**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*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  | Fat Mass  | Percentage Body Fat |
| CHR | SNP | NEA | EA | 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 |

1. **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.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  | Low Birth Weight Twin | High Birth Weight Twin |
| CHR | SNP | NEA | EA | 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 |

1. **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.

|  |  |  |
| --- | --- | --- |
|  | **only MZ** | **only DZ** |
| **SNP** | **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 |

1. ***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 |

1. ***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 |