Table 1: Description of the overall study population, and stratified by time point.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Overall**, N = 283*1* | **A**, N = 140*1* | **B**, N = 143*1* |
| Cohort |  |  |  |
| BIB | 54 (19%) | 27 (19%) | 27 (19%) |
| EDEN | 46 (16%) | 23 (16%) | 23 (16%) |
| KANC | 53 (19%) | 27 (19%) | 26 (18%) |
| RHEA | 58 (20%) | 29 (21%) | 29 (20%) |
| SAB | 72 (25%) | 34 (24%) | 38 (27%) |
| Sex |  |  |  |
| female | 121 (43%) | 60 (43%) | 61 (43%) |
| male | 162 (57%) | 80 (57%) | 82 (57%) |
| Age | 7.36 (6.72, 9.18) | 6.97 (6.44, 8.85) | 7.55 (6.93, 9.62) |
| Ethnicity |  |  |  |
| Caucasian | 261 (92%) | 129 (92%) | 132 (92%) |
| Other | 2 (0.7%) | 1 (0.7%) | 1 (0.7%) |
| Pakistani | 20 (7.1%) | 10 (7.1%) | 10 (7.0%) |
| zBMI | 0.26 (-0.34, 1.09) | 0.28 (-0.34, 1.09) | 0.26 (-0.34, 1.09) |
| hs\_dift\_mealblood\_imp | 2.97 (2.12, 3.75) | 3.25 (2.83, 4.09) | 2.17 (1.63, 3.17) |
| Season |  |  |  |
| autumn | 73 (26%) | 35 (25%) | 38 (27%) |
| spring | 99 (35%) | 50 (36%) | 49 (34%) |
| summer | 28 (9.9%) | 20 (14%) | 8 (5.6%) |
| winter | 83 (29%) | 35 (25%) | 48 (34%) |
| *1*n (%); Median (IQR) | | | |

Table 2: Edge- (top) and node- (bottom) level description of the time-specific networks.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | A | | | B | | |
| **Characteristic** | **Group** | **N** | **N = 4,083***1* | **Group** | **N** | **N = 4,908***1* |
| sign | Edges | 4,083 |  | Edges | 4,908 |  |
| -1 | Edges |  | 1,547 (38%) | Edges |  | 1,956 (40%) |
| 1 | Edges |  | 2,536 (62%) | Edges |  | 2,952 (60%) |
| pcor | Edges | 4,083 | 0.05 (-0.06, 0.06) | Edges | 4,908 | 0.05 (-0.05, 0.06) |
| qval | Edges | 4,083 | 0.024 (0.006, 0.051) | Edges | 4,908 | 0.023 (0.005, 0.048) |
| layer | Nodes | 516 |  | Nodes | 514 |  |
| exposure | Nodes |  | 22 (4.3%) | Nodes |  | 22 (4.3%) |
| methylome | Nodes |  | 237 (46%) | Nodes |  | 238 (46%) |
| serum metabolome | Nodes |  | 177 (34%) | Nodes |  | 174 (34%) |
| urinary metabolome | Nodes |  | 44 (8.5%) | Nodes |  | 44 (8.6%) |
| proteome | Nodes |  | 36 (7.0%) | Nodes |  | 36 (7.0%) |
| degree | Nodes | 516 | 16 (7, 24) | Nodes | 514 | 21 (8, 28) |
| *1*n (%); Median (IQR) | | | | | | |

Table 3: Table listing the number and proportion of the edge types for the merged and time-specific networks. Reported is also the average percent change, defined as the ratio between the number of edges in the merged network and the average number of edges in the time-specific networks.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| layer node x | layer node y | n | p | n A | p A | n B | p B | average change (%) |
| exposure | exposure | 38 | 4 | 64 | 2 | 63 | 1 | 59.8 |
| exposure | serum metabolite | 3 | 0 | 35 | 1 | 72 | 1 | 5.6 |
| exposure | urinary metabolite | 6 | 1 | 58 | 1 | 87 | 2 | 8.3 |
| exposure | protein | 3 | 0 | 33 | 1 | 37 | 1 | 8.6 |
| methylome | exposure | 11 | 1 | 197 | 5 | 254 | 5 | 4.9 |
| methylome | methylome | 329 | 35 | 1416 | 35 | 1735 | 35 | 20.9 |
| methylome | serum metabolite | 40 | 4 | 420 | 10 | 612 | 12 | 7.8 |
| methylome | urinary metabolite | 33 | 3 | 495 | 12 | 599 | 12 | 6.0 |
| methylome | protein | 14 | 1 | 285 | 7 | 277 | 6 | 5.0 |
| serum metabolite | serum metabolite | 360 | 38 | 522 | 13 | 579 | 12 | 65.4 |
| serum metabolite | urinary metabolite | 10 | 1 | 133 | 3 | 166 | 3 | 6.7 |
| urinary metabolite | urinary metabolite | 41 | 4 | 158 | 4 | 154 | 3 | 26.3 |
| protein | serum metabolite | 5 | 1 | 74 | 2 | 90 | 2 | 6.1 |
| protein | urinary metabolite | 1 | 0 | 86 | 2 | 84 | 2 | 1.2 |
| protein | protein | 56 | 6 | 107 | 3 | 99 | 2 | 54.4 |

Table 4: Table listing the five strongest mixed associations in magnitude for the time-specific networks.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| node x | layer x | degree x | node y | layer y | degree y | pcor | qval | visit |
| BPA | exposure | 24 | FGFBasic | proteome | 20 | -0.156 | 0 | A |
| Trimethylamine oxide | urinary metabolome | 30 | OXOMINP | exposure | 21 | -0.108 | 0 | A |
| MBZP | exposure | 38 | BAFF | proteome | 18 | -0.100 | 0 | A |
| MCP1 | proteome | 29 | MBZP | exposure | 38 | 0.100 | 0 | A |
| cg00766289 | methylome | 25 | MEP | exposure | 30 | -0.094 | 0 | A |
| cg08158662 | methylome | 32 | MEP | exposure | 32 | -0.109 | 0 | B |
| cg22507960 | methylome | 17 | BPA | exposure | 31 | -0.099 | 0 | B |
| cg18628367 | methylome | 20 | DETP | exposure | 38 | -0.096 | 0 | B |
| MBZP | exposure | 39 | Acetate | urinary metabolome | 27 | 0.093 | 0 | B |
| DETP | exposure | 38 | cg26767081 | methylome | 32 | 0.092 | 0 | B |

Table 5: Edge- (top) and node- (bottom) level description of the merged network.

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **N** | **N = 950***1* |
| Edges | | |
| sign | 950 |  |
| -1 |  | 182 (19%) |
| 1 |  | 768 (81%) |
| pcor A | 950 | 0.06 (0.05, 0.08) |
| qval A | 950 | 0.009 (0.001, 0.032) |
| pcor B | 950 | 0.06 (0.05, 0.08) |
| qval B | 950 | 0.007 (0.000, 0.030) |
| Nodes | | |
| layer | 462 |  |
| exposure |  | 22 (4.8%) |
| methylome |  | 193 (42%) |
| serum metabolome |  | 169 (37%) |
| urinary metabolome |  | 42 (9.1%) |
| proteome |  | 36 (7.8%) |
| degree | 462 | 4.00 (2.00, 6.00) |
| *1*n (%); Median (IQR) | | |

Table 6: Network-level properties of the merged and time-specific networks.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| network | number of nodes | number of edges | diameter | edge density |
| merged | 462 | 950 | 19 | 0.01 |
| A | 516 | 4083 | 7 | 0.03 |
| B | 514 | 4908 | 7 | 0.04 |

Table 7: Table listing the mixed edges in the merged network, by chemical class and omic layer. Reported are the time-specific partial correlations and q-values. In the case of CpG sites, the mapped genes are also reported.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| chemical class | chemical | omic layer | omic feature | pcor A | pcor B | qval A | qval B | genes |
| OP pesticide metabolite | DEP | Methylome | cg21873275 | 0.076 | 0.053 | 0.001 | 0.047 | - |
|  |  | Proteome | GCSF | 0.084 | 0.080 | 0.000 | 0.000 |  |
|  |  | Serum metabolome | Serotonin | 0.051 | 0.053 | 0.074 | 0.050 |  |
|  |  | Urinary metabolome | N-methylpicolinic acid | 0.062 | 0.083 | 0.017 | 0.000 |  |
| Phenol | ETPA | Methylome | cg04320635 | -0.052 | -0.056 | 0.069 | 0.030 | GSE1;RP11-118F19.1 |
|  |  |  | cg14242246 | 0.060 | 0.056 | 0.021 | 0.033 | C2orf28;SLC5A6 |
|  |  |  | cg24891846 | 0.063 | 0.050 | 0.014 | 0.066 | CACNA1A |
|  | BUPA | Methylome | cg03060555 | 0.069 | 0.082 | 0.005 | 0.000 | ZBTB38 |
|  |  |  | cg04320635 | -0.052 | -0.066 | 0.069 | 0.006 | GSE1;RP11-118F19.1 |
|  |  |  | cg20320656 | 0.063 | 0.052 | 0.015 | 0.054 | LETMD1 |
|  | OXBE | Methylome | cg27466129 | -0.089 | -0.051 | 0.000 | 0.062 | KIAA0513 |
|  |  | Urinary metabolome | Dimethylamine | -0.071 | -0.074 | 0.003 | 0.001 |  |
|  | TRCS | Methylome | cg10072921 | 0.072 | 0.089 | 0.003 | 0.000 | - |
|  |  | Methylome | cg25408086 | 0.065 | 0.054 | 0.010 | 0.039 | CCNT1 |
|  |  | Proteome | Leptin | -0.072 | -0.059 | 0.003 | 0.020 |  |
|  |  | Serum metabolome | Serotonin | -0.055 | -0.054 | 0.049 | 0.042 |  |
| Phthalate metabolite | MBZP | Proteome | EGF | 0.062 | 0.058 | 0.016 | 0.022 |  |
|  |  | Urinary metabolome | N-acetyl neuraminic acid | 0.072 | 0.057 | 0.003 | 0.024 |  |
|  | MEHP | Methylome | cg20080548 | -0.057 | -0.066 | 0.037 | 0.007 | SBSN |
|  |  | Urinary metabolome | Acetate | -0.063 | -0.057 | 0.013 | 0.028 |  |
|  | OHMINP | Serum metabolome | Kynurenine | -0.051 | -0.060 | 0.074 | 0.016 |  |
|  | OXOMINP | Urinary metabolome | 5-oxoproline | 0.060 | 0.056 | 0.023 | 0.031 |  |
|  | MIBP | Urinary metabolome | Scyllo-inositol | -0.051 | -0.077 | 0.081 | 0.001 |  |