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运动诱导的肌肉因子对肥胖相关代谢异常的调控

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摘要：肥胖及相关代谢疾病已经成为危害人体健康的全球性公共卫生问题。运动作为一种有效的、经济的非药物干预手段，对预防和改善肥胖及相关代谢疾病有积极作用。运动通过调控“肌肉因子(myokine)”的分泌增加葡萄糖摄取和利用、脂肪酸氧化及细胞因子间的交互作用等过程发挥调节代谢异常的作用。揭示运动对肌肉因子表达分泌调控的规律，阐明肌肉因子对代谢异常的调控机制，是开发肥胖相关代谢疾病防治新方法和策略的基础。因此，本文对运动调控的肌肉因子及其在运动改善肥胖相关代谢异常中发挥的作用进行综述，拟通过阐明肌肉因子改善代谢异常的机制，为肥胖及相关代谢疾病的防治提供新思路。

关键词：肌肉因子；肥胖；运动；代谢；骨骼肌

Regulation of exercise-induced myokines in obesity-related metabolic abnormalities

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Abstract: Obesity and related metabolic diseases have become a global public health problem that endangers human health. Exercise, as an effective and economical non-drug intervention, has a positive effect on the prevention and improvement of obesity and related metabolic diseases. More and more studies have shown that exercise plays a role in regulating metabolic abnormalities by regulating the secretion of ″myokine″, increasing glucose uptake and utilization, fatty acid oxidation, and the interaction between cytokines. Uncovering the regulation of exercise on the expression and secretion of myokines and elucidating the regulatory mechanism of myokines on metabolic abnormalities is the basis for developing new methods and strategies for the prevention and treatment of obesity-related metabolic diseases. Therefore, this paper reviews the myokines regulated by exercise and their roles in the improvement of obesity-related metabolic abnormalities by exercise, and aims to provide new ideas for the prevention and treatment of obesity and related metabolic diseases by clarifying the mechanism of myokines improving metabolic abnormalities.

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肥胖是一种以机体脂肪过度积累和体重过重为特征的慢性代谢性疾病。随着现代经济的发展，人们生活质量提高，高热量的饮食摄入增加、久坐少动等不健康的生活方式引起机体能量代谢长期失衡，导致肥胖及相关代谢疾病的患病率在全球范围内迅猛增长[1]。肥胖患者体内脂肪异常堆积，常伴有血脂升高、胰岛素敏感性下降等代谢异常。这些代谢异常易诱发其他代谢性疾病，如脂质沉积易诱发高脂血症和非酒精性脂肪肝(nonalcoholic fatty liver disease，NAFLD)、胰岛素信号被抑制易诱发的胰岛素抵抗和2型糖尿病(type 2 diabetes mellitus，T2DM)。此外，肥胖还诱发全身性慢性炎症，增加机体心血管疾病、神经退行性疾病等的患病风险。肥胖及相关代谢疾病严重威胁着人类的生命健康，造成了巨大的经济压力和社会负担，其防治已成为急需解决的公共健康问题。目前，治疗此类疾病的药物大多需要长期服用，且存在机体耐药性、药物副作用大等问题。

运动作为一种健康、经济的干预手段，可以通过刺激骨骼肌产生肌肉因子调控机体代谢，进而起到增加能量消耗、防治肥胖的效果[2]。因此，本文主要针对报道较多的、在代谢疾病中发挥作用的肌肉因子及相关机制等进行综述，以期为运动防治肥胖及相关代谢性疾病提供良好的理论依据。

1 运动诱导的肌肉因子与肥胖相关代谢异常

肌肉因子是指运动的动力器官骨骼肌分泌的细胞因子和活性多肽[3]。它们不仅以自分泌的方式作用于骨骼肌自身，还通过内分泌或旁分泌的方式实现骨骼肌与脂肪组织、肝脏、大脑等之间的相互作用，共同参与机体生理或病理过程的调控[4]。肥胖状态下，机体代谢紊乱，脂肪堆积异常增多，甘油三酯及总胆固醇水平升高，胰岛素敏感性下降，葡萄糖摄取量减少，并常伴有全身性慢性炎症。运动可以调控白介素-6(interleukin-6，IL-6)、鸢尾素(Irisin)、成纤维生长因子21(fibroblast growth factor 21，FGF21)、肌肉生长抑制素(myostatin，MSTN)等肌肉因子的表达水平(表1)，进而调控肥胖相关代谢异常，减轻全身慢性炎症，防治肥胖及相关代谢疾病[2]。

1.1 IL-6

IL-6是首个被发现的肌肉因子，是机体参与免疫应答反应的重要介质。研究表明，运动诱导的IL-6除了具有抗炎、调节免疫细胞生长和分化等作用外，还具有调控葡萄糖稳态及脂质代谢等作用。安静状态下，人体骨骼肌IL-6含量极低；但在运动条件下，肌源性IL-6在c-Jun N末端激酶(c-Jun N kinase，JNK)和激活蛋白1调控下大量表达[23]，成为血液IL-6的主要来源[5]。运动过程中，血浆的IL-6浓度随时间推移呈指数型增加，并在向心运动后即刻或离心运动后约8 h达到峰值，随后迅速下降至运动前水平[5,24,25]。运动强度增大或运动时间延长使其峰值升高。一次急性运动后，循环血液中IL-6水平可升高至安静水平时的100倍[24]。

安静状态下，IL-6可以作为炎症标志物反映机体的炎症水平。流行病学调查显示，肥胖、久坐人群的血浆IL-6基础水平升高，其主要来源于巨噬细胞，与核因子-κB(nuclear factor-κB，NF-κB)通路激活有关，反映机体炎症水平升高[26]。运动中NF-κB信号通路未被激活，且NF-κB的p65亚基与IL-6启动子的结合程度降低[23]，表明运动引起的高水平IL-6具有抗炎效应。长期规律运动能有效累积单次运动带来的益处，降低肥胖、T2DM等代谢异常人群的机体炎症水平，使IL-6基础水平得以恢复，疾病进程得以改善[7-9]。此外，长期运动训练提高了骨骼肌IL-6受体的基础水平[27]，提示IL-6敏感性增强，这可能抵消了IL-6水平的下调。

1.2 Irisin

Irisin是Boström等[28]于2012年发现的肌肉因子，为Ⅲ型纤连球蛋白包含蛋白5(fibronectin type Ⅲ domain-containing protein 5，FNDC5)的水解产物，能够通过增加棕色脂肪组织产热和“白色脂肪棕色化”等机制调节机体代谢。运动时，肌肉的收缩和舒张增加了过氧化物酶体增殖物激活受

表1　运动对相关肌肉因子的调节作用

研究对象	运动类型	运动时间	运动强度	影响	参考文献
健康青年男性	高强度间歇运动	1次急性	大	IL-6↑(s)	[5]
健康青年男性	高强度间歇运动	1次急性	大	IL-6↑(p)	[6]
高脂饮食大鼠	有氧运动	12周	大	IL-6↓(s)	[7]
肥胖老年女性	抗阻运动	8周	中	IL-6↓(p)	[8]
T2DM患者	高强度间歇结合抗阻运动	52周	大	IL-6↓(p)	[9]
T2DM患者	有氧结合抗阻运动	52周	中	IL-6↓(p)	[9]
健康青年男性	有氧运动	1次急性	大	Irisin↑(p)	[10]
健康青年男性	有氧运动	1次急性	小	Irisin↓(p)	[10]
(健康/代谢综合征)中年男性	高强度间歇运动	1次急性	大	Irisin↑(p)	[11]
(健康/代谢综合征)中年男性	有氧运动	1次急性	中	Irisin↑(p)	[11]
(健康/代谢综合征)中年男性	抗阻运动	1次急性	大	Irisin↑(p)	[11]
T2DM大鼠	渐进式抗阻运动	8周	大	Irisin↑(s)	[12]
健康青年男性	有氧运动	8周	中	Irisin↑(p)	[13]
健康青年男性	抗阻运动	8周	大	Irisin↑(p)	[13]
健康青年男性	高强度间歇运动	8周	中	Irisin↑(p)	[13]
T2DM大鼠	渐进式抗阻运动	12周	大	Irisin↓(p)	[14]
超重/肥胖T2DM患者	有氧运动	8周	中	Irisin(p)	[15]
超重/肥胖T2DM患者	抗阻运动	8周	中	Irisin(p)	[15]
代谢综合征的肥胖女性	有氧运动	8周	大	Irisin(p)	[16]
代谢综合征的肥胖女性	抗阻运动	8周	大	Irisin(p)	[16]
代谢综合征的肥胖女性	有氧结合抗阻运动	8周	大	Irisin(p)	[16]
健康小鼠	有氧运动	1次急性	大	FGF21↑(s，p)	[17]
健康青年男性	有氧运动	1次急性	大	FGF21↑(p)	[17]
T2DM大鼠	渐进式抗阻运动	8周	大	FGF21↑(s)	[12]
肥胖小鼠	有氧运动	8周	中	FGF21↑(s)	[18]
肥胖小鼠	有氧运动	8周	中	FGF21↓(p)	[18]
肥胖小鼠	高强度间歇运动	8周	大	FGF21(s)	[18]
肥胖小鼠	高强度间歇运动	8周	大	FGF21↓(p)	[18]
健康青年男性	抗阻运动	1次急性	大	MSTN↓(s)	[19]
(血糖正常/异常)中年男性	有氧运动	1次急性	大	MSTN↓(s)	[20]
(血糖正常/异常)中年男性	有氧运动	1次急性	大	MSTN↑(p)	[20]
(血糖正常/异常)中年男性	有氧结合抗阻运动	12周	中	MSTN↓(s，p)	[20]
胰岛素抵抗中年男性	有氧运动	26周	中	MSTN↓(s，p)	[21]
(健康/T2DM)老年男性	抗阻运动	12周	大	MSTN↓(p)	[22]

“↑”表示升高，“↓”表示下降；用“骨骼肌(skeletal muscle)”首字母“s”表示肌肉因子在骨骼肌的表达水平，用“血浆(plasma)”首字母“p”表示肌肉因子在血浆/血清中的水平

体γ共激活因子-1α(peroxisome proliferator-activated receptor γ coactivator-1α，PGC-1α)水平，上调其下游因子FNDC5表达，促进FNDC5水解生成Irisin。运动生成的Irisin从骨骼肌释放入血，使其循环水平急剧增加，发挥代谢调控作用。在能量消耗相同的情况下，相较于低强度运动，高强度运动后血清中Irisin增加更多[10,11]，提示运动后Irisin水平与运动强度呈正相关。但也有研究显示，运动并不能导致Irisin的变化[29]。鉴于暂无检测Irisin的金方法以及其半衰期仅为1 h，结果矛盾的原因可能与实验样本、采血时间、运动强度、检测方法等相关。

大量研究表明，Irisin水平与BMI、腰围和脂肪量等肥胖相关指标呈负相关[30,31]。FNDC5蛋白补充或注射重组Irisin可使肥胖小鼠体重显著降低[32]。但也有部分研究显示，Irisin水平与肥胖相关指标呈正相关[33]，Polyzos等[34]曾提出“Irisin抵抗”的设想，提示肥胖状态下的Irisin水平可能为代偿性升高。减肥手术后，人体骨骼肌*FNDC5* mRNA水平和循环血液中Irisin水平均降低[35]，这似乎也支持Irisin水平代偿性升高的观点。总的来说，Irisin可以抑制肥胖的发展，有望成为防治肥胖的药物。遗憾的是，目前几乎没有Irisin在肥胖干预方面的临床研究，这可能是未来工作的方向。

对于长期运动后Irisin水平的变化，目前仍存在诸多争议。Boström等[28]最早发现，3周自由跑轮运动使小鼠循环Irisin水平提升65%，10周耐力运动使健康成人循环Irisin水平增加2倍。多数研究支持Boström等[28]的发现，认为定期运动训练提高了循环Irisin水平[12,13]，发挥代谢调控作用。部分研究认为，定期运动训练降低了肥胖人群循环Irisin水平[14]，这可能与“Irisin抵抗”的肥胖患者的高Irisin水平得以改善有关。还有部分研究认为，定期运动训练对循环Irisin无显著影响[15,16]。上述研究的差异可能受运动方案、受试对象的影响，也可能与检测方法不统一，以及人类Irisin前体FNDC5的起始密码子(ATA)与其他哺乳动物中存在的规范的起始密码子(ATG)不同有关。

1.3 FGF21

FGF21是一种可由多种器官合成的多肽激素，具有降血糖、提高胰岛素敏感性，降甘油三酯、提高脂肪利用率等作用。运动后FGF21循环水平立即升高，在运动后1 h达到峰值，约3 h恢复到基线水平[36]。虽然FGF21循环水平升高主要来源于肝脏，但肌源性FGF21也起重要作用[17]，特别是在慢性高胰岛素水平、脂质代谢异常和解耦联蛋白1(uncoupling protein 1，UCP1)缺乏等线粒体应激的条件下[37]。在运动状态下，肌源性FGF21的表达受磷脂酰肌醇3激酶/蛋白质丝氨酸苏氨酸激酶(phosphatidylinositol-3-kinase/protein-serine-threonine kinase，PI3K/Akt)信号通路调控[38,39]，并被释放至循环血液发挥代谢调控作用。

研究表明，运动能够提高正常小鼠[17]、肥胖小鼠[18]、患有心肌和骨骼肌自噬缺陷的肥胖小鼠[40]、糖尿病肥胖大鼠[41]等的骨骼肌中FGF21的表达水平，进而发挥修复线粒体功能、改善胰岛素抵抗等作用。肥胖、T2DM和NAFLD等代谢性疾病患者的FGF21循环水平高，且与BMI、甘油三酯和总胆固醇等相关[42,43]。FGF21高水平可能与其机体存在FGF21抵抗有关[17]。肥胖患者的脂肪组织和骨骼肌中FGF21受体复合物表达受到抑制[44]，长期运动训练可以通过激活过氧化物酶增殖物激活受体-γ(peroxisome proliferater-activated receptor-γ，PPAR-γ)介导FGF受体FGFR1和β-Klotho的表达上调，增强FGF21敏感性，减轻肥胖机体的代谢功能障碍[18,45]。中等强度有氧运动可能产生比高强度间歇运动更好的效果[18]。目前，有关运动与肌源性FGF21表达及其机制的研究尚少，需要进一步探究。

1.4 MSTN

MSTN又名生长分化因子8，主要表达于骨骼肌，不仅能够调节骨骼肌的生长发育，还在糖脂代谢调控中发挥重要作用。肌肉受到机械应力时，JNK通过磷酸化转录因子Smad2诱发肌肉生长，下调MSTN水平[46]。急性运动后，骨骼肌中MSTN表达显著下调，且其减少程度与运动时间呈正相关[19,20]。

研究表明，肥胖人群MSTN浓度升高，且其循环水平与胰岛素敏感性呈负相关[47]。*MSTN*基因敲除小鼠表现为肌肉量增加、脂肪量减少、胰岛素敏感性增强，即使高脂饮食诱导，也不易产生肥胖[48]。长期运动显著降低了骨骼肌及血液中的MSTN基线水平[21,22]，且长期训练后再次进行急性运动，MSTN表达进一步降低[20]。此外，相较于热中性环境，热环境更有利于运动下调MSTN的表达[49]。

1.5 其他肌肉因子

运动能诱导骨骼肌产生并释放大量的肌肉因子，肌肉因子随循环血液到达靶器官，发挥生物作用。除上述肌肉因子外，还有诸多运动诱导的肌肉因子与肥胖密切相关，如Metrnl血清水平与内脏脂肪水平呈负相关[50]，运动能够诱导其升高[6,51]，进而调节脂肪的生成、转运及储存[52]；

Apelin(一种可以由运动诱导、受胰岛素调节的肌肉因子)通过与血管紧张素Ⅱ蛋白J受体结合发挥作用，与肥胖和T2DM密切相关[53,54]；IL-15可作为NAFLD肥胖患者早期动脉粥样硬化的预测因子，在代谢调控和炎症反应中发挥重要作用[55]。此外，BDNF[56]、IL-13[57]等也可由运动诱导、骨骼肌表达和释放，在肥胖相关的代谢调控中发挥重要作用。

除上述肌肉因子外，还有一类新型的信号分子“线粒体衍生肽”，即线粒体DNA编码的肽，其主要分布在骨骼肌、血液等组织中，也在机体能量代谢的调节中发挥重要作用。目前，已被发现的线粒体衍生肽包括MOTS-c、Humanin和SHLP1-6三种[58]。研究表明，在高脂饮食诱导的肥胖小鼠中，MOTS-c的骨骼肌和血浆水平降低，而跑步机训练能够显著上调MOTS-c及相关脂解、致热蛋白的表达，从而调节机体糖脂代谢，增加机体能量消耗[59]。此外，运动还能增加Humanin及SHLP6的表达[60]，进而起到抗炎、胰岛素增敏、调控代谢异常的作用[61]。

2　肌肉因子调控肥胖相关代谢异常的潜在机制

肥胖患者体内脂质异常堆积，胰岛素敏感性降低，并常伴有不同程度的全身性炎症。运动诱导的IL-6、Irisin、FGF21等的上调和MSTN的下调均能激活一磷酸腺苷活化蛋白激酶(AMP-activated protein kinase，AMPK)、PI3K/Akt、UCP1、PGC-1α等信号通路，增加葡萄糖摄取、利用和脂肪酸氧化；此外，肌肉因子还可与胰岛素样生长因子-1(insulin-like growth factor-1，IGF-1)、脂联素(adiponectin，ADPN)等细胞因子交互作用，共同调控机体代谢异常(图1)。

2.1 增加葡萄糖摄取和利用

AMPK信号通路在细胞能量稳态调节中起关键的作用。运动过程中，肌肉因子IL-6[62]、Irisin[63]、FGF21[38]、Metrnl[64]、MOTS-c[65]等表达上调和MSTN表达抑制[66]均能激活AMPK信号通路。AMPK通过磷酸化转录因子开启葡萄糖转运蛋白4(glucose transporter type 4，GLUT4)的转录表达，增加葡萄糖摄取；通过抑制磷酸烯醇式丙酮

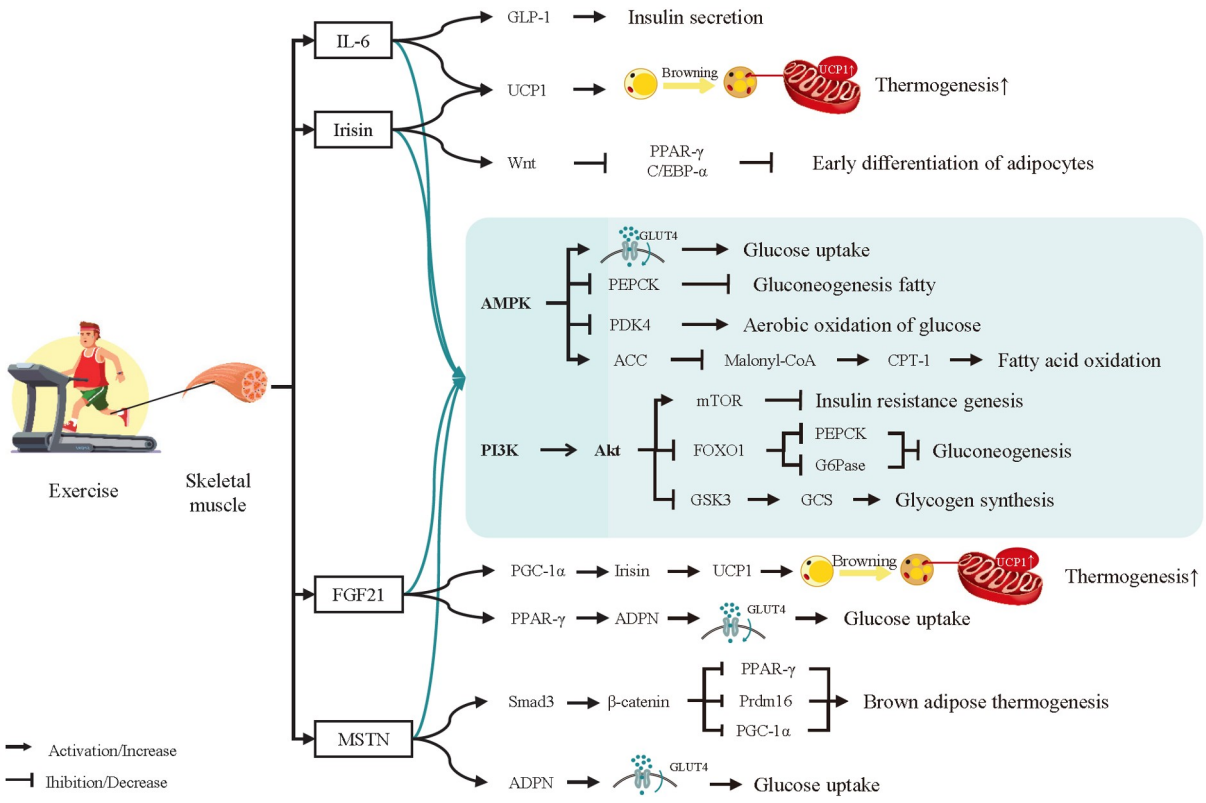

图1　运动诱导的肌肉因子调控肥胖相关代谢的主要机制

酸羧化酶(phosphoenolpyruvate carboxykinase，PEPCK)、葡萄糖-6-磷酸酶(glucose-6-phosphatase，G6Pase)和丙酮酸脱氢酶激酶4(pyruvate dehydrogenase kinase 4，PDK4)的表达抑制糖异生，促进葡萄糖有氧氧化。

PI3K/Akt信号通路与肥胖、T2DM等胰岛素抵抗相关疾病密切相关。运动过程中分泌的IL-6通过激活PI3K/Akt/mTOR，改善胰岛素抵抗[67]。Irisin通过PI3K/Akt/FOXO1介导的PEPCK和G6Pase下调和PI3K/Akt/GSK3介导的糖原合成酶(glycogen synthase，GCS)激活，促进糖原合成，维持机体葡萄糖代谢稳态[68]。肌源性FGF21受PI3K/Akt信号通路的调节[39]，而FGF21又可以通过激活PI3K/Akt信号通路增加骨骼肌和白色脂肪组织中GLUT4的表达，进而增加葡萄糖摄取[69]。不同于上述肌肉因子，MSTN表达上调致使Akt信号转导通路受阻[70]；在抗MSTN多克隆抗体的作用下，高脂饮食诱导的肥胖大鼠可以通过MSTN/PI3K/Akt/mTOR和MSTN/PI3K/Akt/FoxO1信号通路逆转其胰岛素抵抗[71]。

2.2 增加脂肪酸氧化

AMPK信号通路不仅可以调控糖代谢，在脂代谢的调控中也发挥重要作用。运动过程中，肌肉因子通过激活AMPK提高乙酰辅酶A羧化酶(acetyl coenzyme A carboxylase，ACC)的磷酸化水平，抑制ACC活性，降低丙二酰辅酶A(malonyl-CoA)水平，增强肉碱棕榈酰转移酶-1(carnitine palmitoyl transferase-1，CPT-1)的活性，从而导致脂质合成减少和进入线粒体进行β氧化的脂肪酸增加[62,63]。

脂肪组织主要包括棕色脂肪和白色脂肪。白色脂肪组织以甘油三酯的形式储存能量，过多的白色脂肪会导致肥胖。棕色脂肪组织和骨骼肌是人类非战栗产热的重要部位，而UCP1是棕色脂肪组织非战栗产热的主要效应物，具有促使白色脂肪组织褐变的作用。Knudsen等[72]报道，运动训练后小鼠腹股沟白色脂肪组织中*UCP1*基因表达水平升高，而*IL-6*缺陷鼠*UCP1*基因表达水平无变化，提示IL-6参与了白色脂肪组织褐变，在运动调控脂肪代谢中发挥关键作用。此外，Irisin通过激活Wnt信号通路抑制PPAR-γ、C/EBP-α等的表达抑制前脂肪细胞成脂分化[73]，通过PI3K/Akt信号通路改善线粒体呼吸、促进脂肪分解[74]，并能够上调UCP1表达增加产热[75]；MSTN通过诱导Smad3磷酸化，提高β-连环蛋白(β-catenin)含量和稳定性，从而下调*PPAR-γ*、*Prdm16*、*PGC-1α*和*UCP1*等棕色脂肪细胞相关基因的表达[76]，运动下调MSTN水平进而增强脂肪酸氧化。骨骼肌中FGF21的分泌响应于自噬损伤、线粒体功能障碍等应激通路的激活。在慢性高胰岛素水平、脂质代谢异常和UCP1缺乏等线粒体应激条件下，骨骼肌FGF21释放增加，以负反馈的形式改善脂质异常代谢[37]。

2.3 调控细胞因子间的交互作用

Ellingsgaard等[77]发现，运动以IL-6依赖的方式诱导肠道L细胞和胰腺α细胞产生和分泌胰高血糖素样肽-1(glucagon-like peptide-1，GLP-1)，诱导胰岛素分泌，改善胰岛素抵抗并维持葡萄糖稳态。而GLP-1又能刺激β细胞中FNDC5的表达和分泌，参与脂肪分解和褐变，同时上调Irisin表达，与其共同调控糖脂代谢。Irisin通过ERK途径上调IGF-1的表达并下调MSTN的表达[78]；而*MSTN*敲除通过激活肌肉中的AMPK-PGC-1α-FNDC5-Irisin通路，上调肌肉和血清中Irisin的表达[79]，故Irisin与MSTN存在拮抗关系。

ADPN是脂肪细胞分泌的一种细胞因子，在改善糖脂代谢和胰岛素敏感性中发挥重要作用。肥胖患者的基础ADPN水平降低[80]，FGF21增加可以通过激活PPAR-γ增加ADPN的分泌和表达[81]，从而促进脂肪细胞中GLUT4由细胞质向细胞膜迁移，增加葡萄糖摄取，降低血糖水平。MSTN的抑制能够上调ADPN、PPAR-α和PPAR-γ的表达，从而预防HFD诱导的肥胖和胰岛素抵抗[82]。

此外，运动诱导的肌肉因子与炎症因子息息相关。肌源性IL-6能够抑制促炎因子白介素1β(IL-1β)和肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)的表达，促进抗炎因子白细胞介素1受体拮抗剂(IL-1ra)、白介素-10(IL-10)的表达[83]，触发抗炎级联反应，改善胰岛素抵抗，防治慢性代谢性疾病。MD2-TLR4通路激活MyD88依赖性MAPK和NF-κB通路，进而诱导促炎因子表达，被认为是NAFLD的病理机制之一[84]。运动诱导的Irisin通过与MD2结合，使MD2-TLR4的结合被抑制，炎症反

应减弱，进而改善NAFLD[85,86]。FGF21的上调能够显著降低糖尿病小鼠中IL-1β、NF-κB、IL6和IL8的表达，并通过调节AMPK和Akt通路来减轻炎症和氧化应激[87]。此外，有氧运动可以通过下调糖化血红蛋白和血浆炎症因子IL-6、TNF-α和IL-1β的水平，降低肥胖患者的血浆和骨骼肌MSTN水平，从而形成正反馈，使机体代谢趋于稳态[88]。

3 小结与展望

越来越多的研究证实，运动诱导的肌肉因子在调控肥胖相关代谢异常中发挥重要作用。肥胖及相关代谢紊乱会诱导肌肉因子水平的异常，而运动诱导改善肥胖的肌肉因子(如IL-6、Irisin、FGF21)表达增多、抑制加重肥胖的肌肉因子(如MSTN)表达。运动诱导的肌肉因子通过AMPK、PI3K/Akt、UCP1等信号通路增加葡萄糖的摄取与利用、增强脂肪酸氧化、促进白色脂肪组织褐变、增强线粒体功能，发挥改善疾病进程的作用。此外，运动调控不同的细胞因子交互作用，进一步调控能量代谢，改善胰岛素抵抗；并通过下调促炎症因子IL-1β、TNF-α的表达，上调抗炎因子IL-1ra、IL-10等的表达，减缓全身慢性炎症，从而实现逆转肥胖的可能。长期规律运动不仅可以改善肌肉因子的基线水平，还有提高肌肉因子受体敏感性的作用。然而，目前对于不同运动对肌肉因子水平的影响尚不完全统一，最优运动方案(类型、强度、时间和频率等)有待进一步探究。随着生物信息学的发展，人们有望发现更多运动诱导的肌肉因子，并进一步探究其他肌肉因子是否也能够通过相似的途径或通路调控代谢，为运动防治肥胖相关代谢异常提供理论依据。

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