**Supplemental Table 1**: DNA Methylation at LINE-1, *H19*, *HSD11B2* and *IGF2* among all individuals and stratified by sex (after imputation of missing values)1,2.

***Supplemental Table 1:*** Original to this manuscript.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Entire Cohort** | **Boys** | **Girls** | ***P* value3** |
|  | Mean % methylation (SD) | Mean % methylation (SD) | Mean % methylation (SD) |  |
| ***LINE-1* methylation** | N = 243 | N = 114 | N = 129 |  |
| Site 1 | 79.99 (4.11) | 80.56 (4.37) | 79.49 (3.80) | **0.033** |
| Site 2 | 81.92 (2.03) | 82.28 (2.17) | 81.61 (1.83) | **0.015** |
| Site 3 | 78.65 (3.00) | 79.35 (3.06) | 78.03 (2.80) | **<0.001** |
| Site 4 | 73.56 (2.17) | 73.99 (2.00) | 73.18 (2.25) | **0.006** |
|  |  |  |  |  |
| ***H19* methylation** | N= 243 | N= 114 | N=129 |  |
| Site 1 | 58.95 (8.38) | 58.22 (7.70) | 59.60 (8.90) | 0.148 |
| Site 2 | 58.20 (4.86) | 58.27 (3.27) | 58.14 (5.92) | 0.755 |
| Site 3 | 59.26 (3.74) | 59.06 (3.41) | 59.44 (4.00) | 0.443 |
| Site 4 | 56.58 (8.66) | 55.71 (7.76) | 57.35 (9.31) | 0.069 |
|  |  |  |  |  |
| ***HSD11B2* methylation** | N=243 | N=114 | N=129 |  |
| Site 1 | -1.56 (2.16) | -1.55 (2.38) | -1.57 (1.95) | 0.841 |
| Site 2 | 0.09 (0.93) | -0.02 (0.92) | 0.20 (0.93) | 0.087 |
| Site 3 | -2.21 (2.29) | -2.17 (2.37) | -2.25 (2.22) | 0.736 |
| Site 4 | -0.72 (1.77) | -0.66 (1.62) | -0.78 (1.89) | 0.636 |
| Site 5 | 0.18 (4.48) | 0.31 (4.25) | 0.07 (4.68) | 0.556 |
|  |  |  |  |  |
| ***IGF2* methylation** | N=243 | N=114 | N=129 |  |
| Site 1 | 34.91 (12.79) | 34.35 (13.04) | 35.42 (12.54) | 0.319 |
| Site 2 | 44.28 (15.42) | 42.59 (16.80) | 45.79 (13.93) | 0.065 |
| Site 3 | 53.56 (6.71) | 53.25 (7.49) | 53.83 (5.93) | 0.650 |
| Site 4 | 37.00 (4.75) | 36.31 (5.52) | 37.61 (3.86) | **0.006** |
| Site 5 | 53.02 (6.14) | 53.16 (6.60) | 52.90 (5.70) | 0.888 |

**1: Regression imputation method was applied.**

**2: LINE-1, *HSD11B2*, and *H19* data exhibited batch effects and as such were standardized to controls included on experimental plates as previously described (Goodrich et al., 2016), while the *IGF2* data exhibited no batch effect.**

**3: *P*-value of 2-sample t test comparing boys and girls.**

**Supplemental Table 2**: Associations between site-specific visit 1 (early-teen) DNA methylation and visit 1 (early-teen) as well as visit 2 (late-teen) pubertal onset, in adjusted Cox survival model1,2.

***Supplemental Table 2:*** Original to this manuscript.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Boys (N=114)** | | **Pubic Hair** | | **Genital Development** | | **Testicular Volume (L)** | | **Testicular Volume (R)** | |
|  |  | Hazard Ratio(CI) | | Hazard Ratio  (CI) | | Hazard Ratio  (CI) | | Hazard Ratio  (CI) | |
|  |  | Visit 1 | Visit 2 | Visit 1 | Visit2 | Visit 1 | Visit 2 | Visit 1 | Visit 2 |
|  | Site | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted |
| LINE1 | 1 | 0.95  (0.84, 1.08) | 1.03  (0.89, 1.03) | 0.97  (0.89, 1.05) | 1.00  (0.90, 1.03) | 1.01  (0.92, 1.10) | 1.01  (0.92, 1.10) | 0.99  (0.91, 1.08) | 1.03  (0.91, 1.08) |
| 2 | 0.81  (0.59, 1.11) | 0.96  (0.83, 1.10) | 0.88  (0.73, 1.07) | 0.96  (0.83, 1.08) | 1.05  (0.90, 1.22) | 1.08  (0.89, 1.21) | 1.03  (0.89, 1.19) | 1.07  (0.88, 1.18) |
| 3 | 0.93  (0.77, 1,12) | 0.97  (0.89, 1.10) | 0.97  (0.86, 1.10) | 0.95  (0.90, 1.08) | 1.04  (0.93, 1.15) | 1.10  (0.92, 1.14) | 1.02  (0.91, 1.13) | 1.08  (0.91, 1.11) |
| 4 | 1.02  (0.76, 1.37) | 1.02  (0.91, 1.31) | 0.92  (0.77, 1.10) | 1.00  (0.88, 1.15) | 1.04  (0.88, 1.22) | 1.01  (0.87, 1.18) | 1.06  (0.91, 1.23) | 1.03  (0.90, 1.19) |
| *H19* | 1 | 1.01  (0.93, 1.09) | 1.03  (0.99, 1.07) | 1.03  (0.99, 1.08) | 1.00  (0.97, 1.04) | 1.01  (0.96, 1.06) | 1.01  (0.97, 1.06) | 1.03  (0.98, 1.08) | 1.03  (0.98, 1.08) |
| 2 | **0.64**  **(0.43, 0.94)** | 0.96  (0.87, 1.05) | 0.93  (0.84, 1.03) | 0.96  (0.90, 1.03) | 1.08  (0.97, 1.21) | 1.08  (0.97, 1.20) | 1.07  (0.97, 1.18) | 1.07  (0.97, 1.18) |
| 3 | **0.74**  **(0.55, 0.99)** | 0.97  (0.88, 1.06) | 0.93  (0.84, 1.03) | 0.95  (0.89, 1.02) | 1.10  (0.98, 1.24) | 1.10  (0.98, 1.24) | 1.08  (0.97, 1.19) | 1.08  (0.98, 1.19) |
| 4 | 1.02  (0.94, 1.10) | 1.02  (0.98, 1.06) | 1.03  (0.98, 1.07) | 1.00  (0.97, 1.03) | 1.00  (0.96, 1.05) | 1.01  (0.97, 1.06) | 1.02  (0.98, 1.07) | 1.03  (0.98, 1.07) |
| *HSD11B2* | 1 | 0.85  (0.69, 1.03) | 0.89  (0.78, 1.02) | 0.89  (0.76, 1.04) | 0.97  (0.87, 1.08) | 1.01  (0.86, 1.19) | 1.00  (0.85, 1.18) | 0.98  (0.85, 1.14) | 0.97  (0.84, 1.13) |
| 2 | 1.07  (0.62, 1.85) | 0.96  (0.68, 1.34) | 0.96  (0.67, 1.37) | 1.09  (0.81, 1.46) | 0.66  (0.40, 1.08) | 0.66  (0.41, 1.06) | 0.67  (0.43, 1.06) | 0.67  (0.43, 1.04) |
| 3 | 0.86  (0.68, 1.08) | 0.95  (0.84, 1.06) | 0.93  (0.80, 1.08) | 0.90  (0.81, 1.01) | 1.01  (0.87, 1.16) | 1.00  (0.87, 1.15) | 0.99  (0.87, 1.13) | 0.98  (0.86, 1.13) |
| 4 | **1.60**  **(1.05, 2.44)** | **1.20**  **(1.01, 1.43)** | **1.67**  **(1.19, 2.33)** | 1.01  (0.88, 1.16) | 0.99  (0.78, 1.27) | 1.01  (0.78, 1.30) | 1.03  (0.83, 1.29) | 1.05  (0.84, 1.31) |
| 5 | 1.06  (0.91, 1.23) | 0.99  (0.92, 1.07) | 0.96  (0.89, 1.05) | 0.99  (0.93, 1.05) | 0.99  (0.91, 1.07) | 0.98  (0.90, 1.07) | 0.98  (0.90, 1.06) | 0.97  (0.90, 1.06) |
| *IGF2* | 1 | 1.01  (0.97, 1.05) | 1.00  (0.97, 1.03) | 0.99  (0.96, 1.01) | 0.99  (0.96, 1.01) | 1.01  (0.98, 1.04) | 1.01  (0.97, 1.04) | 1.01  (0.98, 1.04) | 1.01  (0.98, 1.04) |
| 2 | 1.01  (0.98, 1.05) | 1.01  (0.99, 1.03) | 1.02  (1.00, 1.05) | 1.01  (0.99, 1.03) | 1.01  (0.98, 1.03) | 1.01  (0.98, 1.03) | 1.00  (0.98, 1.02) | 1.00  (0.98, 1.02) |
| 3 | 0.95  (0.89, 1.01) | 0.96  (0.92, 1.01) | **0.93**  **(0.88, 0.99)** | **0.93**  **(0.89, 0.98)** | 1.03  (0.97, 1.10) | 1.03  (0.96, 1.10) | 1.01  (0.96, 1.07) | 1.01  (0.95, 1.07) |
| 4 | 0.95  (0.87, 1.03) | 1.00  (0.94, 1.07) | 0.95  (0.88, 1.02) | 0.97  (0.92, 1.03) | 1.05  (0.97, 1.13) | 1.04  (0.97, 1.11) | 1.04  (0.97, 1.11) | 1.03  (0.96, 1.10) |
| 5 | 0.99  (0.89, 1.10) | 1.02  (0.96, 1.08) | 0.98  (0.92, 1.05) | 0.99  (0.94, 1.03) | 1.07  (0.99, 1.15) | 1.06  (0.98, 1.14) | 1.05  (0.99, 1.11) | 1.05  (0.98, 1.11) |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Girls (N=129)** | | **Pubic Hair** | | **Breast Development** | | **Menarche (Y/N)** | | **Menarche Age** | |
|  |  | Hazard Ratio  (CI) | | Hazard Ratio  (CI) | | Hazard Ratio  (CI) | | Hazard Ratio  (CI) | |
|  | Site | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted | Adjusted |
| LINE1 | 1 | 0.96  (0.82, 1.12) | 1.00  (0.91, 1.09) | 0.99  (0.92, 1.06) | 0.96  (0.89, 1.05) | 0.97  (0.86, 1.09) | 0.96  (0.89, 1.04) | 0.97  (0.89, 1.07) | 0.97  (0.92, 1.03) |
|  | 2 | 1.05  (0.73, 1.50) | 0.95  (0.76, 1.20) | 0.92  (0.81, 1.04) | 0.88  (0.73, 1.06) | 0.81  (0.58, 1.14) | 0.89  (0.76, 1.05) | 0.88  (0.71, 1.10) | 0.97  (0.86, 1.10) |
|  | 3 | 1.07  (0.86, 1.34) | 0.95  (0.84, 1.08) | **0.89**  **(0.82, 0.97)** | 0.97  (0.87, 1.09) | 0.83  (0.67, 1.03) | 0.98  (0.89, 1.08) | 0.87  (0.72, 1.06) | 0.94  (0.92, 1.10) |
|  | 4 | 1.01  (0.78, 1.31) | 0.92  (0.79, 1.07) | **0.83**  **(0.75, 0.93)** | 0.88  (0.76, 1.02) | 0.85  (0.66, 1.09) | 0.88  (0.77, 1.01) | 0.89  (0.74, 1.06) | 1.01  (0.84, 1.04) |
| *H19* | 1 | 1.03  (0.95, 1.12) | 1.02  (0.98, 1.07) | **1.05**  **(1.02, 1.07)** | 1.02  (0.99, 1.06) | 0.99  (0.94, 1.06) | 1.02  (0.99, 1.06) | 1.01  (0.95, 1.06) | 1.01  (0.99, 1.04) |
|  | 2 | 1.21  (1.00, 1.47) | 1.02  (0.96, 1.07) | 1.02  (0.96, 1.09) | **0.93**  **(0.88, 0.99)** | 0.98  (0.88, 1.09) | 0.99  (0.94, 1.04) | 0.96  (0.85, 1.09) | 1.00  (0.96, 1.04) |
|  | 3 | **1.22**  **(1.01, 1.49)** | 1.07  (0.99, 1.17) | 1.06  (0.99, 1.13) | 0.99  (0.91, 1.07) | 0.99  (0.87, 1.13) | 1.01  (0.93, 1.10) | 0.97  (0.86, 1.09) | 1.01  (0.95, 1.08) |
|  | 4 | 1.03  (0.95, 1.13) | 1.03  (0.98, 1.08) | **1.05**  **(1.03, 1.08)** | 1.03  (0.99, 1.06) | 1.00  (0.94, 1.06) | 1.03  (1.00, 1.06) | 1.01  (0.95, 1.06) | 1.01  (0.99, 1.04) |
| *HSD11B2* | 1 | 0.98  (0.79, 1.22) | 0.97  (0.84, 1.11) | **0.80**  **(0.71, 0.91)** | 0.86  (0.72, 1.02) | 0.93  (0.76, 1.14) | 0.95  (0.80, 1.12) | 0.92  (0.77, 1.10) | 0.98  (0.88, 1.09) |
|  | 2 | 0.87  (0.56, 1.34) | 0.89  (0.58, 1.36) | 0.91  (0.75, 1.11) | 0.88  (0.66, 1.18) | 0.88  (0.58, 1.32) | 0.73  (0.50, 1.08) | 0.93  (0.66, 1.32) | 0.84  (0.63, 1.11) |
|  | 3 | 1.07  (0.87, 1.33) | 1.04  (0.90, 1.20) | **0.87**  **(0.77, 0.98)** | 0.92  (0.79, 1.07) | 0.89  (0.72, 1.11) | 0.91  (0.79, 1.06) | 0.91  (0.77, 1.08) | 0.96  (0.87, 1.06) |
|  | 4 | 1.32  (0.91, 1.90) | 1.06  (0.93, 1.20) | **1.25**  **(1.13, 1.38)** | 1.08  (0.95, 1.24) | 1.18  (0.87, 1.60) | 0.93  (0.76, 1.13) | 1.21  (0.94, 1.57) | 0.90  (0.76, 1.07) |
|  | 5 | 0.97  (0.87, 1.09) | 0.95  (0.87, 1.04) | 0.96  (0.91, 1.01) | 0.99  (0.93, 1.05) | 0.96  (0.87, 1.06) | 0.97  (0.92, 1.03) | 0.99  (0.91, 1.07) | 1.01  (0.96, 1.05) |
| *IGF2* | 1 | 0.99  (0.95, 1.04) | 1.00  (0.97, 1.02) | 1.00  (0.98, 1.02) | 1.00  (0.98, 1.03) | 1.03  (0.99, 1.08) | 1.01  (0.99, 1.03) | 1.02  (0.99, 1.05) | 1.01  (0.99, 1.02) |
|  | 2 | 1.02  (0.98, 1.06) | 1.00  (0.98, 1.03) | 1.01  (1.00, 1.03) | 1.01  (0.99, 1.04) | 0.99  (0.96, 1.03) | 0.99  (0.97, 1.01) | 1.00  (0.97, 1.03) | 0.99  (0.98, 1.01) |
|  | 3 | 0.96  (0.88, 1.04) | 0.98  (0.90, 1.07) | 1.00  (0.95, 1.05) | 0.97  (0.91, 1.04) | **1.12**  **(1.02, 1.22)** | 0.99  (0.94, 1.04) | 1.03  (0.98, 1.09) | 0.98  (0.94, 1.01) |
|  | 4 | 0.99  (0.89, 1.10) | 1.00  (0.93, 1.08) | 0.97  (0.91, 1.04) | 0.94  (0.86, 1.03) | 1.08  (0.95, 1.23) | 0.94  (0.87, 1.03) | 1.03  (0.93, 1.15) | 1.00  (0.93, 1.06) |
|  | 5 | 1.05  (0.94, 1.17) | **1.07**  **(1.01, 1.14)** | 1.01  (0.96, 1.07) | 1.02  (0.96, 1.09) | 1.12  (1.00, 1.26) | 1.00  (0.95, 1.06) | 1.02  (0.96, 1.09) | 0.99  (0.95, 1.03) |

**1: Adjusted for age, BMI and SES status at visit 1 (early-teen).**

**2: Bolded value indicates the association is significant with a *P* value < 0.05.**

**Supplemental Table 3**: Associations between site-specific visit 1 (early-teen) DNA methylation and pubertal progression from visit 1 (early-teen) to visit 2 (late-teen), in adjusted multivariate regression model1,2,3. Odds Ratios are shown from adjusted models for the main effect of DNA methylation along with the interaction between DNA methylation and time between visits.

***Supplemental Table 3:*** Original to this manuscript.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Boys (N=114)** | | **Pubic Hair** | | **Genital Development** | | **Testicular Volume (L)** | | **Testicular Volume (R)** | |
|  |  | Odds Ratio (CI) | | Odds Ratio (CI) | | Odds Ratio (CI) | | Odds Ratio (CI) | |
|  | Site | Main Effect | Site by Time | Main Effect | Site by Time | Main Effect | Site by Time | Main Effect | Site by Time |
| LINE1 | 1 | 1.03  (0.76, 1.39) | 0.97  (0.89, 1.06) | 1.01  (0.86, 1.20) | 0.97  (0.93, 1.01) | 1.05  (0.82, 1.36) | 0.96  (0.89, 1.05) | 1.10  (0.83, 1.47) | 0.94  (0.87, 1.03) |
| 2 | 1.00  (0.52, 1.93) | 0.97  (0.79, 1.19) | 0.96  (0.70, 1.31) | 0.99  (0.92, 1.07) | 1.12  (0.67, 1.87) | 0.94  (0.79, 1.11) | 1.22  (0.66, 2.24) | 0.90  (0.76, 1.08) |
| 3 | 1.03  (0.64, 1.66) | 0.98  (0.85, 1.12) | 0.99  (0.80, 1.22) | 1.00  (0.95, 1.06) | 1.05  (0.71, 1.54) | 0.95  (0.86, 1.06) | 1.11  (0.73, 1.67) | 0.94  (0.84, 1.04) |
| 4 | 1.09  (0.38, 3.12) | 0.98  (0.73, 1.33) | 0.90  (0.63, 1.27) | 1.04  (0.96, 1.14) | 1.11  (0.59, 2.08) | 0.96  (0.81, 1.13) | 1.18  (0.64, 2.16) | 0.97  (0.82, 1.13) |
| *H19* | 1 | 0.99  (0.80, 1.23) | 1.02  (0.96, 1.08) | 1.04  (0.95, 1.14) | 0.99  (0.98, 1.01) | 1.00  (0.85, 1.16) | 1.01  (0.97, 1.05) | 1.00  (0.87, 0.97) | 1.01  (0.97, 1.04) |
| 2 | 0.82  (0.31, 2.14) | 1.06  (0.82, 1.37) | 0.92  (0.73, 1.14) | 1.05  (0.99, 1.12) | 1.07  (0.74, 1.54) | 0.99  (0.89, 1.09) | 1.05  (0.77, 1.43) | 0.98  (0.90, 1.07) |
| 3 | 0.86  (0.36, 2.10) | 1.06  (0.83, 1.35) | 0.95  (0.77, 1.16) | 1.02  (0.97, 1.06) | 1.09  (0.74, 1.61) | 0.98  (0.89, 1.09) | 1.07  (0.77, 1.48) | 0.98  (0.90, 1.07) |
| 4 | 1.00  (0.79, 1.25) | 1.01  (0.95, 1.08) | 1.04  (0.95, 1.13) | 0.99  (0.97, 1.01) | 1.01  (0.87, 1.17) | 1.01  (0.97, 1.05) | 1.01  (0.88, 1.15) | 1.01  (0.97, 1.04) |
| *HSD11B2* | 1 | 0.84  (0.42, 1.68) | 1.04  (0.90, 1.20) | 0.77  (0.53, 1.12) | **1.12**  **(1.01, 1.24)** | 0.94  (0.60, 1.50) | 1.03  (0.92, 1.15) | 0.96  (0.64, 1.45) | 1.03  (0.93, 1.14) |
| 2 | 0.94  (0.25, 3.46) | 1.00  (0.73, 1.37) | 0.70  (0.33, 1.50) | 1.16  (0.94, 1.42) | 0.52  (0.09, 2.97) | 1.41  (0.87, 2.28) | 0.63  (0.17, 2.33) | 1.39  (0.99, 1.95) |
| 3 | 0.87  (0.41, 1.87) | 1.03  (0.88, 1.21) | 0.82  (0.53, 1.25) | 1.07  (0.96, 1.19) | 0.96  (0.61, 1.52) | 0.99  (0.91, 1.08) | 0.98  (0.65, 1.48) | 1.00  (0.91, 1.09) |
| 4 | 1.36  (0.47, 3.96) | 0.97  (0.76, 1.23) | 1.59  (0.92, 2.74) | **0.83**  **(0.72, 0.97)** | 1.08  (0.49, 2.40) | 1.01  (0.85, 1.19) | 1.14  (0.55, 2.38) | 1.00  (0.85, 1.18) |
| 5 | 1.03  (0.74, 1.43) | 0.99  (0.91, 1.07) | 0.97  (0.83, 1.14) | 1.01  (0.97, 1.05) | 1.00  (0.78, 1.29) | 0.94  (0.85, 1.04) | 0.97  (0.78, 1.22) | 0.96  (0.89, 1.04) |
| *IGF2* | 1 | 1.00  (0.90, 1.10) | 1.01  (0.98, 1.03) | 0.99  (0.94, 1.04) | 1.01  (1.00, 1.02) | 0.98  (0.90, 1.07) | 1.01  (0.99, 1.03) | 1.00  (0.92, 1.09) | 1.00  (0.98, 1.02) |
| 2 | 1.00  (0.92, 1.10) | 1.00  (0.97, 1.02) | 1.01  (0.97, 1.06) | 0.99  (0.98, 1.01) | 1.02  (0.95, 1.10) | 1.00  (0.98, 1.02) | 1.01  (0.94, 1.08) | 1.00  (0.98, 1.02) |
| 3 | 0.94  (0.79, 1.13) | 1.02  (0.98, 1.07) | 0.94  (0.85, 1.04) | 1.02  (0.99, 1.04) | 0.96  (0.82, 1.12) | 1.01  (0.98, 1.05) | 0.97  (0.85, 1.12) | 1.02  (0.98, 1.06) |
| 4 | 0.95  (0.78, 1.15) | 1.02  (0.98, 1.06) | 0.93  (0.82, 1.05) | **1.04**  **(1.00, 1.07)** | 1.04  (0.85, 1.27) | 1.01  (0.96, 1.06) | 1.04  (0.87, 1.25) | 1.01  (0.96, 1.06) |
| 5 | 0.96  (0.80, 1.15) | 1.03  (0.99, 1.07) | 1.00  (0.90, 1.11) | 1.01  (0.98, 1.03) | 1.03  (0.86, 1.22) | 1.00  (0.95, 1.04) | 1.01  (0.86, 1.18) | 0.99  (0.94, 1.04) |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Girls (N=129)** | | **Pubic Hair** | | **Breast Development** | | **Menarche (Y/N)** | |  | |
|  |  | Odds Ratio (CI) | | Odds Ratio (CI) | | Odds Ratio (CI) | |
|  | Site | Main effect | Site by Time | Main effect | Site by Time | Main effect | Site by Time |  | |
| LINE1 | 1 | 1.00  (0.73, 1.38) | 1.01  (0.94, 1.08) | 0.96  (0.76, 1.22) | 0.97  (0.91, 1.03) | 1.06  (0.75, 1.51) | 0.98  (0.89, 1.08) |
|  | 2 | 1.03  (0.44, 2.41) | 1.01  (0.82, 1.24) | 0.93  (0.57, 1.50) | 0.94  (0.83, 1.06) | 1.19  (0.49, 2.90) | 0.99  (0.78, 1.26) |
|  | 3 | 1.04  (0.48, 2.25) | 1.00  (0.82, 1.22) | 0.95  (0.69, 1.30) | 0.95  (0.87, 1.04) | 1.17  (0.71, 1.94) | 1.06  (0.92, 1.22) |
|  | 4 | 1.06  (0.41, 2.71) | 1.02  (0.79, 1.32) | 0.93  (0.63, 1.38) | 0.97  (0.89, 1.06) | 1.20  (0.59, 2.42) | 1.03  (0.81, 1.31) |
| *H19* | 1 | 1.03  (0.86, 1.23) | 1.01  (0.97, 1.05) | 1.01  (0.90, 1.13) | 1.01  (0.98, 1.04) | 0.98  (0.82, 1.16) | 1.01  (0.94, 1.07) |
|  | 2 | 1.08  (0.64, 1.82) | 1.03  (0.90, 1.20) | 0.94  (0.81, 1.09) | 0.98  (0.94, 1.02) | 1.01  (0.76, 1.34) | 1.00  (0.93, 1.08) |
|  | 3 | 1.11  (0.64, 1.93) | 1.04  (0.90, 1.20) | 0.95  (0.69, 1.31) | 0.98  (0.90, 1.07) | 0.99  (0.66, 1.48) | 0.99  (0.89, 1.11) |
|  | 4 | 1.02  (0.84, 1.24) | 1.00  (0.96, 1.05) | 1.01  (0.91, 1.12) | 1.01  (0.99, 1.03) | 0.98  (0.82, 1.16) | 1.01  (0.94, 1.07) |
| *HSD11B2* | 1 | 0.92  (0.46, 1.85) | 0.95  (0.80, 1.13) | 0.93  (0.60, 1.43) | 0.95  (0.86, 1.06) | 1.17  (0.64, 2.14) | 1.09  (0.92, 1.30) |
|  | 2 | 0.74  (0.24, 2.25) | 0.99  (0.78, 1.26) | 0.77  (0.32, 1.86) | 0.93  (0.76, 1.15) | 1.29  (0.38, 4.46) | 1.02  (0.62, 1.65) |
|  | 3 | 1.00  (0.44, 2.27) | 1.02  (0.80, 1.29) | 0.91  (0.62, 1.32) | 0.99  (0.90, 1.08) | 1.21  (0.65, 2.24) | 1.04  (0.84, 1.30) |
|  | 4 | 1.24  (0.63, 2.47) | 1.13  (0.93, 1.37) | 1.24  (0.80, 1.93) | 1.15  (0.97, 1.37) | 0.82  (0.42, 1.64) | 0.86  (0.74, 1.00) |
|  | 5 | 0.97  (0.74, 1.27) | 1.02  (0.96, 1.08) | 0.98  (0.82, 1.17) | 1.01  (0.97, 1.04) | 1.05  (0.80, 1.39) | 1.02  (0.95, 1.10) |
| *IGF2* | 1 | 0.99  (0.89, 1.10) | 1.00  (0.97, 1.02) | 0.99  (0.92, 1.07) | 1.00  (0.98, 1.02) | 0.95  (0.84, 1.06) | 0.98  (0.95, 1.02) |
|  | 2 | 1.02  (0.92, 1.13) | 1.01  (0.98, 1.03) | 1.02  (0.96, 1.08) | 1.00  (0.99, 1.01) | 1.01  (0.92, 1.11) | 0.99  (0.96, 1.02) |
|  | 3 | 0.97  (0.80, 1.17) | 1.00  (0.96, 1.04) | 1.01  (0.87, 1.17) | 1.00  (0.97, 1.03) | 0.89  (0.69, 1.16) | 0.93  (0.84, 1.04) |
|  | 4 | 1.01  (0.72, 1.41) | 1.02  (0.93, 1.12) | 0.87  (0.65, 1.18) | 0.98  (0.91, 1.06) | 0.90  (0.65, 1.25) | 0.95  (0.84, 1.07) |
|  | 5 | 1.04  (0.84, 1.29) | 1.01  (0.97, 1.06) | 0.99  (0.86, 1.16) | 1.00  (0.96, 1.03) | 0.87  (0.62, 1.23) | 0.96  (0.88, 1.04) |

**1: Adjusted for age, BMI and SES status at visit 1 (early-teen).**

**2: Bolded value indicates the association is significant with a *P* value < 0.05.**

**3: Model: logit (Y ij) = β0 + β1\*age + β2\*time\_difference + β3\*CpG\_Site + β4\*CpG\_Site\*time\_difference +β5\*age\*time\_difference**

**Supplemental Table 4:** Pyrosequencing assays with primer sequences and details of CpG sites assessed.

**Supplemental Table 4:** Original to this manuscript.



|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **‡Loci are based off of genome build GRCh38/hg38** |  |  |  |  |  |  |
| **†All reverse primers for pyrosequencing are 5'biotinylated. Sequenom primers contain required tag (in lowercase).** | | |  |  |  |  |
| **\*A sequence in the promoter region of nearly all LINE-1s (located throughout the genome) is amplified and sequenced here.**  **The specific sequence, with CpG sites in bold, is as follows: 5'-CTCGTGGTGCGCCGTTTCTTAAGCCG** | | | | | |  |
| **#Due to the resolution capabilities of the EpiTYPER mass spectrometry method, data represent 5 units of methylation that consist of either 1 CpG site or**  **the average of 2 CpG sites. In the loci column, CpG sites that are grouped together are designated with '&'.** | | | | | | |