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·综述·

鱼类疱疹病毒研究进展概述

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摘要：疱疹病毒是双链 DNA 病毒家族成员之一，具有高度的传染性，严重危及人类及动物的健康；其中异疱疹病毒科各成员是引起水生动物病害的主要病原，严重制约全球水产养殖业的健康发展，尤其对我国鱼类养殖产业影响巨大。本文简要概述鱼类疱疹病毒研究发展历程、现状及进展，主要包括鲤疱疹病毒、鮰疱疹病毒、鲑疱疹病毒及其他鱼类疱疹病毒等，以期增强我们对鱼类疱疹病毒研究发展的系统性认知。

关键词: 水生动物；鱼类；病毒病；疱疹病毒

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渔业和水产养殖业为全世界提供了丰富的动物蛋白来源。改革开放四十多年来，中国渔业和水产养殖业快速发展，在世界粮食安全、社会经济发展等领域做出了重要贡献。但仍面临着病毒、细菌和寄生虫等病原生物感染的持续威胁。其中由病毒引起的水产动物疾病，因其发病快、危害大、死亡率高，且尚缺有效的药物治疗措施等特点，被认为是制约水产养殖业可持续发展的重要因素之一[1-2]。

疱疹病毒 (herpesvirus) 是双链 DNA 病毒，完整病毒颗粒由核心、衣壳、被膜及囊膜组成；基因组兼具多样性及结构差异化等特点。依据基因组分析可分为三大类：哺乳类禽类疱疹病毒科 (*Herpesviridae*)、贝类疱疹病毒科 (*Malacoherpesviridae*) 和异疱疹病毒科 (*Alloherpesviridae*)[3]。其中异疱疹病毒科病毒引起的水生动物病害严重制约全球养殖业的发展，尤其对我国鱼类养殖产业影响巨大。根据国际病毒分类委员会 (International Committee on Taxonomy of Viruses, ICTV) 2020 年分类报告 (https://talk.ictvonline.org/taxonomy/)，异疱疹病毒科进一步分为 4 属 13 种，其中 3 属 11 种为鱼类疱疹病毒 (表 1)，各病毒株进化关系详见综述文章[4]。本文内容主要聚焦于鱼类疱疹病毒研究现状及进展，包括鲤疱疹病毒 (*Cyprinid herpesvirus,* CyHV)、鮰疱疹病毒 (*Ictalurid herpesvirus,* IcHV)、鲑疱疹病毒 (*Salmonid herpesvirus,* SalHV) 及其他鱼类疱疹病毒等 (表 1)，简要探讨相关基础研究及防控技术开发的发展趋势。

1　鱼类疱疹病毒分述

1.1　鲤疱疹病毒

鲤疱疹病毒属于异疱疹病毒科鲤疱疹病毒属 (*Cyprinivirus*)。鲤疱疹病毒一般分为鲤疱疹病毒 I 型 (CyHV-1)、鲤疱疹病毒 II 型 (CyHV-2) 和鲤疱疹病毒Ⅲ型 (CyHV-3，亦称为 Koi herpesvirus, KHV)[5]。其基因组为 dsDNA，病毒粒子为正二十面体 (核衣壳 T=16 对称)，有囊膜和外膜包被 (图版)。

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这三类病毒具有一定的宿主选择性，可分别感染鲤、锦鲤、银鲫及金鱼等鱼类，具有温度敏感性；疫病表现出季节流行性特征，且呈现全球分布[6-7]。另外，我国学者分离出一株鲫疱疹病毒，该病毒与鲤疱疹病毒属成员具有较近的亲缘关系[8]。目前针对鲤疱疹病毒研究主要聚焦于新病毒株分离及基因组解析、检测方法建立、免疫学效应及病毒致病机制等方面。

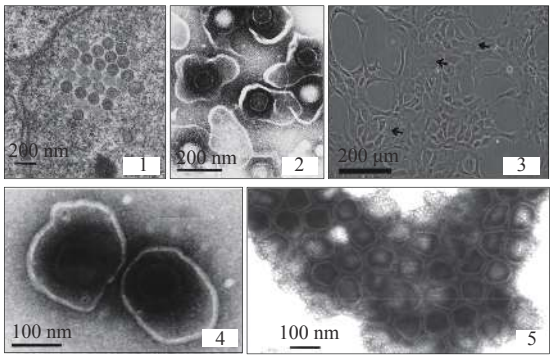
鲤疱疹病毒 I 型 (CyHV-1)　CyHV-1 最早由日本学者在 20 世纪 80 年代从鲤体表瘤状组织中分离鉴定，该病毒可感染鲤科鱼类的幼鱼，诱发鱼体体表瘤状物的产生[9-10]，该病危害较小，致死率低，主要影响鱼体外观；此后在全球范围内陆续报道[11-14]，我国于 1990 年利用电镜技术报道相关病症[14]。CyHV-1 可感染多种鱼类细胞，如锦鲤鳍细胞 (KF-1)、鲤上皮瘤细胞 (EPC)、胖头鳐肌肉细胞 (FHM) 和斑马鱼细胞 (ZF4) 等[15-16]；其感染细胞及鱼体具有温度敏感性特征，最适复制温度 10 ~ 25 °C，超过 30 °C 不能够有效感染[15]。利用原位杂交检测鲤组织中病毒基因组 DNA 初步发现 CyHV-1 存在潜伏感染现象[17]，该病毒感染可通过表型观察及核酸检测方法进行诊断。2013

表 1　鱼类疱疹病毒

Tab. 1　Fish herpesviruses that impact aquaculture and wild fisheries

属 genera	种或株 species or isolates	主要宿主 main host	基因组** genome**	参考文献 references
鲤疱疹病毒属 *Cyprinivirus*	鲤疱疹病毒Ⅰ型 *C. herpesvirus* 1, CyHV-1	鲤 *Cyprinus carpio*	JQ815363 (Isolate NG-J1)	[18]
	鲤疱疹病毒Ⅱ型 *C. herpesvirus* 2, CyHV-2	金鱼和鲫 *Carassius auratus* (goldfish / crucian carp)	JQ815364 (Isolate ST-J1)	[18]
	鲤疱疹病毒Ⅲ型 *C. herpesvirus* 3, CyHV-3 or KHV	(锦)鲤 *C. carpio* (koi carp/common carp)	DQ657948.1 (Isolate KHV-U)	[18]
	鲫疱疹病毒 *Carassius auratus* herpesvirus，CaHV	鲫 *C. auratus*	KU199244	[8]
	鳗鲡疱疹病毒 *Anguillid herpesvirus* 1, AngHV-1	日本鳗鲡和欧洲鳗鲡 *Anguilla japonica*, *A. anguilla*	FJ940765.3 (Isolate CVI500138)	[19]
鮰疱疹病毒属 *Ictalurivirus*	鮰疱疹病毒Ⅰ型 *I. herpesvirus* 1, IcHV-1 or CCV	斑点叉尾鮰 *Ictalurus punctatus*	M75136.1 (Isolate Auburn 1)	[20]
	鮰疱疹病毒Ⅱ型 *I. herpesvirus* 2, IcHV-2	黑鮰 *Ameiurus melas*	MG271984 (Isolate 760/94)	[21]
	鲟鱼疱疹病毒II型 *Acipenserid herpesvirus* 2, AciHV-2	高首鲟 *Acipenser transmontanus*	FJ815289 (Isolate SRWSHV)	[22]
鲑疱疹病毒属 *Salmonivirus*	鲑疱疹病毒Ⅰ型 *S. herpesvirus* 1, SalHV-1	虹鳟 *Oncorhynchus mykiss*	AF023673 (Partial genome)	[23]
	鲑疱疹病毒II型 *S. herpesvirus* 2, SalHV-2	大马哈鱼 *Oncorhynchus* spp.	EU349275 (DNA polymerase)	[4]
	鲑疱疹病毒Ⅲ型 *S. herpesvirus* 3, SalHV-3	突吻红点鲑 *Salvelinus namaycush*	NC043468 (DNA polymerase)	[4]
暂未分类疱疹病毒 unclassified herpesvirus of fish	鲟鱼疱疹病毒Ⅰ型 *A. herpesvirus* 1, AciHV-1	高首鲟 *A. transmontanus*	EF685903.1 (DNA polymerase)	[24]
	鲑疱疹病毒Ⅳ型 *S. herpesvirus* 4, SalHV-4	大西洋鲑 *Salmo salar*	JX886029 (DNA polymerase)	[25]
	鲑疱疹病毒Ⅴ型 *S. herpesvirus* 5, SalHV-5	突吻红点鲑 *S. namaycush*	KP686090 (DNA polymerase)	[26]
	罗非鱼幼鱼脑炎病毒 Tilapia larvae encephalitis virus, TLEV	尼罗罗非鱼 *Oreochromis niloticus*	AY178582 (DNA polymerase)	[27]
	鳕鱼疱疹病毒 Gadid herpesvirus 1, GaHV-1	大西洋鳕鱼 *Gadus morhua*	HQ857783.1 (DNA polymerase)	[28]
	沙丁鱼疱疹病毒 Pilchard herpesvirus，PHV	澳大利亚沙丁鱼 *Sardinops sagax*	AY995177.1 (Terminase gene)	[29]

注：** 鱼类疱疹病毒全基因组或部分基因组 (DNA聚合酶基因或末端酶基因) GenBank登录号
Notes：**The GenBank accession numbers of complete or partial genomes (DNA polymerase gene or terminase gene) of fish herpesviruses



图版　代表性鱼类疱疹病毒粒子及其细胞感染

1. 鲤疱疹病毒 CyHV-3 胞内透射电镜观察[30]；2. CyHV-3 病毒粒子形态特征[30]；3. CyHV-3感染 CCB 细胞[7]；4. IcHV-1 病毒粒子形态特征 (Invasive Species Compendium, N. Fijan)；5. SalHV-3 病毒粒子形态[31]

Plate　Fish herpesvirus particles and the infection in fish cell lines

1. Intracellular observation of CyHV-3 particles by transmission electron microscope, TEM[30]; 2. negative stain of purified CyHV-3 virions[30]; 3. cytopathic effects on CCB cells inoculated with high viral titer of CyHV-3; vacuolated cells indicated by arrows[7]; 4. negatively stained virions of IcHV-1 (Invasive Species Compendium, N. Fijan); 5. negatively stained virions of SalHV-3[31]

年 CyHV-1 基因组完全解析 (NG-J1 分离株)，基因注释相对完全；与 CyHV-2 和 CyHV-3 相比，特殊的是 CyHV-1 编码一个 *JunB* 同源基因，该基因在哺乳动物中是与肿瘤发生密切相关的一个转录调控因子，暗示该基因与 CyHV-1 感染症状相关[18]。目前针对 CyHV-1 感染机制研究较少，多见于与其他疱疹病毒的比较研究[8, 18]；国内流行性调查数据尚缺，仅有少量感染案例报道。

鲤疱疹病毒 II 型 (CyHV-2)　CyHV-2 是引起金鱼和鲫造血器官坏死病的重要病原，该病毒于 1992 年在日本发现后经确认有别于 CyHV-1 分离株，感染症状呈现复杂性特征[32-33]；易感温度 15 ~ 25 °C；在多种鱼类细胞系传代存在弱化现象，通常少于 4 代[33]；近年来，国内外学者建立了 CyHV-2 易感细胞系，如鲫脑细胞系和鳍细胞系等[34-38]。该病毒存在急性感染致病及潜伏感染存活的现象，潜伏感染在应激条件下可再度活化感染[39-40]，这可能与病毒极早期基因及宿主因子有关。国内外 CyHV-2 不同分离株 (ST-J1 和 SY-C1 株) 先后完成全基因测序，二者有高度同源性，属于不同基因亚型[18, 41]。针对 CyHV-2 病原相继开发了多种核酸及免疫学等检测方法[42-46]，但聚合酶链式反应 (polymerase chain reaction，PCR) 及其衍生技术仍然是该病原核酸检测的普适方法。

近年来，应用多组学分析 (转录组、蛋白组等) 促使针对 CyHV-2 病原学研究及与宿主相互关系研究快速发展。在基因组同源分析注释基础上，病毒粒子质谱分析已确认多种病毒结构蛋白 (衣壳、膜蛋白等)，其中包括病毒粒子免疫原性蛋白[47] 为该病毒疫苗开发奠定了重要基础。转录组系统阐明了 CyHV-2 病毒各基因的表达时序[48]，鉴定病毒编码的 micRNA [49] 以及病毒与细胞之间的相互关系，后者主要包括宿主基因及 micRNA 免疫响应等[50-54]；这些研究为进一步了解 CyHV-2 病毒感染宿主策略及宿主抗病毒机制奠定了良好基础。另外，除了通过同源注释的 CyHV-2 病毒功能基因外，该病毒少数基因功能也得到不同程度的分析研究，如病毒 ORF4 基因编码蛋白与肿瘤坏死因子受体具有低同源性，具有促进细胞增殖、抑制细胞凋亡的功能 [55]；ORF104(蛋白激酶同源物) 活化 p38 信号通路等 [56]，诸如此类的基础研究对于明晰 CyHV-2 病毒感染机制具有重要意义。目前，CyHV-2 感染导致的造血器官坏死病严重制约我国鲫养殖业发展，针对该类病害尚无有效的防治方法，我国科研工作者正在尝试开发亚单位和核酸疫苗以及利用中草药提取物来防控该类疫病[57-59]。

鲤疱疹病毒 III 型 (CyHV-3)　20 世纪 90 年代末，首次在德国发现 KHV(CyHV-3) 导致锦鲤大规模死亡，随后在全球范围内暴发，主要包括亚洲、欧洲、美洲等地区；该病毒导致鱼体活力下降、烂鳃、鳃出血、体黑伴有白点和两眼凹陷等临床症状[30, 60]。国内外针对 CyHV-3 引起的疫病已开发出多种病原检测方法；另外，CyHV-3 的检测可参考我国相关标准 (SC/T 7212—2011) 及世界动物卫生组织 (OIE) 疫病名录 (OIE，2019)。

由 CyHV-3 引起的疫病在鲤科鱼类中呈现高暴发、高致死性及影响范围广等特征，因此受到国内外学者的广泛关注；在共同努力下，CyHV-3 逐渐成为研究最为系统和完善的鱼类疱疹病毒之一[61-62]，主要表现在几个方面：①病毒基因组注释完善较早 (早于 CyHV-1 和 CyHV-2，2013年)，2007 年完成 3 株基因组测序 (分别分离自日本、美国、以色列)，参考其他疱疹病毒初步完成基因组注释[60]，应用于 CyHV-1 和 CyHV-2(2013 年) 等鱼类疱疹病毒的基因组比较研究[18]；② CyHV-3 病毒感染机制研究相对全面，包括基因表达特性、病毒结构蛋白解析[63-64]、病毒潜伏感染机制[65-69]、

病毒入侵机制[70-72]、部分编码蛋白功能[73-80]以及病毒基因组复制及转录等[81-83]；③ 可行的重组CyHV-3 病毒技术，2008 年通过大 DNA片段克隆及原核重组技术获得突变病毒[84]，为研究病毒编码蛋白的功能 (病毒感染机制) 以及弱毒株疫苗开发等奠定了重要基础[85-87]。关于 CyHV-3病毒研究的其他方面内容，包括病毒粒子理化性质、感染特性及疫病流行性情况以及防控技术开发等参见以往综述文章[88-89]。

鲫疱疹病毒 (CaHV)　　中国学者于 2016 年报道 CaHV 感染导致鲫急性鳃出血病，发病鱼具有高死亡率的特点，该病毒是新现 (emergence) 鱼类疱疹病毒强毒株。CaHV 与鲤疱疹病毒属成员进化关系最近，基因组大小及排列结构与 CyHV-1、CyHV-2 和 CyHV-3 存在显著差异[8]。目前 CaHV 编码蛋白功能研究已取得重要进展，CaHV 基因组中发现 5 个环指蛋白表现出结构及功能的多样性，暗示其行使多重功能[90]；两次跨膜蛋白 138 L 靶向 FoF1-ATPase 可能与调控线粒体 ATP 合成有关[91]；还发现病毒 GPCR 蛋白具有多重跨膜结构域，其功能可能与宿主细胞信号转导有关[92-93]等；这些工作为研究鱼类疱疹病毒编码蛋白的功能开拓了重要方向。目前针对 CaHV 的防控研究还处于发展阶段，主要涉及抗 CaHV 宿主免疫学研究和抗 CaHV 感染鲫种系筛选等[54, 94]。此外，值得一提的是梭状芽孢杆菌 (*Clostridium bolteae*) 作为一种益生菌能够有效抑制 CaHV 的感染[95]，为防控鲫急性鳃出血病提供了一种可行性方案[96]。

1.2　鮰疱疹病毒

鮰疱疹病毒Ⅰ型 (IcHV-1；又名 channel catfish virus，CCV) 和鮰疱疹病毒Ⅱ型 (IcHV-2；又名 black bullhead virus) 是鮰疱疹病毒属的重要成员，鮰是其主要的天然宿主；基于部分基因组片段分析，IcHV-2 与 IcHV-1 亲缘关系较近[93]。针对 IcHV-1 的生物学研究较早，是鮰疱疹病毒属的模式毒株，IcHV-1 病原检测及防控技术研究为其他鱼类疱疹病毒研究奠定初步基础，本部分详细概述相关内容。

鮰疱疹病毒Ⅰ型 (IcHV-1)　　IcHV-1 是由 Fijan 等[97] 于 1968 年首次从美国患病斑点叉尾鮰幼鱼中分离，该病毒是第一个报道感染鱼类的疱疹病毒，也是鮰疱疹病毒属的典型代表种[98]。IcHV-1 对鱼卵、鱼苗、鱼种等各时期鮰均有危害，而幼鱼较成鱼更易受到感染导致暴发性死亡。IcHV-1 感染可以通过水平或垂直的方式进行传播，同样表现出温度依赖性和潜伏感染的特性。患病鮰在初期表现为摄食性和活力下降、腹部肿胀、鳍条基部和皮下充血，可引起肾脏造血组织和肾管的炎症和坏死等。Wolf 等[98] 利用电镜技术首次观察了棕鮰细胞 (BB) 中感染的 CCV 粒子，研究了病毒粒子的生物学和形态学特征；Booy 等[99]利用冷冻电镜技术和三维图像重建技术分析发现 CCV 病毒粒子衣壳结构与人类单纯疱疹病毒相似。IcHV-1 是直径 175 ~ 200 nm 的二十面体，是一种较大的线性、双链 DNA 病毒，核衣壳由 162 个衣壳粒组成，直径为 100 nm，囊膜包被(图版)，基因组大小约 134 kb，由一个特异性区域和两侧各一个正向重复序列组成，内含 79 个开放阅读框和 76 个编码基因[20, 98]，通过对病毒编码蛋白质的氨基酸序列的分析，一些 ORFs 可能编码与 DNA 有关的酶类，如解旋酶、DNA 聚合酶、胸苷激酶等。Davison 等[100]对纯化的 IcHV-1 病毒粒子进行蛋白质组分析，鉴定了 11 种结构蛋白，如囊膜蛋白 ORF59；衣壳蛋白 ORF27、ORF28、ORF39 和 ORF53；Kunec 等[101] 利用高通量质谱法鉴定了 37 种预测的病毒编码的蛋白，此类研究奠定了鱼类疱疹病毒基因组实验性注释的基础。此外，国外学者借鉴哺乳动物疱疹病毒重组及大 DNA 克隆技术，建立 IcHV-1 病毒重组技术，并应用于病毒编码蛋白功能研究及疫苗开发研究[102-103]。

鮰疱疹病毒病的初步诊断依赖于病鱼的临床症状，最后确诊需要进行病毒分离、免疫学检测、核酸检测等。细胞培养分离技术是最准确的诊断方法；BB 细胞和斑点叉尾鮰卵巢细胞 (CCO) 是常用的检测 CCV 的敏感细胞系，病毒感染能够产生典型的合胞体和核内包涵体。斑点叉尾鮰巨噬细胞、B 淋巴细胞和 T 淋巴细胞也对 IcHV-1 敏感[104]；除了上述敏感细胞系外，研究还发现 CCV 对大鳞大马哈鱼胚胎细胞 (CHSE-214)、草鱼鳍条细胞系 (GCF) 和 EPC 等淡水鱼类细胞系均可以感染，但细胞病变出现时间、病变程度和增殖滴度各有差异，其中 GCF 和 EPC 对 IcHV-1 高敏感[105]。免疫学检测主要通过酶联免疫、间接荧光抗体实验等方法进行抗原抗体反应检测，该类方法应用于 IcHV-1病原检测。采用血清中和实验用于自然和人工感染状态下 IcHV-1 的诊断[106]，以及采用间接荧光抗体染色技术在无症状成鱼卵巢组织中检测 IcHV-1 粒子，提示潜伏病毒可能存在重新激活的风险[107]；在病毒单克隆抗体方面的研究为

IcHV-1 的鉴定、检测和定量研究提供了更好的可能性[108-110]。基于 PCR 的核酸技术是较为精确的检测 IcHV-1 的重要方法；包括普通 PCR 技术、巢式 PCR检测方法、*Taq*Man Real-Time PCR 检测方法、环介导等温扩增技术 (Loop-mediated isothermal amplification, LAMP)、焦磷酸测序检测方法等[111-117]，该类方法检测在保证特异性的基础上兼具较高灵敏度，为 IcHV-1 病毒快速、准确和定量检测提供了重要参考。

疫苗免疫接种是防控 IcHV-1 病毒病的重要手段，目前国外关于 IcHV-1 疫苗的研究主要有几种类型：①弱毒疫苗和灭活疫苗。胡子鲇细胞培养物制备 IcHV-1(V60 株) 弱毒疫苗[118]、胸苷激酶突变的 IcHV-1 弱毒疫苗[119]，均具有较好的免疫保护效果。②亚单位疫苗。利用 CCV 的囊膜部分制备的亚单位疫苗浸泡免疫斑点叉尾鮰鱼卵和幼苗后，免疫保护率超过 80%[120]。③病毒 DNA 疫苗。Nusbaum 等[121] 从 CCV 病毒 ORFs 中筛选了 7 个 DNA 疫苗候选基因，注射免疫 4 ~ 8 cm 的斑点叉尾鮰后，结果显示 ORF59 和 ORF6 的 DNA 疫苗相对保护率较好，最高可达 74%。IcHV-1 防控技术开发为其他鱼类疱疹病毒研究提供了必要参考。

鮰疱疹病毒 Ⅱ 型 (IcHV 2)　IcHV-2 是由 Alborali 等[122] 在意大利养殖的黑鮰中首次被分离，是引起鮰病毒性疾病的重要病原，感染的临床症状及病理现象与 IcHV-1 相似；同时 IcHV-2 基因组序列及结构与 IcHV-1 有较高同源性，其部分基因序列与 IcHV-1 或 AciHV-2 相似度可达 25% ~ 83%；然而 IcHV-2 感染的宿主细胞范围与 IcHV-1 存在差异[21, 122]。以上 2 株鮰疱疹病毒相似特征导致两类病毒病诊断区分有一定困难，鉴于此，国外学者建立了 IcHV-2 特异性的核酸检测方法[123]。最新报道在双须缺鳍鲇 (*Kryptopterus bicirrhis*) 中分离获得一株疱疹病毒 (Silurid herpesvirus 1)，其部分保守基因与 IcHV-2 同源性高达 93%；暗示鮰疱疹病毒较为宽泛的宿主范围[124]。

1.3　鲑疱疹病毒

感染鲑鳟鱼类的疱疹病毒主要有 5 种，分别为鲑疱疹病毒 I ~ V 型，病毒直径 200 ~ 240 nm，有囊膜，在病毒囊膜内部有二十面体的衣壳 (直径为 100 ~ 110 nm)。进化分析显示鲑疱疹病毒可分为 2 支，其中 SalHV-1，-2 亲缘关系较近；另一支为 SalHV-3，-4，-5[23-26]。鲑疱疹病毒致病报道较早 (1970s)，同时也是异疱疹病毒科四大属之一，目前鲑疱疹病毒病研究多聚焦于病毒株分离鉴定、流行病调查及检测技术的开发等。

鲑疱疹病毒 (SalHV-1, -2)　SalHV-1 于 20 世纪 70 年代在华盛顿虹鳟 (*Oncorhynchus mykiss*) 孵化场首次被分离到[125]，1985 年在加利福尼亚地区的虹鳟中再次分离出该病毒[126-128]；SalHV-1 主要对虹鳟幼鱼危害较大，也是鲑疱疹病毒属的典型代表种；SalHV-1 感染通常引起内脏器官水肿，肝脏及脂肪组织充血，组织病理观察可见肾脏和胰腺组织合胞体产生，并且肾脏是该病毒感染的主要靶器官。SalHV-2 是鲑科鱼类重要的病毒性疫病病原之一，20 世纪 70 年代首先从日本十和田湖孵化场大量死亡的淡水饲养的红大麻哈鱼 (*O. nerka*)，以及北海道马苏大麻哈鱼 (*O. masou*) 幼鱼中分离到了 SalHV-2 [129-130]；SalHV-2 感染可分急性型和慢性型两种，急性感染引起皮肤溃疡，内脏器官伴有弥散性出血，口腔和身体表面上皮增生；慢性感染往往以口部为中心形成肿瘤。目前，SalHV-2 主要分离株有马苏大马哈鱼病毒 (*O. masou* virus，OMV)，Yamame 肿瘤病毒 (Yamame tumor virus，YTV) 和银大马哈鱼肿瘤病毒 (Coho salmon tumor virus，CSTV) 等。

SalHV-1 和 SalHV-2 具有相似的细胞感染特性，能够在 CHES-214 和虹鳟性腺细胞 (RTG-2) 中增殖，产生合胞体样细胞病变，因此必须使用血清学或分子生物学方法来加以区分。目前针对 SalHV-1，-2 型的检测方法相对完善，如利用 SalHV-2 单克隆抗体，采用间接免疫荧光抗体技术在海水养殖银大马哈鱼肝脏、脾脏和肾脏等组织快速检测 SalHV-2 感染[131]；利用 PCR 技术能够准确检测出 SalHV-1 和 OMV 感染的马苏大马哈鱼、银大马哈鱼和虹鳟不同组织中的 OMV 特异性片段[132]。

鲑疱疹病毒 (SalHV-3，-4，-5)　SalHV-3 的自然感染宿主为突吻红点鲑，是引起突吻红点鲑表皮增生性疾病的主要病原[31, 133-134]；SalHV-3 感染引起鱼体上皮增生病变，眼、嘴和鳍条等部位出血。目前没有适合培养 SalHV-3 的细胞系，一般通过临床感染症状、电镜观察和 PCR 的方法进行诊断[133, 135-137]。另外，从东欧和美洲鲑鳟鱼中分离出另外 2 株鲑疱疹病毒，分别为大西洋鲑瘤状病毒 (Atlantic salmon papillomatosis virus, ASPV) 和突吻红点鲑疱疹病毒 (Namaycush herpesvirus,

NamHV)；又称为 SalHV-4 和 SalHV-5[25, 26]。据报道 SalHV-4 鱼体感染率可达 80%～90%，致死率超过 50%；体表感染损伤 (瘤状) 致死性较低，真菌和细菌的继发感染可能是主要的致死原因[26, 138]。

1.4　其他鱼类疱疹病毒

除上述三类主要的鱼类疱疹病毒外，仍有一些其他疱疹病毒能够感染特种经济鱼类，包括鳗鲡疱疹病毒 (Eel alloherpesvirus)、鲟鱼疱疹病毒 (Sturgeon alloherpesvirus)、罗非鱼疱疹病毒 (Tilapia herpesvirus) 等 (表 1)。在我国这一类疱疹病毒感染相关鱼类研究相对薄弱或尚未报道，在此针对这些鱼类疱疹病毒的分离鉴定及相关背景进行概述，以期在提高预警防范意识的同时，也为我国鱼类疱疹病毒研究及防控提供一定参考。

鳗鲡疱疹病毒 (AngHV)　鳗鲡疱疹病毒可感染日本鳗鲡和欧洲鳗鲡，两者均属于淡水鳗鲡；从欧洲和亚洲分离的病毒株亲缘关系较近，命名为鳗鲡疱疹病毒Ⅰ型 (AngHV-1)，又名 Herpesvirus anguillae [139]；可导致养殖鳗鲡鳍及皮肤出血、肾脏肿大、腹水等症状，也被认为是野生鳗鲡种群减少的重要因素；鳗鲡源 EK-1、EO 细胞为 AngHV-1 敏感细胞系[140-142]。该病毒基因组在 2010 年测序完成[19]，之后基因功能注释被进一步验证和完善[143]。与 CyHV-1，-2，-3 病毒之间的比较分析表明 AngHV-1 是鲤疱疹病毒属成员之一 [18]；针对该病原流行病学研究国外报道较多[144-148]。近年来我国鳗鲡养殖业快速发展，同时也在包括鳗鲡疱疹病毒分离鉴定，感染模型建立，检测方法及防控技术探索等方面的研究取得一定进展[142, 149-152]。

鲟鱼疱疹病毒 (AciHV)　目前国外已报道 2 株 (种) 分离自鲟鱼的疱疹病毒，分别为鲟鱼疱疹病毒Ⅰ型和Ⅱ型 (AciHV-1，-2)；二者进化关系较远，其中 AciHV-2 与鲴鱼疱疹病毒 (IcHV-1 和 IcHV-2) 进化关系较近[4, 24, 153-154]；尽管有些不同的分类提议，最终国际病毒分类委员会将 AciHV-2 分归为鲴鱼疱疹病毒属[22]。AciHV-1 感染高首鲟，发病幼苗具有较低致死率[155]；与 AciHV-1 相比，AciHV-2 致病性更强[156]，国内外均有报道 AciHV-2 与链球菌 (*Streptococcus*) 混合感染鲟的现象[157-158]。目前国内对于鲟鱼疱疹病毒研究尚处于起步阶段，国外的研究进展为我国鲟养殖业疫病风险预警提供了重要参考。

罗非鱼疱疹病毒 (TLEV) 等　2010 年国外学者认为罗非鱼病毒性脑炎是由一株疱疹病毒引起的，命名为罗非鱼幼鱼脑炎病毒 (TLEV)，暗示其潜在的水平和垂直传播风险[159]；其部分基因片段分析说明 TLEV 与异疱疹病毒科进化距离较远，但仍属于疱疹病毒家族成员，具体分类地位未知[27]。目前，大多数疱疹病毒感染淡水鱼类(表 1)，在海水鱼中报道较少 (部分鲑疱疹病毒)。在 2009 年，大西洋鳕中也发现存在疱疹病毒感染 (GaHV-1)，其分离株与鲴鱼疱疹病毒属或鲑疱疹病毒属病毒株亲缘关系较近[28]。90 年代末，在澳大利亚沙丁鱼中报道疱疹病毒感染对渔业造成严重损失，命名为沙丁鱼疱疹病毒 (PHV)，该疫病持续流行[29, 160-161]，相关机构也提出有益的防控方案[162]；根据现有数据分析该病毒与鲴疱疹病毒成员间进化关系较近[154]。除此之外，仍有一些鱼类可能处在疱疹病毒感染的潜在威胁之下，如河鲈 (*Perca fluviatilis*)、红带平鲉 (*Sebastes proriger*)、大菱鲆 (*Scophthalmus maximus*)、美星鲨 (*Mustelus canis*) 等[6, 163]。

2　小结

本文涉及的部分疱疹病毒对我国鱼类养殖产业造成重大的经济损失，制约相关鱼类产业的健康发展，如我国已将锦鲤疱疹病毒病列入了国家二类动物疫病病种名录。目前，新现和再现 (re-emergence) 鱼类疱疹病毒仍严重危害水产养殖与野生鱼类的健康，对于这些病毒研究进展概述有利于提高我们的预警防范意识。近年来，国内外研究者利用新技术新方法对鱼类疱疹病毒进行不断的深入研究，尤其对鲤疱疹病毒的研究，为我们深入探明鱼类疱疹病毒的病原特性，病毒感染机制等，以及有针对性的开发有效的防控方法奠定了重要基础。本文较为系统地概述鱼类疱疹病毒的基础研究和防控技术开发的背景及发展态势，为后续水产疱疹病毒病害防控研究提供一定参考。

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A brief review on virology researches of fish herpesviruses

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Abstract: Herpesviruses, as the members of the double-stranded DNA viruses, are highly disseminated in nature. Diverse viral isolates of *Alloherpesviridae* family are the main pathogens of aquatic animal diseases, which severely restrict the sustainable development of global aquaculture, particularly a huge impact on the fish aquaculture in China. Thus, this article provides a brief overview on virology researches of fish herpesviruses, including *Cyprinid herpesvirus*, *Ictalurid herpesvirus*, *Salmonid herpesvirus* and other fish herpesviruses. In detail, *Cyprinivirus* includes *C. herpesvirus* 1 (CyHV-1), *C. herpesvirus* 2 (CyHV-2), *C. herpesvirus* 3 (CyHV-3), *Carassius auratus* herpesvirus (CaHV), *Anguillid herpesvirus* 1 (AngHV-1); *Ictalurivirus* involves *I. herpesvirus* 1 (IcHV-1), *I. herpesvirus* 2 (IcHV-2), *Acipenserid herpesvirus* (AciHV-1). *Salmonivirus* consists mainly of *S. herpesvirus* 1,2,3,4,5 (SalHVs). Besides, the article also covers newly identified virus isolates including Tilapia larvae encephalitis virus, TLEV; Gadid herpesvirus 1, and so on, which threaten the health of the farmed and wild fish. This overview of fish herpesviruses discusses the diseases caused by these viruses, the biology of these pathogens, the host-virus interactions, development of detection technology and progress in the prevention strategies. This may be helpful to our understanding of the viral research trends of fish herpesviruses.

Key words: aquatic animals; fish; viral diseases; herpesvirus

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