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·综述·

脂源性外泌体的功能及其在水生动物中的研究进展

卢荣华[1], 吉 红[2], 聂国兴[1*]

(1. 河南师范大学水产学院, 河南 新乡 453007;
2. 西北农林科技大学动物科技学院, 陕西 杨凌 712100)

摘要: 外泌体是一种由多种细胞分泌的30~150 nm的小囊泡, 其通过转运蛋白质、脂质、mRNAs和microRNAs等方式影响或改变受体细胞的行为, 已被证明是一种细胞间通讯的新模式。研究发现外泌体参与了脂肪合成及肥胖、肝脏脂肪变性、胰岛素抵抗、免疫调节、炎症反应、肿瘤发生、血管以及神经生成和成骨等过程。本文阐述了外泌体的形成与生物学特性、分离及鉴定的方法, 重点阐述了脂肪来源的外泌体在机体生理及病理过程中的潜在作用, 并概述了水生动物外泌体的研究进展, 以期为脂肪代谢及有关疾病的病理机制与潜在干预靶标的研究提供新的思路和途径, 也为更多地了解外泌体可能在鱼类糖脂代谢紊乱中的作用提供理论基础。

关键词: 外泌体; 功能; 代谢紊乱; 调控机制; 研究进展

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目前, 我国淡水养殖业迅速发展, 与此同时, 淡水养殖鱼类由于摄入营养成分不均衡或摄入能量过多等问题常引发体内脂质代谢紊乱[1-2], 进而造成鱼类抗应激能力及免疫力等下降。另一方面, 关于养殖鱼类肝脏脂肪代谢紊乱进而引起免疫力下降的分子机制还未完全阐明。研究发现, 肥胖能促进白色脂肪组织的慢性低度炎症, 并且能将M2抗炎表型巨噬细胞转变为M1促炎表型, 这可能与脂肪细胞产生的外泌体数量急剧增多有关。因此了解脂肪组织及其所分泌的外泌体如何调节代谢及免疫反应, 在改善鱼类代谢紊乱及免疫力下降等问题的治疗和预防上具有重要意义。

1 外泌体的形成与生物学特性

1.1 外泌体的形成

外泌体(exosomes)是一类直径为30~150 nm, 密度为1.10~1.18 g/mL的脂质双层膜囊泡样小体[3-5], 具有与细胞相同的拓扑结构。外泌体由细胞质膜和内体膜发育而来, 目前认为外泌体的生物发生有3种模式[3]: ①细胞质膜通过向内出芽的方式形成早期的内体, 内体以内出芽的方式产生腔内小泡形成多泡体(multivesicular bodys, MVBs), 即晚期内体, MVBs与质膜融合向外界分泌纳米级囊泡, 即外泌体; ②从质膜上直接出芽释放外泌体; ③通过在细胞内质膜连接隔室(intracellular plasma membrane–connected compartments, IPMCs)中出芽而延迟释放, 当细胞内质膜连接隔室解除时, 外泌体释放到外界(图1)。

1.2 外泌体的生物学特性

研究发现, 在绵羊网织红细胞、血小板、免疫细胞、神经元、肝细胞、脂肪细胞、肿瘤细胞和间充质干细胞(mesenchymal stem cell, MSC)等诸多细胞中可分泌外泌体[6-8]。外泌体能从几乎所有的体液如血清、尿液、唾液、精液和脑脊液中分离。通过电镜观察其形态为圆形或椭圆形, 可作为载体通过运输转移蛋白质、

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通信作者: 聂国兴, E-mail: niegx@htu.cn

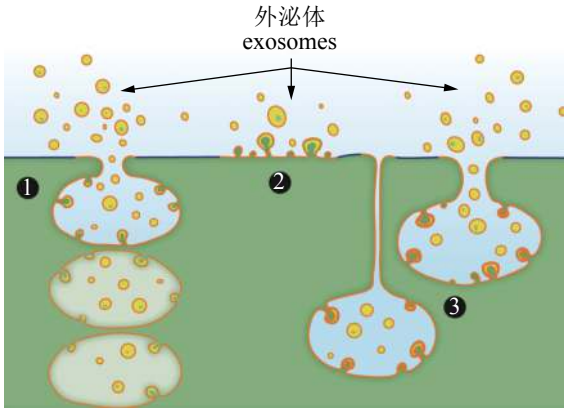

图 1 外泌体来自内体，质膜和外泌体生物发生的三种模式[3]

Fig. 1 Exosomes bud from endosome and plasma membranes, exosome biogenesis occurs by three modes

脂质、mRNAs和microRNAs，甚至DNA片段来影响或改变受体细胞的行为[8-10]。此外，外泌体可作为某些疾病诊断的生物标志物及携带药物或基因递送的载体[8, 11-12]。

外泌体中的四聚体蛋白CD63、CD81/CD82或CD9特别丰富[13]，常作为外泌体的标志物，但CD9已经在较大的囊泡中检测到[14]。外泌体的直径可随亲本细胞状态的变化而改变。由于微粒体、微泡、逆转录病毒样颗粒和凋亡小体的直径与外泌体的直径重叠，因此囊泡大小不能用于识别外泌体[14]。外泌体膜上富含的胆固醇和鞘磷脂以及少量卵磷脂和磷脂酰乙醇胺等脂质也是外泌体具有的显著特征[15]。外泌体含有许多其他类型的跨膜信号蛋白作为信号分子发挥作用[3]，同时也携带细胞因子及富含细胞外基质(extracellular matrix, ECM)蛋白，如纤连蛋白(fibronectin)，肌腱蛋白C(tenascin C)等，外泌体富含的这些内含物表明其能够作为传递复杂的自分泌和旁分泌信号的多重信号平台[16-18]。外泌体的内皮层富含支架蛋白Syntenin和Alix等；其内膜还富含分子伴侣，如主要组织相容性复合体(major histocompatibility complex，MHC) II类蛋白、免疫球蛋白超家族成员8 (immunoglobulin superfamily member 8，IGSF8)和细胞间黏附分子-1 (intracellular adhesion molecule-1，ICAM-1)等。Mathew等[19]首次报道了外泌体中含有热休克蛋白(heat shock proteins，HSPs)。

外泌体中除含有上述各种蛋白质和细胞因子，还含有DNA、mRNAs和microRNAs等物质，其中DNA包括单链DNA、双链DNA、基因组DNA、线粒体DNA等[3]。除此之外，外泌体中还含有丰富的非编码RNA(microRNAs)和一些特异性调节机制[20]。

2 外泌体的分离与鉴定方法

目前分离和鉴定外泌体的方法有很多，如用于表征外泌体物理特征的常用方法包括显微镜(扫描电子显微镜、透射电子显微镜、低温电子显微镜、原子力显微镜)、动态光散射(dynamic light scattering, DLS)、纳米粒子示踪分析(nanoparticle tracking analysis, NTA)、可调电阻脉冲传感技术(tunable resistive pulse sensing, TRPS)和单EV分析(single EV analysis, SEA)以及单粒子干涉反射(single-particle interferometric reflectance, SPIR)方法；富集外泌体常用方法包括普通超速离心、密度梯度超速离心、共沉淀、尺寸排阻色谱(size-exclusion chromatography)和场流分级法(field flow fractionation)，以及一些新的富集方法如微流控过滤(microfluidic filtering)、无接触分选免疫亲和富集(contact-free sorting immunoaffinity enrichment)；检测外泌体标记蛋白的常用方法有常规蛋白质分析(蛋白质印迹和ELISA、质谱分析)、流式细胞术，以及新的蛋白质分析技术，如微粒子流式细胞术(micro particle flow cytometry)、微核磁共振(micro-nuclear magnetic resonance)、纳米等离子外泌体传感技术(nanoplasmonic exosome (nPLEX) sensor)、集成磁电化学外泌体传感技术(integrated magne tic-electrochemical exosome (iMEX) sensor)及ExoScreen等[21]。常见外泌体分离方法的优缺点比较见表1。

3 脂源性外泌体的特征与功能

3.1 脂源性外泌体的特征

脂肪组织不仅是脂肪的储存库，也被称为内分泌器官和免疫器官，在维持全身代谢稳态中发挥关键作用。脂肪组织通过分泌脂肪细胞因子瘦素(leptin)、脂联素(adiponectin)和外泌体等与其他组织器官(脑、肝脏和骨骼肌)进行局部交流，从而影响多种组织。目前在脂肪组织[22]、脂肪细胞[23-24]和脂肪间充质干细胞(Adipose-derived stem cells，ADSCs)[25]的培养液中均发现外泌体。ADSCs是脂肪组织的组分，其分泌的外泌体是ADSCs释放到细胞外基质的膜性囊泡。Katsuda等[26]发现ADSCs衍生的外泌体直径为150~200 nm，比以往报道的外泌体直径大，虽然这些直径不符合

表 1　外泌体的分离方法优缺点比较[5]

Tab. 1　Comparison of the advantages and disadvantages of exosomes isolation methods

方法　method	原理　mechanism	优点　advantage	缺点　disadvantage
普通超速离心法	密度	金标准，操作简单	耗时(>4 h)，产量低，纯度低
密度梯度超速离心法	密度	金标准，纯度高	耗时(>6 h)，产量低
聚乙二醇沉淀法	溶解度	简单，快速(<4 h)	蛋白质污染，纯度低
免疫磁珠捕获	抗原	简单，快速(<4 h)	纯度低，仅使用靶蛋白分离外泌体
尺寸排阻色谱法	大小	简单，快速(<4 h)	低体积样品，(脂)蛋白污染
超滤离心法	大小	大容量样品	缺乏特异性

外泌体的共同标准，但CD63和HSP-70等外泌体标记物表达呈阳性，表明外泌体的大小范围可因特定细胞类型而变化。Durcin等[7]将脂肪细胞来源的EVs分为2个亚群，即大细胞外囊泡(lEVs)和小细胞外囊泡(sEVs)。蛋白质组学分析显示，lEVs和sEVs表现出不同的蛋白质成分特征，sEVs群富集胆固醇，而lEVs含有大量的磷脂酰丝氨酸，这也佐证了根据细胞来源不同，外泌体所携带的特定种类的脂质不同[7, 27]。

3.2　脂源性外泌体的功能

外泌体作为细胞交流的重要载体，可通过运输蛋白质、mRNAs和microRNAs来影响或改变受体细胞的行为[28]，进而参与机体多种生理和病理作用，如脂肪代谢、胰岛素抵抗、脂质毒性、血脂异常、内分泌失调、慢性炎症以及细胞增殖分化、免疫调节、肿瘤和血管发生等[8, 20]。

参与脂肪合成及肥胖的发生　脂肪细胞分泌的外泌体富集了脂肪从头合成相关的关键酶，如脂肪酸合成酶(fatty acid synthase，FASN)，乙酰辅酶A羧化酶(acetyl-CoA carboxylase，ACC)和葡萄糖-6-磷酸脱氢酶(glucose 6-phosphate dehydrogenase，G6PD)，进而促进脂质合成[12, 24]。类似的研究发现，从脂肪细胞释放的外泌体具有抗脂解和增强脂肪生成的作用[29]。在诱导成脂的3T3-L1细胞或血清源外泌体中也发现了一些脂肪合成关键转录因子或细胞因子(例如PPARγ2、脂联素、瘦素、抵抗素)，这些基因的表达随诱导时间的增加而增加[24, 30]。外泌体中还含有丰富的调节脂肪生成的microRNAs，如miR-103、miR-146b、miR-148a和miR-450a等在脂肪细胞介导的外泌体中显著上升[31-34]。Ferrante等[11]发现肥胖和消瘦患者内脏脂肪组织外泌体中出现55个差异表达的microRNAs，其中肥胖患者的外泌体中miR-148b和miR-4269的表达显著下调，而miR-23b和miR-4429的表达上调，这些变化的microRNAs通过调节TGF-β和Wnt/β-catenin信号通路中的mRNAs发挥作用。Dai等[35]研究发现脂肪细胞外泌体通过活化脂肪宿主巨噬细胞分泌促炎细胞因子促进脂肪再生。Barberio等[36]发现脂肪细胞外泌体microRNAs可以部分改变巨噬细胞胆固醇的外排，进而通过破坏胆固醇的清除，最终造成儿童肥胖。Thomou等[37]发现脂肪组织特异性敲除microRNAs合成关键酶Dicer (Dicer KO)的小鼠和患有脂肪营养不良的人类，其循环外泌体中microRNAs水平显著降低。将白色和棕色脂肪组织移植到ADicerKO小鼠体内，可以恢复循环microRNAs水平。通过对Dicer KO小鼠注射正常小鼠血清来源的外泌体也可以得到相似的结果。上述研究表明脂肪组织是构成循环外泌体microRNAs的重要来源，并可以调节远端组织的基因表达，提示脂肪组织分泌的外泌体microRNAs是一种新的脂肪细胞因子形式，这预示脂肪组织产生的这些microRNAs可能有助于诊断肥胖等代谢性疾病。

参与肝脏脂肪变性的调节　肝脏脂肪变性是一种异常的代谢状态，其特征在于肝脏中堆积大量脂肪。已经证明来自肥胖个体的内脏脂肪组织外泌体可能影响非酒精性脂肪肝病(NAFLD)的形成。Povero等[38]从高脂饲喂诱导的NAFLD小鼠模型中分离出外泌体，发现外泌体中含有的蛋白与对照组明显不同，且miR-122和miR-192在血液中被富集，而在肝脏中的水平减少，表明二者参与了NAFLD的形成。Rong等[39]发现从褪黑激素处理的脂肪细胞中分离的外泌体能显著减弱高脂饮食和抵抗素介导的内质网(ER)应激诱导的肝脏脂肪变性，并证明褪黑激素是通过抑制Bmal1的转录和增强m6A RNA去甲基

化进而减少脂肪细胞外泌体中的抵抗素水平，进一步减轻ER应激诱导的肝脏脂肪变性。

参与胰岛素抵抗 肥胖通常会诱导胰岛素抵抗等代谢性疾病的发生。以往研究表明，脂肪组织通过释放细胞因子如肿瘤坏死因子(tumor necrosis factor-alpha，TNF-α)、白细胞介素-6 (interleukin-6，IL-6)、瘦素和脂联素等影响靶组织的胰岛素功能[40-42]。现在有不少研究发现，脂肪组织也可以通过分泌的外泌体诱导机体发生胰岛素抵抗。Deng等[22]发现从肥胖小鼠脂肪组织中分离的含视黄醇结合蛋白4 (RBP-4)的外泌体能通过TLR4/TRIF通路刺激单核细胞向M1型巨噬细胞分化，这些M1型巨噬细胞可以增加TNF-α和 IL-6的分泌，进而导致细胞胰岛素抵抗。最近，Zhang等[43]发现肥胖小鼠脂肪细胞源外泌体可传递miR-155到骨髓巨噬细胞(BMMs)，并通过调控靶基因SOCS1和JAK/STAT通路，诱导BMMs向M1巨噬细胞表型极化。同样，Song等[44]发现小鼠脂肪细胞源外泌体携带的音猬因子(sonic hedgehog)可通过Ptch/PI3K通路介导BMMs向M1巨噬细胞极化，诱导脂肪细胞发生胰岛素抵抗。葡萄糖转运蛋白4(glucose transporter 4，GLUT4)是胰岛素信号传导途径中重要的葡萄糖转运蛋白，下调GLUT4可降低细胞对葡萄糖的摄取，进一步加重胰岛素抵抗。Zhang等[45]发现人M1巨噬细胞释放的外泌体可被脂肪细胞吸收，从而通过激活NF-κB减少GLUT4的转运，诱导脂肪细胞发生胰岛素抵抗；同样的研究发现，给野生型小鼠静脉注射肥胖小鼠脂肪组织巨噬细胞外泌体后，前者葡萄糖清除率和胰岛素的降肝糖能力均降低，PPARγ及GLUT4表达减少，机体胰岛素敏感性降低，而源于正常小鼠和瘦小鼠的同类外泌体则无上述作用，进一步研究发现外泌体中过表达的miR-155是引起PPARγ和GLUT4下调的关键因素[46]。Yu等[47]还发现来自肥胖小鼠脂肪细胞外泌体的miR-27a可以降低骨骼肌中PPARγ的表达，进一步降低GLUT4的表达，增加胰岛素抵抗。有研究发现ob/ob小鼠脂肪组织外泌体中miR-141-3p的表达减少，可通过影响其靶基因*PETN*以及*PETN*作用的PI3K/PDK1/AKT/GSK3信号通路，破坏葡萄糖的吸收及摄取，干扰肝脏胰岛素信号转导造成胰岛素抵抗[48]。Castaño等[49]发现肥胖小鼠血浆外泌体中的miR-122、miR-192、miR-27a-3p和miR-27b-3p等可诱导瘦小鼠葡萄糖耐受不良和胰岛素抵抗，而PPARα的表达降低及血液中游离脂肪酸的升高是关键因素之一。上述研究表明microRNAs可通过旁分泌或内分泌调节机制转移到胰岛素靶细胞中，对细胞及体内胰岛素敏感性和葡萄糖稳态等进行调节。此外，肥胖患者脂肪组织外泌体中含有高浓度的促炎细胞因子[包括IL-6、(单核细胞趋化蛋白1(MCP-1)、RBP-4和脂联素]可诱导肝细胞和肌细胞产生胰岛素抵抗[50]。总之，这些研究表明，肥胖脂肪组织会分泌对机体“有害”的外泌体并通过多种途径诱导胰岛素抵抗的发生(图2)。

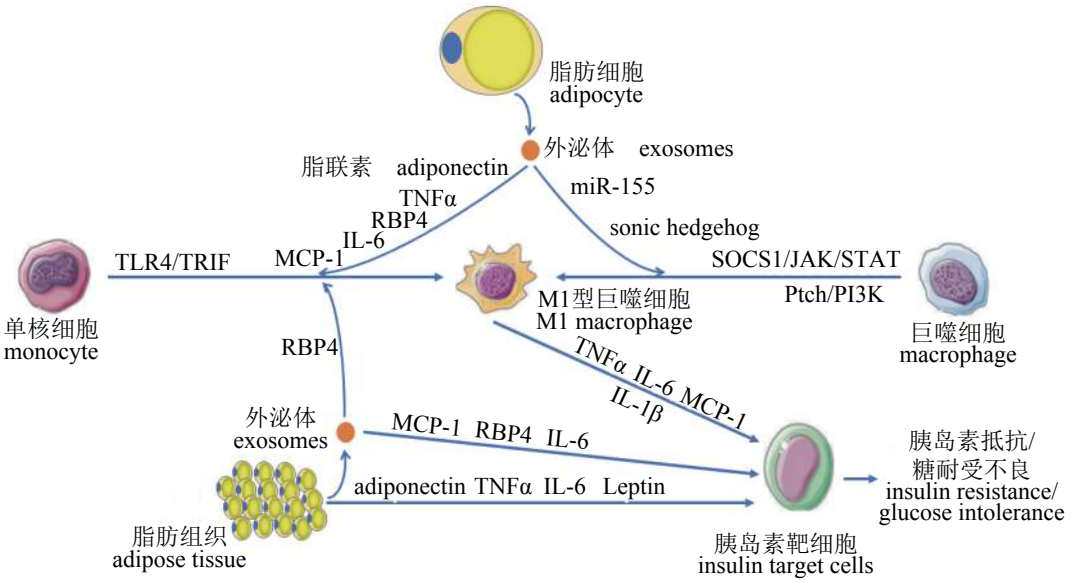

图 2 脂肪细胞产生的异常外泌体可能诱导胰岛素抵抗的机制[5]

Fig. 2 Mechanism of abnormal exosomes produced by adipocytes that may induce insulin resistance

与上述不同的是，ADSCs源外泌体对机体似乎充当着“有益”角色。Shree等[51]通过建立3T3-L1和C2C12细胞的胰岛素抵抗模型，并用脂肪源间充质干细胞的条件培养基(ADSCs-CM)处理模型细胞后发现其恢复了胰岛素敏感性，并认为这可能和GLUT4及磷酸化Akt蛋白表达上调、IL-6和PAI1(纤溶酶原激活物抑制剂-1)表达下调有关。Zhao等[52]发现ADSCs源外泌体通过转移STAT3使巨噬细胞向M2极化，进而改善高脂诱导的肥胖小鼠白色脂肪组织炎症发生及代谢稳态、减少肥胖和减轻肝脏脂肪变性，说明脂肪源性干细胞(ADSCs)在控制肥胖相关炎症和代谢紊乱方面发挥着关键作用。

参与免疫调节　肥胖会促进白色脂肪组织的慢性低度炎症。Kranendonk等[53]证实促进单核细胞向M1巨噬细胞分化的外泌体来自脂肪细胞。脂肪源外泌体中存在免疫调节蛋白如TNF-α、巨噬细胞集落刺激因子(macrophage colony-stimulating factor，MCSF)和RBP-4[53]。肥胖小鼠脂肪外泌体的miR-155诱导巨噬细胞向M1分化，导致脂肪组织中M1-M2巨噬细胞比例不平衡，从而引起慢性炎症[43]。外泌体还可以通过循环运输促炎因子，与远端细胞相互作用促进炎症[10, 54]。来自ADSCs的外泌体能降低体外刺激的T淋巴细胞的增殖速率。此外，ADSCs衍生的外泌体还通过减少干扰素-α(interferon alpha, IFN-α)的分泌来抑制T细胞活化[55]。

参与肿瘤调节　脂肪细胞是多种类型肿瘤微环境中的一员，在某些肿瘤的发展中起作用，特别是乳腺癌、肝癌和恶性黑色素瘤等。ADSCs源外泌体可作为microRNAs的有效转运载体，实现特定microRNAs向肝癌细胞的传递，通过调控肿瘤相关靶基因的表达进而发挥microRNAs的抗肝癌或化疗增敏作用[56]；研究发现过度肥胖者会引发外泌体分泌增多，肿瘤细胞的迁移性增强[57]。前脂肪细胞(3T3-L1)源外泌体能够促进体内乳腺肿瘤的形成和转移[58]。体外培养的3T3-F442A成熟脂肪细胞源外泌体可增加黑色素瘤细胞的迁移和浸润能力[57]。从脂肪细胞分泌的外泌体circRNA(exo-circ-DB)通过抑制miR-34a和激活去泛素化相关的USP7促进肝细胞癌(HCC)的生长并减少DNA损伤，当敲低circ-DB时，脂肪外泌体对HCC细胞的作用则可以逆转[59]。ADSCs源外泌体在大鼠中能显著抑制肝细胞癌发展[60]。从上述可以看出，外泌体像一把“双刃剑”，ADSCs外泌体对肿瘤既有负向调控也有正向的调控作用，与肿瘤进展有密切联系。

参与血管以及神经的生成　研究证明外泌体通过增强细胞增殖和血管生成，促进伤口愈合和肌肉再生。脂肪间充质干细胞可通过促进成纤维细胞的增殖加快皮肤伤口的愈合[61]。ADSCs外泌体促进血管内皮细胞迁移和增殖并刺激新血管形成[62]。黄珍[63]体内实验证实，ADSCs外泌体有助于SVF-CD34+细胞的有效归巢及移植后的造血重建，其机制可能与调节SDF-1/CXCR4信号通路相关。Dai等[35]发现小鼠脂肪组织外泌体可诱导脂肪源性干细胞的脂肪形成，促进主动脉内皮细胞的增殖、迁移和血管的生成。ADSCs及其外泌体的联合治疗可减少大鼠急性缺血性卒中的脑梗面积、帮助神经恢复[64]，可以有效降低毒邪侵袭(谷氨酸兴奋毒损伤)PC12细胞模型的LDH释放率，对PC12细胞具有保护作用，并推测这可能与自噬作用有关[65]。

参与成骨作用　TNF-α预处理的ADSCs外泌体具有促进成骨细胞分化的功能[66]。黄春煌等[67]研究发现，脂肪间充质干细胞条件培养基及其外泌体能够有效促进骨髓间充质干细胞(BMSC)增殖、迁移和成骨向分化，去掉条件培养基中的外泌体后，其作用减弱；在小鼠中的研究发现，脂肪干细胞(ASC)释放的外泌体可以抑制低氧缺血环境下骨细胞凋亡，提示ASC来源的外泌体内含有多种营养物质，可通过调节骨细胞的生理活动以对抗低氧缺血环境导致的细胞凋亡，进而在促进骨组织的修复与再生中发挥作用[68]。

脂肪源性外泌体的其他作用　研究发现大鼠脂肪间充质干细胞来源的外泌体能够减轻肝脏缺血再灌注损伤，并认为其可能是通过缓解氧化应激、抑制炎症反应、抗凋亡而发挥作用[69]。间充质干细胞来源的外泌体可升高心肌组织中ATP的水平，降低心肌氧化应激，增强心肌功能，进而在修复缺血再灌注造成的心肌损伤中起重要作用[70]。Yoshida等[71]给老龄小鼠注射从幼龄小鼠或培养的脂肪细胞中纯化的含烟酰胺磷酸核糖转移酶(eNAMPT)的外泌体，发现老龄小鼠细胞内NAD+生物合成增强，活动能力增强并延长了寿命。此外，ADSCs来源的外泌体在阿尔茨海默症治疗中起重要作用，因外泌体可分泌高水平脑啡肽酶，该酶可降解脑内β淀粉样蛋

白，减少其在脑内的堆积[26]。

外泌体在鱼类中的研究　截止目前，外泌体在鱼类中的研究还非常少。使用差速离心、透射电镜以及标记(HSP-70和乙酰胆碱酯酶)的方法在虹鳟(*Oncorhynchus mykiss*)血液中证实了外泌体的存在，发现血浆外泌体中富含HSP-70蛋白，该蛋白可响应体内热应激在血浆中短暂升高；在原代培养的虹鳟肝细胞中也发现增加环境温度(环境温度+15 °C)提高了肝细胞中HSP-70的表达，并导致HSP-70在外泌体中富集，但皮质醇处理后显著降低了从无应激或热应激的肝细胞释放的外泌体HSP-70的表达，证明了外泌体运输的HSP-70在机体应激反应中的作用[72]。在中华鳖(*Pelodiscus sinensis*)的附睾中发现外泌体的分泌特性及其与成熟精子间的相互作用，认为精子可通过内吞作用或膜融合途径吸收附睾外泌体[73]。在斑马鱼(*Danio rerio*)的研究中发现大脑内皮细胞提取的外泌体可以作为载体携带抗癌药物通过血脑屏障治疗脑癌[74]；在斑马鱼胚胎中用CD63-pHluorin标记可实现对单个内源性外泌体的实时可视化[75]；在大西洋鲑(*Salmo salar*)的研究中发现白细胞来源的外泌体中含有主要组织相容性复合体II类(major histocompatibility complex class II，MHCII)[76]；卢荣华等[77]发现草鱼(*Ctenopharyngodon idella*)脂肪肝细胞源外泌体和免疫作用相关，其能显著提高肝脏组织中促炎因子*TNF-α*、*IL-1β*和*IL-6* mRNA的表达水平。在半滑舌鳎(*Cynoglossus semilaevis*)的血液和精液中分离鉴定了外泌体[78-79]，其精液外泌体中的核苷酸组成主要为microRNAs，并发现4个microRNAs (dre-miR-141-3P、dre-miR-10d-5P、ssa-miR-27b-3P和ssa-miR-23a-3P)可以作为雄性和假雄性半滑舌鳎的性别标记分子[79]。在中国大鲵(*Andrias davidianus*)的胃和睾丸中也分离鉴定了外泌体[80-81]。

4　展望

近年来，有关外泌体的研究在很多领域取得突破，外泌体是一种拥有多重生物功能的活性载体，其生物学功能的研究才刚刚起步，需要进一步研究它们有哪些生理和病理作用，如何与靶细胞相互作用，在水产动物中的作用和调节机制与陆生动物有何异同，如何开发一些与外泌体有关的产品来改善鱼类的糖脂代谢紊乱，比如可通过构建含有能提高胰岛素敏感性miRNA或蛋白质的外泌体，改善鱼类的糖脂代谢紊乱，这为防治鱼类脂肪肝及糖不耐受等问题提供了新的思路，研究来自脂肪组织(细胞)的外泌体可以帮助我们进一步理解代谢性疾病的分子机制。因外泌体在不同生理活动中的显著作用，其在水产动物中的应用前景非常广阔。

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Function of adipose-derived exosomes and related research progress in aquatic animals

LU Ronghua [1], JI hong [2], NIE Guoxing [1*]

(1. *College of Fisheries*, *Henan Normal University*, *Xinxiang* 453007, *China.*;
2. *College of Animal Science and Technology*, *Northwest A & F University*, *Yangling* 712100, *China*)

Abstract: Exosome, a 30-150 nm vesicle, is secreted by a variety of cells, which influences or changes the behavior of recipient cells by transferring proteins, lipids, mRNAs and miRNAs, etc., and has been proved to be a new mode of intercellular communication. Exosomes have been found to be involved in the processes of fat synthesis and obesity, liver steatosis, insulin resistance, immune regulation, inflammatory response, tumorigenesis, vascular and neurogenesis, and osteogenesis. This article mainly expounds the formation and biological characteristics of exosomes, separation and identification method of exosomes. Moreover, it expounds the potential functions of adipose-derived exosome in the physiological and pathological process, and summarizes the research progress of exosomes in aquatic animals. It will provide new approach to lipid metabolism, pathological mechanisms of related diseases and potential intervention target. Also, it will provide basic theoretical knowledge of the role of exosome in glucose and lipid metabolism disturbance of fish.

Key words: exosomes; function; metabolic disorders; regulatory mechanism; research progress

Corresponding author: NIE Guoxing. E-mail: niegx@htu.cn

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