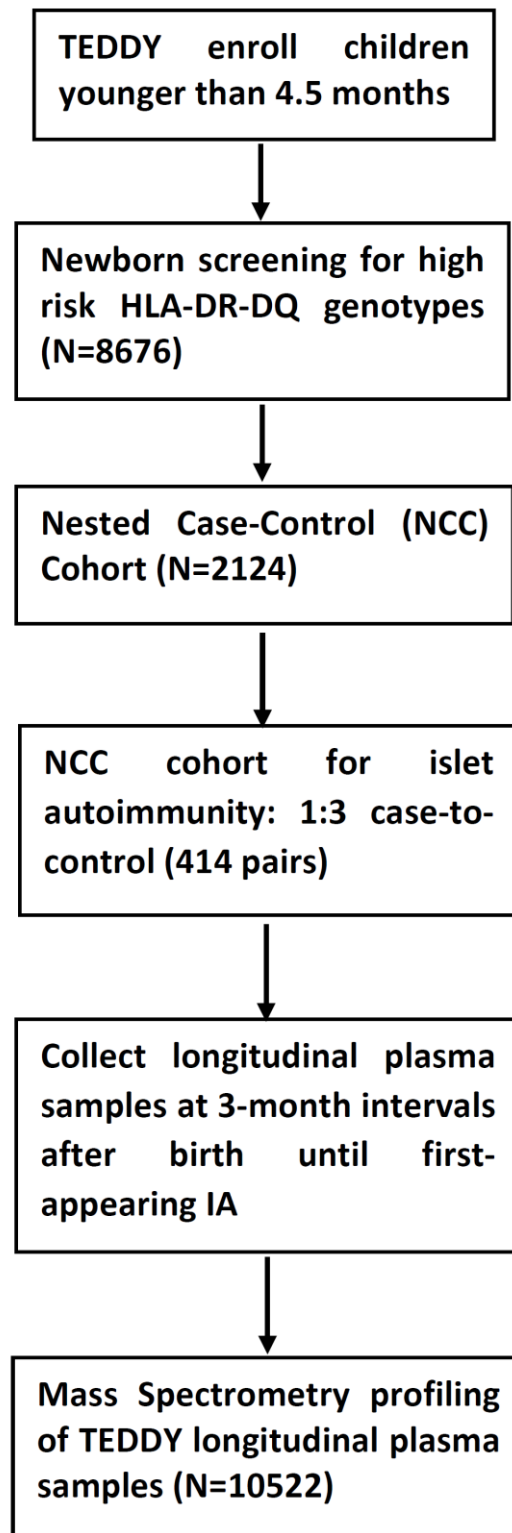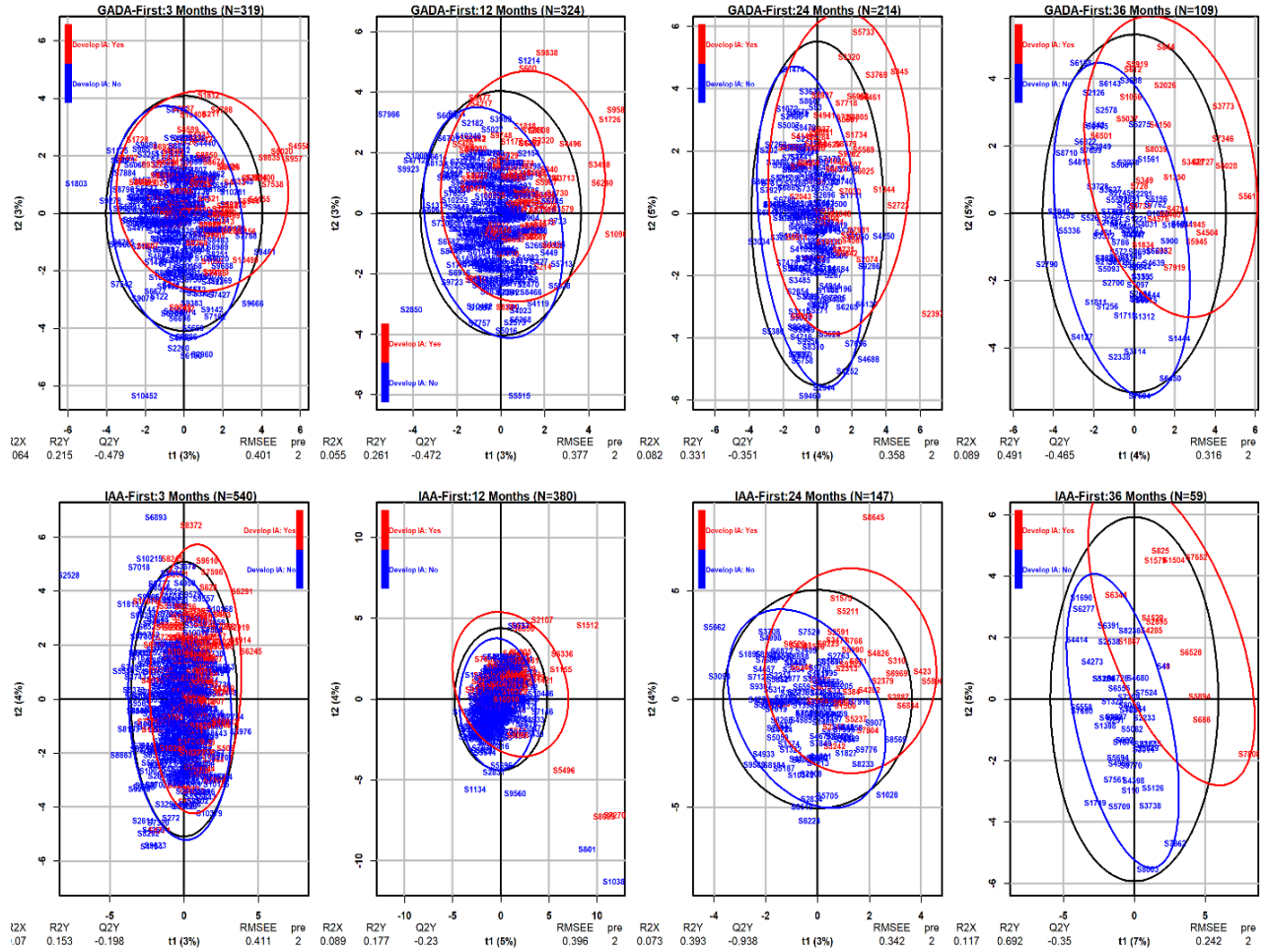SUPPLEMENTARY DATA

**Supplementary Figure 1.** Flowchart for plasma metabolome profiling in the first nested case-control cohort of islet autoimmunity in TEDDY.

```
┌─────────────────────────────┐
│ TEDDY enroll children       │
│ younger than 4.5 months     │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ Newborn screening for high  │
│ risk HLA-DR-DQ genotypes    │
│ (N=8676)                    │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ Nested Case-Control (NCC)   │
│ Cohort (N=2124)             │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ NCC cohort for islet        │
│ autoimmunity: 1:3 case-to-  │
│ control (414 pairs)         │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ Collect longitudinal plasma │
│ samples at 3-month intervals│
│ after birth until first-    │
│ appearing IA                │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ Mass Spectrometry profiling │
│ of TEDDY longitudinal plasma│
│ samples (N=10522)           │
└─────────────────────────────┘
```

SUPPLEMENTARY DATA

**Supplementary Figure 2.** Principal components plot by Partial Least Square Regression with Discriminant Analysis for samples without or prior to seroconversion at 3, 12, 24, 36-month visits, individually. Samples in red are cases developing islet autoimmunity after that visit, while samples in blue are controls matched to the cases.

**Supplementary Figure 3.** Mean abundance of gamma-aminobutyric acid, glutamic acid, glutamine, alpha-ketoglutarate, leucine, and Plasmenyl-PC (ether PC) per time point before seroconversion for cases and controls in GADA-First and IAA-First. Time points are the months to seroconversion within 1 year prior IA.