

- [11] Langley SR, Dwyer J, Drozdov I, et al. Proteomics: from single molecules to biological pathways[J]. *Cardiovasc Res*, 2013, 97(4): 612-622.
- [12] Bagnato C, Thumar J, Mayya V, et al. Proteomics analysis of human coronary atherosclerotic plaque: a feasibility study of direct tissue proteomics by liquid chromatography and tandem mass spectrometry[J]. *Mol Cell Proteomics*, 2007, 6(6): 1088-1102.
- [13] Kakimoto Y, Ito S, Abiru H, et al. Sorbin and SH3 domain-containing protein 2 is released from infarcted heart in the very early phase: proteomic analysis of cardiac tissues from patients[J]. *J Am Heart Assoc*, 2013, 2(6): e000565.
- [14] Sakai J, Ishikawa H, Kojima S, et al. Proteomic analysis of rat heart in ischemia and ischemia-reperfusion using fluorescence two-dimensional difference gel electrophoresis[J]. *Proteomics*, 2003, 3(7): 1318-1324.
- [15] 刘蕾, 王伟, 宋剑南, 等. 心肌梗死小型猪模型差异蛋白质组学研究[J]. 南京医科大学学报: 自然科学版, 2009, 29(4): 459-463.
- [16] 王勇, 吸文静, 郭淑贞, 等. 基于小型猪冠心病心肌缺血模型的血瘀证蛋白质组学研究[J]. 北京中医药大学学报, 2011, 34(7): 460-464.
- [17] Barderas MG, Tuñón J, Dardé VM, et al. Circulating human monocytes in the acute coronary syndrome express a characteristic proteomic profile[J]. *J Proteome Res*, 2007, 6(2): 876-886.
- [18] Parguina AF, Grigorian-Shamajian L, Agra RM, et al. Proteins involved in platelet signaling are differentially regulated in acute coronary syndrome: a proteomic study[J]. *PLoS One*, 2010, 5(10): e13404.
- [19] 高春芳, 郑国宝, 赵光, 等. 急性心肌梗死病程不同时期患者血清蛋白质组学分析[J]. 解放军医学杂志, 2005, 30(6): 465-466.
- [20] Guo W, Xue J, Shi J, et al. Proteomics analysis of distinct portal vein tumor thrombi in hepatocellular carcinoma patients[J]. *J Proteome Res*, 2010, 9(8): 4170-4175.
- [21] Martinez-Pinna R, Madrigal-Matute J, Tarin C, et al. Proteomic analysis of intraluminal thrombus highlights complement activation in human abdominal aortic aneurysms[J]. *Arterioscler Thromb Vasc Biol*, 2013, 33(8): 2013-2020.
- [22] You SA, Archacki SR, Angheloiu G, et al. Proteomic approach to coronary atherosclerosis shows ferritin light chain as a significant marker: evidence consistent with iron hypothesis in atherosclerosis[J]. *Physiol Genomics*, 2003, 13(1): 25-30.
- [23] Distelmaier K, Adlbrecht C, Jakowitsch J, et al. Proteomic profiling of acute coronary thrombosis reveals a local decrease in pigment epithelium-derived factor in acute myocardial infarction[J]. *Clin Sci*, 2012, 123(2): 111-119.
- [24] Alonso-Organ S, Moreno-Luna R, López JA, et al. Proteomic characterization of human coronary thrombus in patients with ST-segment elevation acute myocardial infarction[J]. *J Proteomics*, 2014, 109: 368-381.
- [25] Erogbogbo F, May J, Swihart M, et al. Bioengineering silicon quantum dot theranostics using a network analysis of metabolomic and proteomic data in cardiac ischemia[J]. *Theranostics*, 2013, 3(9): 719-728.
- [26] Vélez P, Parguina AF, Ocaranza-Sánchez R, et al. Identification of a circulating microvesicle protein network involved in ST-elevation myocardial infarction[J]. *Thromb Haemost*, 2014, 112(4): 716-726.

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## 他汀类药物致新发糖尿病机制的研究进展

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### Progress in Research of Mechanism of New-onset Diabetes Mellitus Induced by Statins

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**摘要:** 大量的临床实验结果证实, 他汀类药物不仅能大幅度降低胆固醇, 还可以显著减少心血管事件, 如心绞痛、心肌梗死、冠心病死亡等。然而, 近期的临床研究提示他汀类药物可以增加患者新发糖尿病的风险, 他汀类药物与新发糖尿病的关系引起广泛关注。目前, 他汀类药物引发糖尿病的具体机制仍不清楚。现对近年来有关他汀类药物引发糖尿病的机制研究进展予以综述。

**关键词:** 他汀类药物; 糖尿病; 机制

**Abstract:** A series of large-scale clinical trials have shown that statins can not only greatly reduce cholesterol, but also significantly reduce cardiovascular events, such as angina pectoris, myocardial infarction and coronary heart disease death. However, some recent clinical

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cal researches have indicated that statins increase the risk of new-onset diabetes mellitus. Therefore, the relationship between diabetes mellitus and statins has been of concern. At present, the mechanism of new-onset diabetes mellitus induced by statins is still unclear. This article reviews the recent progress in research of mechanism of new-onset diabetes mellitus induced by statins.

**Key words:** statins; diabetes mellitus; mechanism

他汀类药物,即 3-羟-3-甲基戊二酰辅酶 A(3-hydroxy-3-methylglutaryl coenzyme A, HMG-CoA)还原酶抑制剂,因能有效降低人体内低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)水平,而广泛应用于心血管的一级和二级预防。而新近的研究发现,他汀类药物也可能对人体血糖水平产生影响,导致患者血糖水平升高,增加新发糖尿病的风险。但他汀类药物致新发糖尿病的具体机制仍不清楚,现简要综述他汀类药物致新发糖尿病的相关机制。

## 1 他汀类药物对胰腺 $\beta$ 细胞胰岛素分泌的作用

### 1.1 抑制 $\beta$ 细胞内 ATP 等代谢产物的生成

他汀类药物主要抑制 HMG-CoA 还原酶,因而减少了中间产物甲羟戊酸的合成。甲羟戊酸为类异戊二烯的前体,也是合成辅酶 Q10 的必需物。当甲羟戊酸缺乏时,必然导致细胞内类异戊二烯和辅酶 Q10 合成障碍。辅酶 Q10 是线粒体电子传递链中重要的电子载体,其含量的降低使电子传递减缓,致胰腺  $\beta$  细胞 ATP 生成减少,从而使胰岛素分泌受抑制<sup>[1]</sup>。

### 1.2 抑制 $\beta$ 细胞 L 型钙通道

葡萄糖经葡萄糖转运体-2(glucose transporters-2, GLUT-2)摄入  $\beta$  细胞,由葡萄糖激酶磷酸化为 6-磷酸葡萄糖后启动级联反应,使 ATP 依赖的钾通道关闭,细胞膜去极化,L 型钙通道开放,钙离子内流,致含有胰岛素的微粒分泌<sup>[2]</sup>。葡萄糖可以刺激  $\beta$  细胞内游离钙离子升高,他汀类药物则可能抑制此过程,阻断电压门控钙通道,减少葡萄糖诱导的胰岛素分泌。辛伐他汀能抑制胰岛素分泌,但普伐他汀则无此作用<sup>[3]</sup>。Yada 等<sup>[3]</sup>利用大鼠进行的实验表明:当胰腺  $\beta$  细胞摄取他汀后,胰岛素分泌会减少,这是由于受葡萄糖激动引起的胞浆中钙离子和 L 型钙通道的开放增加这一过程被抑制所致,且这些抑制作用与他汀的脂溶性高低相平行,而水溶性他汀没有类似效应。细胞膜上的胆固醇具有调控细胞功能的效应。胆固醇能维持  $\beta$  细胞电压钙通道的正常功能,且对于胰岛素颗粒的动员及其与细胞膜的融合至关重要。他汀类药物的降脂作用可能导致  $\beta$  细胞膜胆固醇异常<sup>[4]</sup>。Xia 等<sup>[5]</sup>通过抑制  $\beta$  细胞株 MIN6 细胞的鲨烯环氧酶来减少胆固醇分泌,发现胆固醇缺乏时会抑制细胞膜上的电压门控钙通道,减少由葡萄糖刺激的胰岛素释放。而胆固醇充足时,这一现象会逆转,提示胰岛素分泌减少可能与细胞内胆固醇耗尽有关。由于他汀

类药物能大幅度降低胆固醇,因而可能会导致胰岛素释放减少。

### 1.3 诱导 $\beta$ 细胞程序性细胞死亡

与机体其他组织细胞相比,胰腺  $\beta$  细胞容易受到氧化和炎症损伤并且极易程序性细胞死亡<sup>[6]</sup>,而脂蛋白可调节  $\beta$  细胞的生存<sup>[7]</sup>。Rütti 等<sup>[8]</sup>发现,LDL-C 不但减少由葡萄糖刺激的胰岛素分泌,还可抑制  $\beta$  细胞增殖。高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)则可以保护  $\beta$  细胞,避免程序性细胞死亡。尽管他汀类药物具有降胆固醇和抗炎作用,但其在抑制内源性胆固醇合成的同时,还可能会促使外源性胆固醇激活  $\beta$  细胞内有害的免疫炎症反应<sup>[7]</sup>。此外,氧化 LDL-C 可以刺激细胞内的免疫应答,激活炎症的级联反应,损伤  $\beta$  细胞的结构与功能,导致胰岛素分泌减少<sup>[9]</sup>。这种炎症、氧化、程序性细胞死亡之间的相互作用,被血浆来源的 LDL-C 进一步强化。

### 1.4 对腺苷三磷酸结合盒转运体 1 的影响

miRNA-33a 是腺苷三磷酸结合盒转运体 1(ATP-binding cassette transporter A1, ABCA1)重要调节基因,其表达与胰岛细胞和  $\beta$  细胞中的 ABCA1 水平呈负相关<sup>[10-11]</sup>。研究<sup>[11-13]</sup>发现胰岛细胞内 ABCA1 水平的变化影响胰岛细胞内胆固醇稳态进而影响胰岛素分泌和诱导  $\beta$  细胞功能障碍。Allen 等<sup>[14]</sup>证实辛伐他汀和阿托伐他汀诱导肝细胞内 miRNA-33a 的表达,提示他汀类药物可能通过增加 miRNA-33a 的表达进而导致胰岛素分泌减少最终引发糖尿病。

## 2 他汀类药物对周围组织摄取、利用葡萄糖的影响

### 2.1 对脂联素的影响

脂联素是脂肪细胞分泌的具有增加胰岛素敏感性和抗炎作用的细胞因子。Koh 等<sup>[15]</sup>荟萃分析了 24 个他汀类药物试验中糖尿病患者和非糖尿病患者胰岛素敏感性以及相关因素(如脂联素)的改变,发现普伐他汀可增加冠心病患者和葡萄糖耐量受损患者的胰岛素敏感性和脂联素分泌,甚至对无症状的高胆固醇血症患者也有相同作用<sup>[16]</sup>,但对健康的非糖尿病患者无此作用。有研究<sup>[17]</sup>证实瑞舒伐他汀有降低血浆脂联素水平和胰岛素敏感性的作用,而普伐他汀却有升高二者的作用。研究<sup>[18]</sup>发现匹伐他汀可以改善成熟脂肪细胞内激素敏感脂肪酶的表达,增加脂联素分泌,从而升高胰岛素敏感性。

## 2.2 对周围组织摄取葡萄糖的影响

葡萄糖转运蛋白 (glucose transporters, GLUT) 是一组协助转运葡萄糖进入组织的重要蛋白质。其中 GLUT1 主要分布于脑内血管内皮细胞, GLUT2 分布于体内肝脏、肠、肾脏及胰腺  $\beta$  细胞, GLUT3 分布于神经细胞, GLUT4 则主要分布于脂肪细胞、心肌细胞和骨骼肌细胞, 而 GLUT4 活性降低通常被认为与胰岛素抵抗有关<sup>[19]</sup>。当胰岛素释放至细胞外液后, 激活胰岛素受体 (酪氨酸蛋白激酶), 使胰岛素受体底物磷酸化, 这会增加细胞膜外 GLUT4 水平, 导致血糖摄取增加。而类异戊二烯化合物能够上调细胞膜上的 GLUT4 使脂肪细胞对葡萄糖的摄取增加。Nakata 等<sup>[20]</sup>研究发现阿托伐他汀可通过抑制类异戊二烯化合物生成, 进而阻碍 2 型糖尿病小鼠模型的脂肪细胞分化成熟和 GLUT4 表达, 导致脂肪细胞摄取葡萄糖的显著减少进而引起胰岛素抵抗。

## 2.3 抑制外周组织的胰岛素信号转导

他汀类药物还可能通过影响外周胰岛素信号转导来抑制胰岛素分泌。动物实验<sup>[21]</sup>发现高剂量他汀暴露下调骨骼肌中 Akt 和 Foxo 的表达, Akt 和 Foxo 是激活胰岛素受体底物磷酸化的信号转导通路, 进而减少 GLUT4 的表达, 使糖耐量受损。

## 2.4 对周围组织的毒性作用

$\beta$  细胞<sup>[22]</sup>、骨骼肌细胞<sup>[23]</sup> 及脂肪细胞<sup>[24]</sup> 的线粒体功能障碍被认为与糖尿病的发病机制有关。有研究<sup>[25]</sup>表明他汀类药物能产生肌肉毒性作用, 导致骨骼肌细胞线粒体功能障碍, 影响骨骼肌细胞对葡萄糖的摄取和利用, 从而导致胰岛素抵抗及糖尿病。

## 2.5 对解偶联蛋白 3 的影响

解偶联蛋白 3 被认为能阻止线粒体中非酯化型脂肪酸的聚集<sup>[26]</sup>, 研究<sup>[27-28]</sup>发现肌细胞内三酰甘油的聚集能降低骨骼肌对胰岛素的敏感性。Larsen 等<sup>[29]</sup>发现服用辛伐他汀降低解偶联蛋白 3 水平进而导致胰岛素抵抗。有关解偶联蛋白 3 在服用他汀类药物致糖尿病中的作用仍需进一步研究。

## 3 结语

他汀类药物升高血糖的机制主要与其影响胰腺  $\beta$  细胞分泌胰岛素及周围组织对葡萄糖的摄取、利用这两方面机制有关, 但具体机制仍不详, 仍需要进一步深入探讨。

## 【参考文献】

- [1] Sasaki J, Iwashita M, Kono S. Statins: beneficial or adverse for glucose metabolism[J]. *J Atheroscler Thromb*, 2006, 13(3):123-129.
- [2] Kruit JK, Brunham LR, Verchere CB, et al. HDL and LDL cholesterol significantly influence beta-cell function in type 2 diabetes mellitus[J]. *Curr Opin Lipidol*, 2010, 21(3):178-185.

- [3] Yada T, Nakata M, Shiraishi T, et al. Inhibition by simvastatin, but not pravastatin, of glucose-induced cytosolic  $\text{Ca}^{2+}$  signalling and insulin secretion due to blockade of L-type  $\text{Ca}^{2+}$  channels in rat islet beta-cells[J]. *Br J Pharmacol*, 1999, 126(5):1205-1213.
- [4] Mascitelli L, Goldstein MR. Statins, cholesterol depletion and risk of incident diabetes[J]. *Int J Cardiol*, 2011, 152(2):275-276.
- [5] Xia F, Xie L, Mihic A, et al. Inhibition of cholesterol biosynthesis impairs insulin secretion and voltage-gated calcium channel function in pancreatic beta-cells[J]. *Endocrinology*, 2008, 149(10):5136-5145.
- [6] Sjöholm A, Berggren PO, Cooney RV. Gamma-tocopherol partially protects insulin-secreting cells against functional inhibition by nitric oxide[J]. *Biochem Biophys Res Commun*, 2000, 277(2):334-340.
- [7] Roehrich ME, Mooser V, Lenain V, et al. Insulin-secreting beta-cell dysfunction induced by human lipoproteins[J]. *J Biol Chem*, 2003, 278(20):18368-18375.
- [8] Rütli S, Ehses JA, Striber RA, et al. Low- and high-density lipoproteins modulate function, apoptosis, and proliferation of primary human and murine pancreatic beta-cells[J]. *Endocrinology*, 2009, 150(10):4521-4530.
- [9] Kruit JK, Kremer PH, Dai L, et al. Cholesterol efflux via ATP-binding cassette transporter A1 (ABCA1) and cholesterol uptake via the LDL receptor influences cholesterol-induced impairment of beta cell function in mice[J]. *Diabetologia*, 2010, 53(6):1110-1119.
- [10] Rayner KJ, Suarez Y, Davalos A, et al. MiR-33 contributes to the regulation of cholesterol homeostasis[J]. *Science*, 2010, 328(5985):1570-1573.
- [11] Wijesekara N, Zhang LH, Kang MH, et al. miR-33a modulates ABCA1 expression, cholesterol accumulation, and insulin secretion in pancreatic islets[J]. *Diabetes*, 2012, 61(3):653-658.
- [12] Brunham LR, Kruit JK, Pape TD, et al. Beta-cell ABCA1 influences insulin secretion, glucose homeostasis and response to thiazolidinedione treatment[J]. *Nat Med*, 2007, 13(3):340-347.
- [13] Kruit JK, Wijesekara N, Fox JE, et al. Islet cholesterol accumulation due to loss of ABCA1 leads to impaired exocytosis of insulin granules[J]. *Diabetes*, 2011, 60(12):3186-3196.
- [14] Allen RM, Marquart TJ, Albert CJ, et al. miR-33 controls the expression of biliary transporters, and mediates statin- and diet-induced hepatotoxicity[J]. *EMBO Mol Med*, 2012, 4(9):882-895.
- [15] Koh KK, Sakuma I, Quon MJ. Differential metabolic effects of distinct statins[J]. *Atherosclerosis*, 2011, 215(1):1-8.
- [16] Takagi T, Matsuda M, Abe M, et al. Effect of pravastatin on the development of diabetes and adiponectin production[J]. *Atherosclerosis*, 2008, 196(1):114-121.
- [17] Koh KK, Quon MJ, Sakuma I, et al. Differential metabolic effects of rosuvastatin and pravastatin in hypercholesterolemic patients[J]. *Int J Cardiol*, 2013, 166(2):509-515.
- [18] Arnaboldi L, Corsini A. Could changes in adiponectin drive the effect of statins on the risk of new-onset diabetes? The case of pitavastatin[J]. *Atheroscler Suppl*, 2015, 16:1-27.
- [19] Doehner W, Gathercole D, Cicoria M, et al. Reduced glucose transporter GLUT4 in skeletal muscle predicts insulin resistance in non-diabetic chronic heart failure patients independently of body composition[J]. *Int J Cardiol*, 2010, 138(1):19-24.
- [20] Nakata M, Nagasaka S, Kusaka I, et al. Effects of statins on the adipocyte maturation and expression of glucose transporter 4 (SLC2A4): implications in glycaemic control[J]. *Diabetologia*, 2006, 49(8):1881-1892.
- [21] Preiss D, Sattar N. Statins and the risk of new-onset diabetes: a review of recent evidence[J]. *Curr Opin Lipidol*, 2011, 22(6):460-466.
- [22] Supale S, Li N, Brun T, et al. Mitochondrial dysfunction in pancreatic  $\beta$  cells

- [J]. Trends Endocrinol Metab, 2012, 23(9): 477-487.
- [23] Phielix E, Mensink M. Type 2 diabetes mellitus and skeletal muscle metabolic function[J]. Physiol Behav, 2008, 94(2): 252-258.
- [24] Wang CH, Wang CC, Huang HC, et al. Mitochondrial dysfunction leads to impairment of insulin sensitivity and adiponectin secretion in adipocytes[J]. FEBS J, 2013, 280(4): 1039-1050.
- [25] Sirvent P, Fabre O, Bordenave S, et al. Muscle mitochondrial metabolism and calcium signaling impairment in patients treated with statins[J]. Toxicol Appl Pharmacol, 2012, 259(2): 263-268.
- [26] Schrauwen P, Saris WH, Hesselink MK. An alternative function for human uncoupling protein 3: protection of mitochondria against accumulation of nonesterified fatty acids inside the mitochondrial matrix[J]. FASEB J, 2001, 15(13): 2497-2502.
- [27] Krssak M, Falk Petersen K, Dresner A, et al. Intramyocellular lipid concentrations are correlated with insulin sensitivity in humans: a<sup>1</sup>H NMR spectroscopy study[J]. Diabetologia, 1999, 42(1): 113-116.
- [28] Moro C, Bajpeyi S, Smith SR. Determinants of intramyocellular triglyceride turnover: implications for insulin sensitivity[J]. Am J Physiol Endocrinol Metab, 2008, 294(2): e203-e213.
- [29] Larsen S, Stride N, Hey-Mogensen M, et al. Simvastatin effects on skeletal muscle: relation to decreased mitochondrial function and glucose intolerance[J]. J Am Coll Cardiol, 2013, 61(1): 44-53.

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## 心脏核磁共振在急性心肌炎中的研究进展

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### Evolution of Cardiac Magnetic Resonance Imaging in Acute Myocarditis

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**摘要:** 心肌炎是由感染或非感染性疾病引起的心肌组织的炎症反应。在心脏猝死的尸检中心肌炎检出率为 12%, 因此早期准确诊断心肌炎及评估病情程度显得尤其重要。心脏核磁共振对评估疑似心肌炎患者成为一种非侵袭性的基本诊断工具, 具有多参数、多方位的成像特点, 具有良好的软组织对比度和高空间分辨率, 不仅能显示心肌损伤部位、范围, 而且能很好地显示心肌水肿程度及心功能情况, 对心肌炎有着较大的潜在诊断价值, 且对心肌炎的预后评价也有重要价值。

**关键词:** 心肌炎; 心脏核磁共振; 延迟增强

**Abstract:** Myocarditis is a disease characterized by the inflammation and damage of the myocardial tissue caused by infection, toxins, diseases and much more. Myocarditis is detected in 12% of autopsies as being the reason for sudden cardiac deaths. Therefore it is especially important for there to be early and accurate diagnosis, treatment and assessment of the extent of myocarditis. Cardiac magnetic resonance imaging is a noninvasive diagnostic tool for the assessment of patients with suspected myocarditis. Cardiac magnetic resonance imaging offers a multi-parameter and multi-aspect imaging characteristic with an excellent soft tissue contrast and high spatial resolution. It shows the location and the extent of myocardial damage, as well as the extent of myocardial and heart function. Cardiac magnetic resonance imaging has a greater potential diagnostic value for myocarditis and for the prognostic evaluation of myocarditis.

**Key words:** myocarditis; cardiac magnetic resonance; delayed enhancement

#### 1 发生率及病因

心肌炎是一种相对较为常见的影响心肌的炎症性疾病。据报道, 心肌炎在年轻的成人猝死中已达到

12%<sup>[14]</sup>, 是其他心肌病如扩张型心肌病、致心律失常性右室心肌病一个重要的潜在病因。在平素健康患者中, 感染性疾病在心肌炎患者中占了大多数, 通常

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