

Application of lipidomics to reveal differences of facial skin surface lipids between atopic dermatitis and healthy infants

Hecong Wang MD¹  | Le Cui MD¹ | Yan Jia PhD¹  | Ying Gao PhD² |
Gaolei Zhang PhD² | Congfen He PhD¹ 

¹Beijing Key Laboratory of Plant Resources Research and Development, Beijing, China

²Capital Institute of Paediatrics, Beijing, China

Correspondence

Congfen He, Beijing Key Laboratory of Plant Resources Research and Development, School of Science, Beijing Technology and Business University, 11 Fucheng Road, Beijing 100048, China.
Email: congfenhe@126.com

Funding information

National Natural Science Foundation of China, Grant/Award Number: 31501415; Science and Technology Planning Project of Beijing, Grant/Award Number: Z171100001517006; Support Project of High-level Teachers in Beijing Municipal Universities in the Period of 13th Five-year Plan, Grant/Award Number: CIT&TCD201804027; China Cosmetic Collaborative and Innovation Center, BTBU, Grant/Award Number: 19008001060

Abstract

Background: The current knowledge about potential risk factors for atopic dermatitis (AD) is primarily based on the structure and function of the stratum corneum, which is characterized by osmotic defects and abnormal antibacterial function. There are no studies on the difference between facial lipids in infants with AD and healthy infants.

Aims: We sought to explore significantly different lipid markers for infants with AD presenting with lesions and healthy infants aged 0-2 years to guide treatment strategies.

Methods: Twenty-eight patient infants with AD and 32 healthy infants were recruited. Each infant received its surface skin lipids (SSL) on the right cheek. The components of skin lipids were measured by ultra-performance liquid chromatography-quadrupole-time-of-flight mass spectrometry (UPLC-Q-TOF-MS) to explore significantly different lipid markers by analyzing the detection results using orthogonal partial least squares analysis (OPLS-DA).

Results: There were clear distinctions in the components of SSL between the two groups. Twenty-nine significantly different lipid markers ($P \leq .05$) were found.

Conclusion: This study confirmed that there were significant differences in the components of the SSL between AD infants with lesions and healthy infants, but also found lipid types, lipid contents, and lipid structures as AD-related risks.

KEYWORDS

atopic dermatitis, facial surface skin lipids, infants, potential lipid biomarkers, UPLC-Q-TOF-MS

1 | INTRODUCTION

Atopic dermatitis (AD) is a chronic recurrent skin disease, and its main clinical symptoms are dry skin, eczema-like lesions, and persistent itching. Infants have a high incidence of AD in China. The incidence of AD in 1- to 6-month-old infants was 66.39% in Yantai, China.¹ And the incidence of AD in 6- to 12-month-old infants was as high as 75.6% in Tianjin, China.² Worldwide, approximately 2 million children suffer from AD and lifetime prevalence of AD is as high as 20% in 2014.³ The skin of infants is fresher and softer, has

a thinner cuticle, and has lower amounts of lipid components than that of adults.⁴ This results in a weaker skin barrier function in infants and is also one of the possible reasons for the high prevalence of AD in infants.⁴ In 2008, the immunology group of the Chinese Society of Dermatology and Saeki^{5,6} mentioned that it is absolutely necessary for patients with AD to use emollients and moisturizers. This not only prevents evaporation of water but can also decrease stimulation from exogenous factors and promote recovery and improvement of the skin barrier. Recovery of the skin barrier function is key for treating AD.

Skin lipids are an important component of skin and have functions such as maintaining the integrity of the skin and resisting external stimulation.⁷ According to their source, lipids can be classified as sebaceous lipids and intracellular lipids.⁸ These lipids mainly consist of ceramides (Cers), free fatty acids (FFAs), cholesterol (CHOL), cholesterol esters, squalene, triglycerides (TG), wax esters, and diglycerides.⁹

The methods used for the analysis of lipids include thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), gas chromatography mass spectrometer (GC/MS), and liquid chromatograph mass spectrometer (LC/MS).^{10,11} Compared with conventional analysis methods, UPLC-Q-TOF-MS uses a combination of UPLC and high-resolution mass spectrometry to obtain richer and clearer material information and is currently the most commonly used lipid analysis method. OPLS-DA is a supervised data processing method that can maximally highlight the differences between different groups. We have established a series of methods of collection, lipid extraction, data acquisition, and analysis techniques based on UPLC-Q-TOF-MS. In our earlier studies, this method has been used to study the lipids of sensitive skin and normal skin,¹² male and female,¹³ and acne and normal skin in young male.¹⁴ Results showed that facial skin lipids were significantly different in genders. Compared with normal SSL, the sensitive skin and acne had obvious difference.

This study used UPLC-Q-TOF-MS to obtain spectrometry data on the lipids in the facial skin lesions of infants with AD and of healthy infants aged of 0-2 years. The data were combined with the data from OPLS-DA for pattern recognition analysis to determine lipid markers that showed significant differences under screening conditions. We hope that these data can be useful in providing a theoretical basis for the development of skincare products or washing products that can maintain and restore the skin barrier function in infants.

2 | MATERIAL AND METHODS

All patients and volunteers gave informed consent for their participation in the study. The protocols involving human subjects were approved by the Medical Ethics Committee of Capital Institute of Paediatrics and were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

2.1 | Study design

This was a case-control study to search for lipids related to AD, conducted at a university-based hospital. Lipid collection was performed on the right cheek of AD and healthy participants.

2.2 | Investigational products

The instruments used in the experiments were as follows: Liquid chromatography was carried out on ACQUITY UPLC I-Class/Xevo G2-XS Q-TOF, nitrogen-blowing instrument, and vortex shaker.

The reagents used were as follows: methanol, acetone, chloroform (Beijing Chemical Works, analytical grade), ammonium formate, isopropanol, acetonitrile, formic acid (Thermo Fisher Scientific, LC-MS grade), Sebutape[®] (Cuderm Corporation), and distilled water (Watsons).

2.3 | Study population

Infants between 0 and 2 years with AD classified as moderate and severe by the Japanese dermatological association are eligible for this study. There is a total of 28 infants with AD and 32 healthy infants. In order to ensure comparability, target lesions had to be on the right cheek. Before sampling, parents of volunteers were informed of the aim of the study and signed the informed consent form.

Patients with liver and kidney dysfunction and endocrine dysfunction were excluded. Treatment with hormone and other medicines were not allowed unless they were used for more than 1 month.

2.4 | Experimental method

2.4.1 | Sample collection and storage

After the volunteers were enrolled, their faces were washed with clean water. Following this, they were allowed to wait for 30 minutes in a constant temperature and constant humidity environment at a temperature of 24°C and a relative humidity of 50%. The staff applied Sebutape[®] test strips to the right cheek of the volunteers and then removed them after 3 minutes and placed them in sample tubes that were then stored at -80°C. The Sebutape[®] test strips were applied to lesions on the right side of the face in infants in the AD group, while corresponding right facial lipids were collected from the healthy infants.

2.4.2 | Sample processing

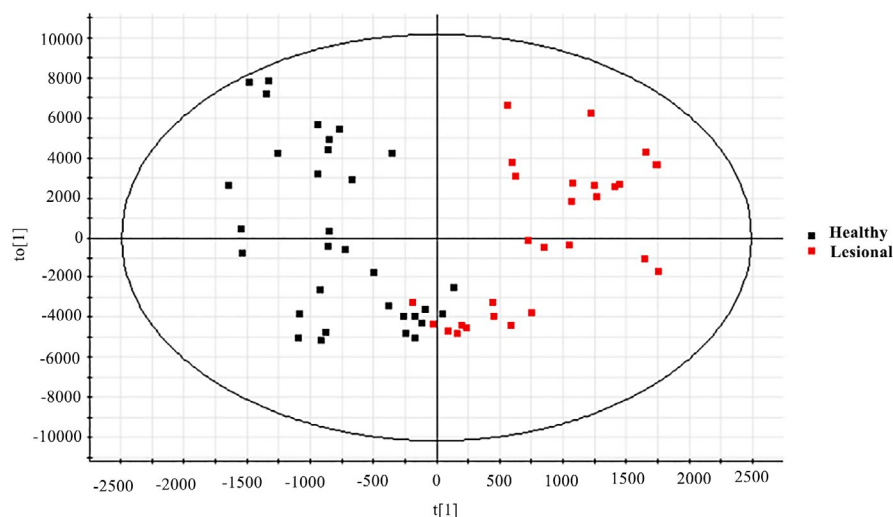
Sample treatment was performed by modified Bligh and Dyer method.¹⁵ The samples were removed from the -80°C freezer, and the mixture of chloroform and methanol was added to them. The mixture was vortexed and allowed to settle for 3 minutes. Next, equal volume of acetone was added, and the mixture was vortexed and allowed to settle for 10 minutes. The Sebutape[®] test strips were removed from the tube, and the lipid extracts were retained and dried with the nitrogen-blowing instrument. Finally, the mixed reagent (methanol:isopropanol) was used to dissolve the lipids for testing.

2.5 | Analysis conditions

2.5.1 | Liquid chromatography conditions

Chromatographic column was Waters ACQUITY UPLC CSH C18 Column, 130 Å, 1.7 µm, 2.1 mm × 50 mm, and the UPLC elution program was as previous study.¹⁵ The flow rate was maintained at 0.3 mL/min. The injection volume was 2.0 µL, and the column was thermostated at 50°C. During UPLC runs, the injector needle was

FIGURE 1 Score graph of SSL between the AD skin lesion group and the healthy group obtained in the positive ion mode. The better the separation between groups in the graph, the greater the differences between groups. Each spot represents a sample, and black represents the healthy group, whereas red represents the AD skin lesion group



washed with the mobile phase. The eluent outlet was connected to Q-TOF-MS for entities detection and characterization.

2.5.2 | Mass spectrometry conditions

Electrospray ionization (ESI) was carried out with positive ion mode acquisition and a mass scan range of 100–1200 m/z ; nitrogen was used for all gas-flow paths. Leucine enkephalin (m/z 554.2771) was used as an external standard for accurate lock mass. Data collection was carried out using the Masslynx 4.1 data management software. Mass spectrometry conditions were as previous study.¹⁵

2.5.3 | Statistical analysis

Data collection was carried out using the Mass Lynx 4.1 software, and data processing was carried out using the Waters Progenesis QI V2.0 and Ezinfo 3.0 software. First, the collected profiled collected raw data were input into the QI software for peak alignment processing; then, the samples were divided into AD lesion and healthy group for peak extraction. After obtaining compound information, the information was input into the Ezinfo software. The S-plot was used for screening of compounds that have greater effects on grouping ($VIP > 2$), and this information was input back into the QI software. Following this, other screening conditions were set ($P \leq .05$, fold difference >2). Compounds that fulfilled the criteria were selected. Finally, these compounds were compared with the Basic Lipids human lipids database to obtain specific information on the characteristics of the lipid components.

3 | RESULTS

3.1 | OPLS-DA analysis of facial lipids from the AD skin lesion group and the healthy group

After the mass spectrometry data of samples from both groups were input into the EZinfo software, the OPLS-DA analysis mode was selected, and the differences in lipid composition between both

groups were assessed using the score graph. We can conclude that the separation of the two samples was good and differences were present (Figure 1).

Since multivariate data analysis indicated significant differences between acne SSL and control, OPLS-DA was performed to select the most important individual lipid species of these subclasses responsible for the discrimination. The selection criteria were $VIP > 1$, $P < .05$, and fold change >2 . Additionally, the same changing trends as the belonging main classes and subclasses were also factors during the screening.

3.2 | Identification of different facial lipid markers in the AD skin lesion group and healthy group

Lipid metabolites that fulfilled the screening criteria were matched to the human lipid database, Basic Lipid. We identified 29 lipid components with significant differences (Table 1).

4 | DISCUSSION

4.1 | Analysis of differences in sphingolipids

Ceramide (Cer) is the lipid component that is predominant in epidermal cells, and it accounts for 50% of intracellular lipids. It is also an important lipid component that maintains the stability of the skin barrier function.¹⁶ Studies have shown that children with AD have abnormal skin barrier function, and lipid content is significantly lower than that of healthy children.¹⁷ In the stratum corneum, long-chain Cers plays an important role in the maintenance of the skin barrier function. The decrease in long-chain Cers and increase in short-chain Cers result in the decrease of the skin barrier function.^{18,19} Our study results show that there are significant differences in the Cers content between the AD skin lesion group and the healthy group, with the Cers content in the healthy group being significantly higher than that in the AD skin lesion group. This suggests that skin barrier dysfunction is present in the skin lesions of infants with AD, and abnormalities in the skin barrier function are closely associated with abnormal Cers metabolism.

TABLE 1 Information table of different facial lipid metabolites in the AD skin lesion group and healthy group

No.	Name	Structure	Mass-to-charge ratio (m/z)	Retention time	Type of lipid
1	Cer(d18:2/20:0)	$C_{38}H_{73}NO_3$	609.5891573	12.78573333	Sphingolipids
2	Cer(d16:1/23:0)	$C_{39}H_{77}NO_3$	608.6026615	11.55683333	
3	Cer(d18:1/18:1(9Z))	$C_{36}H_{69}NO_3$	581.5580923	11.75586667	
4	Cer(d18:1/19:0)	$C_{37}H_{73}NO_3$	580.5682339	10.35231667	
5	SM(d18:0/20:0)	$C_{43}H_{89}N_2O_6P$	778.6770863	16.99715	
6	TG(13:0/14:0/20:2(11Z,14Z))[iso6]	$C_{50}H_{92}O_6$	806.729889	17.72255	Glyceroglycolipids
7	TG(14:0/14:0/15:1(9Z))[iso3]	$C_{46}H_{86}O_6$	752.6817589	17.01303333	
8	TG(13:0/15:1(9Z)/17:1(9Z))[iso6]	$C_{48}H_{88}O_6$	778.6963155	17.13988333	
9	TG(22:3(10Z,13Z,16Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))[iso3]	$C_{69}H_{104}O_6$	1046.811601	17.60971667	
10	TG(14:0/17:0/22:2(13Z,16Z))[iso6]	$C_{56}H_{104}O_6$	890.8211104	17.71478333	
11	TG(14:0/14:0/16:0)[iso3]	$C_{47}H_{90}O_6$	768.7001937	17.71478333	
12	TG(13:0/14:1(9Z)/16:1(9Z))[iso6]	$C_{46}H_{84}O_6$	750.6575605	16.55948333	
13	TG(13:0/14:1(9Z)/20:2(11Z,14Z))[iso6]	$C_{50}H_{90}O_6$	804.7169325	17.30285	
14	TG(15:0/18:0/18:1(9Z))[iso6]	$C_{54}H_{102}O_6$	864.792578	17.84713333	
15	DG(18:4(6Z,9Z,12Z,15Z)/22:1(11Z)/0:0)[iso2]	$C_{43}H_{74}O_5$	688.5863008	13.87246667	
16	DG(15:1(9Z)/17:0/0:0)[iso2]	$C_{37}H_{64}O_5$	589.4796495	12.90948333	
17	DGTS(16:0/18:2(9Z,12Z))	$C_{44}H_{81}NO_7$	758.5928167	10.72358333	
18	PA(22:2(13Z,16Z)/17:0)	$C_{42}H_{79}O_8P$	760.5891955	11.52823333	Glycerophospholipids
19	PA(P-16:0/21:0)	$C_{40}H_{79}O_7P$	703.5589585	9.996533333	
20	PE(18:3(6Z,9Z,12Z)/20:0)	$C_{43}H_{80}NO_8P$	787.5946225	11.88528333	
21	PE(20:2(11Z,14Z)/19:0)	$C_{44}H_{84}NO_8P$	786.6039206	11.89966667	
22	1-(8-[5]-ladderane-octanyl)-2-(8-[3]-ladderane-octanyl)-sn-glycerophosphoethanolamine	$C_{45}H_{76}NO_6P$	758.5531058	10.78008333	
23	21-Methyl-8Z-pentatriacontene	$C_{36}H_{72}$	522.5946218	11.38585	Fatty acyls
24	13-Methyl-1-tritriacontene	$C_{34}H_{68}$	494.5605058	10.28088333	
25	1-Octacosene	$C_{28}H_{56}$	415.4279032	8.089783333	
26	Mayolene-16	$C_{34}H_{60}O_4$	533.4549757	17.29491667	
27	N'-5Z,8Z,11Z,14Z-eicosatetraenoyl-N''-diethyl-ethylenediamine	$C_{26}H_{46}N_2O$	420.4000558	6.852466667	
28	Palmityllaurate	$C_{28}H_{56}O_2$	609.5891573	12.78573333	
29	Type IV cyanolipideicosanoyl ester	$C_{25}H_{45}NO_2$	409.3777697	10.80155	

Abbreviations: AD, atopic dermatitis; Cer, ceramide; DG, diglycerides; PA, phosphatidic acid; PE, phosphatidylethanolamine; SM, sphingomyelin; TG, triglycerides.

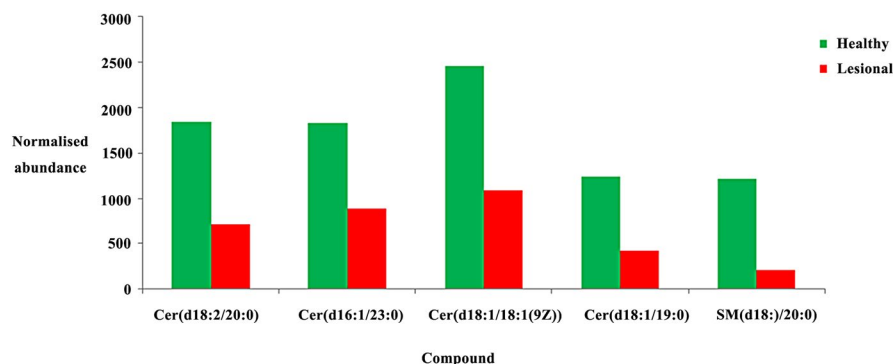
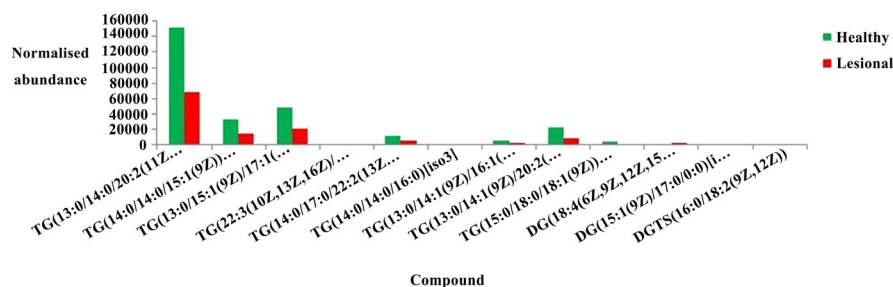
Moreover, the four types of Cers with significant differences between the two groups are long-chain Cers, which is consistent with the existing research results, and indicate that long-chain Cers plays an important role in maintaining barrier function.

Sphingomyelin (SM) produces Cers under the action of sphingomyelinase, which is an important way for skin Cers to form.²⁰ Skin Cers maintain the moisture content of the skin and thus also maintain the skin barrier function. Therefore, an increase in the skin SM content can directly promote the accumulation of skin Cers, thereby indirectly affecting the skin barrier function. The results of this

study show that the SM content (d18:0/20:0) in the healthy group is significantly higher than that in the AD skin lesion group (Figure 2), and this further verifies that SM plays an important role in the maintenance of the skin barrier function.

4.2 | Analysis of the differences in glyceroglycolipids

Triglycerides (TG) are secreted by the lamellar bodies and are important lipid component that maintain the skin barrier

FIGURE 2 Comparison of differences in sphingomyelin between both groups**FIGURE 3** Comparison of differences in glyceroglycolipids between both groups

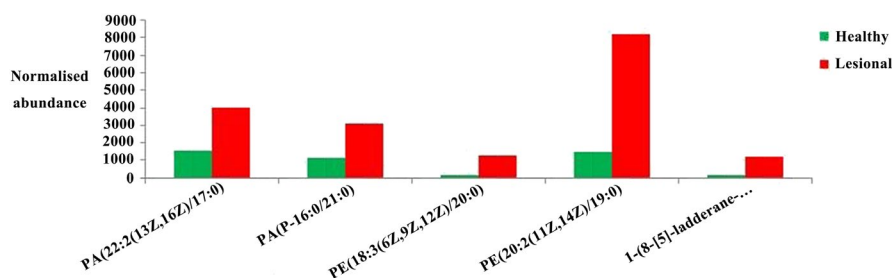
function.²¹ Studies have found that TGs can inhibit the expression of extracellular matrix metalloproteinase-1 (MMP-1) and inflammation-related proteins COX-2 and IL-1 β to protect HaCaT cells that have been irradiated with UV light.²² This study found that there were nine TGs that were different between the AD skin lesion group and the healthy group. The healthy group had a higher content of eight TGs, and the differences were significant (Figure 3). In the AD skin lesion group, the TGs were presented in higher levels, (22:3/22:6/22:6)[ios3], contained more highly unsaturated fatty acid chains than those in the other eight TGs. We hypothesize that TGs with different structures may play different roles in the skin barrier or that the difference in this TG between both groups may be associated with other characteristic reactions in AD.

Diglycerides (DG) are precursors for TG synthesis and form TGs through catalysis by diglycerideacyltransferase. In our study, we found that DG (18:4/22:1/0:0)[ios2] was significantly higher in the AD skin lesion group, whereas DG(15:1/17:0/0:0)[ios2] was significantly higher in the healthy group. We hypothesize that DGs with different structures may have different physiological effects on the skin barrier.

4.3 | Analysis of differences in glycerophospholipids

Phosphatidylethanolamine (PE) and phosphatidylcholine (PC) are phospholipid lipids, which can be used as a cell signal molecule and are also components of the cell membrane. It has the function of maintaining cell membrane integrity and stability.

Phosphatidylethanolamine (PE) and phosphatidic acid (PA) are glycerophospholipids and can act as cell-signaling molecules. They are also components of the cell membrane and maintain its integrity and stability. Studies have found that PE is not only formed as a result of cell apoptosis but can also induce cell apoptosis: PE can activate the Bcl-2/Bax pathway in HepG2 liver cancer cells to promote activation of caspase 3²³ and induce the expression of STAT1 and STAT2,²⁴ leading to apoptosis of cells. PA can increase cell survival and promote cell proliferation in animal cells; they especially promote B-lymphocyte proliferation and strengthen the body's immunity.²⁵ Both PE and PA show antagonism in cell function. This study showed that there were significant differences in the levels of PE and PA between both groups (Figure 4); both were present in higher levels in the AD skin lesion group. We hypothesize that higher levels of PE in the AD skin lesion group may result in excessive apoptosis in the skin

**FIGURE 4** Comparison of differences in glycerophospholipids between both groups

epidermal cells, thereby causing damage to the skin barrier function and difficulty in resisting exogenous stimuli and production of stimulation. At the same time, endogenously produced PA participates in the antagonism of the skin inflammatory reaction due to excessive PE. However, our results showed that the PA levels were much lower than PE, and these results in the skin lesions of patients with AD were in an inflammatory state and defected in skin barrier function.

5 | CONCLUSION

This study used the UPLC-Q-TOF-MS technique in combination with OPLS-DA analysis to obtain good separation and identify human facial SSL components. Upon screening, a total of 29 lipid metabolites that were significantly different between the two groups were obtained. This demonstrated that there were significant differences in facial SSL between 0- and 2-year-old healthy infants and AD infants with skin lesions. Analysis of the different lipids identified was carried out, and we observed that the causes of skin barrier dysfunction in the skin lesions of patients with AD were intimately associated with the type of lipids, lipid content, and lipid structure.

These results were significant in guiding the development of skincare products for infants. However, the studies on the metabolism pathways of some specific structural lipids were still not comprehensive. This study only analyzed the biochemical functions of some types of lipids. It was believed that with the deepening of lipid analysis and identification technology, more research will be conducted on the study of metabolic pathways and biochemical functions of specific structural lipid components in vivo. It will guide us to further understand the difference between lipids in the two groups, define the facial characteristic lipids in infants with AD, and provide ideas for the pathogenesis and treatment of AD.

ACKNOWLEDGMENTS

This work was supported by National Natural Science Foundation of China (31501415); grants from Science and Technology Planning Project of Beijing (Z171100001517006); grants from Support Project of High-level Teachers in Beijing Municipal Universities in the Period of 13th Five-year Plan (CIT&TCD201804027); and grants from China Cosmetic Collaborative and Innovation Center, BTBU (19008001060).

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ORCID

Hecong Wang  <https://orcid.org/0000-0003-2789-1184>

Yan Jia  <https://orcid.org/0000-0001-5641-3478>

Congfen He  <https://orcid.org/0000-0001-5944-4472>

REFERENCES

1. Mao XH. Dalian, China: Dalian Medical University; 2013 (in Chinese).
2. Liu J, Ye T, Li YM, et al. Epidemiological study of the etiological factors of infantile eczema. *Maternal Child Health Care China*. 2008;23(21):3025-3026 (in Chinese).
3. Flohr C, Mann J. New insights into the epidemiology of childhood atopic dermatitis. *Allergy*. 2014;69(1):3-16.
4. Stamatatos GN, Nikolovski J, Mack MC, Kollias N. Infant skin physiology and development during the first years of life: a review of recent findings based on in vivo, studies. *Int J Cosmet Sci*. 2011;33(1):17-24.
5. Immunology group of the Chinese Society of Dermatology. Guidelines for the diagnosis and treatment of atopic dermatitis in China. *Chin J Dermatol*. 2008;41(11):772-773 (in Chinese).
6. Saeki H, Furue M, Furukawa F, et al. Guidelines for management of atopic dermatitis. *J Dermatol*. 2009;36(10):563-577.
7. Motta S, Monti M, Sesana S, Mellesi L, Ghidoni R, Caputo R. Abnormality of water barrier function in psoriasis. *Arch Dermatol*. 1994;130(4):452-456.
8. Van SJ, Janssens M, Gooris GS, Bouwstra JA. The important role of stratum corneum lipids for the cutaneous barrier function. *Biochim Biophys Acta (BBA) - Mol Cell Biol Lipids*. 2014;1841(3):295-313.
9. Brenner M, Hearing VJ. The protective role of melanin against UV damage in human skin. *Photochem Photobiol*. 2008;84(3):539-549.
10. Park H, Zhou Y, Costello CE. Direct analysis of sialylated or sulfated glycosphingolipids and other polar and neutral lipids using TLC-MS interfaces. *J Lipid Res*. 2014;55(4):773-781.
11. Nestola M, Thellmann A. Determination of vitamins D2 and D3 in selected food matrices by online high-performance liquid chromatography-gas chromatography-mass spectrometry (HPLC-GC-MS). *Anal Bioanal Chem*. 2015;407(1):297-308.
12. Fan L, Jia Y, Cui L, Li X, He C. Analysis of sensitive skin barrier function: basic indicators and sebum composition. *Int J Cosmet Sci*. 2018;40(2):117-126.
13. Cui L, He C, Fan L, Jia Y. Application of lipidomics to reveal differences of facial skin surface lipids between male and female. *J Cosmet Dermatol*. 2018;17(6):1254-1261.
14. Gan Y, Zhou M, He C, Chen Z, Jia Y. Lipidomics reveals skin surface lipid abnormality in male youth acne. *Br J Dermatol*. 2018;179(3):732-740.
15. Bligh EG, Dyer WJ. A rapid method of total lipid extraction and purification. *Can J Biochem Physiol*. 1959;37(8):911-917.
16. Cha HJ, He C, Zhao H, Dong Y, An I-S, An S. Intercellular and intracellular functions of ceramides and their metabolites in skin (Review). *Int J Mol Med*. 2016;38(1):16-22.
17. Kezic S, Novak N, Jakasa I, et al. Skin barrier in atopic dermatitis. *Front Biosci*. 2014;19(2):542-556.
18. Mojumdar EH, Kariman Z, van Kerckhove L, Gooris GS, Bouwstra JA. The role of ceramide chain length distribution on the barrier properties of the skin lipid membranes. *Biochim Biophys Acta (BBA) - Biomembranes*. 2014;1838(10):2473-2483.
19. Moore DJ, Rawlings AV. The chemistry, function & (patho)physiology of stratum corneum barrier ceramides. *Int J Cosmet Sci*. 2017;39(4):366-372.
20. Kihara A. Synthesis and degradation pathways, functions, and pathology of ceramides and epidermal acylceramides. *Prog Lipid Res*. 2016;63:50-69.
21. Radner F, Fischer J. The important role of epidermal triacylglycerol metabolism for maintenance of the skin permeability barrier function. *Biochim Biophys Acta - Mol Cell Biol Lipids*. 2014;1841(3):409-415.

22. Jin XJ, Cheng S, Chen Z, et al. Effects of triglycerides metabolism on HaCaT cells after ultraviolet radiation and its possible mechanism. *Prog Modern Biomed*. 2014;14(33):6454-6459 (In Chinese).
23. Yao Y, Huang C, Li Z-F, et al. Exogenous phosphatidylethanolamine induces apoptosis of human hepatoma HepG2 cells via the bcl-2/bax pathway. *World J Gastroenterol*. 2009;15(14):1751-1758.
24. Liu LY, Huang C, Li ZF, et al. STAT1 and STAT2 participation in growth inhibition of human hepatoma HepG2 cells induced by phosphatidylethanolamine. *J Southern Med Univ*. 2011;31(2):256-258 (In Chinese).
25. Ridgway ND. The role of phosphatidylcholine and choline metabolites to cell proliferation and survival. *Crit Rev Biochem Mol Biol*. 2013;48(1):20-38.

How to cite this article: Wang H, Le C, Jia Y, Gao Y, Zhang G, He C. Application of lipidomics to reveal differences of facial skin surface lipids between atopic dermatitis and healthy infants. *J Cosmet Dermatol*. 2019;00:1-7. <https://doi.org/10.1111/jocd.13188>