**Supplementary material**

**Association of exposure to prenatal perﬂuoroalkyl substances and estrogen receptor 1 polymorphisms with the second to fourth digit ratio in school-aged children: the Hokkaido Study**

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**Supplemental Table S1.** Concentrations of maternal plasma PFAS (ng/mL) in the third trimester of pregnancy.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Detection limit (MDL) | *n* (>MDL) | Detection rate (%) | Median | IQR (25th–75th) |
| PFHxS | 0.15 | 846 | 82.6  | 0.31 | 0.25–0.42 |
| PFHxA | 0.10 | 360 | 35.2 | < MDL | < MDL–0.12 |
| PFHpA | 0.10 | 331 | 32.3  | < MDL | < MDL–0.11 |
| PFOS | 0.30 | 1,024 | 100.0  | 6.06 | 4.55–7.91 |
| PFOA | 0.13 | 1,023 | 99.9  | 1.98 | 1.36–2.88 |
| PFNA | 0.31 | 1,021 | 99.7  | 1.06 | 0.82–1.39 |
| PFDA | 0.10 | 1,010 | 98.6  | 0.50 | 0.35–0.65 |
| PFUnDA | 0.11 | 963 | 94.0  | 1.36 | 0.87–1.88 |
| PFDoDA | 0.10 | 903 | 88.2 | 0.17 | 0.1–0.23 |
| PFTrDA | 0.10 | 988 | 96.5 | 0.33 | 0.25–0.46 |
| PFTeDA | 0.10 | 87 | 8.50  | < MDL | < MDL – < MDL |

IQR: Interquartile range.

**Supplemental Table S2.** Characteristics of participants with complete data and children with available 2D:4D data.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Current participants (*n* = 1,024) | Children with 2D:4D data (*n* = 1,899)\* | *p*a |
| **Maternal characteristics** | 31.1 ± 4.2 | 31.2± 4.3 | 0.355 |
| Age at delivery (y) | 20.9 ± 3.2 | 21.0 ± 3.0 | 0.239 |
| Prepregnancy body mass index (kg/m2) |  |  |  |
| Parity |  |  |  |
| Primiparous | 477 (46.6) | 838 (44.1) | <0.001 |
| Multiparous | 542 (52.9) | 993 (52.3) |  |
| Missing data | 5 (0.5) | 68 (3.6) |  |
|  |  |  |  |
| Annual household income (million yen per year) |  |  |  |
| < 5 | 554 (54.1) | 1,016 (53.5) | 0.073 |
| ≥ 5 | 353 (34.5) | 621 (32.7) |  |
| Missing data | 117 (11.4) | 262 (13.8) |  |
|  |  |  |  |
| Education level (y) |  |  |  |
| < 12 | 397 (38.8) | 717 (37.8) | <0.001 |
| ≥ 13 | 620 (60.5) | 1,116 (58.8) |  |
| Missing data | 7 (0.7) | 66 (3.4) |  |
|  |  |  |  |
| Smoking in the first trimester |  |  |  |
| Non−smoker | 576 (56.3) | 1,038 (55.0) | 0.510 |
| Smoker | 228 (22.3) | 416 (22.0) |  |
| Missing data | 220 (21.5) | 445 (23.0) |  |
|  |  |  |  |
| Alcohol consumption in the first trimester |  |  |  |
| Non−drinker | 841 (82.1) | 1,526 (80.0) | <0.001  |
| Drinker | 169 (16.5) | 298 (16.0) |  |
| Missing data | 14 (1.4) | 75 (4.0) |  |
|  |  |  |  |
| **Characteristics of children** |  |  |  |
| Sex |  |  |  |
| Male | 513 (50.1) | 981 (51.7) | 0.305 |
| Female | 511 (49.9) | 918 (48.3) |  |
| Birth weight (g) | 3,059 ± 365 | 3,043 ± 382 | 0.153 |
| Gestational age (wks) | 38.3 ± 2.5 | 38.8 ± 1.4 | 0.705 |
| Mean 2D:4D | 93.9 | 93.9 | 0.711 |

*n* (%) or mean ± SD.

\* Because 20 of the 1,919 participants withdrew from the cohort and their questionnaires were not available, the results of 1,899 participants are shown in the table.

a One sample *t* test.

**Supplemental Table S3.** Maternal plasma PFAS concentration and *ESR1* polymorphisms.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | rs2234693 (T>C) |  |  |  | rs9340799 (A>G) |  |  |  | rs2077647 (A>G) |  |
|  | Genotype  | Median (IQR) | *p* |  | Genotype  | Median (IQR) | *p* |  | Genotype  | Median (IQR) | *p* |
| PFHxS  | TT  | 0.33 (0.26–0.42) | 0.106 |  | AA  | 0.34 (0.27–0.45) | 0.581 |  | AA  | 0.34 (0.26–0.42) | 0.108 |
|  | TC/CC  | 0.34 (0.27–0.45) |  |  | AG/GG  | 0.34 (0.26–0.44) |  |  | AG/GG  | 0.34 (0.27–0.45) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| PFOS | TT  | 6.10 (4.67–7.87) | 0.324 |  | AA | 6.08 (4.58–7.84) | 0.609 |  | AA | 6.21 (4.67–7.84) | 0.222 |
|  | TC/CC  | 6.01 (4.53–7.96) |  |  | AG/GG | 6.03 (4.51–8.18) |  |  | AG/GG | 6.00 (4.51–8.02) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| PFOA | TT | 1.96 (1.35–2.84) | 0.646 |  | AA | 1.98 (1.36–2.88) | 0.992 |  | AA | 1.96 (1.35–2.88) | 0.830 |
|  | TC/CC | 2.00 (1.36–2.90) |  |  | AG/GG | 1.99 (1.35–2.90) |  |  | AG/GG | 1.99 (1.36–2.88) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| PFNA | TT | 1.06 (0.81–1.37) | 0.746 |  | AA | 1.05 (0.81–1.37) | 0.490 |  | AA | 1.06 (0.81–1.37) | 0.653 |
|  | TC/CC | 1.06 (0.82–1.40) |  |  | AG/GG | 1.06 (0.85–1.41) |  |  | AG/GG | 1.06 (0.82–1.40) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| PFDA | TT | 0.49 (0.36–0.66) | 0.504 |  | AA | 0.49 (0.35–0.66) | 0.370 |  | AA | 0.49 (0.35–0.66) | 0.559 |
|  | TC/CC | 0.50 (0.36–0.66) |  |  | AG/GG | 0.50 (0.37–0.66) |  |  | AG/GG | 0.50 (0.35–0.66) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| PFUnDA | TT | 1.41 (1.02–1.84) | 0.996 |  | AA | 1.41 (0.94–1.90) | 0.316 |  | AA | 1.44 (1.06–1.89) | 0.551 |
|  | TC/CC | 1.43 (0.95–1.97) |  |  | AG/GG | 1.44 (0.14–0.23) |  |  | AG/GG | 1.42 (0.93–1.96) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| PFDoDA | TT | 0.18 (0.14–0.24) | 0.769 |  | AA | 0.18 (0.14–0.23) | 0.468 |  | AA | 0.18 (0.14–0.23) | 0.855 |
|  | TC/CC | 0.18 (0.14–0.24) |  |  | AG/GG | 0.18 (0.14–0.25) |  |  | AG/GG | 0.18 (0.14–0.24) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| PFTrDA | TT | 0.34 (0.27–0.44) | 0.943 |  | AA | 0.34 (0.25–0.46) | 0.193 |  | AA | 0.35 (0.27–0.45) | 0.768 |
|  | TC/CC | 0.35 (0.25–0.48) |  |  | AG/GG | 0.35 (0.27–0.48) |  |  | AG/GG | 0.34 (0.25–0.48) |  |
|  |  |  |  |  |  |  |  |  |  |  |  |

Analysis performed using Mann–Whitney *U* tests.

IQR, interquartile range.

**Supplemental Table S4.** Association between *ESR1* polymorphism (dominant model) and 2D:4D.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Genotype model | All a |  | Male b |  | Female b |
| β (95% CI) |  | β (95% CI) |  | β (95% CI) |
| rs2234693 | TT | Reference |  | Reference |  | Reference |
|  | TC/CC | 0.00 (−0.23, 0.24) |  | −0.01 (−0.33, 0.31) |  | 0.01 (−0.34, 0.36) |
|  |  |  |  |  |  |  |
| rs9340799 | AA | Reference |  | Reference |  | Reference |
|  | AG/GG | 0.01 (−0.22, 0.25) |  | −0.03 (−0.35, 0.29) |  | 0.05 (−0.29, 0.40) |
|  |  |  |  |  |  |  |
| rs2077647 | AA | Reference |  | Reference |  | Reference |
|  | AG/GG | −0.02 (−0.25, 0.21) |  | 0.06 (−0.26, 0.38) |  | −0.09 (−0.43, 0.25) |

a Multiple linear regression adjusted for sex, birth weight, maternal age, parity, alcohol consumption, and smoking in the first trimester.

b Multiple linear regression adjusted for birth weight, maternal age, parity, alcohol consumption, and smoking in the first trimester

β (95% CI) represents the percentage change in 2D:4D compared with children in the reference group.

**Supplemental Table S5.** Gene-environment interactions between PFAS and *ESR1* polymorphisms on 2D:4D in all participants.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| rs2234693 |  | rs9340799 |  | rs2077647 |
|  | β (95% CI) |  |  | β (95% CI) |  |  | β (95% CI) |
| PFHxS (ng/mL) | 0.42 (−0.37, 1.22) |  | PFHxS (ng/mL) | 0.37 (−0.44, 1.18) |  | PFHxS (ng/mL) | 0.44 (−0.36, 1.23) |
| rs2234693-TT | 0.00 (−0.23, 0.24) |  | rs9340799−AA | −0.01 (−0.25, 0.22) |  | rs2077647-AA | 0.02 (−0.21, 0.26) |
| PFHxS × rs2234693-TT | 0.06 (−0.72, 0.85) |  | PFHxS × rs9340799-AA | 0.08 (−0.72, 0.88) |  | PFHxS × rs2077647-AA | 0.09 (−0.70, 0.88) |
|  | *Pint* = 0.876 |  |  | *Pint* = 0.853 |  |  | *Pint* = 0.817 |
|  |  |  |  |  |  |  |  |
| PFOS (ng/mL) | 0.63 (−0.65, 1.91) |  | PFOS (ng/mL) | 0.63 (−0.63, 1.89) |  | PFOS (ng/mL) | 0.93 (−0.32, 2.18) |
| rs2234693-TT | −0.00 (−0.23, 0.23) |  | rs9340799-AA  | −0.01 (−0.25, 0.22) |  | rs2077647-AA  | 0.01 (−0.22, 0.25) |
| PFOS × rs2234693-TT | −0.38 (−1.64, 0.87) |  | PFOS ×rs9340799-AA  | 0.46 (−0.77, 1.68) |  | PFOS ×rs2077647-AA  | 0.50 (−0.73, 1.72) |
|  | *Pint* = 0.550 |  |  | *Pint* = 0.466 |  |  | *Pint* = 0.426 |
|  |  |  |  |  |  |  |  |
| PFNA (ng/mL) | 0.51 (−0.77, 1.78) |  | PFNA (ng/mL) | −0.28 (−1.56, 1.0) |  | PFNA (ng/mL) | 0.67 (−059, 1.96) |
| rs2234693-TT | 0.00 (−0.23, 0.24) |  | rs9340799-AA | −0.02 (−0.25, 0.22) |  | rs2077647-AA | 0.03 (−0.21, 0.26) |
| PFNA × rs2234693-TT | 0.55 (−0.68, 1.79) |  | PFNA ×rs9340799-AA  | 1.55 (0.31, 2.79)\* |  | PFNA ×rs2077647-AA  | 1.05 (−0.18, 2.28) |
|  | *Pint* = 0.381 |  |  | *Pint* = 0.015 |  |  | *Pint* = 0.095 |
|  |  |  |  |  |  |  |  |
| PFDA (ng/mL) | −0.11 (−1.07, 0.86) |  | PFDA (ng/mL) | −0.40 (−1.36, 0.56) |  | PFDA (ng/mL) | 0.04 (−0.92, 0.99) |
| rs2234693-TT | −0.00 (−0.24, 0.23) |  | rs9340799-AA | −0.01 (−0.25, 0.22) |  | rs2077647-AA | 0.02 (−0.21, 0.25) |
| PFDA × rs2234693-TT | 0.13 (−0.83, 1.09) |  | PFDA ×rs9340799-AA  | 0.87 (−0.08, 1.82) |  | PFDA ×rs2077647-AA  | 0.64 (−0.31, 1.59) |
|  | *Pint* = 0.788 |  |  | *Pint* = 0.071 |  |  | *Pint* = 0.184 |
|  |  |  |  |  |  |  |  |
| PFUnDA (ng/mL) | 0.37 (−0.23, 0.98) |  | PFUnDA (ng/mL) | 0.25 (−0.30, 0.80) |  | PFUnDA (ng/mL) | 0.45 (−0.14, 1.04) |
| rs2234693-TT | −0.01 (−0.25, 0.22) |  | rs9340799-AA | −0.01 (−0.25, 0.22) |  | rs2077647AA | 0.08 (−0.23, 0.24) |
| PFUnDA × rs2234693-TT | 0.08 (−0.52, 0.69) |  | PFUnDA ×rs9340799-AA | 0.30 (−0.25, 0.85) |  | PFUnDA ×rs2077647-AA | 0.28 (−0.30, 0.87) |
|  | *Pint* = 0.791 |  |  | *Pint* = 0.280 |  |  | *Pint* = 0.340 |
|  |  |  |  |  |  |  |  |
| PFTrDA (ng/mL) | 0.13 (−0.23, 0.24) |  | PFTrDA (ng/mL) | 0.43 (−0.51, 1.38) |  | PFTrDA (ng/mL) | 0.37 (−0.63, 1.37) |
| rs2234693-TT | −0.00 (−0.24, 0.23) |  | rs9340799-AA | −0.01 (−0.24, 0.23) |  | rs2077647-AA | 0.02 (−0.22, 0.25) |
| PFUnDA × rs2234693-TT | −0.70 (−1.70, 0.30) |  | PFUnDA ×rs9340799-AA | 0.01 (−0.92, 0.95) |  | PFUnDA ×rs2077647-AA | −0.16 (−1.16, 0.83) |
|  | *Pint* = 0.171 |  |  | *Pint* = 0.976 |  |  | *Pint* = 0.750 |

Multiple linear regression adjusted for sex, birth weight, maternal age, parity, alcohol consumption, and smoking in the first trimester.

Because PFAS levels were log10-transformed, β (95% CI) represents the expected percentage change in 2D:4D as a result of a 10-fold change in PFAS levels.

\* *p* < 0.05.

**Supplemental Table S6.** Associations between PFAS and 2D:4D in all participants stratified by *ESR1* polymorphisms.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Genotype |  | PFHxS |  | PFOS |  | PFNA |  | PFDA |  | PFUnDA |  | PFTrDA |
|  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |
| rs2234693 | TT | 0.31 (−1.00, 1.63) |  | −0.26 (−2.41, 1.88) |  | 0.52 (−1.60, 0.98) |  | 0.02 (−1.54, 1.57) |  | 0.56 (−0.48, 1.60) |  | −0.41 (−2.15, 1.32) |
|  | TC/CC | 0.49 (−0.42, 1.41) |  | 1.27 (−0.17, 2.70) |  | −0.19 (−1.33, 0.95) |  | −0.19 (−1.33, 0.95) |  | 0.25 (−0.38, 0.43) |  | 0.78 (−0.29, 1.85) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs9340799 | AA | 0.39 (−0.53, 1.30) |  | 1.01 (−0.48, 2.50) |  | 1.21 (−0.26, 2.67) |  | 0.49 (−0.68, 1.66) |  | 0.59 (−0.09, 1.28) |  | 0.51 (−0.65, 1.67) |
|  | AG/GG | 0.45 (−0.88, 1.77) |  | 0.49 (−1.52, 2.51) |  | −1.78 (−3.85, 0.30) |  | −1.23 (−2.73, 0.27) |  | −0.12 (−0.98, 0.73) |  | 0.34 (−1.12, 1.80) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs2077647 | AA | 0.44 (−0.94, 1.83) |  | 1.24 (−0.89, 3.36) |  | 1.55 (−0.68, 3.77) |  | 0.73 (−0.86, 2.33) |  | 0.83 (−0.20, 1.86) |  | 0.49 (−1.30, 2.28) |
|  | AG/GG | 0.41 (−0.49, 1.31) |  | 0.55 (−0.90, 1.99) |  | −0.29 (−1.71, 1.13) |  | −0.61 (−1.74, 0.52) |  | 0.14 (−0.49, 0.76) |  | 0.50 (−0.56, 1.55) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

Multiple linear regression adjusted for sex, birth weight, maternal age, parity, alcohol consumption, and smoking in the first trimester.

Because PFAS levels were log10-transformed, β (95% CI) represents the expected percentage change in 2D:4D in each *ESR1* genotype as a result of a 10-fold change in PFAS levels.

**Supplemental Table S7.** Association between PFAS concentrations and 2D:4D.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | All a |  | Male b |  | Female b |
|  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |
| PFHxS | -0.36 (-0.89, 1.24) |  | -0.23 (-1.78., 1.32) |  | 0.48 (-1.02, 1.98) |
|  |  |  |  |  |  |
| PFOS | 0.76 (-1.00, 2.51) |  | 0.48 (-1.97, 2.93) |  | 1.02 (-1.50, 3.55) |
|  |  |  |  |  |  |
| PFOA | 1.06 (-0.34, 2.45) |  | 1.90 (-0.14, 3.95) |  | 0.41 (-1.54, 2.35) |
|  |  |  |  |  |  |
| PFNA | 1.03 (-0.62, 2.69) |  | 0.77 (-1.68, 3.22) |  | 1.45 (-0.84, 3.75) |
|  |  |  |  |  |  |
| PFDA | -0.18 (-1.48, 1.13) |  | -0.59 (-2.36, 1.19) |  | 0.29 (-1.70, 2.28) |
|  |  |  |  |  |  |
| PFUnDA | 0.18 (-0.53, 0.89) |  | 0.32 (-0.63, 1.26) |  | 0.10 (-0.98, 1.18) |
|  |  |  |  |  |  |
| PFDoDA | 0.55 (-0.37, 1.47) |  | 0.07 (-2.01, 2.15) |  | 1.16 (-0.74, 3.07) |
|  |  |  |  |  |  |
| PFTrDA | 0.37 (-0.86, 1.60) |  | 0.83 (-0.98, 2.64) |  | 0.20 (-1.54, 1.94) |
|  |  |  |  |  |  |

a Multiple linear regression adjusted for sex, birth weight, maternal age, parity, MEHP, alcohol consumption, and smoking in the first trimester.

b Multiple linear regression adjusted for birth weight, maternal age, parity, MEHP, alcohol consumption, and smoking in the first trimester.

Because the PFAS levels were log10-transformed, β (95% CI) represents the expected percentage change in 2D:4D as a result of a 10-fold change in the PFAS levels.

**Supplemental Table S8.** Gene-environment interactions between PFAS and *ESR1* polymorphisms on 2D:4D.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | All a |  | Male b |  | Female b |
|  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |
| PFOA (ng/mL) | 1.01 (-0.53, 2.54) |  | 2.48 (-0.09, 5.05) |  | 0.27 (−1.87, 2.41) |
| rs2234693-TT | -0.09 (−0.45, 0.26) |  | −0.25 (−0.78, 0.29) |  | -0.06 (−0.57, 0.45) |
| PFOA × rs2234693-TT | -0.04 (−1.48, 1.41) |  | 0.79 (−1.66, 3.23) |  | -0.25 (−2.23, 1.74) |
|  | *Pint* = 0.960 |  | *Pint*= 0.528 |  | *Pint*= 0.808 |
|  |  |  |  |  |  |
| PFOA (ng/mL) | 0.84 (−0.58, 2.27) |  | 1.76 (−0.29, 3.80) |  | 0.31 (−1.75, 2.36) |
| rs9340799-AA | −0.11 (−0.44, 0.23) |  | -0.22 (−0.68, 0.24) |  | −0.01 (−0.51, 0.49) |
| PFOA × rs9340799-AA | 0.93 (-0.40, 2.26) |  | 1.60 (−0.31, 3.51) |  | 0.32 (−1.65, 2.29) |
|  | *Pint*= 0.172 |  | *Pint* = 0.099 |  | *Pint* = 0.747 |
|  |  |  |  |  |  |
| PFOA (ng/mL) | 1.29 (-0.20, 2.77) |  | 2.55 (0.27, 4.84)\* |  | 0.64 (−1.47. 2.74) |
| rs2077647-AA | -0.02 (−0.37, 0.33) |  | −0.24 (−0.75, 0.26) |  | 0.09 (−0.42, 0.60) |
| PFOA × rs2077647-AA | 0.66 (-0.74, 2.06) |  | 1.25 (-0.90, 3.41) |  | 0.51 (−-1.47, 2.49) |
|  | *Pint* = 0.352 |  | *Pint* = 0.252 |  | *Pint*= 0.612 |
|  |  |  |  |  |  |
| PFDoDA (ng/mL) | 0.80 (−0.66, 2.26) |  | 0.43 (−1.94, 2.79) |  | 1.19 (−0.77, 3.15) |
| rs2234693-TT | -0.10 (−0.45, 0.25) |  | -0.18 (−0.71, 0.36) |  | −0.03 (−0.52, 0.46) |
| PFDoDA × rs2234693-TT | 0.65 (−0.81, 2.11) |  | 0.76 (−1.59, 3.12) |  | 0.27 (−1.71, 2.24) |
|  | *Pint*= 0.383 |  | *Pint* = 0.524 |  | *Pint*= 0.789 |
|  |  |  |  |  |  |
| PFDoDA (ng/mL) | 0.21 (−1.26, 1.67) |  | −0.17 (−2.32, 1.97) |  | 0.79 (−1.32, 2.90) |
| rs9340799-AA | −0.12 (−0.45, 0.22)  |  | -0.22 (−0.69, 0.25) |  | 0.00 (−0.50, 0.50) |
| PFDoA × 9340799-AA | 1.22 (−0.24, 2.68) |  | 1.09 (−1.04, 3.22) |  | 0.95 (−1.18, 3.07) |
|  | *Pint* = 0.102 |  | *Pint*= 0.314 |  | *Pint*= 0.381 |
|  |  |  |  |  |  |
| PFDoDA (ng/mL) | 0.84 (−0.61, 2.30) |  | 0.60 (−1.67, 2.86) |  | 1.25 (−0.73, 3.23) |
| rs2077647-AA | -0.03 (−0.38, 0.32) |  | −0.19 (−0.70, 0.32) |  | 0.10 (−0.40, 0.60) |
| PFDoDA × rs2077647-AA | 0.79 (−0.67, 2.25) |  | 1.38 (-0.88, 3.64)  |  | 0.12 (−1.87, 2.12) |
|  | *Pint*= 0.290 |  | *Pint*= 0.230 |  | *Pint* = 0.902 |

a Multiple linear regression adjusted for sex, birth weight, maternal age, parity, MEHP, alcohol consumption, and smoking in the first trimester.

b Multiple linear regression adjusted for birth weight, maternal age, parity, MEHP, alcohol consumption, and smoking in the first trimester.

Because the PFAS levels were log10-transformed, β (95% CI) represents the expected percentage change in 2D:4D as a result of a 10-fold change in PFAS levels.

\* *p* < 0.05.

**Supplemental Table S9.** Association between PFAS and 2D:4D stratified by *ESR1* polymorphisms.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Exposure |  | Genotype model | Alla |  | Maleb |  | Femaleb |
|  | β (95% CI) |  | β (95% CI) |  | β (95% CI) |
| PFOA | rs2234693 | TT | 0.65 (-2.16, 3.46) |  | 4.06 (-1.40, 9.53) |  | -0.58 (-4.07, 2.90) |
|  |  | TC/CC | 1.20 (-0.49, 2.89) |  | 1.78 (-0.51, 4.07) |  | 0.48 (-2.11, 3.07) |
|  |  |  |  |  |  |  |  |
|  | rs9340799 | AA | 1.72 (-0.05, 3.49) |  | 3.21 (0.53, 5.90) \* |  | 0.54 (-1.88, 2.96) |
|  |  | AG/GG | -0.11 (-2.50, 2.22) |  | 0.59 (-3.00, 4.19) |  | -0.78 (-4.46, 2.89) |
|  |  |  |  |  |  |  |  |
|  | rs2077647 | AA | 2.12 (-0.55, 4.80) |  | 4.52 (0.05, 9.01) \* |  | 0.60 (-2.97, 4.18) |
|  |  | AG/GG | 0.68 (-1.04, 2.40) |  | 1.16 (-1.24, 3.56) |  | 0.13 (-2.43, 2.68) |
|  |  |  |  |  |  |  |  |
| PFDoDA | rs2234693 | TT | 1.47 (-0.86, 3.80) |  | 1.45 (-3.13, 6.03) |  | 1.39 (-1.44, 4.23) |
|  |  | TC/CC | 0,.25 (-1.50, 2.01) |  | -0.41 (-2.84, 2.03) |  | 0.79 (-1.89, 3.47) |
|  |  |  |  |  |  |  |  |
|  | rs9340799 | AA | 1.39 (-0.29, 3.06) |  | 0.90 (-1.72, 3.52) |  | 1.69 (-0.55, 3.93) |
|  |  | AG/GG | -1.15 (-3.74, 1.44) |  | -1.47 (-5.23, 2.28) |  | -1.17 (-5.22, 2.88) |
|  |  |  |  |  |  |  |  |
|  | rs2077647 | AA | 1.81 (-0.57, 4.20) |  | 2.44 (-1.85, 6.73) |  | 1.53 (-1.53, 4.59) |
|  |  | AG/GG | 0.11 (-1.64, 1.87) |  | -0.86 (-3.35, 1.63) |  | 1.08 (-1.52, 3.69) |
|  |  |  |  |  |  |  |  |

a Multiple linear regression adjusted for sex, birth weight, maternal age, parity, MEHP, alcohol consumption, and smoking in the first trimester.

b Multiple linear regression adjusted for birth weight, maternal age, parity, MEHP, alcohol consumption, and smoking in the first trimester.

Because the PFAS levels were log10-transformed, β (95% CI) represents the expected percentage change in 2D:4D as a result of a 10-fold change in PFAS levels.

\* *p* < 0.05.