

DR JIAN-LIN WU (Orcid ID : 0000-0002-3875-185X)

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Metabolomics reveals a correlation between hydroxyeicosatetraenoic acids (HETEs) and allergic asthma: evidence from three years' immunotherapy

Peiyan Zheng^{1#}, Xiqing Bian^{2#}, Yingying Zhai^{3#}, Cheng Li¹, Na Li², Chuangli Hao⁴, Huimin Huang¹, Wenting Luo¹, Zhifeng Huang¹, Chenxi Liao¹, Mingshan Xue¹, Ming-Quan Guo⁵, Baoqing Sun^{1†}, Jian-Lin Wu^{2†}

¹Department of Allergy and Clinical Immunology, Guangzhou Institute of Respiratory Health, State Key Laboratory of Respiratory Disease, National Clinical Research Center of Respiratory Disease, National Center for Respiratory Medicine, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

²State Key Laboratory for Quality Research in Chinese Medicines, Macau University of Science and Technology, Macao, China

³Pediatric Department, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

⁴Department of Respiratory Diseases, Children's Hospital of Soochow University, Suzhou, China

⁵Key Laboratory of Plant Germplasm Enhancement and Specialty Agriculture, Wuhan Botanical Garden, Sino-Africa Joint Research Center, Chinese Academy of Sciences, Wuhan, China.

[#]These authors contributed equally to the study.

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†Corresponding author: Baoqing Sun, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, sunbaoqing@vip.163.com; Jian-Lin Wu, Macau University of Science and Technology, Macao, jlwu@must.edu.mo

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ABSTRACT

Background: Subcutaneous immunotherapy (SCIT) is an effective, safe, preventative treatment for allergic asthma; however, potential biomarkers for monitoring SCIT have rarely been reported.

Objective: Metabolomics was utilized for the discovery of new biomarkers and analyzing disease pathophysiology of allergic asthma, it was also applied to determine the metabolomic profiles of serum samples from children with asthma undergoing SCIT and identify potential biomarkers for allergic asthma and its therapeutic monitoring.

Methods: Untargeted metabolomics using ultra-high-performance liquid chromatography-quadrupole-time-of-flight mass spectrometry, was performed on 15 asthmatic and 15 healthy pediatric sera to profile carboxylic acids. Statistical analysis combined with pathway enrichment analysis were applied to identify potential biomarkers. Then, targeted metabolomics was performed to study longitudinal changes of eicosanoid profiles on sera from 20 participants with asthma who received SCIT at baseline, 6 months, one, two and three years (ChiCTR-DDT-13003728).

Results: Metabolomic analysis revealed that levels of eicosanoids, particularly 12(S)-hydroxyeicosatetraenoic acid (HETE; AUC = 0.94, $P < 0.0001$) and 15(S)-HETE (AUC = 0.89, $P = 0.0028$), metabolized from arachidonic acid by lipoxygenase and glutathione peroxidase enzymes, were significantly higher in asthma group than in healthy individuals. Furthermore, levels of these important metabolites increased in the first year of SCIT treatment and then decreased from years one to three, being significantly lower after three years of treatment than baseline levels.

Conclusion: 12(S)- and 15(S)-HETEs are potential biomarkers to participate in the pathogenesis and treatment of allergic asthma. Moreover, these metabolites may be a new target for biological indicators to monitor the therapeutic effect of SCIT, particularly in the setting of allergic asthma.

Keywords: Allergic asthma, metabolomics, hydroxyeicosatetraenoic acid, subcutaneous immunotherapy

Key Messages

In our study, metabolomics was applied to hunt for the potential biomarkers for monitoring SCIT. 12(S)- and 15(S)- hydroxyeicosatetraenoic acids are candidate biomarkers for biological indicators for SCIT monitoring, and the metabolic analysis demonstrated that SCIT was useful to treat allergic asthma for at least three years.

Introduction

Allergic asthma is a common chronic disease characterized by airway inflammation. According to World Allergy Organization, 30-40% of the global population suffered from allergic diseases, and the incidence of these allergic diseases is increasing.¹ It is necessary to identify biomarkers using objective measurements in order to guide asthma therapy. Bronchoscopy and exhaled nitric oxide have been used to accurately measure asthma;^{2,3} however, these methods are expensive, invasive, insensitive, and nonspecific for improving patient outcomes.⁴ Consequently, it is important to develop a simple, noninvasive, sensitive, and specific test for patients with allergic asthma.

Clinical epidemiological survey found that house dust mites (HDM) are the most prevalent allergens in patients with asthma.^{5,6} Allergic asthma is often recurrent and requires long-term steroid and antihistamine administration to control its symptoms; however, these drugs are limited by major debilitating side effects, such as skin atrophy, osteoporosis, fatty liver disease, and type 2 diabetes syndrome, and growth inhibition in children.⁷ International consensus has declared that allergy immunotherapy (AIT) is the only treatment that can change the course of allergic diseases.⁸ However, there is currently a lack of objective, highly sensitive, and specific biomarkers for the clinical management of patients receiving AIT.⁹ The European Academy of Allergy and Clinical Immunology proposed a variety of immunological indicators (e.g. allergen-specific IgG4 and the specific IgE/total IgE ratio) to evaluate AIT therapy efficacy;¹⁰ however, there are no validated and generally accepted candidate biomarkers that are predictive or indicative of the clinical response to AIT.¹⁰ Thus, it is necessary to confirm the association of these biomarkers with the clinical response to immunotherapy.

Metabolomics is a key discipline that qualitatively and quantitatively analyzes metabolites.^{11,12} This approach has been widely used to identify novel biomarkers and pathogenic pathways for a number of complex chronic diseases.¹³ Eicosanoids, such as hydroperoxyeicosatetraenoic acids (HPETEs; metabolized from arachidonic acid (AA) by lipoxygenase (LOX) enzymes) and HETEs (metabolized from HPETEs by glutathione peroxidase (GPx) enzymes), have been reported to be involved in the modulation of inflammatory responses, such as asthma.^{14,15} However, the

pathophysiological roles of eicosanoids in asthma and responses to allergic asthma therapy (especially AIT) are not yet completely understood.

In this study (Figure 1), we used a specific and sensitive derivatization method combined with ultra-high-performance liquid chromatography-quadrupole-time-of-flight mass spectrometry (UHPLC-Q-TOF/MS) to analyze the differences between serum metabolites in healthy children and those with HDM allergic asthma. Furthermore, we investigated changes in eicosanoid metabolism in children with allergic asthma during three years of subcutaneous immunotherapy (SCIT).

Methods

Patient characteristics and study design

Fifty pediatric subjects were enrolled in this prospective randomized controlled study (ChiCTR-DDT-13003728). Thirty-five pediatrics with allergic asthma were passed the inclusion and exclusion criteria, including 20 cases were received *Dermatophagoides pteronyssinus* (Der p) SCIT (Alutard, ALK-Abelló, Hørsholm, Demark) of 0, 0.5, 1, 2, and 3 years, 15 asthma pediatric subjects without SCIT, and fifteen healthy pediatric subjects collected for control group. The baseline demographic data of the study participants and relevant information including gender, age, BMI, clinical symptoms, skin prick test, initial diagnosis, family history of allergy, and therapies, were obtained at the time of sample collection. All experiments were conducted in compliance with relevant guidelines and regulation of the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (ethics approval no. GYFYY-2016-61). Written informed consent was obtained from the subject or subject's legal representative.

Inclusion and exclusion criteria

All patients completed questionnaires on their demographics and medical history, and fulfilled the Allergic Rhinitis and its Impact on Asthma (ARIA) criteria for allergic rhinitis and/or the Global Initiative for Asthma (GINA) criteria¹⁶ for asthma. The detailed criteria were as follows: (1) patients aged 5–15 years; (2) a physician-diagnosis of mild to moderate asthma; (3) a history of

atopy to HDM (Der p, and Dermatophagoides farinae (Der f)); sensitization to Der p and Der f as indicated by a skin prick test (SPT) and confirmed by serum sIgE tests at our institution (sIgE $\geq$ 3.5 kU/L). The demographics of the study population are presented in Table 1.

Exclusion criteria followed approved indication for the product in the Summary of Product Characteristics. Patients with severe asthma were excluded. In addition, SCIT cases with missing serum samples during treatment at five time points were excluded.

Sample collection and preparation

All samples were collected and centrifuged at 3000 rpm for 10 min, and then the supernatant was collected and stored at -80 °C before further use. Sample preparation and metabolomics approaches were analyzed using our previously developed UHPLC-Q-TOF/MS approach.¹⁴

A method used to enhance carboxylic acid detection

Serum samples were prepared using our previously developed approach to improve detection of carboxylic acid¹⁷. (2-aminoethyl) trimethylammonium chloride hydrochloride (cholamine) was selected as the derivatization reagent to enhance the sensitivity and separation efficiency of carboxylic acids when analyzed through UHPLC-Q-TOF/MS. 1 μ L was injected directly into the UHPLC-Q-TOF/MS and UHPLC-QQQ-MS.

Metabolomic analysis

Serum samples were measured using a multiplatform analysis: UHPLC-Q-TOF/MS for profiling carboxylic acids and UHPLC-QQQ-MS for quantitation of targeted eicosanoids. The targeted identification of carboxylic acids, including eicosanoids, saturated and unsaturated fatty acids, and bile acids, were shown in Figure S1. The detailed descriptions are available in supplementary material. Raw LC-MS data were acquired and processed using Agilent MassHunter Qualitative Analysis B.06.00 software (Agilent Technology, USA). These metabolites, which have standards, were confirmed through comparison with the relevant standards, others without standards were confirmed *via* LC-MS/MS experiments using 30 eV for fragmentation.

Principal component analysis

SIMCA-P software (version 15.0; Umetrics, Umea, Sweden) were used for multivariate statistical analysis. Unsupervised principal component analysis (PCA) is a statistical procedure that uses an orthogonal transformation to convert the possibly correlated variables into a set of uncorrelated variables called principal components. The greatest variance by any projection is elucidated on the first coordinate (PC1) and the least variance is projected by subsequent PCs.¹⁸ In our study, PCA-X and supervised orthogonal partial least squares-discriminant analysis (OPLS-DA) pattern-recognition methods were used to model the co-variation between healthy and asthma sera. S-plot was used to visualize the relationship between covariance and correlation, and hunt for the metabolites, which have significant differences in asthma compared with healthy children.

Results

Patient characteristics

The study was enrolled 35 asthma pediatric subjects (20 SCIT and 15 Non-SCIT), sex-matched (74.3% male), medians age of 8 (5.0) years old and medians BMI of 15.3 (3.2). Additionally, 71.4% and 22.9% of the asthma patients were combined with allergic rhinitis or both with allergic rhinitis and eczema, respectively. Furthermore, all of patients were sensitized to house dust mites, some of the patients were sensitized to cockroaches, animal epithelium, pollens and molds. Furthermore, initial diagnosis included intermittent asthma (34.3%), mild asthma (45.7%) and moderate asthma (20.0%). In addition, with or without family history of allergic disease were 57.1% and 42.9%. The groups were balanced in terms of gender, age, BMI, and family member with allergic disease, and no statistical difference was observed for any of the clinical data between SCIT and Non-SCIT group. Detailed information is provided in Table 1.

Non-targeted metabolomics analysis of potential systemic biomarkers in allergic asthma

PCA analysis indicated good separation of the healthy and asthmatic groups (Figure 2A), while

the samples in each group clustered tightly together in OPLS-DA score plots, indicating the reliability of our findings (Figure 2B; $R^2Y = 0.893$, $Q^2 = 0.602$). The S-plot suggested that two metabolites were most significantly elevated in asthma group (Figure 2C), which were identified as 12(S)- and 15(S)-HETE by comparing the MS and MS/MS results with the standards. In total, 125 metabolites, including 12(S)- and 15(S)-HETEs, were observed and identified from the characteristic MS/MS fragmentation patterns and comparing the MS data with that in the Lipid Maps and METLIN databases (Table S2 and S5), and are shown in heatmap (Figure 2D).

Next, we used *t*-tests, volcano plots, and ROC curves to confirm these results. Figure 3A gives an overview on fold change and univariate statistical significance in a volcano plot. 42 metabolites were found significantly different and HETEs were up-regulated in asthma (Table S2, Figure 3A). These significantly altered metabolites were then selected for further analysis using SPSS. Nine metabolites (AA; 5(S)-, 15(S)-HPETEs; 5(S)-, 8(S)-, 11(S)-, 12(S)-, 15(S)-HETEs; Figure 3B), which were associated with AA metabolism (Figure 3C), had good AUC values ($P < 0.05$, $|FC| > 1.2$, Table 2) and displayed potential systemic targets abilities to differentiate asthma patients and healthy controls. The metabolites, which had highest importance as calculated by variable importance in projection (VIP score) in the PLS-DA model, are shown in Figure 3D. Importantly, the AUC values, fold changes (FC), and higher VIP score of 12(S)-HETE (AUC = 0.94, FC = 3.19) and 15(S)-HETE (AUC = 0.89, FC = 2.39) indicated that they may be candidate biomarkers to treat allergic asthma, which were consistent with the results of the OPLS-DA analysis.

Longitudinal profiles of targeted eicosanoids metabolomics of SCIT group

SCIT effectively ameliorates symptoms caused by allergens and is effective for treating allergic asthma.¹⁹ As we reported previously,²⁰ levels of the immunostimulatory antibody sIgE showed a slight upward trend during the first year of treatment, but decreased significantly after 1 to 3 years of SCIT. Although several studies have considered IgE and IgG4 to be secondary outcomes, current guidelines do not clearly include biomarkers in the recommendations for clinical trials or clinical responses. There were no significant changes in lung function or sIgE levels during SCIT in these patients (Table S4), however, we conducted targeted metabolomics analysis after up to

three years of SCIT treatment, finding that the levels of 5(S)-, 12(S)-, and 15(S)-HPETEs and 5(S)-, 8(S)-, 11(S)-, 12(S)-, and 15(S)-HETEs dramatically increased during the first year of treatment and then progressively decreased from 1 to 3 years (Figure 4). In particular, the levels of 12(S)-HETE and 15(S)-HETE were significantly lower after three years treatment compared to baseline levels (0Y, $P < 0.05$; Figure 5A).

Discussion

This study performed carboxylic acid metabolomics on serum samples from pediatric subjects with asthma and those treated with SCIT for three years. Metabolomic and multivariate analyses revealed that eicosanoid levels, particularly 12(S)-HETE and 15(S)-HETE, were significantly higher in the asthma group. Moreover, after 3 years of SCIT, the levels of these important metabolites decreased. Barker-Tejeda et al. reported that there is no systemic improvement in arachidonic acid pathway during the first two years in grass-pollen sublingual immunotherapy,²¹ which suggests that longer observations periods for at least three years may be necessary to detect changes in these biomarkers, as seen in our data.

Eicosanoids are a key driver of inflammatory responses,^{22,23} which produced by oxidation of arachidonic acid via LOX and GPx enzymes that are associated with immune regulatory processes and the response of respiratory epithelium. A few of eicosanoids in sera and exhaled breath condensate (EBC) is inflammatory markers which distinguish asthmatics from healthy children.^{23,24} LOXs are categorized as 5-, 8-, 11-, 12-, or 15-LOX according to their specific position of AA oxygenation, and thus metabolize AA into 5(S)-, 8(S)-, 11(S)-, 12(S)-, and 15(S)-HPETEs.²⁵ GPx is thought to be involved in eicosanoid synthesis by regulating LOX activity and metabolizing 5(S)-, 12(S)-, and 15(S)-HPETEs into 5(S)-, 12(S)-, and 15(S)-HETEs (Figure 5B). It has been reported that LOX pathways play important roles in airway inflammation, airway hyperresponsiveness, and airway remodeling during allergic asthma.^{26,27} GPx can also regulate intracellular eicosanoid metabolism through oxidative challenge²⁸ and can react not only with free hydroperoxy fatty acids but also with their esterified form, thus can be a site of eicosanoids synthesis.²⁹ Metabolomics are essential for the identification of biomarkers with good diagnostic performance. Respiratory infection and cell injury may activate the 12/15-LOX pathway in airway epithelial cells, markedly increased their production of AA, 12(S)-HETE and 15(S)-HETE, which

plays a pathophysiological role in asthma.^{30,31} In this study, we found that the levels of 5(S)-, 8(S)-, 11(S)-, 12(S)-, and 15(S)-HETEs, particularly 12(S)- and 15(S)-HETEs, were higher in asthma group. These findings are consistent with previously reported results, which exhibited increased levels of 12/15-LOX and their metabolites 12(S)-/15(S)-HETE.^{32,33} Accordingly, 12(S)-HETE and 15(S)-HETE were attractive targets of allergic asthma and may explain its disease pathogenesis.

AIT is an essential method of treating allergic asthma; however, few studies have specifically evaluated the efficacy and safety of HDM AIT in allergic asthma. Clinical trials of AIT in asthma started as an add-on therapy when evaluating primary end points, such as lung function, number of exacerbations, and reduced need for controller medication.³⁴ Although the EAACI taskforce evaluated all candidate biomarkers used in allergic patients, no validated and generally accepted candidate biomarkers are predictive or indicative of the clinical response to AIT.¹⁰ Although several studies consider some biomarkers (sIgE, tIgE, and IgG4) as secondary outcomes, these clinical observational indexes clearly don't sensitively reflect curative effects during AIT.

To identify improved biomarkers, we conducted targeted metabolomics analysis after up to three years of SCIT treatment. Derivatization-UHPLC-Q-TOF/MS is widely used to efficiently profile metabolites due to its high sensitivity, peak resolution, and reproducibility. However, few studies analyzed metabolic changes during SCIT treatment in children with allergic asthma. In this study, eicosanoids were sensitively detected in patients with asthma before and after SCIT. Particularly, we found that the levels of HETEs, especially 12(S)-, and 15(S)-HETEs, were significantly lower than their baseline levels after 3 years of SCIT, suggesting that their downstream pathways may be involved in the pathogenesis of asthma. These findings are consistent with the results of our previous study,²⁰ in which levels of the immunostimulatory antibody sIgE increased slightly during the early stages of SCIT (0–1 years) but decreased significantly during the middle and late stages (1–3 years), with similar results reported by Jutel and Gleich.^{35,36} Taken together, our results suggested that HETEs participated in the pathogenesis and treatment of allergic asthma and that SCIT was a useful AIT in allergic asthma after three years.

The strength of this study is manifested by its long-term, and longitudinal follow-up. Quality

control samples were prepared to assess the analytical quality of this experiment, and the internal standards were added before sample preparation to reduce the error from operation and equipment. The limitation was the small sample size, which could overcome through validation using patients with SCIT treatment of different years. HETEs were only candidate biomarkers for the monitoring of allergic asthma instead of indication of the asthma severity and clinical effect. Lastly, future prospective studies in bigger cohorts will allow for deeper analysis of the metabolic changes of allergic disease and clarify their relationship with clinical effect.

In conclusion, 12(S)-HETE and 15(S)-HETE, which are metabolized from AA via the LOX and GPx pathways, are potential biomarkers that participate in the pathogenesis and treatment of allergic asthma. Moreover, these metabolites may be a new target for biological indicators to monitor the therapeutic effect of SCIT, particularly in the setting of allergic asthma.

Conflict of Interest: The authors have no conflicts of interest.

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Table 1. Demographic characteristics of the study subjects

Items	Allergic asthma		Healthy control (N = 15)
	SCIT (N = 20)	Without SCIT (N = 15)	
Gender, male (N (%))	17 (85 %)	9 (60 %)	10 (50 %)
Age distribution, medians (IQR)	7 (5.0)	8 (5.0)	8 (6.0)
BMI, medians (IQR)	15.1 (2.5)	15.3 (3.2)	15.5 (2.7)
Pathology, N (%)			
Simply allergic asthma	1 (5 %)	1 (6.7 %)	0
Allergic asthma combined with allergic rhinitis	12 (60 %)	13 (86.7 %)	0
Allergic asthma combined with allergic rhinitis and allergic eczema	7 (35 %)	1 (6.7 %)	0
Allergens (skin prick test), N (%)			
House dust mites	20 (100 %)	15 (100 %)	0
Cockroaches	1 (5 %)	1 (6.7 %)	0
Animal epithelium	4 (20 %)	0 (0 %)	0
Pollens	1 (5 %)	0 (0 %)	0
Molds	1 (5 %)	0 (0 %)	0
Initial diagnosis, N (%)			
Intermittent asthma	10 (50 %)	2 (13.3 %)	0
Mild asthma	6 (30 %)	10 (66.7 %)	0
Moderate asthma	4 (20 %)	3 (20 %)	0
Family history of allergy, N (%)	10 (50 %)	10 (66.7 %)	6 (40 %)

N: number; SCIT: Subcutaneous immunotherapy; IQR: interquartile range; BMI: Body Mass Index. Data are presented with the number (percentage) (N, (%)) or median (IQR).

Table 2. Statistical parameters characterizing the discriminant properties of the selected putative biomarkers

No.	Name	AUC	Accuracy (%)	Precision (%)	95 % CI	FC (Asthma/ healthy)	<i>P</i> value
1	Arachidonic acid	0.85	86.7	86.7	0.74-1.00	1.36	0.0061
2	5(S)-HPETE	0.81	60.0	93.3	0.66-0.97	1.77	0.0039
3	12(S)-HPETE	0.70	53.5	100.0	0.50-0.90	1.29	0.027
4	15(S)-HPETE	0.81	73.3	86.7	0.65-0.97	1.74	0.0045
5	5(S)-HETE	0.85	80.0	80.0	0.71-0.99	2.45	0.0029
6	8(S)-HETE	0.85	100.0	73.3	0.71-1.00	2.43	0.0047
7	11(S)-HETE	0.79	93.3	66.7	0.61-0.96	1.58	0.024
8	12(S)-HETE	0.94	86.7	86.7	0.85-1.00	3.19	<0.0001
9	15(S)-HETE	0.89	93.3	80.0	0.77-1.00	2.39	0.0028

Figure legends

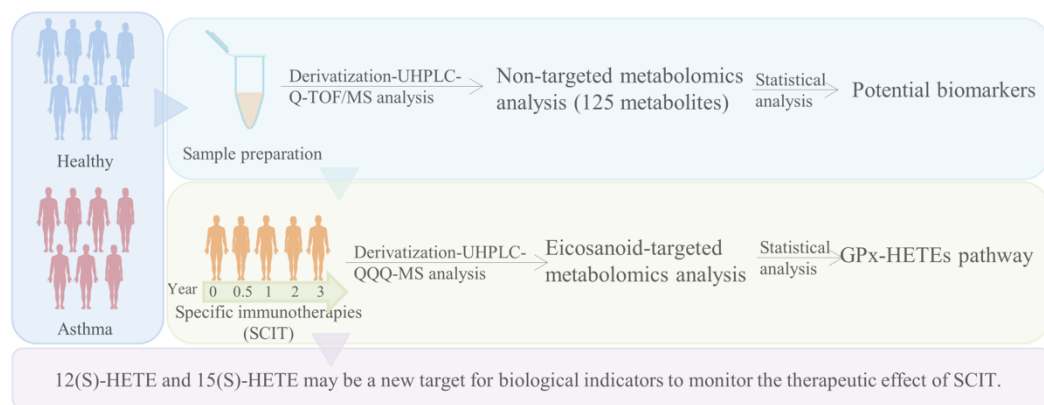
Figure 1. Study design and flow chart.

Figure 2. Results of metabolomics analysis. PCA (**A**) and OPLS-DA (**B**) score plot separating patients with asthma from healthy controls (red: serum of healthy individuals; blue: serum of patients with asthma). (**C**) Loading S-plot of patients with asthma vs healthy controls. (**D**) Heatmap of metabolites identified in the serum of patients with asthma using cholamine derivatization UHPLC-Q-TOF/MS.

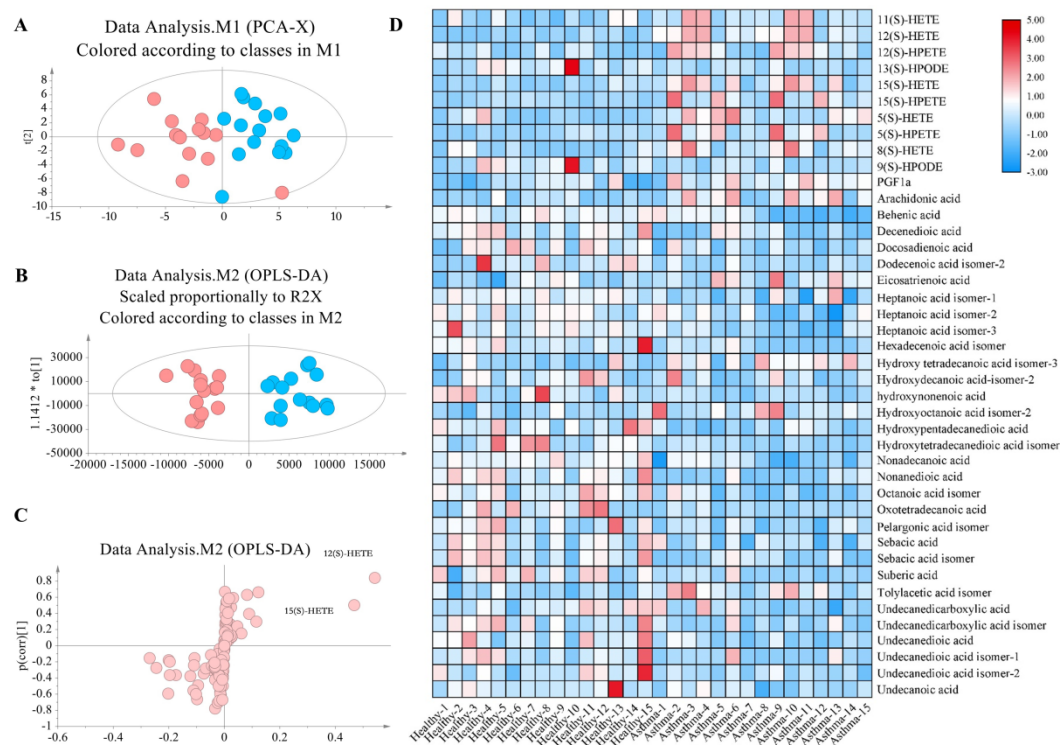
Figure 3. (**A**) Volcano plot showing the metabolic dysregulation in asthma patients, Increased metabolites levels in asthma are labeled as red nodes, decreased levels are marked in blue, not significant metabolites are marked in yellow. (**B**) Changes in eicosanoid levels between healthy individuals and those with allergic asthma. (**C**) Pathway enrichment. (**D**) Variable importance in projection (VIP) scores for top 8 metabolites.

Figure 4. Dynamic changes in serum eicosanoid levels during SCIT. 0Y: baseline; 0.5Y: half of a year of SCIT; 1Y: one year of SCIT; 2Y: two years of SCIT; 3Y: 3 years of SCIT.

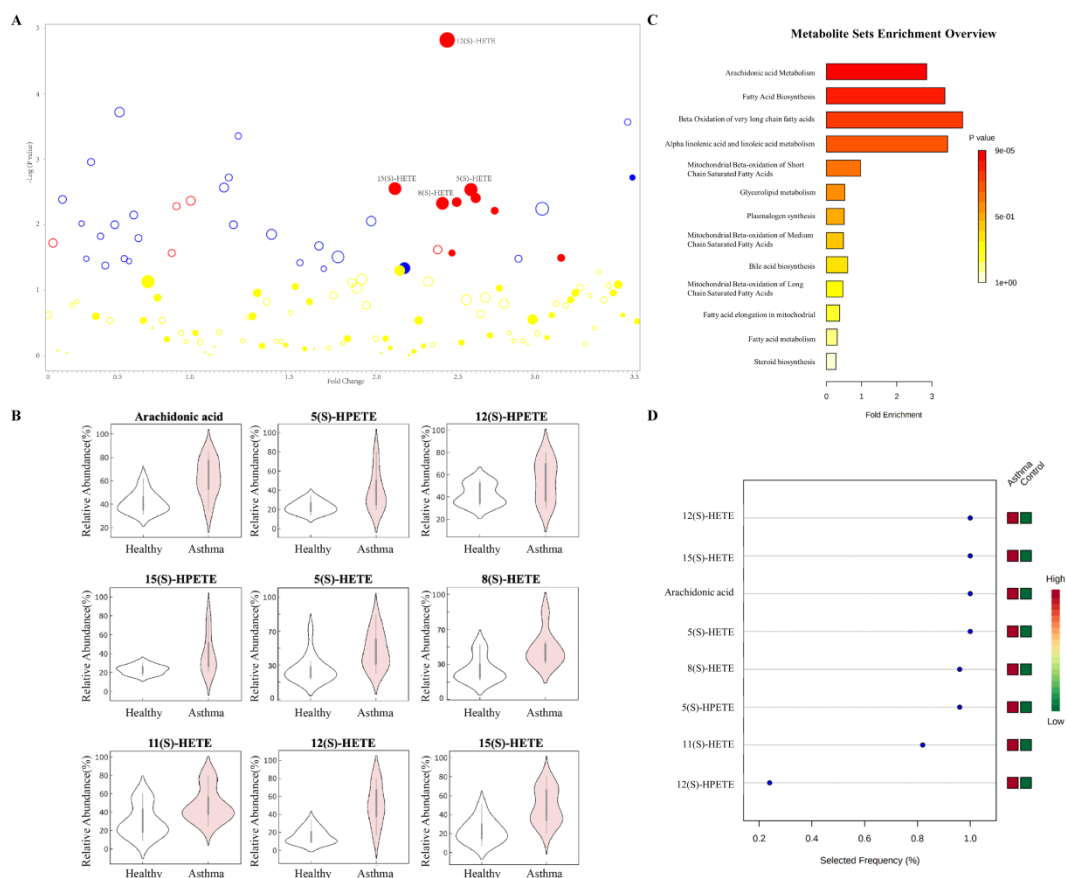
Figure 5. (**A**) Absolute concentrations of targeted eicosanoids in serum samples from patients with allergic asthma during SCIT from years 0 to 3. (**B**) Eicosanoids metabolic pathway.



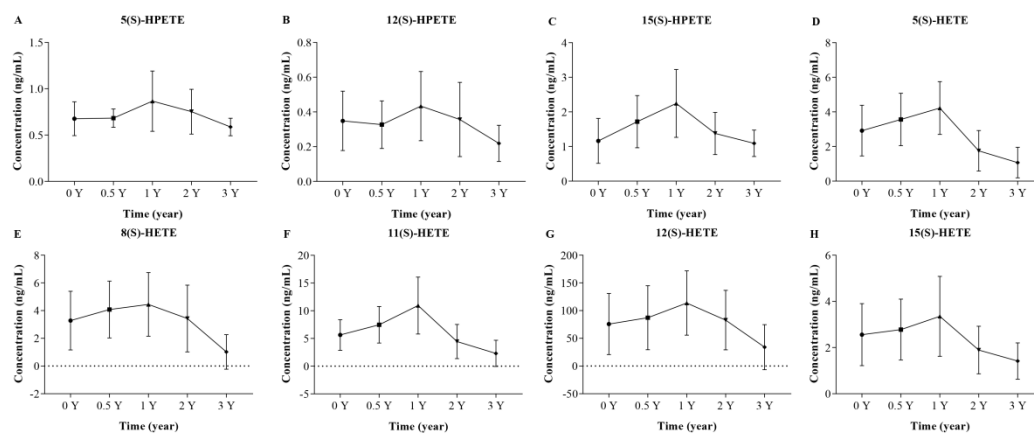
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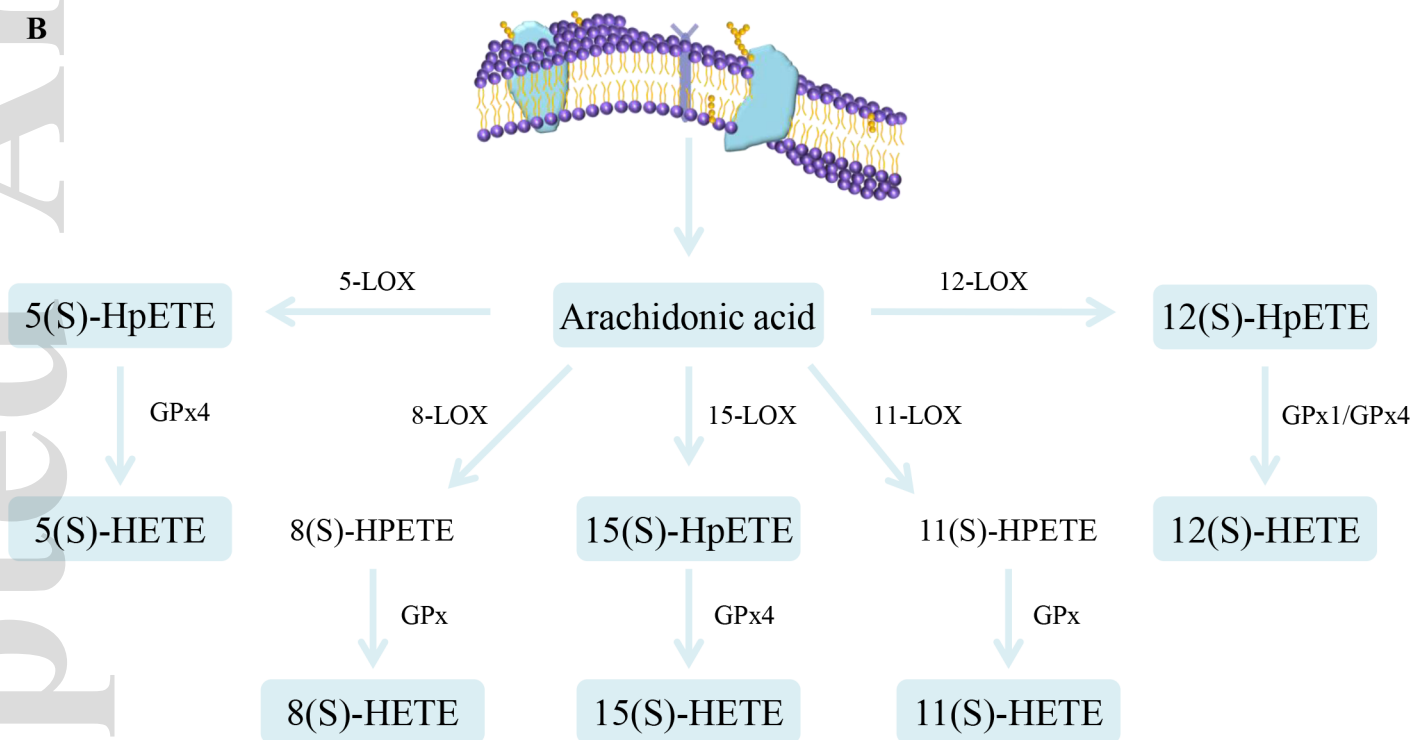
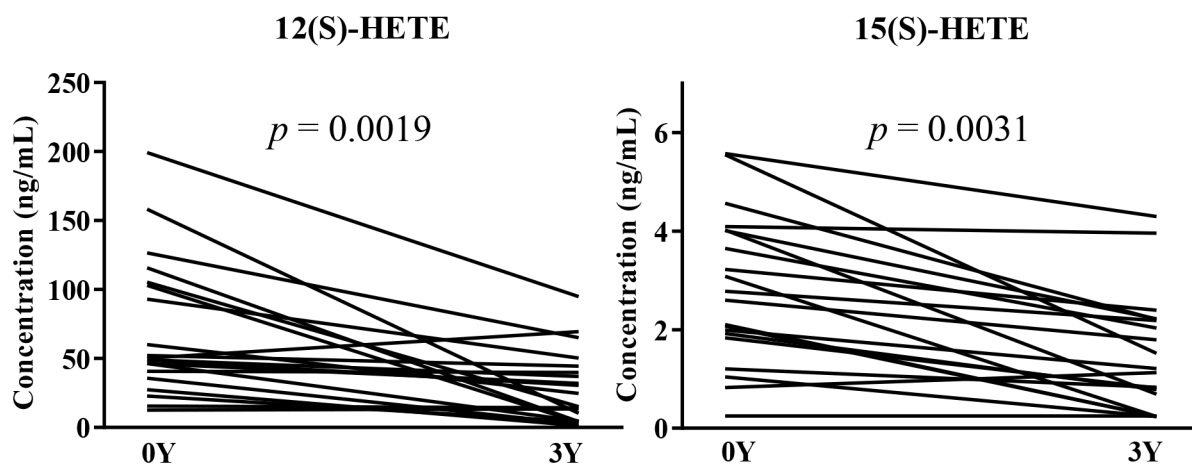
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pai_13569_f5.tif

Metabolomics reveals a correlation between hydroxyeicosatetraenoic acids (HETEs) and allergic asthma: evidence from three years' immunotherapy

Peiyan Zheng^{1#}, Xiqing Bian^{2#}, Yingying Zhai^{3#}, Cheng Li¹, Na Li², Chuangli Hao⁴, Huimin Huang¹, Wenting Luo¹, Zhifeng Huang¹, Chenxi Liao¹, Mingshan Xue¹, Ming-Quan Guo⁵, Baoqing Sun^{1†}, Jian-Lin Wu^{2†}

¹Department of Allergy and Clinical Immunology, Guangzhou Institute of Respiratory Health, State Key Laboratory of Respiratory Disease, National Clinical Research Center of Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

²State Key Laboratory for Quality Research in Chinese Medicines, Macau University of Science and Technology, Macao, China

³Pediatric Department, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China

⁴Department of Respiratory Diseases, Children's Hospital of Soochow University, Suzhou, China

⁵Key Laboratory of Plant Germplasm Enhancement and Specialty Agriculture, Wuhan Botanical Garden, Sino-Africa Joint Research Center, Chinese Academy of Sciences, Wuhan 430074, China.

[#]These authors contributed equally to the study.

[†]Corresponding author: Baoqing Sun, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, sunbaoqing@vip.163.com; Jian-Lin Wu, Macau University of Science and Technology, Macao, jlwu@must.edu.mo

SUPPLEMENTAL MATERIAL

e-Appendix 1. Serum IgE detection

For each subject, the levels of total IgE and sIgE against Der p and Der f in all serum samples were measured using an ImmunoCAP system (Phadia 1000, ThermoFisher Scientific Inc., CA, USA).

e-Appendix 2. SCIT protocol

Patients were treated with a conventional injection schedule of standardized aluminum formulated Der p extract (Alutard, ALK-Abelló, Hørsholm, Demark). The treatment protocol followed the recommended up dosing schedule of 16 weeks before reaching a maintenance dose of 100,000 Alutard-SQ which was maintained every 4-6 weeks for up to 3 years.

e-Appendix 3. Chemicals and materials

Fatty acid standards, including 5(S)-, 8(S)-, 11(S)-, 12(S)-, and 15(S)-HETEs, 5(S)-, 12(S)-, and 15(S)-HPETEs, 9(S)- and 13(S)-HPODEs, 5(S)-, 12(S)-, and 15(S)-hydroxyeicosapentaenoic acids (HEPEs), 13(S)-hydroxyoctadecatrienoic acid (HOTrE); Prostaglandin A2 (PGA2), PGB2, PGD2, PGE2, PGJ2, PGE1, PGF1 α , TXB2, 12(S)-hydroxyheptadecatrienoic acid (HHTrE), and 13,14-dihydro-15-keto PGF2 α , were purchased from Cayman Chemical (Ann Arbor, MI, USA). The isotope-labeled reagents 12(S)-HETE-d8 and PGD2-d4 were used as internal standards. The other standards hexanoic acid, octanoic acid, decanoic acid, dodecanoic acid, myristic acid, stearic acid, heptadecanoic acid, docosahexaenoic acid, eicosapentaenoic acid, docosapentaenoic acid, oleic acid, chenodeoxycholic acid, deoxycholic acid, and isodeoxycholic acid were obtained from Sigma-Aldrich (St. Louis, MO, USA) and J&K Scientific (Beijing, China).

(2-aminoethyl) trimethylammonium chloride hydrochloride (choline), 1-hydroxybenzotriazole hydrate (HOBt), O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU) and triethylamine (TEA) were purchased from Sigma-Aldrich. Acetonitrile (ACN, HPLC grade) and methanol (MeOH, HPLC grade) were obtained from Analaqua Chemicals Supply Inc., Ltd. (Houston, TX, USA). Deionized water was prepared using a Millipore water purification system (Millipore Corp, USA). Mass spectrometry (MS) grade formic acid and other chemical reagents were provided by Sigma-Aldrich.

e-Appendix 4. Sample preparation

All samples were collected and centrifuged at 3000 rpm for 10 min, and then the supernatant was collected and stored at -80 °C before further use. Metabolites were analyzed using our previously developed UHPLC-Q-TOF/MS approach¹. Briefly, 50 µL of each serum sample was mixed with 200 µL of cold ethyl acetate and centrifuged at 13,000 rpm for 5 min (4 °C). Extraction was repeated three times and the combined supernatants were dried under nitrogen stream. The residues of each 50 µL aliquot of serum sample were sequentially mixed with 5 µL of 20 mM HOBt in dimethyl sulfoxide (DMSO), 10 µL of 100 mM cholamine in DMSO containing 200 mM TEA, and 5 µL of 20 mM HATU in DMSO, and then incubated for 1 min at room temperature. Next, 30 µL of acetonitrile was added to make up a final volume of 50 µL, followed by centrifugation at 13,000 rpm for 10 min at 4 °C. Finally, 1 µL was injected directly into the UHPLC-Q-TOF/MS.

Quality control samples were prepared to equilibrate the equipment and to measure the variation of the analytical signal along the analysis, in order to assess the analytical quality of the experiment. In this case, a sample pool was prepared by mixing equal volumes of each sample before derivatization. Then, this pool was prepared and derivatized according to the above mentioned approach.

e-Appendix 5. UHPLC-Q-TOF/MS analysis

Metabolites were separated using an Agilent 1290 Infinity LC system (UHPLC, Santa Clara, CA, USA) consisting of an autosampler, a thermostatically regulated column compartment, and a binary pump with an Agilent Eclipse XDB-C18 column (2.1 × 100 mm, 1.8 µm). The column temperature was maintained at 40 °C and the autosampler was set at 4 °C. Mobile phase A and B were 0.1 % formic acid-containing water and 0.1 % formic acid-containing acetonitrile, respectively, and the gradient was set as follows: 0-1 min, 15-23 % B; 1-8 min, 23-33 % B; 8-8.5 min, 33-35 % B; 8.5-15.5 min, 35-47 % B; 15.5-16 min, 47-50 % B; 16-23 min, 50-85 % B; 23-25 min, 85-95 % B; 25-28.9 min, 95 % B. The injection volume was 1 µL and the flow rate was 0.3 mL/min.

Mass spectrometry was conducted on an Agilent 6550 UHD accurate mass Q-TOF/MS system with a dual jet stream electrospray ion source (dual AJS ESI). The instrument was operated in positive full scan mode with the following MS parameters: dry gas temperature, 250 °C; dry gas flow, 15 L/min; sheath gas temperature, 300 °C; sheath gas flow, 11 L/min; nebulizer pressure, 20 psi; capillary voltage, 5000 V; and nozzle voltage, 500 V. Mass spectra were recorded between 200 and 1000 *m/z*. Accurate mass measurements were obtained by

using a low flow of TOF reference mixture, containing internal reference masses at m/z 922.0098 ($C_{18}H_{18}F_{24}N_3O_6P_3$).

e-Appendix 6. UHPLC-Triple Quadrupole (QQQ)-MS analysis

Agilent 1290 Infinity UHPLC system coupled with an Agilent 6490 triple quadrupole mass spectrometer (Agilent Technologies, Santa Clara, CA) was developed to quantitate the targeted eicosanoids using multiple reaction monitoring (MRM) method. The detailed parameters of HPLC systems was the same as UHPLC-Q-TOF/MS. The gradient was set as follows: 0-0.5 min, 15%-15% B; 0.5-1 min, 15%-24% B; 1-6 min, 24%-33% B; 6-6.5 min, 33%-35% B; 6.5-7.5 min, 35%-42% B; 7.5-14.5 min, 42%-46% B; 14.5-15 min, 46%-50% B; 15-16 min, 50%-95% B; 16-19.9 min, 95%.

Mass spectrometry analysis were obtained in multiple reaction monitoring (MRM) positive ionization mode. The MS parameters were set as follows: drying gas temperature, 225 °C; drying gas flow, 13 L/min; nebulizer pressure, 25 psi; sheath gas temperature, 275 °C; sheath gas flow, 11 L/min; capillary voltage, 4000 V; and nozzle voltage, 500 V. The MRM mode parameters for the targeted eicosanoids were optimized using Agilent optimizer software (Mass Hunter Optimizer), including MRM transitions, collision energy. The selected parameters for all targeted eicosanoids are shown in e-Table 1.

e-Appendix 7. Method validation

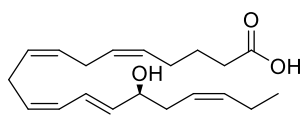
Method validation was performed by studying the linearity, and limit of quantification (LOQ) for targeted eicosanoids. The targeted eicosanoids standards were weighted accurately and dissolved with 70% acetonitrile. Calibration curves were constructed by the peak area of MRM transitions for at least 7 appropriate concentrations of each standard. The LOQ were determined at signal-to-noise ratios (S/N) of 10:1. The linearity range and LOQ was shown in Table S1.

e-Appendix 8. Data preprocessing and statistical analysis

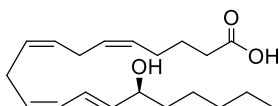
Raw LC-MS data from the control and allergic asthma groups were acquired and processed using Agilent MassHunter Qualitative Analysis B.06.00 software (Agilent Technology, USA). Metabolites were identified using standards, MS/MS spectra, and the Lipid Maps (<http://www.lipidmaps.org/>) and METLIN (<https://metlin.scripps.edu/index.php>) metabolite databases. Multivariate statistical analysis was performed using SIMCA-P software (version 15.0; Umetrics, Umea, Sweden). Unsupervised principal component analysis (PCA) and

supervised orthogonal partial least squares-discriminant analysis (OPLS-DA) pattern-recognition methods were used to model the co-variation between healthy and asthma sera. S-plot was used to visualize the relationship between covariance and correlation. Clinical and metabolomic data were processed using IBM SPSS statistics 20 and GraphPad Prism 5.0 statistical software (GraphPad, Inc., La Jolla, CA, USA). Normally distributed quantitative data were expressed as the mean $\pm$ standard deviation (SD). Student's *t*-tests and volcano plots were used to compare 15 healthy and 15 asthma children sera, respectively. Statistical testing within the chemometric analysis using the ChemRICH platform was determined by Kolmogorv-Smirnov testing. A receiver operating characteristic (ROC) curve and cut-off point were determined using data from the control and allergic asthma groups, with AUC values of ≥ 0.8 representing strong effects. *P* values of < 0.05 were considered statistically significant. Violin plots were analyzed using InstantClue.

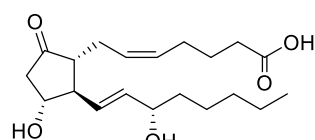
Eicosanoids



15(S)-HEPE

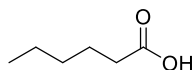


15(S)-HETE

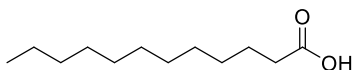


PGE2

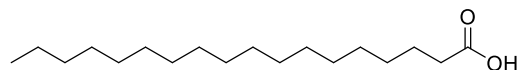
Saturated fatty acids



Hexanoic acid

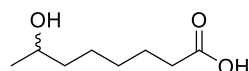


Dodecanoic acid

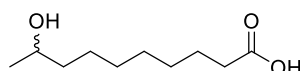


Stearic acid

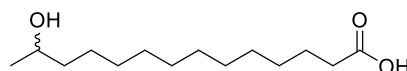
Hydroxysaturated fatty acids



Hydroxyoctanoic acid

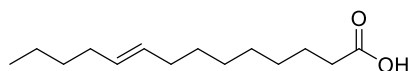


Hydroxydecanoic acid

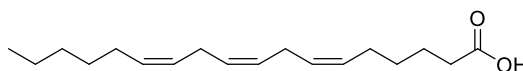


Hydroxytetradecanoic acid

Unsaturated fatty acids

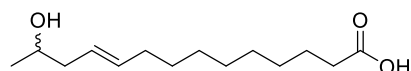


Tetradecenoic acid

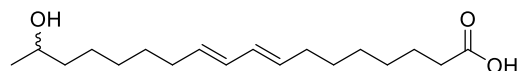


Linolenic acid

Hydroxyunsaturated fatty acids

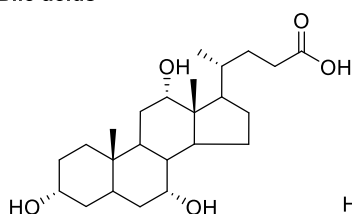


Hydroxytetradecanedioic acid

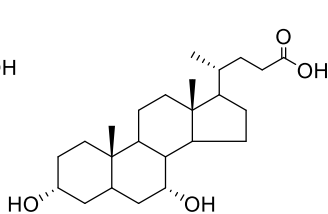


Hydroxyoctadecadienoic acid

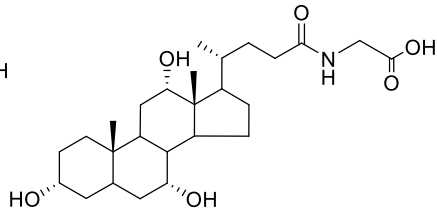
Bile acids



Cholic acid (CA)



Chenodeoxycholic acid (CDCA)



Glycocholic acid (GCA)

Figure S1 The representative structures of carboxylic acids.

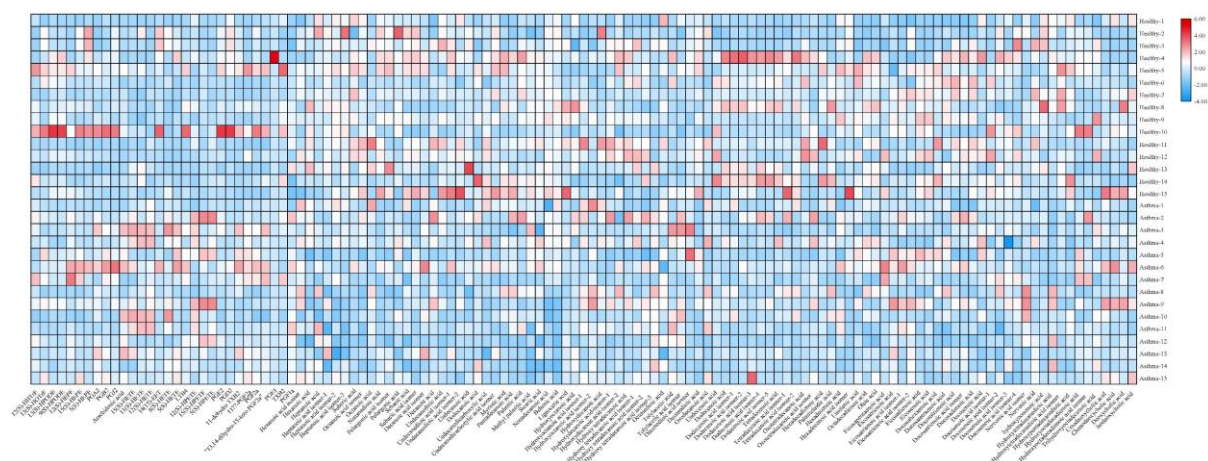


Figure S2. Heatmap of the whole identified metabolites through derivatization UHPLC-Q-TOF/MS

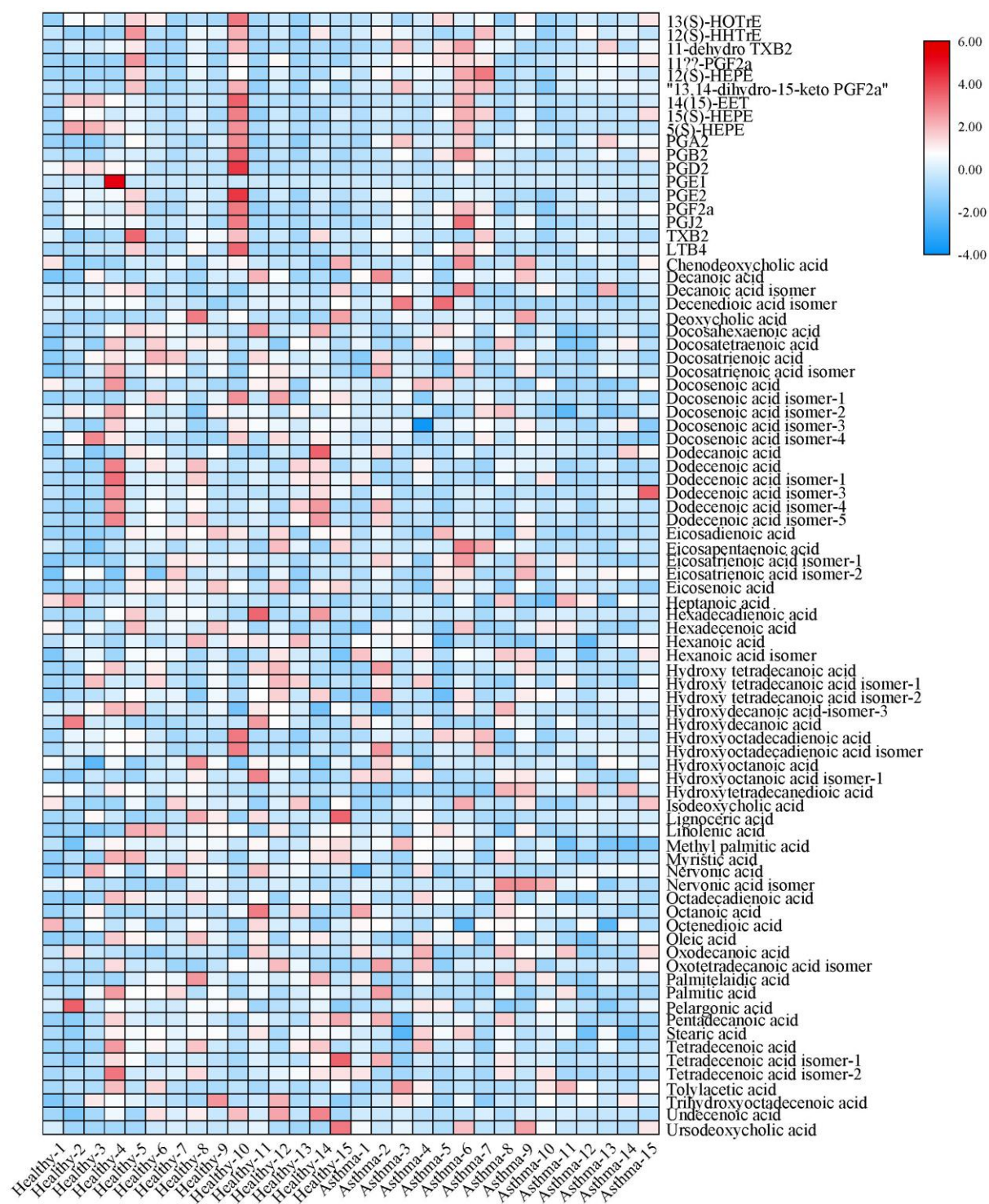


Figure S3. Heatmap of the metabolites except the 42 differentially produced metabolites.

Table S1. List of quantified eicosanoids, MRM parameters, linearity and LOQ

No.	Name	Precursor ions	Product ions	Collision energy (CE)	Linearity (ng/mL)	LOQ (ng/mL)
1	5(S)-HETE	405.4	328.4	12	0.1-20	0.1
2	8(S)-HETE	405.4	328.4	12	0.1-20	0.1
3	11(S)-HETE	405.4	328.4	12	0.1-40	0.1
4	12(S)-HETE	405.4	328.4	12	0.5-200	0.5
5	15(S)-HETE	405.4	328.4	12	0.1-20	0.1
6	5(S)-HPETE	421.4	344.3	10	0.5-40	0.5
7	12(S)-HPETE	421.4	344.3	10	0.1-40	0.1
8	15(S)-HPETE	421.4	344.3	10	0.1-40	0.1

Table S2. Metabolites identified in serum using UHPLC-Q-TOF/MS analysis

Classification	No.	Compound Name	Formula	Derivatization Formula	Precursor Ions [M] ⁺	RT (min)	Fold Change (Asthma/healthy)	p value	MS/MS
Eicosanoids	1	TXB2	C20H34O6	C25H47N2O5	455.3485	5.5	-1.21	0.45	378.26, 360.25, 342.24, 324.22, 306.24, 288.2324, 260.16, 194.11, 152.10, 98.06, 60.07
	2	11 β -PGF2 α	C20H34O5	C25H47N2O4	439.3536	5.73	-1.34	0.29	380.28, 362.27, 344.25, 326.24, 241.19, 208.17, 185.13, 138.09, 98.06, 60.08
	3	PGF1 α	C20H36O5	C25H49N2O4	441.3692	6.6	1.45	0.027	364.28
	4	PGE2	C20H32O5	C25H45N2O4	437.3379	6.84	-1.33	0.29	378.26, 360.25
	5	11-dehydro TXB2	C20H32O6	C25H45N2O5	453.3325	6.97	1.21	0.62	394.16, 376.25, 360.25, 332.26, 288.23, 229.19, 203.18, 138.09, 98.06, 69.63
	6	PGD2	C20H32O5	C25H45N2O4	437.3379	7.43	-2.47	0.074	378.26, 360.25
	7	PGF2 α	C20H34O5	C25H47N2O4	439.3536	7.6	1.16	0.56	362.26, 318.24, 287.85, 273.78, 244.91, 217.59, 203.94, 159.09, 116.03, 89.05, 59.04
	8	13, 14-dihydro-15-keto PGF2 α	C20H34O5	C25H47N2O4	439.3536	8.47	1.45	0.13	379.83, 362.26, 347.27, 263.87, 219.13, 206.0917, 133.08, 60.07
	9	PGA2	C20H30O4	C25H43N2O3	419.3274	9.95	1.53	0.11	360.25, 342.24, 255.17, 198.13, 180.13, 138.08, 124.07, 110.09, 98.06, 60.08
	10	PGB2	C20H30O4	C25H43N2O3	419.3274	10.22	1.41	0.25	342.24, 297.79, 256.84, 214.91, 171.11, 98.06, 60.08
	11	PGE1	C20H34O5	C25H47N2O4	439.3536	10.28	1.00	0.38	380.27, 362.26, 318.24, 260.88, 236.85, 221.09, 188.85, 174.16, 147.10, 60.07

12	PGJ2	C20H30O4	C25H43N2O3	419.3274	10.73	1.16	0.71	364.28, 326.24, 241.19, 182.11, 143.08, 98.06, 60.08
13	12(S)-HHTrE	C17H28O3	C22H41N2O2	365.3168	13.83	1.07	0.76	306.24, 288.23, 260.20, 203.17, 138.09, 119.08, 98.06, 60.08
14	LTB4	C20H32O4	C25H45N2O3	421.343	14.15	1.20	0.63	344.25, 326.24, 282.60, 240.17, 192.14, 178.09, 152.10, 138.09, 98.06, 60.08
15	13(S)-HOTrE	C18H30O3	C23H43N2O2	379.3325	15.36	-1.04	0.9	320.25, 302.24, 285.22, 259.20, 217.19, 189.16, 121.10, 93.06, 60.08
16	12(S)-HEPE	C20H30O3	C25H43N2O2	403.3325	16.64	1.84	0.074	326.24, 284.21, 241.19, 218.15, 192.13, 150.12
17	15(S)-HEPE	C20H30O3	C25H43N2O2	403.3325	17.45	1.13	0.68	326.24, 289.98, 262.13, 244.17, 143.08, 98.06, 60.08
18	15(S)-HETE	C20H32O3	C25H45N2O2	405.3481	18.61	2.39	0.0028	328.26, 300.23, 243.21, 215.17, 173.13, 145.10, 131.08, 117.07, 98.06, 60.08
19	13(S)-HPODE	C18H32O4	C23H45N2O3	397.343	18.97	-2.11	0.046	320.25, 292.26, 250.18, 222.18, 194.15, 180.13, 166.12, 123.11, 98.06, 60.08
20	5(S)-HEPE	C20H30O3	C25H43N2O2	403.3325	19.27	-1.93	0.14	326.24, 298.87, 243.09, 178.12, 147.06, 121.06, 105.07, 69.03
21	9(S)-HPODE	C18H32O4	C23H45N2O3	397.343	19.37	-1.89	0.05	320.01, 292.26, 264.19, 250.18, 208.13, 182.15, 140.91, 122.09, 104.84, 60.08
22	11(S)-HETE	C20H32O3	C25H45N2O2	405.3481	19.65	1.58	0.024	328.26, 243.21, 214.91, 152.10, 98.06, 60.08
23	12(S)-HPETE	C20H32O4	C25H45N2O3	421.343	19.86	1.29	0.027	362.26, 344.25, 333.25, 274.17
24	12(S)-HETE	C20H32O3	C25H45N2O2	405.3481	19.89	3.19	<0.0001	328.26, 300.23, 243.21, 217.14, 138.09, 98.06
25	14(15)-EET	C20H32O3	C25H45N2O2	405.3481	20.46	-1.83	0.28	328.26, 285.22, 243.21, 192.14, 159.11, 131.08, 98.06, 60.08

	26	8(S)-HETE	C20H32O3	C25H45N2O2	405.3481	20.73	2.43	0.0047	346.27, 328.26, 243.21, 219.15, 192.13, 152.10, 138.09, 98.06, 60.08
	27	15(S)-HPETE	C20H32O4	C25H45N2O3	421.343	21.07	1.74	0.0045	362.26, 344.25, 328.26, 293.22, 234.15
	28	5(S)-HETE	C20H32O3	C25H45N2O2	405.3481	21.82	2.45	0.0029	346.27, 328.26, 286.08, 243.21, 201.16, 178.12, 131.08, 98.06, 60.08
	29	5(S)-HPETE	C20H32O4	C25H45N2O3	421.343	22.89	1.77	0.0039	403.33, 344.26, 328.26
	30	Arachidonic acid	C20H32O2	C25H45N2O	389.3526	27.56	1.36	0.0061	330.27, 302.24, 245.22, 218.15, 192.13, 166.12, 152.10, 98.06, 60.08
Saturated fatty acids	31	Heptanoic acid	C7H14O2	C12H27N2O	215.2123	1.8	-1.05	0.61	157.14, 113.09, 85.10, 60.08
	32	Hexanoic acid isomer	C6H12O2	C11H25N2O	201.1966	2.14	1.15	0.17	142.13, 127.10, 99.09, 85.08, 72.08
	33	Hexanoic acid	C6H12O2	C11H25N2O	201.1966	2.34	-1.13	0.15	142.13, 114.11, 99.09, 72.08
	34	Heptanoic acid isomer-1	C7H14O2	C12H27N2O	215.2123	2.49	-1.21	0.0096	157.14, 113.09, 85.10, 60.08
	35	Heptanoic acid isomer-2	C7H14O2	C12H27N2O	215.2123	2.61	-1.18	0.033	157.14, 113.09, 85.10, 60.08
	36	Suberic acid	C8H14O4	C13H27N2O3	259.2021	2.69	-1.49	0.01	200.13, 115.96, 70.97
	37	Heptanoic acid isomer-3	C7H14O2	C12H27N2O	215.2123	3.15	-1.36	0.0011	157.14, 113.09, 85.10, 60.08

38	Nonanedioic acid	C9H16O4	C14H29N2O3	273.2178	3.21	-1.79	0.00019	214.14, 140.07, 114.97, 96.04, 60.08
39	Octanoic acid isomer	C8H16O2	C13H29N2O	229.2279	3.37	-1.31	0.00044	170.15, 141.11, 128.10, 98.06, 84.96, 72.04, 57.07
40	Sebacic acid	C10H18O4	C15H31N2O3	287.2335	3.88	-1.35	0.033	228.16, 172.09, 154.08, 126.09, 84.08, 60.08
41	Sebacic acid isomer	C10H18O4	C15H31N2O3	287.2335	4.19	-1.45	0.01	228.15, 154.08, 126.09, 101.06, 60.08
42	Octanoic acid	C8H16O2	C13H29N2O	229.2279	4.9	1.09	0.69	170.15, 156.89, 129.06, 112.89, 72.93, 57.06
43	Undecanedioic acid	C11H20O4	C16H33N2O3	301.2491	4.93	-1.51	0.0071	242.17, 168.10, 133.08, 101.92, 86.09, 69.06
44	Pelargonic acid isomer	C9H18O2	C14H31N2O	243.2436	5.82	-1.27	0.015	184.17, 141.11, 112.18, 86.06, 71.08, 57.07
45	Undecanedioic acid isomer-1	C11H20O4	C16H33N2O3	301.2491	5.89	-1.64	0.021	242.17, 168.10, 141.10, 98.06, 84.08, 69.06
46	Undecanedioic acid isomer-2	C11H20O4	C16H33N2O3	301.2491	6.49	-1.25	0.036	242.17, 186.14, 168.10, 140.10, 97.06
47	Pelargonic acid	C9H18O2	C14H31N2O	243.2436	7.64	-1.07	0.22	184.17, 141.12, 123.11, 96.92, 71.08, 60.08
48	Decanoic acid isomer	C10H20O2	C15H33N2O	257.2593	9.25	1.11	0.59	198.18, 185.10, 137.13, 109.10, 95.08, 81.07, 60.08
49	Undecanedicarboxylic acid	C13H24O4	C18H37N2O3	329.2804	9.75	-1.22	0.047	285.03, 217.89, 169.01, 95.04, 57.06

50	Decanoic acid	C10H20O2	C15H33N2O	257.2593	10.86	1.31	0.088	198.18, 161.97, 124.87, 109.10, 85.10, 71.08, 60.08
51	Undecanedicarboxylic acid isomer	C13H24O4	C18H37N2O3	329.2804	12.66	-1.41	0.016	307.15, 242.11, 180.06, 99.08, 59.04
52	Undecanoic acid	C11H22O2	C16H35N2O	271.2749	14.16	-1.26	0.038	212.20, 127.12, 96.06, 60.08
53	Dodecanoic acid	C12H24O2	C17H37N2O	285.2904	17.37	1.06	0.79	346.27, 328.26, 286.08, 243.21, 201.16, 178.12, 131.08, 98.06, 60.08
54	Myristic acid	C14H28O2	C19H41N2O	313.3207	23.11	-1.29	0.15	289.98, 273.28, 254.24, 220.16, 138.13, 124.08
55	Pentadecanoic acid	C15H30O2	C20H43N2O	327.3365	25.98	-1.04	0.79	268.26, 210.18, 151.90, 109.10, 85.10, 60.08
56	Palmitic acid	C16H32O2	C21H45N2O	341.3541	28.59	-1.49	0.082	282.27, 224.20, 210.18, 196.17, 182.15, 154.12, 123.11, 98.06, 57.07
57	Methyl palmitic acid	C17H34O2	C22H47N2O	355.3676	30.27	-1.08	0.26	296.29, 252.23, 224.20, 196.17, 168.13, 140.10, 98.06, 57.07
58	Stearic acid	C18H36O2	C23H49N2O	369.385	31.25	-1.1	0.24	310.31, 266.24, 252.23, 238.21, 210.18, 182.15, 154.12, 128.1, 98.06, 57.07
59	Nonadecanoic acid	C19H38O2	C24H51N2O	383.4001	32.35	-1.35	0.00027	324.32, 228.17, 214.12, 181.02, 168.08, 153.01, 128.14, 113.07, 98.06
60	Behenic acid	C22H44O2	C27H57N2O	425.4471	34.79	-1.25	0.0019	366.37, 321.14, 223.02, 154.12, 135.11, 112.12, 85.10, 60.08
61	Lignoceric acid	C24H48O2	C29H61N2O	453.4784	36.17	-1.23	0.3	394.40, 272.29, 223.07, 188.04, 152.10, 117.03, 89.06, 60.08
62	Hydroxyoctanoic acid	C8H16O3	C13H29N2O2	245.2229	1.98	-1.01	0.88	227.21, 169.14, 125.09, 60.08

Hydroxysaturated fatty acids	63	Hydroxyoctanoic acid isomer-1	C8H16O3	C13H29N2O2	245.2229	2.27	1.35	0.25	187.15, 169.14, 60.08
	64	Hydroxyoctanoic acid isomer-2	C8H16O3	C13H29N2O2	245.2229	2.71	1.4	0.0052	227.21, 169.14, 125.09, 60.08
	65	Hydroxydecanoic acid	C10H20O3	C15H33N2O2	273.2542	6.17	-1.01	0.96	255.24, 197.17, 153.12, 125.13, 60.08
	66	Hydroxydecanoic acid isomer-1	C10H20O3	C15H33N2O2	273.2542	6.67	-1.18	0.45	215.18, 197.17, 125.13, 60.08
	67	Hydroxydecanoic acid isomer-2	C10H20O3	C15H33N2O2	273.2542	8.14	-1.39	0.042	255.24, 197.17, 153.12, 125.13, 60.08
	68	Hydroxytetradecanoic acid	C14H28O3	C19H41N2O2	329.3168	10.44	-1.19	0.44	270.24, 214.18, 196.16, 144.91, 111.11, 85.10, 60.08
	69	Hydroxytetradecanoic acid isomer-1	C14H28O3	C19H41N2O2	329.3168	12.29	-1.26	0.29	270.24, 252.23, 146.95, 126.10, 97.10, 60.08
	70	Hydroxytetradecanoic acid isomer-2	C14H28O3	C19H41N2O2	329.3168	14.47	1.09	0.61	270.24, 252.23, 214.91, 129.06, 79.05, 60.08

Unsaturated fatty acids	71	Hydroxytetra- decanoic acid isomer- 3	C14H28O3	C19H41N2O2	329.3168	18.24	1.67	0.004 3	270.24, 230.89, 209.94, 174.09, 152.94, 112.89, 98.05, 59.06
	72	Tolylacetic acid	C9H10O2	C14H23N2O	235.181	2.42	1.41	0.24	177.11, 133.06, 105.06, 60.08
	73	Octenedioic acid	C8H12O4	C13H25N2O3	257.1865	2.59	-1.01	0.83	199.12, 155.06, 127.07, 82.07, 60.08
	74	Tolylacetic acid isomer	C9H10O2	C14H23N2O	235.181	2.67	1.65	0.019	177.11, 133.06, 105.06, 60.08
	75	Decenedioic acid isomer	C10H16O4	C15H29N2O3	285.2178	3.93	-1.1	0.76	226.14, 163.01, 152.07, 85.06, 60.08
	76	Decenedioic acid	C10H16O4	C15H29N2O3	285.2178	4.23	-1.52	0.004 1	226.14, 170.08, 152.07, 124.07, 96.08, 81.03, 60.08
	77	Oxodecanoic acid	C10H18O3	C15H31N2O2	271.2385	5.97	1.4	0.15	213.17, 169.12, 141.12, 60.08
	78	Undecenoic acid	C11H20O2	C16H33N2O	269.259	10.86	-1.36	0.12	210.18, 196.11, 170.08, 126.09, 98.06, 69.07
	79	Dodecenoic acid	C12H22O2	C17H35N2O	283.2742	13.72	-1.59	0.077	224.20, 179.93, 98.06, 70.07
	80	Dodecenoic acid isomer- 1	C12H22O2	C17H35N2O	283.2742	14.04	-1.91	0.093	224.20, 112.09, 98.05, 69.07
	81	Dodecenoic acid isomer- 2	C12H22O2	C17H35N2O	283.2742	14.32	-2.26	0.031	224.20, 138.80, 98.06

	Dodecenoic							
82	acid isomer-3	C12H22O2	C17H35N2O	283.2742	15.28	-1.27	0.55	224.20, 124.11, 98.05
	Dodecenoic							
83	acid isomer-4	C12H22O2	C17H35N2O	283.2742	15.49	-1.47	0.23	224.20, 197.16, 138.12, 112.07, 98.06, 83.08, 60.08
	Oxotetradecanoic acid	C14H26O3	C19H39N2O2	327.3011	15.53	-1.86	0.014	268.22, 226.87, 183.17, 168.01, 144.99, 124.07, 109.10, 95.08, 60.08
	Oxotetradecanoic acid isomer	C14H26O3	C19H39N2O2	327.3011	16.02	1.11	0.6	268.22, 250.21, 202.87, 150.12, 123.11, 89.05, 60.08
86	Dodecenoic acid isomer-5	C12H22O2	C17H35N2O	283.2742	16.13	-1.78	0.13	224.20, 196.12, 180.17, 140.14, 112.07, 98.06, 60.08
87	Tetradecenoic acid	C14H26O2	C19H39N2O	311.3056	19.57	-1.47	0.17	252.23, 181.15, 162.09, 126.09, 98.06, 85.05
88	Tetradecenoic acid isomer-1	C14H26O2	C19H39N2O	311.3056	20.42	-1.07	0.65	252.23, 229.92, 184.20, 152.14, 126.09, 98.06
89	Tetradecenoic acid isomer-2	C14H26O2	C19H39N2O	311.3056	22.05	-1.98	0.068	252.23, 208.20, 185.10, 140.10, 98.06, 69.07
90	Hexadecadienoic acid	C16H28O2	C21H41N2O	337.3217	22.27	-1.69	0.16	278.24, 250.25, 236.20, 180.13, 154.12, 140.10, 124.11, 98.06, 60.08
91	Linolenic acid	C18H30O2	C23H43N2O	363.3375	24.33	-1.12	0.53	304.26, 262.21, 236.20, 208.16, 182.15, 154.12, 140.10, 112.07, 98.06, 60.08

92	Palmitelaidic acid	C16H30O2	C21H43N2O	339.3373	24.95	-1.19	0.46	280.26, 262.25, 236.23, 196.20, 154.12, 126.09, 98.06, 60.08
93	Eicosapentae noic acid	C20H30O2	C25H43N2O	387.3375	24.98	1.17	0.49	328.26, 246.18, 220.16, 192.13, 166.12, 152.10, 138.09, 119.08, 98.06, 60.08
94	Hexadecenoic acid	C16H30O2	C21H43N2O	339.3373	25.39	-1.1	0.6	280.26, 252.27, 236.23, 210.18, 196.20, 182.15, 168.13, 154.12, 140.10, 126.09, 112.07, 98.06, 83.08, 60.08
95	Hexadecenoic acid isomer	C16H30O2	C21H43N2O	339.3373	25.74	-2.63	0.0057	280.26, 252.26, 212.20, 182.19, 163.14, 135.11, 112.07, 98.06, 83.08, 60.08
96	Octadecadenoic acid	C18H32O2	C23H45N2O	365.3539	26.77	-1.13	0.45	306.27, 264.23, 236.20, 208.17, 182.15, 154.12, 98.06, 81.07, 60.08
97	Docosahexaenoic acid	C22H32O2	C27H45N2O	413.3523	27.66	-1.31	0.093	354.27, 246.18, 218.15, 192.13, 166.12, 152.10, 138.09, 119.08, 98.06, 60.08
98	Eicosatrienoic acid	C20H34O2	C25H47N2O	391.3676	29.08	1.38	0.032	332.29, 276.23, 262.21, 248.20, 187.14, 147.11, 121.10, 98.06
99	Eicosatrienoic acid isomer-1	C20H34O2	C25H47N2O	391.3676	29.31	1.2	0.17	332.29, 290.09, 271.24, 245.22, 206.15, 159.11, 121.10, 98.06, 60.08
100	Oleic acid	C18H34O2	C23H47N2O	367.3703	29.55	-1.21	0.24	308.29, 266.24, 238.21, 210.18, 182.15, 154.12, 112.07, 98.06, 69.07
101	Eicosatrienoic acid isomer-2	C20H34O2	C25H47N2O	391.3688	29.9	1.19	0.16	334.31, 214.91, 182.19, 149.02, 123.11, 91.05, 60.08
102	Docosatetraenoic acid	C22H36O2	C27H49N2O	417.3834	30.26	-1.08	0.59	358.31, 330.27, 297.25, 274.21, 208.16, 180.13, 152.10, 98.06, 60.08

103	Eicosadienoic acid	C20H36O2	C25H49N2O	393.3833	30.46	-1.35	0.14	334.31, 278.24, 250.21, 224.20, 196.17, 168.13, 140.10, 126.09, 98.06, 60.08
104	Docosatrienoic acid	C22H38O2	C27H51N2O	419.4001	31.17	-1.27	0.091	360.33, 318.28, 290.26, 60.08
105	Docosatrienoic acid isomer	C22H38O2	C27H51N2O	419.4001	31.52	-1.05	0.66	360.33, 290.26, 60.08
106	Eicosenoic acid	C20H38O2	C25H51N2O	395.3991	31.79	-1.38	0.11	336.32, 294.27, 252.23, 224.20, 196.17, 168.13, 140.10, 98.06, 60.08
107	Docosenoic acid	C22H42O2	C27H55N2O	423.4314	32.09	-1.02	0.67	406.40, 343.19, 252.10, 217.12, 184.07, 123.11, 84.08, 58.06
108	Docosadienoic acid	C22H40O2	C27H53N2O	421.4157	32.26	-1.43	0.033	362.34, 301.21, 276.02, 227.20, 184.07, 123.11, 100.07, 60.08
109	Docosenoic acid isomer-1	C22H42O2	C27H55N2O	423.4314	33.46	-1.31	0.14	364.35, 317.28, 292.08, 233.14, 184.07, 133.08, 89.06, 60.08
110	Nervonic acid isomer	C24H46O2	C29H59N2O	451.4627	33.69	1.18	0.085	392.38, 367.19, 307.29, 239.15, 205.10, 169.08, 133.10, 89.05, 60.08
111	Docosenoic acid isomer-2	C22H42O2	C27H55N2O	423.4314	33.94	-1.11	0.053	364.35, 343.19, 314.14, 239.14, 195.12, 167.03, 133.08, 89.05, 60.08
112	Docosenoic acid isomer-3	C22H42O2	C27H55N2O	423.4314	34.65	-1.05	0.38	364.35, 317.28, 292.08, 184.07, 133.08, 89.06, 60.08
113	Nervonic acid	C24H46O2	C29H59N2O	451.4627	34.91	-1.26	0.11	392.38, 373.30, 311.15, 251.17, 221.19, 177.16, 121.10, 97.10, 60.08

	114	Docosenoic acid isomer-4	C22H42O2	C27H55N2O	423.4314	35.09	-1.12	0.12	350.34, 281.04, 213.10, 123.11, 84.08, 58.06
Hydroxyunsaturated fatty acids	115	Hydroxynonenoic acid	C9H16O3	C14H29N2O2	257.2229	7.26	-1.85	0.0088	239.21, 181.14, 137.09, 60.08
	116	Hydroxytetradecanedioic acid	C14H26O5	C19H39N2O4	359.2909	4.75	-1.04	0.73	300.21, 284.17, 244.15, 208.91, 170.07, 150.09, 89.06, 60.08
	117	Hydroxytetradecanedioic acid isomer	C14H26O5	C19H39N2O4	359.2909	8.74	-1.72	0.0027	300.21, 244.15, 170.08, 152.06, 60.08
	118	Hydroxypentadecanedioic acid	C15H28O5	C20H41N2O4	373.3066	9.58	-1.44	0.0019	356.09, 314.07, 214.14, 173.02, 100.95, 74.09, 60.08
	119	Hydroxyoctadecadienoic acid	C18H32O3	C23H45N2O2	381.3469	17.39	1.17	0.55	304.26, 177.12, 163.14, 149.02, 124.11, 98.06
	120	Hydroxyoctadecadienoic acid isomer	C18H32O3	C23H45N2O2	381.3469	18.02	1.2	0.55	304.26, 152.10, 98.06, 60.08
	121	Trihydroxyoctadecenoic acid	C18H34O5	C23H47N2O4	415.3535	27.79	1.02	0.9	356.27, 273.30, 133.08, 89.06, 71.08, 60.08
	Bile acids	122	Ursodeoxycholic acid	C24H40O4	C29H53N2O3	477.4039	8.19	1.5	0.29

123	Chenodeoxy cholic acid	C24H40O4	C29H53N2O3	477.4039	9.92	1.13	0.71	418.33, 397.73, 366.68, 335.56, 280.21, 239.15, 202.16, 123.08, 60.08
124	Deoxycholic acid	C24H40O4	C29H53N2O3	477.4039	10.73	-1.01	0.98	418.33, 402.26, 372.57, 328.36, 255.13, 213.16, 161.13, 128.10, 60.08
125	Isodeoxycho lic acid	C24H40O4	C29H53N2O3	477.4039	11.25	-1.05	0.86	418.33, 400.32, 351.19, 300.22, 268.36, 161.13, 121.05, 60.08

Table S3. Cluster labels of the metabolites

No.	Compound Name	InChiKeys	Pubchem ID	SMILES	P value	Fold change
1	12(S)-HETE	ZNHVWPKMFKADKW-LQWMCKPYSA-N	5283155	<chem>CCCCC=CCC(C=CC=CCC=CCCC(=O)O)O</chem>	0.0000 15	3.19
2	5(S)-HETE	KGIJOYOSFUGPC-JGKLHWIESA-N	5280733	<chem>CCCCC=CCC=CCC=CC=CC(CCCC(=O)O)O</chem>	0.0029	2.45
3	8(S)-HETE	NLUNAYAEIJYXRB-VYOQERLCSA-N	5283154	<chem>CCCCC=CCC=CC=CC(CC=CCCC(=O)O)O</chem>	0.0047	2.43
4	15(S)-HETE	JSFATNQSLKRBCI-VAEKSGALSA-N	5280724	<chem>CCCCC(C=CC=CCC=CCC=CCCC(=O)O)O</chem>	0.0028	2.39
5	5(S)-HPETE	JNUUNUQHIXOFDA-JGKLHWIESA-N	5280778	<chem>CCCCC=CCC=CCC=CC=CC(CCCC(=O)O)OO</chem>	0.0039	1.77
6	15(S)-HPETE	BFWYTORDSFIVKP-VAEKSGALSA-N	5280893	<chem>CCCCC(C=CC=CCC=CCC=CCCC(=O)O)OO</chem>	0.0045	1.74
7	Hydroxytetradecanoic acid isomer-3	JOSXCARTDOQLV-UHFFFAOYSA-N	3084276	<chem>C(CCCCCC(=O)O)CCCCCO</chem>	0.0043	1.67
8	Tolylacetic acid isomer	GXXXUZIRGXYDFP-UHFFFAOYSA-N	248474	<chem>CC1=CC=C(C=C1)CC(=O)O</chem>	0.019	1.65
9	11(S)-HETE	GCZRCCHPLVMMJE-YZGNWCGPSA-N	5283152	<chem>CCCCC=CC=CC(CC=CCC=CCCC(=O)O)O</chem>	0.024	1.58
10	PGF1alpha	DZUXGQBLFALXCR-CDIPTNKSSA-N	5280939	<chem>CCCCC(C=CC1C(CC(C1CCCCC(=O)O)O)O)O</chem>	0.027	1.45
11	Hydroxyoctanoic acid isomer-2	KDMSVYIHLZKET-UHFFFAOYSA-N	69820	<chem>C(CCCC(=O)O)CCCO</chem>	0.0052	1.40
12	Eicosatrienoic acid	AHANXAKGNAKFSK-PDBXOOCHSA-N	5312529	<chem>CCC=CCC=CCC=CCCCCCCCC(=O)O</chem>	0.032	1.38
13	Arachidonic acid	YZXBAPSDXZZRGB-DOFZRALJSA-N	444899	<chem>CCCCC=CCC=CCC=CCC=CCCC(=O)O</chem>	0.0061	1.36
14	12(S)-HPETE	ZIOZYRSDNLNNJ-LQWMCKPYSA-N	5280892	<chem>CCCCC=CCC(C=CC=CCC=CCCC(=O)O)OO</chem>	0.027	1.29
15	Heptanoic acid isomer-2	MHPUGCYGQWGLJL-UHFFFAOYSA-N	12344	<chem>CC(C)CCCC(=O)O</chem>	0.033	0.85

16	Heptanoic acid isomer-1	CVKMFSAVYPAZTQ-UHFFFAOYSA-N	20653	CCCCC(C)C(=O)O	0.0096	0.83
17	Undecanedicarboxylic acid	HCUZVMHXDRSBKX-UHFFFAOYSA-N	20389	CCCCCCCCCCCC(C(=O)O)C(=O)O	0.047	0.82
18	Behenic acid	UKMSUNONTOPOIO-UHFFFAOYSA-N	8215	CCCCCCCCCCCCCCCCCCCC(=O)O	0.0019	0.80
19	Undecanedioic acid isomer-2	OSYQOBUUFRGFNG-UHFFFAOYSA-N	69957	COC(=O)CCCCCCCCC(=O)O	0.036	0.80
20	Undecanoic acid	ZDPHROOEEOARMN-UHFFFAOYSA-N	8180	CCCCCCCCCCCC(=O)O	0.038	0.79
21	Pelargonic acid isomer	XBUXARJOYUQNTC-UHFFFAOYSA-N	36599	CCCCCCC(CC(=O)O)O	0.015	0.79
22	Octanoic acid isomer	OEOIWYCWDBOPA-UHFFFAOYSA-N	90716	CC(C)CCCCC(=O)O	0.0004 4	0.76
23	Nonadecanoic acid	ISYWECDZWTKEFF-UHFFFAOYSA-N	12591	CCCCCCCCCCCCCCCCCCCC(=O)O	0.0002 7	0.74
24	Sebacic acid	CXMXRPHRNRROMY-UHFFFAOYSA-N	5192	C(CCCCC(=O)O)CCCC(=O)O	0.033	0.74
25	Heptanoic acid isomer-3	DIVCBWJKVSFZKJ-UHFFFAOYSA-N	15271	CCC(C)CCC(=O)O	0.0011	0.74
26	Hydroxydecanoic acid isomer-2	FYSSBMZUBSBFJL-UHFFFAOYSA-N	26612	CCCCCCCC(CC(=O)O)O	0.042	0.72
27	Undecanedicarboxylic acid isomer	DXNCZXXFRKPEPY-UHFFFAOYSA-N	10458	C(CCCCCC(=O)O)CCCCC(=O)O	0.016	0.71
28	Docosadienoic acid	CVCXSNONTRFSEH-UHFFFAOYSA-N	53741802	CCCCCCCCCCCCCCCCCCC=CC=CC(=O)O	0.033	0.70
29	Hydroxypentadecanedioic acid	PWEDZXIZWHL MCP-UHFFFAOYSA-N	23052245	C(CCCCCC(CC(=O)O)O)CCCCC(=O)O	0.0019	0.69
30	Sebacic acid isomer	WUDDSDIHJHPJRP-UHFFFAOYSA-N	19872	CCC(CCCCCC(=O)O)C(=O)O	0.01	0.69
31	Suberic acid	TYFQFVWCELRYAO-UHFFFAOYSA-N	10457	C(CCCC(=O)O)CCC(=O)O	0.01	0.67

32	Undecanedioic acid	LWBHHRRTQZQPDH-UHFFFAOYSA-N	15816	C(CCCCC(=O)O)CCCCC(=O)O	0.0071	0.66
33	Decenedioic acid	XUNMWLWTZWWEIE-UHFFFAOYSA-N	181528	C(CCCCC(=O)O)CCC=CC(=O)O	0.0041	0.66
34	Undecanedioic acid isomer-1	QJGNSTCICFBACB-UHFFFAOYSA-N	12972	CCCCCCCCC(C(=O)O)C(=O)O	0.021	0.61
35	Hydroxytetradecanedioic acid isomer	CEDZIURHISELSQ-UHFFFAOYSA-N	20848956	C(CCCCCC(=O)O)CCCCC(CC(=O)O)O	0.0027	0.58
36	Nonanedioic acid	BDJRBEYXGGNYIS-UHFFFAOYSA-N	2266	C(CCCCC(=O)O)CCCC(=O)O	0.00019	0.56
37	Hydroxynonenic acid	IATDSIZPXXCHKU-UHFFFAOYSA-N	73801896	CCCCCCC=C(C(=O)O)O	0.0088	0.54
38	Oxotetradecanoic acid	WVTQGCAFSDFHWMP-UHFFFAOYSA-N	454062	CCCCCCCC(=O)CCCCCCCC(=O)O	0.014	0.54
39	9(S)-HPODE	JGUNZIWGNMQSBM-UINYOVNOSA-N	9548877	CCCCC=CC=CC(CCCCCCCC(=O)O)OO	0.05	0.53
40	13(S)-HPODE	JDSRHVWSAMTSSN-IRQZEAMPSA-N	5280720	CCCCC(C=CC=CCCCCCCCC(=O)O)OO	0.046	0.47
41	Dodecenoic acid isomer-2	AZCVFLMXESYPIR-NSCUHMNNSA-N	5282734	CC=CCCCCCCCC(=O)O	0.031	0.44
42	Hexadecenoic acid isomer	NNNVXFKZMRGJPM-ZHACJKMWSA-N	5282744	CCCCCCCCC=CCCCC(=O)O	0.0057	0.38
43	Docosenoic acid isomer-2	KJDZDTDNIULJBE-VAWYXSNFSA-N	5312549	CCCCCCCCC=CCCCCCCCC(=O)O	0.053	0.90
44	Tetradecenoic acid isomer-2	IBYFOBGNPINBU-OUKQBFOZSA-N	5282738	CCCCCCCCCCCC=CC(=O)O	0.068	0.51
45	PGD2	BHMBVRSPMRCCGG-OUTUXVNYSAN	448457	CCCCC(C=CC1C(C(CC1=O)O)CC=CCCCC(=O)O)O	0.074	0.40
46	12(S)-HEPE	MCRJLMXYVFDXLS-UOLHMMFFSA-N	5283191	CCC=CCC=CCC(C=CC=CCC=CCCCC(=O)O)O	0.074	1.84
47	Dodecenoic acid	PAWGRNGPMLVJQH-UHFFFAOYSA-N	96204	CCCCCCCCC=CC(=O)O	0.077	0.63

48	Palmitic acid	IPCSVZSSVZVIGE-UHFFFAOYSA-N	985	CCCCCCCCCCCCCCCC(=O)O	0.082	0.67
49	Nervonic acid isomer	GWHCXVQVJPWHRF-UHFFFAOYSA-N	65032	CCCCCCCCC=CCCCCCCCCCCCCCCC(=O)O	0.085	1.18
50	Decanoic acid	GHVNFZFCNZKVNT-UHFFFAOYSA-N	2969	CCCCCCCCCCC(=O)O	0.088	1.31
51	Docosatrenoic acid	WBBQTNCISCKUMU-PDBXOOCHSA-N	5312557	CCC=CCC=CCC=CCCCCCCCCCCCCCCC(=O)O	0.091	0.79
52	Dodecenoic acid isomer-1	PAWGRNGPMLVJQH-ZHACJKMWSA-N	5282729	CCCCCCCCCCC=CC(=O)O	0.093	0.52
53	Docosaheptaenoic acid	MBMBGCFOFBJSGT-KUBAVDMBSA-N	445580	CCC=CCC=CCC=CCC=CCC=CCC=CCCC(=O)O	0.093	0.76
54	PGA2	MYHXHCUNDDAE0Z-FOSBLDSVSA-N	5280880	CCCCCCC(C=CC1C=CC(=O)C1CC=CCCCC(=O)O)O	0.11	1.53
55	Eicosenoic acid	BITHHVVYSMSWAG-KTKRTIGZSA-N	5282768	CCCCCCCCC=CCCCCCCCCCCC(=O)O	0.11	0.72
56	Nervonic acid	GWHCXVQVJPWHRF-KTKRTIGZSA-N	5281120	CCCCCCCCC=CCCCCCCCCCCCCCCC(=O)O	0.11	0.79
57	Undecenoic acid	FRPZMMHWLSIFAZ-UHFFFAOYSA-N	5634	C=CCCCCCCCCCC(=O)O	0.12	0.74
58	Docosenoic acid isomer-4	ZGJQAPUAARZOCF-ARJAWSKDSA-N	5312552	CCC=CCCCCCCCCCCCCCCCCCCC(=O)O	0.12	0.89
59	13, 14-dihydro-15-keto PGF2alpha	VKTIONYPMSCHQI-XAGFEHLVSA-N	5283039	CCCCCCC(=O)CCC1C(CC(C1CC=CCCCC(=O)O)O)O	0.13	1.45
60	Dodecenoic acid isomer-5	GCORITRBZMICMI-HJWRWDBZSA-N	5316956	CCCCCCCCC=CCCC(=O)O	0.13	0.56
61	5(S)-HEPE	FTAGQROYQYQRHF-GHWNLOBHSA-N	5283193	CCC=CCC=CCC=CCC=CC=CC(CCCCC(=O)O)O	0.14	0.52
62	Eicosadienoic acid	XSXIVVZCUAHUJO-HZJYTTRNSA-N	6439848	CCCCCC=CCC=CCCCCCCCCCCC(=O)O	0.14	0.74
63	Docosenoic acid isomer-1	DPUOLQHDNGRHBS-UHFFFAOYSA-N	8216	CCCCCCCCC=CCCCCCCCCCCCCCCC(=O)O	0.14	0.76
64	Hexanoic acid	FUZZWVXGSPDMH-UHFFFAOYSA-N	8892	CCCCCC(=O)O	0.15	0.88
65	Myristic acid	TUNFSRHWOTWDNC-UHFFFAOYSA-N	11005	CCCCCCCCCCCCCCCC(=O)O	0.15	0.78
66	Oxodecanoic acid	JBFDBSZCFDASAE-UHFFFAOYSA-N	259794	CCCCCCCCC(=O)C(=O)O	0.15	1.40

67	Hexadecadienoic acid	OOJGMLFHAQOYIL-SQIWNDBBSA-N	5312421	CCCCCCCCCCCC=CC=CC(=O)O	0.16	0.59
68	Eicosatrienoic acid isomer-2	AHANXAKGNAKFSK-UHFFFAOYSA-N	3210	CCC=CCC=CCC=CCCCCCCCCCC(=O)O	0.16	1.19
69	Hexanoic acid isomer	FGKJLKRYENPLQH-UHFFFAOYSA-N	12578	CC(C)CCC(=O)O	0.17	1.15
70	Tetradecenoic acid	IBYFOBGPINBU-UHFFFAOYSA-N	162384	CCCCCCCCCCCC=CC(=O)O	0.17	0.68
71	Eicosatrienoic acid isomer-1	HOBaelRKJCKHQD-UHFFFAOYSA-N	3011	CCCCC=CCC=CCC=CCCCCCCC(=O)O	0.17	1.20
72	Pelargonic acid	FBUKVWPVBMHYJY-UHFFFAOYSA-N	8158	CCCCCCCCC(=O)O	0.22	0.93
73	Dodecenoic acid isomer-4	IJBFSOLHRKELLR-FPLPWBNSA-N	5312378	CCCCC=CCCC(=O)O	0.23	0.68
74	Stearic acid	QIQXTHQIDYFRH-UHFFFAOYSA-N	5281	CCCCCCCCCCCCCCCCC(=O)O	0.24	0.91
75	Tolylacetic acid	RZWGTXHSYZGXKF-UHFFFAOYSA-N	69519	CC1=CC=CC=C1CC(=O)O	0.24	1.41
76	Oleic acid	ZQPPMHVWECSIRJ-KTKRTIGZSA-N	445639	CCCCCCCC=CCCCCCCC(=O)O	0.24	0.83
77	PGB2	PRFXRIUZNKLRLHM-HKVRTXJWSA-N	5280881	CCCCC(C=CC1=C(C(=O)CC1)CC=CCCCC(=O)O)O	0.25	1.41
78	Hydroxyoctanoic acid isomer-1	NDPLAKGOSZHTPH-UHFFFAOYSA-N	26613	CCCCC(CC(=O)O)O	0.25	1.35
79	Methyl palmitic acid	FXUKWLSZZHVEJD-UHFFFAOYSA-N	22207	CCC(C)CCCCCCCCCCCCC(=O)O	0.26	0.93
80	14(15)-EET	JBSCUHKPLGKXKH-ILYOTBPNSA-N	5283205	CCCCC1C(O1)CC=CCC=CCC=CCCC(=O)O	0.28	0.55
81	11beta-PGF2alpha	PXGPLTODNUVGFL-ZWAKLXPCSA-N	35023007	CCCCC(C=CC1C(CC(C1CC=CCCC(=O)O)O)O)O	0.29	0.75
82	PGE2	XEYBRNLFEZDVAW-ARSRFYASSA-N	5280360	CCCCC(C=CC1C(CC(=O)C1CC=CCCC(=O)O)O)O	0.29	0.75
83	Hydroxytetradecanoic acid isomer-1	ATRNZOYKSNPPBF-UHFFFAOYSA-N	16064	CCCCCCCCCCCC(CC(=O)O)O	0.29	0.79

				CC(CCC(=O)O)C1CCC2C1(CCC3C2C(CC4C3(C		
84	Ursodeoxycholic acid	RUDATBOHQWOJDD-UZVSRGJWSA-N	31401	CCCC(C4)O)C)O)C	0.29	1.50
85	Lignoceric acid	QZZGJDVWLFXDLK-UHFFFAOYSA-N	11197	CCCCCCCCCCCCCCCCCCCCCC(=O)O	0.3	0.81
86	PGE1	GMVPRGQOIIOIMI-DWKJAMRDSA-N	5280723	CCCCC(C=C C1C(CC(=O)C1CCCCCCC(=O)O))O)O	0.38	1.00
87	Docosenoic acid isomer-3	KPGGPQHJCHVLZ-FPLPWBNSLA-N	5312551	CCCCCCC=CCCCCCCCCCCCCCCC(=O)O	0.38	0.95
88	Hydroxytetradecanoi c acid	JYZJYKOZGGEXSX-UHFFFAOYSA-N	1563	CCCCCCCCCCCCC(C(=O)O)O	0.44	0.84
89	TXB2	XNRNNGPBEPNAR-JQLCGNGSA-N	5283137	CCCCC(C=C C1C(C(CC(O1)O)O)CC=CCCCC()=)O)O	0.45	0.83
90	Hydroxydecanoic acid isomer-1	LMHJFKYQYDSOQO-UHFFFAOYSA-N	1825	CCCCC(CCCC(=O)O)O	0.45	0.85
91	Octadecadienoic acid	ADHNUP OJJCKWRT-JLXBFWJWSA-N	5312457	CCCCCCCCCCCCC=CC=CC(=O)O	0.45	0.88
92	Palmitelaidic acid	SECPZKHBN QXJG-BQYQJA HWSA-N	5282745	CCCCC=CCCCCCCC(=O)O	0.46	0.84
93	Eicosapentaenoic acid	JAZBEHYOTPTENJ-JLNKQSITSA-N	446284	CCC=CCC=CCC=CCC=CCC=CCCC(=O)O	0.49	1.17
94	Linolenic acid	DTOSIQBP PRVQHS-PDBXOOCHSA-N	5280934	CCC=CCC=CCC=CCCCCCCC(=O)O	0.53	0.89
95	Dodecenoic acid isomer-3	PAWGRNGPML VJQH-KHPPLWFESA-N	5312376	CCCCCCCC=CC(=O)O	0.55	0.79
96	Hydroxyoctadecadien oic acid	NOCWDMQAHCQAKS-UHFFFAOYSA-N	73746259	CCCCCCCCCCCCC=CC=C(C(=O)O)O	0.55	1.17
97	Hydroxyoctadecadien oic acid isomer	NPDSHTNEKLQQIJ-UINYOVNOSA-N	5312830	CCCCC=CC=CC(CCCCCC(=O)O)O	0.55	1.20
98	PGF2alpha	PXGPLTODNUVGFL-YNNPMVKQSA-N	5280363	CCCCC(C=C C1C(CC(C1CC=CCCC(=O)O)O))O)O	0.56	1.16

99	Decanoic acid isomer	PWKJMPFEQOHBAC-UHFFFAOYSA-N	61840	CCCCC(CC)CCC(=O)O	0.59	1.11
100	Docosatetraenoic acid	FPRKGXIOSIUDSE-UHFFFAOYSA-N	187287	CCCCCCCCCCCCCCC=CC=CC=CC=CC(=O)O	0.59	0.93
101	Oxotetradecanoic acid isomer	FCMLVMXRWKFUTG-UHFFFAOYSA-N	454063	CCCCCCCCC(=O)CCCCC(=O)O	0.6	1.11
102	Hexadecenoic acid	ZVRMGCSSSYZGSM-CCEZHUSRSA-N	5282743	CCCCCCCCCCCCCCC=CC(=O)O	0.6	0.91
103	Heptanoic acid	MNWFXYJYAOYHMED-UHFFFAOYSA-N	8094	CCCCCCC(=O)O	0.61	0.95
104	Hydroxytetradecanoic acid isomer-2	DMCZWEUMVOFXBT-UHFFFAOYSA-N	150961	CCCC(CCCCCCCCCC(=O)O)O	0.61	1.09
105	11-dehydro TXB2	KJYIVXDPWBUBJQ-UHFFFAOYSA-N	1409	CCCCC(C=CC1C(C(CC(=O)O1)O)CC=CCCC C(=O)O)O	0.62	1.21
106	LTB4	VNYSSYRCGWBHLG-AMOLWHMGSA-N	5280492	CCCCC=CCC(C=CC=CC=CC(CCCC(=O)O)O) O	0.63	1.20
107	Tetradecenoic acid isomer-1	YWWVWXASSLXJHU-UHFFFAOYSA-N	68344	CCCCC=CCCCCCCCC(=O)O	0.65	0.93
108	Docosatrenoic acid isomer	WBBQTNCISCKUMU-UHFFFAOYSA-N	3146	CCC=CCC=CCC=CCCCCCCCCCCCC(=O)O	0.66	0.95
109	Docosenoic acid	ATNNLHXCRAAGJS-QZQOTICOSA-N	6433893	CCCCCCCCCCCCCCCCCCCC=CC(=O)O	0.67	0.98
110	15(S)-HEPE	WLKCSMCLEKGITB-DBVSHIMFSA-N	5283192	CCC=CCC(C=CC=CCC=CCC=CCCCC(=O)O)O	0.68	1.13
111	Octanoic acid	WWZKQHOCKIZLMA-UHFFFAOYSA-N	379	CCCCCCCC(=O)O	0.69	1.09
112	PGJ2	UQOQENZLBSFKO-POPPZSFYSA-N	5280884	CCCCC(C=CC1C(C=CC1=O)CC=CCCCC(=O) O)O	0.71	1.16
113	Chenodeoxycholic acid	RUDATBOHQWOJDD-BSWAIDMHSA-N	10133	CC(CCC(=O)O)C1CCC2C1(CCC3C2C(CC4C3(CCC(C4)O)C)O)C	0.71	1.13
114	Hydroxytetradecanoic acid	HWCBZTXSSOIPNB-UHFFFAOYSA-N	10286106	C(CCCCCC(C(=O)O)O)CCCCC(=O)O	0.73	0.96

115	12(S)-HHTrE	KUKJHGXXZWHSBG-WBGSEQOASA-N	5283141	CCCCC(C=CC=CCC=CCCC(=O)O)O	0.76	1.07
116	Decenedioic acid isomer	CXGDCGIPEJKSCK-HNQUOIGGSA-N	6365634	C(CCC(=O)O)CC=CCCC(=O)O	0.76	0.91
117	Dodecanoic acid	POULHZVOKOAJMA-UHFFFAOYSA-N	3893	CCCCCCCCCCCC(=O)O	0.79	1.06
118	Pentadecanoic acid	WQEPLUUGTLDZJY-UHFFFAOYSA-N	13849	CCCCCCCCCCCCCCC(=O)O	0.79	0.96
119	Octenedioic acid	BNTPVRGYUHJFHN-UHFFFAOYSA-N	225490	C(CCC(=O)O)CC=CC(=O)O	0.83	0.99
120	Isodeoxycholic acid	ZHCAAZIHTDCFJX-QLEQUTGBSA-N	164672	CC(CCC(=O)O)C1CCC2C1(C(CC3C2C(CC4C3(CCCC4)C)O)O)C	0.86	0.95
121	Hydroxyoctanoic acid	JKRDADVRIYVCCY-UHFFFAOYSA-N	94180	CCCCCCC(C(=O)O)O	0.88	0.99
122	13(S)-HOTrE	KLLGGGQNRTVBSU-FQSPHKRJSA-N	16061072	CCC=CCC(C=CC=CCCCCCCC(=O)O)O	0.9	0.96
123	Trihydroxyoctadecen oic acid	ZFULIMDGARVKBJ-UHFFFAOYSA-N	1.3E+08	C(CCCCCCCC(O)(O)O)CCCCCCC=CC(=O)O	0.9	1.02
124	Hydroxydecanoic acid	GHPVDCPCKSNJDR-UHFFFAOYSA-N	21488	CCCCCCCCC(C(=O)O)O	0.96	0.99
125	Deoxycholic acid	KXGVEGMKQFWNSR-LLQZFEROSA-N	222528	CC(CCC(=O)O)C1CCC2C1(C(CC3C2CCC4C3(CCC(C4)O)C)O)C	0.98	0.99

Table S4. Demographic characteristics of study subjects in the specific immunotherapy group

Items	0Y	0.5Y ^a	1Y ^b	2Y ^c	3Y	Overall p value
FVC (% pred)	92.6 ±15.5	110.5±5.9*	100.9±12.1	95.4±13.6	96.1 ±13.4	0.214
FEV ₁ (% pred)	93.5 ±14.6	101.4±9.9	100.9±13.1	92.8±13.7	96.6 ±11.7	0.250
FEV ₁ /FVC (%)	95.2 ±12.0	92.2±6.3*	100.7±6.9	98.0±8.7	95.4 ±10.6	0.952
PEF ₂₅₋₇₅ (% pred)	81.0 ±19.5	82.4±20.4	85.2±22.4	78.6±19.2	84.7 ±18.4	0.267
Total IgE, kU/L	427 (641)	593 (1519)	668 (1028)	818 (1095)	529 (1318)	0.232
Der p sIgE, kU/L	52.5 (114.3)	45.4 (75.2)	57.7 (73.6)	51.0 (176.4)	42.4 (108.7)	0.881
Der f sIgE, kU/L	70.3 (104.9)	51.6 (72.5)	72.1 (71.8)	49.4 (87.9)	58.6 (106.0)	0.370

^a: n=6, ^b: n=16, ^c: n=15; *: P<0.05 (compared to 0Y); FVC, forced vital capacity; FEV₁, forced expiratory volume in one second; PEF₂₅₋₇₅, peak expiratory flow; Der p: *Dermatophagoides pteronyssinus*; Der f: *Dermatophagoides farinae*. Normally distributed quantitative data were expressed as the mean ± standard deviation (SD). Non-normally distributed data were expressed as the median ± interquartile range (IQR).

Table S5. Raw data of the identified metabolites in serum using UHPLC-Q-TOF/MS analysis

N o.	Compound Name	Asth ma-1	Asth ma-2	Asth ma-3	Asth ma-4	Asth ma-5	Asth ma-6	Asth ma-7	Asth ma-8	Asth ma-9	Asth ma- 10	Asth ma- 11	Asth ma- 12	Asth ma- 13	Asth ma- 14	Asth ma- 15	Heal thy-1	Heal thy-2	Heal thy-3	Heal thy-4	Heal thy-5	Heal thy-6	Heal thy-7	Heal thy-8	Heal thy-9	Heal thy- 10	Heal thy- 11	Heal thy- 12	Heal thy- 13	Heal thy- 14	Heal thy- 15	
1	TXB2	2067 31	3159 04	2458 97	1785 91	1342 52	1007 96	4600 61	1567 89	1906 08	5512 4	1867 31	2159 04	1458 97	1585 91	1242 52	2503 36	4627 3	7363 1	1148 64	7144 89	1201 39	1047 79	2967 31	2922 30	4888 55	1316 14	1800 52	8022 5	4132 02	1769 02	
2	11β-PGF2a	2470 0	3024 0	4768 0	4270 0	5870 0	6220 0	5562 0	4060 0	7360 0	1516 0	2270 0	2824 0	4368 0	4070 0	5670 2	4765 5	6532 1	4632 5	5743 0	9386 2	3737 2	4364 0	3666 4	1245 0	5064 7	3245 0	4806 0	2343 5	1176 0	4564 7	
3	PGF1a	4100 0	2466 0	1308 0	1004 0	1584 0	2316 0	1160 0	1516 0	1294 0	1698 0	2410 0	1866 0	1508 0	1604 0	1784 0	4280 0	4180 0	4674 0	5280 0	1108 0	1054 0	1054 2	1457 6	1524 0	1328 0	1578 4	5940 6	2154 5	2643 1	1372	
4	PGE2	1153 60	1976 70	2475 90	1097 20	1030 70	1979 30	1674 50	9077 0	7858 0	2645 0	1053 60	1876 70	1475 90	9972 0	1130 70	8528 0	2094 40	1834 70	2188 10	3261 70	1039 20	8998 0	1750 40	1284 20	6348 00	6061 0	1431 90	3309 0	1557 20	9236	
5	11-dehydro TXB2	9100 0	3548 60	2064 0	4852 0	1669 60	2457 00	1057 40	9274 0	5060 0	936 0	2910 0	5548 0	1864 60	2852 0	1069 60	5960 0	7040 0	6450 0	1000 40	1560 67	1045 2	8473 0	8948 0	8320 0	2142 80	1043 5	1042 0	8753 0	9880 3	4946	
6	PGD2	2543 0	4558 0	6406 0	2245 0	5005 0	2242 20	5836 0	6473 0	6012 0	7438 0	6573 0	5558 0	5406 0	3245 0	4905 0	1756 30	2710 60	2788 50	2227 30	1819 30	2709 0	3150 0	6451 0	3046 0	6780 90	4739 21	3728 14	3434 0	1130 0	1758	
7	PGF2a	1141 00	1046 60	2200 00	1225 00	2412 00	3430 60	2668 40	2808 0	1292 60	4560 0	1341 00	1246 60	2000 00	1425 00	2212 00	8072 80	2050 40	1504 20	1491 40	3004 0	6688 0	6846 00	1647 00	9350 0	4689 0	2850 0	8040 0	5096 0	1143 80	4238	
8	13, 14- dehydro-15- keto PGF2a	1079 30	1088 10	2371 50	1239 70	1081 80	2303 10	2397 70	6283 0	9167 0	1308 0	1179 30	1188 10	1371 50	1439 70	1281 80	8138 0	6576 0	6984 0	6075 0	2354 90	4779 0	6226 0	9715 0	7187 0	2555 50	3096 0	1099 30	3883 0	1385 80	4378	
9	PGA2	4980 0	2125 20	3518 40	1542 00	1555 20	3353 00	5746 0	1964 00	2049 60	1748 60	6980 0	1925 20	3318 40	2142 00	2155 20	2374 0	2343 5	4546 7	1005 40	2472 20	1424 00	9146 0	6004 0	1590 80	4782 20	2554 0	1114 20	7540 0	1185 20	8502	
1	PGB2	1110 60	1318 00	2958 00	1035 60	3583 80	5623 80	3350 60	1691 80	1322 40	5004 0	1310 60	1518 00	2758 00	1235 60	3383 80	1117 40	7852 0	4930 0	2088 80	1925 20	1652 80	8084 0	1414 60	1406 60	6873 60	5816 0	1277 60	4392 0	1685 60	5710	
0		5697	5698	5699	5700	5701	5702	5703	5704	5705	5706	5707	5708	5709	5710	5711	5682	5683	5684	7685	5686	5687	5688	5689	5690	5691	5692	5693	5694	5695	5696	
1																																
1	PGI2	2384 0	1744 80	3503 10	1991 80	3960 00	1184 590	4517 80	1940 50	4481 80	4990 0	4384 0	1544 80	2503 00	1791 80	2960 00	4830 0	3946 20	4066 90	3818 50	4142 60	1284 10	1992 70	2980 0	5250 450	1146 0	1653 0	6798 0	2822 0	1032 10	7260	
2		0	80	10	80	00	590	80	50	80		0	80	10	80	00	0	20	90	50	60	10	10	70	0	450	0	0	0	10	0	
1	12(S)-HHTrE	6341 71.4	1014 091	7736 15.6	5515 43.4	2984 71	4226 11.2	1364 066	5513 54	8230 12.2	1633 83.4	4341 71.4	9740 91.4	5736 15.6	7515 43.4	4984 71	5009 62.6	1940 47.8	1977 65.6	1977 09.8	2641 607	1649 77.2	4055 96.8	2630 19.6	8038 19.6	7561 894	1467 87.8	3324 31.4	5963 45.8	2217 140	1077 86.2	4329
3		71.4	091	15.6	43.4	71	11.2	066	54	12.2	83.4	71.4	91.4	15.6	43.4	71	62.6	47.8	65.6	09.8	607	77.2	96.8	19.6	19.6	894	87.8	31.4	45.8	140	86.2	
1	LTB4	5479 0	2236 80	3725 10	9077 0	3641 00	5794 80	3942 60	5124 0	9541 0	5163 0	6479 0	3236 80	2725 10	1907 70	2641 00	3041 0	6924 60	1347 30	1486 00	5354 00	8486 00	1223 00	3894 00	9996 00	9183 50	2804 0	3847 0	3444 0	5404 0	1454	
4		0	80	10	0	00	80	60	0	0	0	0	80	10	70	00	0	0	60	30	00	0	00	00	0	50	0	0	0	0	40	
1	13(S)-HOTrE	1086 24	2015 49	7531 8	1644 00	3470 43	1867 08	2447 70	2793 9	2841 30	3606 6	7862 4	1715 49	1053 18	1344 00	3170 43	2441 4	2533 14	2639 49	1397 90	3588 51	3015 9	4746 2	9838 2	6478 72	5595 3	5601 86	1273 7	2864 39	1389 86	1078	
5		24	49	8	00	43	08	70	9	30	6	4	49	18	00	43	4	14	04	49	90	51	9	2	2	72	3	86	7	39	86	
1	12(S)-HEPE	1404 05	4461 01	2484 54	3528 19	2999 95	7690 05	9570 63	5646 2	1697 74	6988 0	2404 05	3461 01	3484 54	2528 19	1999 95	2886 6	3555 4	3452 7	4148 7	5954 03	1467 93	5459 6	3382 46	1056 73	4171 01	2567 8	2883 76	9376 3	7394 6	3456	
6		05	01	54	19	95	05	63	2	74		05	01	54	19	95	6	4	7	7	03	93	6	46	73	01	8	76	3	6	36	
1	15(S)-HEPE	9980 0	2115 00	1593 20	1306 50	3574 60	5883 90	4874 70	3942 0	2650 90	6020 0	1098 00	1915 00	1393 20	1506 50	4574 60	2503 0	3389 20	3244 70	1931 30	2752 80	1487 70	7705 0	2435 60	7364 0	7423 90	1285 0	1758 90	7483 0	5582 0	2321	
7		0	00	20	50	60	90	70	0	90		00	00	20	50	60	0	20	70	30	80	70	0	60	0	90	0	90	0	0	60	
1	15(S)-HETE	7383 34.6	1578 926	2451 378	1826 906	4501 10.3	1819 172	1003 16.9	7383 34.6	1578 926	2451 378	1826 906	4501 10.3	1819 172	1003 16.9	7367 54	2355 43.4	5810 73.8	4393 96.4	3187 01.7	9127 82.3	4767 10.2	1883 10.3	3680 88.2	1593 54.8	6872 80.5	3567 17.6	4725 78.8	1159 819	7854 32	6793	
8		34.6	926	378	906	10.3	172	16.9	34.6	926	378	906	10.3	172	16.9	54	43.4	73.8	96.4	01.7	82.3	10.2	10.3	88.2	54.8	80.5	17.6	78.8	819	32	71	
1	13(S)-HPODE	4697 7	1209 76	7041 8	1399 5	1169 15	1347 21	1084 81	2778 4	1932 31	3766 7	3697 7	8097 6	1004 18	1199 5	7691 5	3312 9	7596 6	7149 1	2499 24	2593 57	1914 04	9029 8	1311 62	1964 56	6521 32	4119 8	1582 58	3784 8	1179 18	1764	
9		7	76	8	5	15	21	81	4	31	7	7	6	18	5	5	9	6	1	24	57	04	8	62	56	32	8	58	8	18	86	
2	5(S)-HEPE	6133 8	1614 54	1049 82	7261 5	1587 69	8042 79	1665 78	5747 1	3278 25	1507 2	5833 8	1314 54	1349 82	1026 15	1287 69	3288 6	9028 32	8375 76	5925 84	3492 21	1378 20	1069 44	2709 75	8273 4	1024 650	1935 0	2048 70	4269 6	5866 2	1351	
0		8	54	82	5	69	79	78	1	25	2	8	54	82	15	69	6	32	76	84	21	20	44	75	4	650	0	70	6	2	08	
2	9(S)-HPODE	4322 9	9408 3	7145 4	1620 7	1177 19	1355 82	1116 94	2860 0	1787 55	3221 4	5322 9	6408 3	8145 4	7620 7	1077 19	2410 8	6892 7	6686 2	2823 26	2322 78	1510 94	9690 8	1369 82	1820 70	5360 19	4666 9	1462 89	3733 8			

2	12(S)-HPETE	1647	4417	3906	3784	3161	2037	1973	1647	4417	3906	3784	3161	2469	2837	1976	2942	2453	2407	3088	1877	1840	2063	3040	1736	2877	2925	2021	1934	1753	2011
3		05.5	84.9	44.5	19.8	36	50	60	05.5	84.9	44.5	19.8	36	70	60	50	88.2	57.7	34.2	16.9	13.1	30	95.1	99.3	86	05.6	79.8	70	50	40	30
2	12(S)-HETE	3804	3953	5667	5707	1194	3286	2694	3804	3953	5667	5707	1194	3286	2694	1948	6805	6603	6412	6138	1503	8456	1840	7362	1359	6450	2414	1463	1961	5913	1167
4		87.9	12.5	13.1	70.1	75.4	35.7	39.4	87.9	12.5	13.1	70.1	75.4	35.7	39.4	75.3	6.88	1.86	7.89	0.8	76.3	3.75	19.5	5.49	43.5	8.4	97.6	15.1	77.4	4.2	58.5
2	14(15)-EET	3099	1198	1518	4662	2172	1056	1360	2861	3081	6792	6099	9288	1218	1066	2472	1746	8876	9146	5584	3294	9239	1051	2230	1141	1594	1827	2193	1343	5502	4770
5		6	89	57	9	00	561	59	4	33	6	9	57	29	00	9	52	10	29	09	1	68	95	29	341	9	3	4	0	0	
2	8(S)-HETE	1318	2555	4355	2064	2088	1503	1146	1318	2555	4355	2064	2088	1503	2087	1765	1693	2330	2231	5690	4222	1285	4449	1392	2338	1177	4636	2642	3458	9430	1976
6		85	99.9	83.2	13.9	4.01	86.8	53	85	99.9	83.2	13.9	4.01	86.8	45	46	9.16	74.9	57.2	7.94	8.79	23.2	1.94	0.58	8.52	1.84	7.98	4.34	3.6	6.37	62.2
2	15(S)-HPETE	1648	6588	2267	2374	5133	3322	2084	1648	6588	2267	2374	5133	3322	1974	2859	1485	1390	1687	2136	2506	2156	2564	2129	2180	1728	1345	2014	1859	1954	1438
7		93.5	37.5	69.7	74.3	78.2	79	50	93.5	37.5	69.7	74.3	78.2	79	60	30	31.1	64.8	96.1	83	70.8	10.7	54	77.7	71.3	39.6	30	30	40	30	50
2	5(S)-HETE	9131	1147	2617	1780	2541	3174	1046	4131	1147	6172	7806	5412	1946	1643	2065	2022	9676	1431	2462	7542	1598	2248	1013	6503	5598	2863	2097	3124	3475	4657
8		63	195	271	629	294	325	327	63	195	71	29	94	753	829	793	36	73	119	250	83	88	61	47	27	12	80	87	51	83	93
2	5(S)-HPETE	1102	3439	1398	1830	2503	8554	1375	1102	3439	1398	1830	2503	8554	1053	9857	6686	8209	6013	1123	7226	9340	6468	8369	9074	1347	1482	1185	1023	1237	9843
9		42.5	70.9	64.1	89.6	10.3	2.14	30	42.5	70.9	64.1	89.6	10.3	2.14	80	0	0.16	4.13	6.53	89.6	7.28	9.89	1.65	2.75	5.51	54.7	96	96.1	20	40	0
3	Arachidonic acid	4016	5982	9099	6254	7402	9275	3850	4016	5982	9099	6254	7402	9275	3850	6828	4221	4668	4489	3928	7197	3843	5315	5638	5382	6461	3635	4132	4071	5146	4340
0		97.5	71.7	11.8	30.5	27.8	08.5	37.9	97.5	71.7	11.8	30.5	27.8	08.5	37.9	71.8	69.8	96.8	75.1	18.8	73.7	71	05.2	99.5	89.5	38.5	65.2	67	02.1	03.8	62.6
3	Heptanoic acid	1951	1733	2184	2110	1620	2384	1496	2951	1533	1184	3110	2620	1384	2496	2110	2756	3222	2006	2160	2277	1881	2340	2197	2126	1937	1937	1752	2188	1899	1603
1		70	90	90	70	90	20	10	70	90	90	70	90	20	10	70	80	00	80	50	20	00	70	10	10	10	00	30	20	20	60
3	Hexanoic acid	5284	3936	3103	4618	2842	4223	3784	5184	4936	2103	3618	1842	3223	2784	4618	1941	3507	3826	2526	4100	4101	3971	2623	3594	2403	2978	4688	3414	3205	1832
2	isomer	90	30	20	60	60	80	90	90	30	20	60	60	80	90	60	40	00	80	80	40	20	00	30	10	90	90	20	10	40	20
3	Hexanoic acid	2614	2462	2750	2689	1227	1900	1918	1614	1462	2150	2189	1127	2100	2518	2689	1941	2446	2036	1745	2394	1899	2243	3294	2304	2811	2896	2489	3269	2146	1710
3		68	21	92	06	53	63	53	68	21	92	06	53	63	53	06	06	22	93	52	55	64	05	23	59	71	24	60	33	34	94
3	Heptanoic acid isomer-1	2475	1863	2106	2166	1555	2243	2258	1475	2863	2106	1166	2555	3243	1258	2166	2325	2800	2516	2468	2772	2568	2462	2827	2254	2588	2511	2632	2783	2439	2125
4		70	20	30	20	00	50	60	70	20	30	20	00	50	60	20	20	50	20	50	90	90	00	00	20	60	80	70	60	00	70
3	Heptanoic acid isomer-2	1572	1421	1124	1472	1110	1087	1452	9720	8212	8246	1172	8104	4871	1152	1472	1512	1256	1481	1147	1592	1117	1242	1488	1465	1486	1460	1188	1140	1050	1428
5		09	25	61	49	45	11	09	9	5	1	49	5	1	09	49	09	70	94	02	85	47	24	72	56	98	40	54	06	78	12
3	Suberic acid	1476	1534	1752	1785	1197	2737	1087	1176	1234	1152	1485	9276	1237	1387	1185	2920	3022	1922	2566	3083	1976	3181	1607	2505	1134	2883	2849	1076	1284	2453
6		06	44	15	21	69	44	20	06	44	15	21	9	44	20	21	35	5	61	77	67	19	20	58	75	57	63	10	58	51	34
3	Heptanoic acid isomer-3	3003	2350	2887	2843	2001	1900	2479	2103	1750	1987	1343	1701	1300	2779	2843	3011	4984	2759	2470	3255	2272	2733	3323	2951	3432	2781	2789	3330	2736	2524
7		36	53	20	58	27	56	20	36	53	20	58	27	56	20	58	34	14	58	80	12	05	93	43	58	54	99	13	36	96	80
3	Nonanedioic acid	6510	7217	6369	8206	5891	1696	5306	5910	6917	5769	7606	6491	1130	1420	1460	2016	1568	1933	2003	9878	1390	9419	1612	7321	1652	1744	1505	9468	2495	
8		9	7	9	8	7	17	1	9	7	9	8	7	17	61	68	82	00	04	38	52	7	68	1	14	2	73	53	82	6	40
3	Octanoic acid isomer	1209	1858	1572	1604	9433	1489	1205	9877	1058	1372	9649	1003	1289	1005	1404	1779	1620	1424	1707	1891	1126	1582	1507	1470	1504	2134	1897	1726	1484	2031
9		794	644	659	903	97.2	572	920	94.2	644	659	03.2	397	572	920	903	439	949	154	518	601	295	504	424	729	865	431	575	401	071	319
4	Sebacic acid	2802	1230	1463	2229	8294	2212	6115	2202	1830	1763	1929	5894	1912	5815	2049	1845	2988	2471	2960	2820	1659	2081	1099	2378	1008	2277	2575	2041	1371	3094
0		90	60	70	72	1	53	5	90	60	70	72	1	53	5	72	69	15	58	64	21	51	70	59	43	48	09	02	98	72	29
4	Sebacic acid isomer	9886	1128	1083	1297	1970	2537	1978	1688	1828	1053	1177	1210	2237	9483	9972	1779	3075	2515	3015	2804	1213	1940	1113	1991	8405	2350	2520	1949	1510	3432
1		8	12	60	20	95	37	36	68	12	60	20	95	37	6	0	84	66	32	21	76	38	76	18	22	1	92	57	49	14	75
4	Octanoic acid	1785	9085	5883	7580	5913	4490	5189	1385	1108	7883	9580	7913	6490	3189	5580	2972	4992	1210	4248	4164	6499	5063	7027	5312	9783	2124	5860	1469	3737	4045
2		775	62.4	97.4	62	49.4	02.6	00.4	775	562	97.4	62	49.4	02.6	00.4	62	62	66	451	54.6	68	83.2	02.6	60.4	70.6	98.6	952	55.8	743	97.6	98.8
4	Undecanedioic acid	1930	3272	3046	2212	1391	2160	1050	1632	2972	1346	1912	1091	1560	2372	1911	3275	3338	4804	2852	1275	2550	2989	1632	3333	1240	4311	2596	2715	2875	5263
3		33	00	37	98	07	57	06	67	00	37	98	07	57	23	69	13	91	20	55	45	39	20	12	21	23	15	77	75	68	38
4	Pelargonic acid isomer	1296	1830	1809	1933	1189	2142	1802	1096	1530	1609	1533	9895	1942	2102	1633	2019	2207	2128	2542	2797	1546	1975	1451	2272	1442	1401	1821	3269	1632	2423
4		13	84	95	24	54	85	22	13	84	95	24	4	85	22	24	15	12	36	45	26	99	34	64	25	81	79	01	73	19	95
4	Undecanedioic acid isomer-1	1954	3174	3130	3257	2900	8642	1948	1654	2174	2130	2257	1900	6642	2948	2257	3977	4544	7014	8289	7146	3194	4196	1987	4953	1738	4355	5534	4776	3873	1160
5		57	43	31	44	34	34	98	57	43	31	44	34	34	98	53	11	66	67	86	22	94	96	24	80	92	83	86	91	48	417
4	Undecanedioic acid isomer-2	1859	2318	1982	1919	1583	2371	1524	2159	2618	1682	2219	1883	1771	2124	1319</															

4	Decanoic acid	2656	4305	5736	4230	2342	1033	2378	2056	3905	6136	3830	1942	8735	1978	3630	3100	2932	3645	6349	7013	2299	3729	1820	3611	1568	4338	4077	3269	2687	7395
8	isomer	67.8	36.2	40.8	27.4	28.2	525	51	67.8	36.2	40.8	27.4	28.2	24.6	51	27.4	07.8	32.2	66.2	71.4	12.4	51.6	17	51.2	91	04	29.2	27.8	12	35.4	34
4	Undecanedicarboxylic acid	1740	1025	1006	1857	1148	1607	9766	1040	8251	9061	1057	9481	5073	1076	9578	1111	1139	1103	1486	1310	7411	1268	1346	1317	1397	1767	1654	1252	1687	1760
9	Decanoic acid	26	12	13	68	11	30	5	26	2	0	68	1	0	65	5	34	52	69	39	58	2	55	50	13	19	77	92	84	18	26
5	Decanoic acid	1398	2207	8327	1314	5555	1227	1065	1198	1807	1032	9149	7555	1027	8657	1114	2993	4771	1446	8375	6874	1026	7821	5961	1007	1015	1937	1322	5680	7164	5002
0		015	434	98	946	69	606	724	015	434	798	45.8	69	606	23.8	946	09	65.8	909	80.6	09.2	559	38.4	15	014	087	787	923	22.2	97.6	45.4
5	Undecanedicarboxylic acid	2286	1622	1313	1503	1285	3156	1085	1986	1322	2013	1203	1585	2856	1385	1203	2039	3039	2737	3166	3600	1642	3148	1237	2729	1386	1768	2123	1960	1655	4171
1	isomer	01	85	79	24	23	81	55	01	85	79	24	23	81	55	24	76	81	83	41	48	23	56	14	37	36	41	70	44	19	11
5	Undecanoic acid	2474	4361	3331	4535	3090	3868	3786	1474	2361	2331	3535	2890	2868	2786	3535	2993	4215	4709	4010	3478	3389	3565	3405	3606	3613	3530	4135	7955	3168	3602
2		79	23	55	15	75	17	65	79	23	55	15	75	17	46	17	67	71	71	74	94	86	67	05	99	48	20	11	53	88	57
5	Dodecanoic acid	3412	5444	1940	2655	1714	3742	1898	2587	3158	2974	2648	1975	1834	5975	4685	1060	3077	3754	1367	5272	4184	2414	2123	4241	1395	1014	2749	1898	9504	3286
3	Myristic acid	74.8	59.6	27.6	10.9	44.6	24	29.9	51.5	75.4	65.8	76.2	48.2	25.9	46.2	23.5	91.5	29.1	6.28	65.3	54.5	32.2	33.3	89.6	35.9	35.3	86.1	28.8	07	57.1	28.7
5	Pentadecanoic acid	8254	4868	3395	9033	6205	7812	2896	1152	5260	8254	3868	2395	5033	4205	5812	2476	4810	3217	1387	1354	6462	6282	1070	6041	3291	7357	5204	8868	1070	1209
4		44.1	26.3	50.6	79.8	19.2	24.6	20.5	561	76.7	44.1	26.3	50.6	79.8	19.2	24.6	35.3	07	39.1	518	153	39.9	55	520	77.2	71.2	04.3	04.7	67.6	173	810
5	Palmitic acid	3936	5989	1246	3585	3281	3940	2505	5397	3017	3936	3989	2046	2385	2081	2140	1908	1689	2518	5273	3415	3152	3276	3968	3103	2210	3954	3100	2560	4999	6187
5		84.6	80.8	58.5	66.2	50.6	86.8	84.4	97.5	38.1	84.6	80.8	58.5	66.2	50.6	86.8	84.3	50	69.5	09.6	91.1	43.4	56.8	42.5	70.1	36.8	86	66.9	79.8	97.7	01.4
5		4909	1346	2033	4493	2837	3452	2094	7218	1439	4909	9469	1033	2493	1837	2452	4552	2953	7050	1367	7782	7875	9932	3412	7526	2741	6892	3004	5380	7248	5681
6		94	944	32	91	64	57	85	87	12	94	44	32	91	64	57	26	61	25	406	28	27	15	00	62	49	63	80	77	77	33
5	Methyl palmitic acid	2192	2394	2938	2462	2378	2505	1799	2440	1929	2192	1394	1938	1462	1378	1505	1951	1418	2236	2525	2258	2192	2238	2401	2361	2033	2523	2001	2063	2563	2685
7	Stearic acid	64.1	55.7	37.6	37.7	15.9	93.2	74.5	29.4	62	64.1	55.7	37.6	37.7	15.9	93.2	29.1	34.7	00.3	45.5	74.3	95.7	03.6	25.3	05.4	90	19.3	30.5	26.3	60	38.3
5		9137	8943	4386	1239	1042	1243	7393	1036	8063	9137	1044	5386	1039	5422	7432	7642	6573	8431	1131	1041	1079	9848	1049	1070	8590	1168	7586	1020	1043	1040
8		21.8	91.4	72	920	251	245	11.4	817	21.9	21.8	391	72	920	51	45.4	25	38.9	95.1	000	957	307	60	606	978	90.3	036	33	319	701	978
5	Nonadecanoic acid	3667	1143	1136	1172	9683	1097	9886	7667	5439	5364	7723	7683	8970	5886	9723	1040	1207	1098	1096	1101	1120	1181	1066	1304	9728	1072	1160	1200	1116	1375
9		40.2	940	461	365	18.4	054	45.4	40.2	40	61	65	18.4	54	45.4	65	644	452	627	356	793	240	945	904	799	54.2	595	361	923	911	800
6	Behenic acid	2881	2497	2610	2600	2429	2702	2357	1881	1497	1610	1600	1429	1702	1357	1600	2571	2750	2713	2506	2150	2322	2671	2908	2617	2347	2667	2538	2386	2459	2798
0		42	98.9	25.5	00.7	33.5	60.9	46.5	42	98.9	25.5	00.7	33.5	60.9	46.5	00.7	97.8	90	37.3	18	10	10.8	17.4	77.6	80.7	15.9	20.8	94.6	86.1	16.7	62
6	Lignoceric acid	3063	3253	4005	6218	3056	3966	2433	2463	2853	3605	4218	5056	4366	4433	4218	2117	2443	6296	3736	1699	2518	3301	9336	6821	1856	7366	3552	3800	3376	1231
1		13.6	66.2	59.8	91.6	26.2	28.4	98.6	13.6	66.2	59.8	91.6	26.2	28.4	98.6	91.6	00.2	81.4	80.2	18.4	64	23.6	84.8	92.2	45.4	22	17.2	91	37	95.6	144
6	Hydroxyoctanoic acid	1254	1763	1656	1222	1454	1425	1375	1454	1363	1456	1422	1254	1625	1575	1422	1595	1375	1006	1555	1211	1372	1516	1983	1584	1176	1644	1567	1572	1195	1537
2		60	00	60	40	40	40	60	00	60	40	40	40	40	40	60	80	80	00	20	00	60	40	40	40	40	20	40	60	20	80
6	Hydroxyoctanoic acid isomer-1	7728	8150	2789	6961	1541	2349	2554	6728	7150	3789	5961	2541	1349	1554	5961	1052	3106	3236	2068	1208	3718	3291	6699	3156	3621	1189	4595	1871	8376	2165
3		60	20	70	90	70	10	70	60	20	70	90	70	10	70	90	90	0	00	70	50	40	00	10	10	80	340	20	40	0	80
6	Hydroxyoctanoic acid isomer-2	3735	1542	1726	1782	2428	1641	2119	3135	3542	1526	1982	2028	1841	2319	1982	1564	1254	8898	2152	1453	1059	1724	1548	2427	1429	1762	1522	1596	1500	1988
4		00	00	20	80	40	60	60	00	00	20	80	40	60	60	80	40	20	0	20	60	60	20	80	80	00	40	40	60	60	20
6	Hydroxydecanoic acid	6811	5010	2825	6097	1388	1564	1279	5811	4310	1825	5096	2388	2564	2254	4097	2372	1067	3291	3595	1370	1529	1660	2394	3062	2777	9498	5187	3046	1480	2015
5		20	80	50	00	50	70	00	20	80	50	40	50	50	30	00	70	650	90	30	40	80	90	60	40	20	40	50	10	80	60
6	Hydroxydecanoic acid isomer-1	1306	3516	1008	1785	2899	5988	7432	1406	2516	1108	1685	3899	6988	8432	1585	4569	7695	2159	2151	8284	1771	9788	1652	2003	1708	3272	2650	1156	5633	8585
6		07	08	10	67	1	5	5	07	08	10	67	1	5	5	67	6	1	32	29	0	35	7	86	55	75	11	12	19	4	3
6	Hydroxydecanoic acid isomer-2	1065	1074	9013	9323	6308	2120	1064	2732	1382	9843	1074	7308	1120	1293	1032	1393	1343	1987	2720	2624	9819	1352	8950	1602	1534	2129	1891	1263	1674	1775
7		50	31	0	0	0	30	70	10	10	0	30	0	30	10	30	00	80	30	90	20	0	60	0	50	32	60	30	80	32	60
6	Hydroxytetradecanoic acid	5012	3631	1020	1674	2842	1143	1001	1501	2631	1220	1374	8842	9435	8010	1374	5333	6614	2169	2963	1491	2360	1061	9637	1869	7254	2753	3171	1509	8813	5794
8		6	72	14	09	8	52	03	26	72	14	09	8	2	3	09	9	7	70	94	16	88	53	5	85	7	28	28	14	0	9
6	Hydroxytetradecanoic acid isomer-1	7506	2579	1146	3118	4971	1711	8232	4506	1979	8460	2518	7971	1111	5232	2218	6503	9988	3333	1516	1466	2938	1224	7035	2082	8083	2219	3426	3068	9027	1182
9		0	97	09	44	9	44	9	0	97	9	44	9	44	9	44	7	2	54	17	76	56	12	0	93	8	67	72	79	3	78

7	Hydroxytetrad	5389	4016	1737	1394		3161	1152	1538	3016	2737	1994	1239	2161	2152	2394	6561	1197	1459	1967	2707	2074	2249	6240	2408	1251	2685	3478	1659	3481	7128
0	ecanoic acid isomer-2	0	10	30	50		90	70	90	10	30	50	00	90	70	50	0	20	30	90	60	60	70	0	20	90	20	50	90	90	0
7	Hydroxytetrad	1371	3678	2439	3368	6234	3316	1216	4371	3078	3039	3068	3623	2416	4216	2468	7312	1984	3252	1647	1498	1291	1861	8786	2027	7720	1401	1030	3964	1883	1107
1	ecanoic acid isomer-3	12	60	27	37	0	95	59	12	60	27	37	40	95	59	37	8	83	57	99	14	86	50	1	61	5	42	65	50	55	24
7	Tolylacetic	4855	7732	4952	3016	8004	1124	6916	7855	1073	3152	4216	2600	1424	9916	2716	5711	9682	7949	4105	1012	3525	9235	7859	6998	1065	5608	1192	6986	1055	2501
2	acid	8	8	70	05	9	61	8	8	28	70	05	49	61	8	05	7	2	1	89	17	15	8	1	4	72	8	23	4	13	52
7	Octenedioic	2225	2195	1924	1793	2183	1382	2206	2225	2195	1924	1793	2183	1382	2206	1793	2534	1765	2180	1868	2121	1701	1925	2177	1976	1718	2370	1993	1943	1658	1997
3	acid	00	50	70	50	20	50	10	00	50	70	50	20	50	10	50	70	90	90	40	00	00	40	70	60	10	10	50	80	30	00
7	Tolylacetic	2139	4944	6015	3391	2718	2149	8758	1939	3944	5015	2391	3718	1949	9758	2391	2890	2057	1806	1212	3288	1300	1588	8774	1666	1658	1794	2295	8002	9325	2900
4	acid isomer	20	40	50	00	80	50	0	20	40	50	00	80	50	0	00	80	31	20	80	90	30	60	0	80	33	00	80	0	0	50
7	Decenedioic	1589	1834	6129	1883	6615	1776	4425	4678	5342	4290	7839	5650	5764	6425	9839	1752	1896	2160	2664	2565	1151	1543	1082	1395	1000	1978	2141	1767	1408	2818
5	acid isomer	96	29	00	97	07	41	4	3	9	0	7	7	1	4	7	75	66	78	87	32	47	98	05	32	49	93	50	30	62	94
7	Decenedioic	1679	2283	1979	2524	5855	5721	4365	3479	4883	2179	2124	2255	3921	2165	1924	4330	5013	5583	6370	6455	3055	4570	2674	4811	2431	5246	5617	4794	3560	7666
6	acid	29.8	46.2	00.2	01	01	40	62.2	29.8	46.2	00.2	01	01	40	62.2	01	63.6	22.8	89.4	49.4	87.2	96	65	06.6	52.4	47.2	53.8	76	75.6	85.6	57.4
7	Oxodecanoic	6835	3617	3483	8719	1129	1672	1954	7835	5617	4483	7719	9299	1472	2054	6719	2803	6773	3229	2550	1937	1024	2521	2934	2869	8188	7345	3495	2533	2404	2498
7	acid	20	00	60	50	90	20	40	20	00	60	50	0	20	40	50	60	90	90	10	70	50	80	20	0	70	50	70	60	10	
7	Undecenoic	3407	3139	3482	2634	2489	2783	3723	2297	3653	3407	3539	2882	3034	2889	2383	1742	4118	1960	4536	1758	6098	3725	5720	3198	7333	3546	8219	2899	9307	1889
8	acid	87.4	55	27.8	64.4	94	22.8	30	72.6	04.6	87.4	55	27.8	64.4	94	22.8	44.4	5.4	14.8	10.6	34.2	60.2	28.2	49	69.6	66.8	32	72.2	94.8	77.8	10.8
7	Dodecenoic	3399	1150	1820	5258	2017	1767	7565	3986	3656	3399	9503	1620	3258	1017	1567	2184	5674	8254	9593	3256	5720	3631	7201	2747	2135	3209	1638	6446	6226	1396
9	acid	70	39	45	88	82	77	2	89	42	70	9	45	88	82	77	42	3	3	26	24	29	90	08	03	77	95	10	64	73	97
8	Dodecenoic	8506	6502	5615	5604	1229	1421	3029	6236	2031	8506	4502	3615	1604	8291	6217	5492	1073	9272	1662	3796	4422	3528	1004	2378	1339	4422	3175	8112	8994	5107
0	acid isomer-1	40.8	0.4	4.4	22	18.2	79	5.2	90	96.4	40.8	0.4	4.4	22	8.2	9	3.2	22.4	5	854	31.6	85.6	24.8	377	93.6	70	23	23.6	26.4	61.4	73
8	Dodecenoic	2807	2826	6145	7110	1514	3123	1016	2920	1577	7512	6971	2015	2125	1215	8741	2765	5366	4635	8314	1905	2211	1764	5020	1189	6697	2211	1587	4055	4497	2555
1	acid isomer-2	03	158	39	12	76	622	091	13	621	41	12	47	485	488	23	47	12	29	271	026	428	062	585	468	82	115	448	725	326	283
8	Dodecenoic	4986	3045	4038	7879	2963	2007	2177	5421	1203	5126	7822	5478	1974	2245	9214	9191	1081	2174	7549	1605	2794	1939	3780	9595	1296	9600	1505	1920	4799	2854
2	acid isomer-3	6	27	2	1	8	47	26	3	54	4	1	2	21	97	52	4	1	9	17	58	80	09	04	7	88	9	88	97	13	20
8	Dodecenoic	1330	1234	2698	4184	6973	3769	3870	2314	5214	3102	5012	7851	4012	3944	2694	1208	3786	7761	1468	4542	7293	4162	8208	3213	2868	5584	1666	1102	1469	1884
3	acid isomer-4	97	553	99	29	0	69	30	62	36	44	47	2	54	12	81	79	0	2	616	59	93	21	20	26	64	56	00	359	969	01
8	Oxotetradecan	8638	2435	1399	2697	4362	1545	1807	1063	1435	8997	1697	1436	1345	1507	1697	1063	8861	2991	5001	2074	4865	1923	2272	3484	2072	5585	6090	1179	1054	9441
4	oic acid	3	60	79	76	3	34	83	83	60	9	76	23	34	83	76	14	5	37	73	63	59	10	17	32	59	68	38	54	18	2
8	Oxotetradecan	9678	4432	1162	3858	6635	2028	2211	1967	3432	9620	1858	1663	1728	1211	2858	1655	1306	1261	3392	1650	1791	9183	8706	1591	2747	2462	3969	2423	1055	8960
5	oic acid isomer	8	27	01	00	2	34	86	88	27	1	00	52	34	86	00	54	24	21	48	37	69	6	3	07	45	66	07	57	60	0
8	Dodecenoic	9864	1111	1700	2699	4416	4413	3158	1026	8541	2014	3125	5231	3547	2015	2158	7970	2769	4535	1739	4005	7987	3826	1173	2916	2837	4709	1496	7630	1574	2582
6	acid isomer-5	4	385	90	77	5	69	79	84	23	56	46	4	82	54	97	2	1	3	480	72	32	28	587	37	81	60	35	34	456	06
8	Tetradecenoic	6517	3059	1315	1485	4657	5267	7396	8234	3296	6517	2059	1715	8856	2657	3267	1028	1373	1319	1770	8051	1050	6970	1434	5353	3257	6656	2692	1097	1389	3391
7	acid	00.4	47.4	83.6	662	42.8	98.4	5.6	98.8	27	00.4	47.4	83.6	62	42.8	98.4	31.2	44.4	89.4	914	95.6	586	04.8	155	66	49.6	95.8	11.4	212	133	78.8
8	Tetradecenoic	2498	4455	1293	2351	1904	2734	1892	3540	2355	2498	1855	2093	1951	2104	2334	1651	1331	2058	3731	3108	2112	2370	2391	2027	1680	2584	2135	1980	3285	5757
8	acid isomer-1	00.4	55.2	59.4	76	61.4	07.6	56.4	33.6	63.2	00.4	55.2	59.4	76	61.4	07.6	21.2	57.4	44.8	52	60.6	74.6	67	76.6	39.8	34.6	36	84.2	07.6	16.2	13.4
8	Tetradecenoic	4197	4089	1791	1187	2733	1029	1619	4099	1289	4197	2089	2191	7872	1933	6292	2722	8237	6351	7904	1656	2006	2198	4552	1398	5902	1721	2476	3068	4143	4344
9	acid isomer-2	529	58.8	13.4	277	87.4	211	18	822	126	529	58.8	13.4	77	87.4	10.6	14.2	64.6	39	029	027	437	605	617	767	13.2	244	505	424	959	557
9	Hexadecadien	3781	3645	2477	3748	2756	3379	4990	3986	9353	3781	3728	2177	3048	1756	2379	6712	6002	7734	6264	9706	2874	5598	5878	2611	7237	1625	1104	1891	1291	1830
0	oic acid	37	21	89	38	42	91	8	04	7	37	21	89	38	42	91	5	1	7	76	39	68	14	03	24	9	945	38	98	118	30
9	Linolenic acid	3628	4941	1965	5310	6992	4991	3829	1046	6284	2137	2628	3941	2965	3310	4992	1687	2072	9375	1993	8805	8390	3431	4891	6113	5781	2186	6530	2563	5012	5932
1	acid	10.9	28	17.2	57.2	90	64	94.8	74.5	40.8	05.1	10.9	28	17.2	57.2	90	33.5	20.2	6.43	98.6	31	26.9	22.5	35.8	57.6	11.2	04.4	98.6	02.2	12.5	62.6
9	Palmitelaidic	1407	3150	2780	1087	6464	5479	2796	1762	5229	1407	3150	1780	9878	7464	5179	2064	3778	3662	3017	7916	1138	1035	2146	9196	4725	1034	7729	1077	1850	6141
2	acid	272	36.1	04	894	13.3	15	69.3	164	85.4	272	36.1	04	94	13.3	15	34.1	27.5	36.2	16.5	09.9	248	544	840	01.4	72	123	96.8	637	965	17.1
9	Eicosapentaen	4229	5481	4482	6009	4948	1556	1320	7410	6049	2799	3829	3481	2482																	

3	Hexadecenoic acid	6933	3303	3025	2123	6726	4168	1136	1254	2458	3546	3468	2145	1254	1025	2054	3256	1555	2837	1656	4338	2407	2763	2125	4109	2689	1271	2436	1092	1877	1030
4		3.25	57.3	03.2	42.4	2.71	37.1	28.4	84.3	76.2	84.5	21.2	89.6	88.9	48.8	61	22.4	53.7	08.5	34	15.6	02.3	93.1	64.4	28.2	84.5	99.4	27.1	89.3	22.2	49.3
9	Hexadecenoic acid isomer	4557	1655	1126	1102	1448	2489	9940	9821	1027	8657	1125	1024	8423	1025	1024	2151	2069	2482	1611	2976	1021	1278	1290	1790	1257	6734	1942	1001	1051	6240
5		1.5	13.5	43.3	33	88.4	52.3	8.17	.35	9.44	.42	4.86	8.75	.44	4.83	56	51.3	41.8	78.1	43.2	80.8	25	19.5	57.8	92.6	14.8	4.72	01	73.1	88.4	11.1
9	Octadecadienoic acid	1854	1120	1127	2487	1930	1979	7068	2477	9764	1854	6207	6271	1487	1430	9790	7192	6434	9436	2777	2341	1736	1661	2478	1881	1193	2089	8373	1924	2107	1080
6		851	796	171	771	441	097	30.3	994	15.6	851	95.5	70.5	771	441	96.9	52.5	10.3	32.6	693	197	692	694	278	206	775	461	48.9	296	070	965
9	Docosahexaenoic acid	2786	1673	2196	2943	4534	3547	1892	3516	1556	2786	9738	1196	1943	2534	1547	1274	1887	2032	3521	4592	4031	3365	2879	2457	2118	5843	2370	2856	5295	2212
7		34.3	87	03.4	91.7	53.9	37.1	87.1	16.7	36.4	34.3	7	03.4	91.7	53.9	37.1	29	99.3	08.9	64.9	63.3	42.2	00.6	84.9	45	47.8	99.3	73.6	40.1	86.6	89.8
9	Eicosatrienoic acid	1495	1849	1286	1155	2890	2473	1631	1133	3466	1168	1925	1834	2758	1867	2046	7725	1445	1401	8231	2188	1643	2158	1758	2368	2174	1081	1406	9224	1606	1244
8		425	169	414	188	363	812	508	359	204	406	488	652	473	593	875	72.3	675	449	59.6	22.6	641	222	176	744	352	579	139	74.4	184	610
9	Eicosatrienoic acid isomer-1	2102	3310	2464	1271	2961	4081	2192	1622	3509	1957	3105	1867	1532	1352	1682	1051	1350	1278	1399	2298	1611	3026	2964	2232	2807	1941	2024	1477	2091	1633
9		40.1	72.8	92.7	78	14.4	47.7	83.3	53.6	27.5	44.4	46.7	59.4	87.4	47.8	57.3	75.2	36.1	50.1	87.7	68.8	53.3	62.9	34.9	63	12.4	49.5	54.8	46.8	85.1	92.8
1	Oleic acid	1958	1086	7328	2731	1880	2530	7594	2429	1082	1958	9866	4828	1731	1280	2380	7323	9900	1007	3041	2527	2228	1775	3170	2017	1289	2556	1064	2432	2624	1544
0		354	640	72.1	262	463	092	03	593	925	354	40.1	72.1	262	463	092	64.1	79.8	996	803	281	024	606	599	230	637	122	225	565	669	866
0																															
1	Eicosatrienoic acid isomer-2	1173	1734	1146	1018	2039	2131	1099	1210	2477	1201	1857	1532	1958	1876	1768	6373	1849	1806	7098	2009	7479	2288	1289	1574	1342	9294	1641	8736	1301	1404
0		193	843	605	941	573	063	720	630	982	810	625	843	754	423	524	38	365	239	77	954	45	007	113	285	173	33	085	53	699	643
1																															
1	Docosatetraenoic acid	1263	7955	6905	1635	1330	1074	6738	1851	9430	1263	3955	4905	1235	1530	8749	4801	1028	6155	1840	1077	1787	1235	1579	1561	8318	1169	5753	1426	1233	8577
0		997	41.4	29	047	962	982	81	579	15.2	997	41.4	29	047	962	82	87.6	786	56.2	512	644	187	017	201	689	91.2	280	01	564	197	14
2																															
1	Eicosadienoic acid	8877	1629	9317	5308	2760	1535	1319	3845	2194	7996	5254	7851	8524	7632	1012	5479	5687	4638	6795	2057	1742	2146	1873	2596	2164	1113	2376	6231	1961	1996
0		10.4	814	31.5	42.6	139	597	199	60.4	572	78.6	87.9	26.4	61.5	58.1	587	11.4	18	75.2	96.1	583	038	067	386	072	673	142	390	19.5	007	805
3																															
1	Docosatrienoic acid	1942	6713	4396	3740	1692	6140	2980	3942	5713	3396	3440	2692	4140	3980	2740	2072	3056	5798	6389	5150	7757	7113	3882	5191	2670	6672	5054	4136	4998	2903
0		18	81	36	91	01	06	38	18	81	36	91	01	06	38	91	75	98	38	36	67	68	87	67	89	37	22	01	34	61	35
4																															
1	Docosatrienoic acid isomer	1010	4498	2465	2149	1130	3901	1645	1310	3498	1465	1849	1530	2901	2645	1849	8173	1324	2319	4418	2114	3266	2998	1659	2891	1229	3138	3484	2668	2299	1684
0		66	18	21	14	45	90	19	66	18	21	14	45	90	19	14	8	09	41	59	32	61	69	55	43	35	93	93	82	77	92
5																															
1	Eicosenoic acid	1285	1630	1092	4061	2593	1631	1703	4640	2080	6780	1524	9754	1458	8547	5568	5062	6887	5248	6319	2382	2284	2490	1682	2946	2136	1162	2957	6927	2339	2725
6		869	319	602	08.3	945	250	204	53.1	644	09.1	687	23.1	764	62.1	49.5	27.3	35.8	75.2	74.8	883	396	325	244	009	359	426	906	00.1	330	043
1	Docosenoic acid	6113	5517	6509	7669	7429	5777	5942	5607	5037	6765	4976	5287	4852	5123	6782	6940	5903	5570	8340	5320	5877	5429	5884	5271	5265	6903	7056	5055	6559	6136
0		97	40	86	29	31	50	71	35	59	26	53	46	46	54	43	07	46	28	31	10	82	17	11	59	99	03	90	29	38	79
7																															
1	Docosadienoic acid	1496	8800	4970	6921	2057	6546	4277	2496	6800	3970	4921	1957	4546	3277	5921	2207	2913	8228	8457	5887	1052	9187	4132	8121	2820	9565	8104	4730	6088	7647
0		92	70	25	58	76	55	75	92	70	25	58	76	55	75	58	28	57	85	41	68	091	13	36	97	23	66	85	90	10	63
8																															
1	Docosenoic acid isomer-1	1413	1223	1805	4433	1602	1385	1856	1109	1433	9556	9456	1078	8246	1482	7564	5974	8180	7078	8157	1464	2516	1781	9310	1652	3270	1206	3066	7989	2038	2268
0		940	335	651	13	214	491	012	547	119	15	28	245	74	452	23	59	64	27	78	518	300	033	95	704	309	922	479	37	402	032
9																															
1	Nervonic acid isomer	1543	1528	1300	1403	1370	1171	1516	2543	2528	2300	1603	1770	9718	1316	1203	1568	1808	1247	1282	1104	1070	1165	1533	1526	1304	1375	1482	1429	1231	1322
1		30	93	82	89	58	87	79	30	93	82	89	58	7	79	89	20	71	44	91	85	37	73	73	92	69	76	45	31	89	96
0																															
1	Docosenoic acid isomer-2	3700	3778	3585	3897	3052	3451	4564	4801	3676	3126	2485	3542	2946	3125	3945	3668	4433	4026	5042	4266	3627	3726	2964	4370	3914	4030	3535	4342	3612	4182
1		82	65	33	01	49	40	87	20	28	40	76	87	76	87	67	55	94	14	72	85	23	71	52	38	74	26	88	13	38	89
1																															
1	Docosenoic acid isomer-3	1354	1377	1451	5159	1329	1450	1492	1356	1560	1288	1248	1135	1358	1564	1024	1419	1139	1099	1694	1401	1362	1397	1099	1234	1566	1481	1429	1318	1470	1456
1		33	28	83	8	44	93	64	03	07	06	75	47	74	72	85	50	84	32	00	21	06	04	61	37	93	31	32	67	82	98
2																															

1	Nervonic acid	6357	3106	1875	4902	1782	2833	2612	2635	2306	2275	2902	3782	3833	4212	3902	1418	2161	6074	4045	2088	3919	5908	3731	4189	2363	5673	3569	3987	2754	3136
1		0.8	48.6	43.6	31.2	31	00	75.4	70.8	48.6	43.6	31.2	31	00	75.4	31.2	89.8	58.6	29.6	95.4	18.6	58.2	62.2	53.6	24.8	11.6	13.8	91.2	42	69.8	26.4
3																															
1	Docosenoic acid isomer-4	4718	5260	5481	4048	4845	4659	6311	4827	6133	5593	5046	4920	4526	4016	3965	4033	6141	8083	6449	5319	4585	4663	4290	4284	6906	4614	6629	5144	6325	5499
1		4	8	6	7	1	4	6	3	0	0	7	1	8	5	7	8	3	3	5	2	4	1	5	5	5	2	5	3	0	8
4																															
1	Hydroxynone noic acid	1508	1953	1751	1602	6166	1003	3933	1208	1653	1451	1482	1456	7037	6933	1302	3158	3559	3897	1392	1160	8066	2812	5681	2118	2028	1478	5600	3057	1746	1233
1		25	84	97	63	8	74	3	25	84	97	63	68	4	3	63	37	20	63	48	04	4	89	28	60	66	16	4	96	69	24
5																															
1	Hydroxytetradecanedioic acid	1264	1133	1139	1295	1316	1284	1140	2868	2727	1747	1818	2771	1501	2820	1738	2196	2152	1630	2355	2165	1728	2026	2116	1738	1545	1464	1712	1598	1507	1608
1		64	68	04	12	64	48	40	00	60	92	56	12	36	00	56	64	48	40	84	84	88	08	40	96	04	00	40	48	04	72
6																															
1	Hydroxytetradecanedioic acid isomer	1147	1753	1792	1907	1323	1702	1073	1286	8657	1564	1385	9822	1269	7901	1225	2206	9572	1323	2072	4342	2402	3894	4122	1322	1491	1082	2195	2481	2519	2005
1		20	84	48	12	52	00	84	96	6	32	60	4	12	6	60	24	8	60	32	64	72	48	72	08	68	40	76	52	60	52
7																															
1	Hydroxypentadecanedioic acid	2630	1380	1769	1210	1306	2018	1406	2350	1560	2945	2860	2400	1991	1404	1960	3315	2716	2447	2509	3738	2017	2955	2929	1605	3020	2020	2634	2016	4566	3660
1		01	14	07	57	02	66	15	72	23	07	92	50	03	49	92	40	10	20	30	50	90	50	80	70	60	30	09	01	06	95
8																															
1	Hydroxyoctadecanedioic acid	4500	1037	9476	6592	1959	1745	2173	1508	1345	1790	5469	1024	9751	8721	6587	2550	1143	1121	1368	1472	7793	3211	5659	4162	2979	4417	5593	9935	5590	4520
1		20	566	60	07	142	171	499	49	172	39	71	782	23	34	25	87	589	070	159	275	46	32	55	85	133	04	18	1	61	70
9																															
1	Hydroxyoctadecanedioic acid isomer	1095	2718	3509	3627	9301	8203	2158	1164	6858	2461	1027	8421	1125	9426	1027	3024	9475	9462	1433	1352	9261	2932	3677	6019	3011	3869	3705	1341	7393	2750
2		149	104	40	91	99	27	341	52	70	10	854	67	873	57	951	00	24	82	502	470	86	42	74	48	052	20	50	57	31	31
0																															
1	Trihydroxyoctadecenoic acid	1614	2175	3274	2618	1376	2641	1146	2014	1775	2874	2218	2776	2041	3146	2218	9539	1500	3174	2770	2446	2069	1783	1545	4384	1761	2106	3963	1614	2070	1221
2		11	42	57.8	72.4	54	33.8	42.4	11	42	57.8	72.4	54	33.8	42.4	72.4	4	91.6	94.2	64.4	23.8	24	43.2	13.4	73.2	80.4	07	45.6	22.2	71.6	65
1																															
1	Ursodeoxycholic acid	4389	2059	3755	1966	8120	8071	1378	1663	9595	4389	1859	2155	1566	1012	6071	2854	3100	1007	1979	1725	2106	2957	2151	1938	2520	3794	8747	1743	2096	1163
2		28.6	88.2	54.6	59.2	6.6	91.2	13	79.8	62.4	28.6	88.2	54.6	59.2	06.6	91.2	23.2		6.8	2.4	4.4	40	19.4	17.4	56.8	76.6	79	6.6	2	2	455
2																															
1	Chenodeoxycholic acid	4456	3809	4090	8389	1509	2195	3055	4234	1883	4456	2809	3090	6389	2509	1195	1345	3822	2860	8716	5666	4876	9328	2416	8058	1214	5313	3760	4472	1422	1879
2		98	12	28	44	87	386	59	46	972	98	12	28	44	87	386	876	0	6	6	15	50	98	19	68	125	49	55	03	0	767
3																															
1	Deoxycholic acid	2372	1385	6025	2696	3633	4378	5262	3174	1355	2372	2385	4025	3696	2633	3378	2927	2350	2034	5409	8690	1606	6360	1632	3776	6792	2056	1575	1564	4035	1369
2		61	83	50	78	67	78	24	95	902	61	83	50	78	67	78	46	5	1	0	8	77	50	516	05	75	14	94	32	4	642
4																															
1	Isoodeoxycholic acid	1270	2070	7051	8000	3227	1672	4385	3320	1190	1270	1070	5051	7000	4227	1472	1181	2527	1429	1387	8546	2185	1352	7752	6084	7219	1034	6875	1444	7958	1021
2		41	17	85	61	08	614	73	93	074	41	17	85	61	08	614	467	22	14	50	47	00	311	94	46	81	50	76	212	1	798
5																															

Reference

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