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·综述·

鱼类microRNA研究进展

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摘要： microRNA是一种大小为18~25个核苷酸的非编码RNA，调控靶基因的转录后表达，广泛参与多种生理过程。本研究简要综述了microRNA生物学特性、转录后调控机制，详细讨论了第二代测序技术的相关应用、microRNA在鱼类中的表达模式、功能研究，包括渗透压调节、生殖、发育、生长、免疫、代谢等。现有的研究表明，*miR*-200和*miR*-30具有调控血浆离子浓度和渗透压平衡的功能；Dicer1是胚胎发育所必需的，在原肠胚时期，*miR*-20*a*调节头、眼、脊柱、体节的形态发生，*miR*-92调控内胚层的形成，*miR*-10影响体轴形成，*miR*-219影响头部和尾部细胞的凋亡；*miR*-122、*miR*-30、*miR*-145分别影响肝细胞成熟、肝胆管和肠道发育，*miR*-138和*miR*-143调控心脏发育，*miR*-126、*miR*-150、*miR*-451调控血小板、血细胞的发育和成熟，*miR*-10和*miR*-126影响血管生成，*miR*-200、*miR*-183分别影响嗅觉、听觉系统的发育，多个microRNA参与视网膜、肌肉、鱼鳍、肝脏等器官的再生；*miR*-133*a/b*、*miR*-206抑制肌肉细胞分裂，*miR*-214、*miR*-499、*miR*-199、*miR*-3906调控快肌纤维和慢肌纤维的生成；*miR*-430促进原始生殖细胞的生成；多个microRNA参与到禁食和再投喂调控的分解代谢和合成代谢平衡；此外，microRNA通过对免疫因子的调控参与到先天免疫、低氧适应、体色调控、应激反应、肌间刺形成等生理过程中。本研究通过对这些结果进行总结和讨论分析，将有助于对鱼类microRNA研究领域现状的了解和把握，促进鱼类非编码RNA研究的深入。

关键词: microRNA；鱼类；渗透压；发育；生长；生殖；免疫；代谢

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1993年Lee等[1]报道了第一例小非编码RNA研究，在秀丽隐杆线虫(*Caenorhabditis elegans*)体内，小非编码RNA*lin*-4通过与*lin*-14 3′端非编码序列反向互补进而抑制其转录后表达。*let*-7是硬骨鱼中发现的第一种小非编码RNA，具有高度保守的序列和功能，在多种动物(脊椎动物、海鞘类、脊索动物、软体动物、节肢动物、环节动物)体内均有表达[2]。学者们通过生物信息分析和分子克隆的方法发现和确认了几十种该类小RNA分子，并统一将该类分子命名为microRNA[3-5]。

1 microRNA的生物学特性

microRNA具有以下特征：大小为18~25 nt，单链RNA，可以被Northern blot检测出，或者通过PCR克隆得到；成熟体由Dicer酶从具备茎环结构的前体序列加工得来，成熟体来源于前体序列的茎干部分[6]。

microRNA基因由RNA polymerase Ⅱ或者RNA polymerase Ⅲ转录，转录本被称作pri-microRNA[7-8]。RNA polymerase Ⅱ转录的pri-microRNA通常具有poly(A)，α-鹅膏蕈碱可以阻断其转录[7]；少部分

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microRNA由RNA polymerase Ⅲ转录，例如人类(*Homo sapiens*)基因组中最大的microRNA基因簇*C*19*MC*[8]。microRNA基因的转录受到转录因子的调控，转录因子的组合决定了microRNA在不同类型细胞中特异性表达。pri-microRNA大小为数千个碱基，内部具有茎环结构，Drosha酶从pri-microRNA发卡结构处切割，释放出pre-microRNA，大小为600~700 nt，该过程与转录同时进行，剪切后的其余部分被细胞核外切酶体(exosome)降解[6, 9]。经过细胞核加工之后，pre-miRNA通过EXP5(exportin 5) 运输到细胞质中，EXP5属于细胞核转运受体家族，主要负责pre-miRNA核输出，此外也转运少量的tRNA[10]。EXP5特异性识别具有>14 bp dsRNA(double strand RNA)和3′垂悬碱基在1~8 nt的结构，EXP5发挥转运机制与其他核受体家族成员机制相似，在细胞核与pre-miRNA、GTP-RAN相结合，GTP水解后EXP5释放pre-miRNA[6, 9]。pre-microRNA由Dicer酶加工剪切形成5′端和3′端具有垂悬碱基的双链RNA[11]。Dicer是大小为200 ku的核蛋白，属于RnaseⅢ家族，在物种间高度保守，在所有的真核细胞生物中均有表达[11]。microRNA的编码链加载AGO2蛋白后组成miRISC复合体，同时模板链被降解；通过microRNA与靶基因的不完全互补配对，miRISC复合体执行对靶基因mRNA降解、抑制翻译、mRNA脱尾等功能[12]。

2　microRNA转录后调控机制

microRNA通过与靶基因结合形成的miRISC复合小体促进mRNA的降解或者抑制翻译，microRNA与靶基因的结合位点通常位于mRNA 3′UTR (untranslated region)，也有少数结合位点位于5′UTR或CDS(coding sequence)区域[13]。

microRNA一般通过以下几种机制调控靶基因蛋白表达：①抑制翻译起始：靶基因microRNA通过AGO2以及相关蛋白与eIF4E竞争性结合5′GpppN，减少*eIF*4*E*介导的mRNA环化结构形成进而抑制了靶基因mRNA翻译的起始[14]；②阻止核糖体60S亚基组装：核糖体是mRNA翻译成蛋白的细胞器，由60S大亚基和40S小亚基组成，AGO2-Dicer-PAB1复合体通过招募*eIF*6抑制60S亚基形成[15]；③抑制翻译起始：核糖体脱落模型(ribosome drop-off model)认为靶基因microRNA降低翻译复合体的翻译速率，并促进翻译复合体的提前脱落和翻译提前终止[16]；④促进mRNA的脱腺苷化和降解：AGO1通过招募下游蛋白GW182促进mRNA的脱腺苷化和降解[17]。

microRNA根据靶基因mRNA表达水平的高低可以起到开关型或者微调型的调节作用[18]，microRNA对靶基因表达量设定了阈值，mRNA表达量高于阈值时，蛋白产量被强烈抑制；靶基因蛋白表达量接近阈值时对mRNA输入量非常敏感。

3　microRNA在硬骨鱼中的发现

microRNA在硬骨鱼中的发现主要基于三种方法：分子克隆、microarray和第二代测序。表1概括了近年来microRNA在鱼类中的研究进展。第二代测序相对于microarray、传统的桑格测序法具有高灵敏性、较大的检测动态范围、价格低廉的优点，尤其在发现物种特异性microRNA方面具有巨大优势[19]，在鱼类microRNA研究中具有广泛应用。

4　表达模式

microRNA按照特定的时间和空间模式表达，斑马鱼(*Danio rerio*)受精卵受精后的12 h内检测不到microRNA表达；受精后的1~2 d，大部分的microRNA都有表达并且可以被检测出，待到器官发育完成时(受精后96 h)，microRNA表达量明显增加[20]；大部分的microRNA(68%)为组织特异性表达，例如*miR*-140特异性在下颌、头部、鳍的软骨部分表达，*miR*-217的表达局限于外分泌胰腺，*miR*-7局限于内分泌胰腺。位于同一基因簇的microRNA，例如*miR*-200*a*/*b*/429*a*基因簇内的microRNA具有相同的表达模式；但是也有例外，在*miR*-216*a*/216*b*/217基因簇中，*miR*-216*a*/*b*/217均在胰腺中表达，但是*miR*-216*a*/*b*也在肌肉组织中表达[20]。

部分保守的microRNA在不同鱼类中具有类似的表达模式，如*miR*-122、*miR*-722、*miR*-92*a*被报道在大西洋鲑(*Salmo salar*)肝脏中特异性表达，*miR*-16*a*、*miR*-21在其脑中特异性表达[21]。但*miR*-143-1集中在大西洋鲑肾脏、鳃中表达，*miR*-22仅在红肌中表达[21]，这与在斑马鱼中的表达模式不同。值得注意的是，原位杂交显示*miR*-21仅在斑马鱼心脏瓣膜、耳石、菱脑原基中表达，

使用荧光定量PCR显示*miR*-21在大西洋鲑脑中特异性表达[21]，这表明原位杂交技术相对于荧光定量PCR可以揭示microRNA的精细分布。

5 microRNA在鱼类中的功能

5.1 microRNA与渗透压调节

鱼体相对于水体通常是不等渗的，鱼类通过肾脏、鳃保持体内水分和盐的平衡，应对水体渗透压的变化，miR-200家族和miR-30家族被报道参与鱼类渗透压的调节。

miR-200家族在脊椎动物间具有高度的保守性，由5个成员组成：*miR*-200*a*、*miR*-200*b*、*miR*-200*c*、*miR*-141和*miR*-429，成员间具有相似的序列。在斑马鱼中，miR-200家族由2个基因簇组成，*dre-miR*-200*b*/200*a*/429*a*/7149和dre-miR-200*c*/141/429*b*。在不同盐度的刺激下，相对于对照组，*miR*-200敲除(knock-out)后的个体水泡显著性增加，对渗透压变化高度敏感；在低pH的刺激下，与对照组相比，miR-200敲除组Na^+/H^+交换能力下降[22]。*miR*-200通过作用于靶基因*nherf*1发挥调节渗透压的功能，*nherf*1主要在离子细胞(ionocyte)中表达，离子细胞是位于表皮中的角质化细胞，执行的功能类似于哺乳动物的远端肾单位和收集管；*nherf*1调控包括离子通道蛋白(Na^+/H^+离子通道蛋白)、G蛋白偶联受体和一些糖基化跨膜蛋白的转运和膜定位[22]。在尼罗罗非鱼(*Oreochromis niloticus*)体内，*miR*-429通过作用于靶基因*ostf*1调节鱼类对渗透压变化的适应，随着渗透压的升高，*miR*-429表达量相应下降，*ostf*1 mRNA表达量逐渐上升；*miR*-429的敲降(knock-down)引发罗非鱼的耐盐能力下降[23]。

miR-30家族由5个成员组成：*miR*-30*a*、*miR*-30*b*、*miR*-30*c*、*miR*-30*d*和*miR*-30*e*，在肾脏中高丰度表达[24]，具有高度保守性，对于渗透压平衡的维持是必需的。在非洲爪蟾(*Xenopus laevis*)中，*miR*-30调控前肾的发育和渗透压平衡[25]；在罗非鱼中，miR-30c受到渗透压的动态调控，活体注射特异性抑制剂antagomir-30c导致靶基因*hsp*70表达量上升，血浆离子浓度和渗透压升高[24]。

5.2 microRNA与生殖

在多种鱼类中，microRNA参与调控配子形成和性腺发育，多组研究通过第二代测序和荧光定量PCR确定了数种鱼类的性腺microRNA表达谱和卵巢、精巢差异性表达microRNA[26-28]，不同鱼类中的microRNA差异性表达并没有相同之处，这可能是鱼的种类、性腺的不同发育时期造成的。在罗非鱼性别分化的早期阶段，多个microRNA-靶基因被报道参与类固醇生成，包括*miR*-737-*Star*1、*miR*21/200*b*-*Cyp11a*1、*miR*-96/200*b*-*Hsd*3*b*、*miR*-7977-*Foxl*2、*miR*-30*a*-*Cyp*19*a*1*a*、*miR*-212-*Dmrt*1、*miR*-96/499-*AMH*、*miR*-9/27/737*a*-*Hsd*11*b*等[29]。卵巢和精巢(性腺发育Ⅰ/Ⅱ期)microRNA差异性表达谱显示，67种microRNA在卵巢中上调，9种下调；其中多个microRNA被预测参与类固醇生成通路，包括的microRNA-靶基因有*miR*-17-5*p*-*DMRT*1、*miR*-20*a*-*DMRT*1、*miR*-138-*CYP*17*A*2、*miR*-338-*CYP*17*A*2、*miR*-200*a*-*CYP*17*A*2、*miR*-456/138-*AMH*等[30]。

原始生殖细胞(primordial germ cells, PGCs)是产生雄性和雌性生殖细胞的早期细胞，*nanos*和*tdrd*7是维持PGC最重要的基因，具有与体细胞不同的基因表达谱，保守的*miR*-430在体细胞中抑制这2种基因的表达[31-32]，PGCs中的特殊微环境(*Dnd*拮抗*miR*-430的沉默效应[33])抑制了*miR*-430对*nanos*和*tdrd*7的调控，确保了*nanos*和*tdrd*7的特异性表达；其次*miR*-430通过抑制C1q-like调控PGCs的数量[34]。

5.3 microRNA与发育

microRNA广泛参与发育的多个阶段，microRNA在鱼类中参与的发育过程包括形态发生(morphogenesis)、母源mRNA清除、细胞分化、器官再生、变态发育等。

Dicer1是加工microRNA成熟必需的酶，是胚胎发育所必需的，缺失*dicer*1基因会致死，母源的Dicer1加工形成最初的microRNA[35]。microRNA在原肠胚中发挥作用，调控体节、脑和心脏的形态发生，对细胞分化起到微调的功能[36]；*miR*-20*a*通过抑制*vsx*1表达，调控头、眼、脊椎、体节的形态发生[37]；*miR*-92通过调控*gata*5来控制发育，过表达*miR*-92导致内胚层形成减少，抑制*miR*-92表达导致内胚层形成增加、枯否氏泡(Kupffer's vesicle)发育异常[38]；*miR*-10发挥着抑制*HoxB*1和*HoxB*3表达的功能，维持*Hox*基因合理的表达量，对体轴的正常发育具有重要作用[39]，该调控机制在尼罗罗非鱼中也是保守的[40]；*miR*-219

的过表达或沉默均会导致斑马鱼胚胎发育畸形，过表达诱导头部和尾部细胞凋亡[41]。在消化系统中，*miR*-122在肝脏中特异性表达，占肝脏microRNA总量的70%以上，促进肝脏前体细胞的分化和肝细胞成熟[42]，*miR*-30*a*敲降引起肝胆管形态发生的缺陷[43]，*miR*-145通过调控*gata*-6促进表皮和平滑肌细胞分化，促进肠道的发育成熟[44]。在循环系统中，*miR*-138具有调控视黄酸信号通路的功能，是心脏发育和基因在心室特异性表达所必需的[45]；*miR*-143在心脏中高表达，通过抑制*adducin*3调控F-actin的重构，对心房的正常发育必不可少[46]；*miR*-126和*miR*-150协同调控血小板和血细胞生成，敲降*miR*-126导致血细胞增多、血小板生成减少[47]，*miR*-451具有通过调控gata-2促进红细胞成熟的功能[48]，microRNA *Mirn*140的表达是保持血小板形态完整所必需的[49]；Vegf(vascular endothelial growth factor)信号通路是促进血管生成的关键通路，具有促进内皮细胞分裂、迁徙等功能，*miR*-10和*miR*-126通过调控Vegf信号通路促进血管生成[50-51]。在神经系统中，miR-200家族在嗅觉祖细胞中高丰度表达，并促进其终、末端分化[52]，miR-183家族具有影响毛细胞(hair cell)分化方向的功能，调控内耳的发育[53]。

相对于哺乳动物，鱼类具有较强的器官再生能力，microRNA参与多种类型器官的再生，包括视网膜、肌肉和鱼鳍、肝脏等。视网膜再生依赖于缪勒神经胶质细胞(Müller glia)脱分化成为多能祖细胞(multipotent progenitor cell)以及后者的分裂，let-7具有抑制脱分化的功能，视网膜受到损伤之后，*let*-7的表达被Ascl1a抑制从而启动再分化[54]；敲降*dicer*促进多能祖细胞分裂[55]，*miR*-203通过调节Pax6b表达进而抑制多能祖细胞分裂[56]。*miR*-133是一种在肌肉中特异性表达的microRNA，参与肌肉损伤后的再生，斑马鱼心脏损伤后通过心肌细胞的激活和分裂进行再生过程中，抑制*miR*-133则会提升促再生基因*cx*43表达，促进心肌细胞分裂和心肌再生[57]；Fgf(fibroblast growth factor)是调控鱼鳍再生的重要信号通路，在鱼鳍损伤时，该信号通路通过抑制*miR*-133调控促分裂基因表达促进鱼鳍再生[58]；*miR*-378和*miR*-21具有调控DNA合成的功能，在肝脏损伤后促进再生[59]。

在鲆鲽类的变态发育过程中，*miR*-1、*miR*-7、*miR*-9*[*代表microRNA成熟链的互补链(dicer酶切割后形成RNA双链复合体，包括microRNA成熟体和带星号的microRNA)，一般含量较低]、*miR*-21*a*、*miR*-20*c*、*miR*-23*c*、*miR*-128、*miR*-181在变态前高丰度表达，在变态期表达量降低；*miR*-10*b*、*miR*-23*a*、*miR*-26*a*、*miR*-130*d*、*miR*-145、*miR*-200*a*、*miR*-429、*miR*-221、*miR*-724在变态期表达量变化；*miR*-10*b*、*miR*-23*a*、*miR*-26*a*、*miR*-130*d*、*miR*-145、*miR*-200*a*、*miR*-429在变态发育后期发生变化[60]，这些microRNA可能在鲆鲽类变态发育的不同阶段发挥调控功能。

5.4　microRNA与生长

经济鱼类的价值主要是提供肌肉，因此从microRNA角度阐明骨骼肌发育和生长对于水生经济动物品系的选择和育种具有一定的指导意义。Huang等[93]对不同生长速率的尼罗罗非鱼品系的骨骼肌microRNA转录组进行了检测，共检测到16种差异性表达的microRNA。

microRNA参与肌肉细胞分化、分裂和细胞特征自维持，肌肉中特异性表达的microRNA *miR*-133*a/b*[61]、miR-206[62]通过调控*Igf*-1(insulin-like growth factor 1)的表达抑制罗非鱼的生长[62]。*miR*-214通过调控hedgehog信号通路的负调控因子*su*(*fu*)促进慢肌纤维的发育[63]，通过调控N-ras抑制肌细胞分裂进而促进终末端分化的肌管细胞[64]，*miR*-499在慢肌纤维中高表达并维持慢肌纤维特征[65]，miR-3906间接抑制*myf*5，促进快肌纤维分化[66]，通过抑制*homer*-1*b*调控肌细胞内Ca^{2+}稳态和维持快肌纤维特征[67]；*miR*-199通过调控WNT信号通路多个基因平衡成肌细胞的分裂和分化，*miR*-203*b*则通过调控*myoD*抑制成肌细胞的分化[68]。在纳豆芽孢杆菌(*Bacillus natto*)作为益生菌添加剂促进鱼类生长的情况下，*miR*1/133/181在草鱼(*Ctenopharyngodon idella*)骨骼肌中的表达量上调[69]。

5.5　microRNA与免疫

microRNA参与抵抗细菌和病毒侵染的生理过程中，一般对宿主具有保护效应。哈维氏弧菌(*Vibrio harveyi*)是造成水生经济动物病害的主要病原菌之一，在感染弧菌的尖吻鲈(*Lates japonicus*)体内检测到了63种microRNA，其中34种microRNA表达量上升，12种表达量下降，

miR-21家族成员表达量上调幅度最大，达到2.5倍以上[70]；在弧菌诱导斑马鱼的免疫反应中，*miR*-122和*miR*-194下调，并影响多种免疫因子的表达，如*tnf-α*(*tumor necrosis factor α*)、*toll-like receptor*、*interleukin*-22等[71]；使用沙门氏伤寒杆菌(*Salmonella typhimurium*)对斑马鱼胚胎进行攻毒，Toll-like信号通路激活并诱导*miR*-146*a/b*表达上调，敲降*miR*-146导致载脂蛋白家族中6个成员上调[72]。在草鱼体内，过表达*miR*-155/142-3*p*促进肾细胞因子诱导的杀伤细胞(cytokine induced killer，CIK)的活性，这2个microRNA作用于*toll-like receptor* 5 (*tlr*5)调控多种免疫因子的表达，进而增强免疫效应[73]。感染柱状黄杆菌(*Flavobacterium columnare*)诱导鲤(*Cyprinus carpio*)肝脏microRNA表达谱中的30个microRNA表达量发生变化，这些microRNA被预测参与细胞粘连、细胞外基质—受体相互作用(extracellular matrix-receptor interaction)、肌动蛋白细胞骨架、紧密连接、ErbB(erythroblastic leukemia viral oncogene homolog)信号通路的调控[74]。在无乳链球菌(*Streptococcus agalactiae*)感染尼罗罗非鱼6~72 h后，脾脏microRNA表达谱共有1121种microRNA表达量发生变化，这些microRNA主要参与到凋亡、信号通路和免疫反应过程中[75]。

牙鲆(*Paralichthys olivaceus*)被虹彩病毒侵染后，128种宿主microRNA表达量发生变化，这些microRNA的预测靶基因集中在免疫、信号传导、凋亡途径中[76]。在DNA疫苗诱发的免疫反应中，*miR*-155/462/731上调并调控免疫因子的表达，有助于虹鳟(*Oncorhynchus mykiss*)抵御出血性败血症病毒的感染[77]。*MiR*-731在牙鲆被细胞肿大病毒(*Megalocytivirus* sp.)感染后，表达量诱导上调，通过作用*interferon regulatory factor* 7 (*IRF*7)和*p*53，具有抑制抗病毒通路的效应，这可能是细胞肿大病毒在进化中利用宿主microRNA进行自我保护的一种策略[78]。聚肌苷酸胞苷酸(polyinosinic polycytidylic acid，polyi:c)是一种高效的干扰素诱导剂，在使用polyi:c处理泥鳅(*Misgurnus anguillicaudatus*)后，多种microRNA表达量发生变化，这些microRNA通过作用于RIG-Ilike receptor (RLR)信号通路，促进干扰素、细胞因子和凋亡反应，进而增强免疫反应[79]。水泡病毒侵染乌鳢(*Channa argus*)SSN-1细胞系24 h后，共有143种microRNA表达量发生明显变化，其中*miR*-130-5*p*、*miR*-214、*miR*-216*b*对病毒复制具有抑制作用，对宿主具有保护效应[80]。

5.6 microRNA与代谢

在虹鳟体内，*miR*-122具有抑制血糖上升和促进血液中胆固醇浓度上升的功能[81]；鳜(*Siniperca chuatsi*)禁食1周后恢复摄食，*miR*-10*c*、*miR*-107*a*、*miR*-133*a*-3*p*、*miR*-140-3*p*、*miR*-181*a*-5*p*、*miR*-206、*miR*-214表达量发生显著性变化，这些microRNA可能参与禁食和再投喂调控的分解代谢和合成代谢平衡[82]，在斑马鱼体内*miR*-140-5*p*和*let*-7*d*受到禁食诱导，靶向调控代谢的重要基因*AMPK* (adenosine monophosphate-activated protein kinase)[83]；在尼罗罗非鱼体内，microRNA参与到清除活性氧(reactive oxygen species)的过程中，*miR*-223、*miR*-146*a*、*miR*-122、*miR*-16在维生素E缺乏时下调，在维生素E过量摄入时上调[84]。

6 microRNA与其他生理过程

鱼塘水体缺氧是造成“翻塘”，导致鱼类大规模死亡的主要原因之一，研究microRNA调控低氧胁迫(hypoxia)有助于阐释鱼类适应低氧的生理机制。低氧胁迫导致瓦氏黄颡鱼(*Pelteobagrus vachelli*)肝脏中多种microRNA表达量发生变化，其中鉴定到162组microRNA-靶基因具有调控关系，广泛参与到代谢、血管生成、氧气运输等生理过程中[85]。后肠是泥鳅的呼吸器官，在低氧胁迫的情况下共有47种microRNA差异性表达[86]。microRNA同时也被报道参与低氧对雌性生殖系统的生理过程调控，在低氧胁迫下，海水鱼类青鳉(*Oryzias laticeps*)的卵巢中共有43种microRNA差异性表达，生物信息学预测，多种microRNA与类固醇生成基因具有调控关系[87]。

*p*53转录因子是一种肿瘤抑制基因，是应激反应的中心调节基因，*miR*-125*b*通过抑制*p*53蛋白表达，具有抑制细胞凋亡的功能；当DNA受到损伤，*miR*-125*b*表达量下调，促进P53蛋白表达量上升[88]。

miR-429在体色形成中发挥着一定的作用，在鲤和罗非鱼体内，*miR*-429靶向*foxd*3进而间接抑制对黑色素形成必需基因的表达；紫外线可以快速诱导*miR*-429的表达，从而加快黑色素的形成[89]。

在团头鲂(*Megalobrama amblycephala*)体内，*miR*-206-3*p*、*miR*-133-3*p*在肌间刺形成的4个阶段

呈差异性表达，分别作用于*Tgfb*1*r*、*run*2*x*参与肌间刺形成的调控[90]。肌间刺在鱼类的加工和利用中比较难以清除，该项研究有助于阐释肌间刺的形成机制。

表 1　microRNA在鱼类中的发现

Tab. 1　Discoveries of microRNAs in teleost fish

物种 species	组织 tissues	样本类型 sample types	测序方法以及平台 sequencing methods and platform	保守型/个 conserved microRNAs	物种特异性/个 novel microRNAs	参考文献 references
斑马鱼 *Danio rerio*	不同胚胎发育时期样品；成鱼多种组织	不同发育阶段胚胎；成鱼	第二代测序，Roche FLX genome sequencer	192	25	[91]
尼罗罗非鱼 *Orechromis nicotilus*	骨骼肌	成鱼	桑格测序法	25	无	[92]
尼罗罗非鱼 *Orechromis nicotilus*	肌肉	不同生长速率的罗非鱼	第二代测序；SOLiD	184	无	[93]
尼罗罗非鱼 *Orechromis nicotilus*	卵巢、精巢	雄性和雌性罗非鱼	第二代测序；Solexa	525	139	[27]
大西洋鳕 *Gadus morhua*	全鱼	从受精卵到幼鱼，共17个发育阶段	第二代测序；Roche 454 GL FLX sequencer	79	无	[94]
黄颡鱼 *Pelteobagrus fulvidraco*	性腺	雄鱼、雌鱼、超雄鱼	第二代测序；Illumina/Solexa Genome Analyzer	384	113	[95]
团头鲂 *Megalobrama amblycephala*	脑、垂体、肝脏、肌肉	生长速率不同的品系	第二代测序；Solexa	347	22	[96]
斑点叉尾鮰 *Ictalurus punctatus*	多种	成鱼	第二代测序；Solexa	237	45	[97]
大西洋鲑 *Salmo salar*	多种	幼鱼、4月龄鱼	第二代测序；Illumina	459	416	[98]
鳙 *Aristichthys nobilis*	多种	成鱼	第二代测序；Illumina Genome	167	39	[99]
鲢 *Hypophthalmichthys molitrix*	多种	成鱼	第二代测序；Illumina Genome	166	54	[99]
鲤 *Cyprinus carpio*	脾脏	成鱼	第二代测序；Solexa	194	12	[100]
青鳉 *Oryzias laticeps*	全鱼	成鱼	第二代测序；ABI SOLiD platform.	593	425	[101]
尖吻鲈 *Lates japonicus*	全鱼	成鱼	桑格测序法	59	4	[70]
虹鳟 *Oncorhynchus mykiss*	胚胎	胚胎	桑格测序法	14	4	[102]
鲤 *Cyprinus carpio*	多种	成鱼	桑格测序法	92	21	[103]
牙鲆 *Paralichthys olivaceus*	全鱼	不同生长阶段幼鱼	桑格测序法	23	无	[60]

7　小结与展望

综上，microRNA广泛参与硬骨鱼类渗透压调节、生长、发育、免疫、代谢以及其他生理过程。硬骨鱼在脊椎动物中种类最为丰富，是地球生态环境重要组成部分；经济鱼类对人类蛋白质资源的提供具有重要意义，模式鱼类对发育、疾病的研究具有重要价值。因此深入开展对鱼类microRNA的研究，有助于加强对鱼类重要功能基因转录后调控机制的认识，更好地阐释鱼类生理过程的调控机制。目前，microRNA参与硬骨鱼类发育调控的研究报道较多，但与鱼类经济性状相关的研究，如摄食、生长、免疫和营养调控等还有待加强；另外，研究与重要经济性状相关的microRNA分子标记，将为鱼类良种选育和分子育种提供参考依据。

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A review of microRNA research in fish

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Abstract: MicroRNAs, small non-coded RNA of about 18–25 nucleotides, regulate target genes expression by partially complementary binding to 3′UTRs (untranslated regions) and are involved in many biological processes. Recently, microRNAs have been studied broadly in teleosts. This paper briefly reviews the biological property of microRNAs and the post-transcriptional regulation they confer, focusing on microRNAs expression pattern and the discovery of microRNAs in teleost fish by next-generation sequencing. The function studies about microRNA in teleost cover osmotic stress regulation, reproduction, development, growth, immunity, metabolism and other biological processes. Results show that miR-200 and miR-30 family members control the cellular ion balance and salt resistance. Dicer1 is essential to the development of zebrafish, its deletion is lethal and the organogenesis will be impaired. MiR-20a regulates the morphogenesis of head, eye, spinal cord, somite during the gastrula stage; miR-92 controls the formation of endoderm; miR-10 regulates the formation of body axis; miR-219 affects the apoptosis of head and tail, and miR-122, miR-30 and miR-145 respectively adjust maturation of liver cells, the development of liver and intestinal tract. The development of heart is under the control of miR-138 and miR-143; miR-126, miR-150, miR-451 regulate the development and maturation of thrombocytes and hemocytes; miR-10 and miR-126 regulate the formation of blood vessel; miR-200 and miR-183 each regulate the development of olfaction and auditory system. Multiple microRNAs are involved in the process of organ regeneration. MiR-133a/b and miR-206 inhibit the proliferation of myocyte; miR-214/499/199/3906 are involved in the process of quick-twitch and slow-twitch muscle differentiation; miR-430 promotes the generation of primordial germ cell, and microRNAs are also reported to be involved in multiple physiological processes of energy homeostasis, innate immunity, hypoxia adaptation, body color regulation, stress responses, intermuscular bone formation. This paper summarizes those results and will benefit the understanding of the present situation of the microRNAs research in teleost and may be helpful for the promotion of the study in noncoded RNA.

Key words: microRNA; fish; osmotic stress; development; growth; reproduction; immunity; metabolism

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