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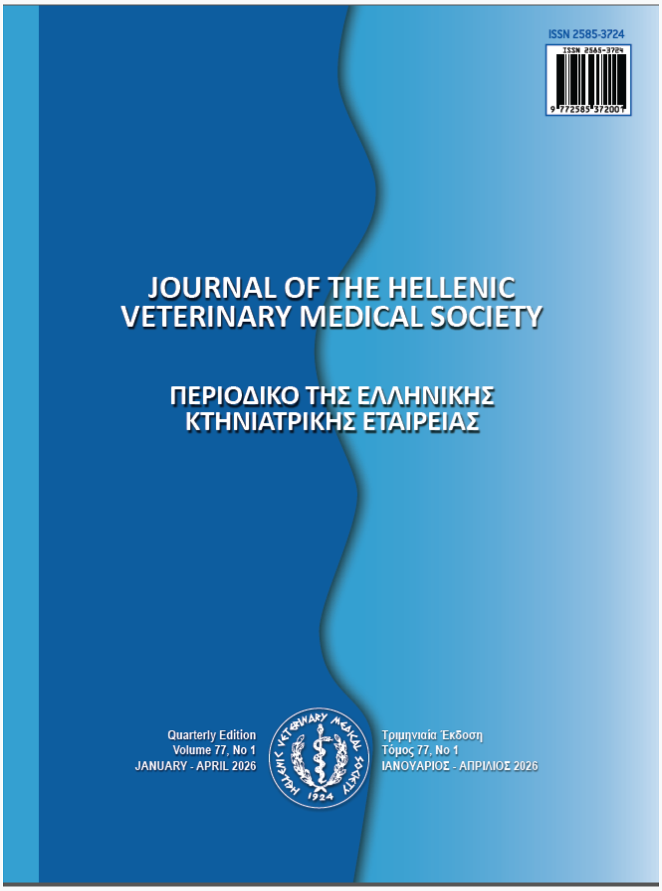

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Anatomy and embryology of fish liver and pancreas with a focus on their use in research

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ABSTRACT: Fish liver and pancreas perform indispensable roles related to food digestion, metabolism, and glucose homeostasis. The fish liver fills the cranial part of the celomic cavity and displays variable lobation and degree of coloration across species. Its development from the gut endoderm is regulated by a cascade of signaling factors, including fibroblast growth factor 10 (Fgf10), GATA-binding factor 6 (Gata6), and hepatocyte nuclear factor 6 (Hnf6). The fish pancreas consists of discrete yellow glandular masses that infiltrate the gut mesentery. The pancreatic tissues may also disseminate into the parenchyma of the liver and spleen, forming hepatopancreas and splenopancreas, in several fishes, e.g., cyprinids. The pancreas originates with two buds from the gut wall close to the area of the developing liver. Specification of pancreatic progenitor cells is regulated by the expression of the transcription factor pancreatic and duodenal homeobox 1 (Pdx1), which initiates a downstream cascade of transcription factors important for pancreatic differentiation. Both organs share several anatomical, developmental, and regenerative mechanisms with higher vertebrates, including humans. These shared similarities made them a target of numerous experimental research studies related to embryogenesis, environmental pollution, and endocrine and metabolic disorders. In this article, we summarize the anatomical, histological, and developmental features involving the liver and pancreas in fish. We also discuss strengths and weaknesses of their use for disease modelling.

Keyword: Brokmann bodies; developmental biology; diabetes; fatty liver; fish model; hepatopancreas

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INTRODUCTION

The fish liver performs several functions that include bile secretion, detoxification, and metabolism of carbohydrates, proteins, and lipids (Genten et al., 2009). In female oviparous fishes, it is responsible for production of yolk precursors, e.g., vitellogenin. The latter are of crucial importance for maintaining embryos and nurturing larvae (Yilmaz et al., 2024).

The gross appearance and area occupied by the liver differ significantly among different types of fish (Bertolucci et al., 2008). Anatomically, the liver is located at the most cranial part of the celomic cavity in most teleost. In many species, it appears divisible into a number of lobes that varies according to the species (Franco-Belussi et al., 2012).

The fish pancreas is composed of endocrine and exocrine portions. The endocrine pancreas consists of pancreatic islets that secrete hormones for regulation of blood glucose levels. These islets comprise insulin-producing beta cells, glucagon-producing alpha cells, somatostatin-producing delta cells, and pancreatic polypeptide-producing PP cells. The latter cell type has not been clearly documented in all fish species (Chanet et al., 2023). On the other hand, the exocrine pancreas includes the pancreatic acini that secrete enzymes necessary for digestion and the duct system that conveys them to the intestine. The ductal epithelium also releases bicarbonate-rich secretion into the gut lumen, further aiding in digestion (Ishiguro et al., 2012).

Unlike the liver, which appears well-organized with distinct localization within the celomic cavity, the fish pancreas displays differences in its spatial distribution. In general, pancreatic tissues in many teleosts, e.g., zebrafish (*Danio rerio*), could be identified as discrete glandular masses interspersed among fats of the gut mesentery (Tocher et al., 2008). In a number of species, e.g., grass carp (*Ctenopharyngodon idella*), clusters of pancreatic tissue, mainly of exocrine nature, invade the subcapsular regions of the spleen and surround the main branches of the portal vein within the liver (Mokhtar, 2015).

The embryonic formation of the liver and pancreas in fish is regulated by a complex network of key transcription factors. These factors are spatiotemporally expressed during sequential steps involving induction of hepatic and pancreatic progenitors as well as their specification and subsequent differentiation (Tao and Peng, 2009; Tiso et al., 2009). Interestingly, a number of these factors is reawakened during damage-induced organ regeneration raising a therapeutic potential for them (Mo et al., 2024).

This review summarizes the structural and developmental events of the liver and pancreas in fish and follows the differentiation process of these organs under control of the transcription factors. It emphasizes the significance of teleost liver and pancreas for disease modeling. The progress in the study of cell lineage will help in creating a role model for better understanding of the disease mechanism and the role of therapeutic agents in minimizing its incidence rate.

LIVER

Anatomical features of fish liver:

The fish liver fills a significant part of the cranial region of the celomic cavity and displays variation in its shape and number of lobes according to species (**Figure 1**). It appears triangular-shaped in Nile tilapia (*Oreochromis niloticus)* (Vicentini et al., 2005) and crescent-shaped in porthole shovelnose catfish (*Hemisorubim platyrhynchos*) (Faccioli et al., 2016). In both species, the liver is bilobed with the left lobe being larger than the right one. Conversely, the right hepatic lobe of grass carp (*Ctenopharyngodon idella*) is more developed than the left hepatic lobe and from which a long process is extended caudally (Mokhtar, 2018). An irregularly shaped liver with three lobes is present in many teleost including zebrafish (*Danio rerio*) and pearl cichlid (*Geophagus brasiliensis)* (Yao et al., 2012). The liver is formed by a single lobe in guppy (*Poecilia reticulata*) (Sousa et al., 2018). In rock goby (*Gobius paganellus)* the liver is pyriform in shape with a smooth dorsal surface and a fissured ventral one (Abusrer and Shtewi, 2023).

In general, the teleost liver is characterized by its reddish coloration due to high vascularization (Bertolucci et al., 2008). The liver color is darker in adult fish compared to juvenile ones (**Figure 2**). The change in liver color occurs in parallel with maturational changes involving other parts of the fish digestive tract (Abdellatif et al., 2024a; Abdellatif et al., 2024b; Fiala et al., 2024). In wild fish, carnivorous species have a reddish-brown liver, while herbivorous species have a light brown one. In farmed fish, especially those of young age, it is lighter in color due to the high fat content of their diets (Taddesse et al., 2014).

It should be noted that in anemia, e.g., those caused by iron deficiency or post-exposure to patho-

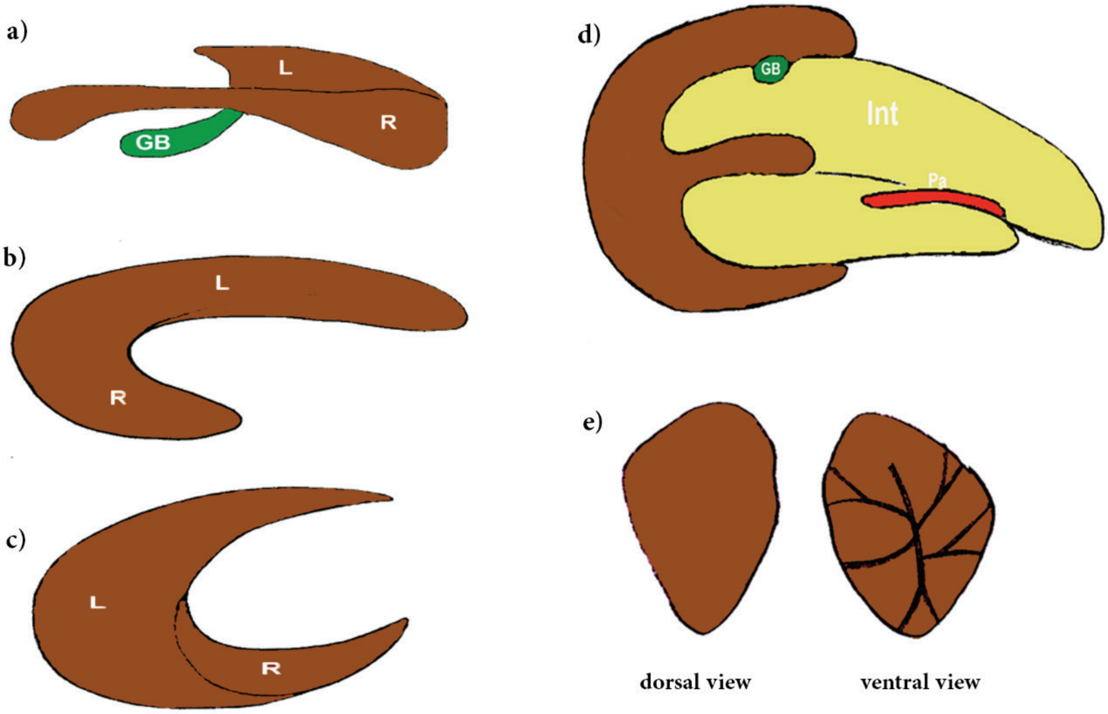

Figure 1. Various forms of liver lobation in teleost. **a**) Grass carp (*Ctenopharyngodon idella*). **b**) Nile tilapia (*Oreochromis niloticus*). **c**) Porthole shovelnose catfish (*Hemisorubim platyrhynchos*). **d**) Zebrafish (*Danio rerio*). **e**) Rock goby (*Gobius paganellus*). GB, gall bladder; Int, intestine; L, left hepatic lobe; Pa, pancreas; R, right hepatic lobe.

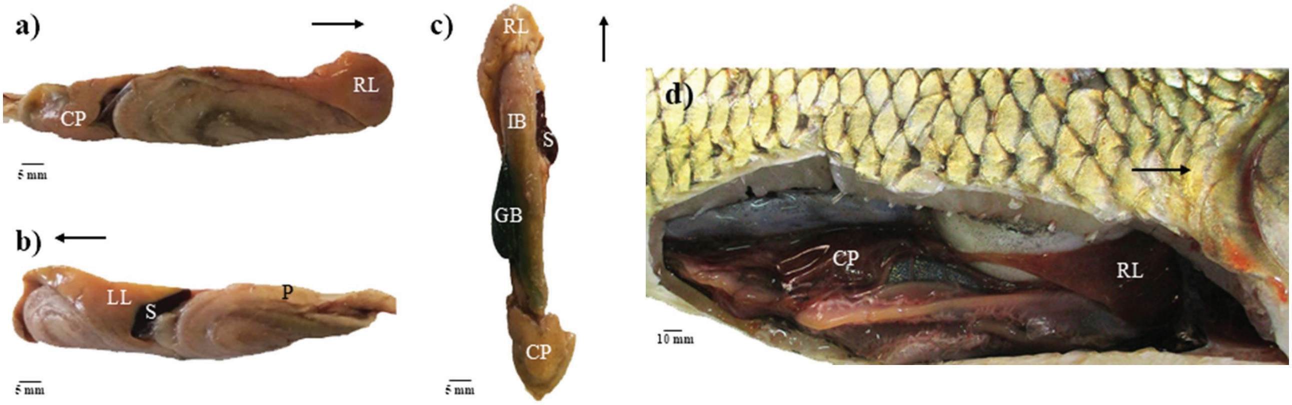

Figure 2. Gross appearance of the liver in juvenile (90 days posthatching) and adult grass carp (*Ctenopharyngodon idella*). Adopted from Fiala (2023). **a**) Right, **b**) left, **c**) ventral views of the liver in juvenile fish. **d**) Right view of the liver in adult fish. The arrow direction indicates the head position. Note the darker coloration of the liver of adult fish compared to that of juvenile ones. RL, right hepatic lobe; LL, left hepatic lobe; CP, caudal process; GB, gall bladder; IB, intestinal bulb; P, pancreas (mesenteric part); S, spleen.

genic viruses, the liver might appear pale in color. However, caution should be applied while interpreting a pale liver color as physiological fluctuations in hepatic glycogen or lipid contents as well as reproductive status can also significantly influence liver color (Buddington and Kuz'mina, 2000).

Histological features of fish liver:

The liver is a parenchymatous organ consisting of parenchyma and stroma. The liver parenchyma is formed mainly by hepatocytes, about 80% of the hepatic parenchyma, which are arranged into hepatic cords, separated from each other by hepatic sinusoids. Phagocytic cells are also found in-between these cords (Franco-Belussi et al., 2012). Except for a limited number of fish species, e.g., lamprey (*Petromyzon marinus*), there is no basal membrane beneath the hepatic sinusoidal lining (Nejedli and Gajger, 2013). Other cells of the liver include Kupffer cells, hepatic stellate cells and endothelial cells which play an important role in proper functioning of hepatocytes (Malik et al., 2002).

The hepatic sinusoids are lined by endothelial cells with spindle-shaped nuclei. Microvillar projections arise from the upper border of hepatocytes and extend into the space of Disse, a space found between the sinusoidal lining and the hepatocytes (Yao et al., 2012).

Typical characteristics of fish hepatocytes include a round central nucleus and eosinophilic cytoplasm containing abundant rough endoplasmic reticulum, lysosomes, and mitochondria (Yao et al., 2012). In female fish the cytoplasm could appear basophilic, especially during breeding season, due to excessive production of vitellogenin. Moreover, the cytoplasm appears vacuolated according to the proportion of the dietary fats (Taddesse et al., 2014). Excessive accumulation of lipid droplets inside the cytoplasm of hepatocytes displaces the nuclei to the periphery of the cells (Azab, 2012).

The hepatocytes display three arrangements: tubular, cord-like, and solid. In the tubular form, the hepatocytes are arranged into a double-layered structure around narrow and irregular sinusoids, e.g., Otocephala. In the cord-like form, the hepatocytes are arranged into a single-layered structure around sinusoids, e.g., Euteleostei. In the solid form, the hepatocytes form several layers around narrow sinusoids, e.g., Elopomorph (Akiyoshi and Inoue, 2004; Noskor et al., 2013).

The liver stroma includes the hepatic capsule and septa. In plectognathid fishes, e.g., fahaka pufferfish (*Tetraodon lineatus*), the liver is covered by a loose connective tissue capsule with a single layer of squamous cells (Azab, 2012), but in Persian tooth-carp (*Acipenser stellatus*) the liver is enclosed by a dense connective tissue capsule with a layer of cuboidal cells (Monsefi et al., 2010). A meshwork of reticular fibers encircles the hepatic sinusoids and the vascular elements of the liver in grass carp (*Ctenopharyngodon idella*) (Mokhtar, 2018). Noteworthy that the fish liver, except for medaka (*Oryzias latipes*), lacks the typical lobulation pattern frequently seen in mammalian liver due to lack of interlobular connective tissue septa (Hardman et al., 2007).

The arrangement of vascular and biliary tracts of the liver differs between fish and mammals. In mammals, the hepatic cords extend from the portal triad toward the hepatic central vein, but in fish the portal triad is not detected (Akiyoshi and Inoue, 2004; Noskor et al., 2013). Moreover, in mammals, portal triads, collections of branches from the portal vein, hepatic artery, and bile duct, are found around each hepatic lobule. In fish, the bile ducts and the hepatic vascular elements are randomly distributed within the hepatic parenchyma (Figueiredo-Fernandes et al., 2007; Noskor et al., 2013). In zebrafish the hepatic artery is not clearly detected, and the hepatocytes are organized in double-layered cords in a radial manner around the central vein (Yao et al., 2012).

Developmental regulation of fish liver:

The process of liver formation involves three sequential stages: hepatoblast specification, hepatocyte differentiation, and liver growth (Field et al., 2003a) (**Figure 3**). The first steps of zebrafish liver formation involve activation of Prox1 and Hhex in the endodermal cells of the hepatic bud at 22 hpf which in turn induces hepatoblast specification (Jin et al., 2023). The hepatic bud appears dorsal to the yolk sac 32-48 hpf. By 32 hpf, the expression of genes responsible for hepatocyte differentiation such as ceruloplasmin and wnt2bb, is noticed (Korzh et al., 2001; Poulain and Ober, 2011). The Gata6 and Hhex further regulate the differentiation of hepatocytes which in turn induces further proliferation of the cells of the developing hepatic bud. The formation of the biliary system is driven by Notch signaling and members of the Onecut (OC) family of transcription factors, e.g., Hnf6. The liver growth commences 60-72 hpf and continues until the liver reaches its mature size (Chu and Sadler, 2009).

The hepatic primordial cells are bipotent cells.

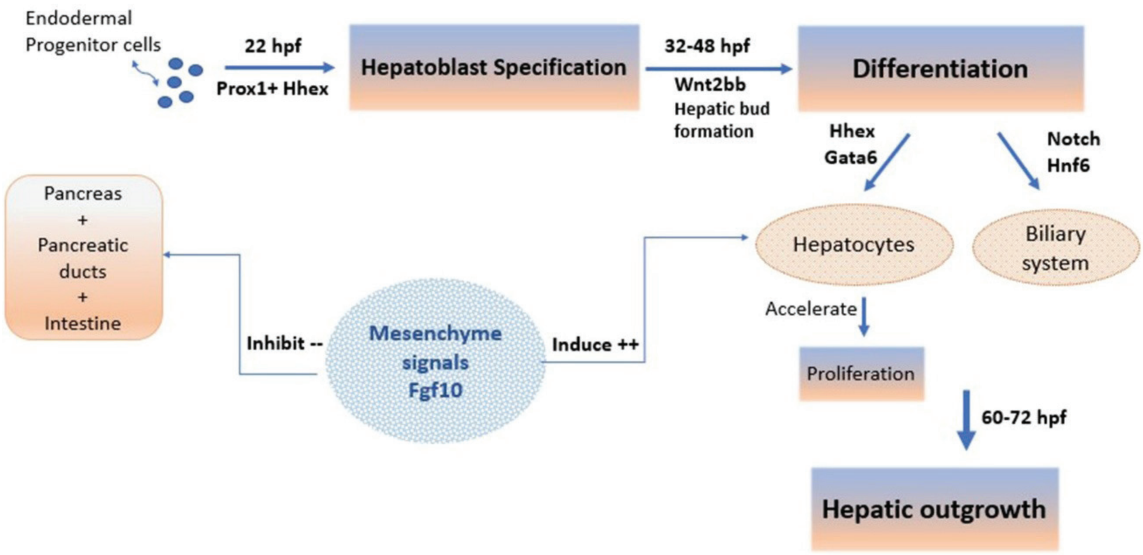

Figure 3. Stages of early development of teleost liver using zebrafish as a model. Fgf10, Fibroblast growth factor 10; Gata6: GATA-binding factor 6; Hhex, Hematopoietically expressed homeobox; Hnf6, Hepatocyte nuclear factor 6; Hpf, hours post fertilization; Prox1, Prospero homeobox protein 1; Wnt2bb, Wingless-type MMTV integration site family, member 2Bb.

They induce the formation of both liver hepatocytes and bile duct cholangiocytes (Gaudio et al., 2009). The precursors of hepatocytes and cholangiocytes detach from the hepatic bud (Duncan, 2003; Zaret, 2002). The hepatic duct is formed from expansion of a stalk connecting the hepatic primordium to the developing gut tube by 34-50 hpf in zebrafish (Field et al., 2003b).

The final stages of hepatic growth require the formation of the vascular tracts (Korzh et al., 2008). This stage includes three different subdivisions: non-vascular, endothelium-dependent and vascular-dependent growth. The vascular-dependent stage of liver growth needs the circulation of the blood into the sinusoids (Korzh et al., 2008).

In most vertebrates, the liver and pancreas share the same origin from the foregut endoderm (Deutsch et al., 2001). The release of Fgf10 by the mesenchyme inhibits the hepatic progenitor cells from differentiating into pancreatic cells (Dong et al., 2007; Yan et al., 2015). Further, mesenchymal molecules play a role in the formation of intrahepatic vascular tracts, Ito cells, and hepatic Kupffer cells (Cassiman et al., 2006).

The process of different organ development in zebrafish occurs during the first 24 hours post fertilization (hpf). The fish larvae are capable of swimming by 24 hpf. Within the first few days post fertilization (dpf) the different systems are formed, and the larvae can depend on external food (Chu and Sadler, 2009).

Using light microscopy, the hepatic primordium is detected from the first day post hatching in porthole shovelnose catfish (*Hemisorubim platyrhynchos*) and appears composed of clusters of undifferentiated cells (Faccioli et al., 2016). Zadmajid et al. (2019) observed the liver of Levantine scraper (*Capoeta damascina*) larvae as a mass of cells between the yolk sac and the developing gut tube. The liver of tomato clownfish (*Amphiprion frenatus*) exhibited a noticeable increase in the number and size of hepatocytes during the early post hatching stage (Putra et al., 2012). The hepatocytes of European catfish (*Silurus glanis L.*) revealed no signs of lipid accumulation at 3-5 days posthatching, but their cytoplasmic glycogen content was evidenced by the end of the first week concomitant with active utilization of exogenous food (Kozarić et al., 2008).

PANCREAS

Anatomical features of fish pancreas:

The fish pancreas consists of endocrine and exocrine compartments which vary in their anatomical arrangement among the different teleost species (Chakrabarti and Ghosh, 2012; Youson et al., 2006).

The exocrine pancreas contributes to food digestion through the discharge of pancreatic secretions rich in several enzymes including trypsin, amylase, and carboxypeptidase A, into the gut lumen. The endocrine portion contains cells that secrete hormones regulating blood glucose levels (Weinrauch et al., 2022).

The distribution of fish pancreatic tissue shows great variation among different species (**Table 1**). In general, it appears in the form of discrete yellow glandular masses that infiltrate the gut mesentery (Hassan, 2013). In zebrafish (*Danio rerio*), the pancreas is organized into 4 lobes: the gallbladder-spleen lobe, the middle lobe, the left lobe, and the ventral lobe (Chen et al., 2007). In grass carp (*Ctenopharyngodon idella*), the pancreas is detected as dispersed masses within the mesentery. In the latter, and similar to most cyprinids, the pancreas also disseminates within the parenchyma of the liver and spleen, forming hepatopancreas and splenopancreas, respectively (Mokhtar, 2015).

The intrahepatic position of fish pancreas has been determined in several fish species including iridescent shark catfish (*Pangasius hypophythalmus*) (Seyrafi et al., 2009), molly (*Poecilia sphenops*) (Hussein et al., 2023), and Nile tilapia (*Oreochromis niloticus*) (Vicentini et al., 2005). The hepatopancreas has been estimated to fill about 5% of total liver area, as in common pandora (*Pagellus erythinus*); that could increase to 14% of total liver area, as in Whiting (*Merlangius merlangus euxinus*) (Nejedli and Gajger, 2013). The splenopancreas has been noted in bassan barbel (*Barbus pectoralis*) (Mahabady et al., 2012), common carp (*Cyprinus carpio*), and binni (*Mesopotamichthys sharpeyi*) (Akoul and Al-Jowari, 2019). In view of this, the fish pancreas has diverse arrangements that may constitute a difficulty during specimen collection and should be thoroughly considered for achieving proper research and diagnostic outcomes.

Table 1. Various forms of pancreas distribution in teleost.

Pancreas form **Species**	**Mesenteric**	**Hepato-pancreas**	**Spleno-pancreas**	**Reference**
Zebrafish (*Danio rerio*)	+ (4 lobes)			(Chen et al., 2007)
Nile tilapia (*Oreochromis niloticus*)		+		(Morrison et al., 2004)
Grass carp (*Ctenopharyngodon idella*)	+	+	+	(Fiala, 2023; Mokhtar, 2015)
Rock Goby (*Gobius paganellus*)		+		(Abusrer and Shtewi, 2023)
Pearl cichlid (*Geophagus brasiliensis*)		+		(Sales et al., 2017)
Iridescent shark catfish (*Pangasius hypophthalmus*)		+		(Seyrafi et al., 2009)
Common pandora (*Pagellus erythinus*)		+ (~5% of total liver area)		(Nejedli and Gajger, 2013)
Whiting (*Merlangius merlangus euxinus*)		+ (~14% of total liver area)		(Nejedli and Gajger, 2013)
Molly (*Poecilia sphenops*)	+	+		(Hussein et al., 2023)
African catfish (*Clarias gariepinus*)	+			(Karkit et al., 2021)
Long Whiskers Catfish (*Mystus gulio*)	+			(Ghosh and Chakrabarti, 2016)
Orangefin labeo (*Labeo calbasu*)	+	+	+	(Ghosh and Chakrabarti, 2016)

Histological features of fish pancreas:

The mesenteric pancreas of fish contains both exocrine and endocrine components. In striped dwarf catfish (*Mystus vittatus*), the exocrine pancreas is composed of serous acini and scattered endocrine islets (Chakrabarti and Ghosh, 2015). In other species, e.g., zebrafish (*Danio rerio*), the endocrine part, often referred to as the Brockman body, is composed of aggregations of several islets, each of which consists mainly of alpha, beta, and delta cells, which are responsible for secretion of glucagon, insulin, and somatostatin hormones, respectively (Yao et al., 2012). These hormone-producing cells were also noticed among the intestinal loops and within the wall of the main pancreatic ducts in common carp (*Cyprinus carpio*) (Akoul and Al-Jowari, 2019; Kong et al., 2002).

The endocrine cells of fish pancreas are characterized by their prominent nuclei and contain abundant smooth endoplasmic reticulum, ribosomes, mitochondria, and zymogen granules within their cytoplasm (Gilloteaux et al., 2008).

In brown spotted grouper (*Epinephelus chlorostigma*), the pancreatic acini appear embedded in the mesenteric adipose tissue. These acini are characterized by their granular cytoplasm. While the endocrine pancreatic islets consist of cellular aggregations and are encircled by connective tissue and blood capillaries to convey the hormones directly to the blood stream (Hassan, 2013).

In grass carp (*Ctenopharyngodon idella*), the pancreatic acini of the hepatopancreas are distributed along the course of portal vein branches. These acini are arranged as clusters of pyramidal cells with basal nuclei and prominent nucleoli and contain eosinophilic zymogen granules within their cytoplasm. The acini are separated from the hepatocytes by a thin connective tissue capsule (**Figure 4**). The intrahepatic part of the pancreas lacks endocrine cells, which appear exclusive to the extrahepatic parts of the pancreas (Mokhtar, 2015).

The distribution of pancreatic acini inside the liver of teleost usually follows the course of portal vein branches; however, they could extend around the hepatic artery and main bile ducts. A species-specific pattern of arrangement has been reported for the intrahepatic pancreas. In Nile tilapia (*Oreochromis niloticus*), the pancreatic acini were detected around the major vascular tracts at the hepatic hilum. These acini follow the venous tract within the hepatic parenchyma and diminish towards the smaller branches, so the efferent vessels appear naked. The hilum is penetrated by the pancreatic-venous biliary arteriolar tract (P-VBAT). This tract is split into smaller tracts such as pancreatic-venous tract (P-VT), pancreatic-venous arteriolar tract (P-VAT), pancreatic-venous biliary tract (P-VBT) and venous tracts (VT) without the pancreas (Akiyoshi and Inoue, 2004; Figueiredo-Fernandes et al., 2007). The perivascular distribution of pancreatic acini were also recorded in grass carp (*Ctenopharyngodon idella*) (Fiala, 2023; Mokhtar, 2015) (**Figure 4**) and guppy (*Poecilia reticulata*) (Sousa et al., 2018).

Developmental regulation of fish pancreas:

In zebrafish, the pancreas originates from the gut endoderm by two buds: the dorsal and ventral pancreatic buds (Tiso et al., 2009) (**Figure 5**). The dorsal pancreatic bud is obviously detected at 24 hpf dorsal to the gut tube and formed from primary endocrine cells, arranged in the form of a principal islet. This bud is displaced to the right side after the gut looping. The ventral pancreatic bud appears 34 hpf rostral to the dorsal one and expands to form the exocrine pancreas around the principal islet (Field et al., 2003b). The duct cell, pancreatic acini, and the second wave endocrine cells originated from the ventral bud. The duct system includes the intra- and extrahepatic ducts which contribute to the formation of second wave endocrine cells (late islets) (Moro et al., 2009; Wang et al., 2011). During early stage of pancreatic formation, the expression of pdx1 is necessary for specification of the endocrine precursors, while ptf1a is required for the exocrine precursors (Biemar et al., 2001; Zecchin et al., 2004).

The progenitors of the endocrine and exocrine cells are segregated at the early stage of pancreas development and remain dispersed in the vicinity of the intestinal tract, and some of them remain attached to the hepatic surface (Faccioli et al., 2016).

In many teleost species, the pancreas appears as a cellular mass located between the yolk sac and the gut tube at hatching time. (Falk-Petersen and Hansen, 2003), In gilthead sea bream (*Sparus aurata*) (Elbal et al., 2004) and spotted wolffish (*Anarhichas minor*) (Falk-Petersen and Hansen, 2003), both endocrine and exocrine cells are distinguished at the time of hatching. In Indian walking catfish (*Clarias magur*) the pancreatic primordium was detected on the first day posthatching and the zymogen granules appeared at a later time (Kumari et al., 2021). In yellow catfish (*Pelteobagrus fulvidraco*), the exocrine acini and zymogen granules were clearly detected

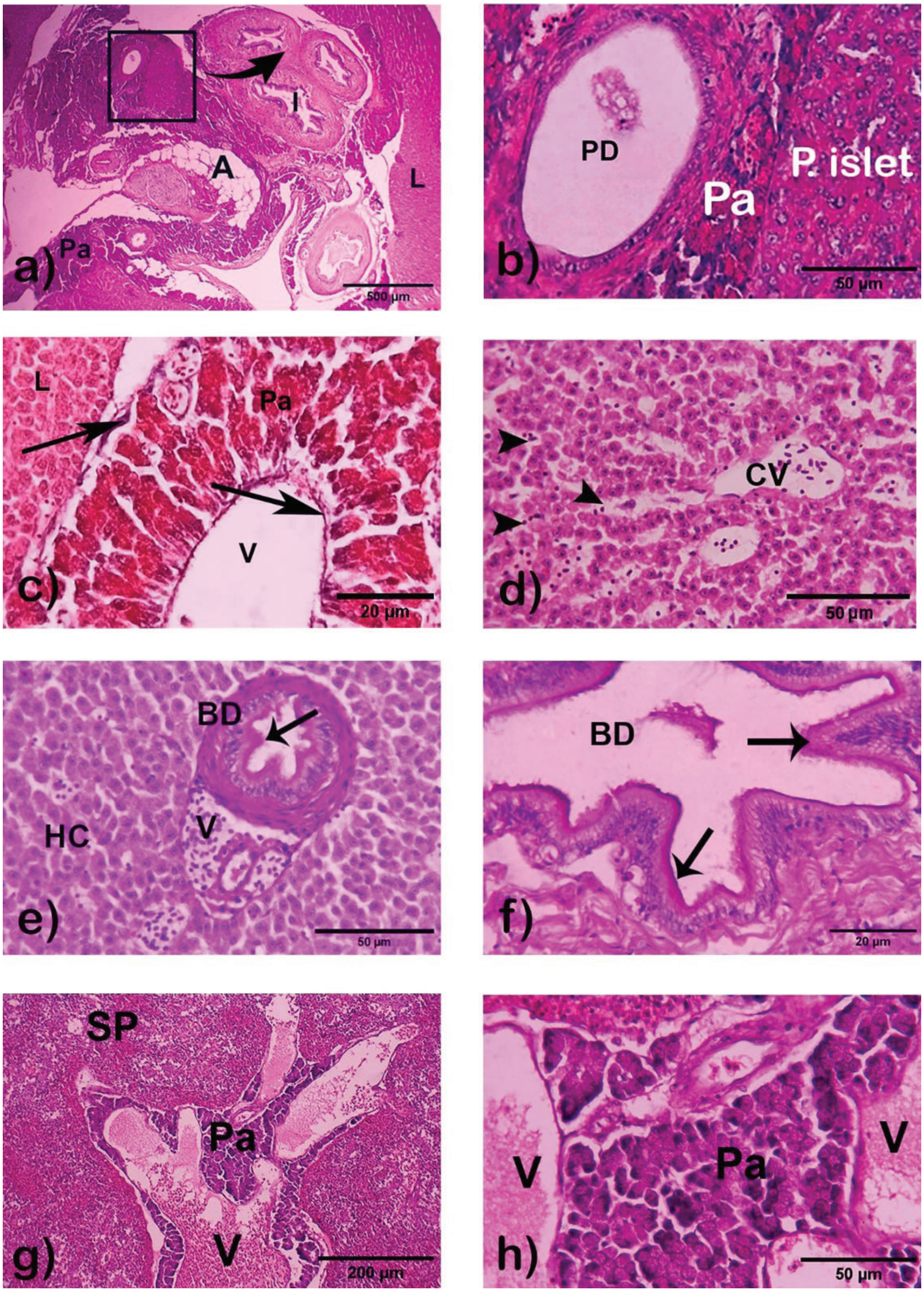

Figure 4. Histological features of the liver and pancreas of an adult grass carp (*Ctenopharyngodon idella*). Adopted from Fiala (2023). **a**) The mesenteric portion of the pancreas consists of pancreatic acini (Pa) in-between the adipose tissue patches (A). I, Intestine; L, liver. H&E stain. **b**) High magnification of Figure 4a showing a large pancreatic islet (P. islet), pancreatic acini (Pa), and a pancreatic duct (PD). **c**) Collagen fibers (arrows) within the wall of an intrahepatic pancreatic-venous tract (P-VT). Masson's trichrome stain. **d**) The hepatic sinusoids (arrowheads) are connected to a centrally located vein (CV). H&E stain. **e, f**) Strong positive PAS staining of apical brush border (arrows) of the intrahepatic (e) and the extrahepatic (f) bile ducts (BD). HC, hepatocytes. PAS stain. **g**) Splenic parenchyma (SP) showing pancreatic tissue, mainly of exocrine nature, (Pa) around branches of the splenic vein (V). H&E stain. **h)** High magnification of Figure 4g showing the structure of an intrasplenic pancreatic-venous tract.

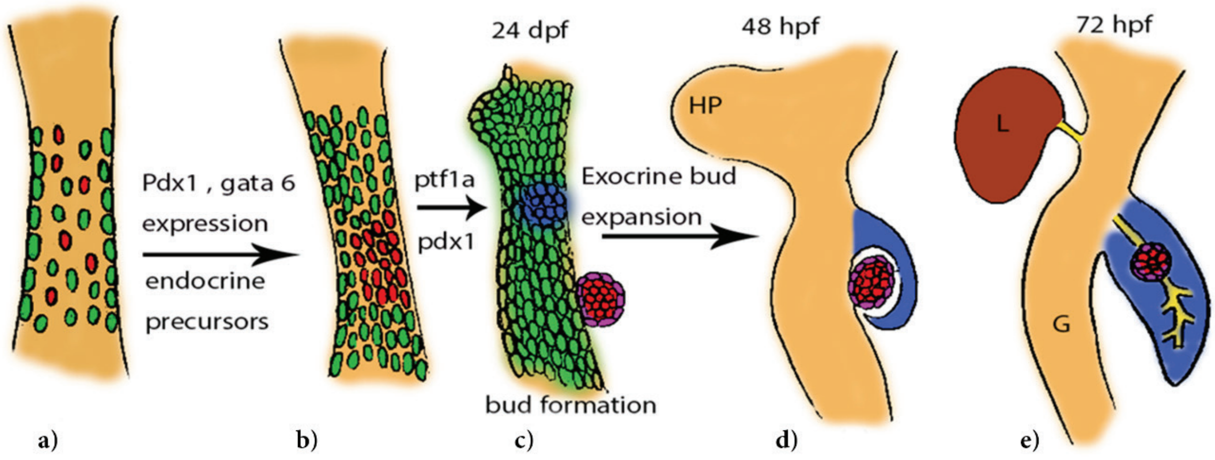

Figure 5. HStages of early development of teleost pancreas using zebrafish as a model. **a**, **b**) The pancreatic precursors emerge from the gut wall after expression of pdx1 (pancreatic and duodenal homeobox 1) and gata 6 (GATA-binding factor 6). **c**) The endocrine bud (red) is displaced posterior to the exocrine one (blue) after the process of gut looping. Ptf1a (pancreas transcription factor 1 subunit alpha) induces exocrine acini, duct cells, and secondary endocrine cells. **d, e**) The hepatic primordium (HP) increases in size, and the exocrine bud expands to enclose the endocrine pancreas. The duct system is formed by this stage and connects the pancreas to the gut lumen. G, gut tube; hpf, hours post fertilization; L, liver.

at 4 days posthatching (dph) and the endocrine cells were noticed at 5 dph (Yang et al., 2010).

The appearance of pancreatocytes shows maturational changes with fish age. In California halibut (*Paralichthys californicus*) (Gisbert et al., 2004) and yellow catfish (*Pelteobagrus fulvidraco*) (Yang et al., 2010), when the larvae start exogenous feeding, the pancreatocytes reveal a pronounced increase in size and a more basophilic staining.

FISH LIVER AND PANCREAS IN DISEASE MODELLING

Zebrafish has been regarded as an important model for liver embryogenesis studies. Reasons for this include the translucent nature of their eggs, the rapid development of their embryos, and the short incubation time, i.e., the time from fertilization to hatching takes 48-72 hours, making them a more efficient model than other animals with in utero developing embryos (Howe et al., 2013). Zebrafish embryos have been used not only to study molecular factors involving liver development under normal circumstances (Yan et al., 2022; Yi et al., 2018), but also under imbalance of several dietary factors including copper, selenium, and alpha-lipoic acid (Li et al., 2022; Tompach et al., 2024; Zhu et al., 2023).

The structure of fish liver shares several similarities with the human liver in terms of hepatocyte organization and mechanisms of nutrient metabolism (Goldsmith and Jobin, 2012). Studying metabolic and lifestyle factors, e.g., exercise, associated with the incidence of non-alcoholic fatty liver disease (NAFLD) using fish as a model is trending (Chang et al., 2023; Zou et al., 2021; Zou et al., 2023). Several teleost species have also been utilized to monitor various mechanisms involving storage and metabolism of lipids and carbohydrates within the liver. Among these species are white-spotted rabbitfish (*Siganus canaliculatus*) (Li et al., 2008), Japanese puffer (*Takifugu rubripes*) (Xu et al., 2020), European seabass (*Dicentrarchus labrax*) (Palma et al., 2019), and zebrafish (*Danio rerio*) (Lyssimachou et al., 2015; Roy et al., 2020). Out of all these species, zebrafish provided the greatest insights into the understanding of hepatic biology due to the availability of fish strains with targeted genetic mutations of factors involved in nutrient metabolism including stearoyl-CoA desaturase (*scd*) (Xu et al., 2023), liver enriched antimicrobial peptide 2 (*leap2*) and its receptor growth hormone secretagogue receptor 1a (*ghsr1a*) (Fei et al., 2024), and liver-enriched gene 1 (*leg1*) (Wang et al., 2025).

The liver of both larval and adult fish has been extensively used to evaluate the effect of various deleterious agents on vertebrates' biology. These agents include endocrine disruptors (e.g., bisphenols) (Liu et al., 2023); heavy metals, e.g., cadmium (Chen et al., 2024); micro- and nanoplastics (Brandts et al., 2022; Wang et al., 2022); organic solvents (e.g., toluene) (Sayed et al., 2023; Su et al., 2023); and fire suppressants (Annunziato et al., 2020; Li et al., 2023). Fish species used for these investigations included zebrafish (*Danio rerio*), Japanese medaka (*Oryzias latipes*), and fathead minnow (*Pimephales promelas*).

The fish pancreas displays considerable morphogenetic and endocrine similarities to the human pancreas, especially those related to the basic organization of endocrine cells as well as developmental pathways governing their development and function (Löhr and Hammerschmidt, 2011). Several researches have utilized fish pancreas as a model for studying vertebrate pancreas biology during diabetes (Krishnan and Rohner, 2019). The availability of genetic manipulation tools pertinent to the zebrafish pancreas has enabled the establishment of therapeutic gadgets for diabetes treatment by defining new sources for insulin production from non-beta cell origins (Ye et al., 2015; Yu et al., 2023).

Various areas of research involving the liver and pancreas of fish are shown in **Figure 6**.

CONCLUSIONS

Morphological and developmental features of fish liver and pancreas, as well as their importance in research studies related to lipid storage and metabolism, regeneration in response to damage-induced toxicity, and diabetes, have been reviewed. The diverse localization of fish pancreas across various fish species suggests caution during representative sampling of the whole organ to achieve sufficient outcomes. Although zebrafish remains an excellent model for most of these studies, characterizing additional fish models warrants future studies.

Understanding the developmental events involving the pancreas will help to improve studies focusing on transdifferentiation of pancreatic endocrine cells. Moreover, characterizing the liver biology of several teleost models will enable researchers to test various therapeutic agents and enrich the field of comparative toxicology. Lastly, broadening the spectrum of knowledge related to the functional anatomy of fish liver and pancreas will accelerate screening of novel approaches for the purposes of hepatic regeneration and experimental diabetes.

LIST OF ABBREVIATIONS

Dph: Day posthatching
Fgf10: Fibroblast growth factor 10
Gata6: GATA-binding factor 6
Ghsr1a: Growth hormone secretagogue receptor 1a
Hhex: Hematopoietically expressed homeobox
Hnf6: Hepatocyte nuclear factor 6
Hpf: Hour post fertilization
Leap2: Liver enriched antimicrobial peptide 2
Leg1: Liver-enriched gene 1
NAFLD: Non-alcoholic fatty liver disease
Oc: Onecut
Pdx1: Pancreatic and duodenal homeobox 1

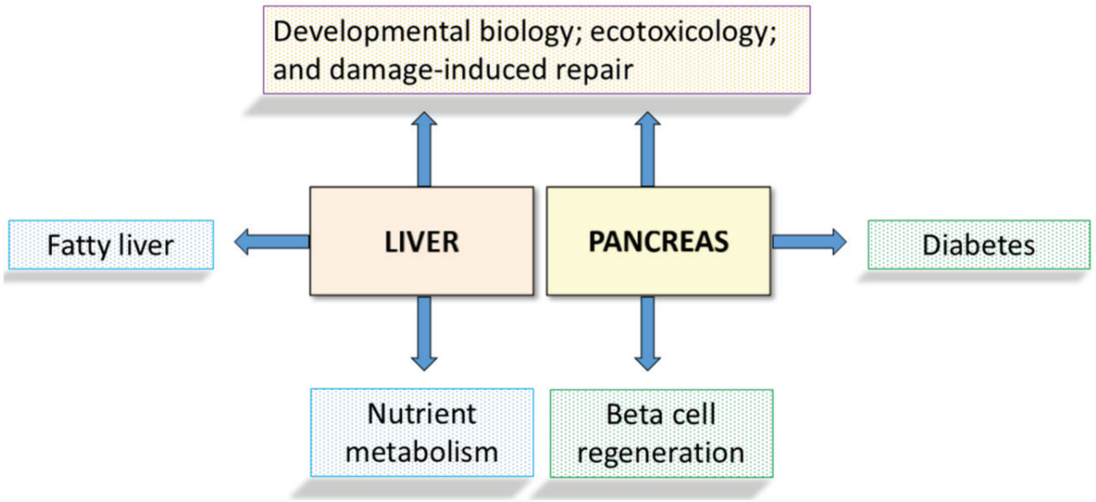

Figure 6. Summary of various research areas involving fish liver and pancreas.

PP: Pancreatic polypeptide
Prox1: Prospero homeobox protein 1
Ptf1a: Pancreas transcription factor 1 subunit alpha
P-VAT : Pancreatic-venous arteriolar tract
P-VBAT: Pancreatic venous biliary arteriolar tract
P-VBT : Pancreatic-venous biliary tract
P-VT: Pancreatic-venous tract
Scd: Stearoyl-CoA desaturase
VT: Venous tract
Wnt2bb: Wingless-type MMTV integration site family, member 2Bb

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All data are included in the published article.

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Authors’ contributions
EF, AA prepared the figures and drafted the manuscript. MS, SE revised the manuscript. All authors accepted the final version of the paper.

REFERENCES

Abdellatif AM, Ateya AI, Hasan KA, Alghamdi MA, Madkour FA (2024a) Spatiotemporal Ultrastructural, Histological, and Morphometric Changes in the Buccal Cavity of Grass Carp (*Ctenopharyngodon idella*) During Fingerling, Yearling, and Adult Stages. Animals 14(21):3162. doi:10.3390/ani14213162

Abdellatif AM, Lashen S, Kandyel RM, Shoeib MB, Madkour FA (2024b) Age-related morphological and ultrastructural changes in the palate and pharyngeal masticatory apparatus of grass carp (*Ctenopharyngodon idella*) juveniles. Tissue Cell 86:102264. doi:10.1016/j.tice.2023.102264

Abusrer SA, Shtewi HH (2023) Morphological and histological structure of hepatopancreas in rock goby *Gobius paganellus* on the western coast of Libya. Open Vet J 13(10):1251-1258. doi:10.5455/OVJ.2023.v13.i10.3

Akiyoshi H, Inoue A (2004) Comparative histological study of teleost livers in relation to phylogeny. Zool. Sci 21(8):841-850.

Akoul MA, Al-Jowari SA-K (2019) Comparative anatomical and histological study of some organs in two fish species *Cyprinus carpio Linnaeus*, 1758 and M*esopotamichthys sharpeyi* (Günther, 1874) (Cypriniformes, Cyprinidae). Bull Iraq nat Hist Mus 15(4):425-441.

Annunziato KM, Doherty J, Lee J, Clark JM, Liang W, Clark CW, Nguyen M, Roy MA, Timme-Laragy AR (2020) Chemical Characterization of a Legacy Aqueous Film-Forming Foam Sample and Developmental Toxicity in Zebrafish (*Danio rerio*). Environ Health Perspect 128(9):97006. doi:10.1289/ehp6470

Azab A (2012) Histological studies on the liver of some Plectognthid fishes (order: Tetraodontiformes), Red Sea, Egypt. Egypt J Aquat Biology Fish 16(4):129-137.

Bertolucci B, Vicentini CA, Vicentini IBF, Bombonato MTS (2008) Light microscopy and ultrastructure of the liver of *Astyanax altiparanae* Garutti and Britski, 2000 (Teleostei, Characidae). Acta Sci Biol Sci 30(1):73-76.

Biemar F, Argenton F, Schmidtke R, Epperlein S, Peers B, Driever W (2001) Pancreas development in zebrafish: early dispersed appearance of endocrine hormone expressing cells and their convergence to form the definitive islet. Dev Biol 230(2):189-203.

Brandts I, Cánovas M, Tvarijonaviciute A, Llorca M, Vega A, Farré M, Pastor J, Roher N, Teles M (2022) Nanoplastics are bioaccumulated in fish liver and muscle and cause DNA damage after a chronic exposure. Environ Res 212(PtA):113433. doi:10.1016/j.envres.2022.113433

Buddington RK, Kuz'mina V. (2000). Digestive System. In Ostrander GK (Ed.), The Laboratory Fish (pp. 173-179). London: Academic Press.

Cassiman D, Barlow A, Vander Borght S, Libbrecht L, Pachnis V (2006) Hepatic stellate cells do not derive from the neural crest. J Hepatol 44(6):1098-1104.

Chakrabarti P, Ghosh SK (2012) Comparative histophysiology of pancreas in *Cirrhinus mrigala* (Hamilton, 1822), *Oreochromis niloticus* (Linnaeus, 1758) and *Wallago attu* (Bloch & Schneider, 1801). Indian J Fish 59(4):93-99.

Chakrabarti P, Ghosh SK (2015) Comparative histological and histochemical studies on the pancreas of *Labeo rohita* (Hamilton, 1822), *Mystus vittatus* (Bloch, 1790) and *Notopterus notopterus* (Pallas, 1769). Int J Aquat Biol 3(1):28-34.

Chanet B, Schnell NK, Guintard C, Chen W-J (2023) Anatomy of the endocrine pancreas in actinopterygian fishes and its phylogenetic implications. Sci Rep 13(1):22501.

Chang C, Li H, Zhang R (2023) Zebrafish facilitate non-alcoholic fatty liver disease research: Tools, models and applications. Liver Int 43(7):1385-1398. doi:10.1111/liv.15601

Chen S, Li C, Yuan G, Xie F (2007) Anatomical and histological observation on the pancreas in adult zebrafish. Pancreas 34(1):120-125.

Chen X, Sun W, Song Y, Wu S, Xie S, Xiong W, Peng C, Peng Y, Wang Z, Lek S, Hogstrand C, Sørensen M, Pan L, Liu D (2024) Acute waterborne cadmium exposure induces liver ferroptosis in Channa argus. Ecotoxicol Environ Saf 283:116947. doi:10.1016/j.ecoenv.2024.116947

Chu J, Sadler KC (2009) New school in liver development: lessons from zebrafish. Hepatology 50(5):1656-1663.

Deutsch G, Jung J, Zheng M, Lóra J, Zaret KSJ (2001) A bipotential precursor population for pancreas and liver within the embryonic endoderm. Development J 128(6):871-881.

Dong PDS, Munson CA, Norton W, Crosnier C, Pan X, Gong Z, Neumann CJ, Stainier DY (2007) Fgf10 regulates hepatopancreatic ductal system patterning and differentiation. Nature Genetics 39(3):397-402.

Duncan SA (2003) Mechanisms controlling early development of the liver. Mech Dev 120(1):19-33. doi:10.1016/s0925-4773(02)00328-3

Elbal M, Hernández MGa, Lozano M, Agulleiro B (2004) Development of the digestive tract of gilthead sea bream (*Sparus aurata L.*). Light and electron microscopic studies. Aquaculture 234(1-4):215-238.

Faccioli CK, Chedid RA, Mori RH, do Amaral AC, Belmont RAF, Vicentini IBF, Vicentini CA (2016) Organogenesis of the digestive system in Neotropical carnivorous freshwater catfish *Hemisorubim platyrhynchos* (Siluriformes: Pimelodidae). Aquaculture 451:205-212.

Falk-Petersen IB, Hansen TK (2003) Early ontogeny of the spotted wolffish (*Anarhichas minor Olafsen*). Aquaculture Research 34(12):1059-1067.

Fei Y, Bao Z, Wang Q, Zhu Y, Lu J, Ouyang L, Hu Q, Zhou Y, Chen L (2024) CRISPR/Cas9-induced LEAP2 and GHSR1a knockout mutant zebrafish displayed abnormal growth and impaired lipid metabolism. Gen Comp Endocrinol 355:114563. doi:10.1016/j.ygcen.2024.114563

Fiala E (2023) Development of the Liver and Pancreas in the Grass Carp Fish. (Master Thesis). Mansoura University, Mansoura, Egypt.

Fiala E, Shoeib MB, Ebada S, Abdellatif AM (2024) Early Post-hatching Development of the Grass Carp Pancreas. MVMJ 25(3):6. doi:10.35943/2682-2512.1245

Field HA, Dong PS, Beis D, Stainier DY (2003b) Formation of the digestive system in zebrafish. II. pancreas morphogenesis. Dev Biol 261(1):197-208.

Field HA, Ober EA, Roeser T, Stainier DY (2003a) Formation of the digestive system in zebrafish. I. Liver morphogenesis. Dev Biol 253(2):279-290.

Figueiredo-Fernandes AM, Fontaínhas-Fernandes AA, Monteiro RA, Reis-Henriques MA, Rocha EJAoA-AA (2007) Spatial relationships of the intrahepatic vascular–biliary tracts and associated pancreatic acini of Nile tilapia, *Oreochromis niloticus* (Teleostei, Cichlidae): A serial section study by light microscopy. Ann Anat 189(1):17-30.

Franco-Belussi L, de Souza Santos LR, Zieri R, Vicentini CA, Taboga SR, de Oliveira C (2012) Liver anatomy, histochemistry, and ultrastructure of *Eupemphix nattereri* (Anura: Leiuperidae) during the breeding season. Zool Sci 29(12):844-848.

Gaudio E, Carpino G, Cardinale V, Franchitto A, Onori P, Alvaro D (2009) New insights into liver stem cells. Digestive and Liver Disease 41(7):455-462.

Genten F, Terwinghe E, Danguy A (2009) Atlas of fish histology. Florida, USA: CRC Press.

Gilloteaux J, Kashouty R, Yono N (2008) The perinuclear space of pancreatic acinar cells and the synthetic pathway of zymogen in *Scorpaena scrofa L.*: Ultrastructural aspects. Tissue Cell 40(1):7-20.

Gisbert E, Piedrahita RH, Conklin DE (2004) Ontogenetic development of the digestive system in California halibut (*Paralichthys californicus*) with notes on feeding practices. Aquaculture 232(1-4):455-470.

Goldsmith JR, Jobin C (2012) Think small: zebrafish as a model system of human pathology. Biomed Res Int 2012(1):817341.

Hardman RC, Volz DC, Kullman SW, Hinton DE (2007) An in vivo look at vertebrate liver architecture: three-dimensional reconstructions from medaka (*Oryzias latipes*). Anat Rec 290(7):770-782. doi:10.1002/ar.20524

Hassan A (2013) Anatomy and histology of the digestive system of the carnivorous fish, the brown-spotted grouper, *Epinephelus chlorostigma* (Pisces; Serranidae) from the Red Sea. Life Sci J 10(2):1-16.

Howe K, Clark MD, Torroja CF, Torrance J, Berthelot C, Muffato M, Collins JE, Humphray S, McLaren K, Matthews L (2013) The zebrafish reference genome sequence and its relationship to the human genome. Nature 496(7446):498-503.

Hussein MM, Sayed RKA, Mokhtar DM (2023) Structural and immunohistochemical characterization of pancreas of Molly fish (*Poecilia sphenops*), with a special reference to its immune role. Microsc Res Tech 86(12):1667-1680. doi:10.1002/jemt.24407

Ishiguro H, Yamamoto A, Nakakuki M, Yi L, Ishiguro M, Yamaguchi M, Kondo S, Mochimaru Y (2012) Physiology and pathophysiology of bicarbonate secretion by pancreatic duct epithelium. Nagoya J Med Sci 74:1-2):1.

Jin Q, Hu Y, Gao Y, Zheng J, Chen J, Gao C, Peng J (2023) Hhex and Prox1a synergistically dictate the hepatoblast to hepatocyte differentiation in zebrafish. Biochem Biophys Res Commun 686:149182. doi:10.1016/j.bbrc.2023.149182

Kong HS, Lee JH, Park KD, Ku SK, Lee HS (2002) Immunohistochemical study of the endocrine cells in the pancreas of the carp, *Cyprinus carpio* (Cyprinidae). J Vet Sci 3(4):303-314.

Korzh S, Emelyanov A, Korzh V (2001) Developmental analysis of ceruloplasmin gene and liver formation in zebrafish. Mech Dev 103(1-2):137-139.

Korzh S, Pan X, Garcia-Lecea M, Winata CL, Pan X, Wohland T, Korzh V, Gong Z (2008) Requirement of vasculogenesis and blood circulation in late stages of liver growth in zebrafish. BMC Dev Biol 8:1-15.

Kozarić Z, Kužir S, Petrinec Z, Gjurčević E, Božić M (2008) The development of the digestive tract in larval European catfish (*Silurus glanis L.*). Anat Histol Embryol 37(2):141-146.

Krishnan J, Rohner N (2019) Sweet fish: Fish models for the study of hyperglycemia and diabetes. J Diabetes 11(3):193-203.

Kumari R, Sharma P, Sarma D, Siddaiah G, Dubey MK, Mir IN, Srivastava P (2021) Ontogeny and development of the gastrointestinal system in Indian walking catfish (*Clarias magur*) during its early development. Fish Physiol Biochem 47:1033-1052.

Li C, Wu Y, Li H, Wang H, Liu JX (2022) Lipid-related metabolism during zebrafish embryogenesis under unbalanced copper homeostasis. Fish Physiol Biochem 48(6):1571-1586. doi:10.1007/s10695-022-01127-8

Li F, Song G, Wang X, Sun Y, Zhou S, Zhang Y, Hua J, Zhu B, Yang L, Zhang W, Zhou B (2023) Evidence for Adverse Effects on Liver Development and Regeneration in Zebrafish by Decabromodiphenyl Ethane. Environ Sci Technol 57(48):19419-19429. doi:10.1021/acs.est.3c06747

Li YY, Hu CB, Zheng YJ, Xia XA, Xu WJ, Wang SQ, Chen WZ, Sun ZW, Huang JH (2008) The effects of dietary fatty acids on liver fatty acid composition and Delta(6)-desaturase expression differ with ambient salinities in *Siganus canaliculatus*. Comp Biochem Physiol B Biochem Mol Biol 151(2):183-190. doi:10.1016/j.cbpb.2008.06.013

Liu J, Lin J, Chen J, Maimaitiyiming Y, Su K, Sun S, Zhan G, Hsu CH (2023) Bisphenol C induces developmental defects in liver and intestine through mTOR signaling in zebrafish (*Danio rerio*). Chemosphere 322:138195. doi:10.1016/j.chemosphere.2023.138195

Löhr H, Hammerschmidt M (2011) Zebrafish in endocrine systems: recent advances and implications for human disease. Annu Rev Physiol 73(1):183-211.

Lyssimachou A, Santos JG, André A, Soares J, Lima D, Guimarães L, Almeida CM, Teixeira C, Castro LF, Santos MM (2015) The Mammalian “Obesogen” Tributyltin Targets Hepatic Triglyceride Accumulation and the Transcriptional Regulation of Lipid Metabolism in the Liver and Brain of Zebrafish. PLoS One 10(12):e0143911. doi:10.1371/journal.pone.0143911

Mahabady MK, Morovvati H, Arefi A, Karamifar M (2012) Anatomical and histomorphological study of spleen and pancreas in Berzem (*Barbus pectoralis*). WJFMS 4(3):263-267.

Malik R, Selden C, Hodgson H (2002) The role of non-parenchymal cells in liver growth. Semin Cell Dev Biol 13(6):425-431. doi:10.1016/s1084952102001301

Mo D, Lv M, Mao X (2024) Using different zebrafish models to explore liver regeneration. Front Cell Dev Biol 12:1485773.

Mokhtar D (2015) Histological, histochemical and ultrastructural characterization of the pancreas of the grass carp (*Ctenopharyngodon idella*). Eur J Anat 19(2):145-153.

Mokhtar D (2018) Cellular and stromal elements organization in the liver of grass carp, *Ctenopharyngodon idella* (Cypriniformes: Cyprinidae). Micron 112(1-14.

Monsefi M, Gholami Z, Esmaeili H-R (2010) Histological and morphological studies of digestive tube and liver of the Persian toothcarp, *Aphanius persicus* (Actinopterygii: Cyprinodontidae). Eur J Biol 69(1):57-64.

Moro E, Gnügge L, Braghetta P, Bortolussi M, Argenton F (2009) Analysis of beta cell proliferation dynamics in zebrafish. Dev Biol 332(2):299-308.

Nejedli S, Gajger IT (2013) Hepatopancreas in some sea fish from different species and the structure of the liver in teleost fish, common pandora, *Pagellus erythinus* (Linnaeus, 1758) and whiting, *Merlangius merlangus euxinus* (Nordmann, 1840). Veterinarski Arhiv 83:441-452.

Noskor SC, Takiue S, Akiyoshi H (2013) Comparative scanning electron microscope studies of hepatic parenchymal architecture in the three infradivisions of teleosts. Bull Faculity of Life and Environmental Science 18:9-16.

Palma PFS, Bock C, Silva TS, Guerreiro PM, Power DM, Pörtner HO, Canário AVM (2019) STC1 and PTHrP Modify Carbohydrate and Lipid Metabolism in Liver of a Teleost Fish. Sci Rep 9(1):723. doi:10.1038/s41598-018-36821-2

Poulain M, Ober EA (2011) Interplay between Wnt2 and Wnt2bb controls multiple steps of early foregut-derived organ development. Development 138(16):3557-3568. doi:10.1242/dev.055921

Putra DF, Abol-Munafi AB, Muchlisin ZA, Chen J-C (2012) Preliminary studies on morphology and digestive tract development of tomato clownfish, *Amphiprion frenatus* under captive condition. AACL Bioflux 5:29-35.

Roy MA, Duche PR, Timme-Laragy AR (2020) The sulfate metabolite of 3,3’-dichlorobiphenyl (PCB-11) impairs Cyp1a activity and increases hepatic neutral lipids in zebrafish larvae (*Danio rerio*). Chemosphere 260:127609. doi:10.1016/j.chemosphere.2020.127609

Sayed AEH, Idriss SK, Abdel-Ghaffar SK, Hussein AAA (2023) Haemato-biochemical, mutagenic, and histopathological changes in *Oreochromis niloticus* exposed to BTX. Environ Sci Pollut Res Int 30(21):59301-59315. doi:10.1007/s11356-023-26604-2

Seyrafi R, Najafi G, Rahmati-Holasoo H, Hajimohammadi B, Shamsadin AS (2009) Histological study of hepatopancreas in iridescent shark catfish (*Pangasius hypophthalmus*). Anim Vet Adv 8(7):1305-1307.

Sousa S, Rocha MJ, Rocha E (2018) Characterization and spatial relationships of the hepatic vascular–biliary tracts, and their associated pancreocytes and macrophages, in the model fish guppy (*Poecilia reticulata*): A study of serial sections by light microscopy. Tissue Cell 50:104-113.

Su L, Sha H, Liu J, Yu L, Li H, Wang R (2023) 2,4-Dinitrotoluene (2,4-DNT) exposure induces liver developmental damage and perturbs lipid metabolism and oxygen transport gene expression in zebrafish (*Danio rerio*). Environ Sci Pollut Res Int 30(30):76104-76111. doi:10.1007/s11356-023-27843-z

Taddesse F, Huh M, Bai SC, Vijverberg J (2014) Histological changes of liver in overfed young nile tilapia. JFAS 9(2):63-74.

Tao T, Peng J (2009) Liver development in zebrafish (*Danio rerio*). J Genet Genom 36(6):325-334. doi:10.1016/S1673-8527(08)60121-6

Tiso N, Moro E, Argenton F (2009) Zebrafish pancreas development. Mol Cell Endocrinol 312(1-2):24-30.

Tocher DR, Bendiksen EÅ, Campbell PJ, Bell JG (2008) The role of phospholipids in nutrition and metabolism of teleost fish. Aquaculture 280(1-4):21-34.

Tompach MC, Gridley CK, Li S, Clark JM, Park Y, Timme-Laragy AR (2024) Comparing the effects of developmental exposure to alpha lipoic acid (ALA) and perfluorooctanesulfonic acid (PFOS) in zebrafish (*Danio rerio*). Food Chem Toxicol 186:114560. doi:10.1016/j.fct.2024.114560

Vicentini C, Franceschini-Vicentini I, Bombonato M, Bertolucci B, Lima S, Santos A (2005) Morphological study of the liver in the teleost *Oreochromis niloticus*. Int J Morphol 23(3):211-216.

Wang C, Hou M, Shang K, Wang H, Wang J (2022) Microplastics (Polystyrene) Exposure Induces Metabolic Changes in the Liver of Rare Minnow (*Gobiocypris rarus*). Molecules 27(3):584. doi:10.3390/molecules27030584

Wang J, Xie A, Fang W, Zhu H, Ye C, Peng J (2025) Zebrafish leg1a and leg1b double null mutant accumulates lipids in the liver. Biochem Biophys Res Commun 751:151418. doi:10.1016/j.bbrc.2025.151418

Wang Y, Rovira M, Yusuff S, Parsons MJ (2011) Genetic inducible fate mapping in larval zebrafish reveals origins of adult insulin-producing β-cells. Development 138(4):609-617.

Weinrauch AM, Fehrmann F, Anderson WG (2022) Sustained endocrine and exocrine function in the pancreas of the Pacific spiny dogfish post-feeding. Fish Physiol Biochem 48(3):645-657. doi:10.1007/s10695-022-01070-8

Xu H, Meng X, Jia L, Wei Y, Sun B, Liang M (2020) Tissue distribution of transcription for 29 lipid metabolism-related genes in *Takifugu rubripes*, a marine teleost storing lipid predominantly in liver. Fish Physiol Biochem 46(4):1603-1619. doi:10.1007/s10695-020-00815-7

Xu SS, Li Y, Wang HP, Chen WB, Wang YQ, Song ZW, Liu H, Zhong S, Sun YH (2023) Depletion of stearoyl-CoA desaturase (scd) leads to fatty liver disease and defective mating behavior in zebrafish. Zool Res 44(1):63-77. doi:10.24272/j.issn.2095-8137.2022.167

Yan C, Zheng W, Gong Z (2015) Zebrafish fgf10b has a complementary function to fgf10a in liver and pancreas development. Mar Biotechnol 17(2):162-167. doi:10.1007/s10126-014-9604-x

Yan L, Gao S, Zhu J, Zhou J (2022) Irf2bp2a regulates liver development via stabilizing P53 protein in zebrafish. Biochim Biophys Acta Gen Subj 1866(10):130186. doi:10.1016/j.bbagen.2022.130186

Yang R, Xie C, Fan Q, Gao C, Fang L (2010) Ontogeny of the digestive tract in yellow catfish *Pelteobagrus fulvidraco* larvae. Aquaculture 302(1-2):112-123.

Yao Y, Lin J, Yang P, Chen Q, Chu X, Gao C, Hu J (2012) Fine structure, enzyme histochemistry, and immunohistochemistry of liver in zebrafish. Anat Rec 295(4):567-576.

Ye L, Robertson MA, Hesselson D, Stainier DY, Anderson RM (2015) Glucagon is essential for alpha cell transdifferentiation and beta cell neogenesis. Development 142(8):1407-1417. doi:10.1242/dev.117911

Yi X, Yu J, Ma C, Li L, Luo L, Li H, Ruan H, Huang H (2018) Yap1/Taz are essential for the liver development in zebrafish. Biochem Biophys Res Commun 503(1):131-137. doi:10.1016/j.bbrc.2018.05.196

Yilmaz O, Sullivan CV, Bobe J, Norberg B (2024) The role of multiple vitellogenins in early development of fishes. Gen Comp Endocrinol 351:114479. doi:10.1016/j.ygcen.2024.114479

Youson J, Al-Mahrouki A, Amemiya Y, Graham L, Montpetit C, Irwin D (2006) The fish endocrine pancreas: review, new data, and future research directions in ontogeny and phylogeny. Gen Comp Endocrinol 148(2):105-115.

Yu J, Ma J, Li Y, Zhou Y, Luo L, Yang Y (2023) Pax4-Ghrelin mediates the conversion of pancreatic ε-cells to β-cells after extreme β-cell loss in zebrafish. Development 150(6): dev201306. doi:10.1242/dev.201306

Zadmajid V, Sørensen SR, Butts IAE (2019) Embryogenesis and early larval development in wild-caught Levantine scraper, *Capoeta damascina* (Valenciennes, 1842). J Morphol 280(1):133-148.

Zaret KS (2002) Regulatory phases of early liver development: paradigms of organogenesis. Nat Rev Genet 3(7):499-512.

Zecchin E, Mavropoulos A, Devos N, Filippi A, Tiso N, Meyer D, Peers B, Bortolussi M, Argenton F (2004) Evolutionary conserved role of ptf1a in the specification of exocrine pancreatic fates. Dev Biol 268(1):174-184.

Zhu Y, Hu J, Zeng S, Gao M, Guo S, Wang M, Hong Y, Zhao G (2023) L-selenomethionine affects liver development and glucolipid metabolism by inhibiting autophagy in zebrafish embryos. Ecotoxicol Environ Saf 252:114589. doi:10.1016/j.ecoenv.2023.114589

Zou Y, Chen Z, Sun C, Yang D, Zhou Z, Peng X, Zheng L, Tang C (2021) Exercise Intervention Mitigates Pathological Liver Changes in NAFLD Zebrafish by Activating SIRT1/AMPK/NRF2 Signaling. Int J Mol Sci 22(20):10940. doi:10.3390/ijms222010940

Zou YY, Tang XB, Chen ZL, Liu B, Zheng L, Song MY, Xiao Q, Zhou ZQ, Peng XY, Tang CF (2023) Exercise intervention improves mitochondrial quality in non-alcoholic fatty liver disease zebrafish. Front Endocrinol 14:1162485. doi:10.3389/fendo.2023.1162485