

Supplementary Material

Variants Close to *NTRK2* Gene are Associated With Birth Weight in Female Twins

Sarah J. Metrustry, Mark H. Edwards, Sarah E. Medland, John W. Holloway, Grant W. Montgomery, Nicholas G. Martin, Tim D. Spector, Cyrus Cooper, and Ana M. Valdes

1. BMI and fat mass in twins

Since our significant SNPs are close to a gene previously associated with obesity, we tested these SNPs with fat mass, lean mass and percentage body fat.

Table S1. Association of fat mass, lean mass and percentage body fat with top SNPs in Twins

CHR	SNP	NEA	EA	Fat Mass		Percentage Body Fat	
				beta	p	beta	p
9	rs7849941	A	T	0.79	0.002	0.85	0.0004
9	rs12340987	A	G	0.57	0.04	0.52	0.05

2. Low birth weight twin and high birth weight twin

We ran two additional GWAS to test these variants- the first on the high birth weight twin only and the second on the low birth weight phenotypes. The results show that it is the low birth weight twin that is more associated with the SNPs identified.

Table S2. Association of the birth-weight of the lowest weight twin and the one with highest weight.

CHR	SNP	NEA	EA	Low Birth Weight Twin		High Birth Weight Twin	
				beta	p	beta	p
9	rs7849941	A	T	-0.13	9.65E-07	-0.10	5.66E-05
9	rs12340987	A	G	-0.14	9.54E-07	-0.06	0.02034

3. Monozygotic and dizygotic females in TwinsUK

Table S3. GWAS results for birth-weight in monozygotic and dizygotic twins

We also tested these two variants with monozygotic (identical) twins and again with non-identical (dizygotic) twins. The results show that it is the identical twin that is more associated with the SNPs identified.

SNP	only MZ			only DZ		
	BETA	SE	p	BETA	SE	P
rs12340987	-0.24	0.05	1.03E-05	-0.09	0.04	2.37E-02
rs7849941	-0.26	0.06	3.09E-06	-0.10	0.04	1.00E-02
rs7852361	-0.26	0.06	4.37E-06	-0.10	0.04	1.14E-02
rs7851300	-0.26	0.06	4.32E-06	-0.10	0.04	1.14E-02

4. Preliminary results: Association on raw birth-weight values

In our preliminary association based on birth-weight values in kg, these are the 4 SNPs that reached genome-wide significance. The analysis was then conducted using z-score values and these results are reported in the manuscript.

		BW: raw values	
SNP	EA	BETA	P
rs12340987	T	-0.11	1.01E-08
rs7849941	C	-0.10	2.01E-08
rs7852361	C	-0.10	4.28E-08
rs7851300	G	-0.10	3.33E-08

5. Comparing analyses with no covariates, adjusting for BMI and also adjusting for both BMI and age (results shown are for the Australian Twin cohort although TwinsUK exhibited comparable results).

		no covars	bmi adj	bmi + age adj
all twins	rs7849941	0.41	0.41	0.41
	rs12340987	0.30	0.30	0.30
mz only	rs7849941	0.67	0.67	0.67
	rs12340987	0.79	0.79	0.79
dz only	rs7849941	0.56	0.56	0.56
	rs12340987	0.36	0.36	0.36
dz-single sex	rs7849941	0.77	0.77	0.77
	rs12340987	0.51	0.50	0.50