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How do limbs, fins, and faces develop and evolve?

鳍与四肢如何发育和演化?

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摘要 鱼鳍如何产生, 又怎样向陆生四足动物的四肢演化? 回答这一科学问题实质上是要理解决定生命这些性状的基因如何受制于自然选择和性选择, 以及由此涉及与发育相关的创新动力和演化机制. 近10年的研究表明, 鳍最早可能是以单鳍褶的形式出现在早期的无颌鱼类中, 尔后在向有颌鱼类和四足动物的演化过程中发生了显著变化, 且在这一演化过程中, 鱼鳍发育必需基因的序列变异、表达模式变化、基因间相互作用甚至部分基因丢失可能起了关键作用. 本文综述了鳍的起源、演化历程和发育模式, 阐述了鳍向四肢演化、鱼鳍两性异形产生和四肢形态演化的分子机制.

关键词 鳍, 肢, 演化, 两性异形, 性别偏向基因

众所周知, 生命起源于水, 生物特别是动物经历了从水生到陆生的演化过程. 远古鱼类是包括人类等在内的所有陆生脊椎动物祖先, 鱼鳍是大部分鱼类用来游泳和维持身体平衡的重要器官, 包括成对的偶鳍和不成对的奇鳍. 其中, 偶鳍沿身体两侧分布, 分为胸鳍和腹鳍, 亦称侧鳍; 奇鳍沿身体正中线生长, 分为背鳍、尾鳍、臀鳍等, 亦称单鳍. 化石、胚胎发育和分子生物学证据表明, 4亿年前, 鱼鳍逐步演化成陆生动物的四肢, 尽管鱼鳍和四肢存在着结构、发育和组织上的差异, 但陆生动物四肢发育过程中所需要的基因, 如*Fgf*, *Wnt*, *Hox*等, 在鱼类的鳍中就已经出现, 并且也是必需的. 目前, 关于鱼鳍如何产生以及如何演化仍具有争议. 比较明确的是, 在自然选择和性选择压力下, 基因驱动了鳍向四肢演化、也导致了鳍的两性异形以及四肢的多态性.

鳍究竟是如何产生的, 偶鳍和奇鳍有着怎样的发育模式, 基因在其中起到了什么作用? 鳍又是怎样向陆生动物的四肢演化的, 如何理解鳍的两性异形现象和肢的形态演化, 一直是近百年来古生物学、比较解剖学、发育生物学、进化生物学等领域中重大命题和长期争论的话题. 随着现代生物学的发展, 特别是基因组比较进化生物学的兴起, 对其演化的历程和发育模式已趋于明晰.

1 鳍的发生和起源

根据化石记录, 类鳍结构最早出现在古老的无颌类中[1,2], 奇鳍和偶鳍的起源相差超过一亿年, 在进化上奇鳍是偶鳍的先驱[3], 且二者有着相似的形态学特征.

关于鱼鳍特别是偶鳍形成目前主要存在两种假说. 其中一种是鳃弓起源学说(gill arch theory), 也被称为“Gegenbaur 假说”, 因为它是由德国解剖生物学家Gegenbaur[4]在1870年提出的. 该假说认为“偶鳍起源于鳃弓结构”[3], 随后, 1877年出现了一种更有影响力的假说——侧褶学说(lateral fin-fold theory), 认为鳍起源于鳃后面鱼体表皮横向或纵向的褶皱[3,5~7],

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这一学说也得到了许多鱼类胚胎发育过程的有力支持[8]，特别是最古老的鱼类——海口鱼(*Haikouichthys ercaicunensis*)和昆明鱼(*Myllokunmingia fengjiaoa*)的发现，使得这种猜想得到了有力证实[9,10]．近年来最新遗传分析结果表明，软骨鱼类鳃弓和偶鳍发育有相同的分子机制[11,12]，揭示了鳃弓与鳍及人类四肢之间可能的演化关系[13]，说明需要重新考虑旧的鳃弓起源学说．

一般说来，鳍的从无到有可分成3个阶段．第一阶段：原始脊索动物如文昌鱼(*Branchiostoma*)中出现沿着背部和腹部中线发育的原始鳍或鳍褶，此时无辐状骨结构[14~16]．第二阶段：无辐状骨的原始鳍开始退化，出现完整的奇鳍和原始的偶鳍，如海口鱼[9,16]．第三阶段：内骨骼辐状骨和外骨骼形成的鳍条明显出现，如七鳃鳗(*Lampetra japonicum*)和盲鳗(*Myxiniformes*)[14,16,17]．在鳍条形成之前，内骨骼和外骨骼有轻微的区别，随着鳍条的逐渐形成，内外骨骼发育模式一致，且形成独立的背鳍、臀鳍以及尾鳍[17]．

2 鳍的发育

通过分子标记对不同类型的细胞进行研究发现，虽然奇鳍和偶鳍分别来源于轴旁中胚层(paraxial mesoderm, PM)和侧板中胚层(lateral plate mesoderm, LPM)，但却共用相同的发育机制[18~20]．在胚胎发育时期，鳍的形成是沿着PM和LPM的中线建立的，脊椎动物鳍条的主要组成部分首先是在中胚层中线组装的，招募与LPM及PM形成相关的物质，由背部向侧部及腹侧部，驱动着鳍的产生[21~25]．

在鳍发育早期，鳍芽(fin bud)的出现标志着鳍的形成，鳍芽受鳍褶控制，成纤维细胞生长因子(fibroblast growth factor, FGF)家族诱导鳍褶的产生和发育，如斑马鱼(*Barchydanio rerio var*)、角鲨鲨鱼(*Heterodontus francisci*)[18,26]．研究结果显示，鳍芽诱导信号始于PM，接着被转入LPM和上覆外胚层(overlying ectoderm, OE)中[27~31]，这其中，鳍芽间介中胚层(intermediate mesoderm, IE)中*Fgf*信号通路、PM中RA信号通路和LPM中的Wnt信号通路等对鳍的发育是必要的，涉及的*Hox*, *Wnt*, *Tbx*, *Pitx*, *dlx*, *Sp*, *Fgf*和*Shh*等基因的表达若受影响，鳍芽就会消失，影响鳍的发育[32]．在随后正常的发育途径中，顶端外胚层嵴(apical ectodermal ridge, AER)组织中心形成“顶褶”(apical fold, AF)结构，该结构由两层上皮细胞组成，这两层上皮细胞之间的IE细胞最终形成鳍条．有颌类的成对附肢的发育依靠AER信号的激活，AER通过FGFs与中胚层的产物协调起作用．如果在背部中线加入FGFs，则能够诱导异常类似AER的结构产生，且激活信号并诱导鳍的产生．在斑马鱼中，FGFs会驱使前端中线鳍褶的扩张，在体侧产生类似鳍褶的结构[33,34]．在中胚层中，Tbx5激活*Fgf10*诱导鳍芽产生．在鸡胚胎中，转录因子Irx3和FoxF1标志着两个腹侧层的形成，从而形成LPM[34]，位于中间中胚层(intermediate mesoderm, IM)的转录因子将视黄酸信号转移到LPM，触发鳍的形成，这是发育为鳍的先决条件．Tulenko等人[20]对猫鲨科(Scyliorhinidae)奇鳍的基因表达模式进行研究时发现，*Tbx18*和*Hoxd*在奇鳍的发育过程中起着定位作用．在鳍的发育过程中，脊椎动物的运动附肢起初是在早期的脊索动物中形成不成对的鳍褶，而后为了适应环境的变化，在身体侧腹面两套运动附肢应运而生．FGF信号是附肢再生的必备条件，但是在再生过程中，FGF精确的功能以及配体仍然是谜[35]．另一个有意思的发现是，在某些派生出的真骨鱼类中，腹鳍细胞会向着胸鳍的位置或者更前端迁移，具体是哪类因子或者哪些临近的细胞起作用还没有得到解答[36]．如果能够通过比较相关基因的功能和表达以及深入探究基因调控网络将会使得整个发育过程得到更加清楚的诠释．

3 鳍向肢的演化

鳍的早期发育与四足动物肢芽的发育非常相似，在后期发育过程中，鳍和四肢之间呈现组织学、结构学和发育学上的不同，那么是什么导致了鳍芽发育为鳍，肢芽发育为四肢，即鳍是如何在历史长河中演化为四肢的？为了回答以上生物学中的基本问题，鱼类和四足类的发育模式以及一些发育相关的关键基因已经被研究，人们正在一步步接近打开这道科学之门的钥匙．

从鳍和肢的结构和组成上来看，它们虽具有许多共同点，但也表现出明显不同，其主要差异有3点：(ⅰ)肢仅由软骨内骨组成但鳍由软骨内骨(组成鳍基骨)和皮骨(组成鳍条)两种骨骼组成[37,38]．(ⅱ)鳍最远端结构是鳍条，而肢则表现为远端或腕指部(autopod)结构．(ⅲ)鳍具有多个前端骨骼元件(anterior skeletal elements)而在四足类前肢的前端却

只有一个近端基骨(proximal basal bone)[39,40].

大量研究表明，基因驱动了鳍向肢的演化，斑马鱼属(*Brachydanio*)、猫鲨属(*Scyliorhinus*)和小鼠(*Mus musculus*)等被认为是研究鳍、鳍肢类似结构、肢演化的模式范例，众多实验也就此展开[14,38,39].

*Hox*基因家族在鳍向肢的演化过程中扮演了重要角色. Saxena和Cooper[37]和Gehrke等[41]发现，斑点雀鳝(*Lepisosteus oculatus*)基因组的*hoxD*和*hoxA*增强子不但能驱动小鼠腕指部报告基因的表达而且还能驱动斑马鱼胸鳍远端部分的表达，但众所周知鱼鳍是没有腕指部的，那这是怎么发生的呢？Nakamura等人[38]最新的研究表明，鳍和指(趾)的骨骼可能由两个相同的基因*Hoxa13*和*Hoxd13*所控制. 他们对斑马鱼和小鼠*Hoxa13*和*Hoxd13*进行敲除后发现，敲除后的小鼠的肢末端不能形成正常的腕指部，而斑马鱼的鳍也出现了骨骼长度减短、鳍条减少的情况. 另外，他们还发现*Hoxa13*和*Hoxd13*被敲除的斑马鱼皮骨减少但出现了更多的软骨内骨，这或许支持了下面一个假说，在进化过程中四足类祖先*Hoxa13*和*Hoxd13*可能发生了某些变异，导致形成鳍条的皮骨不断减少，软骨数目不断增加，最终导致了腕指部的发生. 早期研究表明，在后期，包括*Hoxd13*在内的5′*Hoxd*基因在四足动物肢中因受增强子GCR(global control region)、Prox、保守序列C(conserved sequence C, CsC)以及顶外胚层褶(apical ectodermal fold, AEF)的调节，其表达水平要高于在鳍中的表达水平[42~47]. 这种表达上的变化是否是由于四足类祖先所发生的某些变异所造成的还不得而知，但这种差异或许与腕指部的形成相关.

*And*基因家族中基因丢失也许是从鱼鳍进化到动物四肢的“关键步骤”. Zhang等人[48]和Tulenko等人[49]先后报道了基因*And1*，*And2*和*ScAnd*(putative *And* homologue)，这些基因只存在鱼鳍的发育过程中，在鳍发育后期与皮骨形成相关，且*And1*基因与hoxD转录物共定位，在鱼鳍发育中起关键作用，但在动物的四肢中却没有被发现.

*Gli3-Hand2*相互抑制模式以及*Shh*，5′*Hoxd*以及*Hand2*正反馈调节环表达时间是鱼鳍向四肢演化过程中前端骨骼元件消失的关键. 肢单一近端骨骼元件(即近端基骨)的形成很有可能是鱼鳍前后轴(anterior-posterior，A-P)上某些基因表达模式发生改变所造成的[39,50,51]. 通过对鳍和肢发育相关的基因如*Shh*[52~55]，*Gli3*[54,56~59]，*Hoxd*[60~64]，*Alx4*[57,65,66]和*Pax9*[67~69]等的研究发现，在鼠前肢发育过程中，肢芽前端表达的*Gli3*与后端表达的*Hand2*沿着A-P轴相互抑制，*Shh*，5′*Hoxd*以及*Hand2*形成一个扩大了肢芽后端的区域正反馈调节环，并且抑制前端骨骼元件的形成[58,70,71]. 但在猫鲨鳍芽中，未发现*Hand2*对*Gli3*的抑制作用，*Shh*，5′*Hoxd*以及*Hand2*所形成的正反馈调节环也在后期才出现，并且只能维持很短的时间[39,50,51,72,73]. 在匙吻鲟(*Polyodon spathula*)胸鳍发育过程中，也未发现鳍芽中存在*Gli3-Hand2*的相互抑制[74].

综上所述，在鱼类向陆生动物进化过程中，很多基因是保守的，鱼鳍发育的必需基因如*Fgf*, *Hox*, *Tbx*等也是四足动物肢发育所必需的，就已有的知识来说，基因序列变异、表达模式变化、基因间相互作用甚至部分基因丢失在鳍向肢的演化中起到了关键作用(图1).

4　鳍的两性异形

从不同物种的进化关系来看，鳍伴随着低等无颌类向高等有颌类的进化经历了类鳍结构、奇鳍、偶鳍、肢的演化过程. 在大自然“神奇的魔法”下还演化出了形态多样、色彩丰富的外在特征，有一些鱼类在长期的进化长河中拥有特别的功能，如飞鱼的胸鳍发达如翼，可借助其在空中滑行一段时间；躄鱼也称“跛脚鱼”，底栖鱼类，可借助胸鳍和腹鳍行走；银汉鱼科的一些鱼类如鳉等用臀鳍来输送精子，从而进行生殖；长尾鲨则会用尾鳍进行狩猎等，一般认为是特殊环境造就的适应性进化的结果. 更甚的是，在诸多物种中，同一物种还表现有明显的两性异形(sexual dimorphism)(表1)[97,98].

鳍两性异形的产生可以从选择和个体发生两个角度去理解. 在选择的角度上，目前已经有很多假说被提出来解释鳍的两性异形现象. 性感子孙假说(sexy son hypothesis)[99]认为，选择拥有更长更大鳍的雄性可以将雄性的这些基因遗传给后代，为后代提供更高的繁殖成功率. 性选择的障碍理论(handicap theory)[100]认为，雄性个体所具有的能吸引异性的性征的获得往往伴随着巨大“代价”付出，而这种“代价”是那些缺少某种特质的个体所无法“负担”的，雌性选择这类雄性或许可以获得直接或间接的利益. 这个理论在绿剑尾(*Xiphophorus helleri*)中已

被研究[101]. 负频率依赖选择(negative frequency-dependent selection, NFDS)认为群体中一种表型越是稀少, 相应的表型适合度(fitness of phenotype)也就越高[102], 这是平衡选择(balancing selection)所造成的一种结果[103,104]. Hughes等人[105]通过研究不同色彩雄性孔雀鱼的繁殖适度(reproductive fitness)发现, NFDS是通过两种选择媒介即交配和捕食者来维持孔雀鱼色彩的多样性. Stephanie等人[79], Morgans等人[106]和Leinonen等人[107]的研究表明, 在鳍上性特征的表达(如鳍的颜色、大小)或许是由异性的择偶选择所衡量的, 即性选择影响了生殖特征的量级. 同时在不同群体间捕食压力下, 这种性特征需要在性选择强度和自然选择之间做出“权衡”, 最终表现出一定的“度”.

从个体发生角度而言, 鳍两性异形是由多基因造成的, 受控于不同的数量性状位点(quantitative trait loci, QTL)[108,109]. 目前发现, 性别偏向基因(sex-biased genes)以及受其影响的与生长、性别分化相关基因在两性之间不同的表达水平, 或许最终造成了两性特异的性征[83,110~118]. 对青鳉鱼雄性臀鳍鳍条上乳突状结构发育机制的研究发现, 雄性激素扮演了关键角色[119]. 调节细胞增殖以及骨沉积的*Bmp7*和*Lef1*被雄性激素激活, 最终导致臀鳍乳突状结构形成[120]. 对吉富罗非鱼(*Oreochromis niloticus*)的研究发现, *cyp19a1a*, *foxl2*, *cyp11b2*, *dmrt1*是雌雄性别分化的关键基因[121,122], 这些基因有可能通过影响性腺的形成造成雌雄外在性征的差异. Sharma等人[123]通过研究孔雀鱼性别偏向基因在雌雄个体不同组织表达的转录组数据, 鉴定出了29个在孔雀鱼的尾部偏雄表达且具有编码色素合成功能的蛋白质的基因. Kawajiri等人[124]和Solis等人[125]发现, 青鳉雄性臀鳍长度的变异是多基因的, 被不同的QTL控制, 由性激素介导调节. 对造成三刺棘鱼(*Gasterosteus aculeatus*)包括鳍在内的两性异形的遗传基础研究发现, 雌雄之间在遗传结构上是基本相似的, 对性别异形进化的遗传约束力(genetic constraints)并非像通常认为的那样严重和绝对[76,110,111], 并且与体型适应性改变相关的任何QTL都是在性别决定染色体区域有最大的效应值[108]. 将食蚊鱼的雌性用雄性激素处理, 发现雌性原本圆形的臀鳍演变出了在雄性才有的生殖足结构, 并且与臀鳍生长相关的*shh*, *msxC*, *fgfr1*的表达发生了明显改变, 说明性激素直接造成了雌雄之间臀鳍两性异形现象的发生[126].

5 肢的发育和形态演化

鉴于其发育模式的复杂性、可视性和可操控性, 肢体一直是发育生物学和进化学中的良好模型. 肢发育中的AER组织中心, 极化区(the zone of polarizing activity, ZPA)和趾间细胞凋亡结构域(the domains of interdigital cell death)的变化决定了肢体的形态[127], 如偶蹄动物和澳大利亚蜥蜴趾的丢失与ZPA的改变有关[128~130]; 海豚后肢的缺失与AER的退化有关[131]; 鸭脚蹼和蝙蝠的翅膀则是趾间细胞凋亡发生变化的结果. 肢起源于LPM, 主要沿着3个轴向发育: 由AER组织中心操控的近远端轴向(the proximal-distal axis, P-D轴), 驱使肢从肩膀到手指的发育, AER组织中心保持潜在增殖状态, 与肢体的长度有

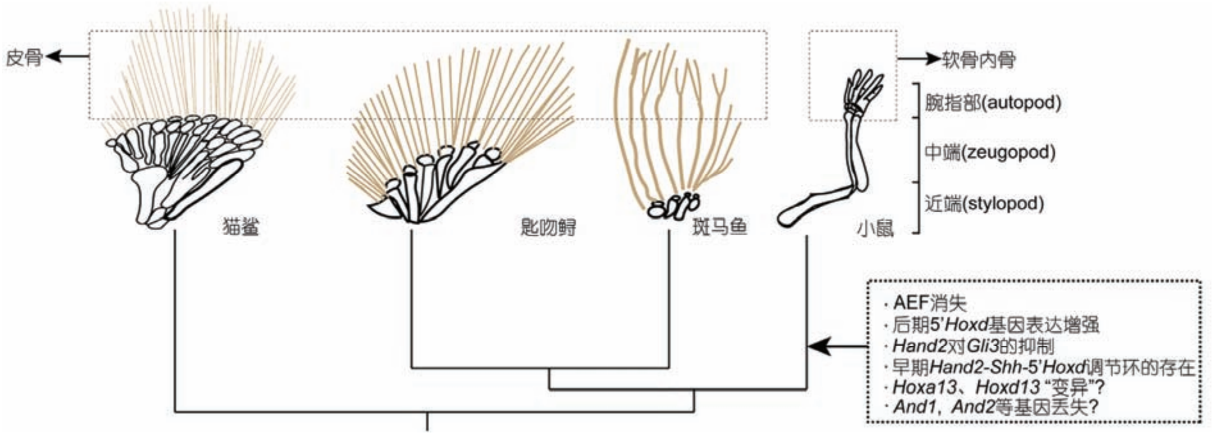

图 1 鳍、鳍肢类似结构和肢的演化关系及其机制[37,38,40,42~51,58,70~74]

Figure 1 Evolutionary relationship and mechanism of fins and limbs[37,38,40,42–51,58,70–74]

表 1　已报道的鳍具有两性异形的鱼类

Table 1　The reported fish species with sexual dimorphism in fins

物种	两性异形	作用	参考文献
孔雀鱼 (*Poecilia reticulate*)	雄性有长臀鳍和尾鳍	影响雌性择偶选择，长臀鳍和尾鳍的雄性具有更多交配机会，两者的改变均是为了适应不断变化的生存环境	[75]
剑尾鱼 (*Xiphophorus helleri*)	雄性臀鳍拥有一个色彩艳丽细长似剑的结构，并特化为生殖足	雌性偏向具有长臀鳍的雄性，且更愿意与之交配	[76]
红大马哈鱼 (*Oncorhynchus nerka*)	雌性的臀鳍会发生额外的发育事件，使得晚期的臀鳍明显大于早期的臀鳍	选择压力使得此次雌性具有繁殖优势	[77]
单鲷类 (*Haplochromines cichlids*)	雄性臀鳍或腹鳍具有像卵一样的彩色斑点即“卵斑”	吸引口含卵子的雌性并完成受精，卵斑的多少决定雌性的偏爱程度	[78]
斑马鱼(*Danio rerio*)	雄性胸鳍会产生表皮角质化结构	刺激卵子排放	[79]
青鳉(*Oryzias latipes*)	雄性臀鳍鳍条上有乳突状结构	吸引雌性，第二性征的特点，生殖多样性	[80]
食蚊鱼(*Gambusia affinis*)	受到雄激素刺激的雄性，臀鳍会延长变成生殖足，正常的雌性有着圆形臀鳍	生殖足可进行体内受精	[81]
带纹矛耙丽鱼 (*Pelvicachromis taeniatus*)	雌性腹鳍异速生长	雄性偏好具有较大腹鳍的雌性	[82]
犹他骨尾鱼(*Gila atraria*)	雄性腹鳍长于雌性	性别分化的副产物	[83]
滇西低线鱲 (*Barilius barna*)	在繁殖季节，雄性的腹鳍有发达的肌肉且腹鳍明显变大	交配	[84]
多幅吉鳉 (*Girardinichthys multiradiatus*)	雄性的背鳍较雌性大	具有较大鳍的雄性更受雌性偏爱且更容易捕食	[85]
大西洋鳕鱼(*Gadus morhu* L.)	雄性的腹鳍远大于雌性的腹鳍	雄性腹鳍会捉住雌性并刺激她排卵，具有较大腹鳍则会使得雄性保持好的身体机能	[86]
鲱形白鲑 (*Coregonus clupeaformis*)	雄性有较大胸鳍和腹鳍	雄性在同性中更具有竞争力，具有更多得到雌性卵的机会	[87]
扁鲨属(*Squatina guggenheim*)	只有成年雄性具有胸鳍	交配	[88]
玛丽鱼(*Poecilia latipinna*)	雄性具有较大的背鳍	雌性的择偶偏向	[89]
肋鳞鱼(*Peltopleurus nuptialis*)	雄性臀鳍变化为生殖足	受精，方便卵运输	[90]
秀美似鳞头鳅 (*Lepidocephalichthys alkaia*)	成熟雄性的胸鳍中两鳍条融合形成凸缘	繁殖	[91]
小点猫鲨(*Scyliorhinus canicula*)	雌性胸鳍表皮变得粗糙形成小齿	交配时便于雄性抓住雌性胸鳍	[92]
长吻雀鳝(*Lepisosteus osseus*)	雄性的臀鳍长于雌性	受精时雄性的长尾鳍不断摆动增加受精率	[93]
莫桑比克罗非鱼 (*Oreochromis mossambicus*)	雄性具有大臀鳍和背鳍	雄性之间竞争繁殖机会，臀鳍和背鳍越大越容易得到繁殖机会	[94]
饰翅多鳍鱼 (*Polypterus ornatipinnis)*	雄性的臀鳍和修饰过的尾鳍	刺激卵排放、收集卵并且臀鳍搅动卵进行受精	[95]
宝石鳊鱼 (*Paedocypris progenetica*)	雄性腹鳍有过度肥厚的肌肉、腹鳍前端角质化	繁殖	[96]

关，主要受Fgf信号通路调控；由ZPA信号中心操控的前后轴向(the anterior-posterior axis, A-P轴)，驱使五指的发育，受Shh信号通路控制；位于OE的背腹轴向(the dorsal-ventral axis, D-V轴)驱使从手背到手掌的发育，受Wnt信号通路调控.

自然界中不同物种的肢体千变万化，如鸟类和蝙蝠中前肢演化成了翅膀；袋鼠的前肢短小灵活适合抓取，后肢强劲适合奔跑；鸭嘴兽四肢短，五趾具钩爪，趾间有蹼；指猴四肢短，腿比臂长，指和趾长(中指特长)；人类上肢和腿截然不同等，但其进化机制和发育过程中的信号通路却非常保守，其多样性的差异主要存在于基因序列及其调控元件小的变化[127,132]．肢体早期发育与*TBX*基因家族的*Tbx4*和*Tbx5*不无关系[133~135]，收到来源于不同位置的*HOX*

基因家族的信号诱导后，*Tbx4*和*Tbx5*所在信号通路分别激活*Fgf10*，*Fgf10*和外胚层中的*Fgf8*相互作用促使肢芽发育成了后肢和前肢，其中*Tbx5*可直接受*HOX*基因家族的信号诱导表达，*Tbx4*的表达是由*HOX*基因家族的信号诱导的*Pitx1*激发的. 前面提到，这些基因同样在鱼类中也有相应的功能，如在斑马鱼中将*Tbx5*敲除会产生没有胸鳍的畸形[136]，将*Tbx4*突变掉则会导致腹鳍缺失[137].

四足动物肢的多样性的形态演化被认为是肢体发育的“升级版”，是长期进化过程中关键基因及其调控序列突变导致的[127,132]，如最新研究结果表明，激活细胞里SHH表达的ZRS增强子在脊椎动物中是高度保守的，蛇的*Zrs*序列在长期进化过程中发生变异(丢失了17个碱基对)甚至丢失，造成*Zrs*失活，不能激活*Shh*表达，并最终导致蛇没有四肢，Kvon等人[138]运用了CRISPR-Cas9技术将蛇的*Zrs*转入小鼠的受精卵内，得到了没有四肢的小鼠，结果表明*Shh*基因及其调控元件的变异在肢体演化过程具有重要作用. *Ptch1*及其调控元件在脊椎动物趾(指)的演化中起决定性作用，相较于小鼠等五趾动物，偶蹄动物如牛、猪等趾头的缺失和*Ptch1*及其调控元件有关[139].

6 展望

鳍到肢的转变是脊椎动物进化史中形态上的重要创新之一，这种转变反映了进化与基因表达时空变化的相关性. 综合过去近20年的研究，造成这种转变的分子机制可归纳为以下两个方面: （ⅰ）A-P轴上*Gli3-Shh*信号通路的存在以及Shh表达时序的改变扩大了肢芽后端的区域，抑制了前端骨骼元件的形成，最终演化为四足动物前肢单一的近端基骨. （ⅱ）P-D轴上*Hox*基因家族转录调节元件的改变导致了*Hox*基因在表达强度以及时空的变化，这种变化伴随着AEF的缩短以及远端外骨骼的形成，最终形成了四足动物肢的远端或腕指部(autopod).

在自然选择和性选择的双重作用下，鳍演变出了色彩绮丽、形态多样的两性异形现象，肢演化出了各种各样的形态. 现有的证据表明，基因及其调控序列在雌雄个体鳍两性异形的发生和四肢的多样性形态演化中扮演了重要角色. 尽管这些发育和演化过程不甚明了，但伴随着大规模全基因组时代的到来，越来越多的关键基因、关键基因上下游基因及它们的调控序列得到克隆、鉴定和生物学上的功能验证，相信最终完整的调控网络机制会得到解析.

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Summary for “鳍与四肢如何发育和演化?”

How do fins and limbs develop and evolve?

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How do fish fins come into being and how do fins evolve into terrestrial tetrapod limbs? To answer this scientific question is substantially to understand how the genes that determine these traits are subject to natural and sexual selection, and how they thereby involve the innovation mechanics and evolution mechanisms with respect to development. Increasing evidence in recent 10 years suggests that fins might be as single fin-fold in early jawless fish, and then get makeable changes on the evolution roads from jawless fish to jaw fish and tetrapods, in which sequence divergence, expression pattern change, cooperative interaction, and even deletion of some required genes for fin development might play critical roles.

The origin of fish fins and tetrapod limbs has been debated for more than three centuries from early natural philosophers and anatomists to modern developmental geneticists. In the recent 10 years, extensive and valuable data have been revealed from a lot of studies on paleontology, comparative anatomy and developmental genetics, and these complementary results have made us to understand the origin and underlying mechanisms behind the formation of the fish fin and tetrapod limb skeletons. It has been certified that fish has evolved to tetrapods and the multiple-basal bones of ancestral fish fins have been reduced to evolve into a single bone of tetrapod limb with fossil records. Similarly, during early embryogenesis, fish fins and tetrapod limbs share similar development mechanism, even though significant differences in histological, developmental and structural patterns exist between them. Many functional genes, such as *Hox*, *And*, *Gli3*, *Hand2*, play key roles in this transition or transformation.

Natural selection and sex selection have led to sexual dimorphism of fish fins and morphological differences of tetrapod limbs. Along with the rapid development of genomics, genome editing and biotechnological manipulation techniques, the genetic basis of sexual dimorphism has been explored. Some gene families and signal pathways, such as *Tbx* gene family, *Hox* gene family, *Ptch1* and its regulation elements, have been identified to involve in the morphological evolution. Significantly, it has been demonstrated that the differential expression of some sex-biased genes and its affected genes which are related with growth and gender differentiation may ultimately lead to sexual dimorphism of the fins.

In this article, we have reviewed origin, evolutionary history and development patterns of fins, and elaborated molecule mechanisms on fin-to-limb evolution, sexual dimorphism of fish fins and morphological evolution of limbs. It is expected that a new era is coming for studies on developmental mechanisms and genetic basis of fin origin and fin-to-limb evolution, and some novel sights will be further provided.

fins, limbs, evolution, sexual dimorphism, sex-bias genes

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