综 述

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鱼类卵子质量研究及其关键科学问题

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摘要: 卵子质量(卵质)是一种复杂的生物学特性, 是决定雌性动物生殖能力的主要因素。鱼类卵质通常指卵子的受精能力及支持胚胎正常发育的能力, 它直接关系到受精卵的形成、胚胎的早期发育及仔、稚、幼鱼的成活与生长, 是决定鱼类繁育成功和养殖效率的首要环节。对卵质进行客观而准确的评估, 提升卵子质量, 以获得大量高质量的成熟卵, 是水产种业和养殖业发展的重要前提。理论上, 鱼类的卵质由卵子中所储存的所有母源物质的集合及其时空分布格局所共同决定。文章综述了鱼类卵子的发生和成熟及鱼类卵质评估标准的研究现状, 重点评述了以斑马鱼为模型所开展的母源因子对卵子质量的调控研究。最后, 提出了鱼类卵质研究中亟待研究和解决的重要科学问题, 即需要重点研究卵原细胞-卵母细胞转换、卵母细胞-卵子转换、卵-胚转换、胚胎-仔鱼转换、仔-稚鱼转换等决定卵质和受到卵质影响的关键生物学事件。

关键词: 卵子质量; 卵子发生和发育; 卵质评价; 母源物质

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卵子质量(卵质), 又称卵子的发育潜能, 是指卵子能够正常受精及支持胚胎发育的能力, 是决定雌性动物生殖能力的主要因素。鱼类是重要的蓝色食物来源[1], 高效繁育是鱼类品种扩繁和种质创新最基本的前提。因此, 可持续绿色发展的水产养殖极大依赖于获得量大质优、可用于高效繁育的成熟鱼卵。硬骨鱼类共有3万多种, 其中用于水产养殖的鱼类400余种。不同的鱼类产出的卵子, 生物学特性往往彼此不同, 它们的受精率、孵化率、存活率以及早期胚胎发育进程都存在很大差异, 因此在学术界和产业界均缺乏清晰可靠的鱼类卵质评价标准。鱼类卵细胞在发育过程中积累了大量的mRNA、蛋白质、激素、脂质、糖类和维生素等母源物质, 这些母源物质不仅支持了卵细胞的发育和成熟, 还对受精后的胚胎发育以及仔稚鱼发育起到重要作用。因此, 从科学本质上而言, 鱼类的卵质是由囤积在卵子中母源物质的集合所共同决定的, 而这些母源物质的囤积不仅受到亲鱼的遗传调控, 也受到生存环境的影响。总之, 从遗传和环境等多角度, 深入探究影响鱼类卵质的因素及其作用机制, 将有助于建立鱼类卵质评价的科学标准, 实现雌性亲鱼的产前诊断, 并提出鱼类卵质提升的可行性途径。

1 鱼类卵子发生概述

鱼类的卵子发生(Oogenesis)是指雌性配子的形成、发育和成熟的过程。这包括原始生殖细胞的形成、原始生殖细胞到卵原细胞的发育和卵原细胞到成熟卵细胞的发育三个阶段[2]。

斑马鱼是开展生殖细胞发育和配子发生研究的良好模型, 以斑马鱼为模型的研究揭示了硬骨鱼类卵子发生的基本规律[3—5]。在胚胎期, 获得母源遗传的生殖质(Germ plasm)的少数细胞被称作原始生殖细胞(Primordial germ cells, PGC); PGC是胚胎期生殖细胞的祖先细胞(Germline progenitor cell, GPC), 在胚胎发育早期与体细胞分开并迁移至生

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殖嵴, 与周围上皮细胞相互作用形成原始性腺; 进一步在原始性腺中转变为卵原细胞(Oogonia); 卵原细胞通过有丝分裂进行增殖和自我更新; 当卵原细胞增殖到一定数目时进入第一次减数分裂, 分化形成卵母细胞。

根据卵母细胞的大小和卵黄的形成状态, 一般人为地将卵子发生过程分为以下几个时期[6](图 1): 初级生长期(Primary growth oocytes, PG), 此时的卵母细胞开始生长; 卵黄增生前期(Primary vitellogenic oocytes, PV), 这一时期皮质泡(Cortical alveoli)产生并填充于卵母细胞的外围, 细胞分裂时相处于减数第一次分裂的间期; 进入卵黄增生期后, 卵母细胞不断地通过内吞作用从血浆中摄取脂质、卵黄蛋白原以及其他分子, 卵母细胞的体积不断增长, 经历卵黄增生早期 (Early vitellogenic oocytes, EV)、卵黄增生中期(Middle vitellogenic oocytes, MV), 直至卵黄颗粒充盈整个卵子, 卵母细胞处于完全生长期(Fully-grown oocytes, FG)。在此之前卵母细胞的减数分裂进程停留在第一次减数分裂的双线期, 染色体的四个拷贝进行活跃的转录, 积累大量的母源mRNA, 但此时的卵母细胞依然不具有受精能力, 称为未成熟的卵母细胞(Immature oocytes)[7]。在成熟诱导激素(Maturation-inducing hormone, MIH)和成熟促进因子(Maturation-promoting factor, MPF)的作用下, 卵母细胞的形态发生剧烈的变化, 其中最显著的事件是生发泡破裂(Germinal vesicle breakdown, GVBD)。经过这一过程, 卵母细胞完成第一次减数分裂, 减数分裂进程推进, 并停留在第二次减数分裂的中期。此时的卵母细胞已具备支持受精及早期胚胎发育所需的母源mRNA、蛋白质、脂质、维生素和激素等物质, 称为成熟期卵(Mature oocyte, M)。随后, 成熟期卵在孕酮(Progestin)的作用下从滤泡细胞(Follicle cells)中脱离, 积聚在卵巢腔中, 在促黄体生成素(Luteinizing hormone, Lh)的刺激下被排出鱼体。排出鱼体的成熟卵子与精子受精后, 便开启新一轮生命个体的发育[8]。

2 评判鱼类卵质的物理指征

衡量卵质优劣, 其最直接的指征是卵子的受精率、胚胎的孵化率以及幼鱼的生存性能, 如畸形率、存活率等。卵子受精率评价的难易程度根据鱼类卵子透明性的差异而有所不同。卵子成功受精之后, 胚胎细胞开始发生卵裂, 对于胚胎透明的鱼类卵子, 其卵裂较易观察, 正常胚胎和非正常胚胎卵裂形态的差异在胚胎发育的早期可被用于评价卵子质量; 对于不透明卵子而言, 可借助染色的方法进行判断。胚胎各个时期的发育状况经常被用于卵子质量的评价, 如在卵裂期观察卵裂以及卵裂球位置是否异常; 在原肠胚时期关注原肠运动以及体轴发育是否异常; 在幼鱼孵化阶段关注胚胎的孵化率以及最终的成活率。从某种程度上来说, 在精子质量一致的前提下, 胚胎畸形率、孵化率和存活率是评价卵子受精后发育潜能的较好指标[9]。

一些研究提示, 可通过某些物理形态特征来判断卵子质量的好坏, 其中比较重要的参数包括卵径大小、卵子色泽、透明度、沉浮性及脂滴(Lipid droplet, 又称“油球”)颗粒的大小和分布等。一般而言, 在相同遗传背景的种群内部, 其卵子直径越小,

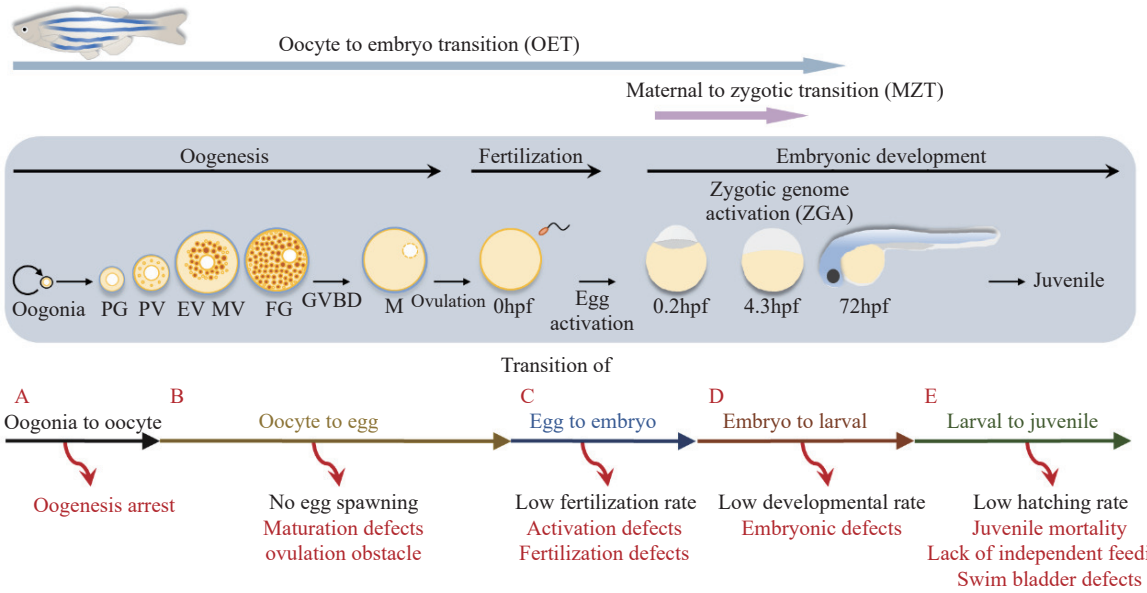

图 1 卵子质量调控及其影响的发育事件

Fig. 1 Regulation of egg quality and its influence on developmental events

越表现出较差的卵质。以斑马鱼为模型的毒理学研究显示, 经药物处理雌鱼的卵子受精率与孵育率降低, 往往伴随着卵子直径的减小与色泽的改变[10—12]。然而, 另一些研究报道, 卵子的直径也并非越大越好。如饥饿胁迫下的斑马鱼(*Danio rerio*)产下的卵子直径增大, 但是其受精卵的孵化时间却相对延后, 幼鱼的存活率显著下降[13]; 在对大菱鲆(*Scophthalmus maximus*)的研究中也发现, 直径较大的卵子往往受精率和孵化率偏低 [14]。其次, 卵子的透明度与色泽也为卵质提供重要参考, 斑马鱼败育的受精卵的卵黄往往在受精之前就表现出较差的透明度, 卵黄物质呈现不均一的状态, 色泽暗沉[15]。不同物种的卵子, 根据其孵化时处于水体的底层还是上层, 分别定义为沉性卵和浮性卵。如产浮性卵的大菱鲆、多锯鲈(*Polyprion oxygeneios*)和红海鲷(*Pagrus pagrus*)等, 具有较高上浮率的卵子其受精率、孵化率等也越高, 因此卵子的上浮率也作为评价这类浮性卵卵质的重要指标[14, 16, 17]。卵的沉浮性一般与其含有的脂滴比重与分布、卵膜间隙的大小等有关。在亚东鲑(*Salmo trutta fario*)的研究中发现脂滴的分布形态与其受精率直接相关, 脂滴均匀分布于卵周的卵子质量优于脂滴聚集分布的卵子[18]; 在金头鲷(*Sparus aurata*)、尖吻重牙鲷(*Diplodus puntazzo*)和河鲈(*Perca fluviatilis* L.)的研究发现, 脂滴的形状和大小与其幼鱼的存活率密切相关[19, 20]。虽然在某种程度上, 卵子的形态特征可用于判断鱼类的卵质, 但是不同的鱼类, 参考标准不尽相同, 且同一物种内部也缺乏可靠的评判标准。因此, 迫切需要从遗传学角度建立统一的、客观的、可靠的鱼类卵质评价标准。

3　卵质决定及其调控的发育事件

从卵原细胞分化到卵母细胞成熟这一阶段, 是决定卵质的关键时期, 主要包括两个发育阶段, 对应两个时相的转换: 卵原细胞-卵母细胞转换(Oogonia-to-oocyte transition, 图 1A), 指的是卵原细胞进入减数分裂并开启卵母细胞的命运的过程, 主要受与卵原细胞分化相关基因的表达调控, 这一过程的失败往往会导致卵子产生的障碍, 雌鱼不孕甚至是性逆转。卵母细胞-卵子转换(Oocyte-to-egg transition, 图 1B)指的是卵母细胞发育为成熟卵子并从滤泡细胞中脱出的过程, 主要受卵母细胞中mRNA、蛋白质、脂类及其他各类物质的调控, 这一过程转换的失败往往伴随着卵子成熟缺陷与排卵障碍[5]。这两个阶段的转换能否成功以及转换完成的程度, 直接决定了卵子质量的优劣; 而卵子质量的优劣, 又调控了卵子受精后的一系列发育事件, 进一步决定受精胚发育的成败。

受到卵质影响的发育学事件可概括为3个主要的发育阶段, 对应3个时相的转换。首先是卵子向胚胎的转换, 也称作“卵-胚转换”(Egg-to-embryo transition, 图 1C), 是胚胎发育中一个最基本的转变, 受精之后两个单倍体的原核结合并开启多细胞生物的发育, 伴随着减数分裂向有丝分裂的转换、胚胎极性的建立、细胞骨架重构、皮质颗粒外排及胞质环流产生等生物学过程[21, 22]。卵-胚转换的失败或障碍往往表现为卵子激活失败、受精率低下或非常早期的胚胎发育异常等。接着是胚胎-仔鱼转换(Embryo-to-larvae transition, 图 1D), 指的是受精卵完成早期胚胎发育进程从而形成一个包含大部分组织器官原基的仔鱼的过程。在这其中最具决定意义的生物学事件是母源合子转换(Maternal-to-zygotic transition, MZT)[23], 即母源mRNA被有秩序地清除同时伴随着合子基因的激活(Zygotic genome activation, ZGA), 这一转换直接决定了母源与合子基因对胚胎发育控制权的交接。胚胎向仔鱼的转换失败或障碍往往表现为胚胎发育的缺陷, 如较高的畸形率、较低的胚胎孵化率或存活率。最后是仔鱼向稚鱼的转换, 也称作仔-稚鱼转换(Larvae-to-juvenile transition, 图 1E), 指的是由从利用母源提供的卵黄营养物质的仔鱼过渡到依靠自主摄食来满足营养需求的稚鱼[24]。这一过渡需要机体在形态、发育与行为上做出一系列的改变, 如消化器官的发育、鱼鳔充气和开口进食等, 因此伴随着大量的能量消耗。这一转换的失败, 其本质是仔鱼对卵黄营养物质的吸收和利用出现障碍, 往往表现为鱼鳔不充气、开口进食失败、低孵化率和高致死率等。

总之, 卵子是雌性配子生长和分化的最终产物, 其经历了卵原细胞-卵母细胞转换, 卵母细胞-卵子转换等重要的发育过程, 其中任一环节出现问题均可能导致卵子发生障碍或卵质变差。卵子受精后, 受精卵将经历卵-胚转换、胚胎-仔鱼转换和仔-稚鱼转换等关键的发育过程, 这些过程的顺利完成都受到卵子中储存的母源物质亦即卵子质量的调控, 其出现问题的表现形式往往表现为低受精率、低存活率和低孵化率等。

4　鱼类卵子质量及其影响的关键事件的遗传调控

4.1　卵细胞转录和囤积的mRNA

卵子发生过程中卵(母)细胞转录产生的mRNA

可分为两大类型, 一类是供卵母细胞自身发育成熟所需; 另一类是在成熟卵中获得有效囤积的mRNA并作为母源物质供给胚胎发育, 即母源mRNA, 其种类和丰度直接决定了卵子的质量, 并影响着后续胚胎发育的进程。

第一类mRNA虽不一定在成熟卵中得到囤积, 但直接决定了卵原细胞-卵母细胞、卵母细胞-卵子等卵子发生过程中的关键转换事件, 其缺失或异常可能导致卵子发育、卵子成熟、或成熟卵受精障碍。例如, 卵母细胞表达的*fancl*、*figla*和*bmp15*等缺失会引起早期卵母细胞发育障碍, 从而导致突变体发生性逆转[25—27]; 卵母细胞表达的RNA结合蛋白编码基因*ptbp1a*的突变, 虽然不影响卵子的成熟, 却导致其激活障碍[28]; 卵母细胞特异表达的*larp6a*和*larp6b*缺失导致卵壳形成和卵壳膨胀障碍, 进而影响到受精卵的发育[29]。有学者利用转录组鉴定到多个与卵子质量调控密切相关的基因, 其中*otulina*和*slc29a1a*等突变体雌鱼所产卵子均表现为受精障碍, 但是其作用机制尚不明确[30]。除此之外, 近期的两项研究发现, 滤泡细胞特异表达的Hippo信号通路调控因子Taz对于成熟卵受精孔的形成至关重要, 母源*taz*的突变导致成熟卵无法正常受精[31, 32]。

后一类在成熟卵中储存的母源mRNA及其调控的信号途径, 则在很大程度上调控了早期胚胎发育的细胞命运和形态建成[33, 34]。例如, 母源的Wnt/β-catenin信号途径是诱导背部体轴发育的初始关键信号, 其本质在于母源β-catenin蛋白在背侧细胞核内的稳定和积累, 母源β-catenin的缺失导致胚胎的严重腹部化[35, 36]。一般认为, 母源储存的β-catenin蛋白以微管依赖的方式从植物极转移到一侧的胚胎细胞从而诱导背部命运[37]。近年的研究表明, 母源β-catenin的激活和活性控制受到母源mRNA翻译产物的严密控制。有研究显示母源表达的Wnt8a能在背侧细胞中特异地激活β-catenin[38], 最新的研究表明一个新的膜蛋白Huluwa(Hwa)能以不依赖于Wnt配体的方式在背侧细胞中特异激活母源β-catenin[39]; 我们实验室近期的研究表明, 母源Nanog通过蛋白互作的方式抑制母源β-catenin在胚胎中的全局性激活, 从而保护了胚胎非背侧组织的正常发育[40]。骨形态发生蛋白(Bone Morphogenetic Protein, BMP)是一种形态发生素, 其主要通过激活下游Smad5、Smad1和Smad9形成的调控网络, 从而形成腹侧至背侧的活性梯度促进腹侧细胞命运[41—44], BMP配体的转录受到*radar*和*pou5f3*等母源mRNA的严密调控[45, 46], *smad5* mRNA也是母源转录的[42, 45, 46]。另一类受到母源调控的胚胎诱导信号是Nodal信号途径[47], Nodal配体通过激活下游转录因子Smad2和Smad3从而激活靶基因的表达, 以活性梯度的方式调控胚胎头尾轴和左右不对称的建立以及中内胚层的形成[48]。

母源合子转换(Maternal-Zygotic Transition, MZT)是鱼类受精胚发育过程中的一个关键事件, 其伴随着母源mRNA的清除与合子基因的激活(Zygotic gene activation, ZGA)。母源mRNA在MZT过程中能否被快速有效地清除, 决定了胚胎是否能够顺利渡过这一时期进而完成后续的发育进程[49—51]。母源mRNA的清除受到多种方式的转录后调控, 包括poly(A)尾的长度、密码子的选择、RNA结合蛋白、RNA的修饰及miR430介导的降解等途径[23]。首先, 母源mRNA的稳定性主要由poly(A)尾的长度来决定, 5′帽子结构m7G通过与poly(A)结合蛋白形成环化结构起始翻译, 短的poly(A)尾将触发翻译抑制及随后的mRNA降解[52]。研究发现当开放阅读框富含不常见密码子时, 将招致CCR4-NOT 复合体对mRNA进行去腺苷酸化, 即母源mRNA密码子的选择性利用可以通过调控Poly(A)的长度影响翻译效率及mRNA的稳定性[53, 54]。其次, mRNA的稳定和降解还受到RNA结合蛋白的调控, 近期的研究还显示相分离也参与母源mRNA稳定性及其翻译活性的调控[49, 55, 56]。有研究显示, 机体还可以通过对mRNA进行多种修饰调控其稳定性, 如mRNA 3′端的尿苷酸化可诱导mRNA在MZT过程中的清除[57]; 5-甲基胞嘧啶(m^5C)修饰的母源mRNA在MZT过程中具有更高的稳定性[58]; Ythdf家族成员和Igf2bp3等作为mRNA N6-腺苷酸甲基化(m^6A)的阅读器蛋白有可能参与调控母源mRNA的稳定性[59—61]。最后, miR-430介导的母源mRNA的清除已被证明在MZT过程中发挥重要作用, 其或通过促进mRNA的去腺苷酸化加速其降解[62], 或通过调控核糖核蛋白复合体的稳定性降低mRNA的翻译效率, 从而加速母源mRNA的降解[63]。miR-430虽然是合子转录的, 但其转录激活受到母源表达的先锋因子(Pioneer factor)Nanog、Pou5f3和Sox19b的严格调控[64], 而这些先锋因子又在MZT时期协同开放染色质, 起始合子基因的转录[49, 64—67]。

总之, 卵母细胞或滤泡细胞mRNA的有序表达及其在时空上的有序囤积调控了卵原细胞-卵母细胞转换和卵母细胞-卵子转换这两个过程, 决定了卵子发生进程和卵质优劣; 储存在成熟卵子中的母源mRNA的种类、丰度和时空分布, 又直接决定着卵子质量和受精胚的早期发育, 特别是卵-胚转换

过程; 母源mRNA的及时清除和合子基因的激活进一步促进了胚胎-仔鱼转换, 使得对胚胎发育的控制权由母源基因向合子基因转换。因此, 卵母细胞表达的mRNA在以上环节的任一节点出现问题, 均会影响卵子支持受精及早期胚胎发育的能力, 严重影响卵子质量, 甚至导致早期胚胎败育。

4.2　母源mRNA的翻译控制及母源蛋白质的积累

母源mRNA的水平伴随着卵母细胞的成熟处在不断的动态变化中, 在卵子发生及早期胚胎发育过程中不断地积累与降解[2], 对这些mRNA的翻译水平进行合理地控制以使其在时空上得以精确地翻译, 对卵子的发生过程十分重要[68]。目前发现的调控母源mRNA翻译控制的主要机制是通过poly(A)尾的长度或通过RNA结合蛋白的调控来实现的。一些母源mRNA, 如*c-mos*和细胞周期相关的mRNA(如*cyclin B1*), 在卵子发生早期具有较短的poly(A)尾, 以维持其处于翻译抑制状态[69, 70], 而在卵子成熟过程中, 其mRNA被多聚腺苷化以延长其poly(A)尾, 促进这些母源mRNA的翻译水平上调, 调控卵子发生过程[71, 72]。RNA结合蛋白通过特定序列结合在母源mRNA的调控序列上抑制特定类型的mRNA的翻译, 如Bruno蛋白在*osk* mRNA定位在卵子的过程中结合在其3′-UTR的重复序列上, 抑制*osk* mRNA的提前翻译, *osk* mRNA的提前成熟和翻译会导致母源性的致死表型[73—75]; Me31B与定位在卵子中的RNA形成核糖核蛋白复合体, 在母源RNA运输至卵子的过程中抑制其翻译, 而缺失Me31B则会导致母源RNA提前成熟和翻译[76]; 斑马鱼Zar1作为RNA结合蛋白与ZP mRNAs结合抑制其在卵子发生过程中的翻译, *zar1*突变会导致卵细胞凋亡和雌性向雄性性逆转[77]等等。最近, 我们发现了一种在全局水平对母源mRNA进行翻译控制的新机制, 即母源因子Nanog在卵子发生过程中抑制翻译延伸因子*eef1a1l2*的转录, 以维持卵子中的母源mRNA的翻译处于合理的水平, 母源*nanog*缺失后导致卵子中翻译机器的活性过度上调, 引起内质网应激(ER stress)和未折叠蛋白响应(Unfolded protein response, UPR), 导致卵母细胞在早期凋亡、卵子成熟度受损, 早期胚胎致死[78]。此外, Ybx1(Y-box binding protein 1)也被发现能够与P-body结合在全局水平抑制母源mRNA的翻译并促进其降解, 缺失母源Ybx1导致卵质下降及早期胚胎败育[15]。因此, 通过不同方式对母源mRNA在卵子发生过程中进行翻译控制, 调控了卵子的发生和卵母细胞的成熟, 决定了卵质。

卵黄蛋白原(Vitellogenin, Vtg)是卵母细胞中储存的最重要的蛋白质之一, 卵黄蛋白原在卵母细胞中的积累与裂解是卵母细胞生长与成熟过程中的重要事件[79, 80]。在卵母细胞生长过程中, 卵母细胞摄取卵黄蛋白原, 并在组织蛋白酶D (Cathepsin D)的作用下转化为卵黄蛋白(Yolk protein, YP), 在卵母细胞成熟(Oocyte maturation, OM)过程中, 一部分卵黄蛋白作为卵子发生及胚胎早期发育的主要营养来源, 另一部分在组织蛋白酶B或L(Cathepsin B, cathepsin L)的作用下完全水解为游离氨基酸(Free amino acid, FAA)或小分子多肽, FAA与一些无机离子共同调节卵母细胞的渗透压, 这是卵母细胞水合作用以及卵子浮力获得的关键步骤。卵子的沉浮性能是界定卵质优劣的关键因素之一, 因此卵质问题往往伴随着卵黄蛋白不能充分裂解造成的浮力改变。研究表明卵子的沉浮性能与组织蛋白酶mRNA的表达水平和蛋白酶活性水平的改变有关[79]。Vtg系统在所有的硬骨鱼类中是由VtgA的两种旁系同源形式(VtgAa和VtgAb)及较小的不完全形式的VtgC组成, 而沉性卵和浮性卵中不同亚型的Vtg的裂解方式也存在差异[81]。鱼类*vtg*基因主要在雌激素的调控下在肝脏中表达[82], 而卵黄蛋白的组成在很大程度上是由肝脏卵黄蛋白原的合成和分泌速率决定的[83]。此外, 在卵母细胞成熟过程中, 卵黄蛋白裂解导致高分子卵黄蛋白向低分子卵黄蛋白转变, 卵母细胞由此变得透明, 也是卵母细胞成熟的标志, 质量较好的卵母细胞往往具有较高的透明程度。斑马鱼中一些基因的突变, 如*over easy* (*ovy*)、*sunny side up* (*ssu*)、*ruehrei* (*rei*)、*souffle* (*suf*), 会导致卵子的透明度变差, 胞质分裂出现障碍, 检测其蛋白质组成发现突变体卵子中高分子卵黄蛋白异常积累, 与未成熟卵母细胞的蛋白质组成类似[84]。高分子卵黄蛋白与低分子卵黄蛋白的比例也作为一项评估卵子质量的指标在一些研究中得以运用[15]。

总之, 在卵原细胞-卵母细胞转换和卵母细胞-卵子转换这两个过程中, 特定母源mRNA的翻译控制和母源蛋白的积累对卵子发生过程至关重要, 母源mRNA翻译控制的失败往往伴随着卵子发生和成熟缺陷, 决定卵质的优劣; 而包括卵黄原蛋白在内的母源蛋白的积累和形态转换失败, 往往会导致较差的卵子质量, 从而影响后续的卵子受精率和胚胎发育效率。

4.3　多不饱和脂肪酸及其代谢产物

脂肪酸的构成可以影响胚胎受精率、孵化率、存活率以及幼鱼的生存能力, 因此调控了卵质的优劣[85]。已有的研究表明, 二十碳五烯酸(EPA,

C20:5n-3)、二十二碳六烯酸(DHA, C22:6n-3)和花生四烯酸(ARA, C20:4n-6)作为多不饱和脂肪酸(Polyunsaturated fatty acids, PUFA)在脊椎动物的生殖中发挥重要作用[86]。鱼类性腺发育过程对DHA有特殊需求, 一些鱼类可以将PUFA从肌肉中选择性地迁移至卵巢以供给卵子的发育与成熟, 为长季节的产卵做准备[87, 88]。

PUFA的产生依赖于去饱和酶与延长酶的协同作用, 斑马鱼中去饱和酶*fadsd6*在卵母细胞成熟阶段表达明显上调, 延长酶*elovl5*在卵黄生成前期与成熟期高表达[86]。对不同卵泡发育阶段的脂肪酸组成分析也表明, 卵黄生成前期和成熟期的卵泡中ARA水平最高, DHA水平在卵黄形成后期和成熟阶段最高, 这些结果提示在卵子发育过程中脂肪酸的储存和重组可能发挥着促进卵母细胞成熟及排卵的重要作用[86, 89]。体外研究的实验证实ARA可以诱发一些鱼类成熟期卵母细胞减数分裂的恢复及成熟后卵子的排出[90, 91]。ARA对卵子排出的重要作用可能是通过它的一类代谢产物——前列腺素(Prostaglandins, PGs)实现的, PGs在包括硬骨鱼类的多种脊椎动物中已经被广泛证明对排卵有不可或缺的作用[92—95]。斑马鱼前列腺素受体Ptger4b与排卵的关系已在核孕酮受体(Progesterone receptor, *pgr*)的基因敲除实验中得到证实, Pgter4拮抗剂可以直接阻断人绒毛膜促性腺激素(Human chorionic gonadotophin, HCG)诱导的排卵[96]。

在多种脊椎动物中转入线虫的ω-3去饱和酶*fat1*可以高效地将n-6 PUFA转化为n-3 PUFA, 优化多不饱和脂肪酸的结构占比[97—99]。转*fat1*小鼠与同时期的野生型小鼠相比卵巢的炎症状态减弱, 且初级卵泡数量与DHA、EPA的水平有很强的正相关关系[100], 提示n-3与n-6 PUFA的占比对脊椎动物的生殖具有重要影响。目前可内源高效合成n-3 PUFA的*fat1*转基因鲤鱼和斑马鱼品系已经构建, 可以作为研究n-3和n-6 PUFA调控鱼类卵子发育与卵子质量的优良模型[101, 102]。综上, 多不饱和脂肪酸及其代谢产物在卵母细胞-卵子转换这一过程中发挥作用, 可能促进卵母细胞的成熟及排卵, 同时脂肪酸也作为亲鱼营养物质在环境对卵质的影响一章中加以讨论。

4.4 生殖激素

鱼类卵泡发育与卵母细胞成熟受到下丘脑-垂体-性腺轴(HPG轴)分泌的多种激素的共同调控, 因此卵子质量与生殖激素有着密不可分的联系。下丘脑产生促性腺激素释放激素(Gonadotropin-releasing hormone, GnRH), 刺激垂体细胞分泌促卵泡激素(Follicle-stimulating hormone, Fsh)和促黄体生成素(Luteinizing hormone, Lh)。Fsh通过刺激卵泡细胞分泌雌二醇(Estradiol, E2)来促进卵泡发育, Lh诱导卵泡细胞产生孕激素等成熟诱导激素(Maturation inducing hormone, MIH)[103, 104]。孕激素可以与其膜受体(Progesterone membrane receptors, mPRs)结合, 进一步刺激促成熟因子(Maturation promoting factor, MPF)的释放, 从而促进卵母细胞恢复减数分裂进程, 继续发育至成熟[105, 106]。在斑马鱼中敲除*fshb*会造成卵巢发育和卵泡成熟迟缓, 卵黄的生成受到影响, 卵母细胞在PG-PV的转化过程中存在明显的阻滞; 将*fsh*的受体*fshr*进行敲除后, 所有的卵泡都滞留在PG期, 之后发生由雌转雄的性逆转[107]; *lhb*敲除之后卵母细胞虽然可以正常发育至FG期, 但难以发生GVBD且不能排卵[108]。在青鳉中对*gnrh1*、*fshb*和*lhb*的敲除也证明Fsh对卵泡的发育和卵黄的积累有重要作用, 而GnRH和Lh对成功排卵是必不可少的, 但GnRH对Fsh的释放并不十分必要[109]。此外, 激活素(Activin)-抑制素(Inhibin)系统在脊椎动物的生殖过程中分别起到刺激和抑制垂体分泌FSH的作用。最新的研究发现共敲除抑制素的α亚基(*inhaa*)和β亚基(*inhab*)之后导致卵泡颗粒细胞肥大及基质细胞的积累[110]; 缺失卵母细胞特异表达的生长分化因子*gdf9*(Growth differentiation factor 9)之后, 卵母细胞的发育也阻滞在PG期, 而共敲除抑制素的α亚基*inhaa*后, *gdf9*突变体的卵泡发生和卵泡激活得到了恢复[111]。近来的研究证实了多肽类神经激素调控了硬骨鱼类的生殖, 分泌神经素(Secretoneurin, SN)作为分泌粒蛋白Ⅱ(Secretogranin-2, SCG2)的衍生神经肽, 被证明在脊椎动物中具有保守的调控垂体促性腺激素的功能, 在鱼类中可以刺激Lh的释放[112, 113]。斑马鱼*scg2*突变遗传模型的构建及相关实验, 直接证实了分泌粒蛋白Ⅱ在下丘脑-垂体生殖调节轴中的重要作用, 并支持了分泌神经素是一种生殖激素的假设[114]。

此外, 卵泡细胞和卵母细胞内产生的多种信号分子也通过旁分泌在局部发挥作用, 共同调节卵泡发育和卵母细胞的成熟[103, 104]。类固醇激素的合成在下丘脑-垂体-性腺调节轴中发挥重要作用, 调控着成鱼性腺发育及生殖行为[115]。芳香化酶Cyp11a作为催化类固醇合成的第一步, 将胆固醇转化为孕烯醇酮(Pregnenolone, P5)。斑马鱼Cyp11a的同源基因Cyp11a2在性腺体细胞中表达, 其缺失之后导致卵巢发育失败及全雄的表型[116]。而Cyp11a的另一同源基因Cyp11a1在早期胚胎的卵黄合胞层(YSL)中表达, 其催化产物P5被证实可以通过与细胞质连

接蛋白1(Cytoplasmic linker protein 1, CLIP-170)结合刺激卵黄微管的聚合与稳定, 从而促进胚胎的外包运动[117, 118]。虽然P5在卵子发生及卵母细胞成熟过程中是否发挥微管稳定剂的作用仍有待研究[119], 但是毫无疑问的是, 母源提供的P5的水平将会直接影响卵子质量的优劣及早期胚胎发育。综上, 生殖激素主要是在卵母细胞-卵子转换这一过程中发挥调控作用, 影响卵子发生、卵母细胞的成熟及排卵过程, 决定卵质。

4.5　卵质域与细胞骨架

卵母细胞中卵质域(Ooplasmic domain)的建立是一个至关重要的发育事件, 在这个过程中, 伴随着卵母细胞的发育, 细胞器、卵黄内容物、母源RNA与蛋白质、脂滴和色素等由原来在卵细胞质(Egg cytoplasm)中的混合状态变为被限制在卵母细胞的特定区域[120, 121], 又称卵质分离(Ooplasmic segregation), 是细胞周期、卵裂、内吞作用、转录起始、翻译等一系列生命进程发生的前提[21, 122]。

鱼类发育过程中卵质域构建的起始, 也是胚胎第一个不对称性的建立始于早期卵母细胞中由母源*bucky ball* (*buc*)基因调控的巴尔比阿尼氏小体(Balbiani body, Bb)的形成, Bb是一个从细胞质中分离出来的非膜性腔室, 紧密聚集了RNA、蛋白质、内质网和线粒体。Bb在发育至I期末期的卵母细胞皮层中解体, 其组分定位于未来的植物极, 这决定了未来胚胎发育的动物-植物(Animal-vegetable axis, AV)轴, 一些重要的母源因子如*cyclin B1*、 *pou2*、*notch*、*zorba*和*vg1* mRNAs定位在动物极, 而*dazl*、*nanos*、*wnt8*、*bruno-like*和*grip2a* mRNAs定位在植物极, 这些极性定位的mRNA与细胞器、细胞骨架一同形成极性卵质域, 进一步支持卵子发生、受精及胚胎发育进程[21, 123—125]。

在鱼类卵子发生及早期胚胎发育过程中, 许多核糖核蛋白颗粒(Ribonucleoprotein granules, RNPs)编码关键的细胞命运决定因子, PGC通过选择性地继承母源生殖质RNP (Germ plasm RNP, GP RNP)复合物而形成, 它的定位直接影响未来胚胎图式的形成[126]。*dazl*、*vasa*、*nanos*、*dnd*和*piwil*是目前在斑马鱼中研究较多的生殖质相关基因, 这些基因对于PGC的成熟与迁移、卵母细胞的产生及维持十分重要。如*vasa*突变体发育为不育雄性, 研究表明Vasa对于卵母细胞的减数分裂及生殖细胞干性的维系十分重要[127]; *nanos1*和*nanos3*对维持卵母细胞的产生具有重要作用[128, 129]。Bb作为卵母细胞中运输生殖质的载体, 它的正常组装对于后代PGC的形成是必须的。Bb正常组装所需蛋白Buc的缺失将导致卵母细胞中出现多个小的巴尔比阿尼氏小体, 生殖质相关的蛋白和mRNA无法汇聚到特定的位置, 卵母细胞极性丧失[130, 131]。Tdrd6a可以与Buc相互作用, 促进Buc蛋白颗粒的增长与迁移, 与Bb的组装直接相关[132]。Rbpms2缺失导致卵母细胞中线粒体及Buc蛋白异常聚集, 不能维持其命运进而性逆转为雄鱼[133]。

许多无膜细胞器以液-液相分离(Liquid to liquid phase transition, LLPS)的方式从细胞质中分离。在秀丽隐杆线虫中, RNA与蛋白质会在细胞的一侧自发地凝聚成小液滴状结构(称为P granules), 其定位决定了第一个生殖细胞的形成。P granules展现出融合(Fusion)、浸润(Wetting)及滴落(Dripping)等液体行为, 随着其成分浓度的变化迅速地发生解体及聚集, 猜测推动其形成的动力为LLPS[134]。近年来, 诸多研究表明核仁凝聚[135]、应激颗粒(Stress granules)的形成[136]及染色质的组装[137]等基本生命过程都涉及LLPS。而Bb与P granules等无膜细胞器的液体性质不同, 其在多种生物中保守存在, 部分由淀粉样纤维组成, 表现出类似于凝胶的固体性质, 与其他无膜细胞器相比这种更加稳定的存在方式可能是卵母细胞作为长寿生殖细胞的可能原因, 但是Bb的形成的动力学基础至今尚不明确[138, 139]。

在卵质分离的过程中, 细胞骨架在卵母细胞极化、母源mRNA与蛋白质的定位中发挥关键作用[140, 141]。微管-肌动蛋白交联因子1a (Macf1a)与角蛋白共定位于Bb, 推测Bb解体时Macf1a可以连接Bb与卵母细胞皮质肌动蛋白, 运输解体后的Bb组分至植物极, Macf1a的缺失与破坏肌动蛋白所产生的表型相似。卵母细胞中*buc*和*macf1a*功能缺失影响细胞骨架网络的组织方向和随后的细胞质分离[141]。Birc5b在星体微管的顶端定位, 介导微丝和微管在皮质区的重组, 它的缺失导致GP RNP在分裂沟处的定位失败, 受精后胞质分裂沟不能形成[142]。综上, 卵质域的正确建立决定了重要母源因子, 尤其是生殖质的定位, 对卵母细胞的产生及极性的确立十分必要, 同时细胞骨架参与了这一过程。卵质域与细胞骨架在卵原细胞-卵母细胞、卵母细胞-卵子转换的过程中发挥调控作用。

4.6　线粒体

线粒体作为供能细胞器, 为多种重要的生物学进程, 如染色质组装、RNA、蛋白质及脂质的合成提供动力学基础[143]。卵母细胞中线粒体及线粒体DNA(mtDNA)拷贝数均显著多于其他类型的细胞, 并在卵母细胞发育的后期其数量急剧增加, 为减数分裂以及受精过程供能; 由于父系线粒体会在精子

进入卵母细胞后退化, 因此卵母细胞线粒体作为母源物质支持早期胚胎发育, 其质量决定了早期胚胎发育的质量[144]。对人和小鼠中的多项研究表明, 线粒体功能障碍是卵母细胞衰老的关键原因。线粒体氧化应激会导致其在卵母细胞减数分裂过程中不能提供足够的ATP供给, 如马达蛋白的活性受损导致纺锤体组装的受损及染色体分离的异常[145]。在正常情况下, 细胞内存在严格的线粒体质量控制机制, 通过其生物发生、动力学(融合与分裂)、线粒体分泌、自噬等多种途径维持整体网络健康[146, 147]。然而, 当线粒体功能受损时, 多种信号通路被破坏导致细胞衰老, 这反过来又会使线粒体质量控制的有效性降低。因此当初级损伤的积累不能被有效修复时, 线粒体系统会趋于崩溃, 进而不再支持卵母细胞的代谢需求, 造成卵母细胞质量降低甚至凋亡[148]。多项研究表明, 卵母细胞中特异性敲除与线粒体融合、裂变相关的基因Drp1、Mfn1/2会造成雌性因卵母细胞发育停滞、卵泡减少而不育; 与线粒体代谢与质量控制相关的线粒体蛋白酶Lonp1的特异性敲除会导致卵巢早衰; 而自噬诱导基因Atg7的缺失也造成严重的卵泡丢失[148—150]。由此可见, 线粒体功能及其质量控制的异常均会导致严重的卵质问题, 是导致雌性育性降低的重要因素。因此对卵母细胞中线粒体的优化是维持卵母细胞储备、提升卵母细胞质量与提升生殖能力的可能途径[151]。

线粒体作为一种真核生物中保守存在的细胞器, 其大量聚集于鱼类卵母细胞的Bb中, 作为重要的母源物质在种系间传递。在以斑马鱼为模型的研究发现, 生殖干祖细胞(Germline stem and progenitor cells, GSPCs)向卵母细胞的分化需要更强的线粒体供能, 生殖细胞特异的线粒体融合因子*pld6*缺失使得GSPCs中线粒体动态失衡, 线粒体拷贝数及ATP合成均减少, 同时, 生殖细胞特有的线粒体云(Mitochondria-nuage)在突变体中缺失, 进而导致piRNA的合成受阻, 在卵母细胞发育早期走向细胞凋亡途径[152]。除此之外, 线粒体对鱼类卵质调控的机制至今鲜有研究。其他物种中的研究结果指向线粒体可能在卵母细胞-卵子转换过程中发挥作用, 线粒体严重异常时将导致卵母细胞染色体倍性异常甚至卵母细胞凋亡。

5 环境因素影响卵质的机制研究

5.1 亲鱼营养

卵子的发育和成熟需要亲鱼卵巢的营养供给, 因此雌鱼的营养状况会影响性腺的发育, 从而限制卵子的数目与质量[153]。蛋白质和脂质是卵黄的主要成分, 在胚胎发育过程中被用作营养来源, 这两者的充足提供有助于提高胚胎及幼鱼的存活率[154]。由于卵子中脂肪酸的含量与构成对后续支持其正常受精与胚胎发育至关重要, 因此雌鱼膳食中不同脂肪酸的含量和占比直接影响着卵子质量。在亲鱼的饲料中添加PUFA可以增加排卵量及受精几率, 提高大菱鲆、军曹鱼(*Rachycentron canadum*)、马拉巴尔红鲷(*Lutjanus malabaricus*)等亲鱼膳食中n-3 PUFA的含量, 其产卵量、卵子直径、受精卵上浮率和孵化率均得到显著提高[155—157], n-3 PUFA对卵质的优化作用可能是通过提升亲鱼卵巢芳香化酶的基因表达水平实现的[158]。膳食中的可消化蛋白(Digestible protein, DP)和可消化能量(Digestible energy, DE)的水平也影响雌鱼的繁殖性能, 用DP含量较低的饲料饲喂雌性尼罗罗非鱼(*Oreochromis niloticus*), 会产生相对较大的卵子, 后代的存活率较高[159]。

维生素是生长和生殖所必需的微量元素, 在饮食摄取中必不可少。斑马鱼的膳食中缺乏维生素E会破坏长链多不饱和脂肪酸(Long chain polyunsaturated fatty acids, LC-PUFA)的合成, 导致ARA和DHA的合成水平下降, 而5-羟基-ARA和7-羟基-DHA的含量加倍, 同时去饱和酶*fads2*和延长酶*elovl2*的mRNA水平补偿性上调, 推测这可能是因为维生素E作为一种脂溶性抗氧化剂, 它的缺失引起了脂质过氧化的增加, 导致PUFA的消耗, 尤其是n-3 PUFA, 因此亲鱼维生素E的摄入缺乏可能通过改变脂肪酸的含量及占比对卵质造成间接影响[160, 161]。维生素A的代谢产物视黄酸(Retinoic acid, RA)参与调节500多个基因的转录, 涉及大量的生物学过程, 其中就包括脊椎动物的卵泡发育[162], 在尼罗罗非鱼中, RA的含量主要由其合成酶基因*aldh1a2*和分解酶基因*cyp26a1*调控, 卵巢进入分化之前通常表现出高*aldh1a2*、低*cyp26a1*的表达模式, 分别对这两个基因进行敲除会导致卵巢进入减数分裂时期的滞后或提前, 在南方鲶和日本比目鱼等其他硬骨鱼类中也是如此, 说明RA的含量变化对于卵母细胞的分化具有调控作用[163—165]。日粮中维生素C的含量也影响亲鱼的生殖能力, 如提高膳食中的维生素C水平可优化尼罗罗非鱼(*Oreochromis niloticus*)、黄鲈(*Perca flavescens*)和大菱鲆(*Scophthalmus maximus*)的生产性能及后代的存活率, 用不含维生素C的饲料饲喂的雌鱼后代存活率降低[166—168]。不同鱼类对各营养成分的需求不尽相同, 探索并开发满足不同鱼类营养需求的饲料来最大限度地提高其卵质

和产卵量也是鱼类养殖营养学的一个重要课题。

5.2　光周期、温度和水体理化因子

季节性是鱼类繁殖的一个共同特征, 在高纬度地区最为明显, 而季节周期主要受光照和温度的影响。许多研究人员强调, 人工光周期(包括对时长和光强的控制)的改变会影响卵子质量, 从而改变仔鱼孵化的成功率。在对美洲红点鲑(*Salvelinus fontinalis*)的研究中发现, 持续的长时间的光照会在卵子发生过程中抑制卵黄生成阶段从而推迟雌鱼的排卵时间, 生殖周期改变的卵子受精后胚胎的存活能力降低[169]; 光照对鱼类生殖周期与卵子质量的影响也存在于海鲈(*Dicentrarchus labrax* L.)和大西洋鳕(*Gadus morhua*)等众多种属中[170, 171]。褪黑素被认为是光周期信息转导到脑-垂体-性腺轴(Hypothalamic-pituitary-gonadal axis, HPG)的介导因子之一, 近年来, 褪黑素在鱼类中的作用得到了广泛的研究。虽然褪黑素可能不驱动生殖的开始, 但是它可以通过反馈控制促性腺激素信号和卵母细胞成熟, 在协调生殖发育方面发挥重要作用[172—174]。哺乳动物中褪黑素不仅可以保护卵母细胞免受氧化应激, 还可能加速卵泡的生长和成熟, 并在排卵前和排卵时保持卵子的完整性[175]。而在鱼类中的研究发现光周期可以改变褪黑素生物合成酶基因和生物钟基因在卵巢中的表达水平[176, 177]。

温度是影响卵子质量的另一个重要环境因素, 一般来说, 生物体内部的生理过程需要在严格的温度范围内发生, 这取决于每个特定过程的相关细胞学机制[178]。鱼类作为一种变温动物其生理活动更容易受到外部温度的影响, 其配子的发生过程也受到温度的严密调控[179]。在对银汉鱼(*Odontesthes bonariensis*)的研究中发现, 在卵黄发生过程中提高温度会引起雌激素水平降低, 导致卵黄发生的损伤从而产生较小的卵子, 幼鱼的存活率显著降低[180]; 对三棘鱼(*Gasterosteus aculeatus*)进行高温胁迫之后, 会导致雌性性腺指数(Gonadosomatic index, GSI)急剧下降, 其胚胎孵化率降低, 且后代存活力差[181]; 在对斑马鱼和大菱鲆的研究中也有类似的发现[182, 183]。目前全球变暖引发的水体温度升高影响水生生态系统的结构和功能已成为事实, 甚至温度升高可能会对一些物种的繁殖产生胁迫, 致使该自然种群的消失[183]。关于温度影响卵子质量的机制研究较少, 但可能涉及相关酶活性的调节[184], 也有证据表明温度也影响了某些基因的转录[185, 186]。

最后, 生殖毒理学的研究表明鱼类卵子质量也受污染水体中重金属离子, 如镉[187, 188]、汞[189]、铜[190]及合成类化学物质, 如磷酸三(1, 3-二氯异丙基)酯(TDCPP)[10]、8-2氟调聚醇[12]等暴露的影响。汞暴露会引起斑马鱼性腺的病理学损伤, 降低过氧化氢酶(Catalase, CAT)、超氧化物歧化酶(Superoxide dismutase, SOD)、谷胱甘肽过氧化物酶(Glutathione peroxidase, GPx)等的活性而引起氧化应激, 并改变HPG轴上一些激素受体如*gnrh2*、*gnrh3*和*lhr*的表达水平[189]。TDCPP可以作为雄激素受体的拮抗剂和雌激素受体的激活剂, 长期暴露于低浓度的TDCPP会改变斑马鱼血浆性激素水平, 导致雌鱼产卵数目减少、且卵子直径变小[10]。镉、双酚A等毒物暴露可能通过表观遗传学调控阻碍卵母细胞成熟并致使其受精能力下降[191, 192]。值得说明的是, 在实验室条件下, 化学物质对鱼类生殖及卵子质量影响的研究多以单因素为变量, 而在自然界中鱼类往往暴露于多重压力之下, 说明单因素实验并不适合评估多种变量对鱼类卵质的实际影响[193], 因此近来也有学者开始进行毒性物质与其他环境因子如温度对卵质共同作用的研究[181]。

5.3　产卵周期

产卵周期对卵子受精率及未来胚胎发育有非常大的影响, 没有及时产出的卵子滞留在卵巢中会逐渐退化甚至被再吸收[194]。虽然卵子能够在体内存活较长时间, 但是在卵子过熟的进程中, 卵巢腔中激素水平的变化、卵子形态学、生理学以及组织学和超微结构的改变都会影响卵子的受精率, 甚至导致幼鱼畸形和染色体倍性的改变[195]。成熟后的卵母细胞在卵巢液中滞留时间过长会导致受精后胚胎畸形率大幅度增加[196, 197]。卵子从腹腔产出后, 与受精的时间间隔也会对卵子质量产生影响, 在亚洲鲶(*Siluriformes, Pangasiidae*)中, 卵排出后间隔3h受精较之于立即受精, 其胚胎的畸形率显著提高, 排出后5h受精的卵子几乎全部畸形[198], 在非洲鲶(*Heterobranchus longifilis*)及虹鳟(*Oncorhynchus mykiss*)中也有相似的结论[194, 199, 200]。鱼类卵母细胞过熟导致卵质变差的机制仍不甚明了, 但是这其中可能涉及卵母细胞老龄化的问题。在哺乳动物中, 卵母细胞的老龄化会改变其甲基化酶活性, 影响其甲基化水平, 进而引起与细胞周期、减数分裂相关的一些基因的表达变化; 老龄化也会改变卵母细胞组蛋白的乙酰化水平, 阻碍组蛋白的泛素化修饰, 扰乱有丝分裂的调节与纺锤体的装配, 造成卵母细胞非整倍性与胚胎死亡, 这也为研究鱼类卵子过熟提供了参考依据[201]。

在自然条件下, 当鱼类无法找到合适的产卵栖息地, 或者当由于人类造成的环境条件延误了产卵时期, 也会导致滞留于卵巢中的卵子过熟从而影响

卵子质量[202]。产卵的最佳周期对不同的类来说不尽相同, 卵子产出后保存的时间也受种属及储存条件(如温度、溶氧量)的影响[203]。因此, 在实验研究的基础上通过不断的实践掌握不同鱼类的卵子成熟规律, 有效地预测并管理产卵时间是优质卵子获得的重要方法。

虽然多种环境因素对鱼类卵质产生不同层次的影响, 但其发挥作用必定通过鱼体的生理和遗传调控来体现。如, 产卵周期对卵质的影响是由于在卵子过熟进程中, 由激素调控的卵子的生化特性发生改变所致; 光照与温度对卵质的影响通过作用于脑-垂体-性腺轴调节卵子的发生与发育, 进而改变其卵子质量[180]。因此, 要了解环境因子对鱼类卵质的影响, 必须要以对卵子发生与发育机制的深刻认识为基础。深入了解鱼类卵子发生、发育的遗传调控机制, 对提高卵子质量和养殖效率有深远意义。

6 总结与展望

卵子的质量直接决定了胚胎发育和幼鱼的存活, 已经成为限制全球水产养殖业发展的一个重要因素[204]。然而, 目前尚无有效指标能够准确评价卵子质量的优劣, 对卵质决定因素的探究也多停留在外在环境因子对某些养殖鱼类卵质的影响研究, 对卵质决定机制的认识仍然不足。本综述主要讨论了包括母源mRNA、蛋白质、脂肪酸、生殖激素、维生素、卵质域、细胞骨架、线粒体等在内的遗传因素, 以及包括亲鱼营养、光周期、温度、水体理化因子和产卵周期等在内的环境因素调控卵质的可能机制(图 2)。而无论是遗传因素还是环境因素, 其对卵子发生和卵质的直接调控以及对早期胚胎和幼苗发育的影响均是作用在从卵原-卵母细胞转换开始到仔-稚鱼转换这5个阶段(图 1)。因此开展鱼类卵子质量的研究, 其科学本质是围绕这5个阶段中的发育生物学事件开展细致的研究, 以探索卵质决定的关键因子及其调控和作用机制。

斑马鱼的基因组清晰, 繁殖周期短, 突变体资源丰富, 遗传学手段成熟[205], 围绕斑马鱼的卵子发生和胚胎发育, 从转录机器及母源mRNA产物、翻译机器及其蛋白产物、脂肪酸合成及代谢产物、生殖激素、卵母细胞胞质结构域构建、环境和表观遗传学调控等角度入手, 充分利用基因编辑、转录组、蛋白组、脂质组等遗传学和多组学手段, 深入探究决定鱼类卵质的遗传和表观遗传学基础, 对于明确硬骨鱼类卵子质量的决定机制具有重要意义, 将为系统评价和提升经济鱼类的卵子质量提供重要指导。

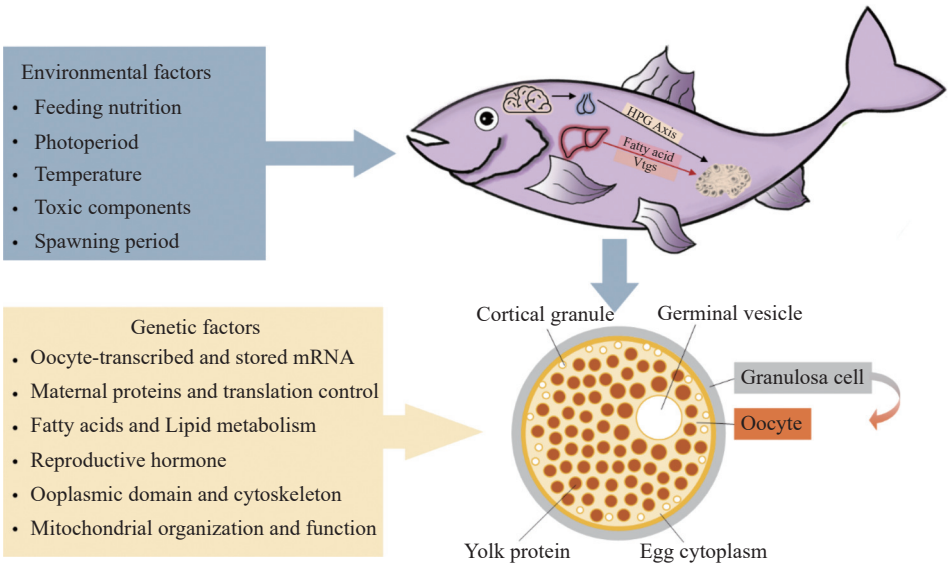

图 2 影响卵子质量的遗传和环境因素

Fig. 2 Genetic and environmental factors that influence egg quality

参考文献:

[1] Naylor R L, Kishore A, Sumaila U R, *et al*. Blue food demand across geographic and temporal scales [J]. *Nature Communications*, 2021(12): 5413.

[2] Lubzens E, Young G, Bobe J, *et al*. Oogenesis in teleosts: how eggs are formed [J]. *General and Comparative Endocrinology*, 2010, **165**(3): 367-389.

[3] Ye D, Zhu L, Zhang Q, *et al*. Abundance of early embryonic primordial germ cells promotes zebrafish female differentiation as revealed by lifetime labeling of germline [J]. *Marine Biotechnology*, 2019, **21**(2): 217-228.

[4] Ye D, Sun Y. Manipulating and visualizing the germline with transgenic lines [J]. *Methods in Molecular Biology*,

2021(2218): 265-276.

[5] Lessman C A. Oocyte maturation: converting the zebrafish oocyte to the fertilizable egg [J]. *General and Comparative Endocrinology*, 2009, **161**(1): 53-57.

[6] Selman K, Wallace R A, Sarka A, *et al*. Stages of oocyte development in the zebrafish, brachydanio rerio [J]. *Journal of Morphology*, 1993, **218**(2): 203-224.

[7] Sen A, Caiazza F. Oocyte maturation: a story of arrest and release [J]. *Frontiers in Bioscience* (Scholar Edition), 2013, **5**(2): 451-477.

[8] Robker R L, Russell D L, Yoshioka S, *et al*. Ovulation: a multi-gene, multi-step process [J]. *Steroids*, 2000, **65**(10/11): 559-570.

[9] Bobe J, Labbé C. Egg and sperm quality in fish [J]. *General and Comparative Endocrinology*, 2010, **165**(3): 535-548.

[10] Wang Q, Lam J C W, Han J, *et al*. Developmental exposure to the organophosphorus flame retardant tris(1, 3-dichloro-2-propyl) phosphate: Estrogenic activity, endocrine disruption and reproductive effects on zebrafish [J]. *Aquatic Toxicology*, 2015(160): 163-171.

[11] Wu H, Rao Q, Zheng J, *et al*. Biochemical and histological alterations in adult zebrafish (*Danio rerio*) ovary following exposure to the tetronic acid insecticide spirotetramat [J]. *Ecotoxicology and Environmental Safety*, 2018(164): 149-154.

[12] Liu C, Deng J, Yu L, *et al*. Endocrine disruption and reproductive impairment in zebrafish by exposure to 8: 2 fluorotelomer alcohol [J]. *Aquatic Toxicology*, 2010, **96**(1): 70-76.

[13] Fan X, Hou T, Sun T, *et al*. Starvation stress affects the maternal development and larval fitness in zebrafish (*Danio rerio*) [J]. *Science of the Total Environment*, 2019(695): 133897.

[14] Forés R, Iglesias J, Olmedo M, *et al*. Induction of spawning in turbot (*Scophthalmus maximus* L.) by a sudden change in the photoperiod [J]. *Aquacultural Engineering*, 1990, **9**(5): 357-366.

[15] Sun J, Yan L, Shen W, *et al*. Maternal Ybx1safeguards zebrafish oocyte maturation and maternal-to-zygotic transition by repressing global translation [J]. *Development*, 2018, **145**(19): dev166587.

[16] Kohn Y Y, Symonds J E. Evaluation of egg quality parameters as predictors of hatching success and early larval survival in hapuku (*Polyprion oxygeneios*) [J]. *Aquaculture*, 2012(342/343): 42-47.

[17] Aristizabal E, Suárez J, Vega A, *et al*. Egg and larval quality assessment in the Argentinean red porgy (*Pagrus pagrus*) [J]. *Aquaculture*, 2009, **287**(3/4): 329-334.

[18] Mansour N, Lahnsteiner F, Patzner R A. Distribution of lipid droplets is an indicator for egg quality in brown trout, *Salmo trutta fario* [J]. *Aquaculture*, 2007, **273**(4): 744-747.

[19] Lahnsteiner F, Patarnello P. The shape of the lipid vesicle is a potential marker for egg quality determination in the gilthead seabream, *Sparus aurata*, and in the sharpsnout seabream, *Diplodus puntazzo* [J]. *Aquaculture*, 2005, **246**(1/2/3/4): 423-435.

[20] Żarski D, Palińska K, Targońska K, *et al*. Oocyte quality indicators in Eurasian perch, *Perca fluviatilis* L., during reproduction under controlled conditions [J]. *Aquaculture*, 2011, **313**(1/2/3/4): 84-91.

[21] Lindeman R E, Pelegri F. Vertebrate maternal-effect genes: insights into fertilization, early cleavage divisions, and germ cell determinant localization from studies in the zebrafish [J]. *Molecular Reproduction and Development*, 2010, **77**(4): 299-313.

[22] Fuentes R, Fernández J. Ooplasmic segregation in the zebrafish zygote and early embryo: pattern of ooplasmic movements and transport pathways [J]. *Developmental Dynamics*, 2010, **239**(8): 2172-2189.

[23] Yartseva V, Giraldez A J. The maternal-to-zygotic transition during vertebrate development: a model for reprogramming [J]. *Current Topics in Developmental Biology*, 2015(113): 191-232.

[24] Mawed S A, Zhang J, Ren F, *et al*. *atg7* and *beclin1* are essential for energy metabolism and survival during the larval-to-juvenile transition stage of zebrafish [J]. *Aquaculture and Fisheries*, 2022, **7**(4): 359-372.

[25] Rodríguez-Marí A, Cañestro C, Bremiller R A, *et al*. Sex reversal in zebrafish fancl mutants is caused by Tp53-mediated germ cell apoptosis [J]. *PLoS Genetics*, 2010, **6**(7): e1001034.

[26] Qin M, Zhang Z, Song W, *et al*. Roles of figla/figla in juvenile ovary development and follicle formation during zebrafish gonadogenesis [J]. *Endocrinology*, 2018, **159**(11): 3699-3722.

[27] Dranow D B, Hu K, Bird A M, *et al*. Bmp15 is an oocyte-produced signal required for maintenance of the adult female sexual phenotype in zebrafish [J]. *PLoS Genetics*, 2016, **12**(9): e1006323.

[28] Mei W, Lee K W, Marlow F L, *et al*. hnRNP I is required to generate the Ca^{2+} signal that causes egg activation in zebrafish [J]. *Development*, 2009, **136**(17): 3007-3017.

[29] Hau H T A, Ogundele O, Hibbert A H, *et al*. Maternal Larp6 controls oocyte development, chorion formation and elevation [J]. *Development*, 2020, **147**(4): dev187385.

[30] Cheung C T, Nguyen T V, Le Cam A, *et al*. What makes a bad egg? Egg transcriptome reveals dysregulation of translational machinery and novel fertility genes important for fertilization [J]. *BMC Genomics*, 2019, **20**(1): 584.

[31] Xia P, Gütl D, Zheden V, *et al*. Lateral inhibition in cell specification mediated by mechanical signals modulating TAZ activity [J]. *Cell*, 2019, **176**(6): 1379-1392.e14.

[32] Yi X, Yu J, Ma C, *et al*. The effector of Hippo signaling,

Taz, is required for formation of the micropyle and fertilization in zebrafish [J]. *PLoS Genetics*, 2019, **15**(1): e1007408.

[33] Langdon Y G, Mullins M C. Maternal and zygotic control of zebrafish dorsoventral axial patterning [J]. *Annual Review of Genetics*, 2011(45): 357-377.

[34] Fuentes R, Tajer B, Kobayashi M, *et al*. The maternal coordinate system: molecular-genetics of embryonic axis formation and patterning in the zebrafish [J]. *Current Topics in Developmental Biology*, 2020(140): 341-389.

[35] Ryu S L, Fujii R, Yamanaka Y, *et al*. Regulation of dharma/bozozok by the Wnt pathway [J]. *Developmental Biology*, 2001, **231**(2): 397-409.

[36] Fekany K, Yamanaka Y, Leung T, *et al*. The zebrafish bozozok locus encodes *Dharma*, a homeodomain protein essential for induction of gastrula organizer and dorsoanterior embryonic structures [J]. *Development*, 1999, **126**(7): 1427-1438.

[37] Schneider S, Steinbeisser H, Warga R M, *et al*. β-catenin translocation into nuclei demarcates the dorsalizing centers in frog and fish embryos [J]. *Mechanisms of Development*, 1996, **57**(2): 191-198.

[38] Lu F I, Thisse C, Thisse B. Identification and mechanism of regulation of the zebrafish dorsal determinant [J]. *Proceedings of the National Academy of Sciences of the United States of America*, 2011, **108**(38): 15876-15880.

[39] Yan L, Chen J, Zhu X, *et al*. Maternal Huluwa dictates the embryonic body axis through β-catenin in vertebrates [J]. *Science*, 2018, **362**(6417): eaat1045.

[40] He M, Zhang R, Jiao S, *et al*. Nanog safeguards early embryogenesis against global activation of maternal β-catenin activity by interfering with TCF factors [J]. *PLoS Biology*, 2020, **18**(7): e3000561.

[41] Zinski J, Bu Y, Wang X, *et al*. Systems biology derived source-sink mechanism of BMP gradient formation [J]. *eLife*, 2017(6): e22199.

[42] Kramer C, Mayr T, Nowak M, *et al*. Maternally supplied Smad5 is required for ventral specification in zebrafish embryos prior to zygotic bmp signaling [J]. *Developmental Biology*, 2002, **250**(2): 263-279.

[43] Wei C Y, Wang H P, Zhu Z Y, *et al*. Correction: Transcriptional factors Smad1 and Smad9 act redundantly to mediate zebrafish ventral specification downstream of Smad5 [J]. *The Journal of Biological Chemistry*, 2020, **295**(52): 18650.

[44] Tucker J A, Mintzer K A, Mullins M C. The BMP signaling gradient patterns dorsoventral tissues in a temporally progressive manner along the anteroposterior axis [J]. *Developmental Cell*, 2008, **14**(1): 108-119.

[45] Sidi S, Goutel C, Peyriéras N, *et al*. Maternal induction of ventral fate by zebrafish *radar* [J]. *Proceedings of the National Academy of Sciences of the United States of America*, 2003, **100**(6): 3315-3320.

[46] Reim G, Brand M. Maternal control of vertebrate dorsoventral axis formation and epiboly by the POU domain protein Spg/Pou2/Oct4 [J]. *Development*, 2006, **133**(14): 2757-2770.

[47] Xu P, Zhu G, Wang Y, *et al*. Maternal Eomesodermin regulates zygotic nodal gene expression for mesendoderm induction in zebrafish embryos [J]. *Journal of Molecular Cell Biology*, 2014, **6**(4): 272-285.

[48] Schier A F. Nodal signaling in vertebrate development [J]. *Annual Review of Cell and Developmental Biology*, 2003(19): 589-621.

[49] Lee M T, Bonneau A R, Giraldez A J. Zygotic genome activation during the maternal-to-zygotic transition [J]. *Annual Review of Cell and Developmental Biology*, 2014(30): 581-613.

[50] Liu C, Ma Y, Shang Y, *et al*. Post-translational regulation of the maternal-to-zygotic transition [J]. *Cellular and Molecular Life Sciences*, 2018, **75**(10): 1707-1722.

[51] Vastenhouw N L, Cao W X, Lipshitz H D. The maternal-to-zygotic transition revisited [J]. *Development*, 2019, **146**(11): dev161471.

[52] Vasudevan S, Seli E, Steitz J A. Metazoan oocyte and early embryo development program: a progression through translation regulatory cascades [J]. *Genes & Development*, 2006, **20**(2): 138-146.

[53] Bazzini A A, Del Viso F, Moreno-Mateos M A, *et al*. *Codon* identity regulates mRNA stability and translation efficiency during the maternal-to-zygotic transition [J]. *The EMBO Journal*, 2016, **35**(19): 2087-2103.

[54] Mishima Y, Tomari Y. *Codon* usage and 3' UTR length determine maternal mRNA stability in zebrafish [J]. *Molecular Cell*, 2016, **61**(6): 874-885.

[55] Shi B, Heng J, Zhou J Y, *et al*. Phase separation of Ddx3xb helicase regulates maternal-to-zygotic transition in zebrafish [J]. *Cell Research*, 2022, **32**(8): 715-728.

[56] Despic V, Neugebauer K M. RNA tales - how embryos read and discard messages from mom [J]. *Journal of Cell Science*, 2018, **131**(5): jcs201996.

[57] Chang H, Yeo J, Kim J G, *et al*. Terminal uridylyltransferases execute programmed clearance of maternal transcriptome in vertebrate embryos [J]. *Molecular Cell*, 2018, **70**(1): 72-82.e7.

[58] Yang Y, Wang L, Han X, *et al*. RNA 5-methylcytosine facilitates the maternal-to-zygotic transition by preventing maternal mRNA decay [J]. *Molecular Cell*, 2019, **75**(6): 1188-1202.e11.

[59] Ren F, Lin Q, Gong G, *et al*. Igf2bp3 maintains maternal RNA stability and ensures early embryo development in zebrafish [J]. *Communications Biology*, 2020(3): 94.

[60] Ivanova I, Much C, Di Giacomo M, *et al*. The RNA m^6A reader YTHDF2 is essential for the post-transcriptional regulation of the maternal transcriptome and oocyte

competence [J]. *Molecular Cell*, 2017, **67**(6): 1059-1067.e4.

[61] Kontur C, Jeong M, Cifuentes D, *et al*. Ythdf m^6A readers function redundantly during zebrafish development [J]. *Cell Reports*, 2020, **33**(13): 108598.

[62] Giraldez A J, Mishima Y, Rihel J, *et al*. Zebrafish miR-430 promotes deadenylation and clearance of maternal mRNAs [J]. *Science*, 2006, **312**(5770): 75-79.

[63] Bazzini A A, Lee M T, Giraldez A J. Ribosome profiling shows that miR-430 reduces translation before causing mRNA decay in zebrafish [J]. *Science*, 2012, **336**(6078): 233-237.

[64] Lee M T, Bonneau A R, Takacs C M, *et al*. Nanog, Pou5f1 and SoxB1 activate zygotic gene expression during the maternal-to-zygotic transition [J]. *Nature*, 2013, **503**(7476): 360-364.

[65] Miao L, Tang Y, Bonneau A R, *et al*. The landscape of pioneer factor activity reveals the mechanisms of chromatin reprogramming and genome activation [J]. *Molecular Cell*, 2022, **82**(5): 986-1002.e9.

[66] Veil M, Yampolsky L Y, Grüning B, *et al*. Pou5f3, SoxB1, and Nanog remodel chromatin on high nucleosome affinity regions at zygotic genome activation [J]. *Genome Research*, 2019, **29**(3): 383-395.

[67] Pálfy M, Schulze G, Valen E, *et al*. Chromatin accessibility established by Pou5f3, Sox19b and Nanog primes genes for activity during zebrafish genome activation [J]. *PLoS Genetics*, 2020, **16**(1): e1008546.

[68] Vardy L, Orr-Weaver T L. Regulating translation of maternal messages: multiple repression mechanisms [J]. *Trends in Cell Biology*, 2007, **17**(11): 547-554.

[69] Richter J D, Lasko P. Translational control in oocyte development [J]. *Cold Spring Harbor Perspectives in Biology*, 2011, **3**(9): a002758.

[70] Weill L, Belloc E, Bava F A, *et al*. Translational control by changes in poly(A) tail length: recycling mRNAs [J]. *Nature Structural & Molecular Biology*, 2012, **19**(6): 577-585.

[71] McGrew L L, Dworkin-Rastl E, Dworkin M B, *et al*. Poly(A) elongation during *Xenopus* oocyte maturation is required for translational recruitment and is mediated by a short sequence element [J]. *Genes & Development*, 1989, **3**(6): 803-815.

[72] Sheets M D, Fox C A, Hunt T, *et al*. The 3′-untranslated regions of c-mos and cyclin mRNAs stimulate translation by regulating cytoplasmic polyadenylation [J]. *Genes & Development*, 1994, **8**(8): 926-938.

[73] Kim-Ha J, Kerr K, MacDonald P M. Translational regulation of *oskar* mRNA by Bruno, an ovarian RNA-binding protein, is essential [J]. *Cell*, 1995, **81**(3): 403-412.

[74] Snee M, Benz D, Jen J, *et al*. Two distinct domains of Bruno bind specifically to the oskar mRNA [J]. *RNA Biology*, 2008, **5**(1): 1-9.

[75] Castagnetti S, Hentze M W, Ephrussi A, *et al*. Control of oskar mRNA translation by Bruno in a novel cell-free system from *Drosophila* ovaries [J]. *Development*, 2000, **127**(5): 1063-1068.

[76] Nakamura A, Amikura R, Hanyu K, *et al*. Me31B silences translation of oocyte-localizing RNAs through the formation of cytoplasmic RNP complex during *Drosophila* oogenesis [J]. *Development*, 2001, **128**(17): 3233-3242.

[77] Miao L, Yuan Y, Cheng F, *et al*. Translation repression by maternal RNA binding protein Zar1 is essential for early oogenesis in zebrafish [J]. *Development*, 2017, **144**(1): 128-138.

[78] He M, Jiao S, Zhang R, *et al*. Translational control by maternal Nanog promotes oogenesis and early embryonic development [J]. *Development*, 2022, **149**(24): dev201213.

[79] Carnevali O, Cionna C, Tosti L, *et al*. Role of cathepsins in ovarian follicle growth and maturation [J]. *General and Comparative Endocrinology*, 2006, **146**(3): 195-203.

[80] Sun C, Zhang S. Immune-relevant and antioxidant activities of vitellogenin and yolk proteins in fish [J]. *Nutrients*, 2015, **7**(10): 8818-8829.

[81] Reading B J, Hiramatsu N, Sawaguchi S, *et al*. Conserved and variant molecular and functional features of multiple egg yolk precursor proteins (vitellogenins) in white perch (*Morone americana*) and other teleosts [J]. *Marine Biotechnology*, 2009, **11**(2): 169-187.

[82] Wang H, Tan J T T, Emelyanov A, *et al*. Hepatic and extrahepatic expression of vitellogenin genes in the zebrafish, *Danio rerio* [J]. *Gene*, 2005(356): 91-100.

[83] Yilmaz O, Patinote A, Nguyen T, *et al*. Multiple vitellogenins in zebrafish (*Danio rerio*): quantitative inventory of genes, transcripts and proteins, and relation to egg quality [J]. *Fish Physiology and Biochemistry*, 2018, **44**(6): 1509-1525.

[84] Wagner D S, Dosch R, Mintzer K A, *et al*. Maternal control of development at the midblastula transition and beyond: mutants from the zebrafish II [J]. *Developmental Cell*, 2004, **6**(6): 781-790.

[85] Yanes-Roca C, Rhody N, Nystrom M, *et al*. Effects of fatty acid composition and spawning season patterns on egg quality and larval survival in common snook (*Centropomus undecimalis*) [J]. *Aquaculture*, 2009, **287**(3/4): 335-340.

[86] Ishak S D, Tan S H, Khong H K, *et al*. Upregulated mRNA expression of desaturase and elongase, two enzymes involved in highly unsaturated fatty acids biosynthesis pathways during follicle maturation in zebrafish [J]. *Reproductive Biology and Endocrinology*, 2008(6): 56.

[87] Huynh M D, Kitts D D, Hu C, *et al*. Comparison of fatty acid profiles of spawning and non-spawning Pacific herring, *Clupea harengus* pallasi [J]. *Comparative Bio-*

chemistry and Physiology Part B, *Biochemistry & Molecular Biology*, 2007, **146**(4): 504-511.

[88] Garrido S, Rosa R, Ben-Hamadou R, *et al*. Effect of maternal fat reserves on the fatty acid composition of sardine (*Sardina pilchardus*) oocytes [J]. *Comparative Biochemistry and Physiology Part B*, *Biochemistry & Molecular Biology*, 2007, **148**(4): 398-409.

[89] Monroig Ó, Rotllant J, Sánchez E, *et al*. Expression of long-chain polyunsaturated fatty acid (LC-PUFA) biosynthesis genes during zebrafish *Danio rerio* early embryogenesis [J]. *Biochimica et Biophysica Acta* (BBA) - *Molecular and Cell Biology of Lipids*, 2009, **1791**(11): 1093-1101.

[90] Patiño R, Yoshizaki G, Bolamba D, *et al*. Role of arachidonic acid and protein kinase C during maturation-inducing hormone-dependent meiotic resumption and ovulation in ovarian follicles of Atlantic croaker [J]. *Biology of Reproduction*, 2003, **68**(2): 516-523.

[91] Ann Sorbera L, Francisco Asturiano J, Carrillo M, *et al*. Effects of polyunsaturated fatty acids and prostaglandins on oocyte maturation in a marine teleost, the European sea bass (*Dicentrarchus labrax*) [J]. *Biology of Reproduction*, 2001, **64**(1): 382-389.

[92] Richards J S. Sounding the alarm-does induction of prostaglandin endoperoxide synthase-2 control the mammalian ovulatory clock [J]? *Endocrinology*, 1997, **138**(10): 4047-4048.

[93] Lister A L, Van Der Kraak G. An investigation into the role of prostaglandins in zebrafish oocyte maturation and ovulation [J]. *General and Comparative Endocrinology*, 2008, **159**(1): 46-57.

[94] Takahashi T, Fujimori C, Hagiwara A, *et al*. Recent advances in the understanding of teleost medaka ovulation: the roles of proteases and prostaglandins [J]. *Zoological Science*, 2013, **30**(4): 239-247.

[95] Kim S O, Duffy D M. Mapping PTGERs to the ovulatory follicle: regional responses to the ovulatory PGE2-signal [J]. *Biology of Reproduction*, 2016, **95**(2): 33.

[96] Tang H, Liu Y, Li J, *et al*. Gene knockout of nuclear progesterone receptor provides insights into the regulation of ovulation by LH signaling in zebrafish [J]. *Scientific Reports*, 2016(6): 28545.

[97] Kang J X, Wang J, Wu L, *et al*. Fat-1 mice convert n-6 to n-3 fatty acids [J]. *Nature*, 2004, **427**(6974): 504.

[98] Lai L, Kang J X, Li R, *et al*. Generation of cloned transgenic pigs rich in omega-3 fatty acids [J]. *Nature Biotechnology*, 2006, **24**(4): 435-436.

[99] Wu X, Ouyang H, Duan B, *et al*. Production of cloned transgenic cow expressing omega-3 fatty acids [J]. *Transgenic Research*, 2012, **21**(3): 537-543.

[100] Hohos N M, Cho K J, Swindle D C, *et al*. Fat-1 transgene is associated with improved reproductive outcomes [J]. *Endocrinology*, 2018, **159**(12): 3981-3992.

[101] Pang S C, Wang H P, Li K Y, *et al*. Double transgenesis of humanized *fat1* and *fat2* genes promotes *Omega*-3 polyunsaturated fatty acids synthesis in a zebrafish model [J]. *Marine Biotechnology*, 2014, **16**(5): 580-593.

[102] Zhang X, Pang S, Liu C, *et al*. A novel dietary source of EPA and DHA: metabolic engineering of an important freshwater species-common carp by *fat1*-transgenesis [J]. *Marine Biotechnology*, 2019, **21**(2): 171-185.

[103] Clelland E, Peng C. Endocrine/paracrine control of zebrafish ovarian development [J]. *Molecular and Cellular Endocrinology*, 2009, **312**(1/2): 42-52.

[104] Ge W. Gonadotropins and their paracrine signaling network in the zebrafish ovary [J]. *Fish Physiology and Biochemistry*, 2005, **31**(2/3): 209-214.

[105] Hanna R N, Zhu Y. Controls of meiotic signaling by membrane or nuclear progestin receptor in zebrafish follicle-enclosed oocytes [J]. *Molecular and Cellular Endocrinology*, 2011, **337**(1/2): 80-88.

[106] Patiño R, Yoshizaki G, Thomas P, *et al*. Gonadotropic control of ovarian follicle maturation: the two-stage concept and its mechanisms [J]. *Comparative Biochemistry and Physiology Part B*, *Biochemistry & Molecular Biology*, 2001, **129**(2/3): 427-439.

[107] Zhang Z, Lau S W, Zhang L, *et al*. Disruption of zebrafish follicle-stimulating hormone receptor (fshr) but not luteinizing hormone receptor (lhcgr) gene by TALEN leads to failed follicle activation in females followed by sexual reversal to males [J]. *Endocrinology*, 2015, **156**(10): 3747-3762.

[108] Zhang Z, Zhu B, Ge W. Genetic analysis of zebrafish gonadotropin (FSH and LH) functions by TALEN-mediated gene disruption [J]. *Molecular Endocrinology*, 2015, **29**(1): 76-98.

[109] Takahashi A, Kanda S, Abe T, *et al*. Evolution of the hypothalamic-pituitary-gonadal axis regulation in vertebrates revealed by knockout medaka [J]. *Endocrinology*, 2016, **157**(10): 3994-4002.

[110] Zhao C, Zhai Y, Geng R, *et al*. Genetic analysis of activin/inhibin β subunits in zebrafish development and reproduction [J]. *PLoS Genetics*, 2022, **18**(12): e1010523.

[111] Chen W, Zhai Y, Zhu B, *et al*. Loss of growth differentiation factor 9 causes an arrest of early folliculogenesis in zebrafish-a novel insight into its action mechanism [J]. *PLoS Genetics*, 2022, **18**(12): e1010318.

[112] Zhao E, Basak A, Wong A O L, *et al*. The secretogranin II-derived peptide secretoneurin stimulates luteinizing hormone secretion from gonadotrophs [J]. *Endocrinology*, 2009, **150**(5): 2273-2282.

[113] Zhao E, Grey C L, Zhang D, *et al*. Secretoneurin is a potential paracrine factor from lactotrophs stimulating gonadotropin release in the goldfish pituitary [J]. *American Journal of Physiology Regulatory*, *Integrative and Comparative Physiology*, 2010, **299**(5): R1290-R1297.

[114] Mitchell K, Zhang W S, Lu C, *et al*. Targeted mutation of secretogranin-2 disrupts sexual behavior and repro-

duction in zebrafish [J]. *Proceedings of the National Academy of Sciences of the United States of America*, 2020, **117**(23): 12772-12783.

[115] Zhang Q, Ye D, Wang H, *et al*. Zebrafish cyp11c1 knockout reveals the roles of 11-ketotestosterone and cortisol in sexual development and reproduction [J]. *Endocrinology*, 2020, **161**(6): bqaa048.

[116] Wang Y, Ye D, Zhang F, *et al*. Cyp11a2 is essential for oocyte development and spermatogonial stem cell differentiation in zebrafish [J]. *Endocrinology*, 2022, **163**(2): bqab258.

[117] Hsu H J, Liang M R, Chen C T, *et al*. Pregnenolone stabilizes microtubules and promotes zebrafish embryonic cell movement [J]. *Nature*, 2006, **439**(7075): 480-483.

[118] Weng J H, Liang M R, Chen C H, *et al*. Pregnenolone activates CLIP-170 to promote microtubule growth and cell migration [J]. *Nature Chemical Biology*, 2013, **9**(10): 636-642.

[119] Hsu H J, Hsiao P, Kuo M W, *et al*. Expression of zebrafish *cyp11a1* as a maternal transcript and in yolk syncytial layer [J]. *Gene Expression Patterns*, 2002, **2**(3/4): 219-222.

[120] Costello D P. Ooplasmic segregation in relation to differentiation [J]. *Annals of the New York Academy of Sciences*, 1948, **49**(Art 5): 663-683.

[121] Fernández J, Valladares M, Fuentes R, *et al*. Reorganization of cytoplasm in the zebrafish oocyte and egg during early steps of ooplasmic segregation [J]. *Developmental Dynamics*, 2006, **235**(3): 656-671.

[122] Abrams E W, Mullins M C. Early zebrafish development: it's in the maternal genes [J]. *Current Opinion in Genetics & Development*, 2009, **19**(4): 396-403.

[123] Escobar-Aguirre M, Elkouby Y M, Mullins M C. Localization in oogenesis of maternal regulators of embryonic development [J]. *Advances in Experimental Medicine and Biology*, 2017(953): 173-207.

[124] Ge X, Grotjahn D, Welch E, *et al*. *Hecate*/Grip2a acts to reorganize the cytoskeleton in the symmetry-breaking event of embryonic axis induction [J]. *PLoS Genetics*, 2014, **10**(6): e1004422.

[125] Howley C, Ho R K. mRNA localization patterns in zebrafish oocytes [J]. *Mechanisms of Development*, 2000, **92**(2): 305-309.

[126] Extavour C G, Akam M. Mechanisms of germ cell specification across the metazoans: epigenesis and preformation [J]. *Development*, 2003, **130**(24): 5869-5884.

[127] Hartung O, Forbes M M, Marlow F L. Zebrafish Vasa is required for germ-cell differentiation and maintenance [J]. *Molecular Reproduction and Development*, 2014, **81**(10): 946-961.

[128] Draper B W, McCallum C M, Moens C B. *nanos1* is required to maintain oocyte production in adult zebrafish [J]. *Developmental Biology*, 2007, **305**(2): 589-598.

[129] Beer R L, Draper B W. *nanos3* maintains germline stem cells and expression of the conserved germline stem cell gene *nanos2* in the zebrafish ovary [J]. *Developmental Biology*, 2013, **374**(2): 308-318.

[130] Heim A E, Hartung O, Rothhämel S, *et al*. Oocyte polarity requires a Bucky ball-dependent feedback amplification loop [J]. *Development*, 2014, **141**(4): 842-854.

[131] Marlow F L, Mullins M C. Bucky ball functions in Balbiani body assembly and animal-vegetal polarity in the oocyte and follicle cell layer in zebrafish [J]. *Developmental Biology*, 2008, **321**(1): 40-50.

[132] Roovers E F, Kaaij L J T, Redl S, *et al*. Tdrd6a regulates the aggregation of buc into functional subcellular compartments that drive germ cell specification [J]. *Developmental Cell*, 2018, **46**(3): 285-301.e9.

[133] Kaufman O H, Lee K, Martin M, *et al*. rbpms2 functions in Balbiani body architecture and ovary fate [J]. *PLoS Genetics*, 2018, **14**(7): e1007489.

[134] Brangwynne C P, Eckmann C R, Courson D S, *et al*. Germline P granules are liquid droplets that localize by controlled dissolution/condensation [J]. *Science*, 2009, **324**(5935): 1729-1732.

[135] Berry J, Weber S C, Vaidya N, *et al*. RNA transcription modulates phase transition-driven nuclear body assembly [J]. *Proceedings of the National Academy of Sciences of the United States of America*, 2015, **112**(38): E5237-E5245.

[136] Molliex A, Temirov J, Lee J, *et al*. Phase separation by low complexity domains promotes stress granule assembly and drives pathological fibrillization [J]. *Cell*, 2015, **163**(1): 123-133.

[137] Sabari B R, Dall'Agnese A, Boija A, *et al*. Coactivator condensation at super-enhancers links phase separation and gene control [J]. *Science*, 2018, **361**(6400): eaar3958.

[138] Jamieson-Lucy A H, Kobayashi M, James Aykit Y, *et al*. A proteomics approach identifies novel resident zebrafish Balbiani body proteins Cirbpa and Cirbpb [J]. *Developmental Biology*, 2022(484): 1-11.

[139] Boke E, Ruer M, Wühr M, *et al*. Amyloid-like self-assembly of a cellular compartment [J]. *Cell*, 2016, **166**(3): 637-650.

[140] Gupta T, Marlow F L, Ferriola D, *et al*. Microtubule actin crosslinking factor 1 regulates the balbiani body and animal-vegetal polarity of the zebrafish oocyte [J]. *PLoS Genetics*, 2010, **6**(8): e1001073.

[141] Escobar-Aguirre M, Zhang H, Jamieson-Lucy A, *et al*. Microtubule-actin crosslinking factor 1 (Macf1) domain function in Balbiani body dissociation and nuclear positioning [J]. *PLoS Genetics*, 2017, **13**(9): e1006983.

[142] Nair S, Marlow F, Abrams E, *et al*. The chromosomal passenger protein birc5b organizes microfilaments and germ plasm in the zebrafish embryo [J]. *PLoS Genetics*, 2013, **9**(4): e1003448.

[143] Tilg H, Moschen A R, Roden M. NAFLD and diabetes

mellitus [J]. *Nature Reviews Gastroenterology & Hepatology*, 2017, **14**(1): 32-42.

[144] Shoubridge E A, Wai T. Mitochondrial DNA and the mammalian oocyte [J]. *Current Topics in Developmental Biology*, 2007, **77**: 87-111.

[145] Zhang X, Wu X Q, Lu S, *et al*. Deficit of mitochondria-derived ATP during oxidative stress impairs mouse MII oocyte spindles [J]. *Cell Research*, 2006, **16**(10): 841-850.

[146] Picca A, Mankowski R T, Burman J L, *et al*. Mitochondrial quality control mechanisms as molecular targets in cardiac ageing [J]. *Nature Reviews Cardiology*, 2018, **15**(9): 543-554.

[147] Jiao H, Jiang D, Hu X, *et al*. Mitocytosis, a migrasome-mediated mitochondrial quality-control process [J]. *Cell*, 2021, **184**(11): 2896-2910.e13.

[148] Shen Q, Liu Y, Li H, *et al*. Effect of mitophagy in oocytes and granulosa cells on oocyte quality [J]. *Biology of Reproduction*, 2021, **104**(2): 294-304.

[149] Hou X, Zhu S, Zhang H, *et al*. Mitofusin1 in oocyte is essential for female fertility [J]. *Redox Biology*, 2019(21): 101110.

[150] Song Z H, Yu H Y, Wang P, *et al*. Germ cell-specific Atg7 knockout results in primary ovarian insufficiency in female mice [J]. *Cell Death & Disease*, 2015, **6**(1): e1589.

[151] van der Reest J, Nardini Cecchino G, Haigis M C, *et al*. Mitochondria: Their relevance during oocyte ageing [J]. *Ageing Research Reviews*, 2021(70): 101378.

[152] Zhang R, Tu Y X, Ye D, *et al*. A germline-specific regulator of mitochondrial fusion is required for maintenance and differentiation of germline stem and progenitor cells [J]. *Advanced Science*, 2022, **9**(36): e2203631.

[153] Johnston T A, Wiegand M D, Leggett W C, *et al*. Hatching success of walleye embryos in relation to maternal and ova characteristics [J]. *Ecology of Freshwater Fish*, 2007, **16**(3): 295-306.

[154] Coldebella I J, Neto J R, Mallmann C A, *et al*. The effects of different protein levels in the diet on reproductive indexes of *Rhamdia quelen* females [J]. *Aquaculture*, 2011, **312**(1/2/3/4): 137-144.

[155] Chee W L, Turchini G M, Teoh C Y, *et al*. Dietary arachidonic acid and the impact on growth performance, health and tissues fatty acids in Malabar red snapper (*Lutjanus malabaricus*) fingerlings [J]. *Aquaculture*, 2020(519): 734757.

[156] Araújo B C, Honji R M, Rombenso A N, *et al*. Influences of different arachidonic acid levels and temperature on the growth performance, fatty acid profile, liver morphology and expression of lipid genes in cobia (*Rachycentron canadum*) juveniles [J]. *Aquaculture*, 2019(511): 734245.

[157] Ma A J, Chen C, Lei J L, *et al*. The effect of protein and n-3HUFA on the reproduction of turbot (*Scophthalmus maximus*) [J]. *Marine Fisheries Research*, 2005, **26**(1): 7-12. [马爱军, 陈超, 雷霁霖, 等. 饲料蛋白质含量和n-3HUFA水平对大菱鲆亲鱼产卵的影响 [J]. 海洋水产研究, 2005, **26**(1): 7-12.]

[158] Orlando T M, Fontes T V, Paulino R R, *et al*. Effects of the dietary linoleic acid to linolenic acid ratio for Nile tilapia (*Oreochromis niloticus*) breeding females [J]. *Aquaculture*, 2020(516): 734625.

[159] Allan Bombardelli R, dos Reis Goes E S, de Negreiros Sousa S M, *et al*. Growth and reproduction of female Nile tilapia fed diets containing different levels of protein and energy [J]. *Aquaculture*, 2017(479): 817-823.

[160] Lebold K M, Jump D B, Miller G W, *et al*. Vitamin E deficiency decreases long-chain PUFA in zebrafish (*Danio rerio*) [J]. *The Journal of Nutrition*, 2011, **141**(12): 2113-2118.

[161] Lebold K M, Kirkwood J S, Taylor A W, *et al*. Novel liquid chromatography-mass spectrometry method shows that vitamin E deficiency depletes arachidonic and docosahexaenoic acids in zebrafish (*Danio rerio*) embryos [J]. *Redox Biology*, 2014(2): 105-113.

[162] Blomhoff R, Blomhoff H K. Overview of retinoid metabolism and function [J]. *Journal of Neurobiology*, 2006, **66**(7): 606-630.

[163] Li M, Feng R, Ma H, *et al*. Retinoic acid triggers meiosis initiation via *stra8*-dependent pathway in Southern catfish, *Silurus meridionalis* [J]. *General and Comparative Endocrinology*, 2016(232): 191-198.

[164] Feng R, Fang L, Cheng Y, *et al*. Retinoic acid homeostasis through aldh1a2 and cyp26a1 mediates meiotic entry in Nile tilapia (*Oreochromis niloticus*) [J]. *Scientific Reports*, 2015(5): 10131.

[165] Yamaguchi T, Kitano T. High temperature induces *cyp26b1* mRNA expression and delays meiotic initiation of germ cells by increasing cortisol levels during gonadal sex differentiation in Japanese flounder [J]. *Biochemical and Biophysical Research Communications*, 2012, **419**(2): 287-292.

[166] Lee K J, Dabrowski K. Long-term effects and interactions of dietary vitamins C and E on growth and reproduction of yellow perch, *Perca flavescens* [J]. *Aquaculture*, 2004, **230**(1/2/3/4): 377-389.

[167] Sarmento N L A F, Martins E F F, Costa D C, *et al*. Reproductive efficiency and egg and larvae quality of Nile tilapia fed different levels of vitamin C [J]. *Aquaculture*, 2018(482): 96-102.

[168] Wang Y Y, Zhao C N. Key techniques for cultivating turbot parent fish [J]. *Shandong Fisheries*, 2010, **27**(12): 22. [王远洋, 赵城南. 大菱鲆亲鱼培育关键技术 [J]. 齐鲁渔业, 2010, **27**(12): 22.]

[169] Holcombe G W, Pasha M S, Jensen K M, *et al*. Effects of photoperiod manipulation on brook trout reproductive development, fecundity, and circulating sex steroid concentrations [J]. *North American Journal of Aquacul-*

ture, 2000, **62**(1): 1-11.

[170] Carrillo M, Bromage N, Zanuy S, *et al*. The effect of modifications in photoperiod on spawning time, ovarian development and egg quality in the sea bass (*Dicentrarchus labrax* L.) [J]. *Aquaculture*, 1989, **81**(3/4): 351-365.

[171] Lasse Taranger G, Carrillo M, Schulz R W, *et al*. Control of puberty in farmed fish [J]. *General and Comparative Endocrinology*, 2010, **165**(3): 483-515.

[172] Chattoraj A, Bhattacharyya S, Basu D, *et al*. Melatonin accelerates maturation inducing hormone (MIH): induced oocyte maturation in carps [J]. *General and Comparative Endocrinology*, 2005, **140**(3): 145-155.

[173] Sébert M E, Legros C, Weltzien F A, *et al*. Melatonin activates brain dopaminergic systems in the eel with an inhibitory impact on reproductive function [J]. *Journal of Neuroendocrinology*, 2008, **20**(7): 917-929.

[174] Maitra S K, Chattoraj A, Mukherjee S, *et al*. Melatonin: a potent candidate in the regulation of fish oocyte growth and maturation [J]. *General and Comparative Endocrinology*, 2013(181): 215-222.

[175] Rocha R M P, Lima L F, Alves A M C V, *et al*. Interaction between melatonin and follicle-stimulating hormone promotes *in vitro* development of caprine preantral follicles [J]. *Domestic Animal Endocrinology*, 2013, **44**(1): 1-9.

[176] Ceinos R M, Chivite M, López-Patiño M A, *et al*. Differential circadian and light-driven rhythmicity of clock gene expression and behaviour in the turbot, *Scophthalmus maximus* [J]. *PLoS One*, 2019, **14**(7): e0219153.

[177] Ahmad Khan Z, Yumnamcha T, Rajiv C, *et al*. Melatonin biosynthesizing enzyme genes and clock genes in ovary and whole brain of zebrafish (*Danio rerio*): differential expression and a possible interplay [J]. *General and Comparative Endocrinology*, 2016(233): 16-31.

[178] Pörtner H O, Farrell A P. Ecology. Physiology and climate change [J]. *Science*, 2008, **322**(5902): 690-692.

[179] Ficke A D, Myrick C A, Hansen L J. Potential impacts of global climate change on freshwater fisheries [J]. *Reviews in Fish Biology and Fisheries*, 2007, **17**(4): 581-613.

[180] Elisio M, Chalde T, Miranda L A. Effects of short periods of warm water fluctuations on reproductive endocrine axis of the pejerrey (*Odontesthes bonariensis*) spawning [J]. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, 2012, **163**(1): 47-55.

[181] Hani Y M I, Turies C, Palluel O, *et al*. Effects of a chronic exposure to different water temperatures and/or to an environmental cadmium concentration on the reproduction of the threespine stickleback (*Gasterosteus aculeatus*) [J]. *Ecotoxicology and Environmental Safety*, 2019(174): 48-57.

[182] Li Q H, Sun J, Li Y Z, *et al*. Effects of nutrition enhancement, light and temperature control on gonad development and ovum quality in *Scophthalmus maximus* spawner [J]. *Journal of Southern Agriculture*, 2013, **44**(6): 1030-1035. [李庆华, 孙建, 李仰真, 等. 营养强化和控光控温对大菱鲆亲鱼性腺发育及卵子质量的影响 [J]. 南方农业学报, 2013, **44**(6): 1030-1035.]

[183] Cardoso P G, Rodrigues D, Madureira T V, *et al*. Warming modulates the effects of the endocrine disruptor progestin levonorgestrel on the zebrafish fitness, ovary maturation kinetics and reproduction success [J]. *Environmental Pollution*, 2017(229): 300-311.

[184] Pankhurst N W, Porter M R. Cold and dark or warm and light: variations on the theme of environmental control of reproduction [J]. *Fish Physiology and Biochemistry*, 2003, **28**(1): 385-389.

[185] Lahiri K, Froehlich N, Heyd A, *et al*. Developmental stage-specific regulation of the circadian clock by temperature in zebrafish [J]. *BioMed Research International*, 2014(2014): 930308.

[186] Lahiri K, Vallone D, Gondi S B, *et al*. Temperature regulates transcription in the zebrafish circadian clock [J]. *PLoS Biology*, 2005, **3**(11): e351.

[187] Tilton S C, Foran C M, Benson W H. Effects of cadmium on the reproductive axis of Japanese medaka (*Oryzias latipes*) [J]. *Comparative Biochemistry and Physiology Part C*: *Toxicology & Pharmacology*, 2003, **136**(3): 265-276.

[188] Wu S M, Tsai P J, Chou M Y, *et al*. Effects of maternal cadmium exposure on female reproductive functions, gamete quality, and offspring development in zebrafish (*Danio rerio*) [J]. *Archives of Environmental Contamination and Toxicology*, 2013, **65**(3): 521-536.

[189] Zhang Q F, Li Y W, Liu Z H, *et al*. Reproductive toxicity of inorganic mercury exposure in adult zebrafish: Histological damage, oxidative stress, and alterations of sex hormone and gene expression in the hypothalamic-pituitary-gonadal axis [J]. *Aquatic Toxicology*, 2016(177): 417-424.

[190] Cao J, Wang G, Wang T, *et al*. Copper caused reproductive endocrine disruption in zebrafish (*Danio rerio*) [J]. *Aquatic Toxicology*, 2019(211): 124-136.

[191] Ma Y, Liu H, Wu J, *et al*. The adverse health effects of bisphenol A and related toxicity mechanisms [J]. *Environmental Research*, 2019(176): 108575.

[192] Cheng Y, Zhang J, Wu T, *et al*. Reproductive toxicity of acute Cd exposure in mouse: resulting in oocyte defects and decreased female fertility [J]. *Toxicology and Applied Pharmacology*, 2019(379): 114684.

[193] Gunderson A R, Armstrong E J, Stillman J H. Multiple stressors in a changing world: the need for an improved perspective on physiological responses to the dynamic marine environment [J]. *Annual Review of Marine Science*, 2016(8): 357-378.

[194] Aegerter S, Jalabert B. Effects of post-ovulatory oocyte ageing and temperature on egg quality and on the occur-

rence of triploid fry in rainbow trout, *Oncorhynchus mykiss* [J]. *Aquaculture*, 2004, **231**(1/2/3/4): 59-71.

[195] Mohagheghi Samarin A, Policar T, Lahnsteiner F. Fish oocyte ageing and its effect on egg quality [J]. *Reviews in Fisheries Science & Aquaculture*, 2015, **23**(3): 302-314.

[196] Linhart O, Billard R. Survival of ovulated oocytes of the European catfish *(Silurus glanis*) after *in vivo* and *in vitro* storage or exposure to saline solutions and urine [J]. *Aquatic Living Resources*, 1995, **8**(4): 317-322.

[197] Rizzo E, Godinho H P, Sato Y. Short-term storage of oocytes from the neotropical teleost fish *Prochilodus marggravii* [J]. *Theriogenology*, 2003, **60**(6): 1059-1070.

[198] Legendre M, Slembrouck J, Subagja J, *et al*. Ovulation rate, latency period and ova viability after GnRH-or hCG-induced breeding in the Asian catfish *Pangasius hypophthalmus* (Siluriformes, Pangasiidae) [J]. *Aquatic Living Resources*, 2000, **13**(3): 145-151.

[199] Legendre M, Otémé Z. Effect of varying latency period on the quantity and quality of ova after hCG-induced ovulation in the African catfish, *Heterobranchus longifilis* (Teleostei, Clariidae) [J]. *Aquatic Living Resources*, 1995, **8**(4): 309-316.

[200] Rime H, Guitton N, Pineau C, *et al*. Post-ovulatory ageing and egg quality: a proteomic analysis of rainbow trout coelomic fluid [J]. *Reproductive Biology and Endocrinology*, 2004(2): 26.

[201] Chamani I J, Keefe D L. Epigenetics and female reproductive aging [J]. *Frontiers in Endocrinology*, 2019(10): 473.

[202] Gaudemar B, Beall E. Effects of overripening on spawning behaviour and reproductive success of Atlantic salmon females spawning in a controlled flow channel [J]. *Journal of Fish Biology*, 1998, **53**(2): 434-446.

[203] Linhart O, Shelton W L, Tučková V, *et al*. Effects of temperature on *in vitro* short-term storage of sterlet sturgeon (*Acipenser ruthenus*) *Ova* [J]. *Zuchthygiene*, 2016, **51**(1): 165-170.

[204] Migaud H, Bell G, Cabrita E, *et al*. Gamete quality and broodstock management in temperate fish [J]. *Reviews in Aquaculture*, 2013(5): S194-S223.

[205] Sun Y, Zhang B, Luo L, *et al*. Systematic genome editing of the genes on zebrafish Chromosome 1 by CRISPR/Cas9 [J]. *Genome Research*, 2019, **30**(1): 118-126.

RESEARCH PROGRESS AND SEVERAL KEY SCIENTIFIC QUESTIONS IN STUDIES OF FISH EGG QUALITY

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Abstract: Egg quality is a complex biological characteristic, which determines the reproductive capacity of females. Fish egg quality refers to the fertilizing ability of eggs and the ability to support the normal development of embryos and larvae. It is directly related to the formation of fertilized eggs, the early development of embryos, and the survival and development of larvae and juvenile fish. It is the key-link that determines the success of fish breeding and breeding efficiency. It is an important prerequisite for the development of aquaculture industry to evaluate egg quality objectively and accurately, to improve egg quality and to obtain a large number of mature eggs with high quality. In theory, fish egg quality is determined by all deposited maternal materials and their spatial and temporal distribution patterns in the egg. In this paper, the research status of fish oogenesis, maturation and the evaluation criteria of egg quality are summarized. In addition, the regulation of egg quality by maternal factors based on zebrafish model is highlighted. Finally, the key scientific questions involved in fish oocyte quality that need to be studied and solved are proposed, i.e., the main biological events that determine and are affected by egg quality, including oogonia-to-oocyte transition, oocyte-to-egg transition, egg-to-embryo transition, embryo-to-larval transition, and larval-to-juvenile transition.

Key words: Egg quality; Oogenesis; Evaluation of egg quality; Maternal material