohort

Richardson AS,<sup>1,2</sup> North, KE,<sup>3,4</sup> Graff M,<sup>1,4</sup> Young KM,<sup>1,4</sup> Mohlke KL,<sup>3,5</sup> Lange LA,<sup>3,5</sup> Lange EM,<sup>3,5</sup> Harris KM,<sup>1,6</sup> Gordon-Larsen P<sup>1,2</sup>

<sup>1</sup>Carolina Population Center, <sup>2</sup>Department of Nutrition Gillings School of Global Public Health, <sup>3</sup>Carolina Center for Genome Sciences, <sup>4</sup>Department of Epidemiology, <sup>5</sup>Department of Genetics, University of North Carolina, Chapel Hill, <sup>6</sup>Department of Sociology

North Carolina, USA

**Table S1.** List of 41 well-established adiposity related SNPs considered for interaction with MVPA in the current study

SNP	Nearby gene	Chromosome	Position
rs10146997	NRXN3	14	79014915
rs10508503 <sup>2</sup>	PTER	10	16339957
rs10767664	BDNF	11	27682562
rs1077393	NCR3_BAT2	6	31718508
rs10938397	GNPDA2	4	45023455
rs10968576	LRRN6C	9	28404339
rs12444979 <sup>2</sup>	GPRC5B	16	19841101
rs12970134 <sup>1</sup>	MC4R	18	56035730
rs13078807 <sup>1</sup>	CADM2	3	85966840
rs13107325 <sup>2</sup>	SLC39A8	4	103545887
rs1424233	MAF	16	78240252
rs1514175 <sup>1</sup>	TNNI3K	1	74703665
rs1555543 <sup>1</sup>	PTBP2	1	96656818
rs1805081	NPC1	18	19394430
rs206936	NUDT3	6	34410847
rs2112347 <sup>1</sup>	POC5 (formerly FLJ35779)	5	7505998
rs2241423	MAP2K5	15	65873892
rs2287019	QPCTL	19	50894012
rs2444217	ADCY9	16	3978388
rs2568958 <sup>1,</sup>	NEGR1	1	72477137
rs2605100	LYPLAL1	1	216032619
rs2890652 <sup>1</sup>	LRP1B	2	142793663
rs29941 <sup>1</sup>	KCTD15	19	39001372
rs3810291	TMEM160	19	52260843
rs3817334	MTCH2	11	47607569
rs4712652	PRL	6	22186594
rs4771122 <sup>1</sup>	MTIF3	13	26918180
rs4788102 <sup>2</sup>	SH2B1	16	28780899
rs4929949 <sup>1</sup>	RPL27A	11	8561169
rs543874 <sup>1</sup>	SEC16B/LZTR2	1	174621137
rs545854	MSRA	8	9897490
rs571312 <sup>1</sup>	MC4R	18	55990749
rs6548238 <sup>2</sup>	TMEM18	1	624905
rs713586	POMC	2	25069659
rs7138803	FAIM2	12	48533735
rs7359397 <sup>1</sup>	SH2B1_APOB48	16	28793160
rs7647305	ETV5	3	187316992
rs867559	LMX1B	9	126544879
rs887912 <sup>1</sup>	FANCL	2	59214528
rs987237	TFAP2B	6	50911009

rs9939609 FTO 16 52378028

Abbreviations: SNP, single nucleotide polymorphism, MVPA, moderate to vigorous physical activity, EA, European Americans, AA, African Americans, HA, Hispanic Americans
Sorted by rs number

<sup>1</sup> Not considered for interaction assessment in AA

<sup>2</sup> Not considered for interaction assessment in HA

<sup>3</sup> Not considered for interaction in EA

**Table S2**. Allele frequencies for 41 well-established adiposity related SNPs<sup>1</sup> by race/ethnicity

race/ethnicity				
Nearby gene	SNP	European	African	Hispanic
		American	American	American
ADCY9	rs2444217	0.57	0.57	0.57
BDNF	rs10767664	0.79	0.79	0.79
CADM2	rs13078807	0.20	0.20	0.20
ETV5	rs7647305	0.79	0.79	0.79
FAIM2	rs7138803	0.38	0.38	0.38
FANCL	rs887912	0.28	0.28	0.28
FTO	rs9939609	0.39	0.39	0.39
GNPDA2	rs10938397	0.43	0.43	0.43
GPRC5B	rs12444979	0.86	0.86	0.86
KCTD15	rs29941	0.68	0.68	0.68
LMX1B	rs867559	0.19	0.19	0.19
LRP1B	rs2890652	0.16	0.16	0.16
LRRN6C	rs10968576	0.31	0.31	0.31
LYPLAL1	rs2605100	0.29	0.29	0.29
MAF	rs1424233	0.48	0.48	0.48
MAP2K5	rs2241423	0.77	0.77	0.77
MC4R	rs12970134	0.26	0.26	0.26
MC4R	rs571312	0.23	0.23	0.23
MSRA	rs545854	0.16	0.16	0.16
MTCH2	rs3817334	0.40	0.40	0.40
MTIF3	rs4771122	0.22	0.22	0.22
NCR3_BAT2	rs1077393	0.49	0.49	0.49
NEGR1	rs2568958	0.63	0.63	0.63
NPC1	rs1805081	0.60	0.60	0.60
NRXN3	rs10146997	0.79	0.79	0.79
NUDT3	rs206936	0.21	0.21	0.21
POC5	rs2112347	0.63	0.63	0.63
POMC	rs713586	0.48	0.48	0.48
PRL	rs4712652	0.42	0.42	0.42
PTBP2	rs1555543	0.59	0.59	0.59
PTER	rs10508503	0.92	0.92	0.92
QPCTL	rs2287019	0.82	0.82	0.82
RPL27A	rs4929949	0.51	0.51	0.51
SEC16B/LZTR2	rs543874	0.20	0.20	0.20
SH2B1	rs4788102	0.39	0.39	0.39
SH2B1_APOB48	rs7359397	0.39	0.39	0.39
SLC39A8	rs13107325	0.08	0.08	0.08
TFAP2B	rs987237	0.18	0.18	0.18
TMEM160	rs3810291	0.67	0.67	0.67
TMEM18	rs6548238	0.83	0.83	0.83
TNNI3K	rs1514175	0.44	0.44	0.44

Abbreviations: BMI, body mass index, SNP, single nucleotide polymorphism, MVPA, moderate to vigorous physical activity, CI confidence interval Sorted by nearby gene 

¹Considered for interaction assessment 41 SNPs in EA, 37 in HA, and 19 in AA

**Table S3.** Estimated main effects<sup>1</sup> of 41 well-established adiposity related SNPs<sup>2</sup> on adolescent BMI-for-age Z scores, by race/ethnicity

			BMI-for-age Z scores									
Nearby gene	SNP	Europe	European American			frican American			Hispanic American			
		β	(95% CI)	р	β	(95% CI)	р	β	(95% CI)	р		
ADCY9	rs2444217	-0.03	(-0.07,0.02)	0.2264	0.06	(-0.03,0.14)	0.1894	-0.04	(-0.13,0.05)	0.3830		
BDNF	rs10767664	0.06	(0.00,0.11)	0.0336	-0.04	(-0.19,0.10)	0.5692	0.10	(0.00, 0.21)	0.0561		
CADM2	rs13078807	0.06	(0.01,0.11)	0.0229				0.08	(-0.04,0.20)	0.2157		
ETV5	rs7647305	0.03	(-0.02,0.08)	0.2283	0.09	(0.01,0.16)	0.0195	0.00	(-0.11,0.10)	0.9346		
FAIM2	rs7138803	0.03	(-0.02,0.07)	0.2610	0.12	(0.02, 0.22)	0.0138	-0.01	(-0.11,0.09)	0.8483		
FANCL	rs887912	0.06	(0.02,0.11)	0.0090				-0.06	(-0.17,0.05)	0.3057		
FTO	rs9939609	0.16	(0.12,0.21)	1.86E-13	0.02	(-0.05, 0.09)	0.5276	0.09	(0.00, 0.18)	0.0621		
GNPDA2	rs10938397	0.05	(0.00, 0.09)	0.0347	0.12	(0.04,0.21)	0.0051	0.06	(-0.03,0.15)	0.1958		
GPRC5B	rs12444979	0.06	(0.00, 0.12)	0.0476				0.12	(-0.03,0.26)	0.1073		
KCTD15	rs29941	0.03	(-0.02,0.07)	0.2322				0.02	(-0.07,0.11)	0.6703		
LMX1B	rs867559	0.03	(-0.02,0.08)	0.3031	-0.01	(-0.08,0.07)	0.9002	0.02	(-0.07,0.11)	0.6286		
LRP1B	rs2890652	0.04	(-0.02,0.09)	0.2124				0.09	(-0.04,0.21)	0.1785		
LRRN6C	rs10968576	0.01	(-0.04,0.05)	0.8087	0.10	(0.00, 0.19)	0.0397	0.05	(-0.05,0.15)	0.3403		
LYPLAL1	rs2605100	-0.01	(-0.06,0.04)	0.6153				0.00	(-0.09,0.09)	0.9497		
SEC16B/LZTR2	rs543874	0.09	(0.04, 0.14)	0.0010				0.10	(-0.01,0.21)	0.0734		
MAF	rs1424233	0.00	(-0.04,0.04)	0.9368	0.03	(-0.05,0.11)	0.5060	0.06	(-0.02,0.15)	0.1462		
MAP2K5	rs2241423	0.06	(0.01,0.11)	0.0127	0.06	(-0.02,0.13)	0.1277	-0.05	(-0.14,0.04)	0.2465		
MC4R	rs12970134	0.07	(0.02, 0.12)	0.0036				0.06	(-0.05,0.17)	0.3199		
MC4R	rs571312	0.10	(0.05, 0.15)	0.00007				0.10	(-0.02,0.21)	0.1024		
MSRA	rs545854	0.03	(-0.02,0.09)	0.2492				-0.02	(-0.12,0.08)	0.6522		
MTCH2	rs3817334	0.03	(-0.01,0.07)	0.1678	0.05	(-0.03,0.13)	0.2590	0.03	(-0.06,0.12)	0.4806		
MTIF3	rs4771122	-0.01	(-0.06,0.04)	0.7929				0.10	(-0.01,0.21)	0.0694		

Table S3. (continued)

						BMI-for-age Z se	cores			
Nearby gene	SNP	Europe	an American		African	American		Hispani	c American	
		β	(95% CI)	р	β	(95% CI)	р	β	(95% CI)	р
NCR3_BAT2	rs1077393	0.00	(-0.05,0.04)	0.8537	0.02	(-0.06,0.09)	0.6383	0.05	(-0.04,0.13)	0.2619
NEGR1	rs2568958	0.05	(0.00, 0.09)	0.0407				0.05	(-0.05,0.14)	0.3276
NPC1	rs1805081	0.01	(-0.03,0.06)	0.5600				0.04	(-0.06,0.14)	0.4118
NRXN3	rs10146997	-0.03	(-0.09,0.02)	0.2230	-0.02	(-0.09, 0.06)	0.6654	-0.05	(-0.15,0.06)	0.3795
NUDT3	rs206936	0.06	(0.00,0.11)	0.0376	-0.02	(-0.09, 0.05)	0.5967	-0.02	(-0.11,0.07)	0.6274
POC5	rs2112347	0.02	(-0.02,0.07)	0.3654				0.04	(-0.05,0.13)	0.4195
POMC	rs713586	0.06	(0.02,0.11)	0.0043	0.00	(-0.10,0.10)	0.9766	-0.03	(-0.12,0.05)	0.4403
PRL	rs4712652	0.03	(-0.01,0.08)	0.1132	-0.02	(-0.09, 0.06)	0.6544	-0.01	(-0.09,0.08)	0.8699
PTBP2	rs1555543	0.05	(0.01,0.10)	0.0160				0.07	(-0.02,0.16)	0.1164
PTER	rs10508503	0.12	(0.04, 0.20)	0.0024	-0.17	(-0.43,0.10)	0.2264			
QPCTL	rs2287019	0.03	(-0.02,0.09)	0.2111				0.01	(-0.12,0.13)	0.9157
RPL27A	rs4929949	-0.02	(-0.06,0.02)	0.3014				0.01	(-0.08,0.09)	0.8980
SEC16B/LZTR2	rs543874	0.09	(0.04, 0.14)	0.0010				0.10	(-0.01,0.21)	0.0734
SH2B1	rs4788102	0.01	(-0.03,0.05)	0.6631	0.01	(-0.07, 0.09)	0.8391			
SH2B1_APOB48	rs7359397	0.01	(-0.03,0.06)	0.5874				0.08	(-0.01,0.16)	0.0899
SLC39A8	rs13107325	0.04	(-0.04,0.12)	0.3314						
TFAP2B	rs987237	0.10	(0.05, 0.16)	0.0002				0.12	(0.02,0.21)	0.0156
TMEM160	rs3810291	0.04	(-0.01,0.08)	0.0923	0.06	(-0.03,0.15)	0.1842	-0.04	(-0.13,0.05)	0.3849
TMEM18	rs6548238	0.15	(0.09, 0.20)	1.28E-07						
TNNI3K	rs1514175	0.06	(0.02,0.11)	0.0040				0.01	(-0.07,0.10)	0.7708

Abbreviations: SNP, single nucleotide polymorphism, MVPA, moderate to vigorous physical activity, BMI, body mass index, CI confidence interval Sorted by nearby gene

<sup>&</sup>lt;sup>1</sup>Main effect model: Multivariable linear model of adolescent BMI regressed on SNP, controlling for age, sex, MVPA, current smoking, screen time, region, indicator for self-reported heights and weights, oversampling of highly educated African Americans (AA stratum only), Hispanic subpopulation ancestry, as well as an indicator for foreign born (n= 268, HA stratum only). Random

intercepts allowed for individual, family and school with no sample weighting. Models run separately for each SNP and race/ethnicity. P values corrected for multiple testing are  $\alpha$  equal to 0.05/number of SNPs tested (0.0012 in EA, 0.0026 in AA, 0.0014 in HA)  $^2$ Considered for interaction assessment 41 SNPs in EA, 37 in HA, and 19 in AA

**Table S4.** Estimated main effects<sup>1</sup> of 41 well-established adiposity related SNPs<sup>2</sup> on adolescent weight-for-age Z scores, by race/ethnicity

		Weight-for-age Z scores								
Nearby gene	SNP	Europe	an American		African	American		Hispani	ic American	
		β	(95% CI)	р	β	(95% CI)	р	β	(95% CI)	р
ADCY9	rs2444217	-0.02	(-0.06,0.02)	0.3809	0.04	(-0.05,0.12)	0.4020	-0.04	(-0.13,0.05)	0.3787
BDNF	rs10767664	0.06	(0.01,0.11)	0.0262	-0.02	(-0.16,0.13)	0.8048	0.10	(-0.01,0.21)	0.0896
CADM2	rs13078807	0.05	(0.00, 0.10)	0.0416				0.18	(0.05, 0.30)	0.0052
ETV5	rs7647305	0.04	(-0.01,0.09)	0.1398	0.08	(0.01,0.15)	0.0231	-0.06	(-0.18,0.05)	0.2707
FAIM2	rs7138803	0.04	(0.00,0.08)	0.0710	0.14	(0.05, 0.24)	0.0024	0.06	(-0.04,0.16)	0.2448
FANCL	rs887912	0.06	(0.01,0.10)	0.0116				-0.01	(-0.12,0.10)	0.8646
FTO	rs9939609	0.14	(0.10,0.18)	2.16E-11	0.01	(-0.06,0.08)	0.7419	0.08	(-0.02,0.17)	0.1058
GNPDA2	rs10938397	0.04	(0.00,0.08)	0.0418	0.13	(0.04, 0.21)	0.0037	0.07	(-0.02,0.16)	0.1279
GPRC5B	rs12444979	0.06	(0.01,0.12)	0.0315				0.05	(-0.10,0.20)	0.5082
KCTD15	rs29941	0.03	(-0.01,0.07)	0.1816				0.02	(-0.07,0.11)	0.6809
LMX1B	rs867559	0.02	(-0.03,0.07)	0.4011	-0.03	(-0.10,0.05)	0.5140	-0.02	(-0.11,0.07)	0.6297
LRP1B	rs2890652	0.03	(-0.03,0.08)	0.3410				0.15	(0.03, 0.28)	0.0180
LRRN6C	rs10968576	0.00	(-0.04,0.04)	0.9598	0.10	(0.01, 0.19)	2.60E-02	0.04	(-0.06,0.15)	4.03E-01
LYPLAL1	rs2605100	0.00	(-0.04,0.05)	0.9555				0.02	(-0.07,0.11)	0.6848
MAF	rs1424233	0.00	(-0.04,0.04)	0.9396	0.01	(-0.07,0.08)	0.8378	0.01	(-0.08,0.10)	0.8544
MAP2K5	rs2241423	0.05	(0.01, 0.10)	0.0268	0.06	(-0.01,0.13)	0.0868	-0.01	(-0.10,0.08)	0.8739
MC4R	rs12970134	0.07	(0.02, 0.11)	0.0054				0.13	(0.02, 0.24)	0.0256
MC4R	rs571312	0.10	(0.05, 0.14)	0.00009				0.19	(0.07,0.31)	0.0015
MSRA	rs545854	0.02	(-0.03,0.08)	0.4510				-0.03	(-0.13,0.07)	0.5276
MTCH2	rs3817334	0.03	(-0.01,0.07)	0.1448	0.05	(-0.03,0.13)	0.2322	0.01	(-0.08,0.10)	0.8593
MTIF3	rs4771122	0.01	(-0.04,0.06)	0.6344		·		0.08	(-0.03,0.19)	0.1721

Table S4. (continued)

					V	Veight-for-age Z	scores			
Nearby gene	SNP	Europe	an American		African	American		Hispani	c American	
		β	(95% CI)	р	β	(95% CI)	р	β	(95% CI)	р
NCR3_BAT2	rs1077393	-0.03	(-0.08,0.01)	0.0903	0.00	(-0.07,0.08)	0.9009	0.02	(-0.07,0.10)	0.7255
NEGR1	rs2568958	0.05	(0.01, 0.09)	0.0243				0.02	(-0.07,0.12)	0.6196
NPC1	rs1805081	0.01	(-0.03,0.05)	0.5297				0.05	(-0.05,0.15)	0.3717
NRXN3	rs10146997	-0.02	(-0.08,0.03)	0.3385	-0.02	(-0.09, 0.05)	0.6035	-0.04	(-0.15,0.07)	0.4479
NUDT3	rs206936	0.06	(0.01,0.11)	0.0182	-0.02	(-0.09, 0.05)	0.6086	0.01	(-0.08,0.10)	0.7895
POC5	rs2112347	0.03	(-0.01,0.07)	0.1905				0.00	(-0.09,0.10)	0.9215
POMC	rs713586	0.05	(0.01, 0.09)	0.0123	0.00	(-0.09,0.10)	0.9229	-0.04	(-0.13,0.04)	0.3293
PRL	rs4712652	0.01	(-0.03,0.05)	0.5911	-0.03	(-0.10,0.05)	0.5115	0.00	(-0.09,0.09)	0.9956
PTBP2	rs1555543	0.04	(0.00,0.08)	0.0737				0.06	(-0.03,0.15)	0.1897
PTER	rs10508503	0.07	(0.00, 0.15)	0.0644	-0.08	(-0.34,0.18)	0.5483			
QPCTL	rs2287019	0.02	(-0.03,0.07)	0.4858				0.03	(-0.10,0.16)	0.6267
RPL27A	rs4929949	-0.01	(-0.05,0.03)	0.7876				0.00	(-0.08,0.09)	0.9292
SEC16B/LZTR2	rs543874	0.08	(0.03, 0.13)	0.0011				0.10	(-0.01,0.21)	0.0880
SH2B1	rs4788102	0.01	(-0.03,0.05)	0.5821	0.04	(-0.04,0.12)	0.2987			
SH2B1_APOB48	rs7359397	0.01	(-0.03,0.05)	0.5697				0.02	(-0.07,0.11)	0.6129
SLC39A8	rs13107325	0.02	(-0.06,0.09)	0.6786						
TFAP2B	rs987237	0.10	(0.05, 0.16)	0.0001				0.11	(0.01,0.21)	0.0249
TMEM160	rs3810291	0.01	(-0.03,0.06)	0.5621	0.08	(-0.01,0.16)	0.0892	-0.03	(-0.12,0.06)	0.5129
TMEM18	rs6548238	0.16	(0.10,0.21)	9.54E-09						
TNNI3K	rs1514175	0.05	(0.01,0.09)	0.0099				0.02	(-0.07,0.10)	0.7106

Abbreviations: SNP, single nucleotide polymorphism, MVPA, moderate to vigorous physical activity, BMI, body mass index, CI confidence interval Sorted by nearby gene

<sup>&</sup>lt;sup>1</sup>Main effect model: Multivariable linear model of adolescent BMI regressed on SNP, controlling for age, sex, MVPA, current smoking, screen time, region, indicator for self-reported heights and weights, oversampling of highly educated African Americans (AA stratum only), Hispanic subpopulation ancestry, as well as an indicator for foreign born (n= 268, HA stratum only). Random

intercepts allowed for individual, family and school with no sample weighting. Models run separately for each SNP and race/ethnicity. P values corrected for multiple testing are  $\alpha$  equal to 0.05/number of SNPs tested (0.0012 in EA, 0.0026 in AA, 0.0014 in HA)  $^2$ Considered for interaction assessment 41 SNPs in EA, 37 in HA, and 19 in AA

**Table S5**. Estimated main effects<sup>1</sup> of 41 well-established adiposity related SNPs<sup>2</sup> on adolescent height-for-age Z scores, by race/ethnicity

•					H	Height-for-age Z	scores				
Nearby gene	SNP	Europe	European American			African American			Hispanic American		
	β	(95% CI)	р	β	(95% CI)	р	β	(95% CI)	р		
ADCY9	rs2444217	0.02	(-0.02,0.06)	0.4076	-0.01	(-0.10,0.08)	0.8216	0.00	(-0.09,0.08)	0.9645	
BDNF	rs10767664	0.02	(-0.03,0.07)	0.4704	0.03	(-0.12,0.18)	0.6696	0.04	(-0.07,0.14)	0.4930	
CADM2	rs13078807	0.01	(-0.04,0.06)	0.8116				0.23	(0.11,0.35)	0.0001	
ETV5	rs7647305	0.04	(-0.01,0.08)	0.1412	0.01	(-0.06, 0.09)	0.7184	-0.12	(-0.23,-0.01)	0.0267	
FAIM2	rs7138803	0.04	(0.00,0.08)	0.0383	0.13	(0.04, 0.23)	0.0067	0.10	(0.01,0.20)	0.0309	
FANCL	rs887912	-0.01	(-0.05,0.03)	0.6693				0.09	(-0.02,0.20)	0.1018	
FTO	rs9939609	0.01	(-0.03,0.05)	0.5066	-0.01	(-0.09, 0.06)	0.6826	-0.01	(-0.10,0.08)	0.8574	
GNPDA2	rs10938397	0.01	(-0.03,0.05)	0.6197	0.01	(-0.08,0.10)	0.8536	0.05	(-0.04,0.14)	0.2674	
GPRC5B	rs12444979	0.01	(-0.05,0.06)	0.7446				-0.11	(-0.25,0.03)	0.1368	
KCTD15	rs29941	0.01	(-0.03,0.05)	0.6046				-0.02	(-0.11,0.07)	0.6824	
LMX1B	rs867559	-0.01	(-0.05,0.04)	0.8092	-0.03	(-0.11,0.05)	0.4663	-0.09	(-0.18,-0.01)	0.0297	
LRP1B	rs2890652	-0.02	(-0.07,0.04)	0.5715				0.16	(0.04, 0.28)	0.0092	
LRRN6C	rs10968576	-0.01	(-0.06, 0.03)	0.5457	0.06	(-0.03,0.15)	0.2079	-0.01	(-0.11,0.09)	0.8010	
LYPLAL1	rs2605100	-0.01	(-0.05,0.04)	0.7606				0.06	(-0.03,0.15)	0.1656	
MAF	rs1424233	0.02	(-0.02,0.06)	0.4234	-0.02	(-0.10,0.06)	0.5713	-0.09	(-0.18,-0.01)	0.0305	
MAP2K5	rs2241423	0.00	(-0.05,0.05)	0.9674	0.04	(-0.03,0.12)	0.2820	0.11	(0.02, 0.19)	0.0123	
MC4R	rs12970134	0.03	(-0.02,0.07)	0.2686				0.14	(0.03, 0.24)	0.0123	
MC4R	rs571312	0.03	(-0.01,0.08)	0.1533				0.20	(0.09,0.31)	0.0006	
MSRA	rs545854	-0.02	(-0.08,0.03)	0.4261				-0.06	(-0.15,0.04)	0.2456	
MTCH2	rs3817334	0.01	(-0.03,0.05)	0.7510	0.04	(-0.04,0.12)	0.3213	-0.02	(-0.11,0.06)	0.6258	
MTIF3	rs4771122	0.04	(0.00, 0.09)	0.0794				-0.04	(-0.14,0.07)	0.5046	

Table S5. (continued)

			Height-for-age Z scores								
Nearby gene	SNP	Europe	European American		African	African American			Hispanic American		
		β	(95% CI)	р	β	(95% CI)	р	β	(95% CI)	р	
NCR3_BAT2	rs1077393	-0.08	(-0.12,-0.04)	0.00007	-0.03	(-0.10,0.05)	0.4733	-0.07	(-0.15,0.01)	0.0808	
NEGR1	rs2568958	0.02	(-0.02,0.06)	0.4016				-0.06	(-0.15,0.03)	0.2095	
NPC1	rs1805081	0.01	(-0.03,0.05)	0.5053				0.01	(-0.08,0.10)	0.8197	
NRXN3	rs10146997	0.02	(-0.02,0.07)	0.3155	-0.01	(-0.09,0.06)	0.7078	0.01	(-0.09,0.11)	0.8205	
NUDT3	rs206936	0.02	(-0.03,0.07)	0.3607	0.01	(-0.07,0.08)	0.8316	0.06	(-0.02,0.15)	0.1558	
POC5	rs2112347	0.01	(-0.04,0.05)	0.8007				-0.06	(-0.14,0.03)	0.2118	
POMC	rs713586	0.00	(-0.04,0.04)	0.9175	-0.01	(-0.11,0.09)	0.8284	0.00	(-0.08,0.09)	0.9557	
PRL	rs4712652	-0.07	(-0.11,-0.03)	0.0012	-0.03	(-0.10,0.05)	0.5199	0.01	(-0.07,0.10)	0.7501	
PTBP2	rs1555543	-0.01	(-0.05,0.03)	0.4687				-0.01	(-0.09,0.08)	0.8865	
PTER	rs10508503	-0.07	(-0.14,0.00)	0.0590	0.21	(-0.06,0.49)	0.1217				
QPCTL	rs2287019	-0.02	(-0.07,0.03)	0.4095				0.05	(-0.07,0.18)	0.3757	
RPL27A	rs4929949	0.03	(-0.01,0.06)	0.1927				-0.02	(-0.11,0.06)	0.5515	
SEC16BLZTR2	rs543874	0.03	(-0.02,0.08)	0.2482				0.00	(-0.10,0.10)	0.9993	
SH2B1	rs4788102	0.00	(-0.04,0.04)	0.9138	0.04	(-0.04,0.12)	0.3338				
SH2B1_APOB48	rs7359397	-0.01	(-0.05,0.03)	0.7390				-0.04	(-0.12,0.05)	0.3970	
SLC39A8	rs13107325	-0.08	(-0.15,0.00)	0.0380							
TFAP2B	rs987237	0.03	(-0.02,0.08)	0.2913				0.02	(-0.07,0.11)	0.7010	
TMEM160	rs3810291	-0.04	(-0.08,0.00)	0.0527	0.06	(-0.03,0.16)	0.1612	0.02	(-0.07,0.10)	0.6956	
TMEM18	rs6548238	0.07	(0.02,0.12)	0.0058							
TNNI3K	rs1514175	0.01	(-0.03,0.05)	0.7563				0.01	(-0.08,0.09)	0.8786	

Abbreviations: SNP, single nucleotide polymorphism, MVPA, moderate to vigorous physical activity, BMI, body mass index, CI confidence interval Sorted by nearby gene

<sup>&</sup>lt;sup>1</sup>Main effect model: Multivariable linear model of adolescent BMI regressed on SNP, controlling for age, sex, MVPA, current smoking, screen time, region, indicator for self-reported heights and weights, oversampling of highly educated African Americans (AA stratum only), Hispanic subpopulation ancestry, as well as an indicator for foreign born (n= 268, HA stratum only). Random

intercepts allowed for individual, family and school with no sample weighting. Models run separately for each SNP and race/ethnicity. P values corrected for multiple testing are  $\alpha$  equal to 0.05/number of SNPs tested (0.0012 in EA, 0.0026 in AA, 0.0014 in HA)  $^2$ Considered for interaction assessment 41 SNPs in EA, 37 in HA, and 19 in AA

Table S6. Genotype frequencies for the 3 adiposity related loci with observed nominally significant (p<0.05) interactions by MVPA and race/ethnicity

	Low MVPA (<5 bouts /wk)	High MVPA (5+ bouts/wk)	Total
	( 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	(= = = = = = = = = = = = = = = = = = =	
European American			
FTO (rs9939609)			
TT	661 (36.0)	1,190 (37.3)	1,851 (36.8)
AT	888 (48.4)	1,518 (47.5)	2,406 (47.8)
AA	286 (15.6)	486 (15.2)	772 (15.4)
Total, N	1,835	3,194	5,029
GNPDA2 (rs10938397)			
AA	583 (31.8)	1,031 (32.2)	1,614 (32.0)
AG	933 (50.8)	1,589 (49.6)	2,522 (50.1)
GG	320 (17.4)	581 (18.2)	901 (17.9)
Total, N	1,836	3,201	5,037
Hispanic American			
1.7TD2/05C46B (ro542974)			
<i>LZTR2/SEC16B</i> (rs543874) AA		E01 (GC 9)	970 (67.4)
, , ,	369 (68.3)	501 (66.8)	870 (67.4)
AG	149 (27.6)	221 (29.5)	370 (28.7)
GG	22 (4.1)	28 (3.7)	50 (3.9)
Total, N	540	750	1,290

Unless otherwise noted, No and column percentages presented 

1 Interaction model: Multivariable linear model of adolescent BMI regressed on SNP, MVPA, and SNP-by-MVPA interaction, controlling for age, sex, current smoking, screen time, region, indicator for self-reported heights and weights, oversampling of highly educated African Americans (AA stratum only), Hispanic subpopulation ancestry, as well as an indicator for foreign born (HA stratum only). Random effects allowed for individual, family and school with no sample weighting. Models were run separately for each SNP and race/ethnicity. Likelihood ratio tests were used to assess statistical interaction between the main effects (no interaction term) model and the interaction model, separately for each SNP by race/ethnicity. P values corrected for multiple testing are α equal to 0.05/number of SNPs tested (0.0012 in EA and 0.0014 in HA).

High MVPA: less than 5 bouts per week of MVPA, low MVPA: less than 5 bouts per week of MVPA

**Table S7.** Model results for the three nominally significant interactions (p<0.05)<sup>1</sup> between adiposity related loci by MVPA<sup>2</sup> in association with BMI-for-age Z scores in the overweight/obese<sup>3</sup> European Americans and Hispanic Americans

	β (95% CI)
European American	
FTO (rs9939609 per copy of A allele)	0.08 (0.02, 0.13)
MVPA (high versus low)	-0.11 (-0.19,02)
rs9939609 x MVPA	-0.05 (-0.12, 0.22)
p for interaction <sup>1</sup>	0.18
GNPDA2 (rs10938397 per copy of G allele)	0.07 (0.01, 0.12)
MVPA (high versus low)	-0.10 (-0.18, -0.02)
rs10938397 x MVPA	-0.05 (-0.12, -0.02)
p for interaction <sup>1</sup>	0.18
Hispanic American	
LZTR2/SEC16B (rs543874 per copy of G allele)	0.01 (-0.10, 0.12)
MVPA (high versus low)	0.01 (-0.10, 0.12)
rs5438749 x MVPA	0.00 (-0.16, -0.16)
p for interaction <sup>1</sup>	0.99

Abbreviations: SNP, single nucleotide polymorphism, BMI, body mass index, MVPA, moderate to vigorous physical activity, CI, confidence interval, EA, European Americans, HA, Hispanic Americans

<sup>&</sup>lt;sup>1</sup> Beta estimates are presented for the SNP, MVPA, SNP by MVPA interaction terms, and main effects in the interacted multivariable linear model of adolescent BMI-for-age Z scores regressed on SNP, MVPA, and SNP-by-MVPA interaction, controlling for age, sex, current smoking, screen time, region, indicator for self-reported heights and weights, oversampling of highly educated African Americans (AA stratum only), Hispanic subpopulation ancestry, as well as an indicator for foreign born (HA stratum only). Random effects allowed for individual, family and school with no sample weighting. Models were run separately for each SNP and race/ethnicity. Likelihood ratio tests were used to assess statistical interaction between the main effects (no interaction term) model and the interaction model, separately for each SNP by race/ethnicity. P values corrected for multiple testing are α equal to 0.05/number of SNPs tested (0.0012 in EA and 0.0014 in HA).

<sup>&</sup>lt;sup>2</sup> High MVPA: 5 or more bouts per week of MVPA, low MVPA: less than 5 bouts per week of MVPA

<sup>&</sup>lt;sup>3</sup> Overweight and obese defined by (BMI>=25 kg/m2; IOTF cut-off points)[33]. Sample sizes were in EA: 1,442 and in HA: 451.