Advances in Clinical Medicine 临床医学进展, 2022, 12(10), 9288-9293
Published Online October 2022 in Hans. http://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2022.12101343

Hans汉斯

脂肪细胞因子在心血管疾病中的研究进展

樊纯祯[1]，王军珂[2]，戴红艳[3*]

[1]青岛大学附属青岛市市立医院，山东 青岛
[2]青岛大学青岛医学院，山东 青岛
[3]青岛市市立医院心脏中心，山东 青岛

收稿日期：2022年9月18日；录用日期：2022年10月8日；发布日期：2022年10月17日

摘 要

心血管疾病(Cardiovascular disease, CVD)在我国患病率和致死率一直高居榜首，至今仍处于上升阶段，影响个人健康的同时也加重了社会负担。而肥胖是心血管病的独立危险因素。脂肪组织不仅可以储存脂肪，也是重要的内分泌器官，能分泌大量的脂肪因子，对调控代谢、抗炎症反应、抗氧化应激等方面有重要作用。随着脂肪细胞因子与代谢综合征、卒中等关系的深入研究，人们对其与心血管疾病的关系也愈发关注。本文总结了几种脂肪细胞因子在心血管疾病中的研究进展，包括脂联素(Adiponectin)、瘦素(leptin)、白脂素(Asprosin)。

关键词

心血管疾病，脂肪细胞因子，脂联素，瘦素，白脂素

Research Progress of Adipocytokines in Cardiovascular Diseases

Chunzhen Fan[1], Junke Wang[2], Hongyan Dai[3*]

[1]The Affiliated Qingdao Municipal Hospital of Qingdao University, Qingdao Shandong
[2]Qingdao Medical College of Qingdao University, Qingdao Shandong
[3]Heart Center of Qingdao Municipal Hospital, Qingdao Shandong

Received: Sep. 18th, 2022; accepted: Oct. 8th, 2022; published: Oct. 17th, 2022

Abstract

Cardiovascular disease (CVD) has the highest morbidity and mortality in my country, and it is still

*通讯作者。

文章引用: 樊纯祯, 王军珂, 戴红艳. 脂肪细胞因子在心血管疾病中的研究进展[J]. 临床医学进展, 2022, 12(10): 9288-9293. DOI: 10.12677/acm.2022.12101343

on the rise. It affects individual health and also increases social burden. Obesity is an independent risk factor for cardiovascular disease. Adipose tissue can not only store fat, but also an important endocrine organ, which can secrete a large number of adipokines, which play an important role in regulating metabolism, anti-inflammatory response, and anti-oxidative stress. With the in-depth study of the relationship between adipocytokines and metabolic syndrome, stroke, etc., people are paying more and more attention to the relationship between adipocytokines and cardiovascular diseases. This paper summarizes the research progress of several adipocytokines in cardiovascular diseases, including Adiponectin, leptin, Asprosin.

Keywords

Cardiovascular Disease, Adipocytokines, Adiponectin, Leptin, Asprosin

1. 引言

《全球心血管疾病和危险因素负担1990~2019》提示血管疾病患病人数从1990年的2.71亿增加到2019年的5.23亿，其中因心血管疾病死亡的人数占全球总死亡人数的1/3左右。根据《中国心血管健康与疾病报告2021》[1]显示我国每5例死亡中就有2例死于心血管疾病。鉴于其严重程度，心血管疾病越来越被重视，世界卫生组织于2010年发现50岁之前严格控制CVD的发病危险因素，可以预防90%的动脉粥样硬化性心血管疾病[2]，而肥胖是导致心血管病、高脂血症、糖尿病、代谢综合征等多种疾病的重要原因。

脂肪组织不仅可以储存脂肪，也是重要的内分泌器官，以自分泌、旁分泌等多种方式分泌脂肪因子，对调控代谢、抗炎症反应、抗氧化应激等方面有重要作用[3]。近年来，研究发现脂肪细胞因子与心血管疾病的发生、发展着密切的联系，其在心血管疾病中扮演着复杂且重要的角色，有望成为治疗靶点。许多学者认为脂肪细胞因子是“脂肪–心血管轴”的中介[4]。本文旨在论述几种脂肪细胞因子在心血管疾病中的研究进展。

2. 脂联素在心血管疾病中的研究进展

脂联素(Adiponectin, ADPN)是由脂肪组织分泌的血浆蛋白，有抗糖尿病、抗炎及抗动脉粥样硬化等作用[5] [6] [7]。研究表明，高脂联素水平能降低冠状动脉疾病风险，可作为冠心病患者临床预后的预测因子[8] [9]。进一步研究发现，脂联素的抗动脉粥样硬化特性是在通过磷脂酰肌醇 3-激酶依赖途径和AMPK 途径内皮细胞中产生一氧化氮[10]。而一氧化氮可使血管松弛，并对血管壁产生抗炎和抗血栓作用[11]。另外，脂联素可通过其受体(AdiopRs)改善脂毒性，Kim Y [12]等研究发现，脂联素受体激动剂通过增加 AdipoR 表达和激活 AMPK-PPARα/PGC-1α 等通路，调节心脏的氧化应激、炎症和细胞凋亡，从而改善心脏脂质代谢、肥大和功能参数。研究表明[13]，脂联素能够抑制巨噬细胞平滑肌细胞增殖和TNF-α表达，从而抑制巨噬细胞转化为泡沫细胞。Naryzhnaya NV [14]等研究表明，血清脂联素水平下降是严重冠状动脉粥样硬化患者心外膜脂肪组织(EAT)脂肪细胞氧化应激强度的重要独立决定因素。另有研究发现脂联素可预测心衰患者[15]的死亡率和发病率，同时也是急性心肌梗死患者[16]心血管风险的独立预测因子。可以肯定的是脂联素与心血管疾病密切相关。但由于试验方法存在局限且研究样本量较少有可能形成试验误差。因此，可进一步增加样本量并改进试验方法，采用前瞻性研究、细胞研究和动物研究深入

探讨脂联素与心血管疾病的关系，并加大对分子机制的研究。

3. 瘦素在心血管疾病中的研究进展

1994 年，发现了第一个脂肪因子瘦素[17]。有研究[18]发现瘦素通过下丘脑发送营养状况信号从而调节体重，下丘脑产生神经递质调节摄入食物和消耗能量的平衡。瘦素的外周作用包括刺激炎症反应、氧化应激、动脉粥样硬化形成和血栓形成[19]。Sathish 等学者[20]研究发现瘦素可诱导炎症和内皮功能障碍，引起血管收缩，也可促进血管平滑肌细胞迁移和增殖，增加动脉粥样硬化斑块的易损性和破裂风险。瘦素对平滑肌细胞增殖的刺激作用是通过结合瘦素受体(Lep-R)并通过诱导细胞周期蛋白 D1 的表达来介导的，细胞周期蛋白 D1 通过 MAPK 途径促进细胞增殖[21]。此外，瘦素通过增加细胞粘附分子和组织因子的表达影响冠状动脉的内皮细胞[22]。然而关于瘦素与心血管疾病的临床研究却得到了相互矛盾的结果。有研究表明[23]，空腹血浆瘦素水平升高可预测冠心病患者短期内急性冠脉综合征或心力衰竭的发生。冠状动脉粥样硬化的存在、严重程度和病变复杂性与冠心病患者的瘦素水平较高有关[24]。射血分数保留型心衰和射血分数降低型心衰患者的瘦素水平也高于对照组[25]。Aurelian 等[26]在杰克逊心脏研究(JHS)中评估了瘦素与非裔美国人心血管事件风险的前瞻性关联表明瘦素与冠心病无关。也有一项荟萃分析[27]纳入了 13 项研究，共 4257 名心血管疾病患者和 26710 名对照者，采用随机效应模型的 meta 分析表明，瘦素可显著增加冠心病的风险(OR = 1.16, 95% CI 1.02~1.32)，但进一步调整其他心血管危险因素后并没有发现相关性(OR = 1.16, 95% CI 0.97~1.40)，表明瘦素水平与冠心病的风险没有关系。另一项前瞻性巢式病例对照研究的结果表明，在平均 11.4 年的随访时间内，6502 名参与者的血清瘦素水平与 CVD 风险之间没有相关性[28]。目前有关瘦素与冠心病的研究有一定的矛盾，其之间是否存在相关性，以及瘦素是否可以作为预测和诊断冠心病的生物标志物还需扩大样本量或多中心进一步验证。

4. 白脂素在心血管疾病中的研究进展

白脂素(Asprosin)由全身白色脂肪组织合成，是 2016 年 Romere C [29]等在研究新生儿型早衰症(neonatal progeroid syndrome, NPS)患者时发现的新型脂肪因子，它是原纤维蛋白-1 (fibrillin-1, FBN-1)第 65 和 66 位外显子编码后再进行剪切修饰而成，可通过激活 G 蛋白-cAMP-PKA 信号通路促进肝脏释放葡萄糖，引起血中胰岛素水平增高。此外，Asprosin 能穿过血脑屏障，促进食欲从而引起体重增加[30]。据报道，Asprosin 与多种心血管疾病密切相关，其中可能与冠心病的发病机制有关，尤其是通过胰岛素抵抗和血脂异常[31]。Asprosin 是维持能量代谢稳态的关键调节因子[32]。据报道[33] Asprosin 可能通过激活蛋白激酶(PK)A 通路使血管平滑肌细胞表型维持分化状态，从而抑制动脉粥样硬化。Asprosin 也可通过抑制 AMPK-mTOR 途径自噬，促进β细胞凋亡[34]，并通过 TLR4/JNK 介导的途径与 Toll 样受体 4(TLR4)结合，从而增加促炎性细胞因子和活性氧(ROS)的产生[35]。J. Zou 等学者研究表明[36]，Asprosin 通过上调抑制巨噬细胞中的脂质积累并降低 apoE-/-小鼠的动脉粥样硬化负担。通过激活 p38/Elk-1 信号通路表达 ABCA1 和 ABCG1。Guven C 等研究表明[37]，高血清 Asprosin 水平联合冠状动脉狭窄数量可诊断冠心病的严重程度。徐佰达[38]等的临床试验结果提示血浆 Asprosin 对冠心病有保护作用，对治疗缺血性心脏病存在潜在价值。Wang 等研究表示[39]，血浆 Asprosin 可作为动脉粥样硬化的重要标志物。Zhang Z [40]发现 Asprosin 通过激活 ERK1/2-SOD2 途径抑制细胞凋亡，从而改善了心肌梗死(myocardial infarction, MI)的间充质基质细胞(mesenchymal stromal cell, MSC)的存活。X. Deng 等[41]研究发现 T2DM 合并颈动脉斑块患者血清 Asprosin 水平显著升高，提示其可能在 T2DM 颈动脉斑块的发生发展中发挥作用，主要通过调节高血糖和胰岛素抵抗参与了动脉粥样硬化的发生发展。以上研究均表明，Asprosin 与心血管疾病关系密切，但横断面研究存在局限性，仅用于判断其相关性，不能说明 Asprosin 与心血管疾病发病的

因果关系，仍需更大样本量的前瞻性研究或动物实验进一步明确 Asprosin 与心血管疾病的关系。

5. 总结与展望

脂肪细胞因子对心血管疾病的重要作用逐渐得到了证实。脂联素、瘦素、白脂素等作为重要的脂肪细胞因子，与冠心病、动脉粥样硬化、房颤、高血压、心力衰竭等心血管疾病的相关性也得到证实。脂肪细胞因子也可能通过改善胰岛素抵抗、抗炎、抗动脉粥样硬化、改善内皮功能等，在心血管疾病中起到积极的诊疗作用。但脂肪细胞因子能否评估心血管疾病的风险及预后，仍需要多中心、大规模的临床研究证实。

参考文献

[1] 中国心血管健康与疾病报告编写组. 中国心血管健康与疾病报告 2021 概要[J]. 中国循环杂志, 2022, 37(6): 553-578.

[2] Reamy, B.V., Williams, P.M. and Kuckel, D.P. (2018) Prevention of Cardiovascular Disease. *Primary Care*, **45**, 25-44. https://doi.org/10.1016/j.pop.2017.11.003

[3] Watanabe, T., Watanabe-Kominato, K., Takahashi, Y., Kojima, M. and Watanabe, R. (2017) Adipose Tissue-Derived Omentin-1 Function and Regulation. *Comprehensive Physiology*, **7**, 765-781. https://doi.org/10.1002/cphy.c160043

[4] Van de Voorde, J., Pauwels, B., Boydens, C. and Decaluwe, K. (2013) Adipocytokines in Relation to Cardiovascular Disease. *Metabolism*, **62**, 1513-1521. https://doi.org/10.1016/j.metabol.2013.06.004

[5] Kern, P.A., Lu, T., Rassouli, N. and Ranganathan, G. (2003) Adiponectin Expression from Human Adipose Tissue: Relation to Obesity, Insulin Resistance, and Tumor Necrosis Factor-Alpha Expression. *Diabetes*, **52**, 1779-1785. https://doi.org/10.2337/diabetes.52.7.1779

[6] Lee, B. and Shao, J. (2014) Adiponectin and Energy Homeostasis. *Reviews in Endocrine and Metabolic Disorders*, **15**, 149-156. https://doi.org/10.1007/s11154-013-9283-3

[7] Ohashi, K., Ouchi, N. and Matsuzawa, Y. (2012) Anti-Inflammatory and Anti-Atherogenic Properties of Adiponectin. *Biochimie*, **94**, 2137-2142. https://doi.org/10.1016/j.biochi.2012.06.008

[8] Inoue, T., Kotooka, N., Morooka, T., Komoda, H., Uchida, T., Aso, Y., *et al*. (2007) High Molecular Weight Adiponectin as a Predictor of Long-Term Clinical Outcome in Patients with Coronary Artery Disease. *American Journal of Cardiology*, **100**, 569-574. https://doi.org/10.1016/j.amjcard.2007.03.062

[9] Zhang, M., Chen, X., Zhu, Y., Yin, L., Quan, Z., Ou, Y., *et al*. (2022) Causal Associations of Circulating Adiponectin with Cardiometabolic Diseases and Osteoporotic Fracture. *Scientific Reports*, **12**, Article No. 6689. https://doi.org/10.1038/s41598-022-10586-1

[10] Di Chiara, T., Licata, A., Argano, C., Duro, G., Corrao, S. and Scaglione, R. (2014) Plasma Adiponectin: A Contributing Factor for Cardiac Changes in Visceral Obesity-Associated Hypertension. *Blood Pressure*, **23**, 147-153. https://doi.org/10.3109/08037051.2013.823767

[11] Chen, Z., Peng, I.C., Sun, W., Su, M.I., Hsu, P.H., Fu, Y., *et al*. (2009) AMP-Activated Protein Kinase Functionally Phosphorylates Endothelial Nitric Oxide Synthase Ser633. *Circulation Research*, **104**, 496-505. https://doi.org/10.1161/CIRCRESAHA.108.187567

[12] Kim, Y., Lim, J.H., Kim, E.N., Hong, Y.A., Park, H.J., Chung, S., *et al*. (2022) Adiponectin Receptor agonist Ameliorates Cardiac Lipotoxicity via Enhancing Ceramide Metabolism in Type 2 Diabetic Mice. *Cell Death & Disease*, **13**, Article No. 282. https://doi.org/10.1038/s41419-022-04726-8

[13] Ouchi N KS, Arita, Y., Nishida, M., Matsuyama, A., Okamoto, Y., Ishigami, M., Kuriyama, H., *et al*. (2001) Adipocyte-Derived Plasma Protein, Adiponectin, Suppresses Lipid Accumulation and Class A Scavenger Receptor Expression in Human Monocyte-Derived Macrophages. *Circulation*, **103**, 1057-1063. https://doi.org/10.1161/01.CIR.103.8.1057

[14] Naryzhnaya, N.V., Koshelskaya, O.A., Kologrivova, I.V., Suslova, T.E., Kharitonova, O.A., Andreev, S.L., *et al*. (2022) Production of Reactive Oxygen Species by Epicardial Adipocytes Is Associated with an Increase in Postprandial Glycemia, Postprandial Insulin, and a Decrease in Serum Adiponectin in Patients with Severe Coronary Atherosclerosis. *Biomedicines*, **10**, Article No. 2054. https://doi.org/10.3390/biomedicines10082054

[15] George, J., Patal, S., Wexler, D., Sharabi, Y., Peleg, E., Kamari, Y., *et al*. (2006) Circulating Adiponectin Concentrations in Patients with Congestive Heart Failure. *Heart*, **92**, 1420-1424. https://doi.org/10.1136/hrt.2005.083345

[16] Kojima, S., Funahashi, T., Otsuka, F., Maruyoshi, H., Yamashita, T., Kajiwara, I., *et al*. (2007) Future Adverse Cardiac

Events Can Be Predicted by Persistently Low Plasma Adiponectin Concentrations in Men and Marked Reductions of Adiponectin in Women after Acute Myocardial Infarction. *Atherosclerosis*, **194**, 204-213. https://doi.org/10.1016/j.atherosclerosis.2006.07.028

[17] Zhang Y PR, Maffei, M., Barone, M., Leopold, L. and Friedman, J.M. (1994) Positional Cloning of the Mouse Obese Gene and Its Human Homologue. *Nature*, **372**, 425-32. https://doi.org/10.1038/372425a0

[18] Friedman, J.M. (1998) Leptin, Leptin Receptors, and the Control of Body Weight. *Nutrition Reviews*, **56**, S38-S46. https://doi.org/10.1111/j.1753-4887.1998.tb01685.x

[19] Liberale, L., Bonaventura, A., Vecchie, A., Casula, M., Dallegri, F., Montecucco, F., *et al*. (2017) The Role of Adipocytokines in Coronary Atherosclerosis. *Current Atherosclerosis Reports*, **19**, Article No. 21. https://doi.org/10.1007/s11883-017-0657-y

[20] Vasamsetti, S.B., Natarajan, N., Sadaf, S., Florentin, J. and Dutta, P. (2022) Regulation of Cardiovascular Health and Disease by Visceral Adipose Tissue-Derived Metabolic Hormones. *The Journal of Physiology*. https://doi.org/10.1113/JP282728

[21] Huang, F., Xiong, X., Wang, H., You, S. and Zeng, H. (2010) Leptin-Induced Vascular Smooth Muscle Cell Proliferation via Regulating Cell Cycle, Activating ERK1/2 and NF-κB. *Acta Biochim Biophys Sin* (*Shanghai*), **42**, 325-331. https://doi.org/10.1093/abbs/gmq025

[22] Cirillo, P., Angri, V., De Rosa, S., Cali, G., Petrillo, G., Maresca, F., *et al*. (2010) Pro-Atherothrombotic Effects of Leptin in Human Coronary Endothelial Cells. *Thrombosis and Haemostasis*, **103**, 1065-1075. https://doi.org/10.1160/TH09-06-0392

[23] Puurunen, V.P., Kiviniemi, A., Lepojarvi, S., Piira, O.P., Hedberg, P., Junttila, J., *et al*. (2017) Leptin Predicts Short-Term Major Adverse Cardiac Events in Patients with Coronary Artery Disease. *Annals of Medicine*, **49**, 448-454. https://doi.org/10.1080/07853890.2017.1301678

[24] Hasan-Ali, H., Abd El-Mottaleb, N.A., Hamed, H.B. and Abd-Elsayed, A. (2011) Serum Adiponectin and Leptin as Predictors of the Presence and Degree of Coronary Atherosclerosis. *Coronary Artery Disease*, **22**, 264-269. https://doi.org/10.1097/MCA.0b013e3283452431

[25] Faxen, U.L., Hage, C., Andreasson, A., Donal, E., Daubert, J.C., Linde, C., *et al*. (2017) HFpEF and HFrEF Exhibit Different Phenotypes as Assessed by Leptin and Adiponectin. *International Journal of Cardiology*, **228**, 709-716. https://doi.org/10.1016/j.ijcard.2016.11.194

[26] Bidulescu, A., Liu, J., Chen, Z., Hickson, D.A., Musani, S.K., Samdarshi, T.E., *et al*. (2013) Associations of Adiponectin and Leptin with Incident Coronary Heart Disease and Ischemic Stroke in African Americans: The Jackson Heart Study. *Frontiers in Public Health*, **1**, Article No. 16. https://doi.org/10.3389/fpubh.2013.00016

[27] Yang, H., Guo, W., Li, J., Cao, S., Zhang, J., Pan, J., *et al*. (2017) Leptin Concentration and Risk of Coronary Heart Disease and Stroke: A Systematic Review and Meta-Analysis. *PLOS ONE*, **12**, e0166360. https://doi.org/10.1371/journal.pone.0166360

[28] Seven, E., Husemoen, L.L., Sehested, T.S., Ibsen, H., Wachtell, K., Linneberg, A., *et al*. (2015) Adipocytokines, C-Reactive Protein, and Cardiovascular Disease: A Population-Based Prospective Study. *PLOS ONE*, **10**, Article ID: e0128987. https://doi.org/10.1371/journal.pone.0128987

[29] Romere, C., Duerrschmid, C., Bournat, J., Constable, P., Jain, M., Xia, F., *et al*. (2016) Asprosin, a Fasting-Induced Glucogenic Protein Hormone. *Cell*, **165**, 566-579. https://doi.org/10.1016/j.cell.2016.02.063

[30] Duerrschmid, C., He, Y., Wang, C., Li, C., Bournat, J.C., Romere, C., *et al*. (2017) Asprosin Is a Centrally Acting Orexigenic Hormone. *Nature Medicine*, **23**, 1444-1453. https://doi.org/10.1038/nm.4432

[31] Moradi, N., Fouani, F.Z., Vatannejad, A., Bakhti Arani, A., Shahrzad, S. and Fadaei, R. (2021) Serum Levels of Asprosin in Patients Diagnosed with Coronary Artery Disease (CAD): A Case-Control Study. *Lipids in Health and Disease*, **20**, Article No. 88. https://doi.org/10.1186/s12944-021-01514-9

[32] Ovali, M.A. and Bozgeyik, I. (2022) Asprosin, a C-Terminal Cleavage Product of Fibrillin 1 Encoded by the FBN1 Gene, in Health and Disease. *Molecular Syndromology*, **13**, 175-183. https://doi.org/10.1159/000520333

[33] Zhu, Q., Ni, X.Q., Lu, W.W., Zhang, J.S., Ren, J.L., Wu, D., *et al*. (2017) Intermedin Reduces Neointima Formation by Regulating Vascular Smooth Muscle Cell Phenotype via cAMP/PKA Pathway. *Atherosclerosis*, **266**, 212-222. https://doi.org/10.1016/j.atherosclerosis.2017.10.011

[34] Wang, R. and Hu, W. (2021) Asprosin Promotes Beta-Cell Apoptosis by Inhibiting the Autophagy of Beta-Cell via AMPK-mTOR Pathway. *Journal of Cellular Physiology*, **236**, 215-221. https://doi.org/10.1002/jcp.29835

[35] Lee, T., Yun, S., Jeong, J.H. and Jung, T.W. (2019) Asprosin Impairs Insulin Secretion in Response to Glucose and viability through TLR4/JNK-mediated inflammation. *Molecular and Cellular Endocrinology*, **486**, 96-104. https://doi.org/10.1016/j.mce.2019.03.001

[36] Zou, J., Xu, C., Zhao, Z.W., Yin, S.H. and Wang, G. (2022) Asprosin Inhibits Macrophage Lipid Accumulation and

Reduces Atherosclerotic Burden by Up-Regulating ABCA1 and ABCG1 Expression via the p38/Elk-1 Pathway. *Journal of Translational Medicine* **20**, Article No. 337. https://doi.org/10.1186/s12967-022-03542-0

[37] Guven, C. and Kafadar, H. (2022) Evaluation of Plasma Asprosin Concentration in Patients with Coronary Artery Disease. *Brazilian Journal of Cardiovascular Surgery*, **37**, 493-500. https://doi.org/10.21470/1678-9741-2021-0003

[38] 徐佰达, 叶挺, 王倩, 马涛, 刘洁, 宗刚军. 血浆白脂素水平与冠心病的关系[J]. 心脏杂志, 2019, 31(4): 428-431.

[39] Wang, H.H., Luo, W.Y., Lin, M., Li, X.J., Xiang, G.D. and Triganti, D.T. (2021) Plasma Asprosin, CCDC80 and ANGPTL4 Levels Are Associated with Metabolic and Cardiovascular Risk in Patients with Inflammatory Bowel Disease. *Physiological Research*, **70**, 203-211. https://doi.org/10.33549/physiolres.934547

[40] Zhang, Z., Tan, Y., Zhu, L., Zhang, B., Feng, P., Gao, E., *et al*. (2019) Asprosin Improves the Survival of Mesenchymal Stromal Cells in Myocardial Infarction by Inhibiting Apoptosis via the Activated ERK1/2-SOD2 Pathway. *Life Sciences*, **231**, Article ID: 116554. https://doi.org/10.1016/j.lfs.2019.116554

[41] Deng, X., Zhao, Z., Zhao, L., Wang, C., Li, Y., Cai, Z., *et al*. (2022) Association between Circulating Asprosin Levels and Carotid Atherosclerotic Plaque in Patients with Type 2 Diabetes. *Clinical Biochemistry*. https://doi.org/10.1016/j.clinbiochem.2022.04.018