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· 综述 ·

## 水产动物营养与免疫研究进展

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**摘要:** 营养与饲料对水产养殖的贡献越来越重要, 饲料组成不仅影响水产动物的营养, 而且会影响水产动物的免疫与抗病能力; 而营养状况更是决定水产养殖动物抵抗疾病能力的重要因素之一。本文综述了近5年水产动物营养与免疫方面的主要研究进展, 如: 多种必需营养素(蛋白质/氨基酸、脂肪、碳水化合物、维生素、矿物元素)、添加剂(酶制剂、植物精油、免疫多糖)、发酵饲料对免疫和抗病能力的影响等。提出了组学和生物信息技术在水产动物上的应用, 将有利于探讨水产养殖饲料的营养含量、鱼类肠道菌群和由此产生的代谢产物之间的关系, 为研究鱼类营养与免疫之间的复杂关系提供参考。

**关键词:** 水产动物; 营养; 免疫; 进展

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### 1 蛋白质(氨基酸)与免疫

#### 1.1 蛋白质(必需氨基酸)对水产动物免疫和抗病的影响

蛋白质(必需氨基酸)是水产动物维持生长、生殖等关键生理途径的重要调节因子, 也是构成

机体免疫系统的物质基础。近年来, 关于氨基酸营养与免疫系统的相关研究成为水产养殖动物研究的热点。适宜蛋白质或氨基酸可通过影响红螯螯虾(*Cherax quadricarinatus*)<sup>[1]</sup>、拉萨裸裂尻鱼(*Schizopygopsis younghusbandi*)<sup>[2]</sup>和日本沼虾(*Macrobrachium nipponensis*)<sup>[3]</sup>超氧化物歧化酶、过氧

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化氢酶、谷胱甘肽过氧化物酶等抗氧化酶系统, 增强机体抗氧化能力。饲料蛋白质水平过高或过低则会抑制水产动物如皱纹盘鲍 (*Haliotis discus hannai*) 等的 TOR 信号转导、细胞凋亡、免疫和抗应激<sup>[4]</sup>。赖氨酸、蛋氨酸等限制性氨基酸通过增加溶菌酶活力和酸性磷酸酶活性, 以及补体 3 和免疫球蛋白 M 的合成提高欧洲鲈 (*Dicentrarchus labrax*)<sup>[5]</sup>、草鱼 (*Ctenopharyngodon idella*)<sup>[6]</sup>、团头鲂 (*Megalobrama amblycephala*)<sup>[7]</sup>、大口黑鲈 (*Micropterus salmoides*)<sup>[8]</sup>、杂交石斑鱼 (*Epinephelus fuscoguttatus* ♀ × *E. lanceolatus* ♂)<sup>[9]</sup>、南亚野鲮 (*Labeo rohita*)<sup>[10]</sup>、虹鳟 (*Oncorhynchus mykiss*)<sup>[11]</sup> 等机体的非特异性免疫力。

精氨酸可有效缓解尼罗罗非鱼 (*Oreochromis niloticus*) 对无乳链球菌 (*Streptococcus agalactiae*)<sup>[12]</sup>、印度鲤 (*Cirrhinus mrigala*)<sup>[13]</sup> 对嗜水气单胞菌 (*Aeromonas hydrophila*) 感染作用, 降低死亡率。其他必需氨基酸也通过影响血清免疫、抗氧化、炎症反应、紧密连接蛋白等多种途径调控免疫力。在欧洲鲈对美人鱼发光杆菌杀鱼亚种菌株<sup>[5]</sup>、草鱼对柱状黄杆菌<sup>[14]</sup>、中华绒螯蟹 (*Eriocheir sinensis*) 对嗜水气单胞菌<sup>[15]</sup> 等中的研究均证实适宜饲料蛋白或必需氨基酸水平可有效缓解病原菌感染的负面反应, 降低死亡率。

## 1.2 蛋白质 (必需氨基酸) 对水产动物免疫的作用机制

近年来的研究发现, 蛋白质 (必需氨基酸) 可以通过 TOR 信号通路提高杂交江鲢 (*Pelteobagrus vachelli* ♀ × *Leiocassis longirostris* ♂)<sup>[16]</sup>、斜带石斑鱼 (*Epinephelus coioides*)<sup>[17]</sup> 等水产动物的免疫力。此外, 精氨酸、苏氨酸、亮氨酸等在团头鲂、草鱼、杂交江鲢中可以激活 Nrf2-Keap1 通路及下游基因, 增强机体抗氧化和免疫力<sup>[14, 16, 18-19]</sup>。也有报道指出, TOR 信号通路发挥免疫调控作用与 Nrf2 信号通路有关。Liang 等<sup>[20]</sup> 研究发现亮氨酸可以通过激活 TOR 提高 Nrf2 的表达进而调节抗氧化酶基因的表达, 增强机体免疫力。

Liang 等<sup>[18, 21]</sup> 研究表明, 适宜的精氨酸水平显著抑制团头鲂 *NF-κB* 基因的表达, 并与 *IL-1β* 和 *TNF-α* 等促炎因子的 mRNA 水平呈正相关。饲料赖氨酸水平通过影响尼罗罗非鱼血清 *IL-1β*、*IL-6*、*IL-10* 及肝脏 *NF-κB* 信号通路核心基因的表达来增强机体免疫力<sup>[22]</sup>。除了以上 3 条主要的信号通路以外, 蛋白质 (必需氨基酸) 发挥免疫调控作用

还与 ERK<sup>[23]</sup>、AMPK-NO<sup>[21]</sup>、Sirt1/ERK/90RSK<sup>[16]</sup> 和 STATs 信号通路<sup>[24]</sup> 有关。目前的研究仍然局限在对抗氧化和免疫因子转录或蛋白表达水平的影响上, 蛋白质 (必需氨基酸) 与免疫靶基因的相互作用机制还有待进一步研究。

## 2 脂肪与免疫

### 2.1 脂肪对水产动物免疫的影响

脂肪不仅参与细胞和组织构成, 提供能量和必需脂肪酸, 还是多种免疫因子的重要合成要素, 在动物发育和免疫调控中起关键调控作用。对团头鲂<sup>[25]</sup>、大口黑鲈<sup>[26]</sup>、草鱼<sup>[27]</sup>、花鲈 (*Lateolabrax japonicus*)<sup>[28]</sup> 等不同食性鱼类的研究发现, 高脂饲料对鱼类的免疫损伤作用主要体现在诱导脂肪代谢紊乱、肝脏脂肪过度沉积; 诱导炎症、细胞凋亡和氧化应激损伤; 诱导肠道微生物紊乱, 损伤肠道屏障功能。此外, 甲壳动物体内不饱和脂肪酸含量高, 并且无分化的脂肪细胞, 脂肪均以脂滴的形式储存于肝胰腺中, 更易受高脂诱导产生氧化应激损伤。高脂饲料可诱导罗氏沼虾肝胰腺细胞凋亡增加, 脂滴自噬增加, 抑制抗氧化酶系统, 导致肝胰腺氧化应激损伤<sup>[29]</sup>。

不同脂肪源的脂肪酸组成以及不同水产动物的必需脂肪酸需求均存在差异, 不适宜的脂肪源会导致机体脂肪代谢紊乱和氧化应激损伤。在大黄鱼 (*Larimichthys crocea*) 饲料中使用菜籽油、棕榈油和亚麻籽油高水平替代鱼油均导致肝脏氧化损伤, 并激活促炎因子表达<sup>[30-32]</sup>。对于甲壳动物, 饲料中鱼油对中华绒螯蟹促生长, 提高抗氧化能力和抗低盐应激方面要优于亚麻籽油和豆油等植物油, 并且摄食鱼油的蟹体内 n-3 长链多不饱和脂肪酸 (LCPUFA) 含量更高<sup>[33-34]</sup>。对于罗氏沼虾、克氏原螯虾 (*Procambarus clarkii*) 等淡水虾类, 在饲料中使用不饱和度较低的动植物油源部分替代鱼油, 其养殖效果与抗氧化能力优于鱼油<sup>[35-36]</sup>。此外, 鱼油等富含 LCPUFA 脂肪源的氧化也是导致水产动物组织损伤和氧化应激的重要因素。对团头鲂的研究发现, 摄食氧化鱼油可诱导组织氧化应激损伤和炎症<sup>[37]</sup>。

饲料中添加适宜的脂肪酸组成具有抑制炎症反应、减轻疾病等作用, 缺乏必需脂肪酸会导致水产动物生长缓慢、脂肪代谢异常与免疫力低下<sup>[38-39]</sup>。大西洋鲑 (*Salmo salar*)、卵形鲳鲹 (*Trachinotus ovatus*)、长江鲟 (*Acipenser dabryanus*)、泥

鳅 (*Misgurnus anguillicaudatus*) 等对 EPA 和 DHA 等 n-3 LCPUFA 需求高, 饲料中适宜 n-3LCPUFA 可显著提高抗氧化、免疫和抗炎相关通路, 提高机体抗应激和抗病力<sup>[38-40]</sup>。饲料中不同脂肪酸比例对免疫同样具有调控作用。适宜亚麻酸/亚油酸比例可提高细鳞鲑 (*Brachymystax lenok*) 非特异免疫力<sup>[25]</sup>。在大西洋鲑饲料中通过增加 EPA 和 DHA 提高 n-3/n-6 脂肪酸比例可增强肠道屏障功能和健康<sup>[41]</sup>。过量共轭亚油酸会导致草鱼肝细胞线粒体空泡化, 内质网肿胀, 排列过于紧密; 肌细胞肌节结构松散, 肌原纤维降解<sup>[42]</sup>。

## 2.2 脂肪对水产动物免疫的作用机制

目前, 脂肪对水产动物免疫调控的分子机制研究主要集中在对抗氧化、炎症相关通路, 脂肪酸代谢相关通路, 细胞自噬和凋亡相关通路等的影响上。在水产动物高脂模型中的研究发现, 高脂饲料通过激活 *apo1*, *atgl*, *PPAR $\alpha$* , *PPAR $\gamma$* , *cpt-1*, *acc*, *cyp7 $\alpha$* , *rxr*, *cebpa* 等脂肪合成相关基因促进花鲈脂肪的过度沉积, 通过激活 *IL-1 $\beta$* , *TGF- $\beta$* , *TNF- $\alpha$* , *caspase 9*, *ERK*, *caspase 3*, *caspase 8* 等炎症和凋亡相关基因诱导细胞凋亡<sup>[28]</sup>。在甲壳动物中高脂饲料可下调罗氏沼虾肝胰腺 *Imd-relish* 和 *Toll-dorsal* 信号通路抑制抗氧化酶系统, 以及通过 *iNOS/NO* 通路诱导肝胰腺脂滴自噬和细胞凋亡<sup>[29]</sup>。

DHA 和 EPA 等 n-3LCPUFA 可抑制致病菌诱导大西洋鲑白细胞的炎症因子和 TLRs 信号通路的表达, 降低对疾病的敏感性。过量亚油酸诱导大黄鱼肝胰腺炎症, 激活自噬可下调 *TNF- $\alpha$*  和 *IL-1 $\beta$*  等促炎因子表达, 缓解炎症发生<sup>[43]</sup>。

## 3 碳水化合物与免疫

### 3.1 碳水化合物对水产动物免疫的影响

糖是有机体重要的能源和碳源, 糖代谢的中间产物又可以转变为其他含碳化合物, 如: 氨基酸、脂肪、核苷等, 为动物提供营养物质。但是, 鱼类对碳水化合物的利用受到一系列复杂因素的影响, 包括养殖品种的生物特性、饲料成分、加工方式和饲养环境等<sup>[44-45]</sup>。饲料中适宜的糖水平可以提高杂交石斑鱼、日本沼虾溶菌酶活性和抗氧化酶活性等非特异免疫力指标<sup>[46-47]</sup>。高糖摄入可降低鱼体的抗氧化能力、白细胞呼吸爆发活性等非特异免疫力, 导致代谢应激, 对鱼体健康

造成不利影响。高糖摄入还会降低鱼肝中 AMPK 的磷酸化, 诱导促炎因子的快速表达<sup>[48]</sup>, 且糖酵解和磷酸化的失衡会激活巨噬细胞进而诱导炎症表型<sup>[49]</sup>。糖耐量试验也发现, 高糖可引起鱼类肝脏细胞、外周白细胞的呼吸爆发和氧化应激损伤<sup>[50]</sup>。但是也有研究发现, 南亚野鲮可以耐受饲料中 45% 糊化淀粉, 且不会影响鱼类生长和抗氧化酶活性, 还会增强鱼体对嗜水气单胞菌的抵抗力<sup>[51]</sup>。对大口黑鲈幼鱼的研究发现, 高淀粉饲料 (19%) 会降低其肝功能和免疫力, 诱发肝组织核迁移和空泡化病理学现象, 添加胆汁酸可以缓解其糖不耐受的应激反应<sup>[52]</sup>, 添加白藜芦醇可有效降低促炎细胞因子的表达<sup>[53]</sup>。

### 3.2 碳水化合物对水产动物免疫的作用机制

在传统的免疫学研究基础上, 借助高通量测序和转录组技术研究发现, 饲料高碳水化合物通过调控 NF- $\kappa$ B、趋化因子、细胞因子 (SOCS3)、Toll 样受体 (TLR) 等信号通路诱导肝脏代谢功能损伤和免疫炎症反应<sup>[54-55]</sup>。高糖可以通过 PI3K/Akt/Nrf2 引起鱼类肝脏细胞、外周白细胞的呼吸爆发和氧化应激损伤, 还能影响 cAMP/PKA 通路, 并通过 MAPK/ACC/PGC-1 $\alpha$  通路和 p38MAPK 参与呼吸爆发功能及其关键酶 p47phox 的调控<sup>[50]</sup>。应用全基因组测序技术研究发现饲料碳水化合物显著改变了胰岛素受体 substrate-1 (IRS1)、PI3K 等通路及其下游 TGF- $\beta$  信号基因的 DNA 甲基化<sup>[56-57]</sup>, 也有研究发现 miRNA (miR34a 等) 通过调控 *Sirt1/foxO1* 及其下游基因的表达诱导高糖的免疫应激反应<sup>[58]</sup>。此外, 高糖饲料通过抑制 *Sirt1* 的表达调节胰岛素通路, 并介导 *FoxO1* 或 *PI3KR1/Akt* 通路诱导免疫抑制, 且白藜芦醇 (*SIRT1* 激活剂) 可以激活 AMPK/SIRT1/PGC-1 $\alpha$  网络, 降低 *IL-10* 和 *TNF- $\beta$*  等促炎因子的表达<sup>[53]</sup>。随着系统营养代谢观念的提出, 认为葡萄糖可以通过肠-肝轴调控鱼体胆汁酸循环, 胆汁酸作为代谢调节剂或营养信号分子影响鱼类葡萄糖、能量代谢和炎症反应<sup>[59]</sup>。此外, 也有报道指出饲料中较高的玉米淀粉可能通过影响肠道微生物而增加肠道通透性, 降低其对病原菌入侵的抵抗<sup>[60]</sup>。

饲料中添加高剂量的碳水化合物会影响水产动物的免疫, 不同食性鱼类的免疫作用机制有一定的差别, 随着系统营养学观念的逐渐深入和生物技术手段在营养研究中的应用, 未来通过营养规划、基因修饰等手段研究鱼类饲料碳水化合物



对免疫和微生物屏障的调控机理将受到关注。

## 4 维生素与免疫

### 4.1 维生素对水产动物免疫的影响

维生素作为辅酶及活性物质,对水产动物的代谢和免疫均产生重要的影响。维生素 E 能提高印度鲤<sup>[61]</sup>、网纹鸭嘴鲶<sup>[62]</sup>(*Pseudoplatystoma reticulatum*)和多鳞鳢(*Sillago sihama*)<sup>[63]</sup>血清 ALP 活性、球蛋白含量、肝脏 AKP 活性、补体 C3 和免疫球蛋白 IgM 含量,增强鱼体免疫功能。叶酸可增强西伯利亚鲟(*Acioenser baerii*)的溶菌酶活性和免疫球蛋白含量<sup>[64]</sup>。适量维生素 B<sub>6</sub>能提高鲤体内溶菌酶和碱性磷酸酶活性,增强其天然免疫力<sup>[65]</sup>。通过提高溶菌酶等免疫指标,维生素 C 可增强黄鳝<sup>[66]</sup>、尼罗罗非鱼<sup>[67]</sup>和多鳞鳢<sup>[68]</sup>等的非特异性免疫力。

对甲壳动物的研究表明,维生素 A<sup>[69]</sup>、维生素 E<sup>[70]</sup>、维生素 D<sub>3</sub><sup>[71]</sup>、肌醇<sup>[72]</sup>等增强虾蟹 LZM、ACP 等活性,上调 NF- $\kappa$ B 通路基因 *Toll*, *MyD88*, *Relish*, *LZM*, *HSP90* 表达,提高非特异性免疫功能。维生素 C 可以提高克氏原螯虾体内 LZM、ACP 和 AKP 活性,及对白斑综合征病毒的抵抗力<sup>[73]</sup>。维生素 B<sub>2</sub> 可缓解外界环境导致的苏氏圆腹鲢(*Pangasianodon hypophthalmus*)免疫力低下<sup>[74]</sup>。肌醇能提高凡纳滨对虾应对氨氮、低氧胁迫和黄曲霉毒素时所产生的免疫应答能力<sup>[75]</sup>。维生素 E 缺乏或维生素 B<sub>6</sub> 缺乏会对草鱼天然免疫屏障及鳃、肠黏膜免疫屏障产生损伤,降低其免疫功能<sup>[76-77]</sup>。

### 4.2 维生素调控水产动物免疫的作用机制

近些年研究表明,维生素对水产动物免疫的调控机制主要通过以下途径:(1)肠道免疫屏障作用,调节抗菌肽基因在肠道中的表达,维持微生物的动态平衡<sup>[78-79]</sup>;(2)调控补体系统、溶菌酶和酸性磷酸酶活性等,提高免疫功能、抗氧化和抗病力<sup>[76]</sup>;(3)通过 *Toll*、NF- $\kappa$ B 通路,上调 NF- $\kappa$ B 相关蛋白 p65、I $\kappa$ B $\alpha$ 、I $\kappa$ B $\beta$ 、I $\kappa$ B $\gamma$ 、Kelch 1b、肌球蛋白轻链激酶、p38MAPK 表达,调控细胞因子及体内抗菌化合物的合成,提高鱼类免疫力<sup>[76]</sup>;(4)在甲壳动物中,通过上调 *Toll2*、*Relish*、*MyD88* 等免疫基因的表达,激活酚氧化酶系统,增强免疫力<sup>[71, 78-79]</sup>。然而,维生素在体内的作用并不是单一的,维生素与维生素、维生素与其他营养素之间的协同作用需要进一步研究。

## 5 矿物元素与免疫

### 5.1 矿物营养元素对水产动物免疫与抗病的影响

矿物元素对水产动物的免疫机能具有十分重要的作用。与水产动物免疫相关的矿物元素主要为锌、硒、铜、铁、磷等,并主要受饲料矿物元素添加水平和化学形态的影响。研究发现饲料中添加适宜水平的锌可提高日本沼虾、杂交鳢(*Channa maculate* ♀ × *C. argus* ♂) 苗种血浆 LZM 和补体 C3 活性,并提高抗氧化能力,减少脂质过氧化物的产生<sup>[80-81]</sup>。饲料添加适宜剂量的硒可上调团头鲂幼鱼肝脏抗炎细胞因子、*Nrf2*、*Keap-1* 的转录,同时抑制促炎细胞因子、*IL-8*、*TNF- $\alpha$*  和 *TGF- $\beta$*  的转录<sup>[82]</sup>。饲料中添加适宜剂量铜显著提高凡纳滨对虾肝胰腺的 Cu/Zn-SOD 酶活性及转录水平<sup>[83]</sup>,铜过量会诱导伊朗裂臀鱼(*Schizothorax zarudnyi*)发生氧化应激<sup>[84]</sup>。饲料中添加适宜剂量的铁可上调中华绒螯蟹幼蟹铁蛋白 *ferritin-1* 和 *ferritin-2* 的转录水平,下调铁调节蛋白 *irp* 及炎症相关因子 *toll2*、*myd88*、*GRISH* 和 *litaf* 的转录水平,减轻了 LPS 诱导的炎症反应<sup>[85]</sup>。铁含量过高可显著下调免疫相关基因 *TLR*、*Lec*、*Muc-1*、*Muc-2*、*proPO* 和 *ALF* 的转录,损害凡纳滨对虾的肠道免疫功能(病原体识别、抗菌能力和黏液稳态),增加脂质过氧化物的产生<sup>[86]</sup>。也有研究表明,铁超载破坏了大西洋鲑的免疫反应,导致感染鲑鱼立克次氏体(*Piscirickettsia salmonis*)后的耐受性下降并导致死亡率增加<sup>[87]</sup>。缺磷加剧了嗜水气单胞菌诱导的草鱼肠道炎症反应,加剧肠道免疫屏障和物理屏障功能受损<sup>[88]</sup>。缺磷还降低暗纹东方鲀(*Takifugu obscurus*)感染嗜水气单胞菌后的存活率和总血细胞计数,加剧氧化应激、炎症反应和细胞凋亡,损害免疫系统<sup>[89]</sup>。

纳米颗粒形态的矿物营养元素在水产动物免疫调控和抗应激方面的研究是近期研究的热点。在尼罗罗非鱼饲料中添加低剂量纳米氧化锌(30 mg/kg)显著提升血清 LZM 活性和 IgM 含量,上调脾脏细胞表面趋化因子、*TLR7*、*IgM* 和 *IFN- $\gamma$*  基因表达水平。但是高剂量(60 mg/kg)会上调 *IL8* 和 *IL-1 $\beta$*  基因表达,诱导炎症发生<sup>[90]</sup>。尼罗罗非鱼饲料中添加 1.0 mg/kg 纳米硒,免疫调节硒蛋白(*GPx2*、*SelJ*、*SelL*、*SelK*、*SelS*、*SelW* 和 *Sepp1a*)及其合成因子(*SPS1* 和 *Scl*)的转录表达

显著上调<sup>[91]</sup>; 并通过下调 *Caspase1*、*P450* 和 *HSP70* 表达缓解因感染导致的细胞凋亡, 增强抗嗜水气单胞菌感染的能力, 降低感染率<sup>[92-93]</sup>。

## 5.2 矿物元素对水产动物免疫的作用机制

不同矿物元素对水产动物不同器官免疫功能的调控路径和分子机制有所不同。日本沼虾雌虾上的研究表明, 锌通过调控肝胰腺 Toll 样受体通路相关基因 (*TLR3*、*MyD88*、*IRAK4*、*TRAF6*、*MAPK3K7*、*MAPK14*) 调控对虾非特异性免疫<sup>[80]</sup>。凡纳滨对虾饲料中添加氨基酸螯合锌通过介导肝胰腺锌信号通路 (*mt*、*mtf1*、*zip3*、*zip9*、*zip11*、*zip14*) 激活免疫相关基因 (*Toll*、*IMD*、*LZM*、*proPO*、*ALP* 和 *Cu/Zn-SOD*) 表达<sup>[94]</sup>。草鱼饲料硒缺乏下调抗菌肽和硒蛋白 (*hepcidin*、*Mucin2*、 *$\beta$ -defensin-1*、*Leap2A*、*Leap2B*、*SelK*、*SelS*、*SelP*、*SelW*) 基因表达, 并通过介导 *IKK $\alpha$* 、 *$\beta$* 、 *$\gamma$ /I $\kappa$ B $\alpha$ /NF- $\kappa$ B* 信号通路及 *TOR/(S6K1, 4E-BP1)* 信号通路上调促炎细胞因子并下调抗炎细胞因子的转录水平加重炎症反应, 损害免疫功能<sup>[95]</sup>。饲料中铜通过介导吞噬体和 *IL-17* 信号通路调控凡纳滨对虾的免疫反应<sup>[96]</sup>。饲料中铁缺乏通过介导肠道 *IKK $\beta$* 、*IKK $\gamma$ /I $\kappa$ B $\alpha$ /NF- $\kappa$ Bp65* 通路和 *TOR/(S6K1, 4EBP)* 信号通路上调促炎细胞因子转录, 下调抗炎细胞因子转录, 加重肠道炎症, 降低免疫力<sup>[97-98]</sup>。饲料中钙和维生素 D<sub>3</sub> 通过钙依赖的 *TLR-NF $\kappa$ B* 途径增强中华绒螯蟹抗菌能力和非特异性免疫力<sup>[99]</sup>。

研究发现, 矿物元素通过抑制凋亡和自噬对机体发挥保护作用, 矿物元素锌可通过抑制鲤 *PERK/IRE1* 介导的凋亡及自噬, 对重金属砷诱导的氧化应激、内质网应激、脾脏毒性和免疫毒性发挥保护作用<sup>[100]</sup>。锌通过抑制内质网应激 (*GRP78*、*p-PERK*、*p-eIF2 $\alpha$* )、凋亡 (*Caspase3/9*、*Bcl-2*、*Bax*) 和自噬 (*LC-3*、*p62*) 相关蛋白的表达缓解砷诱导的鲤鳃组织损伤<sup>[101]</sup>。关于矿物元素介导凋亡和自噬发挥水产动物器官损伤和免疫毒性的保护作用研究尚处于起步阶段, 需要进一步研究。

此外, 矿物元素介导水产动物肠道微生物的改变调控宿主的免疫及对病原菌的抵抗。锌可通过改变杂交石斑鱼肠道微生物区系丰度介导宿主对病原菌的抵抗<sup>[102]</sup>。饲料中过量补铁破坏凡纳滨对虾肠道微生物群稳态, 损害对虾肠道的免疫功能 (病原体识别、抗菌能力和黏液稳态)<sup>[86]</sup>。Ma 等<sup>[103]</sup> 首次使用 16S 微生物组、宏基因组和转录组联合分

析方法探索了锌对卵形鲳鲂肠-肝轴的影响, 低剂量锌提高了肠道核心菌群 (变形菌、梭杆菌、厚壁菌和拟杆菌) 的丰度, 高剂量锌导致肠道微生物群失调, 激活细菌 VI 型分泌杀菌系统 (T6SSs), 触发宿主肝脏的氧化应激反应、免疫和抗病毒机能。

矿物元素主要通过参与免疫相关酶的合成, 影响水生动物免疫器官的发育, 对维持机体内源性抗氧化系统和缓解细胞氧化损伤起重要作用。目前, 对纳米颗粒形态矿物营养元素的作用机制研究还不够深入, 对“矿物元素-微生物-宿主免疫轴”作为新切入点仍需进一步研究。

## 6 添加剂与水产动物免疫

在后抗生素时代, 养殖业涉及的饲料安全成为重要的问题, 除了基本营养素之外, 酶制剂、植物精油和免疫多糖类绿色功能性饲料添加剂的开发和应用逐渐成为水产动物营养领域的研究热点。酶制剂种类繁多, 主要包括非淀粉多糖 (NSP) 酶、植酸酶、蛋白酶、淀粉酶和脂肪酶。其中大多数酶制剂的作用原理是针对性降解植物原料中的抗营养物质, 或补充动物机体内源消化酶的不足, 提高胃肠道对饲料养分的消化吸收率<sup>[104]</sup>。NSP 酶降解 NSP 后会产生具有益生元特性的寡聚糖<sup>[105]</sup>, 如: 低聚木糖<sup>[106]</sup>、壳寡糖<sup>[107]</sup>、甘露寡糖<sup>[108]</sup> 和  $\beta$ -葡聚糖<sup>[109]</sup> 等, 这些寡糖可以减少水产动物肠道内有害菌的附着和定植, 促进有益菌的定植, 提高肠道健康水平, 间接提高水产动物的非特异性免疫力。但是酶制剂在生产实践中受到饲料加工热敏性的限制, 并未在水产饲料中广泛应用, 未来加工工艺和设备的提升是解决液体酶制剂在水产饲料中广泛应用的关键突破口。植物精油属于植物次生代谢物的挥发性芳香物质混合物, 是水产养殖中很有前景的膳食补充剂和潜在的饲用抗生素替代品。研究表明, 水产动物饲料中补充精油可提高宿主的抗氧化和免疫指标活性<sup>[110]</sup>、抗应激能力<sup>[111]</sup> 及抗病力<sup>[112]</sup>。此外, 近期在尼罗罗非鱼<sup>[113]</sup>、凡纳滨对虾<sup>[114]</sup>、大菱鲆<sup>[115]</sup>、锦鲤<sup>[116]</sup> 等水产动物上的研究发现, 植物精油还可通过调节鱼类肠道微生物群结构, 间接调节宿主的免疫系统和健康状态。免疫多糖的种类十分丰富, 在水产养殖中研究和应用较多的免疫多糖包括玉屏风多糖<sup>[117]</sup>、黄芪多糖<sup>[118]</sup>、 $\beta$ -葡聚糖<sup>[109]</sup>、蒲公英多糖<sup>[119]</sup>、硫酸多糖<sup>[120]</sup> 等。在鲫 (*Carassius auratus*)<sup>[121]</sup>、三疣梭子蟹 (*Portunus trituberculatus*)<sup>[122]</sup>、

西伯利亚鲟 (*A. baerii*)<sup>[123]</sup>、克氏原螯虾<sup>[124]</sup>等多种水产动物上的研究证实,免疫多糖主要通过促进免疫细胞因子的合成、分泌等来提高抗氧化酶及溶菌酶活性,增强 T-淋巴细胞、白细胞、巨噬细胞等免疫细胞的功能并激活补体系统。关于免疫多糖的功能研究还有待进一步探索。

## 7 发酵饲料与免疫

近年来,通过生物发酵技术降低饲料原料中的抗营养因子,释放活性物质,调控水产动物免疫与健康成为水产营养领域的研究热点。全价配合饲料经发酵后,粗蛋白、可溶性蛋白、多不饱和脂肪酸等营养物质显著提高<sup>[125]</sup>。在配合饲料中拌喂 20% 以下发酵饲料显著提高中华绒螯蟹抗氧化和免疫机能<sup>[126]</sup>。目前,发酵饲料的主要研究方向为发酵植物性饲料原料替代饲料中鱼粉对水产动物免疫和肠道健康的影响。研究表明,使用米曲霉 (*Aspergillus oryzae*) 发酵菜籽粕可替代真鲷 (*Pagrus major*) 饲料中 50% 鱼粉,并显著降低体内 MDA、活性氧、杀菌活性和呼吸爆发水平<sup>[127]</sup>。使用发酵辣木叶 (*Moringa oleifera*) 替代饲料中 40%~60% 的鱼粉可显著降低异育银鲫嗜水气单胞菌攻毒死亡率,激活 SOD、CAT、溶菌酶、补体 C3 等免疫酶,抑制脾脏 TLR2 信号通路表达<sup>[128]</sup>。使用发酵豆粕替代饲料中适宜量鱼粉显著提高了花鲈、大口黑鲈等的抗氧化能力、先天性免疫、肠道健康、脂质和蛋白代谢<sup>[129]</sup>。

此外,一些发酵成分还可用作免疫增强剂。在点带石斑鱼和尖吻鲈 (*Lates calcarifer*) 上的研究中发现,在饲料中添加 1%~3% 发酵柠檬皮<sup>[130-131]</sup>、斑马鱼 (*Danio rerio*) 饲料中添加乳酸菌发酵硒 (3 mg/kg)<sup>[132]</sup>、凡纳滨对虾饲料中添加 0.2%~0.8% 发酵开菲尔 Kefir<sup>[133]</sup>、鲇 (*Clarias gariepinus*) 饲料中添加 2.5% 芽孢杆菌和乳球菌发酵蚯蚓<sup>[134]</sup>等可提高鱼虾的非特异性免疫力、抗氧化能力及其抗病力。目前,生物发酵全价配合饲料和饲料原料对水产动物生长、免疫、抗病和肠道健康领域已有广泛研究,但目前的研究多集中于表型指标,缺乏对调控机理的研究。此外,行业内还缺乏针对发酵菌种的安全性评估体系,有待进一步研究。

## 8 营养与免疫研究展望

目前,评价营养素等提高水产动物免疫与抗病力的研究,主要还是集中在生化和转录水平。

有关水产动物营养与免疫之间相互作用的基础研究和应用研究仍滞后于哺乳动物,仅有部分研究利用转录组、代谢组和蛋白组学,获得了与营养调控和免疫调控相关的差异分子、小分子代谢物和蛋白,同时逐渐开始关注肠道菌群与机体免疫之间的关系。多组学和生物信息技术在水产动物中的应用,将为研究鱼类营养和免疫之间的复杂关系提供重要技术支撑,有利于探讨水产养殖饲料的营养含量、鱼类肠道菌群和由此产生的代谢物之间的关系,以及这些次级代谢产物对鱼类的健康与抵抗力的影响。

(作者声明本文无实际或潜在的利益冲突)

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## Research progress in nutrition and immunity of aquatic animals

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**Abstract:** With the increasing importance of contribution of nutrition and feed science and technology to aquaculture, feed composition affects not only the nutritional status of aquatic animals, but also their immunity and disease resistance, and the former is one of the most important factors in determining the ability of aquaculture animals to resist disease. This paper reviews the major research progress in aquatic animal nutrition and immunity in the last five years, such as multiple essential nutrients (proteins/amino acids, fats, carbohydrates, vitamins, minerals), additives (enzyme preparations, essential oils, immune polysaccharides), fermented feeds, and their effects on immunity and disease resistance. In our opinion, the application of omics and bioinformatics to aquatic animals will facilitate the exploration of the relationships among the nutritional composition of aquaculture feeds, the fish gut flora and the derived metabolites, and provide important technical support for the study of the complicated relationships between nutrition and immunity in fish.

**Key words:** aquatic animals; nutrition; immunity; progress

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