



SHANGHAI JIAO TONG UNIVERSITY SCHOOL OF MEDICINE 学者介绍



欧阳凤秀 博士
OUYANG Feng-xiu Ph.D

研究员、博士生导师
Professor, Doctoral Supervisor

ORCID ID: 0000-0003-1980-5928



欧阳凤秀 (1971—), 上海交通大学医学院附属新华医院教育部和上海市环境与儿童健康重点实验室研究员, 复旦大学流行病学与卫生统计学博士。2004—2011 年曾在美国哈佛大学公共卫生学院和美国西北大学医学院儿童医院先后进行博士后及专职科研工作。2013 年曾到美国约翰·霍普金斯大学公共卫生学院做短期访问教授。现任中华医学会儿科分会临床流行病学学组(筹)副组长、中华医学会临床流行病学和循证医学分会学组委员、全国卫生产业企业管理协会抗衰老分会理事、上海市微量元素学会理事。长期从事生命早期暴露因素与胎儿生长、儿童健康的流行病学研究, 探讨肥胖/代谢综合征等疾病的相关遗传、环境因素及生物标志物, 以期进行早期综合干预。在国际著名学术期刊 *Environmental Health Perspectives*、*American Journal of Clinical Nutrition*、*Journal of Allergy and Clinical Immunology*、*Bulletin of the World Health Organization* 及国内权威期刊发表论文 90 余篇, 其中 SCI 收录 70 余篇。主持国家重点研发计划“政府间国际科技创新合作”重点专项 1 项、国家自然科学基金委员会与美国国立卫生研究院合作研究重点项目 1 项、国家自然科学基金青年及面上项目 3 项、国际原子能机构国际合作项目 2 项、美国盖茨基金会项目 1 项。承担国家自然科学基金中加国际合作重大项目子课题 1 项。入选上海浦江人才计划, 2015 年、2019 年上海市教育委员会高峰高原学科建设计划。

该研究依托上海交通大学医学院“双一流”暨高水平地方高校建设高原学科—公共卫生与预防医学学科项目。

代表性论著

1. Tang N, Fan P, Yu X, Ma R, Tao Y, Wang W, Ouyang F. Effects of long-term triclosan exposure on microbiota in zebrafish[J]. *Front Microbiol*, 2021, 12: 604313.
2. Ouyang F, Zhang GH, Du K, Shen L, Ma R, Wang X, Wang X, Zhang J. Maternal prenatal urinary bisphenol A level and child cardio-metabolic risk factors: a prospective cohort study [J]. *Environ Pollut*, 2020, 265: 115008.
3. Ouyang F, Tang N, Zhang HJ, Wang X, Zhao S, Wang W, Zhang J, Cheng W. Maternal urinary triclosan level, gestational diabetes mellitus and birth weight in Chinese women [J]. *Sci Total Environ*, 2018, 626: 451–457.
4. Wang X, Ouyang F, Feng L, Wang X, Liu Z, Zhang J. Maternal urinary triclosan concentration in relation to maternal and neonatal thyroid hormone levels: a prospective study[J]. *Environ Health Perspect*, 2017, 125 (6): 067017.
5. Ouyang F, Longnecker MP, Venners SA, Johnson S, Korrick S, Zhang J, Xu X, Christian P, Wang MC, Wang X. Preconception serum 1,1,1-trichloro-2,2,bis (p-chlorophenyl) ethane and B-vitamin status: independent and joint effects on women's reproductive outcomes[J]. *Am J Clin Nutr*, 2014, 100(6): 1470–1478.



综述

孕期多不饱和脂肪酸对母婴健康影响的研究进展

马蕊, 陈书进, 欧阳凤秀

上海交通大学医学院附属新华医院环境与儿童健康教育部和上海市重点实验室, 上海 200092

[摘要] 孕期营养与妊娠结局及子代健康密切相关。长链多不饱和脂肪酸 (polyunsaturated fatty acids, PUFAs) 主要包括二十二碳六烯酸 (docosahexaenoic acid, DHA)、二十碳五烯酸 (eicosapentaenoic acid, EPA)、花生四烯酸 (arachidonic acid, AA)、 α -亚麻酸 (α -linolenic acid, ALA) 及亚油酸 (linoleic acid, LA)。人体 DHA、EPA 和 AA 主要通过膳食摄入或由必需脂肪酸 ALA 及 LA 合成。PUFAs 是体内胆固醇酯、磷脂及脂肪的重要组成部分, 参与细胞膜的构成, 可作为第二信使使前体传递信号; 可转化合成激素及 PUFAs 衍生物, 通过多种途径, 发挥复杂的生物学功能。妇女孕期 n-3 PUFAs (EPA、DHA) 不足, 可能与先兆子痫、早产及产后抑郁的发病风险增高有关, 并影响儿童心血管远期健康, 但这些相关性还存在一定的争议。母亲孕期 n-3 PUFAs (EPA、DHA) 的摄入可能与儿童喘息及哮喘风险降低有关, 而 n-6 PUFAs (AA) 摄入量过多可能与哮喘、过敏性鼻炎的风险增加有关。对 DHA 不足的早产儿, 及时补充 DHA 可促进神经发育。目前缺乏孕妇及新生儿这一敏感人群 PUFAs 正常参考范围, 有必要进一步研究和建立相关标准, 以便合理指导孕妇孕期 PUFAs 营养。

[关键词] 多不饱和脂肪酸; 母婴健康; 二十二碳六烯酸

[DOI] 10.3969/j.issn.1674-8115.2021.12.020 **[中图分类号]** R151 **[文献标志码]** A

Research progress in the association between maternal prenatal polyunsaturated fatty acids and maternal and infant health

MA Rui, CHEN Shu-jin, OUYANG Feng-xiu

Ministry of Education-Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China

[Abstract] The nutritional status during pregnancy is closely related to the pregnancy outcome of the mother and the health of the offspring. Long chain polyunsaturated fatty acids (PUFAs) mainly include docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), arachidonic acid (AA), α -linolenic acid (ALA) and linoleic acid (LA). DHA, EPA and AA in human body are mainly from diet or synthesized from essential fatty acids ALA and LA. As the important components of cholesterol esters, phospholipids and fat in human body, PUFAs play complex biological functions through a variety of ways. For instance, PUFAs can participate in the composition of cell membrane, work as the second messenger precursors to transmit signals, and transform into hormones and PUFAs derivatives. Lack of PUFAs (EPA and DHA) during pregnancy may be related to the increased risk of preeclampsia, preterm delivery and postpartum depression, and affect the long-term cardiovascular health of children, but these correlations are still controversial. The increased intake of n-3 PUFAs (EPA and DHA) during pregnancy might be associated with the reduced risk of wheezing and asthma, while the increased intake of n-6 PUFAs (AA) might be associated with the increased risk of asthma and allergic rhinitis. For premature infants with insufficient DHA, timely supplementation of DHA could promote neurodevelopment. At present, there is a lack of normal reference range of PUFAs for pregnant women and newborns as the sensitive population. Thus, it is necessary to further study and establish the normal reference range of PUFAs in order to reasonably guide the nutrition of PUFAs during pregnancy.

[Key words] polyunsaturated fatty acid (PUFA); maternal and infant health; docosahexaenoic acid (DHA)

多不饱和脂肪酸 (polyunsaturated fatty acids, PUFAs) 是一类碳链中含有 2 个或 2 个以上不饱和双键的脂肪酸, 其中碳链长度为 18~22 个碳原子的 PUFAs 又称为长链 PUFAs。PUFAs 主要包括二十二碳六烯酸

(docosahexaenoic acid, DHA)、二十碳五烯酸 (eicosapentaenoic acid, EPA)、花生四烯酸 (arachidonic acid, AA)、 α -亚麻酸 (α -linolenic acid, ALA) 及亚油酸 (linoleic acid, LA)。PUFAs 是磷脂、脂肪和胆固醇酯

[基金项目] 国家自然科学基金 (81961128023); 国家重点研发计划“政府间国际科技创新合作”重点专项 (2017YFE0124700); 上海市教育委员会高峰高原学科建设计划 (20152518)。

[作者简介] 马蕊 (1991—), 女, 博士生; 电子信箱: marui9145@126.com。

[通信作者] 欧阳凤秀, 电子信箱: ouyangfengxiu@xinhumed.com.cn。

[Funding Information] National Natural Science Foundation of China (81961128023); National Key Research and Development Program of China (2017YFE0124700); Shanghai Municipal Education Commission—Gaofeng Clinical Medicine Grant Support (20152518)。

[Corresponding Author] OUYANG Feng-xiu, E-mail: ouyangfengxiu@xinhumed.com.cn。

的重要组成成分,可通过供能、改变细胞膜的构成、作为第二信使前体传递信号、转化合成激素及PUFAs衍生物,发挥复杂的生物学功能^[1]。在母婴健康方面,流行病学研究显示母亲孕期摄入DHA不足,可能与先兆子痫^[2]、早产^[3]、低出生体质量儿^[4]、产后抑郁^[5]的发生有关,也可能影响子代的神经发育^[6]、心血管健康^[7]及过敏性疾病^[8]的患病风险。相反,母亲孕期摄入AA和LA过多可能与子代患过敏性疾病风险增加有关^[9]。由于胎儿和新生儿体内的酶系统尚未发育成熟,无法合成足够的DHA、EPA及AA以供机体利用^[10]。因此在生命早期,胎儿主要依靠母体PUFAs经胎盘转运;出生后婴儿主要依靠母乳喂养获得PUFAs^[11]。然而,孕妇普遍存在DHA、EPA摄入不足的情况^[12]。

本文主要综述PUFAs的种类,孕妇及新生儿脐带血脂肪酸水平的特点与现状,PUFAs对母婴健康的影响及其可能的机制。

1 PUFAs的主要种类及来源

根据PUFAs第1个不饱和碳键(即碳双键)在碳链上的位置,长链PUFAs分为n-3族(主要包括DHA、EPA、ALA)、n-6族(主要包括AA、LA)、n-7族以及n-9族。由于人体无法从头合成PUFAs,体内所需的DHA、EPA及AA可通过膳食摄入或分别从各自的合成前体ALA及LA经过一系列复杂的酶促反应合成(图1)。

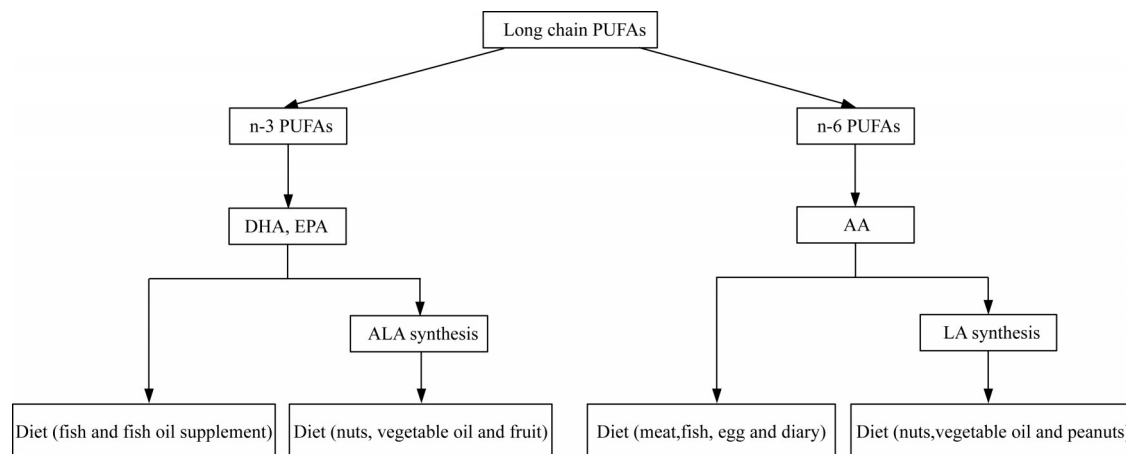


图1 人体n-3及n-6多不饱和脂肪酸主要种类及来源示意图

Fig 1 Main types and sources of human n-3 PUFAs and n-6 PUFAs

2 孕妇血PUFAs水平

妊娠期为一特殊生理时期,由于母体是胎儿营养及PUFAs的提供者,胎儿在孕晚期对DHA等PUFAs的需求增多,因此孕期妇女必须摄入足够的PUFAs以保证胎儿的需要。母体血浆中非酯化PUFAs的胎盘转运是胎儿PUFAs的主要来源,其先穿过合胞滋养层,扩散至胎盘绒毛基质,随后通过胎儿毛细血管内皮进入胎儿血循环^[13]。鉴于胎儿发育对PUFAs的需求,孕妇PUFAs缺乏与不足仍是值得关注的问题。

血脂肪酸水平是反映膳食脂肪酸摄入量的生物标志物^[14]。血浆和血清脂肪酸浓度主要反映机体近几周的脂肪酸摄入水平,红细胞脂肪酸的含量可以反映过去几个月的脂肪酸摄入水平。脂肪酸常采用液相色谱、气相色谱及色谱质谱联用进行检测^[15-16]。血脂肪酸浓度可表示为绝对值或目的脂肪酸占总脂肪酸浓度的百分比^[17]。由于提取方法、检测仪器等方面的差异^[15-16],采用百分比

表示血脂肪酸浓度有一定的可比性。

孕期血脂肪酸水平往往低于一般人群。按一般成人红细胞DHA、EPA和AA的正常参考值,孕妇DHA、EPA水平往往较低,而AA水平正常甚至较高。一项比利时开展的孕早期妇女队列研究^[18]发现,大多数(71.3%)孕妇的红细胞n-3 PUFAs水平低于一般人群。例如年轻成人DHA的实验室参考值(reference values, RV)为5.27%~8.87%,EPA的RV为0.75%~2.34%,AA的RV为11.0%~13.4%。而孕妇人群中,54.9%孕妇红细胞DHA水平低于RV,86.9%孕妇EPA水平低于RV。与之相反,77.9%孕妇AA水平高于RV^[18]。正常健康孕妇孕期血DHA水平平均为2.01%~7.44%,EPA水平平均为0.24%~0.98%,AA水平平均为4.94~15.61%(表1)。孕妇血DHA、EPA及AA水平往往低于一般人群。随着妊娠的进展,胎儿发育对脂肪酸的需求增加,孕妇血红细胞DHA及AA水平趋于降低^[19]。

此外,多胎妊娠婴儿PUFAs特别是DHA浓度往往低

表 1 健康孕妇妊娠期血 PUFAs 水平

Tab 1 Blood PUFAs levels of healthy pregnant women during pregnancy

| Author (Year) | Region | Sample size/n | Pregnancy | Sample | DHA/% | EPA/% | AA/% |
|-----------------------|-------------|---------------|---------------|-------------|------------------|------------------|------------------|
| Araujo (2020) [20] | Norway | 247 | 17–40 week | Erythrocyte | 6.92 (mean) | 0.79 (mean) | 10.84 (mean) |
| Nita (2020) [21] | Japan | 416 | 24–30 week | Erythrocyte | 7.44±1.12 | 0.74 (0.55–1.04) | 11.38±1.03 |
| Hoge (2018) [18] | Belgium | 122 | 1st trimester | Erythrocyte | 5.27±1.42 | 0.51±0.25 | 14.30±1.26 |
| Kitamura (2017) [22] | Japan | 213 | 1st trimester | Erythrocyte | 6.23±1.14 | 0.98±0.38 | 10.96±1.43 |
| Barrera (2018) [23] | Chile | 60 | 2nd trimester | Erythrocyte | 4.16±0.60 | 0.98±0.10 | 12.90±1.20 |
| Much (2013) [24] | Germany | 102 | 2nd trimester | Erythrocyte | 4.54±1.24 | 0.41±0.15 | 12.51±2.30 |
| Steer (2012) [25] | England | 4 346 | ≥20 weeks | Erythrocyte | 2.01 (1.24–3.05) | 0.24 (0.16–0.36) | 6.09 (3.89–8.36) |
| Kitamura (2017) [22] | Japan | 213 | 3rd trimester | Erythrocyte | 5.86±1.01 | 0.80±0.39 | 8.83±1.36 |
| Gellert (2016) [26] | Germany | 213 | 3rd trimester | Erythrocyte | 6.10±1.29 | 0.52±0.19 | 13.88±1.68 |
| Matsumoto (2020) [27] | Japan | 204 | 24–30 weeks | Plasma | 5.66 (median) | 0.85 (median) | 8.28 (median) |
| Voortman (2018) [28] | Netherlands | 6 999 | 2nd trimester | Plasma | 4.67 (median) | 0.44 (median) | 9.72 (median) |
| Wolfe (2011) [29] | America | 52 | Delivery | Serum | 2.07 (median) | 0.27 (median) | 4.94 (median) |

Note: Data are expressed as mean, $\bar{x}\pm s$, median or median (interquartile range, IQR). Inclusion criteria: studies were published from 2011 to 2021, and the subjects were perinatal women with a sample size of ≥ 50 . The total fatty acid levels of red blood cells, plasma or serum samples were detected and expressed as % (percentage of all fatty acids).

于单胎妊娠^[30]，可能是由于多胎妊娠胎儿对 PUFAs 需求总量更高。此外，经产妇新生儿 DHA 水平往往低于初产妇孕育的新生儿^[31]。因此，孕妇孕期有必要补充富含 PUFAs 的食品或补充剂，改善母体 PUFAs 储备消耗过度甚至不足的情况。目前尚无孕妇血脂脂肪酸正常参考值标准，有必要建立孕妇血 PUFAs 的正常参考值范围，为合理指导孕妇孕期补充 PUFAs 提供依据。

3 新生儿脐带血 PUFAs 水平

由于脐动脉中流动的是静脉血，临床评估新生儿脂

肪酸水平，常检测脐动脉血脂肪酸浓度^[32]。新生儿脐带血 DHA 水平平均为 2.45%~7.54%，EPA 水平平均为 0.08%~1.06%，AA 水平平均为 7.62%~18.03%（表 2）。新生儿血 EPA、DHA 及 AA 水平高于母亲^[29]。既往美国一项研究^[29]报道，母亲分娩前血 EPA、DHA 及 AA 浓度百分比的中位数分别为 0.27%、2.07% 和 4.94%，新生儿脐带血 EPA、DHA 及 AA 浓度百分比中位数分别为 1.06%、3.24% 和 9.64%，母亲血与脐带血 DHA 和 AA 的相关系数分别为 0.52 和 0.49。目前，我国新生儿脐血 PUFAs 浓度的相关研究和数据较少，有待进一步研究。

表 2 新生儿脐带血 PUFAs 水平

Tab 2 Umbilical cord blood PUFAs levels of newborns

| Author (Year) | Region | Sample size/n | Sample | DHA/% | EPA/% | AA/% |
|-----------------------|---------|---------------|-------------|------------------|------------------|-------------------|
| Nita (2020) [21] | Japan | 383 | Erythrocyte | 6.79±0.93 | 0.28 (0.20–0.39) | 15.35±1.28 |
| Kitamura (2018) [33] | Japan | 114 | Erythrocyte | 7.54±0.08 | 0.43±0.02 | 16.03±0.11 |
| Much (2013) [24] | Germany | 65 | Erythrocyte | 2.54±2.19 | 0.08±0.06 | 7.62±4.85 |
| Matsumoto (2020) [27] | Japan | 203 | Plasma | 5.98 (median) | 0.60 (median) | 17.06 (median) |
| Montes (2013) [34] | Spain | 170 | Plasma | 4.53±1.12 | 0.19±0.11 | 14.13±1.84 |
| Steer (2012) [25] | England | 3 394 | Plasma | 2.45 (1.85–3.44) | 0.19 (0.14–0.25) | 8.94 (7.16–11.53) |
| Kohlboeck (2011) [35] | Germany | 416 | Serum | 7.15±1.33 | 0.30±0.13 | 18.03±1.55 |
| Wolfe (2011) [29] | America | 52 | Serum | 3.24 (median) | 1.06 (median) | 9.64 (median) |

Note: The data are expressed as $\bar{x}\pm s$, median or median (IQR). Inclusion criteria: studies were published from 2011 to 2021, and the subjects were newborns with a sample size of ≥ 50 . The total fatty acid levels of red blood cells, plasma or serum samples were detected and expressed as % (percentage of all fatty acids).

4 PUFAs与母婴健康的关系

流行病学研究显示,母亲孕期补充DHA可减少产后抑郁、先兆子痫、早产及低出生体质量儿的发生^[2-5],促进子代神经生长发育和心血管健康,降低过敏性疾病的发病风险^[6-8]。母亲孕期LA、AA摄入量过多可能与子代过敏性疾病患者风险增加有关^[9]。

4.1 PUFAs与孕妇健康及出生结局的关联

4.1.1 产后抑郁 产后抑郁常发生在产后1个月内,可持续数月甚至数年^[36]。既往的生态学研究^[37]发现,人均海产品消费量较低的南非与消费量较高的冰岛相比,南非产后抑郁的患病率高出8.8倍(分别为24.5%和2.5%),提示摄入海产品(富含n-3 PUFAs)可能降低产后抑郁患病率。另一项小样本($n=72$)研究^[5]也发现,妊娠早期n-3 PUFAs水平低或合并高水平n-6 PUFAs,与产后抑郁风险升高有关。孕妇血DHA浓度与产后抑郁患病风险呈负相关^[38]。孕期补充DHA可降低产后抑郁的发病风险^[39];然而,也有研究未发现两者之间具有相关性^[40]。

4.1.2 先兆子痫 先兆子痫发生在约3%的妊娠妇女中,对母婴健康均有负面影响^[41]。Kulkarni等^[42]发现,先兆子痫患者及子代脐带血的DHA浓度均低于正常组。另有研究^[43]报道,先兆子痫孕妇妊娠晚期血红细胞n-6和n-3长链PUFAs浓度均低于正常孕妇,且子代脐带血DHA水平和n-3 PUFAs也降低。先兆子痫孕妇及其胎儿长链PUFAs的浓度更低,可能与母体合成水平下降有关^[43]。一篇系统综述^[2]报道,孕妇补充n-3 PUFAs可降低子痫前期的发生风险($RR=0.82$, $95\%CI$ 0.70~0.97),但与妊娠高血压综合征无关($RR=0.98$, $95\%CI$ 0.90~1.07)。上述研究提示孕妇孕期摄入n-3 PUFAs对预防先兆子痫发生可能有一定的积极作用。

4.1.3 早产 全球每年约发生1 500万例早产,是导致婴儿早期并发症和死亡的主要原因^[44];其中早期早产约占所有早产的20%,是新生儿死亡和儿童残疾的最大负担^[45]。Middleton等^[3]对随机对照试验研究进行系统综述和meta分析,发现孕妇n-3 PUFAs补充组较未补充组,早产($RR=0.89$, $95\%CI$ 0.81~0.97)和早期早产($RR=0.58$, $95\%CI$ 0.44~0.77)发生率均更低。然而,同年一项随机临床试验报道,孕妇从妊娠20周之前到34周补充n-3 PUFAs,对早产发生率无影响^[46]。因此,孕期补充n-3 PUFAs是否能减少早产的发生,尚无定论。

4.1.4 出生体质量 胎儿正常发育对其未来健康至关重要

要^[47]。Cinelli等^[4]发现母亲和新生儿红细胞DHA、AA浓度与出生体质量呈正相关。妊娠期补充DHA和EPA可减少低出生体质量儿的风险($RR=0.90$, $95\%CI$ 0.82~0.99)^[3]。

4.2 PUFAs对儿童健康的影响

4.2.1 婴幼儿神经发育及孤独症谱系障碍 DHA是视觉系统中视网膜光感受器和大脑皮质灰质的重要成分^[48]。人群研究发现,母亲妊娠期补充DHA,对婴幼儿的问题解决^[49]、动作^[50]及智力^[51]的发育有着积极影响。然而,一篇纳入15项随机对照研究的系统综述^[52]发现,含DHA、AA的配方奶粉喂养对足月婴儿的神经发育没有影响。而对于缺乏DHA的早产儿,配方奶粉或母乳中添加PUFAs有助于其神经发育^[6]。孤独症谱系障碍儿童补充n-3 PUFAs和n-6 PUFAs,可减轻孤独症谱系障碍症状(标准化均数差=-0.13, $95\%CI$ -0.34~-0.02)^[53]。目前,临床上建议患孤独症儿童补充n-3 PUFAs,并将其作为一种减轻核心症状的安全有效方法^[54]。

4.2.2 心血管健康 EPA和DHA对成人心血管健康的有益作用已被证实^[55],但在子代心血管健康方面尚无定论。相较于成人,婴儿心脏神经的支配由交感神经占优势,因此心率更快^[56]。既往研究^[7]发现孕晚期母亲血DHA、EPA浓度与子代6个月时的心率呈负相关,与心率变异性呈正相关,而AA的结果相反。出生后补充鱼油(n-3 PUFAs的浓缩来源)组婴儿的心率低于未补充鱼油组^[57]。食物富含DHA的足月儿与缺乏DHA摄入的足月儿相比,在4~6个月龄时的心率更低,心率变异性更高^[58]。

母亲孕中期血总n-3 PUFAs及DHA浓度百分比与其子代6岁时的收缩压呈负相关,n-6 PUFAs浓度百分比与收缩压呈正相关,未发现n-3 PUFAs和n-6 PUFAs与舒张压的关联^[59]。另有研究^[60]发现,脐带血AA水平及AA:DHA比值与9岁儿童舒张压呈负相关,与收缩压无关;DHA与舒张压和收缩压无关。此外,也有研究^[61]发现脐带血n-3 PUFAs及n-6 PUFAs水平与子代血压无关。

4.2.3 过敏性疾病 Pham等^[8]提出孕期n-3 PUFAs的摄入,可能影响子代免疫系统的发育,与过敏性疾病的遗传易感性存在交互作用。日本大阪妇幼健康研究^[62]发现,母亲孕期LA摄入量与子代患湿疹的风险呈正相关;荷兰队列研究^[63]报道孕妇血n-6 PUFAs与n-3 PUFAs比值与子代湿疹患病风险呈负相关。近期美国的一项研究^[9]报道,孕妇孕中期血n-6 PUFAs水平与子代患哮喘风险呈正相关,而n-3 PUFAs则相反。芬兰队列研究^[64]

发现, 孕妇高 n-6 PUFAs 和 n-3 PUFAs 摄入与 5 岁儿童过敏性鼻炎患病风险增加有关。

5 PUFAs 健康影响的可能作用机制

已知 AA 是促炎症前列腺素和白三烯的前体^[65], 具有促炎症作用; 而 EPA 和 DHA 通过诱导白介素-10 (interleukin-10, IL-10) 产生并抑制 IL-1 β 、肿瘤坏死因子 α (tumor necrosis factor- α , TNF- α) 的产生^[66], 减轻炎症反应。

5.1 作为过氧化物酶体增殖物激活受体的配体

过氧化物酶体增殖物激活受体 (peroxisome proliferator-activated receptors, PPARs) 属于配体依赖性转录因子核激素受体超家族, 在许多细胞生理过程 (如葡萄糖稳态、细胞分化、炎症反应等) 中发挥调控作用^[67]。EPA、DHA、AA 及其衍生物均是 PPARs 的天然配体^[68]。LA 和 EPA 通过调节 PPAR- α 促进小鼠胚胎干细胞血管细胞分化^[69]; DHA 和 EPA 通过调节 PPAR- γ 抑制转化生长因子 β 1 诱导的促肝纤维化作用, 对肝脏有保护作用^[70]; 此外, DHA 可上调 PPAR- γ , 改善小鼠胰岛素抵抗, 减轻炎症反应^[71]。

5.2 通过调节多种信号通路发挥作用

基础研究发现, n-3 PUFAs 可介导多种信号通路活化, 发挥减轻神经、肝脏、肾脏损伤等作用。例如, DHA 可调节 c-Jun 氨基末端激酶 (c-Jun N-terminal kinase, JNK) 信号通路介导的微管蛋白 Tau 磷酸化, 减轻脑损伤^[72]; DHA 还通过调节活性氧/JNK 信号通路, 减轻由甲基汞诱导的神经细胞损伤^[73]。在肝肾损伤方面, 有研究^[74]发现 DHA 和 EPA 治疗通过调节核因子 E2 相关因子 2 和核因子 κ B 信号通路减轻损伤。此外, DHA 还能调节 mTOR、B 淋巴细胞瘤-2 基因 (B-cell lymphoma-2, BCL-2) /BCL-2 相关蛋白 X 通路, 发挥抗炎、抗纤维化等作用^[75-76]。目前, 关于 n-6 PUFAs 对信号通路调节作用的研究较少。有研究^[77]发现 AA 可通过激活 WNT 信号, 对

肠上皮细胞增殖起正调控作用, 而对肠上皮细胞分化起负调控作用。

5.3 PUFAs 衍生物的健康保护作用

PUFAs 衍生的类内源性介质被称为“特异性促炎症消退介质” (specialized pro-resolving mediator, SPM), 具有限制炎症细胞浸润、活化, 促进组织内稳态恢复等作用^[78]。Resolvin D1 (RvD1) 由 DHA 合成, 通过抑制 TNF- α 诱导的 IL-1 β 产生^[79], 减少中性粒细胞浸润^[80], 从而减轻由缺血或脓毒症引起的器官损伤^[79, 81-82]。Maresin1 也是由 DHA 合成的 SPM, 研究发现其具有与 RvD1 类似的抗脓毒症损伤等作用^[83]。目前关于 SPM 的相关研究多为基础研究, 后续值得在动物及人群中继续探索。

5.4 通过激活 G 蛋白偶联受体 120 作用发挥保护性作用

G 蛋白偶联受体 120 (G protein-coupled receptor 120, GPR120) 是一种长链脂肪酸受体, 作为 n-3 PUFAs 的受体/传感器, 具有调节脂肪酸的抗炎、胰岛素增敏等作用^[84-85]。例如, Fan 等^[86]发现 DHA 和 AA 通过 GPR120 与核苷酸结合寡聚化结构域样受体蛋白 3 相互作用, 减轻脂多糖诱导的肝巨噬细胞 (库普弗细胞) 损伤; Chen 等^[87]发现 DHA 通过 GPR120/细胞外信号调节激酶通路, 减轻四氯化碳引起的肝脏氧化损伤。

6 结语

多不饱和脂肪酸是重要的营养素, 孕期 DHA 不足或缺乏可能与子痫、早产、低出生体质量及母亲产后抑郁发病风险增高有关, 并可影响子代神经发育、远期心血管健康以及增加过敏性疾病的发病风险。相反, 母亲孕期 LA、AA 摄入量过多可能与子代患湿疹、哮喘、过敏性鼻炎的风险增加有关。因此, 有必要建立孕妇及新生儿脐带血 PUFAs 的正常参考值范围, 以期早期发现母婴营养问题, 合理指导和干预。

参·考·文·献

- [1] Zhao WN, Hylton NK, Wang J, et al. Activation of WNT and CREB signaling pathways in human neuronal cells in response to the Omega-3 fatty acid docosahexaenoic acid (DHA)[J]. Mol Cell Neurosci, 2019, 99: 103386.
- [2] Bakouei F, Delavar MA, Mashayekh-Amiri S, et al. Efficacy of n-3 fatty acids supplementation on the prevention of pregnancy induced-hypertension or preeclampsia: a systematic review and meta-analysis[J]. Taiwan J Obstet Gynecol, 2020, 59(1): 8-15.
- [3] Middleton P, Gomersall JC, Gould JF, et al. Omega-3 fatty acid addition during pregnancy[J]. Cochrane Database Syst Rev, 2018, 11(11): CD003402.
- [4] Cinelli G, Fabrizi M, Ravà L, et al. Association between maternal and foetal

- erythrocyte fatty acid profiles and birth weight[J]. *Nutrients*, 2018, 10(4): 402.
- [5] Hoge A, Tabar V, Donneau AF, et al. Imbalance between omega-6 and omega-3 polyunsaturated fatty acids in early pregnancy is predictive of postpartum depression in a Belgian cohort[J]. *Nutrients*, 2019, 11(4): 876.
- [6] Wang Q, Cui Q, Yan C. The effect of supplementation of long-chain polyunsaturated fatty acids during lactation on neurodevelopmental outcomes of preterm infant from infancy to school age: a systematic review and meta-analysis[J]. *Pediatr Neurol*, 2016, 59: 54-61. e1.
- [7] Drewery ML, Gaitán AV, Spedale SB, et al. Maternal n-6 and n-3 fatty acid status during pregnancy is related to infant heart rate and heart rate variability: an exploratory study[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2017, 126: 117-125.
- [8] Pham MN, Bunyavanich S. Prenatal diet and the development of childhood allergic diseases: food for thought[J]. *Curr Allergy Asthma Rep*, 2018, 18(11): 58.
- [9] Rosa MJ, Hartman TJ, Adgent M, et al. Prenatal polyunsaturated fatty acids and child asthma: effect modification by maternal asthma and child sex[J]. *J Allergy Clin Immunol*, 2020, 145(3): 800-807. e4.
- [10] Basak S, Mallick R, Duttaroy AK. Maternal docosahexaenoic acid status during pregnancy and its impact on infant neurodevelopment[J]. *Nutrients*, 2020, 12(12): 3615.
- [11] Shrestha N, Holland OJ, Kent NL, et al. Maternal high linoleic acid alters placental fatty acid composition[J]. *Nutrients*, 2020, 12(8): 2183.
- [12] Zhang ZY, Fulgoni VL, Kris-Etherton PM, et al. Dietary intakes of EPA and DHA omega-3 fatty acids among US childbearing-age and pregnant women: an analysis of NHANES 2001–2014[J]. *Nutrients*, 2018, 10(4): 416.
- [13] Lewis RM, Wadsack C, Desoye G. Placental fatty acid transfer[J]. *Curr Opin Clin Nutr Metab Care*, 2018, 21(2): 78-82.
- [14] Metherel AH, Armstrong JM, Patterson AC, et al. Assessment of blood measures of n-3 polyunsaturated fatty acids with acute fish oil supplementation and washout in men and women[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2009, 81(1): 23-29.
- [15] Micalizzi G, Ragosta E, Farnetti S, et al. Rapid and miniaturized qualitative and quantitative gas chromatography profiling of human blood total fatty acids[J]. *Anal Bioanal Chem*, 2020, 412(10): 2327-2337.
- [16] Hoving LR, Heijink M, van Harmelen V, et al. GC-MS analysis of medium- and long-chain fatty acids in blood samples[J]. *Methods Mol Biol*, 2018, 1730: 257-265.
- [17] Petenuci ME, Dos Santos VJ, Gualda IP, et al. Fatty acid composition and nutritional profiles of *Brycon* spp. from central Amazonia by different methods of quantification[J]. *J Food Sci Technol*, 2019, 56(3): 1551-1558.
- [18] Hoge A, Bernardy F, Donneau AF, et al. Low omega-3 index values and monounsaturated fatty acid levels in early pregnancy: an analysis of maternal erythrocytes fatty acids[J]. *Lipids Health Dis*, 2018, 17(1): 63.
- [19] Kawabata T, Kagawa Y, Kimura F, et al. Polyunsaturated fatty acid levels in maternal erythrocytes of Japanese women during pregnancy and after childbirth[J]. *Nutrients*, 2017, 9(3): 245.
- [20] Araujo P, Kjelleve M, Nerhus I, et al. Fatty acid reference intervals in red blood cells among pregnant women in Norway-cross sectional data from the 'little in Norway' cohort[J]. *Nutrients*, 2020, 12(10): 2950.
- [21] Nita R, Kawabata T, Kagawa Y, et al. Associations of erythrocyte fatty acid compositions with FADS1 gene polymorphism in Japanese mothers and infants[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2020, 152: 102031.
- [22] Kitamura Y, Kogomori C, Hamano H, et al. Relationship between changes in fatty acid composition of the erythrocyte membranes and fatty acid intake during pregnancy in pregnant Japanese women[J]. *Ann Nutr Metab*, 2017, 70(4): 268-276.
- [23] Barrera C, Valenzuela R, Chamorro R, et al. The impact of maternal diet during pregnancy and lactation on the fatty acid composition of erythrocytes and breast milk of Chilean women[J]. *Nutrients*, 2018, 10(7): 839.
- [24] Much D, Brunner S, Vollhardt C, et al. Effect of dietary intervention to reduce the n-6/n-3 fatty acid ratio on maternal and fetal fatty acid profile and its relation to offspring growth and body composition at 1 year of age[J]. *Eur J Clin Nutr*, 2013, 67(3): 282-288.
- [25] Steer CD, Hibbeln JR, Golding J, et al. Polyunsaturated fatty acid levels in blood during pregnancy, at birth and at 7 years: their associations with two common FADS2 polymorphisms[J]. *Hum Mol Genet*, 2012, 21(7): 1504-1512.
- [26] Gellert S, Schuchardt JP, Hahn A. Higher omega-3 index and DHA status in pregnant women compared to lactating women: results from a German nation-wide cross-sectional study[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2016, 109: 22-28.
- [27] Matsumoto A, Kawabata T, Kagawa Y, et al. Associations of umbilical cord fatty acid profiles and desaturase enzyme indices with birth weight for gestational age in Japanese infants[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2021, 165: 102233.
- [28] Voortman T, Tieleman MJ, Stroobant W, et al. Plasma fatty acid patterns during pregnancy and child's growth, body composition, and cardiometabolic health: the Generation R Study[J]. *Clin Nutr*, 2018, 37(3): 984-992.
- [29] Wolfe MD, Chuang LT, Rayburn WF, et al. Low fatty acid concentrations in neonatal cord serum correlate with maternal serum[J]. *J Matern Fetal Neonatal Med*, 2012, 25(8): 1292-1296.
- [30] Otto SJ, Houwelingen AC, Antal M, et al. Maternal and neonatal essential fatty acid status in phospholipids: an international comparative study[J]. *Eur J Clin Nutr*, 1997, 51(4): 232-242.
- [31] Kim H, Oh B, Park-Min KH. Regulation of osteoclast differentiation and activity by lipid metabolism[J]. *Cells*, 2021, 10(1): 89.
- [32] Bruschi M, Santucci L, Petretto A, et al. Association between maternal omega-3 polyunsaturated fatty acids supplementation and preterm delivery: a proteomic study[J]. *FASEB J*, 2020, 34(5): 6322-6334.
- [33] Kitamura Y, Kogomori C, Hamano H, et al. Fatty acid composition of the erythrocyte membranes varies between early-term, full-term, and late-term infants in Japan[J]. *Ann Nutr Metab*, 2018, 73(4): 335-343.
- [34] Montes R, Chisaguano AM, Castellote AI, et al. Fatty-acid composition of maternal and umbilical cord plasma and early childhood atopic eczema in a Spanish cohort[J]. *Eur J Clin Nutr*, 2013, 67(6): 658-663.
- [35] Kohlboeck G, Glaser C, Tiesler C, et al. Effect of fatty acid status in cord blood serum on children's behavioral difficulties at 10 y of age: results from the LISAPLUS Study[J]. *Am J Clin Nutr*, 2011, 94(6): 1592-1599.
- [36] Stewart DE, Vigod SN. Postpartum depression: pathophysiology, treatment, and emerging therapeutics[J]. *Annu Rev Med*, 2019, 70: 183-196.
- [37] Hibbeln JR. Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national, ecological analysis[J]. *J Affect Disord*, 2002, 69(1/2/3): 15-29.
- [38] Otto SJ, de Groot RH, Hornstra G. Increased risk of postpartum depressive symptoms is associated with slower normalization after pregnancy of the functional docosahexaenoic acid status[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2003, 69(4): 237-243.
- [39] Hsu MC, Tung CY, Chen HE. Omega-3 polyunsaturated fatty acid supplementation in prevention and treatment of maternal depression: putative mechanism and recommendation[J]. *J Affect Disord*, 2018, 238: 47-61.
- [40] Trujillo J, Vieira MC, Lepsch J, et al. A systematic review of the associations between maternal nutritional biomarkers and depression and/or anxiety during pregnancy and postpartum[J]. *J Affect Disord*, 2018, 232: 185-203.
- [41] Turbeville HR, Sasser JM. Preeclampsia beyond pregnancy: long-term consequences for mother and child[J]. *Am J Physiol Renal Physiol*, 2020, 318(6): F1315-F1326.
- [42] Kulkarni AV, Mehendale SS, Yadav HR, et al. Circulating angiogenic factors and their association with birth outcomes in preeclampsia[J]. *Hypertens Res*, 2010, 33(6): 561-567.
- [43] Mackay VA, Huda SS, Stewart FM, et al. Preeclampsia is associated with compromised maternal synthesis of long-chain polyunsaturated fatty acids, leading to offspring deficiency[J]. *Hypertension*, 2012, 60(4): 1078-1085.
- [44] Vogel JP, Chawanpaiboon S, Moller AB, et al. The global epidemiology of preterm birth[J]. *Best Pract Res Clin Obstet Gynaecol*, 2018, 52: 3-12.
- [45] Martin JA, Osterman MJK. Describing the increase in preterm births in the United States, 2014–2016[J]. *NCHS Data Brief*, 2018(312): 1-8.
- [46] Makrides M, Best K, Yelland L, et al. A randomized trial of prenatal n-3 fatty acid supplementation and preterm delivery[J]. *N Engl J Med*, 2019, 381(11): 1035-1045.
- [47] Kesavan K, Devaskar SU. Intrauterine growth restriction: postnatal monitoring and outcomes[J]. *Pediatr Clin North Am*, 2019, 66(2): 403-423.
- [48] Sun GY, Simonyi A, Fritsche KL, et al. Docosahexaenoic acid (DHA): an essential nutrient and a nutraceutical for brain health and diseases[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2018, 136: 3-13.
- [49] Braarud H, Markhus M, Skotheim S, et al. Maternal DHA status during pregnancy has a positive impact on infant problem solving: a Norwegian prospective observation study[J]. *Nutrients*, 2018, 10(5): 529.
- [50] Ogaz-González R, Mérida-Ortega Á, Torres-Sánchez L, et al. Maternal dietary intake of polyunsaturated fatty acids modifies association between prenatal DDT exposure and child neurodevelopment: a cohort study[J]. *Environ Pollut*, 2018, 238: 698-705.
- [51] Colombo J, Shaddy DJ, Gustafson K, et al. The Kansas University DHA Outcomes Study (KUDOS) clinical trial: long-term behavioral follow-up of the effects of prenatal DHA supplementation[J]. *Am J Clin Nutr*, 2019, 109(5): 1380-1392.
- [52] Jasani B, Simmer K, Patole SK, et al. Long chain polyunsaturated fatty acid

- supplementation in infants born at term[J]. *Cochrane Database Syst Rev*, 2017, 3(3): CD000376.
- [53] de Andrade Wobido K, de Sá Barreto da Cunha M, Miranda SS, et al. Non-specific effect of omega-3 fatty acid supplementation on autistic spectrum disorder: systematic review and meta-analysis[J]. *Nutr Neurosci*, 2021: 1-13.
- [54] Infante M, Sears B, Rizzo AM, et al. Omega-3 PUFAs and vitamin D co-supplementation as a safe-effective therapeutic approach for core symptoms of autism spectrum disorder: case report and literature review[J]. *Nutr Neurosci*, 2020, 23(10): 779-790.
- [55] Innes JK, Calder PC. Marine omega-3 (N-3) fatty acids for cardiovascular health: an update for 2020[J]. *Int J Mol Sci*, 2020, 21(4): 1362.
- [56] Bar-Haim Y, Marshall PJ, Fox NA. Developmental changes in heart period and high-frequency heart period variability from 4 months to 4 years of age[J]. *Dev Psychobiol*, 2000, 37(1): 44-56.
- [57] Vuholm S, Teisen MN, Mølgaard C, et al. Sleep and physical activity in healthy 8–9-year-old children are affected by oily fish consumption in the FiSK Junior randomized trial[J]. *Eur J Nutr*, 2021, 60(6): 3095-3106.
- [58] Pivik RT, Dykman RA, Jing H, et al. Early infant diet and the omega 3 fatty acid DHA: effects on resting cardiovascular activity and behavioral development during the first half-year of life[J]. *Dev Neuropsychol*, 2009, 34(2): 139-158.
- [59] Vidakovic AJ, Gishti O, Steenweg-de Graaff J, et al. Higher maternal plasma n-3 PUFA and lower n-6 PUFA concentrations in pregnancy are associated with lower childhood systolic blood pressure[J]. *J Nutr*, 2015, 145(10): 2362-2368.
- [60] Seggers J, Kikkert HK, de Jong C, et al. Neonatal fatty acid status and cardiometabolic health at 9 years[J]. *Early Hum Dev*, 2016, 100: 55-59.
- [61] Lauritzen L, Eriksen SE, Hjorth MF, et al. Maternal fish oil supplementation during lactation is associated with reduced height at 13 years of age and higher blood pressure in boys only[J]. *Br J Nutr*, 2016, 116(12): 2082-2090.
- [62] Umehara M, Yamagishi K, Iso H. Intake of fish and long-chain n-3 polyunsaturated fatty acids and risk of diseases in a Japanese population: a narrative review[J]. *Eur J Clin Nutr*, 2021, 75(6): 902-920.
- [63] Mensink-Bout SM, Voortman T, Dervishaj M, et al. Associations of plasma fatty acid patterns during pregnancy with respiratory and allergy outcomes at school age[J]. *Nutrients*, 2020, 12(10): 3057.
- [64] Nwaru BI, Erkkola M, Lumia M, et al. Maternal intake of fatty acids during pregnancy and allergies in the offspring[J]. *Br J Nutr*, 2012, 108(4): 720-732.
- [65] Innes JK, Calder PC. Omega-6 fatty acids and inflammation[J]. *Prostaglandins Leukot Essent Fatty Acids*, 2018, 132: 41-48.
- [66] Céspedes N, Tamayo A, Rodriguez MJ, et al. EPA plus DHA improves survival related to a decrease of injury after extended liver ischemia in Sprague-Dawley rats[J]. *Ann Hepatol*, 2020, 19(2): 172-178.
- [67] Hong F, Pan SJ, Guo Y, et al. PPARs as nuclear receptors for nutrient and energy metabolism[J]. *Molecules*, 2019, 24(14): 2545.
- [68] Korbecki J, Bobiński R, Dutka M. Self-regulation of the inflammatory response by peroxisome proliferator-activated receptors[J]. *Inflamm Res*, 2019, 68(6): 443-458.
- [69] Taha A, Sharifpanah F, Wartenberg M, et al. Omega-3 and Omega-6 polyunsaturated fatty acids stimulate vascular differentiation of mouse embryonic stem cells[J]. *J Cell Physiol*, 2020, 235(10): 7094-7106.
- [70] Hu SQ, Bae M, Park YK, et al. N-3 PUFAs inhibit TGFβ1-induced profibrogenic gene expression by ameliorating the repression of PPARγ in hepatic stellate cells[J]. *J Nutr Biochem*, 2020, 85: 108452.
- [71] Wei WT, Hu MJ, Huang J, et al. Anti-obesity effects of DHA and EPA in high fat-induced insulin resistant mice[J]. *Food Funct*, 2021, 12(4): 1614-1625.
- [72] Zhu W, Zhao L, Li T, et al. Docosahexaenoic acid ameliorates traumatic brain injury involving JNK-mediated Tau phosphorylation signaling[J]. *Neurosci Res*, 2020, 157: 44-50.
- [73] Zhang H, Wang SS, Wang YQ, et al. DHA ameliorates MeHg-induced PC12 cell apoptosis by inhibiting the ROS/JNK signaling pathway[J]. *Mol Med Rep*, 2021, 24(2): 558.
- [74] Eraky SM, Abo El-Magd NF. Omega-3 fatty acids protect against acetaminophen-induced hepatic and renal toxicity in rats through HO-1-Nrf2-BACH1 pathway[J]. *Arch Biochem Biophys*, 2020, 687: 108387.
- [75] Shan C, Wang R, Wang S, et al. Endogenous production of n-3 polyunsaturated fatty acids protects mice from carbon tetrachloride-induced liver fibrosis by regulating mTOR and Bcl-2/Bax signalling pathways[J]. *Exp Physiol*, 2021, 106(4): 983-993.
- [76] Ahn YJ, Lim JW, Kim H. Docosahexaenoic acid induces expression of NAD(P)H: quinone oxidoreductase and heme oxygenase-1 through activation of Nrf2 in cerulein-stimulated pancreatic acinar cells[J]. *Antioxidants*, 2020, 9(11): 1084.
- [77] Wang Q, Lin Y, Sheng X, et al. Arachidonic acid promotes intestinal regeneration by activating WNT signaling[J]. *Stem Cell Reports*, 2020, 15(2): 374-388.
- [78] Flitter BA, Fang X, Matthay MA, et al. The potential of lipid mediator networks as ocular surface therapeutics and biomarkers[J]. *Ocul Surf*, 2021, 19: 104-114.
- [79] Chen JJ, Chen J, Jiang ZX, et al. Resolvin D1 alleviates cerebral ischemia/reperfusion injury in rats by inhibiting NLRP3 signaling pathway[J]. *J Biol Regul Homeost Agents*, 2020, 34(5). DOI: 10.23812/20-392-A.
- [80] Liu GJ, Tao T, Zhang XS, et al. Resolvin D1 attenuates innate immune reactions in experimental subarachnoid hemorrhage rat model[J]. *Mol Neurobiol*, 2021, 58(5): 1963-1977.
- [81] Wang ML, Liu ML, Zhang JS, et al. Resolvin D1 protects against sepsis-induced cardiac injury in mice[J]. *BioFactors*, 2020, 46(5): 766-776.
- [82] Zhuo YZ, Zhang SK, Li CX, et al. Resolvin D1 promotes SIRT1 expression to counteract the activation of STAT3 and NF-κB in mice with septic-associated lung injury[J]. *Inflammation*, 2018, 41(5): 1762-1771.
- [83] Xia H, Wang F, Wang M, et al. Maresin1 ameliorates acute lung injury induced by sepsis through regulating Th17/Treg balance[J]. *Life Sci*, 2020, 254: 117773.
- [84] Kang S, Huang J, Lee BK, et al. Omega-3 polyunsaturated fatty acids protect human hepatoma cells from developing steatosis through FFA4 (GPR120)[J]. *Biochim Biophys Acta Mol Cell Biol Lipids*, 2018, 1863(2): 105-116.
- [85] Castilla-Madriral R, Barrenetxe J, Moreno-Aliaga MJ, et al. EPA blocks TNF-α-induced inhibition of sugar uptake in Caco-2 cells via GPR120 and AMPK[J]. *J Cell Physiol*, 2018, 233(3): 2426-2433.
- [86] Fan G, Li Y, Chen J, et al. DHA/AA alleviates LPS-induced Kupffer cells pyroptosis via GPR120 interaction with NLRP3 to inhibit inflammasome complexes assembly[J]. *Cell Death Dis*, 2021, 12(1): 73.
- [87] Chen JL, Wang DP, Zong YB, et al. DHA protects hepatocytes from oxidative injury through GPR120/ERK-mediated mitophagy[J]. *Int J Mol Sci*, 2021, 22(11): 5675.

[收稿日期] 2021-08-04

[本文编辑] 崔黎明