Plasma metabolome and circulating vitamins stratified onset age of an initial islet autoantibody and progression to type 1 diabetes: the TEDDY study

Short title: Metabolic and vitamins signatures for islet autoimmunity characteristics

Qian Li[1*], Xiang Liu[1*], Jimin Yang[1], Iris Erlund[2], Åke Lernmark[3], William Hagopian[4], Marian Rewers[5], Jin-Xiong She[6], Jorma Toppari[7,8], Anette-G. Ziegler[9,10,11], Beena Akolkar[12], Jeffrey P. Krischer[1], and the TEDDY Study Group[+]

Affiliations

[1]Health Informatics Institute, University of South Florida, Tampa, FL, USA.

[2]Department of Government Services, Finnish Institute for Health and Welfare, Helsinki, Finland

[3]Department of Clinical Sciences, Clinical Research Centre, Skåne University Hospital, Lund University, Malmo, Sweden

[4]Pacific Northwest Research Institute, Seattle, Washington, USA

[5]Barbara Davis Center for Childhood Diabetes, University of Colorado Denver, Aurora, Colorado, USA

[6]Center for Biotechnology and Genomic Medicine, Medical College of Georgia, Augusta University, Augusta, Georgia, USA

[7]Department of Pediatrics, Turku University Hospital, Turku, Finland.

[8]Department of Physiology, University of Turku, Turku, Finland.

[9]Institute of Diabetes Research, Helmholtz Zentrum München, Munich, Germany

[10]Forschergruppe Diabetes, Technical University of Munich, Klinikum Rechts der Isar, Munich, Germany

[11]Forschergruppe Diabetes e.V. at Helmholtz Zentrum München, Munich, Germany

Diabetes Publish Ahead of Print, published online October 26, 2020

[12]National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland

* These authors contributed equally.

[+] A complete list of the TEDDY Study Group can be found in Acknowledgements.

Corresponding Author: Qian Li, Ph.D.
Email: Qian.Li@epi.usf.edu
Telephone: 813-396-9638
Fax: 813-396-9601

ABSTRACT

Children's plasma metabolome, especially lipidome reflects gene regulation and dietary exposures, heralding the development of islet autoantibodies (IA) and type 1 diabetes (T1D). The TEDDY study enrolled 8676 newborns by screening HLA-DR-DQ genotypes at six clinical centers in four countries; profiled metabolome and measured concentrations of ascorbic acid, 25-hydroxyvitamin D (25(OH)D), erythrocyte membrane fatty acids following birth until IA seroconversion under nested case-control design. We grouped children having an initial autoantibody only against insulin (IAA-first) or glutamic acid decarboxylase (GADA-first) by unsupervised clustering of temporal lipidome, identifying a subgroup of children having early onset of each initial autoantibody, i.e., IAA-first by 12 months and GADA-first by 21 months, consistent with population-wide early seroconversion age. Differential analysis showed that infants having reduced plasma ascorbic acid and cholesterol experienced IAA-first earlier, while early onset of GADA-first was preceded by reduced sphingomyelins at infancy. Plasma 25(OH)D prior to either autoantibody was lower in T1D progressors compared to non-progressors, with simultaneous lower diglycerides, lysophosphatidylcholines, triglycerides, alanine before GADA-first. Plasma ascorbic acid and 25(OH)D at infancy were lower in HLA-DR3/DR4 children among IA cases but not in matched controls, implying gene expression dysregulation of circulating vitamins as latent signals for IA or T1D progression.

Type 1 diabetes (T1D) is an autoimmune disease developing in young children due to the interaction between genetic risks and environmental exposures, with appearance of beta cell autoantibodies or islet autoantibodies (IA) as the established precursors. The population-wide early onset of distinct initial autoantibodies had been reported at different ages throughout early childhood, i.e. an autoantibody against insulin (IAA-first) by age of 15 months and an autoantibody against glutamic acid decarboxylase (GADA-first) before 24 months (1). Distinct type or onset age of an initial autoantibody can be a result of either genetic variation or immune response to early environmental exposures.

IAA-first was found related to HLA DR4-DQ8 and the *INS* gene polymorphism, while GADA-first was related to HLA DR3-DQ2 polymorphisms in the *ERBB3*, *SH2B3* and *BACH2* gene polymorphisms (2). Age of IA seroconversion was recently found associated with afterwards progression to T1D (3), regardless of the type of initial autoantibodies. Furthermore, nutrients or dietary pattern had been found as one of the critical exposure-related factors predictive of IA or T1D in early childhood (4; 5). Recent studies in T1D have reported the impact of diet or blood concentrations of nutrient biomarkers on disease outcomes, such as infant formula type (6), gluten intake amount (7), vitamin C (ascorbic acid) (8), vitamin D (9), probiotics (10) and omega-3 fatty acids (11-13). The aforementioned results had not reported potential etiology, causes or molecular signatures for the population-wide skewed seroconversion age of either autoantibody, which might be also predictive of further progression to T1D.

The exposures to ascorbic acid, vitamin D and fatty acids can be assessed either at the intake level using dietary assessment tools or at biomarker level quantified by immunoassay platforms (14) and chromatographic methods (15; 16). These micronutrients and fatty acids are usually considered positively associated with the actual intake amount, as well as regulated by protein-coding genes and metabolic pathways, such as vitamin C transport genes *SLC23A1*, *SLC2A1*, *SLC2A2*, and 25-hydroxyvitamin D (or 25(OH)D) receptor genes *VDR, RXRA*. A secondary set of biomarkers for nutrient sources is the lipidome profiled from plasma or serum, which is related to both nutrients or energy sources and metabolic activity. As structural components of cell membranes, complex lipids are involved in a variety of metabolic pathways (17) and play an important role in children's growth and disease development. Previous studies had found that heterogeneity of lipidome profiles signaled the underlying development of or recovery from diseases (18-20). Therefore, children's lipidome reflect metabolism of nutrients, as a link between gene regulation of nutrient biomarkers and characteristics related to primary endpoints, i.e. IA or T1D.

Previous studies in type 1 diabetes rarely integrated dietary biomarkers and lipidome profiles due to either limited blood samples or cohort size (5; 11; 19). The Environmental Determinants of Diabetes in the Young (TEDDY) study measured concentrations of dietary biomarkers in plasma or on red blood cell membrane for the enrolled participants by immunoassay and chromatographic methods, as well as profiled untargeted plasma metabolome by mass spectrometry platforms (21). In the present study, we hypothesized that plasma ascorbic acid, 25(OH)D and erythrocyte omega-3 fatty acids, i.e., alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), docosapentaenoic acid (DPA) are nutrients (or biomarkers) interacting with lipidome followed by the development of IA and progression to T1D.

Our present analyses were performed on GADA-first and IAA-first children and their matched controls. We first adopted an unsupervised clustering approach to group GADA-first and IAA-first children based on their temporal lipidomic profiles at and prior to seroconversion, and further identified nutritional and metabolic signatures for IA-related outcomes, as well as assessed the association of HLA-DR-DQ haplotypes or genotypes with the identified signatures.

Methods

TEDDY nested case-control study

TEDDY is an observational prospective study of children at increased genetic risk of type 1 diabetes conducted in six clinical research centers: three in U.S. (Colorado, Georgia/Florida, and Washington) and three in Europe (Finland, Germany, and Sweden). A total of 8676 children were enrolled and followed prospectively from 3 months to 15 years of age for blood samples collection and islet autoantibodies measurement at 3-month intervals before 4 years of age and at 6-month interval thereafter. All children who were persistently positive for any autoantibody were followed every 3 months until the age of 15 years. Detailed study design and methods have been previously published (22). Written informed consents were obtained for all study participants from a parent or a primary caretaker, separately, for genetic screening and participation in the prospective follow-up, beginning at birth. Autoantibodies were measured in two laboratories by radiobinding assays (22; 23). Persistent IA was defined as confirmed positive autoantibodies (IAA, GADA, or IA-2A) in at least two consecutive samples by both laboratories, with the date of seroconversion defined as that of the first positive sample. Type 1 diabetes was diagnosed using the American Diabetes Association criteria (24).

For biomarker discovery, a nested case-control (NCC) design using risk set sampling was conducted based on data collected as of May 31, 2012 (25). Four hundred and eighteen IA case subjects were selected, and each was matched with 3 control subjects who had not developed IA by the age when the case subject experienced the first-appearing autoantibodies. Matching factors were clinical centers, gender and first-degree relatives' status of T1D. For case subjects selected in NCC design, plasma ascorbic acid, 25(OH)D, and erythrocyte fatty acids were measured from the children's blood samples annually from the end of infancy (i.e. at 12-, 24-, 36-, 48-, 60- month), while the children's metabolome including lipidome were profiled at each 3-month visit following birth up to seroconversion. Nutrient biomarkers and metabolome were also measured at the same age (or visits) for matched control subjects. The concentrations of nutrient biomarkers during infant age (i.e. at 3-, 6-, 9- month) were also available at different frequencies (9; 26). Bar plots in **Figure 1** present the numbers of subjects having biomarkers and lipidome measured, individually, per time point within 1 year prior to seroconversion. Each matched case-control pair had blood samples collected at the same ages, although random missing visits occurred.

Nutrient biomarkers and metabolome profiling

Nutrient biomarkers were profiled at the Biochemistry Laboratory, Genomics and Biomarkers Unit, National Institute for Health and Welfare (THL), Helsinki, Finland. Plasma ascorbic acid was determined by an ion-paired, reversed-phase, high-performance liquid chromatographic method using electrochemical detection, while plasma 25(OH)D was measured using the ARCHITECT 25-OH Vitamin D chemiluminescent microparticle immunoassay (CMIA). Omega-3 fatty acids were analyzed from erythrocytes stabilized in 2-propanol and butylated hydroxytoluene. Erythrocyte fatty acids composition was analyzed using an Agilent 6890 gas chromatograph with a split injector and hydrogen as the carrier gas, employing a capillary column Omegawax 320 (length: 30 m, I.D.: 0.32 mm, phase layer: 0.25 µm; Supelco, Bellefonte, PA, USA). Data were analyzed using OpenLab CDS Chemstation software (Agilent, Palo Alto, USA). The percentage composition of fatty acid methyl esters was normalized to 100% in each sample. Samples of the cases and their controls at each age point were processed in the same batch for all analytes.

TEDDY subjects' plasma samples selected under NCC design were shipped to NIH West Coast Metabolomics Center at University of California Davis (UCD) and processed by following standard laboratory protocols. Prior to sample shipment, the TEDDY Data Coordinating Center (DCC) designed laboratory running batches by assigning plasma samples of matched subjects to the same batch. Mass spectrometry processing at UCD followed the order of designed batches to ensure that disease outcomes did not confound with run-order.

The primary metabolites assay was profiled by gas chromatography time-of-flight mass spectrometry (GC-TOF MS) on Leco Pegasus III instrument annotated by BinBase (27). The complex lipids (lipidome) assay was analyzed by charged surface hybrid column with electrospray ionization (CSH-ESI) on Agilent ultra high pressure liquid chromatography quadrupole time-of-flight mass spectrometry (UHPLC-QTOF MS) instruments annotated with LipidBlast (28). Peaks from GC-TOF MS platform were automatically detected and deconvoluted from co-eluting peaks by the Leco ChromaTOF software (v3.0). Raw data output from CSH-ESI-QTOF instruments were processed in an untargeted manner by Agilent's software MassHunter Qual (v. B.05.00) to find peaks. Peak features were then imported into MassProfilerProfessional for peak alignments to seek which peaks are present in multiple chromatograms. These peaks are then collated and constrained within the MassHunter quantification software (v. B.05.01) on the accurate mass precursor ion level, using the MS information and the LipidBlast library. We applied a comprehensive normalization pipeline Systematic Error Removal Using Random Forest (SERRF) (29) to the raw quantified intensity of metabolites, successfully removing laboratory run-order effect in terms of a quality control (QC) metric, i.e., reduced coefficient of variation of internal standard compounds. The normalized data still contained missing abundance, which were filled by the values generated from a label-free missing value imputation tool GMSimpute (30).

Unsupervised clustering of temporal lipidomic profiles

To screen potential linkage among lipidome, nutrients, and IA-related outcomes, an unsupervised clustering approach was first applied to the GADA-first and IAA-first children (n=165) having plasma lipidome profiled at three consecutive visits within 6 months before or at seroconversion, labeled as visit 0, -3, -6. Previous results had shown strong infant-age pattern in TEDDY children's lipidome (21), which may be a result of growth and dietary exposure changes similar to that in gut microbiome (31). The aim of this analysis was to detect latent subgroups of children having stratified blood concentrations of nutrients or distinct endpoint outcomes, instead of grouping lipidome profiles only representative of age or growth phases (31). Hence, we merged every child's multi-visit lipidomes into one temporal lipidomic profile, consisting of three consecutive measurements of 208 lipid species with dimension of $m=3\times208=624$.

Temporal lipidomic profiles of the children who experienced seroconversion by the end of infancy might be grouped into a cluster due to infant-age patterns. On the other hand, a cluster of children consisting of both pre- and post-infancy seroconversion may represent young age and other characteristics. Existing studies (32; 33) reported strong association among lipid species profiled from each sample. Thus, to account for the strong associations among lipid species and temporal measurements, we employed Gaussian model-based clustering to group (n=165) temporal lipidomic profiles. The clustering was performed by R package mclust (34) and the optimal number of clusters was selected between 1 to 10 according to Bayesian Information Criterion.

Cluster-wise lipidomic, nutritional signatures and correlation analysis

We first employed the Bioconductor package limma (35) to perform lipidome-wide differential analysis to identify lipidomic signatures that defined each cluster of children. Classes of lipidomic signatures were further confirmed by enrichment analysis from ChemRICH (36) with filters: altered lipid species ratio>0.3, increased or decreased species ratio >0.3, and Benjamini-Hochberg (BH) procedure (37) adjusted p-value <0.05. Next, the concentration of each nutrient biomarker measured within 12 months before seroconversion was compared between clusters of children by linear regression, adjusted by the age of biomarker measurement with statistical significance at $P<0.05$. A nutrient biomarker with concentration stratified by the clusters is a nutritional signature for the corresponding subgroup(s) of children. The cluster-wise nutritional and lipidomic signatures revealed the latent relation between nutrient biomarkers and lipid species.

We further confirmed the lipidome-nutrients connectivity by Spearman's correlation coefficients (rho) of pairwise lipid species and nutrient biomarkers based on IAA-first, GADA-first cases (n=191) and matched controls (n=517) , who had both types of analytes measured within 12 months before seroconversion. Connectivity (or correlation) threshold was determined by rho >0.1 or <-0.1. The concentration of each nutrient biomarker was the log-scaled measurement (or the average of more than one measurement) within 12 months prior to seroconversion for cases and at the same age for matched controls, while the lipidome was selected at the last visit (3 months) prior to seroconversion and at the same age of matched controls.

Differential abundance analysis for IA-related outcomes

Demographic characteristics and IA-related outcomes per cluster, such as the type of an initial autoantibody, seroconversion age, and further progression to T1D were first identified by Kruskal-Wallis test, Fisher's exact test and Cox regression with statistical significance at $P<0.05$. We further performed differential analysis on metabolome (i.e. primary metabolites and lipidome) and nutrient biomarkers against the identified endpoint outcomes among GADA-first and IAA-first cases, using limma or linear regression. Metabolites associated with endpoint outcomes were selected by adjusted $P<0.2$, while association between nutrient biomarkers and endpoint outcomes were analyzed by linear regression and selected by $P<0.05$. Prognostic effect was further confirmed by Cox regression. Age at analytes measurements, country, family history of T1D, gender, and HLA DR-DQ haplotypes were included in differential or Cox analysis as covariates.

Results

Clusters of children defined by temporal lipidomic profiles

The unsupervised clustering algorithm grouped 165 TEDDY children's temporal lipidomic profiles before GADA-first or IAA-first as Clusters I-IV, visualized by T-distributed

Stochastic Neighbor Embedding (tSNE) plot in **Figure 2a** and the heatmap in **Figure 2b**. Children in Clusters I and II were not clearly distinguished from each other on the tSNE plot, but they were well separated from Clusters III-IV. In addition, a clear border between Cluster IV and the others was observed (**Figure 2a)**. The distribution of clusters in the tSNE plot agreed to the lipidomic patterns in **Figure 2b**, i.e. Clusters I and II shared similar patterns in TG, but a remarkable difference between Clusters I-II and Clusters III-IV was observed in TG. Heatmap at visits -3, -6 presented contrast of Clusters II vs I and Clusters IV vs III in TG.

Cluster-wise lipidomic, nutrient signatures and connectivity

We further performed lipidome-wide differential and enrichment analyses at visits -3, -6 to identify the most differentiated lipid classes as top signatures for Clusters III-IV vs Clusters I-II, Cluster II vs Cluster I, and Clusters IV vs Cluster III, Cluster III vs Cluster I, and Cluster IV vs Cluster I. Differential analysis results were listed in Supplemental **Tables S1-S10** and the differentially abundant lipid classes at both visits -3 and -6 were summarized in Supplemental **Table S11**, verifying lipidomic signatures illustrated in **Figure 2b.** Compared to the reference Cluster I, lipidomic signatures for Cluster II were increased phosphatidylcholines (PC) and sphingomyelins (SMd), while higher triacylglycerols (TG), diglycerides (DG) and lower PC, Cholesterol Esters (CE) were signatures for Cluster IV. Cluster III compared to the other clusters had increased TG, DG, lysoPC, and plasmalogens, as a result of young-age (21) lipidome profiles (at seroconversion) as shown in **Table 1**. A higher level of ascorbic acid was observed in Cluster III (*P*=0.0024) and Cluster IV (*P*=0.0031), while 25(OH)D concentration was elevated only in Cluster IV (*P*=0.0093**)**. Ascorbic acid was also found decreasing along with growth, being consistent with higher ascorbic acid and young age at measurement in Cluster III. Cluster

IV had lower composition of omega-3 fatty acids ALA, EPA, DHA, DPA (*P*=0.0006, <0.001, 0.0156, 0.0007) with mean levels shown in **Table 1**, and were positively associated with measurement age (*P*<0.001).

Spearman correlation coefficients among nutrient biomarkers and lipidome were listed in Supplemental **Table S12** and visualized in **Supplemental Figure**, including the pair-wise correlation between dietary biomarkers. Higher levels of TG, DG, ascorbic acid and 25(OH)D in Clusters III-IV were consistent with TG and DG positive correlations with ascorbic acid and 25(OH)D, while omega-3 fatty acids showed positive connectivity with most of CE lipid species and negative connectivity with DG (**Table S12**). The simultaneous higher levels of ascorbic acid, 25(OH)D and reduced omega-3 fatty acids observed in Cluster IV was consistent with the correlations among these nutrient biomarkers (**Table S12)**.

Cluster-wise characteristics related to IA

The association of identified clusters with country, family history of T1D, initial autoantibody type, seroconversion age were shown in **Table 1**. Most subjects in Cluster I experienced seroconversion after 15 months of age regardless of the type of initial autoantibodies. Cluster II had relatively lower proportion of first degree relatives in T1D (*P*=0.0498). The cluster-wise seroconversion age for each initial autoantibody were presented in **Figure 2c** and **Table 1**. Cluster III compared to others was a subgroup with younger seroconversion age (*P*<0.0001) for either IAA-first or GADA-first. Half of GADA-first children's (n=21) temporal lipidomic profiles in Cluster III were post-infancy, although the lipidomic profiles for half of IAA-first children (n=30) in this cluster were at infant age. Hence, Cluster III not only represented younger age of lipidome or children, but also included the earliest seroconversion of each autoantibody. A subgroup analysis showed that seroconversion among Clusters I, II, IV was age-independent. Relatively higher ascorbic acid, 25(OH)D and lower omega-3 fatty acids were found in US participants compared to other countries, while most of participants in Cluster IV were from US (*P*=0.0005). This explained the nutritional signatures (higher ascorbic acid, 25(OH)D and lower omega-3 fatty acids) identified in Cluster IV.

A Kaplan-Meier curve (**Figure 2d**) showed that subjects in Cluster III compared to other clusters had higher risk of T1D progression from the onset of initial autoantibody, as a result of early seroconversion in Cluster III (3). A subsequent question is whether the subjects in the other Clusters (I, II, IV) had similar risk of progression to T1D from the initial autoantibody, since they experienced seroconversion at similar age. Therefore, we compared the risk of progression from seroconversion to T1D among Clusters I, II, and IV throughout the follow-up from seroconversion to December 31, 2019, adjusting for the age at seroconversion, type of the initial autoantibody, first-degree relatives with T1D, gender, HLA haplotypes (DR3/DR4 vs others). Supplemental **Table S13** showed that Cluster IV compared to Cluster I had relatively slower T1D progression after the initial autoantibody (hazard ratio (95% CI): 0.3672 (0.1617, 0.8335), *P*=0.0166). Therefore, we identified distinct clusters of children representing earlier seroconversion of either IAA-first or GADA-first, fewer first degree relatives in T1D, and slower progression to T1D.

Metabolites and circulating vitamins preceding early seroconversion and T1D progression

Children in Cluster III developed IAA-first at mean age of 12.3 months and GADA-first at mean age of 20.6 months, being consistent with the population-wide early onset of either initial autoantibody (2). This subgroup of TEDDY children revealed an analytical definition of early onset of IAA-first and GADA-first. To identify metabolic or nutritional signatures for early onset of an initial autoantibody instead of age, we first defined IAA-first cases as 'Early IAA' (n=68), 'Late IAA' (n=134) by seroconversion before or after 12 months of age, and GADA-first as 'Early GADA' (n=43), 'Late GADA' (n=93) by seroconversion before or after 21 months of age. Differential abundance analysis between 'Early-' and 'Late-' onset of each initial autoantibody was performed on analytes measured at the same age during infancy, with country, gender, first degree of relatives in T1D and HLA haplotype included as covariates. Log fold change (logFC) in **Figure 3a** showed that children having reduced plasma ascorbic acid at age 6 months (P=0.0362) or less abundant cholesterol metabolite at age 9 months (P<0.0001, BH adjusted P<0.2) developed afterwards IAA-first earlier ('Early IAA'), while less abundant sphingomyelins species at age 9 months (BH adjusted P<0.2) were found associated with the following early onset of GADA-first ('Early GADA'). The cholesterol metabolite associated with 'Early IAA' was the free form of cholesterol profiled by GC-TOF MS (InChIKey: HVYWMOMLDIMFJA-DPAQBDIFSA-N), different from cholesterol ester (CE) lipid species profiled by UHPLC-QTOF MS platform.

Differential analysis also found children who experienced T1D progresssion (n=171) after either type of initial autoantibody had reduced 25(OH)D (P=0.0029) within one year prior to seroconversion compared to the non-progressors (n=167), while multiple lipid species in lysoPC and DG 34:1 at 6 months prior to GADA-first were less abundant in T1D progressors than non-progressors (**Figure 3b)**. Age of measurement, country, gender and first degree relatives with T1D were included as covariates in the differential analysis of progression. Relatively higher abundance (logFC in **Figure 3b**) of lipid species before IAA-first onset in T1D progressors compared to non-progressors was not confirmed with statistical significance. Reduced abundance of other lipid species in DG, TG 56:8, and amino acid alanine at 6 months before GADA-first onset were also found signaling afterwards T1D progression by Cox regression analysis (BH adjusted $P<0.2$), with hazard ratio presented in **Figure 4**. The prognostic signatures for T1D progression following GADA-first (lysoPC and DG 34:1) identified in differential analysis were also confirmed by Cox regression. Our analysis did not find metabolic signatures for T1D progression following IAA-first. These results agreed to the higher 25(OH)D and slower T1D progression observed in Cluster IV.

A further analysis on the analytes measured at infant age among IAA-first and GADA-first cases revealed that HLA-DR3/DR4 haplotype and the corresponding alleles (at HLA genes DRB1, DQA1, DQB1) were associated with reduced 25(OH)D at age of 6 months (**Table 2**), although ascorbic acid at the same age was only associated with HLA-DR3/DR4 haplotype. Association between HLA-DR3/DR4 and circulating vitamins was not observed in matched controls.

Discussion

Our analysis in the present study revealed the relationship among HLA DR3/DR4 genotypes, circulating vitamins, metabolome, islet autoimmunity and further progression to T1D in early childhood. We provided an analytical definition for early seroconversion of IAA-first (12 months) and GADA-first (21 months), respectively. We identified reduced ascorbic acid, cholesterol metabolite and SMd species as early-seroconversion signatures for IAA-first and GADA-first (**Figure 3**), while 25(OH)D and multiple metabolites before either initial autoantibody were predictive of further progression to T1D.

Multiple metabolites near the onset of GADA-first were found as prognostic signature for T1D (**Figure 4)**. The association between reduced amino acid alanine and T1D progression was consistent with the negative association between alanine and GADA-first risk reported in (21). Our previous analysis on primary metabolites in TEDDY (21) also found alanine negatively associated with the risk of IAA-first. Higher pseudo uridine was found associated with T1D progression following GADA-first, which was also a risk marker for development of T2D or renal dysfunction in T1D or T2D (38; 39). Pseudo uridine is typically the most abundant marker of modified RNA bases in human plasma. Erythritol-a critical sugar alcohol-was also found positively associated with T1D progression after GADA-first. Furthermore, results in **Table 2** not only confirmed previous findings that lower circulating vitamins were associated with higher IA risk (9; 26), but also implied that HLA-DR3/DR4 potentially linked to the gene expression dysregulation of these circulating vitamins.

Our analysis found reduced ascorbic acid only preceding early seroconversion of IAA-first, consistent with the conclusion that ascorbic acid only reduced the risk of IAA-first from a recent analysis in TEDDY (26). Previous results about the role of ascorbic acid in T1D were unclear. A previous study (40) showed that ascorbic acid level was significantly increased in plasma and spleen of the diabetes-prone rats compared to the control group. Higher ascorbate concentration in mouse was also found to have immediate inhibition on insulin secretion, but was completely reversible (41), which was associated with hyperpolarization of the pancreatic beta-cell. On the other hand, oral ascorbic acid supplementation was reported to provide an effective prophylaxis against exercise-induced free radical-mediated lipid peroxidation in type 1 diabetes (8).

A recent study in TEDDY provided evidence for the association between 25(OH)D and islet autoimmunity (9) without analyzing the risk of T1D. The protective effect of 25(OH)D on T1D was reported in a Norwegian birth control study (42) and in a non-Hispanic White population in the U.S. (43), but not in other studies (44-48). Our present study shed light on the potential causes for previous inconsistent conclusions about 25(OH)D and the overall risk for T1D, that is the time between 25(OH)D measurement and clinical onset of T1D. Our findings underscored the importance of when to relate 25(OH)D to T1D, i.e. within one year prior to, at (or immediately after) seroconversion, at a second islet autoantibody (49) or before the onset of multiple positive autoantibodies (50; 51).

One of our aims in the present analyses was to identify potential metabolic and nutritional markers for the subtypes of islet autoimmunity. Hence, we focused on TEDDY children who developed GADA only (33%) or IAA only (49%) as the initial autoantibody to ensure heterogeneity among subjects in clustering, without considering the simultaneous onset of GADA and IAA (14%) or other autoantibodies at seroconversion. Future studies on lipidome and dietary biomarkers under TEDDY NCC design should include all subjects having positively-confirmed IA and their matched controls for sufficient statistical power. The TEDDY full cohort is dominated by White Non-Hispanic (>90%), hence, sample size in other race or ethnicity groups was too small to assess whether our findings were relevant to races. Another limitation of present study existed in the prognostic analysis on either metabolome or nutrient biomarkers, which was conducted within the TEDDY NCC design for IA (at 1:3 case-to-control ratio). The population-wide risk of progression from initial autoantibody to T1D might differ from that in TEDDY NCC as it only represents a subgroup of the full TEDDY cohort who seroconverted at an early age (<5 years). Future prognostic analysis on metabolome or nutrient biomarkers should be extended to a larger cohort for reproducibility and validation.

Conclusion

Infants having reduced plasma ascorbic acid and cholesterol experienced seroconversion of IAA-first earlier, while early onset of GADA-first was preceded by reduced sphingomyelins at infancy. Either IAA-first or GADA-first children with further T1D progression compared to non-progressors had lower plasma 25(OH)D prior to the onset of each autoantibody. Plasma ascorbic acid and 25(OH)D were negatively associated with HLA-DR3/DR4 among infants who later experienced IAA-first and GADA-first, implying dysregulation of gene expression potentially linked to reduced circulating vitamins.

Data Availability Statement

The datasets generated and analyzed during the current study will be made available in the NIDDK Central Repository at https://www.niddkrepository.org/studies/teddy.

Funding

The TEDDY Study is funded by U01 DK63829, U01 DK63861, U01 DK63821, U01 DK63865, U01 DK63863, U01 DK63836, U01 DK63790, UC4 DK63829, UC4 DK63861, UC4 DK63821, UC4 DK63865, UC4 DK63863, UC4 DK63836, UC4 DK95300, UC4 DK100238, UC4 DK106955, UC4 DK112243, UC4 DK117483, and Contract No. HHSN267200700014C from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Institute of Environmental Health Sciences (NIEHS), Centers for Disease Control and Prevention (CDC), and JDRF. This work supported in part by the NIH/NCATS Clinical and Translational Science Awards to the University of Florida (UL1 TR000064) and the University of Colorado (UL1 TR002535).

Author Contributions

AL, WH, MR, JS, JT, AZ, BA, JK provided conception and design of the study. QL, XL, JK developed analytical plan and interpreted the results. QL conducted analysis programming and drafted the manuscript with XL. JY interpreted results, provided inputs in discussion and edited the manuscript. AL, MR, JS, JT, AZ facilitated physical data collection from patients. QL, XL, JY, IE, AL, WH, MR, JS, JT, AZ, BA, JK reviewed, edited, and approved the final draft of the manuscript.

Guarantor Statement

Qian Li is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Competing Interests

The authors declare no competing interests.

Acknowledgements

The TEDDY Study Group

Colorado Clinical Center: Marian Rewers, M.D., Ph.D., PI[1,4,5,6,9,10], Aaron Barbour, Kimberly Bautista[11], Judith Baxter[8,911], Daniel Felipe-Morales, Kimberly Driscoll, Ph.D.[8], Brigitte I. Frohnert, M.D.[2,13], Marisa Stahl, M.D.[12], Patricia Gesualdo[2,6,11,13], Michelle Hoffman[11,12,13], Rachel Karban[11], Edwin Liu, M.D.[12], Jill Norris, Ph.D.[2,3,11], Stesha Peacock, Hanan Shorrosh, Andrea Steck, M.D.[3,13], Megan Stern, Erica Villegas[2], Kathleen Waugh[6,7,11]. University of Colorado, Anschutz Medical Campus, Barbara Davis Center for Childhood Diabetes.

Finland Clinical Center: Jorma Toppari, M.D., Ph.D., PI[¥^1,4,10,13], Olli G. Simell, M.D., Ph.D., Annika Adamsson, Ph.D.[^11], Suvi Ahonen[*±§], Mari Åkerlund[*±§], Leena Hakola[*], Anne Hekkala,

M.D.[µ¤], Henna Holappa[µ¤], Heikki Hyöty, M.D., Ph.D.*[±6], Anni Ikonen[µ¤], Jorma Ilonen, M.D., Ph.D.[¥¶3], Sinikka Jäminki*[±], Sanna Jokipuu[^], Leena Karlsson[^], Jukka Kero M.D., Ph.D.[¥^], Miia Kähönen[µ¤11,13], Mikael Knip, M.D., Ph.D.*[±5], Minna-Liisa Koivikko[µ¤], Merja Koskinen*[±], Mirva Koreasalo*[±§2], Kalle Kurppa, M.D., Ph.D.*[±12], Jarita Kytölä*[±], Jutta Laiho, Ph.D.*[6], Tiina Latva-aho[µ¤], Katri Lindfors, Ph.D.*[12], Maria Lönnrot, M.D., Ph.D.*[±6], Elina Mäntymäki[^], Markus Mattila*, Maija Miettinen[§2], Katja Multasuo[µ¤], Teija Mykkänen[µ¤], Tiina Niininen[±*11], Sari Niinistö[±§2], Mia Nyblom*[±], Sami Oikarinen, Ph.D.*[±6], Paula Ollikainen[µ¤], Zhian Othmani[^], Sirpa Pohjola [µ¤], Petra Rajala[^], Jenna Rautanen[±§], Anne Riikonen*[±§2], Eija Riski[^], Miia Pekkola[*±], Minna Romo[^], Satu Ruohonen[^], Satu Simell, M.D., Ph.D.[¥12], Maija Sjöberg[^], Aino Stenius[µ¤11], Päivi Tossavainen, M.D.[µ¤], Mari Vähä-Mäkilä[¥], Sini Vainionpää[^], Eeva Varjonen[^11], Riitta Veijola, M.D., Ph.D.[µ¤13], Irene Viinikangas[µ¤], Suvi M. Virtanen, M.D., Ph.D.*[±§2].
[¥]University of Turku, *Tampere University, [µ]University of Oulu, [^]Turku University Hospital, Hospital District of Southwest Finland, [±]Tampere University Hospital, [¤]Oulu University Hospital, §National Institute for Health and Welfare, Finland, [¶]University of Kuopio.

Georgia/Florida Clinical Center: Jin-Xiong She, Ph.D., PI[1,3,4,10], Desmond Schatz, M.D.*[4,5,7,8], Diane Hopkins[11], Leigh Steed[11,12,13], Jennifer Bryant[11], Katherine Silvis[2], Michael Haller, M.D.*[13], Melissa Gardiner[11], Richard McIndoe, Ph.D., Ashok Sharma, Stephen W. Anderson, M.D.[^], Laura Jacobsen, M.D.*[13], John Marks, DHSc.*[11,13], P.D. Towe*. Center for Biotechnology and Genomic Medicine, Augusta University. *University of Florida, [^]Pediatric Endocrine Associates, Atlanta.

Germany Clinical Center: Anette G. Ziegler, M.D., PI[1,3,4,10], Ezio Bonifacio Ph.D.*[5], Cigdem Gezginci, Anja Heublein, Eva Hohoff[¥2], Sandra Hummel, Ph.D.[2], Annette Knopff[7], Charlotte Koch, Sibylle Koletzko, M.D.[¶12], Claudia Ramminger[11], Roswith Roth, Ph.D.[8], Jennifer Schmidt, Marlon Scholz, Joanna Stock[8,11,13], Katharina Warncke, M.D.[13], Lorena Wendel, Christiane Winkler, Ph.D.[2,11]. Forschergruppe Diabetes e.V. and Institute of Diabetes Research, Helmholtz Zentrum München, Forschergruppe Diabetes, and Klinikum rechts der Isar, Technische Universität München. *Center for Regenerative Therapies, TU Dresden, [¶]Dr. von Hauner Children's Hospital, Department of Gastroenterology, Ludwig Maximillians University Munich, [¥]University of Bonn, Department of Nutritional Epidemiology.

Sweden Clinical Center: Åke Lernmark, Ph.D., PI[1,3,4,5,6,8,9,10], Daniel Agardh, M.D., Ph.D.[6,12], Carin Andrén Aronsson, Ph.D.[2,11,12], Maria Ask, Rasmus Bennet, Corrado Cilio, Ph.D., M.D.[5,6], Susanne Dahlberg, Helene Engqvist, Emelie Ericson-Hallström, Annika Björne Fors, Lina Fransson, Thomas Gard, Monika Hansen, Hanna Jisser, Fredrik Johansen, Berglind Jonsdottir, M.D., Ph.D.[11], Helena Elding Larsson, M.D., Ph.D.[6,13], Marielle Lindström, Markus Lundgren, M.D., Ph.D.[13], Marlena Maziarz, Ph.D., Maria Månsson-Martinez, Jessica Melin[11], Zeliha Mestan, Caroline Nilsson, Karin Ottosson, Kobra Rahmati, Anita Ramelius, Falastin Salami, Anette Sjöberg, Birgitta Sjöberg, Carina Törn, Ph.D.[3], Åsa Wimar[13]. Lund University.

Washington Clinical Center: William A. Hagopian, M.D., Ph.D., PI[1,3,4,5,6,7,10,12,13], Michael Killian[6,7,11,12], Claire Cowen Crouch[11,13], Jennifer Skidmore[2], Masumeh Chavoshi, Arlene Meyer, Jocelyn Meyer, Denise Mulenga[11], Nole Powell, Jared Radtke, Matei Romancik, Shreya Roy, Davey Schmitt, Sarah Zink. Pacific Northwest Research Institute.

Pennsylvania Satellite Center: Dorothy Becker, M.D., Margaret Franciscus, MaryEllen Dalmagro-Elias Smith[2], Ashi Daftary, M.D., Mary Beth Klein, Chrystal Yates. Children's Hospital of Pittsburgh of UPMC.

Data Coordinating Center: Jeffrey P. Krischer, Ph.D.,PI[1,4,5,9,10], Sarah Austin-Gonzalez, Maryouri Avendano, Sandra Baethke, Brant Burkhardt, Ph.D.[5,6], Martha Butterworth[2], Joanna Clasen, David Cuthbertson, Christopher Eberhard, Steven Fiske[8], Jennifer Garmeson, Veena Gowda, Kathleen Heyman, Belinda Hsiao, Christina Karges, Francisco Perez Laras, Qian Li, Ph.D.[2,3,12], Shu Liu, Xiang Liu, Ph.D.[2,3,8,13], Kristian Lynch, Ph.D. [5,6,8], Jamie Malloy, Cristina McCarthy[11], Hemang Parikh, Ph.D.[3], Cassandra Remedios, Chris Shaffer, Laura Smith, Ph.D.[8,11], Susan Smith[11], Noah Sulman, Ph.D., Roy Tamura, Ph.D.[1,2,11,12,13], Dena Tewey, Michael Toth, Ulla Uusitalo, Ph.D.[2], Kendra Vehik, Ph.D.[4,5,6,8,13], Ponni Vijayakandipan, Jimin Yang, Ph.D., R.D.[2]. *Past staff: Michael Abbondondolo, Lori Ballard, Rasheedah Brown, Stephen Dankyi, David Hadley, Ph.D., Hye-Seung Lee, Ph.D., Colleen Maguire, Wendy McLeod, Aubrie Merrell, Steven Meulemans, Ryan Quigley.* University of South Florida.

Project scientist: Beena Akolkar, Ph.D.[1,3,4,5,6,7,9,10]. National Institutes of Diabetes and Digestive and Kidney Diseases.

Autoantibody Reference Laboratories: Liping Yu, M.D.^[5], Dongmei Miao, M.D.^, Polly Bingley, M.D., FRCP*[5], Alistair Williams*, Kyla Chandler*, Ilana Kelland*, Yassin Ben Khoud*, Huma Zahid*, Matthew Randell *. ^Barbara Davis Center for Childhood Diabetes, University of Colorado Denver, *Bristol Medical School, University of Bristol, UK.

Dietary Biomarkers Laboratory: Iris Erlund, Ph.D.[2] , Irma Salminen, Jouko Sundvall, Jaana Leiviskä, Nina Kangas, Petra Arohonka. National Institute for Health and Welfare, Helsinki, Finland.

HLA Reference Laboratory: William Hagopian[3], MD, PhD, Masumeh Chavoshi, Jared Radtke, Sarah Zink. Pacific Northwest Research Institute, Seattle WA. (Previously Henry Erlich,

Ph.D.[3], Steven J. Mack, Ph.D., Anna Lisa Fear. Center for Genetics, Children's Hospital Oakland Research Institute.)

Metabolomics Laboratory: Oliver Fiehn, Ph.D., Bill Wikoff, Ph.D., Brian Defelice, Dmitry Grapov, Ph.D., Tobias Kind, Ph.D., Mine Palazoglu, Luis Valdiviez, Benjamin Wancewicz, Gert Wohlgemuth, Joyce Wong. UC Davis Metabolomics Center.

Repository: Sandra Ke, Niveen Mulholland, Ph.D. NIDDK Biosample Repository at Fisher BioServices.

Other contributors: Thomas Briese, Ph.D.[6], Columbia University. Suzanne Bennett Johnson, Ph.D.[8,11], Florida State University. Eric Triplett, Ph.D.[6], University of Florida.

Committees:

[1]Ancillary Studies, [2]Diet, [3]Genetics, [4]Human Subjects/Publicity/Publications, [5]Immune Markers, [6]Infectious Agents, [7]Laboratory Implementation, [8]Psychosocial, [9]Quality Assurance, [10]Steering, [11]Study Coordinators, [12]Celiac Disease, [13]Clinical Implementation.

REFERENCE

1. Krischer JP, Lynch KF, Schatz DA, Ilonen J, Lernmark Å, Hagopian WA, Rewers MJ, She J-X, Simell OG, Toppari J, Ziegler A-G, Akolkar B, Bonifacio E, the TSG: The 6 year incidence of diabetes-associated autoantibodies in genetically at-risk children: the TEDDY study. Diabetologia 2015;58:980-987
2. Krischer JP, Lynch KF, Schatz DA, Ilonen J, Lernmark Å, Hagopian WA, Rewers MJ, She J-X, Simell OG, Toppari J, Ziegler A-G, Akolkar B, Bonifacio E, Group tTS: The 6 year incidence of diabetes-associated autoantibodies in genetically at-risk children: the TEDDY study. Diabetologia 2015;58:980-987
3. Liu X, Vehik K, Huang Y, Larsson HE, Toppari J, Ziegler AG, She J-X, Rewers M, Hagopian WA, Akolkar B, Krischer JP: Distinct Growth Phases in Early Life Associated With the Risk of Type 1 Diabetes: The TEDDY Study. Diabetes Care 2020:dc191670
4. Pundziūtė-Lyckå A, Persson L-Å, Cedermark G, Jansson-Roth A, Nilsson U, Westin V, Dahlquist G: Diet, Growth, and the Risk for Type 1 Diabetes in Childhood. A matched case-referent study 2004;27:2784-2789
5. Rewers M, Ludvigsson J: Environmental risk factors for type 1 diabetes. Lancet 2016;387:2340-2348
6. Hummel S, Beyerlein A, Tamura R, Uusitalo U, Andrén Aronsson C, Yang J, Riikonen A, Lernmark Å, Rewers MJ, Hagopian WA, She J-X, Simell OG, Toppari J, Ziegler A-G, Akolkar B, Krischer JP, Virtanen SM, Norris JM: First Infant Formula Type and Risk of Islet Autoimmunity in The Environmental Determinants of Diabetes in the Young (TEDDY) Study. Diabetes Care 2017;40:398-404
7. Lund-Blix NA, Dong F, Mårild K, Seifert J, Barón AE, Waugh KC, Joner G, Størdal K, Tapia G, Stene LC, Johnson RK, Rewers MJ, Norris JM: Gluten Intake and Risk of Islet Autoimmunity and Progression to Type 1 Diabetes in Children at Increased Risk of the Disease: The Diabetes Autoimmunity Study in the Young (DAISY). Diabetes Care 2019;42:789-796
8. Davison GW, Ashton T, George L, Young IS, McEneny J, Davies B, Jackson SK, Peters JR, Bailey DM: Molecular detection of exercise-induced free radicals following ascorbate prophylaxis in type 1 diabetes mellitus: a randomised controlled trial. Diabetologia 2008;51:2049
9. Norris JM, Lee H-S, Frederiksen B, Erlund I, Uusitalo U, Yang J, Lernmark Å, Simell O, Toppari J, Rewers M, Ziegler A-G, She J-X, Onengut-Gumuscu S, Chen W-M, Rich SS, Sundvall J, Akolkar B, Krischer J, Virtanen SM, Hagopian W: Plasma 25-Hydroxyvitamin D Concentration and Risk of Islet Autoimmunity. Diabetes 2018;67:146-154
10. Uusitalo U, Liu X, Yang J, Aronsson CA, Hummel S, Butterworth M, Lernmark Å, Rewers M, Hagopian W, She J-X, Simell O, Toppari J, Ziegler AG, Akolkar B, Krischer J, Norris JM, Virtanen SM, Group TS: Association of Early Exposure of Probiotics and Islet Autoimmunity in the TEDDY Study. JAMA Pediatr 2016;170:20-28
11. Miller MR, Yin X, Seifert J, Clare-Salzler M, Eisenbarth GS, Rewers M, Norris JM: Erythrocyte membrane omega-3 fatty acid levels and omega-3 fatty acid intake are not associated with conversion to type 1 diabetes in children with islet autoimmunity: The Diabetes Autoimmunity Study in the Young (DAISY). Pediatric Diabetes 2011;12:669-675
12. Niinistö S, Takkinen H-M, Erlund I, Ahonen S, Toppari J, Ilonen J, Veijola R, Knip M, Vaarala O, Virtanen SM: Fatty acid status in infancy is associated with the risk of type 1 diabetes-associated autoimmunity. Diabetologia 2017;60:1223-1233
13. Virtanen S, Niinistö S, Nevalainen J, Salminen I, Takkinen H-M, Kääriä S, Uusitalo L, Alfthan G, Kenward M, Veijola R, Simell O, Ilonen J, Knip M: Serum fatty acids and risk of advanced B-cell autoimmunity: A nested case-control study among children with HLA-conferred susceptibility to type i diabetes. European journal of clinical nutrition 2010;64:792-799
14. Lequin RM: Enzyme Immunoassay (EIA)/Enzyme-Linked Immunosorbent Assay (ELISA). Clinical Chemistry 2005;51:2415-2418

15. Salminen I, Alfthan G: Plasma ascorbic acid preparation and storage for epidemiological studies using TCA precipitation. Clinical Biochemistry 2008;41:723-727
16. Elorinne A-L, Alfthan G, Erlund I, Kivimäki H, Paju A, Salminen I, Turpeinen U, Voutilainen S, Laakso J: Food and Nutrient Intake and Nutritional Status of Finnish Vegans and Non-Vegetarians. PLOS ONE 2016;11:e0148235
17. van Meer G, Voelker DR, Feigenson GW: Membrane lipids: where they are and how they behave. Nat Rev Mol Cell Biol 2008;9:112-124
18. Orešič M, Simell S, Sysi-Aho M, Näntö-Salonen K, Seppänen-Laakso T, Parikka V, Katajamaa M, Hekkala A, Mattila I, Keskinen P, Yetukuri L, Reinikainen A, Lähde J, Suortti T, Hakalax J, Simell T, Hyöty H, Veijola R, Ilonen J, Lahesmaa R, Knip M, Simell O: Dysregulation of lipid and amino acid metabolism precedes islet autoimmunity in children who later progress to type 1 diabetes. The Journal of Experimental Medicine 2008;205:2975-2984
19. Pflueger M, Seppänen-Laakso T, Suortti T, Hyötyläinen T, Achenbach P, Bonifacio E, Orešič M, Ziegler A-G: Age- and Islet Autoimmunity–Associated Differences in Amino Acid and Lipid Metabolites in Children at Risk for Type 1 Diabetes. Diabetes 2011;60:2740-2747
20. Kyle JE, Burnum-Johnson KE, Wendler JP, Eisfeld AJ, Halfmann PJ, Watanabe T, Sahr F, Smith RD, Kawaoka Y, Waters KM, Metz TO: Plasma lipidome reveals critical illness and recovery from human Ebola virus disease. Proceedings of the National Academy of Sciences 2019;116:3919-3928
21. Li Q, Parikh H, Butterworth MD, Lernmark Å, Hagopian W, Rewers M, She J-X, Toppari J, Ziegler A-G, Akolkar B, Fiehn O, Fan S, Krischer JP: Longitudinal Metabolome-Wide Signals Prior to the Appearance of a First Islet Autoantibody in Children Participating in the TEDDY Study. Diabetes 2020:db190756
22. Group TTS: The Environmental Determinants of Diabetes in the Young (TEDDY) study: study design. Pediatric Diabetes 2007;8:286-298
23. Group TS: The Environmental Determinants of Diabetes in the Young (TEDDY) Study. Annals of the New York Academy of Sciences 2008;1150:1-13
24. Standards of Medical Care in Diabetes—2014. Diabetes Care 2014;37:S14-S80
25. Lee H-S, Burkhardt BR, McLeod W, Smith S, Eberhard C, Lynch K, Hadley D, Rewers M, Simell O, She J-X, Hagopian B, Lernmark A, Akolkar B, Ziegler A-G, Krischer JP, the TSG: Biomarker discovery study design for type 1 diabetes in The Environmental Determinants of Diabetes in the Young (TEDDY) study. Diabetes/metabolism research and reviews 2014;30:424-434
26. Mattila M, Erlund I, Lee H-S, Niinistö S, Uusitalo U, Andrén Aronsson C, Hummel S, Parikh H, Rich SS, Hagopian W, Toppari J, Lernmark Å, Ziegler AG, Rewers M, Krischer JP, Norris JM, Virtanen SM, Group ftTS: Plasma ascorbic acid and the risk of islet autoimmunity and type 1 diabetes: the TEDDY study. Diabetologia 2019;
27. Skogerson K, Wohlgemuth G, Barupal DK, Fiehn O: The volatile compound BinBase mass spectral database. BMC bioinformatics 2011;12:321-321
28. Kind T, Liu K-H, Lee DY, DeFelice B, Meissen JK, Fiehn O: LipidBlast in silico tandem mass spectrometry database for lipid identification. Nature methods 2013;10:755-758
29. Fan S, Kind T, Cajka T, Hazen SL, Tang WHW, Kaddurah-Daouk R, Irvin MR, Arnett DK, Barupal DK, Fiehn O: Systematic Error Removal Using Random Forest for Normalizing Large-Scale Untargeted Lipidomics Data. Analytical Chemistry 2019;91:3590-3596
30. Li Q, Fisher K, Meng W, Fang B, Welsh E, Haura EB, Koomen JM, Eschrich SA, Fridley BL, Chen YA: GMSimpute: a generalized two-step Lasso approach to impute missing values in label-free mass spectrum analysis. Bioinformatics 2019;
31. Stewart CJ, Ajami NJ, O'Brien JL, Hutchinson DS, Smith DP, Wong MC, Ross MC, Lloyd RE, Doddapaneni H, Metcalf GA, Muzny D, Gibbs RA, Vatanen T, Huttenhower C, Xavier RJ, Rewers M, Hagopian W, Toppari J, Ziegler A-G, She J-X, Akolkar B, Lernmark A, Hyoty H, Vehik K, Krischer JP,

Petrosino JF: Temporal development of the gut microbiome in early childhood from the TEDDY study. Nature 2018;562:583-588
32. La Torre D, Seppänen-Laakso T, Larsson HE, Hyötyläinen T, Ivarsson SA, Lernmark Å, Orešič M: Decreased Cord-Blood Phospholipids in Young Age–at–Onset Type 1 Diabetes. Diabetes 2013;62:3951-3956
33. Kulkarni H, Mamtani M, Wong G, Weir JM, Barlow CK, Dyer TD, Almasy L, Mahaney MC, Comuzzie AG, Duggirala R, Meikle PJ, Blangero J, Curran JE: Genetic correlation of the plasma lipidome with type 2 diabetes, prediabetes and insulin resistance in Mexican American families. BMC Genet 2017;18:48-48
34. Scrucca L, Fop M, Murphy TB, Raftery AE: mclust 5: clustering, classification and density estimation using Gaussian finite mixture models. The R journal 2016;8:289
35. Smyth GK: limma: Linear Models for Microarray Data. In *Bioinformatics and Computational Biology Solutions Using R and Bioconductor* Gentleman R, Carey VJ, Huber W, Irizarry RA, Dudoit S, Eds. New York, NY, Springer New York, 2005, p. 397-420
36. Barupal DK, Fiehn O: Chemical Similarity Enrichment Analysis (ChemRICH) as alternative to biochemical pathway mapping for metabolomic datasets. Scientific Reports 2017;7:14567
37. Benjamini Y, Yekutieli D: False Discovery Rate–Adjusted Multiple Confidence Intervals for Selected Parameters. Journal of the American Statistical Association 2005;100:71-81
38. Niewczas MA, Mathew AV, Croall S, Byun J, Major M, Sabisetti VS, Smiles A, Bonventre JV, Pennathur S, Krolewski AS: Circulating Modified Metabolites and a Risk of ESRD in Patients With Type 1 Diabetes and Chronic Kidney Disease. Diabetes Care 2017;40:383-390
39. Solini A, Manca ML, Penno G, Pugliese G, Cobb JE, Ferrannini E: Prediction of Declining Renal Function and Albuminuria in Patients With Type 2 Diabetes by Metabolomics. The Journal of Clinical Endocrinology & Metabolism 2016;101:696-704
40. Behrens WA, Madere R: Vitamin C and vitamin E status in the spontaneously diabetic BB rat before the onset of diabetes. Metabolism 1991;40:72-76
41. Bergsten P, Moura AS, Atwater I, Levine M: Ascorbic acid and insulin secretion in pancreatic islets. Journal of Biological Chemistry 1994;269:1041-1045
42. Tapia G, Mårild K, Dahl SR, Lund-Blix NA, Viken MK, Lie BA, Njølstad PR, Joner G, Skrivarhaug T, Cohen AS, Størdal K, Stene LC: Maternal and Newborn Vitamin D–Binding Protein, Vitamin D Levels, Vitamin D Receptor Genotype, and Childhood Type 1 Diabetes. Diabetes Care 2019;42:553-559
43. Munger KL, Levin LI, Massa J, Horst R, Orban T, Ascherio A: Preclinical Serum 25-Hydroxyvitamin D Levels and Risk of Type 1 Diabetes in a Cohort of US Military Personnel. American Journal of Epidemiology 2013;177:411-419
44. Simpson M, Brady H, Yin X, Seifert J, Barriga K, Hoffman M, Bugawan T, Barón AE, Sokol RJ, Eisenbarth G, Erlich H, Rewers M, Norris JM: No association of vitamin D intake or 25-hydroxyvitamin D levels in childhood with risk of islet autoimmunity and type 1 diabetes: the Diabetes Autoimmunity Study in the Young (DAISY). Diabetologia 2011;54:2779
45. Mäkinen M, Mykkänen J, Koskinen M, Simell V, Veijola R, Hyöty H, Ilonen J, Knip M, Simell O, Toppari J: Serum 25-Hydroxyvitamin D Concentrations in Children Progressing to Autoimmunity and Clinical Type 1 Diabetes. The Journal of Clinical Endocrinology & Metabolism 2016;101:723-729
46. Thorsen SU, Mårild K, Olsen SF, Holst KK, Tapia G, Granström C, Halldorsson TI, Cohen AS, Haugen M, Lundqvist M, Skrivarhaug T, Njølstad PR, Joner G, Magnus P, Størdal K, Svensson J, Stene LC: Lack of Association Between Maternal or Neonatal Vitamin D Status and Risk of Childhood Type 1 Diabetes: A Scandinavian Case-Cohort Study. American Journal of Epidemiology 2017;187:1174-1181
47. Thorsen SU, Pipper CB, Johannesen J, Mortensen HB, Pociot F, Svensson J: 25-Hydroxyvitamin D, Autoantigenic and Total Antibody Concentrations: Results from a Danish Case–control Study of Newly Diagnosed Patients with Childhood Type 1 Diabetes and their Healthy Siblings. Scandinavian Journal of Immunology 2018;87:46-53

48. Mäkinen M, Löyttyniemi E, Koskinen M, Vähä-Mäkilä M, Siljander H, Nurmio M, Mykkänen J, Virtanen SM, Simell O, Hyöty H, Ilonen J, Knip M, Veijola R, Toppari J: Serum 25-Hydroxyvitamin D Concentrations at Birth in Children Screened for HLA-DQB1 Conferred Risk for Type 1 Diabetes. The Journal of Clinical Endocrinology & Metabolism 2019;104:2277-2285
49. Vehik K, Lynch KF, Schatz DA, Akolkar B, Hagopian W, Rewers M, She JX, Simell O, Toppari J, Ziegler AG, Lernmark A, Bonifacio E, Krischer JP, Group TS: Reversion of beta-Cell Autoimmunity Changes Risk of Type 1 Diabetes: TEDDY Study. Diabetes Care 2016;39:1535-1542
50. Ziegler AG, Rewers M, Simell O, Simell T, Lempainen J, Steck A, Winkler C, Ilonen J, Veijola R, Knip M, Bonifacio E, Eisenbarth GS: Seroconversion to multiple islet autoantibodies and risk of progression to diabetes in children. Jama 2013;309:2473-2479
51. Krischer JP, Liu X, Vehik K, Akolkar B, Hagopian WA, Rewers MJ, She JX, Toppari J, Ziegler AG, Lernmark A, Group TS: Predicting Islet Cell Autoimmunity and Type 1 Diabetes: An 8-Year TEDDY Study Progress Report. Diabetes Care 2019;42:1051-1060

Table 1: **Characteristics of Clusters I-IV.**

Characteristics		Cluster I	Cluster II	Cluster III	Cluster IV	P-value*
	N (%)	43 (26.1)	51(30.9)	48 (29.1)	23 (13.9)	
ALA (composition %)	Mean (SD)	0.15 (0.04)	0.15 (0.06)	0.11 (0.04)	0.11 (0.04)	
EPA (composition %)	Mean (SD)	0.60 (0.29)	0.48 (0.37)	0.50 (0.25)	0.27 (0.14)	
DHA (composition %)	Mean (SD)	3.98 (1.04)	3.92 (1.18)	4.96 (1.04)	3.39 (0.83)	
DPA (composition %)	Mean (SD)	2.11 (0.40)	1.85 (0.54)	1.77 (0.44)	1.65 (0.56)	
Seroconversion age (month)	Mean (SD)	30.1 (10.9)	25.0 (11.3)	14.8 (8.4)	27.9 (10.8)	<0.0001
Country	US	2 (4.7)	10 (19.6)	12 (25.0)	20 (87.0)	<0.0001
	Finland	19 (44.2)	16 (31.4)	19 (39.6)	2 (8.7)	
	Germany	2 (4.7)	1 (2.0)	5 (10.4)	0 (0.0)	
	Sweden	20 (46.5)	24 (47.1)	12 (25.0)	1 (4.3)	
First degree relatives with type 1 diabetes	Yes	8 (18.6)	6 (11.8)	16 (33.3)	7 (30.4)	0.0498
	No	35 (81.4)	45 (88.2)	32 (66.7)	16 (69.6)	
Sex	Female	22 (51.2)	29 (56.9)	19 (39.6)	11 (47.8)	0.3829
	Male	21 (48.8)	22 (43.1)	29 (60.4)	12 (52.2)	
HLA DR-DQ genotype	DR3/DR4	23 (53.5)	23 (45.1)	22 (45.8)	11 (47.8)	0.8541
	Other	20 (46.5)	28 (54.9)	26 (54.2)	12 (52.2)	
Type of initial autoantibody	IAA	27 (62.8)	30 (58.8)	33 (68.8)	8 (34.8)	0.0519
	GADA	16 (37.2)	21 (41.2)	15 (31.3)	15 (65.2)	
Ascorbic acid (umol/L)	Mean (SD)	42.99 (20.5)	47.75 (23.5)	63.70 (23.4)	61.96 (22.5)	
25(OH)D (nmol/L)	Mean (SD)	50.53 (16.4)	53.67 (15.8)	49.98 (20.6)	62.73 (21.5)	

Data are presented as number (percentage) unless otherwise indicated. The composition of each fatty acid was the ratio of each fatty acid abundance over the total abundance of all fatty acids.

*P-values were from Pearson's Chi-square test for categorical variables or Kruskal-Wallis test for continuous variables. Association test on country and clusters was confirmed by excluding Germany because of small sample size and sparse cells (n<2) in contingency table.

Table 2: Association between HLA haplotypes/genotypes and plasma 25(OH)D, ascorbic acid at age of 6 months for IAA-first and GADA-first children.

HLA haplotypes or genotypes (%)	Plasma 25(OH)D (nmol/L)		Plasma ascorbic acid (umol/L)	
	Mean (SD)	P-value	Mean (SD)	P-value
DR3/DR4 (51%)	49.62 (21.18)	0.018	55.51 (27.99)	0.04+
Others (49%)	56.62 (24.88)		62.37 (28.54)	
DRB1*0301 (64%)	51.23 (20.49)	0.023	58.90 (29.00)	0.845
Others (36%)	56.24 (27.34)		58.90 (27.54)	
DQA1*0501 (64%)	51.43 (20.56)	0.033	58.92 (28.80)	0.856
Others (36%)	56.00 (27.43)		58.85 (27.87)	
DQB1*201 (64%)	51.43 (20.56)	0.033	58.92 (28.80)	0.856
Others (36%)	56.00 (27.43)		58.85 (27.87)	

Association analysis per circulating nutrient was performed by linear regression on each genetic factor with covariates of country, gender, and family history of T1D.

+Association between HLA DR3/DR4 and ascorbic acid was *P*=0.001 for GADA-first children.

Figures

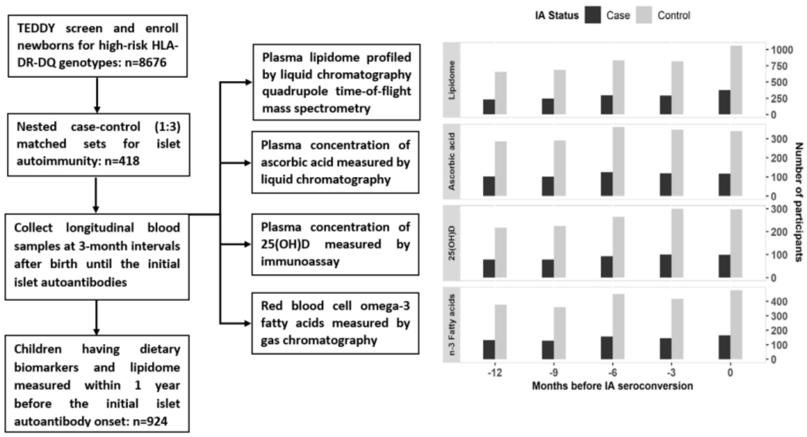
Figure 1: TEDDY study design and distribution of participants having nutrient biomarkers and lipidome measured.

Figure 2: Clusters identified by temporal lipidomic profiles of 165 TEDDY children.

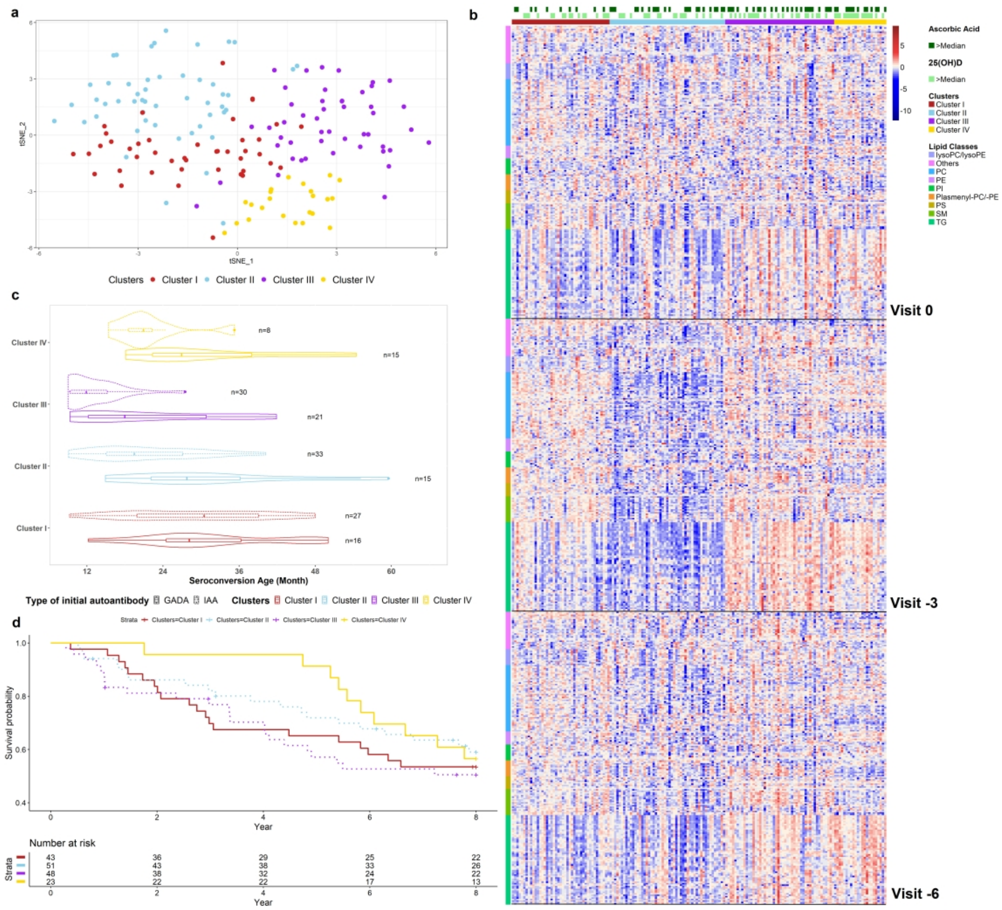
(a) T-distributed Stochastic Neighbor Embedding plot based on longitudinal lipidome, with axes representing two dimensions of distances. (b) Heatmap for longitudinal lipidome with columns as subjects and rows as lipids per visit. (c) Distribution of seroconversion age for each type of initial autoantibody per cluster. (d) Kaplan-Meier curve for progression from the initial autoantibody to T1D.

Figure 3: Metabolites and circulating vitamins preceding (a) early seroconversion or (b) further progression to T1D.

Figure 4: Hazard ratio for metabolites associated with progression risk from GADA-first seroconversion to T1D.

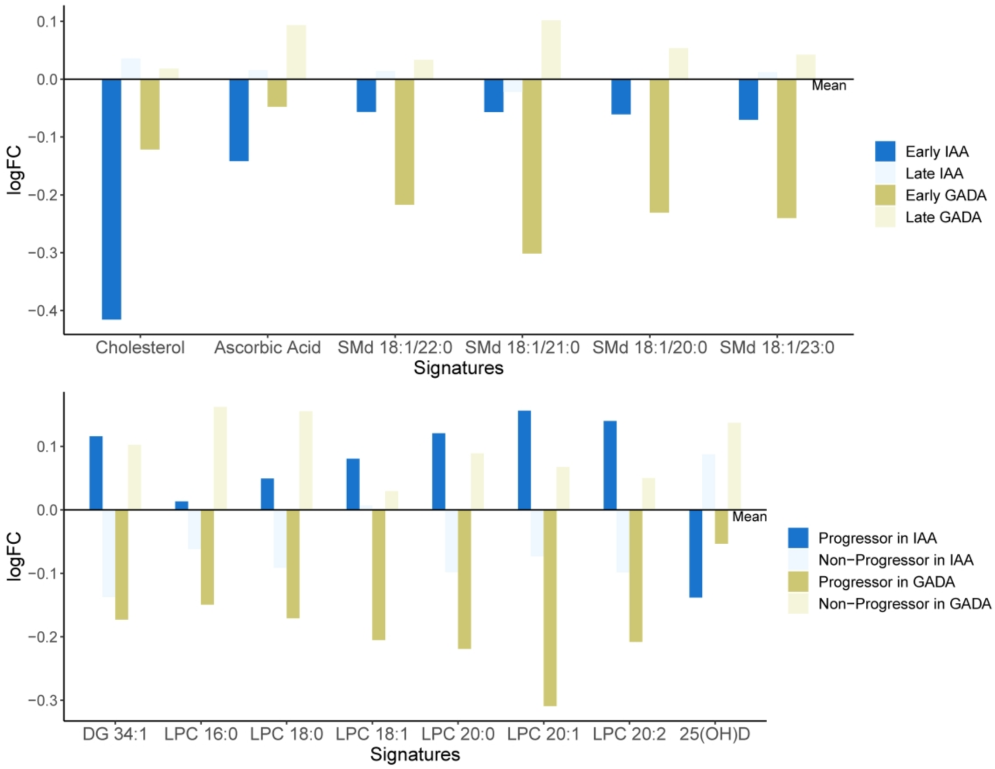


TEDDY study design and distribution of participants having nutrient biomarkers and lipidome measured.



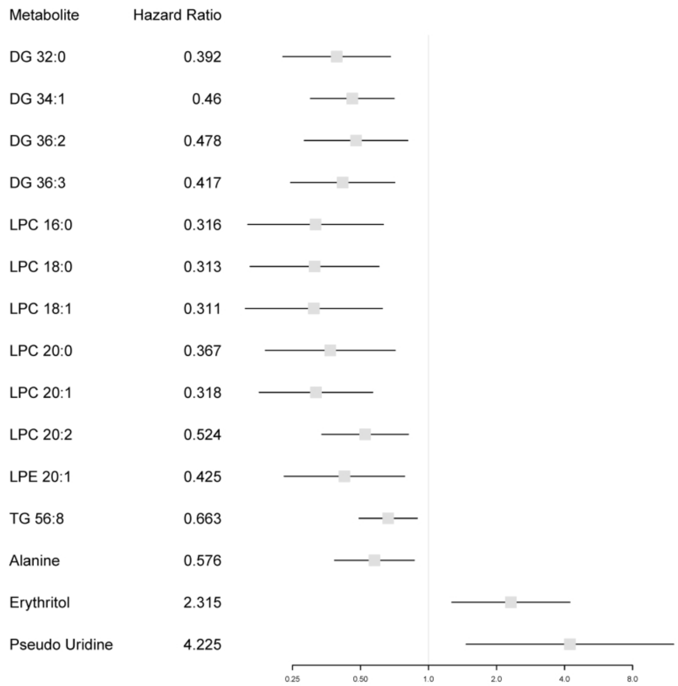
Clusters identified by temporal lipidomic profiles of 165 TEDDY children

558x508mm (300 x 300 DPI)



Metabolites and circulating vitamins preceding (a) early seroconversion or (b) further progression to T1D.

279x215mm (300 x 300 DPI)



Hazard ratio of metabolites associated with progression to T1D following GADA-first seroconversion.

279x215mm (300 x 300 DPI)

The TEDDY Study Group

Colorado Clinical Center: Marian Rewers, M.D., Ph.D., PI[1,4,5,6,9,10], Aaron Barbour, Kimberly Bautista[11], Judith Baxter[8,911], Daniel Felipe-Morales, Kimberly Driscoll, Ph.D.[8], Brigitte I. Frohnert, M.D.[2,13], Marisa Stahl, M.D.[12], Patricia Gesualdo[2,6,11,13], Michelle Hoffman[11,12,13], Rachel Karban[11], Edwin Liu, M.D.[12], Jill Norris, Ph.D.[2,3,11], Stesha Peacock, Hanan Shorrosh, Andrea Steck, M.D.[3,13], Megan Stern, Erica Villegas[2], Kathleen Waugh[6,7,11]. University of Colorado, Anschutz Medical Campus, Barbara Davis Center for Childhood Diabetes.

Finland Clinical Center: Jorma Toppari, M.D., Ph.D., PI[¥^1,4,10,13], Olli G. Simell, M.D., Ph.D., Annika Adamsson, Ph.D.[^11], Suvi Ahonen[*±§], Mari Åkerlund[*±§], Leena Hakola[*], Anne Hekkala, M.D.[μ¤], Henna Holappa[μ¤], Heikki Hyöty, M.D., Ph.D.[*±6], Anni Ikonen[μ¤], Jorma Ilonen, M.D., Ph.D.[¥¶3], Sinikka Jäminki[*±], Sanna Jokipuu[^], Leena Karlsson[^], Jukka Kero M.D., Ph.D.[¥^], Miia Kähönen[μ¤11,13], Mikael Knip, M.D., Ph.D.[*±5], Minna-Liisa Koivikko[μ¤], Merja Koskinen[*±], Mirva Koreasalo[*±§2], Kalle Kurppa, M.D., Ph.D.[*±12], Jarita Kytölä[*±], Jutta Laiho, Ph.D.[*6], Tiina Latva-aho[μ¤], Katri Lindfors, Ph.D.[*12], Maria Lönnrot, M.D., Ph.D.[*±6], Elina Mäntymäki[^], Markus Mattila[*], Maija Miettinen[§2], Katja Multasuo[μ¤], Teija Mykkänen[μ¤], Tiina Niininen[±*11], Sari Niinistö[±§2], Mia Nyblom[*±], Sami Oikarinen, Ph.D.[*±6], Paula Ollikainen[μ¤], Zhian Othmani[^], Sirpa Pohjola[μ¤], Petra Rajala[^], Jenna Rautanen[±§], Anne Riikonen[*±§2], Eija Riski[^], Miia Pekkola[*±], Minna Romo[^], Satu Ruohonen[^], Satu Simell, M.D., Ph.D.[¥12], Maija Sjöberg[^], Aino Stenius[μ¤11], Päivi Tossavainen, M.D.[μ¤], Mari Vähä-Mäkilä[¥], Sini Vainionpää[^], Eeva Varjonen[^11], Riitta Veijola, M.D., Ph.D.[μ¤13], Irene Viinikangas[μ¤], Suvi M. Virtanen, M.D., Ph.D.[*±§2]. [¥]University of Turku, [*]Tampere University, [μ]University of Oulu, [^]Turku University Hospital, Hospital District of Southwest Finland, [±]Tampere University Hospital, [¤]Oulu University Hospital, §National Institute for Health and Welfare, Finland, [¶]University of Kuopio.

Georgia/Florida Clinical Center: Jin-Xiong She, Ph.D., PI[1,3,4,10], Desmond Schatz, M.D.[*4,5,7,8], Diane Hopkins[11], Leigh Steed[11,12,13], Jennifer Bryant[11], Katherine Silvis[2], Michael Haller, M.D.[*13], Melissa Gardiner[11], Richard McIndoe, Ph.D., Ashok Sharma, Stephen W. Anderson, M.D.[^], Laura Jacobsen, M.D.[*13], John Marks, DHSc.[*11,13], P.D. Towe[*]. Center for Biotechnology and Genomic Medicine, Augusta University. [*]University of Florida, [^]Pediatric Endocrine Associates, Atlanta.

Germany Clinical Center: Anette G. Ziegler, M.D., PI[1,3,4,10], Ezio Bonifacio Ph.D.[*5], Cigdem Gezginci, Anja Heublein, Eva Hohoff[¥2], Sandra Hummel, Ph.D.[2], Annette Knopff[7], Charlotte Koch, Sibylle Koletzko, M.D.[¶12], Claudia Ramminger[11], Roswith Roth, Ph.D.[8], Jennifer Schmidt, Marlon Scholz, Joanna Stock[8,11,13], Katharina Warncke, M.D.[13], Lorena Wendel, Christiane Winkler, Ph.D.[2,11]. Forschergruppe Diabetes e.V. and Institute of Diabetes Research, Helmholtz Zentrum München, Forschergruppe Diabetes, and Klinikum rechts der Isar, Technische Universität München. [*]Center for Regenerative Therapies, TU Dresden, [¶]Dr. von Hauner Children's Hospital, Department of Gastroenterology, Ludwig Maximillians University Munich, [¥]University of Bonn, Department of Nutritional Epidemiology.

Sweden Clinical Center: Åke Lernmark, Ph.D., PI[1,3,4,5,6,8,9,10], Daniel Agardh, M.D., Ph.D.[6,12], Carin Andrén Aronsson, Ph.D.[2,11,12], Maria Ask, Rasmus Bennet, Corrado Cilio, Ph.D., M.D.[5,6], Susanne Dahlberg, Helene Engqvist, Emelie Ericson-Hallström, Annika Björne Fors, Lina Fransson, Thomas Gard, Monika Hansen, Hanna Jisser, Fredrik Johansen, Berglind Jonsdottir, M.D., Ph.D.[11], Helena Elding Larsson, M.D., Ph.D.[6,13], Marielle Lindström, Markus Lundgren, M.D., Ph.D.[13], Marlena Maziarz, Ph.D., Maria Månsson-Martinez, Jessica Melin[11], Zeliha Mestan, Caroline Nilsson, Karin Ottosson, Kobra Rahmati, Anita Ramelius, Falastin Salami, Anette Sjöberg, Birgitta Sjöberg, Carina Törn, Ph.D.[3], Åsa Wimar[13]. Lund University.

Washington Clinical Center: William A. Hagopian, M.D., Ph.D., PI[1,3,4,5,6,7,10,12,13], Michael Killian[6,7,11,12], Claire Cowen Crouch[11,13], Jennifer Skidmore[2], Masumeh Chavoshi, Arlene Meyer, Jocelyn Meyer, Denise Mulenga[11], Nole Powell, Jared Radtke, Matei Romancik, Shreya Roy, Davey Schmitt, Sarah Zink. Pacific Northwest Research Institute.

Pennsylvania Satellite Center: Dorothy Becker, M.D., Margaret Franciscus, MaryEllen Dalmagro-Elias Smith[2], Ashi Daftary, M.D., Mary Beth Klein, Chrystal Yates. Children's Hospital of Pittsburgh of UPMC.

Data Coordinating Center: Jeffrey P. Krischer, Ph.D.,PI[1,4,5,9,10], Sarah Austin-Gonzalez, Maryouri Avendano, Sandra Baethke, Brant Burkhardt, Ph.D.[5,6], Martha Butterworth[2], Joanna Clasen, David Cuthbertson, Christopher Eberhard, Steven Fiske[8], Jennifer Garmeson, Veena Gowda, Kathleen Heyman, Belinda Hsiao, Christina Karges, Francisco Perez Laras, Qian Li, Ph.D.[2,3,12], Shu Liu, Xiang Liu, Ph.D.[2,3,8,13], Kristian Lynch, Ph.D. [5,6,8], Jamie Malloy, Cristina McCarthy[11], Hemang Parikh, Ph.D.[3], Cassandra Remedios, Chris Shaffer, Laura Smith, Ph.D.[8,11], Susan Smith[11], Noah Sulman, Ph.D., Roy Tamura, Ph.D.[1,2,11,12,13], Dena Tewey, Michael Toth, Ulla Uusitalo, Ph.D.[2], Kendra Vehik, Ph.D.[4,5,6,8,13], Ponni Vijayakandipan, Jimin Yang, Ph.D., R.D.[2]. *Past staff: Michael Abbondondolo, Lori Ballard, Rasheedah Brown, Stephen Dankyi, David Hadley, Ph.D., Hye-Seung Lee, Ph.D., Colleen Maguire, Wendy McLeod, Aubrie Merrell, Steven Meulemans, Ryan Quigley.* University of South Florida.

Project scientist: Beena Akolkar, Ph.D.[1,3,4,5,6,7,9,10]. National Institutes of Diabetes and Digestive and Kidney Diseases.

Autoantibody Reference Laboratories: Liping Yu, M.D.^[5], Dongmei Miao, M.D.^, Polly Bingley, M.D., FRCP*[5], Alistair Williams*, Kyla Chandler*, Ilana Kelland*, Yassin Ben Khoud*, Huma Zahid*, Matthew Randell *. ^Barbara Davis Center for Childhood Diabetes, University of Colorado Denver, *Bristol Medical School, University of Bristol, UK.

HLA Reference Laboratory: William Hagopian[3], MD, PhD, Masumeh Chavoshi, Jared Radtke, Sarah Zink. Pacific Northwest Research Institute, Seattle WA. (Previously Henry Erlich, Ph.D.[3], Steven J. Mack, Ph.D., Anna Lisa Fear. Center for Genetics, Children's Hospital Oakland Research Institute.)

Metabolomics Laboratory: Oliver Fiehn, Ph.D., Bill Wikoff, Ph.D., Brian Defelice, Dmitry Grapov, Ph.D., Tobias Kind, Ph.D., Mine Palazoglu, Luis Valdiviez, Benjamin Wancewicz, Gert Wohlgemuth, Joyce Wong. UC Davis Metabolomics Center.

Repository: Sandra Ke, Niveen Mulholland, Ph.D. NIDDK Biosample Repository at Fisher BioServices.

Other contributors: Thomas Briese, Ph.D.[6], Columbia University. Suzanne Bennett Johnson, Ph.D.[8,11], Florida State University. Eric Triplett, Ph.D.[6], University of Florida.

Committees:
[1]Ancillary Studies, [2]Diet, [3]Genetics, [4]Human Subjects/Publicity/Publications, [5]Immune Markers, [6]Infectious Agents, [7]Laboratory Implementation, [8]Psychosocial, [9]Quality Assurance, [10]Steering, [11]Study Coordinators, [12]Celiac Disease, [13]Clinical Implementation.

S1. Lipidome differential abundance analysis: Cluster III-IV vs I-II at Visit -3

Compound	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	4.39E-09	0.75137
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	5.94E-13	0.693041
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	8.76E-06	0.742769
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.110328	0.917769
CE 22:6	VOEVEGPN	14274978	CC/C=C\C/(	0.001532	0.763868
Ceramide d	NAJHAHQN	52931115	CCCCCCCC(	0.039554	1.100939
Ceramide d	KEPQASGD	5283567	CCCCCCCC(	0.000528	1.141423
Ceramide d	ZJVVOYPTF	5283571	CCCCCCCC(	0.032614	1.073382
Ceramide d	VJSBNBBOS	5283568	CCCCCCCC(	0.889757	0.989796
Cer (d18:1/	YDNKGFDK	5283564	CCCCCCCC(	0.001	1.131904
Cholesterol	HVYWMON	5997	C[C@H](CC	0.38498	0.993437
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	2.72E-11	1.538416
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	1.28E-08	1.295189
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	1.52E-08	1.567162
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.532202	0.979919
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	9.24E-07	1.463127
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	1.55E-09	1.536843
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.000115	1.601475
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	4.52E-05	1.911112
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.773387	0.98579
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.21574	1.064225
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.854141	0.963199
FA 18:0	QIQXTHQID	5281	CCCCCCCC(	0.27671	1.074383
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.648159	1.059221
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.21505	1.072858
GlcCer d18:	YIGARKIIFO	6321359	CCCCCCCC(	0.900131	1.005879
GlcCer d18:	POQRWMR	6321361	CCCCCCCC(	0.889757	1.006896
GlcCer d18:	WBOZIXHP	6321360	CCCCCCCC(	0.239499	0.931431
LPC 18:0	IHNKQIMG'	497299	CCCCCCCC(	0.063141	1.110357
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.030279	1.116345
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	1.28E-05	1.312807
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.239499	1.067781
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.690852	1.032259
LPC 20:2	YYQVCMM	52924053	CCCCC/C=C	0.006069	1.166911
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.147429	1.147976
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	1.34E-08	1.489798
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.459218	0.9913
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.020825	1.136247
PC 16:0/16	KILNVBDSW	452110	CCCCCCCC(	2.95E-06	1.1481
PC 18:1/16	WTJKGGKO	5497103	CCCCCCCC(	0.510341	1.015283
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	6.99E-05	1.59087
PC 30:0	RFVFQQWK	129657	CCCCCCCC(	2.85E-06	1.429326
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.040921	1.144294
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	0.005063	1.204455
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	7.34E-05	1.33875
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	0.245764	1.089213
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	7.39E-09	1.287684
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.000619	1.039928
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.682969	0.975954
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	0.000167	1.198858

PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.1701	1.06482
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.002447	1.126559
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.001489	1.149403
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.204256	1.058696
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	3.56E-07	1.137051
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.106268	0.984382
PC 36:6	SPWBDEZM	52922847	CCCCC/C=C	0.021459	1.199528
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	1.17E-05	1.202419
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.931477	1.007105
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	1.74E-05	1.244065
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.000118	1.157204
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.891668	0.986946
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	3.82E-08	1.176849
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.599162	1.049834
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.006107	1.147644
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	0.122465	0.814687
PC 40:2	AEUCYCQY	24779063	CCCCCCCC/	0.000789	1.193451
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.002086	1.273798
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.000232	1.244977
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.614843	1.032369
PC 42:1	PAHPUCKP	24778881	CCCCCCCC(	0.001325	0.85131
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.121507	1.073896
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.278061	0.896171
PC 44:3	GZZUNXHF	52923541	CCCCCCCC(	0.306818	0.951613
PC 44:4	UIAAGLPOL	52923481	CCCCCCCC(	0.267869	1.049898
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	0.208447	0.953824
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	0.079467	0.930838
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	3.48E-06	0.813811
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.705037	0.984466
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.29515	1.048912
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.047857	1.120965
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.345429	1.038928
PE 34:2	HBZNVZIRJ	46891780	CCCCCCCC(	0.000764	1.354763
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	0.015182	1.17878
PE 36:3	GKAFCSRKI	71728379	CCCCCCCC/	0.158296	0.963803
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.000187	1.257664
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	1.73E-05	1.238737
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.002242	1.567292
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.038984	1.175365
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.003933	1.170119
Phosphatid	RYHJACYQT	52926457	CCCCCCCC(	0.044758	1.033086
Plasmenyl-I	IQACMFWA	6443157	CCCCCCCC(	0.001094	0.811781
Plasmenyl-I	JCIBOIAZHL	70698851	CCCCCC/C=	0.001532	0.879872
Plasmenyl-I	FHHVIBPVB	24779390	CCCCCCCC(	0.016582	1.160033
Plasmenyl-I	XVXISDREV	52925079	CCCCCCCC(	0.659617	1.026425
Plasmenyl-I	UUYSKERSK	52925126	CCCCCCCC(	0.001559	1.208821
Plasmenyl-I	RLLOITCRN	52925061	CCCCCCCC(	0.900131	0.98145
Plasmenyl-I	URPXXNCT	86289532	CCCCCCCC(	0.000941	1.220175
Plasmenyl-I	KCNBSSYOJ	52925089	CCCCCCCC(	0.010344	1.16687
Plasmenyl-I	WVGALBKS	5283497	CCCCCCCC(	0.064299	1.151726
Plasmenyl-I	CVCZYWPC	52925119	CCCCCCCC(	0.186277	1.143191
Plasmenyl-I	FIJFPUAJUE	42607458	CCCCCCCC(	0.046714	1.166424

PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.822245	0.995348
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.744213	0.996391
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.002393	1.111152
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.000204	1.050857
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	6.39E-05	1.086991
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.604812	1.024013
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	1.38E-06	1.194458
PS 42:8	ROCNHMA:	52925757	CCCCC/C=C	0.016763	1.156969
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.52985	0.975875
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.000682	1.187239
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.545386	1.034211
SM d16:1/2	LKQLRGMN	6453725	CCCCCCCC(	1.63E-06	1.192861
SM d16:1/2	NBEADXWA	6443882	CCCCCCCC(	5.26E-05	1.157524
SM d18:1/1	KYICBZWZC	11433862	CCCCCCCC(	4.72E-06	1.318584
SM d18:1/1	RWKUXQNI	9939941	CCCCCCCC(	0.003492	1.06552
SM d18:1/1	YLWSJLLZU	52931235	CCCCCCCC(	0.003165	1.085097
SM d18:1/2	AADLTHQN	44260124	CCCCCCCC(	0.000378	1.157267
SM (d18:1/	MDRFMTLY	52931179	CCCCCCCC(	0.03259	1.073777
SM d18:1/2	YXSZOBWV	52931193	CCCCCCCC(	0.005271	1.185417
SM d18:1/2	FJJANLYCZU	44260125	CCCCCCCC(	0.239499	1.038936
SM d18:1/2	SXZWBNWT	46891684	CCCCCCCC(	0.379458	1.041124
SM d18:1/2	QEDPUVGS	44260127	CCCCCCCC(	0.939645	1.003722
SM d18:2/2	JBDGKEXQK	52931209	CCCCCCCC(	0.52985	1.028844
SM d18:2/2	DACOGJME	52931217	CCCCCCCC(	0.326514	0.954436
SM (d18:2/	TXFLWJQV(	52931215	CCCCCCCC/	0.854141	0.993043
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	8.26E-12	4.608674
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	3.68E-14	5.458299
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	7.77E-14	3.167979
TG 46:1	RSDIQTNCD	56936558	CCCCCCCC(	1.14E-13	4.279262
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	2.68E-14	4.559742
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	1.12E-15	3.958115
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	3.32E-11	2.07289
TG 48:1	FEKLSEFRU	9543986	CCCCCCCC(	1.77E-15	2.522005
TG 48:2	RUOVJPPU)	9543987	CCCCCCCC(	4.86E-16	3.241376
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	1.61E-14	3.991588
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	1.03E-11	2.658089
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	6.18E-14	2.916437
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	5.18E-15	2.526939
TG 50:0	QRJMBNGC	3246958	[2H]C([2H])	8.90E-13	2.996094
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	1.79E-12	1.556498
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	3.08E-16	1.639809
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	4.20E-20	2.383584
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	3.60E-18	2.771783
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	3.60E-18	2.775953
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	1.61E-14	2.902122
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	8.11E-14	2.205386
TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	6.46E-20	2.140056
TG 51:4	IIRQXNVLA)	9544052	CCCCCCCC/	3.56E-20	2.314796
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	7.44E-11	2.92463
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	3.28E-16	2.852622
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	1.54E-06	1.15934
TG 52:4	WHSWXEY\	25240364	CCCCCCCC/	1.48E-10	1.588669

TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	2.57E-09	1.814894
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	3.46E-11	2.052724
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	1.58E-12	3.161209
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	3.08E-14	2.0061
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCCC/	2.14E-17	2.133285
TG 53:4	BMSDHYZL(	9544152	CCCCCCCC/	3.08E-18	1.855889
TG 53:5	QHYAATSKY	9544183	CCCCCCC/C	3.38E-13	2.084983
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	1.02E-06	1.718828
TG 54:1	YFFIQXNTT'	16058371	CCCCCCCC(	4.86E-16	3.466638
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	7.34E-16	2.360601
TG 54:3	PHYFQTYBJ	5497163	CCCCCCCC/	1.08E-09	1.41406
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	1.56E-06	1.418404
TG 54:5	VVEBTVMJI	25240373	CCCCCCCC/	8.94E-10	1.696558
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	8.03E-08	1.972463
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.001159	1.635533
TG 56:1	OCYFAHIHV	9544345	CCCCCCCC(	7.77E-14	2.688962
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	8.94E-14	2.60813
TG 56:3	QXMHHXQ	9544447	CCCCCCCC/	1.51E-10	2.082477
TG 56:4	YONCDTJKI	25240379	CCCCCCCC/	4.43E-05	1.61151
TG 56:5	UHEJWASO	25240380	CCCCCCCC/	6.11E-05	1.520603
TG 56:6	ZTNDRFCAE	9544625	CCCCC/C=C	0.197245	1.136074
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	1.56E-07	1.588702
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	1.17E-05	1.764582
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	4.85E-10	2.109749
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	5.25E-11	2.161522
TG 58:3	RFMSTHTU	9544748	CCCCCCCC/	2.03E-11	2.365491
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	2.86E-09	2.135111
TG 58:6	GSNFRUMS	9544977	CCCCCCCC/	7.34E-16	2.272505
TG 58:8	KWIGMCRV	9545124	CCCCCCCC(	1.74E-05	1.581893
TG 58:9	RVXFSLZMZ	9545200	CCCCCCCC/	2.03E-07	1.795798
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	4.09E-11	1.857481
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.000838	1.483517
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	5.15E-09	1.987051
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	1.68E-06	1.540777

S2. Lipidome differential abundance analysis: Clusters III-IV vs I-II at Visit -6

Compound Na	InChiKeys	Pubchem II	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	7.90E-06	0.772319
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	7.37E-07	0.704609
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	1.27E-08	0.660296
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.592621	0.962253
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	0.016991	0.800401
Ceramide d18	NAJHAHQN	52931115	CCCCCCCC(	0.813017	1.011932
Ceramide d40	KEPQASGD	5283567	CCCCCCCC(	0.013288	1.102974
Ceramide d42	ZJVVOYPTF	5283571	CCCCCCCC(	0.239809	1.045112
Ceramide d42	VJSBNBBOS	5283568	CCCCCCCC(	0.904742	0.993306
Cer (d18:1/16	YDNKGFDK	5283564	CCCCCCCC(	0.260395	1.047674
Cholesterol	HVYWMOM	5997	C[C@H](CC	0.182963	0.989292
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	5.34E-07	1.435697
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	4.24E-05	1.267374
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	2.29E-06	1.472847
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.260395	1.045987
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.001864	1.257284
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	0.000142	1.307094
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.476711	1.107565
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.003133	1.677244
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.888956	0.993078
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.743592	0.98096
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.757266	0.947691
FA 18:0	QIQXTHQID	5281	CCCCCCCC(	0.602401	1.04074
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.526121	0.923843
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.349628	1.068603
GlcCer d18:1/	YIGARKIIFO	6321359	CCCCCCCC(	0.695493	1.018783
GlcCer d18:1/	POQRWMR	6321361	CCCCCCCC(	0.925936	0.996413
GlcCer d18:1/	WBOZIXHP	6321360	CCCCCCCC(	0.148708	0.915453
LPC 18:0	IHNKQIMG	497299	CCCCCCCC(	0.016043	1.160414
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.204669	1.075794
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.006163	1.204312
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.402435	1.058512
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.304444	1.081791
LPC 20:2	YYQVCMM	52924053	CCCCC/C=C	0.004003	1.217272
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.73157	1.034165
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.005547	1.263206
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.887424	0.998211
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.34121	1.061934
PC 16:0/16:0	KILNVBDSW	452110	CCCCCCCC(	0.005547	1.101663
PC 18:1/16:0	WTJKGGKO	5497103	CCCCCCCC(	0.035651	0.950224
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.015226	1.345779
PC 30:0	RFVFQQWK	129657	CCCCCCCC(	0.005253	1.25748
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.461017	0.948107
PC 32:2	GPWHCUUI	24778764	CCCCCC/C=	0.800209	1.019879
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.001797	1.272563
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	0.51772	0.950593
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	1.24E-06	1.296864
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.90403	0.998327
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.005414	0.838673
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	0.075268	1.092653

PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.028751	1.142851
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.453142	1.040944
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.000603	1.060113
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.453791	1.028753
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.00082	1.084721
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.676473	1.006939
PC 36:6	SPWBDEZN	52922847	CCCCC/C=C	0.785197	1.027905
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.077009	1.092132
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.162819	1.127304
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	2.78E-06	1.28661
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.000807	1.161885
PC 38:3	OJHJKEBRZ!	52922741	CCCCCCCC/	0.417097	1.087069
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	3.07E-06	1.17167
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.695493	0.958598
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.038062	1.116069
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	0.22813	0.839644
PC 40:2	AEUCYCQY,	24779063	CCCCCCCC/	0.000576	1.226207
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.008531	1.225614
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.000147	1.282056
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.582256	0.964728
PC 42:1	PAHPUCKP'	24778881	CCCCCCCC(	1.23E-05	0.804014
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.346309	1.04663
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.198476	0.866062
PC 44:3	GZZUNXHF.	52923541	CCCCCCCC(	0.370821	0.953177
PC 44:4	UIAAGLPOI	52923481	CCCCCCCC(	0.417097	1.039343
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	0.053368	0.927781
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	0.003214	0.882673
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	3.52E-07	0.761345
PC p36:3	SOUZQPFU.	53481701	CCCCCCCC(	0.622977	0.980083
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.557393	1.031923
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.293972	1.076388
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.582256	1.023703
PE 34:2	HBZNVZIRJ'	46891780	CCCCCCCC(	0.204669	1.149493
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	0.729816	1.02908
PE 36:3	GKAFCSRKI	71728379	CCCCCCCC/	0.982602	0.99934
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.029809	1.170159
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	0.013092	1.136971
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.000831	1.311241
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.053539	1.167597
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.025039	1.125047
Phosphatidylg	RYHJACYQT	52926457	CCCCCCCC(	0.90403	0.998178
Plasmenyl-PC	IQACMFWA	6443157	CCCCCCCC(	1.47E-06	0.736259
Plasmenyl-PC	JCIBOIAZHL	70698851	CCCCCC/C=	6.18E-06	0.803494
Plasmenyl-PC	FHHVIBPVB	24779390	CCCCCCCC(	0.013523	1.15635
Plasmenyl-PE	XVXISDREV	52925079	CCCCCCCC(	0.145402	0.914884
Plasmenyl-PE	UUYSKERSK	52925126	CCCCCCCC(	0.053539	1.146846
Plasmenyl-PE	RLLOITCRN	52925061	CCCCCCCC(	0.406449	0.882378
Plasmenyl-PE	URPXXNCT)	86289532	CCCCCCCC(	0.053539	1.142125
Plasmenyl-PE	KCNBSSYOJ	52925089	CCCCCCCC(	0.012579	1.19191
Plasmenyl-PE	WVGALBKS	5283497	CCCCCCCC(	0.075193	1.155027
Plasmenyl-PE	CVCZYWPC	52925119	CCCCCCCC(	0.31359	1.116817
Plasmenyl-PE	FIJFPUAJUI	42607458	CCCCCCCC(	0.024805	1.195181

PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.024805	0.958439
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.808517	0.997481
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.556898	1.027874
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.002941	1.042086
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.003203	1.114676
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.139372	1.078042
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	1.11E-06	1.21493
PS 42:8	ROCNHMA:	52925757	CCCCC/C=C	0.018367	1.178071
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.808471	0.987405
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.008819	1.138058
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.644787	1.027784
SM d16:1/20:(	LKQLRGMN	6453725	CCCCCCCC(	3.42E-05	1.190051
SM d16:1/20::	NBEADXWA	6443882	CCCCCCCC(	0.008819	1.104084
SM d18:1/14:(	KYICBZWZC	11433862	CCCCCCCC(	4.80E-05	1.268406
SM d18:1/16:(	RWKUXQNI	9939941	CCCCCCCC(	0.106434	1.036458
SM d18:1/16::	YLWSJLLZU	52931235	CCCCCCCC(	0.084102	1.050291
SM d18:1/20:(	AADLTHQN	44260124	CCCCCCCC(	8.87E-05	1.168119
SM (d18:1/20	MDRFMTLY	52931179	CCCCCCCC(	0.107442	1.05587
SM d18:1/21:(	YXSZOBWV	52931193	CCCCCCCC(	0.04626	1.120596
SM d18:1/22:(	FJJANLYCZU	44260125	CCCCCCCC(	0.555508	1.019012
SM d18:1/23:(	SXZWBNWT	46891684	CCCCCCCC(	0.277222	0.950146
SM d18:1/24:(	QEDPUVGS	44260127	CCCCCCCC(	0.62046	0.982326
SM d18:2/23:(	JBDGKEXQK	52931209	CCCCCCCC(	0.218894	0.949569
SM d18:2/24:(	DACOGJME	52931217	CCCCCCCC(	0.10105	0.930055
SM (d18:2/24	TXFLWJQV(	52931215	CCCCCCC/	0.384679	0.968769
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	5.27E-08	4.085405
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	1.27E-08	4.478217
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	2.28E-07	2.594801
TG 46:1	RSDIQTNCD	56936558	CCCCCCCC(	1.92E-08	3.420166
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	1.26E-09	3.810371
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	1.26E-09	3.359684
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	1.36E-05	1.724092
TG 48:1	FEKLSEFRU(	9543986	CCCCCCCC(	6.67E-08	2.08152
TG 48:2	RUOVJPPU)	9543987	CCCCCCCC(	1.27E-08	2.576339
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	2.11E-09	3.259001
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	1.82E-05	2.043826
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	6.69E-06	2.096691
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	1.69E-06	1.913353
TG 50:0	QRJMBNGG	3246958	[2H]C([2H])	3.80E-07	2.490418
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	8.03E-07	1.380022
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	1.19E-07	1.412852
TG 50:3	UFHNZOAC	25240357	CCCCCCC/	1.26E-09	1.944126
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	1.26E-09	2.261952
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	1.47E-07	2.120645
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	1.35E-06	2.20325
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	2.00E-05	1.688369
TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	1.46E-07	1.675631
TG 51:4	IIRQXNVLA)	9544052	CCCCCCC/	1.29E-08	1.862196
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	5.27E-08	2.961686
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	1.27E-08	2.342822
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.001798	1.102208
TG 52:4	WHSWXEYY	25240364	CCCCCCC/	1.24E-06	1.40384

TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.002297	1.446108
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	1.96E-06	1.876186
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	4.36E-07	2.574173
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	0.0001	1.633555
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCC/	3.88E-07	1.674987
TG 53:4	BMSDHYZL(	9544152	CCCCCCC/	2.76E-07	1.554978
TG 53:5	QHYAATSK'	9544183	CCCCCC/C	7.31E-07	1.843477
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	4.03E-05	1.706099
TG 54:1	YFFIQXNTT'	16058371	CCCCCCCC(	2.43E-08	2.782084
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	4.48E-08	1.948152
TG 54:3	PHYFQTYBJ	5497163	CCCCCCC/	6.18E-06	1.325279
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	0.002297	1.285794
TG 54:5	VVEBTVMJI	25240373	CCCCCCC/	4.03E-05	1.421759
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.001072	1.611801
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.024486	1.42419
TG 56:1	OCYFAHIHV	9544345	CCCCCCCC(	3.26E-06	2.095931
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	2.78E-06	2.114167
TG 56:3	QXMHHXQ	9544447	CCCCCCC/	4.00E-05	1.733719
TG 56:4	YONCDTJKI:	25240379	CCCCCCC/	0.01165	1.33534
TG 56:5	UHEJWASO	25240380	CCCCCCC/	2.32E-05	1.53088
TG 56:6	ZTNDRFCAI	9544625	CCCCC/C=C	0.90403	1.012979
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	7.37E-07	1.554752
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	1.95E-07	1.994256
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	0.000421	1.619062
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	4.43E-05	1.727571
TG 58:3	RFMSTHTU	9544748	CCCCCCC/	1.99E-05	1.944719
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	3.12E-05	1.792646
TG 58:6	GSNFRUMS	9544977	CCCCCCC/	1.11E-06	1.762502
TG 58:8	KWIGMCRV	9545124	CCCCCCCC(	5.87E-05	1.547059
TG 58:9	RVXFSLZMZ	9545200	CCCCCCC/	1.24E-06	1.724265
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	0.002452	1.457369
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.000224	1.525376
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	0.011833	1.421467
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	0.067587	1.219911

S3. Lipidome differential abundance analysis: Cluster II vs I at Visit -3

Compound Name	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	0.016764	0.879489
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	0.028446	1.129656
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	7.12E-09	0.669618
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	7.54E-05	0.782046
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	0.827243	0.973267
Ceramide d18:1/23	NAJHAHQN	52931115	CCCCCCCC(	8.64E-06	0.783512
Ceramide d40:1	KEPQASGD	5283567	CCCCCCCC(	0.000233	0.832545
Ceramide d42:1	ZJVVOYPTF	5283571	CCCCCCCC(	0.339109	0.954667
Ceramide d42:2	VJSBNBBOS	5283568	CCCCCCCC(	6.60E-05	0.754069
Cer (d18:1/16:0)	YDNKGFDK	5283564	CCCCCCCC(	0.000656	0.850138
Cholesterol	HVYWMON	5997	C[C@H](CC	0.093216	1.017346
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	0.001006	0.780218
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.252787	0.942376
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	0.134347	0.852051
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.459945	1.029306
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.180117	0.872144
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	0.218082	1.120076
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.29057	0.80272
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.973673	1.009052
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.987543	0.99885
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.922319	0.992517
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.946849	1.021743
FA 18:0	QIQXTHQIE	5281	CCCCCCCC(	0.841441	1.020697
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.856769	1.033207
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.100705	1.124102
GlcCer d18:1/22:0	YIGARKIIFO	6321359	CCCCCCCC(	0.015533	0.88006
GlcCer d18:1/24:0	POQRWMR	6321361	CCCCCCCC(	0.037719	0.893995
GlcCer d18:1/24:1	WBOZIXHP	6321360	CCCCCCCC(	0.00032	0.791742
LPC 18:0	IHNKQIMG	497299	CCCCCCCC(	0.708438	0.969833
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.134347	0.905012
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.578314	0.951046
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.16081	1.100605
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.51764	1.063816
LPC 20:2	YYQVCMM	52924053	CCCCC/C=C	0.346061	1.072982
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.037346	0.739125
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.175005	0.877558
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.628056	0.991525
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.506626	0.947488
PC 16:0/16:0	KILNVBDSW	452110	CCCCCCCC(	3.26E-09	0.800338
PC 18:1/16:0	WTJKGGKO	5497103	CCCCCCCC(	5.54E-06	0.872222
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	2.18E-08	0.410256
PC 30:0	RFVFQQWK	129657	CCCCCCCC(	1.12E-11	0.497244
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	9.95E-10	0.589645
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	5.57E-07	0.671623
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	2.26E-10	0.530681
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	1.67E-12	0.549168
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	2.67E-09	0.729062
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.011919	0.960998
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	1.17E-07	0.716099
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	8.45E-09	0.712487

PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	5.57E-07	0.767793
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	2.26E-10	0.726244
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.011143	0.829745
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.000702	0.826459
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.000165	0.870143
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.110868	1.019238
PC 36:6	SPWBDEZN	52922847	CCCCC/C=C	1.25E-08	0.570562
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	8.05E-09	0.743345
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.004941	0.785523
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	2.83E-08	0.707237
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	2.88E-09	0.755453
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.005301	0.799102
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.000578	0.875542
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	2.74E-06	0.604539
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.007953	0.847891
PC 38:8	QQNHCRBC	52922865	CC/C=C\C/(	8.45E-09	0.408655
PC 40:2	AEUCYCQY/	24779063	CCCCCCCC/	4.41E-05	0.760692
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.002212	0.736816
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.000103	0.730511
PC 40:7	BPUROMFC	24778982	CCCCC/C=C	0.035524	0.857048
PC 42:1	PAHPUCKP	24778881	CCCCCCCC(	0.973673	0.996397
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.533103	1.040342
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	2.40E-06	0.579764
PC 44:3	GZZUNXHF	52923541	CCCCCCCC(	0.002893	0.839673
PC 44:4	UIAAGLPOL	52923481	CCCCCCCC(	0.841441	1.012534
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	0.030578	0.905075
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	6.25E-05	0.814452
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	0.059135	0.898134
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.00452	0.863708
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.01222	0.865207
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.000671	0.771654
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.216561	0.940131
PE 34:2	HBZNVZIRJ	46891780	CCCCCCCC(	0.005372	0.716345
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	4.38E-10	0.619251
PE 36:3	GKAFCSRKI	71728379	CCCCCCCC/	0.856769	0.992141
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.00232	0.773702
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	2.40E-11	0.667505
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.228638	0.736067
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.004499	0.757216
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.002893	0.816993
Phosphatidylglycer	RYHJACYQT	52926457	CCCCCCCC(	0.25202	1.025351
Plasmenyl-PC 34:2	IQACMFWA	6443157	CCCCCCCC(	0.626602	0.953596
Plasmenyl-PC 36:6	JCIBOIAZHL	70698851	CCCCCC/C=	0.000428	0.838361
Plasmenyl-PC 38:5	FHHVIBPVE	24779390	CCCCCCCC(	0.000111	0.740084
Plasmenyl-PE 36:3	XVXISDREV	52925079	CCCCCCCC(	0.000695	0.782141
Plasmenyl-PE 36:5	UUYSKERSK	52925126	CCCCCCCC(	0.001838	0.791826
Plasmenyl-PE 36:6	RLLOITCRN	52925061	CCCCCCCC(	1.78E-05	0.49585
Plasmenyl-PE 38:5	URPXXNCT	86289532	CCCCCCCC(	3.49E-05	0.761787
Plasmenyl-PE 38:6	KCNBSSYOJ	52925089	CCCCCCCC(	0.03863	0.865823
Plasmenyl-PE 38:7	WVGALBKS	5283497	CCCCCCCC(	0.012961	0.812022
Plasmenyl-PE 40:6	CVCZYWPC	52925119	CCCCCCCC(	0.005339	0.703702
Plasmenyl-PE 40:7	FIJFPUAJUD	42607458	CCCCCCCC(	0.00018	0.729175

PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.000869	0.918083
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.996965	1.000047
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	1.88E-08	0.778701
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.020074	0.956232
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.006218	0.925916
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	3.38E-05	0.80185
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	0.03877	0.907646
PS 42:8	ROCNHMA:	52925757	CCCCC/C=C	0.039517	0.880565
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.210179	0.97855
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	6.95E-10	0.665254
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.098143	0.903841
SM d16:1/20:0	LKQLRGMN	6453725	CCCCCCCC(	2.29E-07	0.794908
SM d16:1/20:1	NBEADXWA	6443882	CCCCCCCC(	2.42E-07	0.803857
SM d18:1/14:0	KYICBZWZC	11433862	CCCCCCCC(	9.30E-08	0.645479
SM d18:1/16:0	RWKUXQNI	9939941	CCCCCCCC(	1.48E-05	0.883546
SM d18:1/16:1	YLWSJLLZU	52931235	CCCCCCCC(	1.33E-05	0.86112
SM d18:1/20:0	AADLTHQN	44260124	CCCCCCCC(	1.56E-05	0.795163
SM (d18:1/20:1)	MDRFMTLY	52931179	CCCCCCCC(	0.000112	0.854348
SM d18:1/21:0	YXSZOBWV	52931193	CCCCCCCC(	8.96E-07	0.681675
SM d18:1/22:0	FJJANLYCZU	44260125	CCCCCCCC(	0.030684	0.913782
SM d18:1/23:0	SXZWBNWT	46891684	CCCCCCCC(	1.46E-06	0.792221
SM d18:1/24:0	QEDPUVGS	44260127	CCCCCCCC(	0.841441	1.016878
SM d18:2/23:0	JBDGKEXQK	52931209	CCCCCCCC(	3.07E-12	0.720783
SM d18:2/24:0	DACOGJME	52931217	CCCCCCCC(	0.00351	0.858531
SM (d18:2/24:1)	TXFLWJQV(	52931215	CCCCCCC/	2.15E-05	0.854614
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	2.15E-05	0.316805
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	2.40E-06	0.280122
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	1.13E-07	0.353046
TG 46:1	RSDIQTNCD	56936558	CCCCCCCC(	4.81E-06	0.31546
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	0.00018	0.410531
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	5.65E-05	0.456498
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	1.49E-05	0.534723
TG 48:1	FEKLSEFRU(	9543986	CCCCCCCC(	5.56E-07	0.464367
TG 48:2	RUOVJPPU:	9543987	CCCCCCCC(	1.46E-06	0.421898
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	0.003576	0.546875
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	1.41E-09	0.366346
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	2.47E-11	0.322813
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	3.07E-12	0.384357
TG 50:0	QRJMBNGG	3246958	[2H]C([2H])	4.65E-05	0.449577
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	0.000826	0.740835
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	0.000966	0.761313
TG 50:3	UFHNZOAC	25240357	CCCCCCC/	0.004713	0.731599
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	0.004522	0.700066
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	0.009552	0.719996
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	1.41E-09	0.362155
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	9.33E-10	0.452964
TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	1.58E-07	0.618763
TG 51:4	IIRQXNVLA:	9544052	CCCCCCC/	2.00E-05	0.650398
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	0.001007	0.534072
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	0.000125	0.532181
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.158367	0.934337
TG 52:4	WHSWXEY\	25240364	CCCCCCC/	0.926481	1.010811

TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.841441	0.968829
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	4.82E-06	0.582144
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	3.71E-07	0.355708
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	1.21E-07	0.554688
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCC/	1.56E-05	0.620427
TG 53:4	BMSDHYZL(	9544152	CCCCCCC/	0.000719	0.759466
TG 53:5	QHYAATSK'	9544183	CCCCCC/C	0.03877	0.790022
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	0.110868	0.808225
TG 54:1	YFFIQXNTT'	16058371	CCCCCCCC(	0.00031	0.520301
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	0.003811	0.673609
TG 54:3	PHYFQTYBJ	5497163	CCCCCCC/	0.619861	1.043373
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	0.087893	1.183123
TG 54:5	VVEBTVMJI	25240373	CCCCCCC/	0.253218	1.144303
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.103198	1.318936
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.129439	0.75154
TG 56:1	OCYFAHIHV	9544345	CCCCCCCC(	0.012614	0.666726
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	0.156953	0.810185
TG 56:3	QXMHHXQ	9544447	CCCCCCC/	0.17857	0.820229
TG 56:4	YONCDTJKI.	25240379	CCCCCCC/	0.035524	1.372494
TG 56:5	UHEJWASO	25240380	CCCCCCC/	0.850719	0.967437
TG 56:6	ZTNDRFCAI	9544625	CCCCC/C=C	0.003811	0.732942
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	0.038323	0.79291
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	0.742322	0.937541
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	0.004437	0.685921
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	0.514376	0.907156
TG 58:3	RFMSTHTU	9544748	CCCCCCC/	0.841609	0.967022
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	0.708438	0.941601
TG 58:6	GSNFRUMS	9544977	CCCCCCC/	0.000125	0.629132
TG 58:8	KWIGMCRV	9545124	CCCCCCCC(	0.29057	0.865204
TG 58:9	RVXFSLZMZ	9545200	CCCCCCC/	0.637884	0.931976
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	0.003576	0.71895
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.0255	0.726909
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	0.613855	0.916811
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	0.000732	0.669517

S4. Lipidome differential abundance analysis: Cluster II vs I at Visit -6

Compound Name	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	0.036617	0.849871
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	0.285244	0.903377
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	0.001221	0.741456
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.012325	0.778534
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	0.05687	0.775108
Ceramide d18:1/23:0	NAJHAHQN	52931115	CCCCCCCC(	0.07448	0.875606
Ceramide d40:1	KEPQASGD	5283567	CCCCCCCC(	0.912796	0.988613
Ceramide d42:1	ZJVVOYPTF	5283571	CCCCCCCC(	0.926176	1.00869
Ceramide d42:2	VJSBNBBOS	5283568	CCCCCCCC(	0.318108	0.922811
Cer (d18:1/16:0)	YDNKGFDK	5283564	CCCCCCCC(	0.787339	0.977626
Cholesterol	HVYWMON	5997	C[C@H](CC	0.131726	1.021012
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	0.912796	1.018229
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.949806	0.992424
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	0.973098	1.007226
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.565923	0.958589
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.926176	1.015418
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	0.1639	1.177581
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.947868	0.990033
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.620779	1.212549
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.877799	0.985478
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.481913	1.072449
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.314694	1.312824
FA 18:0	QIQXTHQID	5281	CCCCCCCC(	0.427385	1.111632
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.231618	1.256797
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.342926	1.11731
GlcCer d18:1/22:0	YIGARKIIFO	6321359	CCCCCCCC(	0.713641	0.97142
GlcCer d18:1/24:0	POQRWMR	6321361	CCCCCCCC(	0.333725	0.941838
GlcCer d18:1/24:1	WBOZIXHPI	6321360	CCCCCCCC(	0.166955	0.898661
LPC 18:0	IHNKQIMG'	497299	CCCCCCCC(	0.587976	1.072826
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.894283	1.01922
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.737538	1.045725
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.036617	1.240552
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.138713	1.196326
LPC 20:2	YYQVCMM	52924053	CCCCC/C=C	0.28386	1.141945
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.595521	0.912003
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.216983	1.196738
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.81908	1.006075
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.492142	1.078532
PC 16:0/16:0	KILNVBDSW	452110	CCCCCCCC(	0.255426	0.938166
PC 18:1/16:0	WTJKGGKO	5497103	CCCCCCCC(	0.079507	0.92546
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.042046	0.653448
PC 30:0	RFVFQQWK	129657	CCCCCCCC(	0.005784	0.699133
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.005165	0.739979
PC 32:2	GPWHCUUI	24778764	CCCCCC/C=	0.022679	0.781243
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.003758	0.703087
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	0.000815	0.692784
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	0.182231	0.901456
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.497121	0.984281
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.012325	0.799153
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	0.01203	0.829336

PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.096632	0.834658
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.131726	0.886024
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.663186	0.983866
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.21907	0.929828
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.052211	0.916757
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.528527	0.97855
PC 36:6	SPWBDEZN	52922847	CCCCC/C=C	0.004327	0.644394
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.072208	0.859841
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.022787	0.745374
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	0.008749	0.800503
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.151234	0.902563
PC 38:3	OJHJKEBRZ:	52922741	CCCCCCCC/	0.060703	0.766782
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.285244	0.939951
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.010195	0.687306
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.166955	0.885655
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	0.00038	0.47281
PC 40:2	AEUCYCQY/	24779063	CCCCCCCC/	0.285244	0.901388
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.183458	0.85124
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.05687	0.827615
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.52391	0.931221
PC 42:1	PAHPUCKP'	24778881	CCCCCCCC(	0.877799	0.980111
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.481913	1.055839
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.122194	0.745424
PC 44:3	GZZUNXHF:	52923541	CCCCCCCC(	0.285244	0.923126
PC 44:4	UIAAGLPOL	52923481	CCCCCCCC(	0.65345	1.036835
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	0.817596	0.981439
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	0.083147	0.890737
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	0.682928	0.961115
PC p36:3	SOUZQPFU.	53481701	CCCCCCCC(	0.175834	0.916101
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.285244	0.912817
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.170634	0.854914
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.995255	1.000589
PE 34:2	HBZNVZIRJ'	46891780	CCCCCCCC(	0.850368	0.95179
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	0.00038	0.69152
PE 36:3	GKAFCSRKN	71728379	CCCCCCCC/	0.73538	0.978799
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.44991	0.904108
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	0.005165	0.803061
PE 38:4	ANRKEHNW	46891781	CCCCCCCC(	0.912796	0.974887
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.1639	0.8248
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.216647	0.892963
Phosphatidylglycerol	RYHJACYQT	52926457	CCCCCCCC(	0.861125	1.006687
Plasmenyl-PC 34:2	IQACMFWA	6443157	CCCCCCCC(	0.469004	1.089305
Plasmenyl-PC 36:6	JCIBOIAZHL	70698851	CCCCCC/C=	0.560197	0.950018
Plasmenyl-PC 38:5	FHHVIBPVB	24779390	CCCCCCCC(	0.05687	0.837974
Plasmenyl-PE 36:3	XVXISDREV	52925079	CCCCCCCC(	0.570073	0.939454
Plasmenyl-PE 36:5	UUYSKERSK	52925126	CCCCCCCC(	0.926176	0.983596
Plasmenyl-PE 36:6	RLLOITCRN	52925061	CCCCCCCC(	0.096645	0.700975
Plasmenyl-PE 38:5	URPXXNCT)	86289532	CCCCCCCC(	0.973098	1.006795
Plasmenyl-PE 38:6	KCNBSSYOJ	52925089	CCCCCCCC(	0.392306	1.100938
Plasmenyl-PE 38:7	WVGALBKS	5283497	CCCCCCCC(	0.995255	0.999161
Plasmenyl-PE 40:6	CVCZYWPC	52925119	CCCCCCCC(	0.393372	0.875785
Plasmenyl-PE 40:7	FIJFPUAJUD	42607458	CCCCCCCC(	0.285244	0.884224

PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.05687	0.938175
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.518723	0.987708
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.285244	0.924442
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.973098	0.99844
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.285244	0.944732
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.09647	0.873078
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	0.478197	0.946087
PS 42:8	ROCNHMA;	52925757	CCCCC/C=C	0.381665	0.924368
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.728141	1.032216
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.000484	0.774256
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.850368	0.977276
SM d16:1/20:0	LKQLRGMN	6453725	CCCCCCCC(	0.005165	0.85368
SM d16:1/20:1	NBEADXWA	6443882	CCCCCCCC(	0.01967	0.882164
SM d18:1/14:0	KYICBZWZC	11433862	CCCCCCCC(	0.01203	0.788302
SM d18:1/16:0	RWKUXQNI	9939941	CCCCCCCC(	0.223529	0.96087
SM d18:1/16:1	YLWSJLLZU	52931235	CCCCCCCC(	0.036617	0.918915
SM d18:1/20:0	AADLTHQN	44260124	CCCCCCCC(	0.09289	0.901547
SM (d18:1/20:1)	MDRFMTLY	52931179	CCCCCCCC(	0.015301	0.892686
SM d18:1/21:0	YXSZOBWV	52931193	CCCCCCCC(	0.003758	0.775027
SM d18:1/22:0	FJJANLYCZL	44260125	CCCCCCCC(	0.850368	0.986552
SM d18:1/23:0	SXZWBNWT	46891684	CCCCCCCC(	0.005165	0.846447
SM d18:1/24:0	QEDPUVGS	44260127	CCCCCCCC(	0.877799	0.987196
SM d18:2/23:0	JBDGKEXQK	52931209	CCCCCCCC(	3.03E-06	0.776136
SM d18:2/24:0	DACOGJME	52931217	CCCCCCCC(	0.221787	0.92569
SM (d18:2/24:1)	TXFLWJQV(	52931215	CCCCCCCC/	0.094827	0.922201
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	0.866753	0.89568
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	0.927592	0.946288
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	0.433823	0.764434
TG 46:1	RSDIQTNCD	56936558	CCCCCCCC(	0.73538	0.856029
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	0.886552	1.07806
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	0.926176	1.045249
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	0.314694	0.801903
TG 48:1	FEKLSEFRU(	9543986	CCCCCCCC(	0.318108	0.788587
TG 48:2	RUOVJPPU;	9543987	CCCCCCCC(	0.599844	0.850027
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	0.800464	1.113117
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	0.216983	0.722939
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	0.095895	0.642202
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	0.084472	0.683375
TG 50:0	QRJMBNGG	3246958	[2H]C([2H])	0.480248	0.791653
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	0.432945	0.906405
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	0.644899	0.941102
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	0.995255	0.999261
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	0.877799	1.049623
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	0.912796	1.040118
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	0.131726	0.670519
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	0.095078	0.715316
TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	0.285244	0.845864
TG 51:4	IIRQXNVLA;	9544052	CCCCCCCC/	0.654767	0.912815
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	0.595521	0.834024
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	0.595521	0.859711
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.975821	1.002207
TG 52:4	WHSWXEY\	25240364	CCCCCCCC/	0.168631	1.182454

TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.518723	1.155877
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	0.560197	0.879729
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	0.453711	0.781242
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	0.09289	0.705594
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCC/	0.510795	0.88742
TG 53:4	BMSDHYZL(	9544152	CCCCCCC/	0.936834	0.984842
TG 53:5	QHYAATSK'	9544183	CCCCCC/C	0.285244	1.249068
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	0.975821	1.0084
TG 54:1	YFFIQXNTT'	16058371	CCCCCCCC(	0.737538	0.886745
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	0.912796	0.966395
TG 54:3	PHYFQTYBJ	5497163	CCCCCCC/	0.216983	1.141157
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	0.034957	1.287006
TG 54:5	VVEBTVMJI	25240373	CCCCCCC/	0.318108	1.157737
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.094421	1.485038
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.886552	1.049284
TG 56:1	OCYFAHIHV	9544345	CCCCCCCC(	0.73538	1.118162
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	0.711121	1.126632
TG 56:3	QXMHHXQI	9544447	CCCCCCC/	0.552353	1.153279
TG 56:4	YONCDTJKI.	25240379	CCCCCCC/	0.131726	1.322042
TG 56:5	UHEJWASO	25240380	CCCCCCC/	0.926176	0.976652
TG 56:6	ZTNDRFCAI	9544625	CCCCC/C=C	0.377853	0.8869
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	0.592466	0.915804
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	0.579053	1.140488
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	0.599844	1.129498
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	0.216983	1.302105
TG 58:3	RFMSTHTU	9544748	CCCCCCC/	0.131726	1.414972
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	0.160805	1.353964
TG 58:6	GSNFRUMS	9544977	CCCCCCC/	0.285244	0.822734
TG 58:8	KWIGMCRV	9545124	CCCCCCCC(	0.807554	0.944915
TG 58:9	RVXFSLZMZ	9545200	CCCCCCC/	0.973098	1.008998
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	0.311159	1.237195
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.285244	0.825574
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	0.20479	1.297874
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	0.850368	1.050386

S5. Lipidome differential abundance analysis: Cluster IV vs III at Visit -3

Compound	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	0.831464	1.02648
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	0.533761	1.069278
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	0.228606	1.183057
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.104064	1.174652
CE 22:6	VOEVEGPN	14274978	CC/C=C\C/(	7.77E-06	0.501577
Ceramide d	NAJHAHQN	52931115	CCCCCCCC(	0.000358	1.325989
Ceramide d	KEPQASGD	5283567	CCCCCCCC(	0.783725	1.020967
Ceramide d	ZJVVOYPTF	5283571	CCCCCCCC(	0.681479	1.025614
Ceramide d	VJSBNBBOS	5283568	CCCCCCCC(	2.67E-05	0.631829
Cer (d18:1/	YDNKGFDK	5283564	CCCCCCCC(	0.370016	0.93716
Cholesterol	HVYWMON	5997	C[C@H](CC	0.509958	1.011612
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	0.163914	0.848311
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.256573	0.896176
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	0.015775	0.73269
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.486742	0.954292
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.031462	0.749353
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	0.243923	0.85734
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.406927	0.903359
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.699355	1.123274
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.847776	1.019981
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.253118	0.894245
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.109729	0.633234
FA 18:0	QIQXTHQID	5281	CCCCCCCC(	0.670394	0.945948
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.064763	0.703627
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.509099	0.930506
GlcCer d18:	YIGARKIIFO	6321359	CCCCCCCC(	0.001116	0.783857
GlcCer d18:	POQRWMR	6321361	CCCCCCCC(	0.001545	0.801763
GlcCer d18:	WBOZIXHP	6321360	CCCCCCCC(	7.92E-06	0.635673
LPC 18:0	IHNKQIMG	497299	CCCCCCCC(	0.10824	0.84704
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.008131	0.794522
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.0234	0.781269
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.000181	0.708909
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	8.61E-05	0.598274
LPC 20:2	YYQVCMM	52924053	CCCCC/C=C	0.014789	0.78019
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.783725	1.033852
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.228606	0.863925
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.319579	1.022003
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.005896	0.778606
PC 16:0/16	KILNVBDSW	452110	CCCCCCCC(	0.001303	0.870805
PC 18:1/16	WTJKGGKO	5497103	CCCCCCCC(	0.746083	0.988789
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.949711	1.018463
PC 30:0	RFVFQQWI	129657	CCCCCCCC(	0.100609	1.167227
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.027456	1.220782
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	0.010077	1.343121
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.325127	1.105436
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	1.13E-06	1.651007
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	0.000671	0.800189
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.949711	0.997627
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.442292	1.088212
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	2.74E-05	1.356389

PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.008131	1.221718
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.573618	0.962795
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.183721	0.965524
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.228606	1.095458
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.240608	1.039816
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.155977	0.969698
PC 36:6	SPWBDEZM	52922847	CCCCC/C=C	0.509099	0.911076
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.418668	1.064076
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	2.74E-05	1.719626
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	0.000101	1.34916
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.180249	0.917535
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.013304	1.55524
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.913467	0.992005
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.494881	1.113084
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	7.35E-09	0.636537
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	0.965278	0.980901
PC 40:2	AEUCYCQY	24779063	CCCCCCCC/	0.062925	0.844326
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	6.19E-08	0.524834
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.00519	0.783386
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.002941	0.740885
PC 42:1	PAHPUCKP	24778881	CCCCCCCC(	0.067928	0.859261
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.32678	1.089973
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.00206	1.66389
PC 44:3	GZZUNXHF	52923541	CCCCCCCC(	0.002108	0.786287
PC 44:4	UIAAGLPOL	52923481	CCCCCCCC(	0.161459	0.888416
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	0.000671	0.81214
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	2.35E-05	0.769924
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	0.973571	1.005675
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.709424	1.026698
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.008784	0.828315
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.161459	1.143588
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.001761	0.808063
PE 34:2	HBZNVZIRJ	46891780	CCCCCCCC(	0.607208	1.090075
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	2.23E-08	1.784614
PE 36:3	GKAFCSRKN	71728379	CCCCCCCC/	0.772167	0.987747
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.029916	1.227283
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	9.49E-05	1.330652
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.284065	1.137817
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.000695	0.646973
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	7.64E-06	0.669916
Phosphatid	RYHJACYQT	52926457	CCCCCCCC(	0.626355	0.983359
Plasmenyl-I	IQACMFWA	6443157	CCCCCCCC(	0.428452	1.099065
Plasmenyl-I	JCIBOIAZHL	70698851	CCCCCC/C=	0.955045	0.992454
Plasmenyl-I	FHHVIBPVE	24779390	CCCCCCCC(	0.639299	1.058898
Plasmenyl-I	XVXISDREV	52925079	CCCCCCCC(	0.533761	1.062745
Plasmenyl-I	UUYSKERSK	52925126	CCCCCCCC(	0.001545	0.723352
Plasmenyl-I	RLLOITCRN	52925061	CCCCCCCC(	0.004431	0.533827
Plasmenyl-I	URPXXNCT	86289532	CCCCCCCC(	0.026403	0.76859
Plasmenyl-I	KCNBSSYOJ	52925089	CCCCCCCC(	0.00092	0.690195
Plasmenyl-I	WVGALBKS	5283497	CCCCCCCC(	1.17E-11	0.442122
Plasmenyl-I	CVCZYWPC	52925119	CCCCCCCC(	0.287625	0.829094
Plasmenyl-I	FIJFPUAJUI	42607458	CCCCCCCC(	7.76E-07	0.515072

PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.714363	1.011236
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.430645	1.018041
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.949711	0.993684
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.988046	0.999713
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.100609	1.060725
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.001623	1.237185
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	0.840343	1.01703
PS 42:8	ROCNHMA;	52925757	CCCCC/C=C	2.74E-05	0.61134
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.474865	1.076405
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.087081	1.137585
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.099515	0.839273
SM d16:1/2	LKQLRGMN	6453725	CCCCCCCC(	0.013055	0.857884
SM d16:1/2	NBEADXWA	6443882	CCCCCCCC(	0.681479	0.968765
SM d18:1/1	KYICBZWZC	11433862	CCCCCCCC(	0.248261	0.904177
SM d18:1/1	RWKUXQNI	9939941	CCCCCCCC(	0.022316	0.9211
SM d18:1/1	YLWSJLLZU	52931235	CCCCCCCC(	0.029322	0.898453
SM d18:1/2	AADLTHQN	44260124	CCCCCCCC(	0.008754	0.841931
SM (d18:1/	MDRFMTLY	52931179	CCCCCCCC(	0.126081	0.91169
SM d18:1/2	YXSZOBWV	52931193	CCCCCCCC(	0.0234	1.248914
SM d18:1/2	FJJANLYCZU	44260125	CCCCCCCC(	0.342374	0.946757
SM d18:1/2	SXZWBNWT	46891684	CCCCCCCC(	0.009095	1.23674
SM d18:1/2	QEDPUVGS	44260127	CCCCCCCC(	0.061875	0.8534
SM d18:2/2	JBDGKEXQK	52931209	CCCCCCCC(	0.012442	1.200443
SM d18:2/2	DACOGJME	52931217	CCCCCCCC(	7.77E-06	0.699736
SM (d18:2/	TXFLWJQV(	52931215	CCCCCCCC/	8.91E-05	0.799113
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	0.332761	0.685329
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	0.180978	0.62129
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	0.988046	1.004723
TG 46:1	RSDIQTNCD	56936558	CCCCCCCC(	0.08363	0.6183
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	0.129916	0.610791
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	0.329211	0.741751
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	0.988046	0.997642
TG 48:1	FEKLSEFRU	9543986	CCCCCCCC(	0.687656	0.939672
TG 48:2	RUOVJPPUX	9543987	CCCCCCCC(	0.406927	0.835149
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	0.104064	0.59946
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	0.163476	1.398678
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	0.027456	1.551178
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	0.00528	1.56929
TG 50:0	QRJMBNGC	3246958	[2H]C([2H])	0.412993	0.816259
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	0.331649	0.927416
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	0.505028	0.950638
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	0.978807	0.99407
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	0.562159	0.87872
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	0.103003	0.714705
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	0.194891	1.297585
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	0.041646	1.353236
TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	0.004273	1.401183
TG 51:4	IIRQXNVLA;	9544052	CCCCCCCC/	0.11462	1.240708
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	0.160026	0.649216
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	0.087081	0.744602
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.041679	0.923792
TG 52:4	WHSWXEYY	25240364	CCCCCCCC/	0.160026	0.835075

TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.100609	0.745574
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCCC	0.973571	1.013268
TG 53:1	WWJIBIGW	9544081	CCCCCCCCC	0.681479	1.121131
TG 53:2	RSINITWKV	9544102	CCCCCCCCC	0.406927	1.129881
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCCC/	0.282363	1.147964
TG 53:4	BMSDHYZL	9544152	CCCCCCCC/	0.08726	1.212213
TG 53:5	QHYAATSKY	9544183	CCCCCCC/C	0.319579	0.819183
TG 54:0	DCXXMTOC	11146	CCCCCCCCC	0.105381	0.705746
TG 54:1	YFFIQXNTT	16058371	CCCCCCCCC	0.120977	0.684957
TG 54:2	RYNHWWN	16058372	CCCCCCCCC	0.018789	0.707641
TG 54:3	PHYFQTYBJ	5497163	CCCCCCCC/	0.021924	0.811859
TG 54:4	BRLGHZXET	9544255	CCCCCCCCC	0.087081	0.807366
TG 54:5	VVEBTVMJI	25240373	CCCCCCCC/	0.01369	0.715356
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.080827	0.683943
TG 54:8	BMPVTDW	9544413	CCCCC/C=C	0.211453	0.683727
TG 56:1	OCYFAHIHV	9544345	CCCCCCCCC	0.001481	0.524481
TG 56:2	PDEQUPGH	9544390	CCCCCCCCC	0.000388	0.460605
TG 56:3	QXMHHXQ	9544447	CCCCCCCC/	0.000269	0.513557
TG 56:4	YONCDTJKI	25240379	CCCCCCCC/	0.050868	0.666901
TG 56:5	UHEJWASO	25240380	CCCCCCCC/	0.366272	0.852561
TG 56:6	ZTNDRFCAE	9544625	CCCCC/C=C	0.687656	1.089993
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	0.000388	0.601209
TG 56:8	UBGUHMD	9544762	CCCCCCCCC	2.94E-06	0.38474
TG 58:1	OWZMHFA	25240381	CCCCCCCCC	0.011199	0.56761
TG 58:2	GXWBCAVC	9545277	CCCCC/C=C	0.003063	0.538166
TG 58:3	RFMSTHTU	9544748	CCCCCCCC/	0.008131	0.528091
TG 58:4	CCKRHDUC	9544835	CCCCCCCCC	0.001875	0.47542
TG 58:6	GSNFRUMS	9544977	CCCCCCCC/	0.099515	0.764903
TG 58:8	KWIGMCRV	9545124	CCCCCCCCC	0.000933	0.538267
TG 58:9	RVXFSLZMZ	9545200	CCCCCCCC/	3.63E-05	0.450498
TG 60:1	YNDXXWKS	9544965	CCCCCCCCC	0.062441	0.734739
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.000195	0.463602
TG 60:2	QPNVLDQS	9545040	CCCCCCCCC	0.043286	0.666242
TG 62:1	TZLOSVAFX	9545526	CCCCCCCCC	0.366358	0.867621

S6. Lipidome differential abundance analysis: Cluster IV vs Cluster III at Visit -6

Compound	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	0.039663	0.794468
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	0.922514	0.973971
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	0.267575	1.175011
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.251371	0.870734
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	1.18E-07	0.44871
Ceramide d	NAJHAHQN	52931115	CCCCCCCC(	0.003854	1.259907
Ceramide d	KEPQASGD.	5283567	CCCCCCCC(	0.873349	1.016887
Ceramide d	ZJVVOYPTF	5283571	CCCCCCCC(	0.95428	1.006814
Ceramide d	VJSBNBBOS	5283568	CCCCCCCC(	0.000155	0.673621
Cer (d18:1/	YDNKGFDK	5283564	CCCCCCCC(	0.629944	0.959428
Cholesterol	HVYWMON	5997	C[C@H](CC	0.482621	1.014484
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	0.501575	1.122385
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.516886	1.094812
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	0.961195	0.986419
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.298651	0.932405
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.988142	0.998297
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	0.239842	1.168996
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.792789	1.114807
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.586649	1.14704
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.1786	0.879828
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.024277	0.82511
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.010263	0.522461
FA 18:0	QIQXTHQID	5281	CCCCCCCC(	0.482621	0.912815
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.000753	0.555962
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.152694	0.854083
GlcCer d18:	YIGARKIIFO	6321359	CCCCCCCC(	0.016411	0.824295
GlcCer d18:	POQRWMR	6321361	CCCCCCCC(	0.006733	0.819384
GlcCer d18:	WBOZIXHP	6321360	CCCCCCCC(	5.23E-05	0.635149
LPC 18:0	IHNKQIMG'	497299	CCCCCCCC(	0.71631	1.041303
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.2774	0.896483
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.353485	0.879869
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.389801	0.908814
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.012442	0.755502
LPC 20:2	YYQVCMM.	52924053	CCCCC/C=C	0.378893	0.89319
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.014026	1.387694
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.927113	0.976231
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.288974	1.026127
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.089046	0.848826
PC 16:0/16	KILNVBDSW	452110	CCCCCCCC(	0.002383	0.829044
PC 18:1/16	WTJKGGKO	5497103	CCCCCCCC(	0.309127	0.960467
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.792789	0.939846
PC 30:0	RFVFQQWK	129657	CCCCCCCC(	0.965195	0.990236
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.951551	1.012474
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	0.000808	1.453684
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.470385	0.897017
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	0.000317	1.426883
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	0.003806	0.750195
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.153129	1.037226
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.013475	1.32123
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	2.20E-07	1.450202

PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.199282	1.126261
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.298651	0.908792
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.975626	0.998742
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.184792	1.085115
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.771712	1.012699
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.611283	0.989161
PC 36:6	SPWBDEZN	52922847	CCCCC/C=C	0.827189	0.963452
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.004242	1.235134
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.009634	1.405929
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	0.007867	1.24324
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.259831	0.904123
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.650572	1.099496
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.342904	0.936964
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.377555	1.193307
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	2.71E-10	0.632764
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	0.523556	0.843516
PC 40:2	AEUCYCQY,	24779063	CCCCCCCC/	0.03118	0.803584
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	4.01E-09	0.505872
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.002644	0.709925
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.038094	0.822668
PC 42:1	PAHPUCKP'	24778881	CCCCCCCC(	0.616487	0.948589
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.970562	0.994973
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.00052	1.651305
PC 44:3	GZZUNXHF	52923541	CCCCCCCC(	0.000162	0.719859
PC 44:4	UIAAGLPOl	52923481	CCCCCCCC(	0.015074	0.828886
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	6.60E-05	0.765203
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	2.93E-05	0.748533
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	0.128064	1.166259
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.95428	0.993294
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.004242	0.812224
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.586665	1.071902
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.006073	0.831865
PE 34:2	HBZNVZIRJ'	46891780	CCCCCCCC(	0.038094	1.410796
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	1.21E-08	1.874651
PE 36:3	GKAFCSRKN	71728379	CCCCCCCC/	0.771712	1.024275
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.55888	1.090492
PE 38:2	CLPMAPXZl	9546825	CCCCCCCC(	1.59E-05	1.39803
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.027075	1.307296
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.006033	0.714391
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	4.01E-09	0.656578
Phosphatid	RYHJACYQT	52926457	CCCCCCCC(	0.965195	1.002123
Plasmenyl-I	IQACMFWA	6443157	CCCCCCCC(	0.066272	1.209061
Plasmenyl-I	JCIBOIAZHL	70698851	CCCCCC/C=	0.230468	1.118269
Plasmenyl-I	FHHVIBPVE	24779390	CCCCCCCC(	0.817116	0.968915
Plasmenyl-I	XVXISDREV	52925079	CCCCCCCC(	0.049024	1.215157
Plasmenyl-I	UUYSKERSK	52925126	CCCCCCCC(	0.009197	0.752016
Plasmenyl-I	RLLOITCRN	52925061	CCCCCCCC(	0.00396	0.513961
Plasmenyl-I	URPXXNCT	86289532	CCCCCCCC(	0.000922	0.693715
Plasmenyl-I	KCNBSSYOJ	52925089	CCCCCCCC(	6.60E-05	0.617893
Plasmenyl-I	WVGALBKS	5283497	CCCCCCCC(	1.07E-12	0.418126
Plasmenyl-I	CVCZYWPC	52925119	CCCCCCCC(	0.134586	0.730958
Plasmenyl-I	FIJFPUAJUD	42607458	CCCCCCCC(	3.71E-08	0.48299

PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.961195	1.002689
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.445852	0.982833
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.482621	0.942043
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.665254	1.010984
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.801927	0.975494
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.259831	1.105205
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	0.128064	0.909057
PS 42:8	ROCNHMA:	52925757	CCCCC/C=C	0.000209	0.599918
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.629944	1.054881
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.975626	1.002981
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.025222	0.801782
SM d16:1/2	LKQLRGMN	6453725	CCCCCCCC(	4.52E-05	0.739921
SM d16:1/2	NBEADXWA	6443882	CCCCCCCC(	0.01264	0.84254
SM d18:1/1	KYICBZWZC	11433862	CCCCCCCC(	0.026057	0.81947
SM d18:1/1	RWKUXQNI	9939941	CCCCCCCC(	0.138751	0.935792
SM d18:1/1	YLWSJLLZU	52931235	CCCCCCCC(	0.01532	0.882562
SM d18:1/2	AADLTHQN	44260124	CCCCCCCC(	0.000123	0.77328
SM (d18:1/	MDRFMTLY	52931179	CCCCCCCC(	0.003854	0.84286
SM d18:1/2	YXSZOBWV	52931193	CCCCCCCC(	0.479021	1.083759
SM d18:1/2	FJJANLYCZU	44260125	CCCCCCCC(	0.937122	0.992101
SM d18:1/2	SXZWBNWT	46891684	CCCCCCCC(	0.001634	1.286026
SM d18:1/2	QEDPUVGS	44260127	CCCCCCCC(	0.586649	1.039696
SM d18:2/2	JBDGKEXQK	52931209	CCCCCCCC(	0.358745	1.073907
SM d18:2/2	DACOGJME	52931217	CCCCCCCC(	8.45E-07	0.696423
SM (d18:2/	TXFLWJQV(	52931215	CCCCCCCC/	5.23E-05	0.7865
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	0.503374	1.383598
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	0.913319	1.082826
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	0.101164	1.586314
TG 46:1	RSDIQTNCD	56936558	CCCCCCCC(	0.95428	0.965896
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	0.937984	1.050094
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	0.58693	1.23053
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	0.019717	1.574958
TG 48:1	FEKLSEFRU	9543986	CCCCCCCC(	0.531687	1.160783
TG 48:2	RUOVJPPU)	9543987	CCCCCCCC(	0.623093	1.157797
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	0.937984	0.95298
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	0.006033	2.222938
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	0.01264	1.948494
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	0.006033	1.809979
TG 50:0	QRJMBNGC	3246958	[2H]C([2H])	0.019717	1.90572
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	0.626174	1.060266
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	0.650572	1.054306
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	0.195557	1.246218
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	0.346643	1.254177
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	0.629944	1.148633
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	0.039663	1.746196
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	0.016251	1.61606
TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	0.000384	1.717509
TG 51:4	IIRQXNVLA)	9544052	CCCCCCCC/	0.000753	1.729886
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	0.019717	2.186391
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	0.516886	1.184847
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.751172	0.980768
TG 52:4	WHSWXEYY	25240364	CCCCCCCC/	0.183789	1.165271

TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.58693	1.144258
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	0.003854	2.000213
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	0.022556	2.002175
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	0.033028	1.560926
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCC/	0.003854	1.600562
TG 53:4	BMSDHYZL(	9544152	CCCCCCC/	0.000266	1.622173
TG 53:5	QHYAATSK\	9544183	CCCCCC/C	0.029472	1.520155
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	0.016411	1.782369
TG 54:1	YFFIQXNTT\	16058371	CCCCCCCC(	0.028414	1.887606
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	0.516886	1.151792
TG 54:3	PHYFQTYBJ	5497163	CCCCCCC/	0.665254	1.055438
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	0.445852	1.151995
TG 54:5	VVEBTVMJI	25240373	CCCCCCC/	0.720864	1.067168
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.444802	1.260415
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.983551	1.007121
TG 56:1	OCYFAHIH\	9544345	CCCCCCCC(	0.193892	1.458497
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	0.586649	1.208637
TG 56:3	QXMHHXQ	9544447	CCCCCCC/	0.720864	0.896008
TG 56:4	YONCDTJKI	25240379	CCCCCCC/	0.767674	1.079483
TG 56:5	UHEJWASO	25240380	CCCCCCC/	0.345326	0.839326
TG 56:6	ZTNDRFCAI	9544625	CCCCC/C=C	0.975626	0.990971
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	0.00052	0.618295
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	0.000247	0.469532
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	0.06566	1.603379
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	0.578287	1.188781
TG 58:3	RFMSTHTU	9544748	CCCCCCC/	0.470332	1.298339
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	0.792789	0.914042
TG 58:6	GSNFRUMS	9544977	CCCCCCC/	0.628209	0.880105
TG 58:8	KWIGMCR\	9545124	CCCCCCCC(	0.037842	0.661107
TG 58:9	RVXFSLZMZ	9545200	CCCCCCC/	0.000384	0.518596
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	0.027075	1.580031
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	3.99E-06	0.421284
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	0.109763	1.568478
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	0.007867	1.621068

S7. Lipidome differential abundance analysis: Cluster III vs Cluster I at Visit -3

Compound	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFI	5283632	CCCCCCCC/	1.50E-06	0.694895
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	7.95E-06	0.724539
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	6.87E-08	0.565856
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.00014	0.762359
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	0.623644	0.941255
Ceramide d	NAJHAHQN	52931115	CCCCCCCC(	0.021025	0.880199
Ceramide d	KEPQASGD	5283567	CCCCCCCC(	0.624297	1.026465
Ceramide d	ZJVVOYPTF	5283571	CCCCCCCC(	0.394709	1.038161
Ceramide d	VJSBNBBOS	5283568	CCCCCCCC(	0.835563	0.985438
Cer (d18:1/	YDNKGFDK	5283564	CCCCCCCC(	0.269306	1.058485
Cer (d18:1/	KEPQASGD	5283567	CCCCCCCC(	0.502671	1.02991
Cer (d18:1/	VJSBNBBOS	5283568	CCCCCCCC(	0.897431	0.992183
Cholesterol	HVYWMON	5997	C[C@H](CC	0.933125	0.999006
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	0.000187	1.418206
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.000176	1.299483
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	3.65E-05	1.58908
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.837176	1.010598
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.000146	1.491566
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	4.72E-07	1.717922
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	1.21E-05	1.469062
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.002506	1.849502
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.745722	0.978881
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.197781	1.098978
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.653918	1.129969
FA 18:0	QIQXTHQID	5281	CCCCCCCC(	0.302404	1.106124
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.261722	1.208194
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.050236	1.170147
GlcCer d18:	YIGARKIIFO	6321359	CCCCCCCC(	0.802421	1.015551
GlcCer d18:	POQRWMR	6321361	CCCCCCCC(	0.762285	1.017807
GlcCer d18:	WBOZIXHP	6321360	CCCCCCCC(	0.485044	0.950316
LPC 18:0	IHNKQIMG	497299	CCCCCCCC(	0.082298	1.152391
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.03561	1.139309
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	4.36E-05	1.383886
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.000907	1.25739
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.010053	1.260773
LPC 20:2	YYQVCMM	52924053	CCCCC/C=C	0.000365	1.313883
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.749277	0.963877
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.00011	1.455223
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.160297	0.979801
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.006542	1.196657
PC 16:0/16	KILNVBDSV	452110	CCCCCCCC(	0.086553	1.064051
PC 18:1/16	WTJKGGKO	5497103	CCCCCCCC(	0.008269	0.946151
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.86339	0.975265
PC 30:0	RFVFQQWI	129657	CCCCCCCC(	0.413709	0.930571
PC 32:0	KILNVBDSV	452110	CCCCCCCC(	0.090816	1.090143
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.002508	0.805387
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	0.144374	0.882053
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.351506	0.918977
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	2.77E-07	0.668884
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	0.004424	1.166035

PC 34:1	WTJKGGKO	5497103	CCCCCCCC(	0.002174	0.904911
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.261722	1.018506
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.002227	0.79223
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	0.050763	0.903663
PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.008176	0.864652
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.353902	0.958777
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.015234	1.050586
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.22119	0.9269
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.20548	1.041146
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.783277	1.004575
PC 36:6	SPWBDEZM	52922847	CCCCC/C=C	0.378241	0.911788
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.953524	1.003303
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.002508	0.741183
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	0.228547	0.935601
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.640823	1.021972
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.045839	0.757388
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.018689	1.097823
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.01014	0.771719
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.001018	1.214725
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	8.10E-05	0.50448
PC 40:2	AEUCYCQY	24779063	CCCCCCCC/	0.22119	1.086828
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.001451	1.329943
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.058733	1.136364
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.589512	1.046357
PC 42:1	PAHPUCKP	24778881	CCCCCCCC(	0.084442	0.892436
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.321972	1.066991
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	7.95E-06	0.56534
PC 44:3	GZZUNXHF	52923541	CCCCCCCC(	0.28374	0.935647
PC 44:4	UIAAGLPOl	52923481	CCCCCCCC(	0.106508	1.098317
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	0.477083	0.966589
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	0.045971	0.906355
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	1.75E-05	0.766324
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.047087	0.901508
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.629349	1.030679
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.351506	0.932474
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.174678	1.076518
PE 34:2	HBZNVZIRJ	46891780	CCCCCCCC(	0.417685	1.099324
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	0.000104	0.753396
PE 36:3	GKAFCSRKN	71728379	CCCCCCCC/	0.202595	0.963526
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.793173	1.023993
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	0.071612	0.906873
PE 38:4	ANRKEHNW	46891781	CCCCCCCC(	0.040542	1.272861
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.159724	1.163871
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.009545	1.193887
Phosphatid	RYHJACYQT	52926457	CCCCCCCC(	0.011327	1.052923
Plasmenyl-I	IQACMFWA	6443157	CCCCCCCC(	0.003662	0.76728
Plasmenyl-I	JCIBOIAZHL	70698851	CCCCCC/C=	4.18E-05	0.801571
Plasmenyl-I	FHHVIBPVE	24779390	CCCCCCCC(	0.708507	0.967157
Plasmenyl-I	XVXISDREV	52925079	CCCCCCCC(	0.078409	0.88078
Plasmenyl-I	UUYSKERSK	52925126	CCCCCCCC(	0.029279	1.18284
Plasmenyl-I	RLLOITCRN	52925061	CCCCCCCC(	0.301222	0.822028
Plasmenyl-I	URPXXNCT	86289532	CCCCCCCC(	0.13175	1.146407

Plasmenyl-I	KCNBSSYOJ	52925089	CCCCCCCC(	0.020888	1.216854
Plasmenyl-I	WVGALBKS	5283497	CCCCCCCC(	0.001451	1.340015
Plasmenyl-I	CVCZYWPC	52925119	CCCCCCCC(	0.97521	1.003892
Plasmenyl-I	FIJFPUAJUI	42607458	CCCCCCCC(	0.046734	1.218355
PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.002718	0.946814
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.5323	0.990662
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.463476	0.972138
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.144374	1.025742
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.421635	1.02281
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.001292	0.847866
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	0.015017	1.127101
PS 42:8	ROCNHMA;	52925757	CCCCC/C=C	0.005599	1.266439
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.378241	0.94173
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.116294	0.912775
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.502671	1.036187
SM d16:1/2	LKQLRGMN	6453725	CCCCCCCC(	0.033315	1.106807
SM d16:1/2	NBEADXWA	6443882	CCCCCCCC(	0.485044	1.038841
SM d18:1/1	KYICBZWZC	11433862	CCCCCCCC(	0.284814	1.074311
SM d18:1/1	RWKUXQNI	9939941	CCCCCCCC(	0.397616	1.023176
SM d18:1/1	YLWSJLLZU	52931235	CCCCCCCC(	0.36657	1.035862
SM (d18:1/	LKQLRGMN	6453725	CCCCCCCC(	0.158116	1.079894
SM (d18:1/	NBEADXWA	6443882	CCCCCCCC(	0.417985	1.048644
SM d18:1/2	AADLTHQN	44260124	CCCCCCCC(	0.139373	1.080517
SM (d18:1/	MDRFMTLY	52931179	CCCCCCCC(	0.748281	1.01585
SM d18:1/2	YXSZOBWV	52931193	CCCCCCCC(	0.144374	0.895998
SM d18:1/2	FJJANLYCZL	44260125	CCCCCCCC(	0.86339	1.007028
SM d18:1/2	SXZWBNW	46891684	CCCCCCCC(	0.005125	0.856502
SM d18:1/2	QEDPUVGS	44260127	CCCCCCCC(	0.356494	1.066252
SM d18:2/2	JBDGKEXQI	52931209	CCCCCCCC(	3.41E-05	0.811893
SM d18:2/2	DACOGJME	52931217	CCCCCCCC(	0.819164	0.986367
SM (d18:2/	TXFLWJQV(	52931215	CCCCCCCC/	0.646154	0.980616
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	0.000446	2.791828
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	3.27E-05	3.192822
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	0.002227	1.798017
TG 46:1	RSDIQTNCI	56936558	CCCCCCCC(	1.99E-05	2.673984
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	5.34E-06	3.300037
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	4.02E-06	2.849342
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	0.008269	1.47708
TG 48:1	FEKLSEFRU	9543986	CCCCCCCC(	5.97E-05	1.697284
TG 48:2	RUOVJPPU	9543987	CCCCCCCC(	1.04E-05	2.151436
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	1.16E-06	3.395699
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	0.099012	1.38278
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	0.067177	1.369838
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	0.050763	1.299853
TG 50:0	QRJMBNGC	3246958	[2H]C([2H])	0.000305	2.0737
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	0.000112	1.355398
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	1.42E-06	1.437662
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	4.28E-08	2.01571
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	1.55E-07	2.381925
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	4.28E-08	2.589768
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	0.008966	1.537243
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	0.03561	1.301138

TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	3.42E-05	1.478632
TG 51:4	IIRQXNVLA:	9544052	CCCCCCCC/	1.39E-06	1.709262
TG 52:0	SDNYRTVJC	545690	CCCCCCCCC	0.00014	2.393617
TG 52:1	NPCZZYKITI	25240360	CCCCCCCCC	6.98E-07	2.228981
TG 52:2	KGLAHZTW	25240361	CCCCCCCCC	0.000198	1.146462
TG 52:3	KGLAHZTW	25240361	CCCCCCCCC	4.28E-08	1.268962
TG 52:4	WHSWXEY\	25240364	CCCCCCCC/	2.63E-07	1.69404
TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	1.28E-06	1.961983
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCCC	0.004424	1.524026
TG 53:1	WWJIBIGW	9544081	CCCCCCCCC	0.003059	1.738648
TG 53:2	RSINITWKV	9544102	CCCCCCCCC	0.001451	1.400573
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCCC/	6.13E-06	1.57456
TG 53:4	BMSDHYZL(	9544152	CCCCCCCC/	1.28E-06	1.501919
TG 53:5	QHYAATSK\	9544183	CCCCCCC/C	3.33E-07	1.957159
TG 54:0	DCXXMTOC	11146	CCCCCCCCC	0.000636	1.714324
TG 54:1	YFFIQXNTT'	16058371	CCCCCCCCC	9.40E-07	2.749142
TG 54:2	RYNHWWN	16058372	CCCCCCCCC	6.87E-08	2.130968
TG 54:3	PHYFQTYBJ	5497163	CCCCCCCC/	1.18E-07	1.548087
TG 54:4	BRLGHZXET	9544255	CCCCCCCCC	2.26E-06	1.665431
TG 54:5	VVEBTVMJI	25240373	CCCCCCCC/	2.96E-08	2.034496
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	3.76E-07	2.592273
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.025919	1.58433
TG 56:1	OCYFAHIH\	9544345	CCCCCCCCC	2.04E-07	2.659857
TG 56:2	PDEQUPGH	9544390	CCCCCCCCC	2.96E-08	2.990844
TG 56:3	QXMHHXQ	9544447	CCCCCCCC/	9.12E-08	2.320804
TG 56:4	YONCDTJKI.	25240379	CCCCCCCC/	6.76E-06	2.181896
TG 56:5	UHEJWASO	25240380	CCCCCCCC/	0.004901	1.572738
TG 56:6	ZTNDRFCAI	9544625	CCCCC/C=C	0.658297	0.933418
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	1.91E-05	1.65177
TG 56:8	UBGUHMD	9544762	CCCCCCCCC	3.76E-07	2.321815
TG 58:1	OWZMHFA	25240381	CCCCCCCCC	1.11E-05	2.065736
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	1.56E-07	2.505924
TG 58:3	RFMSTHTU	9544748	CCCCCCCC/	1.18E-07	2.856581
TG 58:4	CCKRHDUC	9544835	CCCCCCCCC	4.02E-07	2.629362
TG 58:6	GSNFRUMS	9544977	CCCCCCCC/	4.72E-07	1.927599
TG 58:8	KWIGMCR\	9545124	CCCCCCCCC	0.000153	1.78732
TG 58:9	RVXFSLZMZ	9545200	CCCCCCCC/	5.24E-07	2.237908
TG 60:1	YNDXXWKS	9544965	CCCCCCCCC	6.76E-05	1.716094
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.003524	1.600619
TG 60:2	QPNVLDQS	9545040	CCCCCCCCC	1.75E-05	2.162106
TG 62:1	TZLOSVAFX	9545526	CCCCCCCCC	0.029279	1.297729

S8. Lipidome differential abundance analysis: Cluster III vs Cluster I at Visit -6

Compound	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	0.00027	0.7617925
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	3.35E-05	0.6725358
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	7.78E-09	0.532799
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.06667	0.8785684
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	0.340932	0.9036995
Ceramide d	NAJHAHQN	52931115	CCCCCCCC(	0.038854	0.8736686
Ceramide d	KEPQASGD	5283567	CCCCCCCC(	0.118459	1.0902116
Ceramide d	ZJVVOYPTF	5283571	CCCCCCCC(	0.345602	1.0477229
Ceramide d	VJSBNBBOS	5283568	CCCCCCCC(	0.266516	1.0807833
Cer (d18:1/	YDNKGFDK	5283564	CCCCCCCC(	0.357889	1.0488692
Cer (d18:1/	KEPQASGD	5283567	CCCCCCCC(	0.163074	1.0773135
Cer (d18:1/	VJSBNBBOS	5283568	CCCCCCCC(	0.448828	1.0554526
Cholesterol	HVYWMON	5997	C[C@H](CC	0.774678	0.9958667
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	0.000768	1.3966137
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.022811	1.2256577
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	0.000435	1.4851765
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.358485	1.0457007
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.017767	1.2684648
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	0.001016	1.3578618
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.830894	1.063454
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.014972	1.7811785
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.724734	1.0269485
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.250894	1.0843708
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.165194	1.3556099
FA 18:0	QIQXTHQID	5281	CCCCCCCC(	0.184774	1.1353046
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.099615	1.264869
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.034344	1.1943816
GlcCer d18:	YIGARKIIFO	6321359	CCCCCCCC(	0.279517	1.0676627
GlcCer d18:	POQRWMR	6321361	CCCCCCCC(	0.631422	1.0288342
GlcCer d18:	WBOZIXHP	6321360	CCCCCCCC(	0.993239	1.0007292
LPC 18:0	IHNKQIMG	497299	CCCCCCCC(	0.035402	1.1898242
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.131871	1.1261307
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.011381	1.286114
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.006532	1.227266
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.00181	1.3056466
LPC 20:2	YYQVCMM	52924053	CCCCC/C=C	0.000446	1.3569215
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.284001	0.8846888
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.007844	1.4033866
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.724734	0.9931643
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.053683	1.1667286
PC 16:0/16	KILNVBDSW	452110	CCCCCCCC(	0.008094	1.1307987
PC 18:1/16	WTJKGGKO	5497103	CCCCCCCC(	0.001149	0.923098
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.607188	1.090044
PC 30:0	RFVFQQWK	129657	CCCCCCCC(	0.751802	1.038836
PC 32:0	KILNVBDSW	452110	CCCCCCCC(	0.003369	1.2053386
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.00109	0.8019694
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	0.007844	0.7902205
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.369281	1.0888384
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	6.58E-06	0.6942205
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	0.00014	1.3455075

PC 34:1	WTJKGGKO	5497103	CCCCCCCC(	0.000896	0.8838999
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.225746	0.9781325
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	2.51E-05	0.6785378
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	0.012609	0.8751758
PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.976468	0.9969555
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.961654	1.0054702
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.060058	1.051227
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.452994	0.9631097
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.302321	1.030537
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.947596	0.9986826
PC 36:6	SPWBDEZM	52922847	CCCCC/C=C	0.088996	0.8196831
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.328038	0.9396872
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.175106	0.8607269
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	0.38551	1.0626389
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.054852	1.1354997
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.396339	0.9127272
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.001333	1.1571073
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.021868	0.7386157
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.000374	1.2118967
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	0.002922	0.5909313
PC 40:2	AEUCYCQY/	24779063	CCCCCCCC/	0.006149	1.2441294
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.000111	1.4004809
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.004282	1.2927758
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.916759	0.9887284
PC 42:1	PAHPUCKP'	24778881	CCCCCCCC(	0.001423	0.8090131
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.240404	1.0797056
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.00039	0.6277071
PC 44:3	GZZUNXHF:	52923541	CCCCCCCC(	0.860564	1.0152419
PC 44:4	UIAAGLPOU	52923481	CCCCCCCC(	0.04664	1.1263809
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	0.980128	1.001569
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	0.073186	0.9105108
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	2.56E-05	0.7089221
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.18817	0.9366166
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.38551	1.050542
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.71309	0.9666399
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.088996	1.0869542
PE 34:2	HBZNVZIRJ'	46891780	CCCCCCCC(	0.993239	1.0010273
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	2.06E-05	0.6872644
PE 36:3	GKAFCSRKI	71728379	CCCCCCCC/	0.752859	0.9801437
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.491652	1.0772202
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	0.096598	0.9055888
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.114898	1.1857443
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.142959	1.1728005
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.000647	1.2125064
Phosphatid	RYHJACYQT	52926457	CCCCCCCC(	0.970787	1.0011059
Plasmenyl-I	IQACMFWA	6443157	CCCCCCCC(	0.000183	0.7252335
Plasmenyl-I	JCIBOIAZHL	70698851	CCCCCC/C=	8.90E-05	0.7536584
Plasmenyl-I	FHHVIBPVE	24779390	CCCCCCCC(	0.452994	1.0614039
Plasmenyl-I	XVXISDREV	52925079	CCCCCCCC(	0.02395	0.8302969
Plasmenyl-I	UUYSKERSI	52925126	CCCCCCCC(	0.005816	1.2465311
Plasmenyl-I	RLLOITCRN	52925061	CCCCCCCC(	0.617307	0.9027806
Plasmenyl-I	URPXXNCT:	86289532	CCCCCCCC(	0.001533	1.2904986

Plasmenyl-I	KCNBSSYOJ	52925089	CCCCCCCC(	4.96E-05	1.467691
Plasmenyl-I	WVGALBKS	5283497	CCCCCCCC(	6.58E-06	1.5313326
Plasmenyl-I	CVCZYWPC	52925119	CCCCCCCC(	0.343844	1.1503252
Plasmenyl-I	FIJFPUAJUD	42607458	CCCCCCCC(	0.000245	1.4152303
PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.000295	0.9250157
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.84302	0.9963828
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.964542	1.0042162
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.082031	1.0375257
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.144112	1.0895397
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.678873	0.9695739
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	5.86E-05	1.2159249
PS 42:8	ROCNHMA:	52925757	CCCCC/C=C	0.003181	1.3320688
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.916759	0.9873024
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.916759	0.9895998
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.250894	1.0903498
SM d16:1/2	LKQLRGMN	6453725	CCCCCCCC(	0.000314	1.2041097
SM d16:1/2	NBEADXWA	6443882	CCCCCCCC(	0.090182	1.0903456
SM d18:1/1	KYICBZWZC	11433862	CCCCCCCC(	0.014424	1.1891017
SM d18:1/1	RWKUXQNI	9939941	CCCCCCCC(	0.286626	1.0362932
SM d18:1/1	YLWSJLLZU	52931235	CCCCCCCC(	0.267078	1.0446242
SM (d18:1/	LKQLRGMN	6453725	CCCCCCCC(	0.000456	1.2029487
SM (d18:1/	NBEADXWA	6443882	CCCCCCCC(	0.049611	1.1123923
SM d18:1/2	AADLTHQN	44260124	CCCCCCCC(	0.000647	1.2001588
SM (d18:1/	MDRFMTLY	52931179	CCCCCCCC(	0.288607	1.0493321
SM d18:1/2	YXSZOBWV	52931193	CCCCCCCC(	0.537838	0.9507833
SM d18:1/2	FJJANLYCZU	44260125	CCCCCCCC(	0.762839	1.0141561
SM d18:1/2	SXZWBNW	46891684	CCCCCCCC(	0.000206	0.8000529
SM d18:1/2	QEDPUVGS	44260127	CCCCCCCC(	0.403027	0.963257
SM d18:2/2	JBDGKEXQI	52931209	CCCCCCCC(	6.48E-05	0.8086867
SM d18:2/2	DACOGJME	52931217	CCCCCCCC(	0.970787	1.0028005
SM (d18:2/	TXFLWJQV(	52931215	CCCCCCCC/	0.970787	1.0021295
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	0.000153	3.4641456
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	4.12E-05	4.2354683
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	0.0038	1.9315018
TG 46:1	RSDIQTNCD	56936558	CCCCCCCC(	4.96E-05	3.1790717
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	6.58E-06	3.906618
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	2.06E-05	3.2176691
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	0.081849	1.3201928
TG 48:1	FEKLSEFRU	9543986	CCCCCCCC(	0.000617	1.7435737
TG 48:2	RUOVJPPU)	9543987	CCCCCCCC(	0.000113	2.2495888
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	6.58E-06	3.5084154
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	0.212242	1.3231648
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	0.175106	1.3284334
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	0.146655	1.2841548
TG 50:0	QRJMBNGG	3246958	[2H]C([2H])	0.013989	1.7803219
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	0.001214	1.2838025
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	0.000163	1.3438577
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	2.81E-05	1.8096021
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	2.56E-05	2.1579053
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	8.90E-05	2.0712899
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	0.056233	1.4806697
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	0.231561	1.2050256

TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	0.039091	1.2842254
TG 51:4	IIRQXNVLA:	9544052	CCCCCCCC/	0.001933	1.4839756
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	0.004397	2.0831546
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	0.000149	2.0429578
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.00919	1.1104913
TG 52:3	KGLAHZTW	25240361	CCCCCCCC(	0.000307	1.1469505
TG 52:4	WHSWXEY\	25240364	CCCCCCCC/	3.58E-05	1.4631491
TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.0038	1.497528
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	0.054912	1.3981391
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	0.013815	1.7980368
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	0.302321	1.1703661
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCCC/	0.016483	1.3480189
TG 53:4	BMSDHYZL(	9544152	CCCCCCCC/	0.005831	1.318456
TG 53:5	QHYAATSK\	9544183	CCCCCCC/C	0.000123	1.8160141
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	0.041734	1.421236
TG 54:1	YFFIQXNTT'	16058371	CCCCCCCC(	0.000963	2.1216244
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	0.000105	1.8267815
TG 54:3	PHYFQTYBJ	5497163	CCCCCCCC/	4.96E-05	1.3990368
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	0.002615	1.4083748
TG 54:5	VVEBTVMJI	25240373	CCCCCCCC/	0.000228	1.507273
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.000159	1.8532214
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.059644	1.4584968
TG 56:1	OCYFAHIH\	9544345	CCCCCCCC(	0.000867	1.9705944
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	0.000149	2.1211649
TG 56:3	QXMHHXQ	9544447	CCCCCCCC/	7.01E-05	1.9410184
TG 56:4	YONCDTJKI.	25240379	CCCCCCCC/	0.004161	1.5157019
TG 56:5	UHEJWASO	25240380	CCCCCCCC/	0.000142	1.5996189
TG 56:6	ZTNDRFCAE	9544625	CCCCC/C=C	0.781923	0.9519092
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	6.94E-06	1.7321198
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	2.59E-08	2.7360087
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	0.028609	1.4843504
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	0.000123	1.8849885
TG 58:3	RFMSTHTU	9544748	CCCCCCCC/	0.000108	2.1573186
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	4.43E-05	2.1754202
TG 58:6	GSNFRUMS	9544977	CCCCCCCC/	0.000606	1.6524232
TG 58:8	KWIGMCR\	9545124	CCCCCCCC(	0.000337	1.7154499
TG 58:9	RVXFSLZMZ	9545200	CCCCCCCC/	5.96E-07	2.143353
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	0.037955	1.4104758
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	8.90E-05	1.8189858
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	0.054912	1.4152962
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	0.60471	1.0713888

S9. Lipidome differential abundance analysis: Cluster IV vs Cluster I at Visit -3

Compound	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	5.56E-06	0.713295
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	0.001758	0.774733
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	1.38E-05	0.66944
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.105839	0.895506
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	8.22E-07	0.472112
Ceramide d	NAJHAHQN	52931115	CCCCCCCC(	0.020816	1.167135
Ceramide d	KEPQASGD.	5283567	CCCCCCCC(	0.433464	1.047987
Ceramide d	ZJVVOYPTF	5283571	CCCCCCCC(	0.22498	1.064752
Ceramide d	VJSBNBBOS	5283568	CCCCCCCC(	1.38E-05	0.622628
Cer (d18:1/	YDNKGFDK	5283564	CCCCCCCC(	0.914756	0.99197
Cer (d18:1/	KEPQASGD.	5283567	CCCCCCCC(	0.174235	1.076033
Cer (d18:1/	VJSBNBBOS	5283568	CCCCCCCC(	2.33E-05	0.710909
Cholesterol	HVYWMON	5997	C[C@H](CC	0.433464	1.010607
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	0.104184	1.20308
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.053025	1.164565
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	0.261182	1.164303
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.475419	0.964406
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.361456	1.11771
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	0.001742	1.472843
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.001758	1.32709
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	3.87E-05	2.077497
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.979316	0.99844
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.845185	0.982756
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.279159	0.715535
FA 18:0	QIQXTHQIE	5281	CCCCCCCC(	0.697608	1.046336
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.433464	0.850117
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.343603	1.088829
GlcCer d18:	YIGARKIIFO	6321359	CCCCCCCC(	0.001521	0.796047
GlcCer d18:	POQRWMR	6321361	CCCCCCCC(	0.005893	0.81604
GlcCer d18:	WBOZIXHP	6321360	CCCCCCCC(	5.90E-07	0.604091
LPC 18:0	IHNKQIMG'	497299	CCCCCCCC(	0.827859	0.976122
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.179621	0.905206
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.408665	1.081188
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.174235	0.891375
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.011101	0.754287
LPC 20:2	YYQVCMM.	52924053	CCCCC/C=C	0.797472	1.025079
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.979316	0.996506
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.034305	1.257204
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.96402	1.001359
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.388439	0.931724
PC 16:0/16	KILNVBDSV	452110	CCCCCCCC(	0.071107	0.926581
PC 18:1/16	WTJKGGKO	5497103	CCCCCCCC(	0.011101	0.935544
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.975543	0.993271
PC 30:0	RFVFQQWI	129657	CCCCCCCC(	0.45819	1.086188
PC 32:0	KILNVBDSV	452110	CCCCCCCC(	0.035751	0.891513
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.875954	0.983202
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	0.063343	1.184704
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.913897	1.01587
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	0.248881	1.104332
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	0.233231	0.933049

PC 34:1	WTJKGGKO	5497103	CCCCCCCC(	0.027503	0.913451
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.350984	1.016088
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.037572	0.862114
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	0.000992	1.225718
PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.388439	1.05636
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.121553	0.923106
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.563463	1.014366
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.827859	1.015379
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.034305	1.082601
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.168696	0.974134
PC 36:6	SPWBDEZM	52922847	CCCCC/C=C	0.127005	0.830708
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.254159	1.067591
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.020816	1.274558
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	0.000297	1.262276
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.254159	0.937695
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.156602	1.177921
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.03459	1.089045
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.248881	0.858989
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.001057	0.773217
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	2.33E-05	0.494845
PC 40:2	AEUCYCQY/	24779063	CCCCCCCC/	0.27447	0.917637
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.001632	0.697999
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.112801	0.890212
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.006247	0.775231
PC 42:1	PAHPUCKP\	24778881	CCCCCCCC(	0.001521	0.766836
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.041286	1.162991
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.669224	0.940664
PC 44:3	GZZUNXHF	52923541	CCCCCCCC(	6.83E-05	0.735687
PC 44:4	UIAAGLPOL	52923481	CCCCCCCC(	0.757351	0.975762
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	1.38E-05	0.785005
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	8.23E-08	0.697825
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	0.001035	0.770673
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.248881	0.925577
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.03165	0.853727
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.433464	1.066366
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.034305	0.869895
PE 34:2	HBZNVZIRJ\	46891780	CCCCCCCC(	0.015826	1.198346
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	0.000305	1.344521
PE 36:3	GKAFCSRKI	71728379	CCCCCCCC/	0.238446	0.95172
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.020752	1.256729
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	0.00131	1.206732
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.013014	1.448283
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.018552	0.752994
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.007858	0.799804
Phosphatid	RYHJACYQT	52926457	CCCCCCCC(	0.212978	1.035401
Plasmenyl-I	IQACMFWA	6443157	CCCCCCCC(	0.115494	0.84329
Plasmenyl-I	JCIBOIAZHL	70698851	CCCCCC/C=	0.000281	0.795523
Plasmenyl-I	FHHVIBPVE	24779390	CCCCCCCC(	0.80207	1.024121
Plasmenyl-I	XVXISDREV	52925079	CCCCCCCC(	0.475419	0.936045
Plasmenyl-I	UUYSKERSI	52925126	CCCCCCCC(	0.076944	0.855609
Plasmenyl-I	RLLOITCRN	52925061	CCCCCCCC(	1.78E-05	0.438821
Plasmenyl-I	URPXXNCT	86289532	CCCCCCCC(	0.105839	0.881117

Plasmenyl-I	KCNBSSYOJ	52925089	CCCCCCCCC(	0.036546	0.839866
Plasmenyl-I	WVGALBKS	5283497	CCCCCCCCC(	3.76E-06	0.592449
Plasmenyl-I	CVCZYWPC	52925119	CCCCCCCCC(	0.248881	0.832321
Plasmenyl-I	FIJFPUAJUD	42607458	CCCCCCCCC(	2.33E-05	0.627541
PS 38:3	BQBTWCBZ	52925523	CCCCCCCCC(	0.05865	0.957452
PS 38:4	SVOUGFFD	24779545	CCCCCCCCC(	0.591738	1.008534
PS 40:3	BTIQFPURP	52925502	CCCCCCCCC(	0.475419	0.965998
PS 40:4	GBBNRADS	52925748	CCCCCCCCC(	0.213197	1.025448
PS 40:6	LYYHRRPTE	24779546	CCCCCCCCC(	0.003796	1.084921
PS 42:5	VNQACVFLI	52925755	CCCCCCCCC(	0.434164	1.048967
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	0.00505	1.146295
PS 42:8	ROCNHMA:	52925757	CCCCC/C=C	0.002152	0.774225
PS p34:0	OHPHIZCKA	52926194	CCCCCCCCC(	0.475419	1.013683
SM 33:1	LQINJRUGT	52931139	CCCCCCCCC(	0.56119	1.038359
SM 34:0	QHZIGNLCL	9939965	CCCCCCCCC(	0.208542	0.869643
SM d16:1/2	LKQLRGMN	6453725	CCCCCCCCC(	0.269616	0.949512
SM d16:1/2	NBEADXWA	6443882	CCCCCCCCC(	0.915207	1.006393
SM d18:1/1	KYICBZWZC	11433862	CCCCCCCCC(	0.737402	0.971367
SM d18:1/1	RWKUXQNI	9939941	CCCCCCCCC(	0.05865	0.942448
SM d18:1/1	YLWSJLLZU	52931235	CCCCCCCCC(	0.075681	0.930673
SM (d18:1/	LKQLRGMN	6453725	CCCCCCCCC(	0.345919	0.947214
SM (d18:1/	NBEADXWA	6443882	CCCCCCCCC(	0.978642	1.001834
SM d18:1/2	AADLTHQN	44260124	CCCCCCCCC(	0.071107	0.909722
SM (d18:1/	MDRFMTLY	52931179	CCCCCCCCC(	0.0893	0.92614
SM d18:1/2	YXSZOBWV	52931193	CCCCCCCCC(	0.19211	1.119025
SM d18:1/2	FJJANLYCZU	44260125	CCCCCCCCC(	0.214833	0.95341
SM d18:1/2	SXZWBNWT	46891684	CCCCCCCCC(	0.284084	1.05927
SM d18:1/2	QEDPUVGS	44260127	CCCCCCCCC(	0.393112	0.90994
SM d18:2/2	JBDGKEXQH	52931209	CCCCCCCCC(	0.599407	0.974631
SM d18:2/2	DACOGJME	52931217	CCCCCCCCC(	3.73E-07	0.690196
SM (d18:2/	TXFLWJQV(	52931215	CCCCCCCC/	1.76E-06	0.783623
TG 42:0	DUXYWXYC	11148	CCCCCCCCC(	0.064653	1.913322
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCCC(	0.034305	1.983667
TG 46:0	JWVXCFSNI	91865745	CCCCCCCCC(	0.015826	1.806509
TG 46:1	RSDIQTNCD	56936558	CCCCCCCCC(	0.065762	1.653325
TG 46:2	XUEMVUXN	56936582	CCCCCCCCC(	0.014889	2.015632
TG 46:3	AQARPXOE	56936561	CCCCCCCCC(	0.003255	2.113504
TG 48:0	PVNIQBQSY	11147	CCCCCCCCC(	0.03165	1.473596
TG 48:1	FEKLSEFRU(	9543986	CCCCCCCCC(	0.007118	1.594891
TG 48:2	RUOVJPPU:	9543987	CCCCCCCCC(	0.003255	1.796771
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	0.004545	2.035586
TG 49:0	TTWJTJMW	9543988	CCCCCCCCC(	0.003255	1.934064
TG 49:1	VYYGQDOP	9543991	CCCCCCCCC(	0.000232	2.124863
TG 49:2	QZYSUBAQ	9543993	CCCCCCCCC(	1.38E-05	2.039847
TG 50:0	QRJMBNGG	3246958	[2H]C([2H])	0.036546	1.692677
TG 50:1	YHMDGPZC	25240460	CCCCCCCCC(	0.031649	1.257018
TG 50:2	QEZWFCZN	9544010	CCCCCCCCC(	0.002424	1.366696
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	5.56E-06	2.003757
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	7.15E-05	2.093046
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	0.000962	1.850921
TG 51:1	OZAXLAGN	9544006	CCCCCCCCC(	0.000601	1.994703
TG 51:2	NSNSZGBC(	9544013	CCCCCCCCC(	0.000146	1.760746

TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	8.23E-08	2.071834
TG 51:4	IIRQXNVLA:	9544052	CCCCCCCC/	3.69E-07	2.120695
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	0.089684	1.553975
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	0.010346	1.659704
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.247729	1.059092
TG 52:3	KGLAHZTW	25240361	CCCCCCCC(	0.001521	1.202054
TG 52:4	WHSWXEY\	25240364	CCCCCCCC/	0.005598	1.414651
TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.020816	1.462804
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	0.015826	1.544248
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	0.003427	1.949252
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	0.000235	1.582481
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCCC/	5.21E-06	1.807538
TG 53:4	BMSDHYZL(	9544152	CCCCCCCC/	2.49E-07	1.820646
TG 53:5	QHYAATSK\	9544183	CCCCCCC/C	0.013854	1.603272
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	0.312217	1.209877
TG 54:1	YFFIQXNTT	16058371	CCCCCCCC(	0.011101	1.883044
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	0.011101	1.50796
TG 54:3	PHYFQTYBJ	5497163	CCCCCCCC/	0.014889	1.256828
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	0.014932	1.344612
TG 54:5	VVEBTVMJI	25240373	CCCCCCCC/	0.011973	1.455389
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.011973	1.772967
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.728161	1.083249
TG 56:1	OCYFAHIH\	9544345	CCCCCCCC(	0.109637	1.395045
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	0.076944	1.377599
TG 56:3	QXMHHXQ	9544447	CCCCCCCC/	0.298663	1.191864
TG 56:4	YONCDTJKI.	25240379	CCCCCCCC/	0.069235	1.455109
TG 56:5	UHEJWASO	25240380	CCCCCCCC/	0.174235	1.340855
TG 56:6	ZTNDRFCAI	9544625	CCCCC/C=C	0.913897	1.01742
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	0.974161	0.993058
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	0.572568	0.893294
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	0.433464	1.172532
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	0.084805	1.348603
TG 58:3	RFMSTHTU	9544748	CCCCCCCC/	0.020773	1.508534
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	0.248881	1.250052
TG 58:6	GSNFRUMS	9544977	CCCCCCCC/	0.011101	1.474425
TG 58:8	KWIGMCR\	9545124	CCCCCCCC(	0.831671	0.962055
TG 58:9	RVXFSLZMZ	9545200	CCCCCCCC/	0.974161	1.008172
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	0.112801	1.260882
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.073692	0.742051
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	0.073692	1.440487
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	0.352235	1.125937

S10. Lipidome differential abundance analysis: Cluster IV vs Cluster I at Visit -6

Compound	InChiKeys	Pubchem ID	SMILES	pvalue	foldchange
CE 18:1	RJECHNNFF	5283632	CCCCCCCC/	2.40E-07	0.60522
CE 18:2	NAACPBBQ	5287939	CCCCC/C=C	7.62E-05	0.65503
CE 18:3	FYMCIBHUI	6436907	CC/C=C\C/(	9.78E-05	0.626045
CE 20:4	IMXSFYNM	6479222	CCCCC/C=C	0.005452	0.765
CE 22:6	VOEVEGPM	14274978	CC/C=C\C/(	1.96E-11	0.405499
Ceramide d	NAJHAHQN	52931115	CCCCCCCC(	0.17868	1.100741
Ceramide d	KEPQASGD	5283567	CCCCCCCC(	0.098506	1.108622
Ceramide d	ZJVVOYPTF	5283571	CCCCCCCC(	0.377088	1.054862
Ceramide d	VJSBNBBOS	5283568	CCCCCCCC(	0.000157	0.728039
Cer (d18:1/	YDNKGFDK	5283564	CCCCCCCC(	0.931401	1.006314
Cer (d18:1/	KEPQASGD	5283567	CCCCCCCC(	0.031366	1.144091
Cer (d18:1/	VJSBNBBOS	5283568	CCCCCCCC(	0.000186	0.716538
Cholesterol	HVYWMON	5997	C[C@H](CC	0.487026	1.010291
DG 32:0	JEJLGIQLPY	644078	CCCCCCCC(	3.89E-05	1.567538
DG 34:0	VYQDALBE(	3246945	CCCCCCCC(	0.001453	1.341865
DG 34:1	YEJYLHKQO	5282283	CCCCCCCC(	0.001104	1.465007
DG 36:0	UHUSDOQ(	102615	CCCCCCCC(	0.639992	0.975016
DG 36:2	AFSHUZFNI	9543716	CCCCCCCC/	0.03182	1.266304
DG 36:3	BLZVZPYMI	9543722	CCCCCCCC/	7.26E-05	1.587335
DG 38:5	GRGDLDNR	9543784	CCCCC/C=C	0.035239	1.185546
DG 38:6	YDVDXUYJF	9543795	CCCCC/C=C	0.016507	2.043084
DG 40:1	VFUWCRM	9543793	CCCCCCCC(	0.186292	0.903538
FA 16:0	IPCSVZSSVZ	985	CCCCCCCC(	0.177008	0.894725
FA 16:1	SECPZKHBE	445638	CCCCCC/C=	0.153503	0.708253
FA 18:0	QIQXTHQIE	5281	CCCCCCCC(	0.810347	1.036323
FA 18:1	ZQPPMHVV	445639	CCCCCCCC/	0.05664	0.703219
FA 22:4	TWSWSIQA	5497181	CCCCC/C=C	0.877567	1.020101
GlcCer d18:	YIGARKIIFO	6321359	CCCCCCCC(	0.049128	0.880069
GlcCer d18:	POQRWMR	6321361	CCCCCCCC(	0.008954	0.843011
GlcCer d18:	WBOZIXHP	6321360	CCCCCCCC(	5.24E-06	0.635613
LPC 18:0	IHNKQIMG'	497299	CCCCCCCC(	0.043058	1.238967
LPC 18:1	YAMUFBLW	16081932	CCCCCCCC/	0.931401	1.009557
LPC 18:2	SPJFYYJXNF	11005824	CCCCC/C=C	0.286251	1.131611
LPC 20:0	UATOAILW	24779473	CCCCCCCC(	0.267082	1.115356
LPC 20:1	GJTDRNFW	24779475	CCCCCCCC(	0.931401	0.986419
LPC 20:2	YYQVCMM:	52924053	CCCCC/C=C	0.094174	1.211988
LPE 18:0	BBYWOYAF	46891690	CCCCCCCC(	0.13597	1.227678
LPE 18:2	DBHKHNGE	52925130	CCCCC/C=C	0.039579	1.37003
LPE 20:0	HEQMDGO	52925131	CCCCCCCC(	0.373929	1.019113
LPE 20:1	JEAGLCKGA	52925139	CCCCCCCC/	0.931401	0.99035
PC 16:0/16	KILNVBDSV	452110	CCCCCCCC(	0.177008	0.937481
PC 18:1/16	WTJKGGKO	5497103	CCCCCCCC(	0.000402	0.886605
PC 28:0	CITHEXJVP(	5459377	CCCCCCCC(	0.931401	1.024473
PC 30:0	RFVFQQWI	129657	CCCCCCCC(	0.877567	1.028692
PC 32:0	KILNVBDSV	452110	CCCCCCCC(	0.085105	0.890828
PC 32:1	QIBZFHLFH	6443788	CCCCCCCC(	0.029455	0.811973
PC 32:2	GPWHCUU	24778764	CCCCCC/C=	0.22634	1.148731
PC 32:3	UXEFXNOSI	52922763	CCCCCCCC(	0.898138	0.976706
PC 33:1	GXTATYLPY	24778662	CCCCCCCC(	0.931401	0.990571
PC 34:0	PZNPLUBHI	24778686	CCCCCCCC(	0.931401	1.009393

PC 34:1	WTJKGGKO	5497103	CCCCCCCC(	0.001842	0.859373
PC 34:2	JLPULHDHA	5287971	CCCCCCCC(	0.489541	1.014544
PC 34:3	CNNSEHUK	24778699	CCCCCCCC(	0.249254	0.896505
PC 35:2	ZSKWZJYU\	52922491	CCCCCCCC(	0.000304	1.269182
PC 36:0	NRJAVPSFF	94190	CCCCCCCC(	0.169448	1.122832
PC 36:1	ATHVAWFA	24778825	CCCCCCCC(	0.255433	0.913763
PC 36:2	SNKAWJBJ(	10350317	CCCCCCCC/	0.160983	1.049905
PC 36:3	BXRLDROZ\	24778937	CCCCCCCC/	0.489278	1.045085
PC 36:4	IIZPXYDJLKI	10747814	CCCCCCCC(	0.191894	1.043624
PC 36:5	DYDDZDMJ	24778771	CCCCCC/C=	0.489278	0.987858
PC 36:6	SPWBDEZN	52922847	CCCCC/C=C	0.111017	0.789725
PC 37:2	MCZUABD\	52922735	CCCCCCCC(	0.054186	1.16064
PC 37:3	OOYQEEUL	52922851	CCCCCCCC(	0.111017	1.210121
PC 37:4	QRPUCJXFF	52922853	CCCCCCCC(	0.000304	1.321115
PC 38:2	KXXLFCAPK	24779263	CCCCCCCC(	0.744487	1.026632
PC 38:3	OJHJKEBRZ	52922741	CCCCCCCC/	0.980497	1.00354
PC 38:4	DNYKSJQVE	52923291	CCCCCCCC(	0.060809	1.084168
PC 38:5	YLWBKBDN	53479033	CCCCCC/C=	0.293884	0.881395
PC 38:6	PLZBTDKJYI	52923295	CCCCC/C=C	0.000186	0.766845
PC 38:8	QQNHCRB(	52922865	CC/C=C\C/(	0.000157	0.49846
PC 40:2	AEUCYCQY	24779063	CCCCCCCC/	0.997308	0.999763
PC 40:5	LJFKFKIYUJI	52923133	CCCCCCCC/	0.000402	0.708464
PC 40:6	TYRTWVKQ	52923195	CCCCC/C=C	0.356469	0.917774
PC 40:7	BPUROMF(	24778982	CCCCC/C=C	0.03143	0.813395
PC 42:1	PAHPUCKP	24778881	CCCCCCCC(	0.000137	0.767421
PC 42:4	SGYNBRXE(	24779052	CCCCCCCC(	0.311561	1.074277
PC 42:6	DSVRMAGY	52923651	CCCCC/C=C	0.898138	1.036536
PC 44:3	GZZUNXHF	52923541	CCCCCCCC(	2.59E-06	0.730831
PC 44:4	UIAAGLPOL	52923481	CCCCCCCC(	0.27117	0.933641
PC p34:1	OIICTMOQI	11125520	CCCCCCCC(	1.76E-05	0.766404
PC p34:2	KMNVIRCH	52923934	CCCCCCCC(	1.29E-08	0.681547
PC p34:3	QLEHHUPU	24779386	CCCCCCCC(	0.020138	0.826787
PC p36:3	SOUZQPFU	53481701	CCCCCCCC(	0.15078	0.930336
PC p36:4	IOYKZPNDX	24779388	CCCCCCCC(	0.027555	0.853276
PC p38:3	WOSDZWB	52925093	CCCCCCCC(	0.693293	1.036143
PC p38:4	BAKDTVUH	52925117	CCCCCCCC(	0.06259	0.904199
PE 34:2	HBZNVZIRJ	46891780	CCCCCCCC(	0.009712	1.412245
PE 36:2	DXXUYBAIS	52924894	CCCCCCCC(	0.005257	1.288381
PE 36:3	GKAFCSRKI	71728379	CCCCCCCC/	0.943754	1.003936
PE 36:4	DUQDVNA(	52924875	CCCCCCCC(	0.113782	1.1747
PE 38:2	CLPMAPXZI	9546825	CCCCCCCC(	0.000609	1.266041
PE 38:4	ANRKEHNV	46891781	CCCCCCCC(	0.000139	1.550118
PE 38:6	LFGBKOUQ	52924893	CCCCC/C=C	0.170081	0.837839
PE 40:6	FEABWDMI	52924379	CCCCC/C=C	0.001176	0.796105
Phosphatid	RYHJACYQT	52926457	CCCCCCCC(	0.931401	1.003231
Plasmenyl-I	IQACMFWA	6443157	CCCCCCCC(	0.201204	0.876851
Plasmenyl-I	JCIBOIAZHL	70698851	CCCCCC/C=	0.026038	0.842793
Plasmenyl-I	FHHVIBPVE	24779390	CCCCCCCC(	0.786319	1.028411
Plasmenyl-I	XVXISDREV	52925079	CCCCCCCC(	0.931401	1.008941
Plasmenyl-I	UUYSKERSK	52925126	CCCCCCCC(	0.527951	0.937412
Plasmenyl-I	RLLOITCRN	52925061	CCCCCCCC(	0.00011	0.463994
Plasmenyl-I	URPXXNCT	86289532	CCCCCCCC(	0.202463	0.895239

Plasmenyl-I	KCNBSSYOJ	52925089	CCCCCCCC(	0.330218	0.906876
Plasmenyl-I	WVGALBKS	5283497	CCCCCCCC(	8.37E-06	0.64029
Plasmenyl-I	CVCZYWPC	52925119	CCCCCCCC(	0.203711	0.840839
Plasmenyl-I	FIJFPUAJUL	42607458	CCCCCCCC(	0.000104	0.683542
PS 38:3	BQBTWCBZ	52925523	CCCCCCCC(	0.005244	0.927503
PS 38:4	SVOUGFFD	24779545	CCCCCCCC(	0.216373	0.979278
PS 40:3	BTIQFPURP	52925502	CCCCCCCC(	0.439782	0.946015
PS 40:4	GBBNRADS	52925748	CCCCCCCC(	0.104949	1.048922
PS 40:6	LYYHRRPTE	24779546	CCCCCCCC(	0.110191	1.062839
PS 42:5	VNQACVFLI	52925755	CCCCCCCC(	0.327481	1.071578
PS 42:6	WOBFEYJLJ	52925756	CCCCC/C=C	0.035239	1.105345
PS 42:8	ROCNHMA:	52925757	CCCCC/C=C	0.00159	0.799131
PS p34:0	OHPHIZCKA	52926194	CCCCCCCC(	0.695617	1.041486
SM 33:1	LQINJRUGT	52931139	CCCCCCCC(	0.931401	0.99255
SM 34:0	QHZIGNLCL	9939965	CCCCCCCC(	0.035239	0.874222
SM d16:1/2	LKQLRGMN	6453725	CCCCCCCC(	0.013243	0.890946
SM d16:1/2	NBEADXWA	6443882	CCCCCCCC(	0.103146	0.918659
SM d18:1/1	KYICBZWZC	11433862	CCCCCCCC(	0.786319	0.974433
SM d18:1/1	RWKUXQNI	9939941	CCCCCCCC(	0.384994	0.969755
SM d18:1/1	YLWSJLLZU	52931235	CCCCCCCC(	0.042903	0.921945
SM (d18:1/	LKQLRGMN	6453725	CCCCCCCC(	0.035036	0.894607
SM (d18:1/	NBEADXWA	6443882	CCCCCCCC(	0.056084	0.899243
SM d18:1/2	AADLTHQN	44260124	CCCCCCCC(	0.165084	0.928059
SM (d18:1/	MDRFMTLY	52931179	CCCCCCCC(	0.008954	0.88444
SM d18:1/2	YXSZOBWV	52931193	CCCCCCCC(	0.780349	1.03042
SM d18:1/2	FJJANLYCZL	44260125	CCCCCCCC(	0.931401	1.006145
SM d18:1/2	SXZWBNWT	46891684	CCCCCCCC(	0.666508	1.028889
SM d18:1/2	QEDPUVGS	44260127	CCCCCCCC(	0.980497	1.001495
SM d18:2/2	JBDGKEXQI	52931209	CCCCCCCC(	0.004917	0.868454
SM d18:2/2	DACOGJME	52931217	CCCCCCCC(	2.45E-07	0.698374
SM (d18:2/	TXFLWJQV(	52931215	CCCCCCCC/	8.37E-06	0.788175
TG 42:0	DUXYWXYC	11148	CCCCCCCC(	7.30E-05	4.792985
TG 44:1	UZLGGKDLJ	56936554	CCCCCCCC(	0.000133	4.586274
TG 46:0	JWVXCFSNI	91865745	CCCCCCCC(	0.000139	3.063968
TG 46:1	RSDIQTNCL	56936558	CCCCCCCC(	0.000771	3.070653
TG 46:2	XUEMVUXN	56936582	CCCCCCCC(	2.96E-05	4.102316
TG 46:3	AQARPXOE	56936561	CCCCCCCC(	1.76E-05	3.959437
TG 48:0	PVNIQBQSY	11147	CCCCCCCC(	0.000402	2.079248
TG 48:1	FEKLSEFRU	9543986	CCCCCCCC(	0.000787	2.023911
TG 48:2	RUOVJPPU:	9543987	CCCCCCCC(	0.000137	2.604568
TG 48:3	SKGWNZXC	9543989	CCCCCC/C=	4.75E-05	3.343449
TG 49:0	TTWJTJMW	9543988	CCCCCCCC(	0.00011	2.941314
TG 49:1	VYYGQDOP	9543991	CCCCCCCC(	0.000137	2.588445
TG 49:2	QZYSUBAQ	9543993	CCCCCCCC(	4.75E-05	2.324293
TG 50:0	QRJMBNGC	3246958	[2H]C([2H])	4.93E-05	3.392795
TG 50:1	YHMDGPZC	25240460	CCCCCCCC(	0.00159	1.361172
TG 50:2	QEZWFCZN	9544010	CCCCCCCC(	0.000459	1.416837
TG 50:3	UFHNZOAC	25240357	CCCCCCCC/	4.04E-06	2.25516
TG 50:4	PVMBAGXV	25240359	CCCCCC/C=	8.37E-06	2.706395
TG 50:5	AFTBPUXZT	9544045	CCCCCC/C=	0.000231	2.379153
TG 51:1	OZAXLAGN	9544006	CCCCCCCC(	0.000112	2.58554
TG 51:2	NSNSZGBC(	9544013	CCCCCCCC(	0.000181	1.947393

TG 51:3	ISSGPXMQ(	9544023	CCCCCCC/C	4.84E-07	2.205668
TG 51:4	IIRQXNVLA.	9544052	CCCCCCCC/	1.03E-06	2.567109
TG 52:0	SDNYRTVJC	545690	CCCCCCCC(	5.33E-06	4.554591
TG 52:1	NPCZZYKITI	25240360	CCCCCCCC(	9.78E-05	2.420592
TG 52:2	KGLAHZTW	25240361	CCCCCCCC(	0.085105	1.089134
TG 52:3	KGLAHZTW	25240361	CCCCCCCC(	0.000748	1.183677
TG 52:4	WHSWXEY\	25240364	CCCCCCCC/	2.09E-05	1.704965
TG 52:5	CQZAAIKPS	25240366	CCCCCC/C=	0.014963	1.713559
TG 53:0	ZJUXHXMIK	9544181	CCCCCCCC(	1.76E-05	2.796576
TG 53:1	WWJIBIGW	9544081	CCCCCCCC(	2.77E-05	3.599985
TG 53:2	RSINITWKV	9544102	CCCCCCCC(	0.000112	1.826855
TG 53:3	ZNQBEJJYV.	9544126	CCCCCCCC/	2.27E-06	2.157588
TG 53:4	BMSDHYZL(	9544152	CCCCCCCC/	2.45E-07	2.138764
TG 53:5	QHYAATSK\	9544183	CCCCCCC/C	2.86E-05	2.760623
TG 54:0	DCXXMTOC	11146	CCCCCCCC(	5.30E-05	2.533167
TG 54:1	YFFIQXNTT\	16058371	CCCCCCCC(	3.64E-06	4.00479
TG 54:2	RYNHWWN	16058372	CCCCCCCC(	9.56E-05	2.104073
TG 54:3	PHYFQTYBJ	5497163	CCCCCCCC/	0.000139	1.476597
TG 54:4	BRLGHZXET	9544255	CCCCCCCC(	0.000104	1.62244
TG 54:5	VVEBTVMJI	25240373	CCCCCCCC/	0.001176	1.608514
TG 54:6	HBOQXIRUI	5322095	CCCCC/C=C	0.000721	2.335829
TG 54:8	BMPVTDW(	9544413	CCCCC/C=C	0.177008	1.468882
TG 56:1	OCYFAHIH\	9544345	CCCCCCCC(	6.03E-05	2.874106
TG 56:2	PDEQUPGH	9544390	CCCCCCCC(	0.000104	2.563719
TG 56:3	QXMHHXQ	9544447	CCCCCCCC/	0.015981	1.739167
TG 56:4	YONCDTJKI	25240379	CCCCCCCC/	0.011013	1.636174
TG 56:5	UHEJWASO	25240380	CCCCCCCC/	0.060809	1.342603
TG 56:6	ZTNDRFCAI	9544625	CCCCC/C=C	0.735942	0.943314
TG 56:7	DODZUDCY	9544695	CCCCC/C=C	0.666508	1.070961
TG 56:8	UBGUHMD	9544762	CCCCCCCC(	0.27117	1.284644
TG 58:1	OWZMHFA	25240381	CCCCCCCC(	4.64E-05	2.379976
TG 58:2	GXWBCAV(	9545277	CCCCC/C=C	0.000326	2.240839
TG 58:3	RFMSTHTU	9544748	CCCCCCCC/	6.92E-05	2.80093
TG 58:4	CCKRHDUC	9544835	CCCCCCCC(	0.0021	1.988425
TG 58:6	GSNFRUMS	9544977	CCCCCCCC/	0.01613	1.454305
TG 58:8	KWIGMCR\	9545124	CCCCCCCC(	0.375358	1.134095
TG 58:9	RVXFSLZMZ	9545200	CCCCCCCC/	0.548178	1.111535
TG 60:1	YNDXXWKS	9544965	CCCCCCCC(	0.000402	2.228595
TG 60:11	ASSZWZBQ	9545730	CCCCC/C=C	0.072323	0.766309
TG 60:2	QPNVLDQS	9545040	CCCCCCCC(	0.000326	2.219861
TG 62:1	TZLOSVAFX	9545526	CCCCCCCC(	0.001088	1.736794

S11: Differential abundant lipid classes between clusters, identified by ChemRICH at visits -3 and -6.

Clusters to compare	Visit	Lipid class	Class size	p-value
III-IV vs I-II	**-3**	Unsaturated triglycerides	53	6.2E-45
		Saturated triglycerides	8	2.2E-20
		Unsaturated phosphatidylcholines	40	2.6E-12
	-6	Unsaturated triglycerides	53	3.3E-41
		Saturated phosphatidylcholines	5	2E-08
		Saturated triglycerides	8	1.1E-07
II vs I	**-3**	Unsaturated phosphatidylcholines	40	7.5E-24
		sphingomyelins	15	1.8E-12
	-6	Unsaturated phosphatidylcholines	40	3.1E-08
		sphingomyelins	15	0.000047
III vs I	**-3**	Unsaturated triglycerides	53	3.5E-39
		Saturated triglycerides	8	9.2E-09
		Unsaturated diglycerides	6	0.000023
		lysophosphatidylcholines	6	3.1E-07
	-6	Unsaturated triglycerides	53	3.2E-32
		Saturated triglycerides	8	3.5E-06
		lysophosphatidylcholines	6	5.3E-06
IV vs I	**-3**	Unsaturated triglycerides	53	7.9E-21
		Saturated triglycerides	8	0.000052
		Unsaturated phosphatidylcholines	40	2.5E-10
		cholesterol esters	5	0.000013
	-6	Unsaturated triglycerides	53	3.1E-31
		Saturated triglycerides	8	2.2E-20
		Unsaturated phosphatidylcholines	40	1.2E-06
		Unsaturated diglycerides	6	0.000042
		cholesterol esters	5	4.8E-12
IV vs III	**-3**	galactosylceramides	3	3.7E-09
		plasmalogens	8	2.8E-07
	-6	galactosylceramides	3	4.4E-06
		plasmalogens	8	6.2E-06

Adjusted p-value	Key lipid species	Differential species	Increased species
9.3E-44	TG 51:4	52	52
1.6E-19	TG 46:0	8	8
1.3E-11	PC 38:4	23	19
4.9E-40	TG 46:2	51	51
1.5E-07	PC 34:0	5	5
4.2E-07	TG 42:0	8	8
1.1E-22	PC 33:1	34	0
6.6E-12	SM d18:2/23:0	13	0
4.7E-07	PC 38:8	12	0
0.00035	SM d18:2/23:0	8	0
5.3E-38	TG 54:5	50	50
6.9E-08	TG 52:0	7	7
0.00007	DG 36:3	5	5
1.2E-06	LPC 18:2	5	5
4.8E-31	TG 56:8	44	44
0.000018	TG 42:0	5	5
0.00002	LPC 20:2	5	5
1.2E-19	TG 51:3	33	33
0.00011	TG 49:0	5	5
1.9E-09	PC p34:2	18	6
0.000033	CE 22:6	4	0
4.7E-30	TG 53:4	44	44
1.6E-19	TG 52:0	8	8
4.3E-06	PC p34:2	15	2
0.00013	DG 36:3	5	5
2.4E-11	CE 22:6	5	0
2.8E-08	GlcCer d18:1/24:1	3	0
0.000001	Plasmenyl-PE 38:7	7	0
0.000031	GlcCer d18:1/24:1	3	0
0.000031	Plasmenyl-PE 38:7	7	0

S12. Spearman correlation coefficient (rho) among nutrient biomarkers and lipidome

	Ascorbic Ac	25(OH)D	ALA	EPA	DHA	DPA
CE18:1	-0.089	-0.08757	0.172391	0.218428	0.008736	0.184539
CE18:2	-0.07653	0.068338	0.070974	-0.04731	-0.12594	-0.01031
CE18:3	-0.21943	0.057001	0.522954	0.360069	-0.11357	0.316715
CE20:4	0.011124	-0.06344	-0.11955	0.041201	0.013447	0.106502
CE22:6	-0.03803	-0.1068	0.049446	0.350347	0.423698	0.104642
Ceramided18:1/23:0	-0.05984	0.171771	0.040676	-0.08075	-0.20695	0.031948
Ceramided40:1	0.043492	0.169991	-0.07349	-0.12548	-0.12514	-0.02951
Ceramided42:1	0.015058	0.135447	-0.04425	-0.10408	-0.14192	0.015523
Ceramided42:2	-0.09625	-0.08768	0.255723	0.3583	0.177973	0.233819
Cerd18:1/16:0	-0.02953	0.121644	-0.02823	0.028124	-0.00357	0.072879
Cerd18:1/22:0	0.04769	0.19296	-0.11119	-0.17947	-0.15874	-0.03763
Cerd18:1/24:1	-0.11031	-0.05232	0.261187	0.359526	0.185964	0.231267
DG32:0	0.036313	0.038718	-0.04742	0.073185	0.115511	0.082896
DG34:0	-0.00027	-0.00957	-0.16639	-0.00648	0.070239	0.030523
DG34:1	-0.02147	0.049066	0.041579	0.133502	0.138376	0.104873
DG36:0	-0.05124	-0.04266	-0.02385	-0.00773	0.039994	-0.00117
DG36:2	-0.04146	0.087784	0.121152	0.090961	0.083428	0.033473
DG36:3	0.074541	0.184318	-0.12366	-0.23557	-0.02339	-0.17652
DG38:5	0.093812	0.106496	-0.18273	-0.12854	0.032629	-0.08512
DG38:6	0.091619	0.121926	-0.26972	-0.29313	-0.03359	-0.19054
DG40:1	0.020544	-0.04066	0.04339	0.054722	0.029418	0.040178
FA16:0	0.013874	0.002947	-0.0426	-0.02573	0.042546	-0.01407
FA16:1	-0.00341	-0.10314	-0.07347	0.03091	0.06876	0.025058
FA18:0	0.006299	-0.01909	-0.01678	-0.01202	0.024324	0.025593
FA18:1	-0.01787	-0.02408	-0.05155	-0.00879	0.068591	-0.02594
FA22:4	0.003426	-0.04785	-0.1877	-0.08871	0.060339	-0.05844
LPC16:0	-0.07114	0.102454	0.156521	0.143787	0.065924	0.188022
LPC18:0	-0.00372	0.081695	0.021545	0.115343	0.146723	0.11842
LPC18:1	0.008121	0.057885	0.127924	0.116119	0.136851	0.063573
LPC18:2	0.099839	0.10739	-0.11584	-0.09949	0.056881	-0.10326
LPC20:0	0.062864	0.122509	0.002361	0.010343	0.114794	-0.0491
LPC20:1	-0.05398	0.059037	0.145948	0.179899	0.192129	0.103434
LPC20:2	0.043682	0.043728	-0.09259	-0.02257	0.120267	-0.01401
LPE18:0	-0.05798	0.179444	0.147096	0.074333	-0.00395	0.158171
LPE18:2	0.096611	0.079724	-0.07202	-0.09752	0.007515	-0.08472
LPE20:0	-0.06673	-0.00086	0.146934	0.056266	0.010731	0.046289
LPE20:1	0.02476	0.07491	0.093116	0.098224	0.131945	0.050834
PC16:0/16:0	0.062472	-0.06756	-0.10074	0.086027	0.187926	0.023747
PC18:1/16:0	-0.10366	-0.09252	0.355691	0.279239	0.015064	0.210979
PC28:0	0.151588	-0.14666	-0.09853	0.022162	0.08182	-0.01257
PC30:0	0.136768	-0.1557	-0.12156	0.064335	0.092918	0.051469
PC32:0	0.072416	-0.08284	-0.10304	0.129254	0.203788	0.071346
PC32:1	0.003827	-0.19067	0.173615	0.241346	0.028246	0.214531
PC32:2	0.115463	-0.02707	0.012482	-0.08608	-0.10249	-0.02142
PC32:3	0.161478	-0.18437	-0.14803	0.072055	0.131923	0.038838
PC33:1	-0.08811	-0.03962	0.186506	0.224604	-0.08051	0.26729
PC34:0	0.048331	-0.09557	-0.13452	0.140182	0.147285	0.133902
PC34:1	-0.06696	-0.07946	0.329847	0.257073	0.012489	0.170558
PC34:2	0.055973	0.128396	0.018641	-0.1423	-0.10513	-0.10086
PC34:3	-0.0996	-0.01402	0.480691	0.306445	-0.0829	0.280411

PC35:2	-0.01707	0.097413	-0.0141	-0.01989	-0.16269	0.079059
PC36:0	-0.05433	0.063601	0.1308	0.120565	-0.14183	0.19123
PC36:1	-0.0111	-0.07478	0.187168	0.277116	0.075601	0.177132
PC36:2	0.103704	0.066462	-0.12491	-0.05198	0.021852	-0.07012
PC36:3	-0.02635	0.118971	0.155754	-0.06079	-0.18927	0.027187
PC36:4	0.111182	0.016433	-0.1728	-0.06827	-0.00213	-8.66E-05
PC36:5	0.010411	-0.086	0.041234	0.073041	0.079109	0.003361
PC36:6	0.025445	-0.10776	0.102553	0.308258	0.310617	0.124135
PC37:2	-0.02326	0.124429	0.0787	0.056747	-0.04204	0.056043
PC37:3	-0.05036	0.09971	0.051677	-0.00459	-0.2122	0.088634
PC37:4	0.055677	0.072877	-0.16732	-0.03896	-0.04866	0.073756
PC38:2	0.026987	-0.07233	0.02153	0.205681	0.134872	0.142502
PC38:3	-0.04894	0.041427	0.100317	0.085845	-0.17581	0.185307
PC38:4	0.145749	-0.00794	-0.28502	-0.09677	0.040035	-0.03606
PC38:5	-0.12494	-0.03935	0.270385	0.315944	-0.03301	0.277276
PC38:6	0.024371	-0.10391	-0.04421	0.342644	0.519564	0.086101
PC38:8	-0.204	-0.1065	0.448604	0.588876	0.085591	0.430626
PC40:2	0.0811	-0.15725	0.026792	0.231435	0.207544	0.192906
PC40:5	0.070882	-0.10112	-0.10094	0.312767	0.526634	0.057391
PC40:6	0.024151	-0.06934	-0.04294	0.299252	0.352753	0.140559
PC40:7	-0.03639	0.06236	0.143994	0.20692	0.269484	0.00723
PC42:1	-0.14717	0.124034	0.320574	0.154455	-0.08787	0.090323
PC42:4	0.088217	0.15197	-0.25874	-0.30279	-0.08653	-0.17865
PC42:6	-0.08671	0.014291	0.289745	0.192824	-0.1282	0.198997
PC44:3	-0.07248	0.003923	0.170006	0.215554	0.099995	0.096013
PC44:4	0.073442	0.064688	-0.18839	-0.16352	0.109121	-0.18745
PCp34:1	-0.01196	0.050859	0.146857	0.096404	0.04326	0.010554
PCp34:2	-0.0344	-0.14564	0.181071	0.331512	0.215199	0.186449
PCp34:3	-0.08825	0.110429	0.277768	0.09102	-0.22684	0.152873
PCp36:3	-0.02785	-0.01952	-0.02571	0.064514	-0.0402	0.147157
PCp36:4	0.129993	-0.06959	-0.22672	0.001073	0.120441	0.018242
PCp38:3	0.030427	-0.02748	-0.15028	-0.02833	-0.12233	0.10323
PCp38:4	0.077842	-0.01148	-0.06877	0.01031	0.035293	0.028547
PE34:2	0.016038	0.116116	0.108539	-0.05854	-0.09226	-0.04867
PE36:1	-0.08159	-0.02318	0.188384	0.199281	-0.08801	0.248689
PE36:2	-0.06163	0.096359	0.068136	-0.00481	-0.21703	0.133458
PE36:3	-0.05332	-0.01236	0.012112	0.051422	0.022679	0.04148
PE36:4	-0.03287	0.053766	0.065698	-0.00244	-0.03639	0.022711
PE38:2	-0.01765	0.085742	-0.00937	0.01579	-0.11392	0.093789
PE38:4	-0.01727	0.053921	-0.00981	-0.03749	-0.05805	-0.00055
PE38:6	-0.05916	-0.0735	0.142005	0.311339	0.333627	0.094883
PE40:6	0.05058	-0.12272	-0.10496	0.317902	0.542944	0.05134
Phosphatidylglycerol29:(	0.072907	-0.01725	-0.07254	-0.07603	-0.01256	-0.06507
PI34:1	-0.09847	0.013887	0.315776	0.287332	-0.01335	0.229672
PI34:2	0.05707	0.159963	-0.00385	-0.1801	-0.1346	-0.137
PI36:1	-0.1623	0.063469	0.395779	0.298722	-0.09364	0.241936
PI36:2	-0.02686	0.223579	0.094863	-0.16554	-0.21967	-0.07709
PI36:3	0.084468	0.139441	-0.04057	-0.20949	-0.14556	-0.14911
PI36:4	0.140084	0.03243	-0.13736	-0.02259	0.119291	-0.05442
PI38:4	0.126014	0.078601	-0.20031	-0.09022	0.065191	-0.07352
PI38:5	0.038996	0.017474	-0.14161	-0.08505	-0.01263	-0.03422
PI40:8	0.005835	0.004057	-0.10394	-0.13387	-0.083	-0.04401

PIp36:5	-0.14425	-0.00467	0.134063	-0.02556	-0.06802	-0.04483
Plasmenyl-PC34:2	-0.17357	0.100374	0.290598	0.090265	-0.27355	0.148907
Plasmenyl-PC36:6	-0.08874	0.106148	0.278422	0.125839	-0.18476	0.167912
Plasmenyl-PC38:5	0.079203	-0.07437	-0.20941	0.024165	0.001529	0.133081
Plasmenyl-PE36:3	-0.08293	0.05817	0.117416	0.075046	-0.18377	0.16137
Plasmenyl-PE36:5	0.04987	-0.001	-0.25008	0.005842	0.158641	-0.01594
Plasmenyl-PE36:6	-0.15605	-0.12075	0.254722	0.575094	0.25089	0.352658
Plasmenyl-PE38:5	0.022156	-0.06027	-0.18703	0.058075	0.079398	0.078828
Plasmenyl-PE38:6	0.080349	-0.04641	-0.22563	0.004225	0.087428	0.018685
Plasmenyl-PE38:7	0.02942	-0.10639	-0.13623	0.277655	0.498211	0.039334
Plasmenyl-PE40:6	-0.01283	-0.0711	-0.06514	0.132899	-0.02438	0.202865
Plasmenyl-PE40:7	-0.00658	-0.14354	-0.11401	0.321793	0.381906	0.15679
PS38:3	-0.05267	-0.06206	0.287234	0.232424	0.019248	0.123613
PS38:4	0.006261	0.043841	-0.00751	-0.0208	0.011826	-0.07347
PS40:3	0.004913	-0.10057	0.124159	0.234267	0.08617	0.117538
PS40:4	0.110937	0.066221	-0.11654	-0.10057	-0.00642	-0.1546
PS40:6	0.120023	0.063313	-0.27317	-0.20207	-0.05922	-0.09389
PS42:5	-0.03695	0.034567	0.087235	0.109925	-0.13365	0.186211
PS42:6	0.179927	0.016188	-0.39768	-0.17983	0.04458	-0.10865
PS42:8	0.063205	-0.1119	-0.11063	0.298248	0.552265	0.008263
PSp34:0	-0.04331	0.071314	0.053749	-0.0491	-0.07385	0.000523
SM33:1	0.007261	0.077808	-0.08411	0.048675	-0.01964	0.106743
SM34:0	-0.02301	-0.00396	-0.08667	0.099664	0.174408	0.02816
SMd16:1/20:0	0.072439	-0.09123	-0.21214	0.058204	0.196165	0.042005
SMd16:1/20:1	0.070068	-0.0823	-0.14814	0.07999	0.097823	0.120754
SMd18:1/14:0	0.167503	-0.01395	-0.22862	-0.08223	0.135902	-0.12336
SMd18:1/16:0	0.016526	0.019944	-0.02193	0.133818	0.125485	0.127231
SMd18:1/16:1	0.095887	-0.04683	-0.04309	0.144563	0.190142	0.091433
SMd18:1/18:0	0.065829	-0.08967	-0.20682	0.025419	0.160468	0.018933
SMd18:1/18:1	0.085473	-0.11457	-0.20337	0.086558	0.158014	0.089249
SMd18:1/20:0	0.096355	0.064269	-0.17448	-0.10138	0.088111	-0.11819
SMd18:1/20:1	0.028206	-0.03737	0.015152	0.135899	0.082384	0.115666
SMd18:1/21:0	0.025477	0.16697	-0.09769	-0.16812	-0.1012	-0.10489
SMd18:1/22:0	-0.02213	0.1549	-0.05081	-0.08375	-0.07811	-0.00458
SMd18:1/23:0	-0.09493	0.178268	0.05917	-0.06231	-0.16675	0.038372
SMd18:1/24:0	-0.02366	0.109625	-0.05254	-0.09695	-0.08915	-0.01724
SMd18:2/23:0	-0.0947	0.084393	0.172445	0.123251	-0.09429	0.154989
SMd18:2/24:0	-0.0791	-0.07903	0.241069	0.351795	0.204572	0.212457
SMd18:2/24:1	-0.02128	-0.08441	0.221215	0.350671	0.222077	0.215445
TG42:0	0.119605	0.004208	-0.20072	-0.07514	0.067507	-0.07075
TG44:1	0.13634	-0.00786	-0.20106	-0.0606	0.088199	-0.06475
TG46:0	0.087751	-0.00835	-0.13024	0.009606	0.073686	0.013593
TG46:1	0.127753	-0.03076	-0.17143	-0.02191	0.118147	-0.04128
TG46:2	0.140292	0.008496	-0.2302	-0.12114	0.078505	-0.1094
TG46:3	0.129642	0.032439	-0.20445	-0.1192	0.05948	-0.09886
TG48:0	0.016425	0.027134	-0.08097	0.031195	0.05107	0.039066
TG48:1	0.107776	-0.04885	-0.13246	0.028539	0.114693	0.00817
TG48:2	0.125895	0.006362	-0.16919	-0.07044	0.072918	-0.06129
TG48:3	0.139823	0.026229	-0.23818	-0.14797	0.07986	-0.14
TG49:0	0.032921	0.014335	-0.06694	0.068772	0.023393	0.101462
TG49:1	0.023575	0.019391	-0.05542	0.077569	0.027789	0.109588
TG49:2	0.047228	0.01969	-0.10178	0.038702	0.014189	0.0905

TG50:0	0.00813	0.023371	-0.09544	0.036307	0.061008	0.040402
TG50:1	0.042713	-0.0179	-0.07787	0.065653	0.133261	0.029315
TG50:2	0.07597	-0.02504	-0.08957	0.021896	0.106813	-0.00185
TG50:3	0.124976	0.061202	-0.19906	-0.1453	0.049562	-0.12341
TG50:4	0.13834	0.058387	-0.19812	-0.14775	0.065987	-0.13916
TG50:5	0.125605	0.056388	-0.15647	-0.12162	0.07991	-0.11575
TG51:1	0.024739	0.002614	-0.06632	0.094581	0.047333	0.119315
TG51:2	-0.01247	0.034416	-0.00975	0.103067	0.01342	0.134147
TG51:3	0.038713	0.097145	-0.1365	-0.06555	-0.03574	0.018808
TG51:4	0.075749	0.091489	-0.13523	-0.07481	0.018456	-0.02551
TG52:0	0.016654	0.023111	-0.14635	0.003084	0.034467	0.024496
TG52:1	0.04586	-0.00261	-0.10468	0.060169	0.115152	0.046754
TG52:2	-0.02378	0.039788	0.065845	0.085962	0.131746	-0.0066
TG52:3	0.071422	0.121736	-0.15062	-0.14051	0.073171	-0.14555
TG52:4	0.120568	0.095336	-0.20999	-0.25302	0.02934	-0.1967
TG52:5	0.038004	0.101456	0.016113	-0.03932	0.072855	-0.07389
TG53:0	0.046116	-0.01309	-0.0831	0.015853	-0.00533	0.071715
TG53:1	0.052661	-0.0054	-0.08737	0.086831	0.053447	0.10475
TG53:2	-0.02871	0.042046	-0.00711	0.101236	0.015691	0.118207
TG53:3	0.010089	0.095209	-0.07231	-0.01223	-0.01506	0.041402
TG53:4	0.054202	0.094294	-0.12769	-0.09951	-0.04617	-0.02266
TG53:5	0.066997	0.029301	-0.08647	-0.03884	0.055005	-0.04191
TG54:0	-0.00815	0.050438	-0.09561	0.007693	0.018635	0.031272
TG54:1	0.043975	0.049707	-0.09306	0.005313	0.048001	0.019346
TG54:2	0.043613	0.064126	-0.04421	0.020845	0.087737	-0.00787
TG54:3	0.052892	0.130346	-0.02922	-0.11257	0.022701	-0.13864
TG54:4	0.073771	0.134735	-0.10445	-0.20345	0.005046	-0.19766
TG54:5	0.110289	0.136573	-0.16689	-0.22619	0.015574	-0.17404
TG54:6	0.086683	0.130603	-0.13094	-0.20043	0.006128	-0.17302
TG54:8	-0.01233	0.009115	0.016859	0.108152	0.090874	0.051462
TG56:1	0.06381	0.073045	-0.05132	-0.02255	0.061964	-0.03104
TG56:2	0.049261	0.075762	-0.02909	-0.01	0.072019	-0.03502
TG56:3	0.009499	0.068652	0.038422	0.029012	0.098717	-0.02168
TG56:4	0.076303	0.119924	-0.04016	-0.14563	0.05939	-0.15693
TG56:5	0.019306	0.085369	-0.02099	0.087464	0.126653	0.065279
TG56:6	0.012111	0.085109	0.008604	0.014346	-0.03968	0.051075
TG56:7	0.067886	-0.0263	-0.12426	0.171841	0.335907	0.016535
TG56:8	0.042866	-0.03798	-0.14723	0.139147	0.389057	-0.03335
TG58:1	0.080823	0.053372	-0.01859	-0.02934	0.037959	-0.03524
TG58:2	0.07046	0.08044	-0.05377	-0.0405	0.094874	-0.07253
TG58:3	0.072795	0.096444	-0.07306	-0.1025	0.04928	-0.10459
TG58:4	0.071826	0.024929	-0.02231	-0.02693	0.104655	-0.05062
TG58:6	0.075046	-0.03591	-0.09591	0.046428	0.127185	0.058411
TG58:8	-0.0149	-0.03486	-0.04612	0.199672	0.335743	0.023184
TG58:9	0.05727	0.009696	-0.1267	0.12748	0.366458	-0.04275
TG60:1	0.054307	0.07795	0.003668	-0.04179	0.005331	-0.0393
TG60:11	0.036346	-0.07887	-0.07298	0.286925	0.402477	0.093355
TG60:2	0.067565	0.086537	-0.02373	-0.08039	0.025312	-0.08775
TG62:1	0.013295	0.05965	0.101699	0.022851	-0.02944	0.036699
Ascorbic Acid	1	0.008033	-0.23238	-0.19369	0.07356	-0.23717
25(OH)D	0.008033	1	-0.07434	-0.20987	-0.13678	-0.13887
ALA	-0.23238	-0.07434	1	0.626388	-0.0311	0.597693

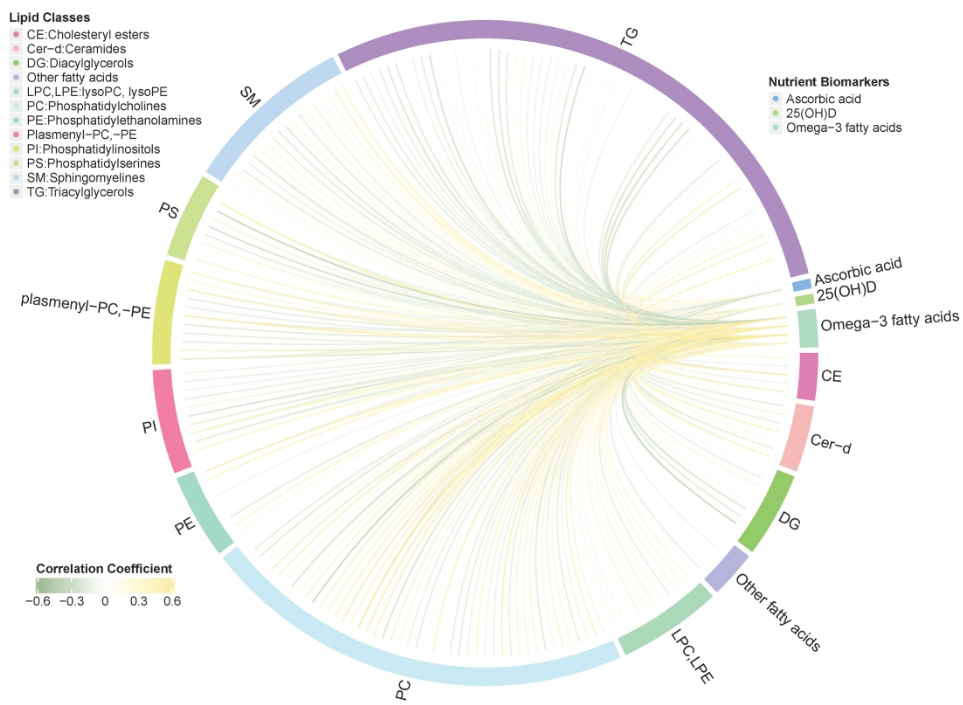
EPA	-0.19369	-0.20987	0.626388	1	0.439355	0.764018
DHA	0.07356	-0.13678	-0.0311	0.439355	1	0.08474
DPA	-0.23717	-0.13887	0.597693	0.764018	0.08474	1

rho>0.1 rho<-0.1

S13. Cox proportional hazard analysis on Clusters I, II, IV, age at seroconversion, first degree relatives, Sex,

Factor		HR (95% CI)	P-value
Cluster	II vs. I	0.55 (0.28, 1.08)	0.0825
	IV vs. I	**0.37 (0.16, 0.83)**	**0.0166**
Age at seroconversion (/month)		**0.92 (0.89, 0.96)**	**<0.001**
First degree relatives with T1D	Yes vs. No	1.82 (0.91, 3.64)	0.0896
Sex	Male vs. female	0.96 (0.53, 1.72)	0.8835
HLA DR-DQ genotype	DR3/DR4 vs. other	**3.04 (1.59, 5.78)**	**<0.001**
Type of initial autoantibody	IAA vs. GADA	0.73 (0.40, 1.33)	0.3052

, HLA genotype, type of the initial autoantibody



Circos plot for connectivity between lipidome and nutrients.

279x215mm (300 x 300 DPI)