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Review

# Maternal immunity in fish

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ABSTRACT

Both innate and adaptive immune-relevant factors are transferred from mother to offspring in fishes. These maternally-transferred factors include IgM, lysozymes, lectin, cathelicidin and complement components. Recently, yolk proteins, phosvitin and lipovitellin, have been shown to be maternally-transferred factors, functioning in the defense of teleost larvae against pathogens. Among these factors, the mode of action of complement components and yolk proteins has been explored, whereas that of all the other factors remains elusive. At present, the transfer mechanisms of maternally-derived immune factors are largely unknown although those of IgM and yolk protein transmission from mother to offspring have been reported in some fishes. Maternal transfer of immunity is affected by many elements, including biological factors, such as age and maturation, and environmental conditions experienced by brood fish, such as pathogens and nutritional supply. Practically, the manipulation of maternal immunity transfer can be used to enhance the survival rate of fish larvae.



**Contents**



## 1. Introduction

Maternal immunity refers to the immunity transferred across the placenta, colostrum, milk or eggs from mother to offspring, which is supposed to play a key role to protect the vulnerable offspring against pathogenic attacks. Maternal immunity was initially described in mammals and birds more than 100 years ago (Ehrlich, 1892; Klemperer, 1893), and has now been documented among different vertebrates such as mammals (Leach et al., 1990; Dardillat et al., 1978; Gustafsson et al., 1994; Sadeharju et al., 2007), birds (Kissling et al., 1954; reviewed in Brambell, 1970; Heller et al., 1990; Bencina et al., 2005; Hamal et al., 2006), reptiles (Schumacher et al., 1999), amphibians (Poorten and Kuhn, 2009) and fishes (reviewed in Zapata et al., 2006; reviewed in Swain and Nayak, 2009) as well as in invertebrates including insect (Moret and Schmid-Hempel, 2001; Zanchi et al., 2011), shrimp (Huang and Song, 1999) and amphioxus (Liang et al., 2009).

*Abbreviations:* Vg, vitellogenin; Pv, phosvitin; Lv, lipovitellin; CP, classical pathway; AP, alternative pathway; LP, lectin pathway; MBL, mannose-binding lectin; PAMPs, pathogen-associated molecular patterns; LPS, lipopolysaccharide; LTA, lipoteichoic acid; PGN, peptidoglycan.

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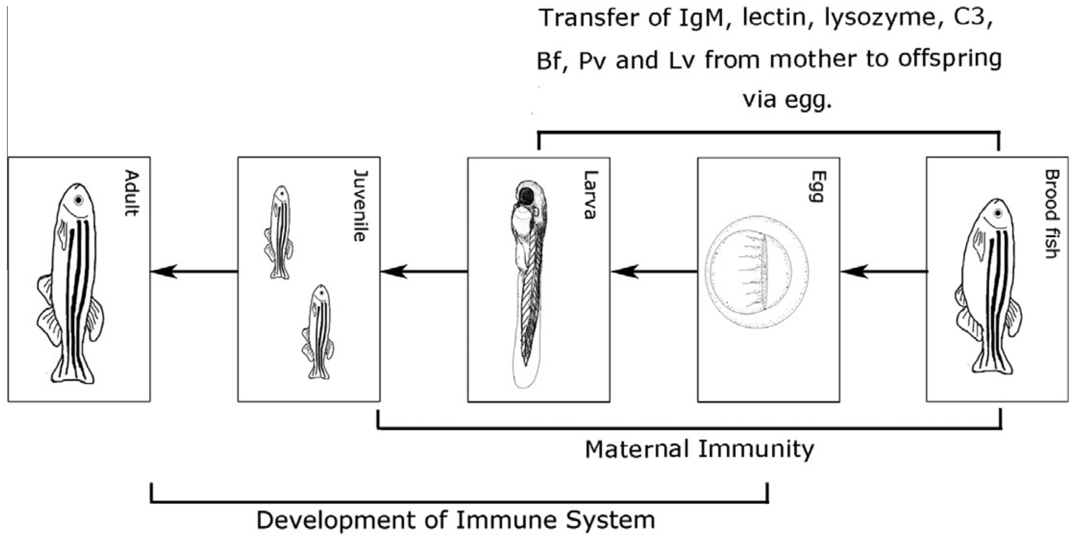


**Fig. 1.** A diagram showing the transfer and persistence of maternal immunity with respect to acquisition of immunocompetence at the different stages of development. Both innate and adaptive immune-relevant factors are transferred from mother to offspring, which play a critical role to protect the vulnerable offspring against pathogenic attacks before full development and maturation of immune system in fish.

Fish eggs are in most cases cleidoic, i.e. closed free-living system following fertilization; they are therefore supposed to depend upon the maternal provision of immune-relevant molecules for protection against invading pathogens before full maturation of immunological systems (Fig. 1). In the past two decades, the massive increase in aquaculture has put a greater emphasis on studies of the immune system and defense mechanisms against diseases associated with fish. As a result, a great stride has been made in recent years on the defense roles of maternally-derived factors in embryos and larvae in fishes, and our knowledge as such has dramatically increased. Below we will discuss the transfer of maternally-derived immune factors, mode of action of maternally-derived factors, mode of maternally-derived factor transfer, factors affecting maternal immunity transfer and possible application in fish culture, with a special emphasis on vitellogenin (Vg)-derived proteins and complement.

## 2. Transfer of maternally-derived immune factors

Previous studies on several fish species have shown that maternal IgM is able to be transferred from mother to offspring (Van Loon et al., 1981; Bly et al., 1986; Mor and Avtalion, 1990; Fuda et al., 1992; Castillo et al., 1993; Breuil et al., 1997; Olsen and Press, 1997; Hanif et al., 2004; Picchietti et al., 2004, 2006; Swain et al., 2006). Likewise, maternal transfer of the innate immune factors including the complement component C3 (Ellingsen et al., 2005; Huttenhuis et al., 2006; Løvoll et al., 2007; Wang et al., 2008, 2009), lectins (Bildfell et al., 1992; Tateno et al., 2002; Jung et al., 2003; Dong et al., 2004; Hasan et al., 2009), lysozymes (Yousif et al., 1991, 1994; Wang and Zhang, 2010) and cathelicidin (Seppola et al., 2009) to offspring has also been reported in different teleost species. Moreover, immunization of parents results in a significant increase in IgM levels (Mor and Avtalion, 1990; Sin et al., 1994; Oshima et al., 1996; Hanif et al., 2004) and lysozyme activities (Hanif et al., 2004) in the eggs compared to control. These maternally-derived immune factors have been elegantly reviewed by Mulero et al. (reviewed in Mulero et al., 2007) and Swain and Nayak (reviewed in Swain and Nayak, 2009). Here we will only describe the transfer of Vg-derived proteins and complement components because their immunological function in fish embryos and larvae has been experimentally tested.

### 2.1. Vg-derived proteins

Vg is an egg yolk precursor protein, present in the females of all oviparous species including fish, amphibians, reptiles, birds, most invertebrates and the platypus. Vg is usually synthesized extra-ovarianly and transported by the circulation system to the ovary, where it is internalized into growing oocytes and proteolytically cleaved to generate yolk proteins, phosvitin (Pv) and lipovitellin (Lv), that are later used as the nutrients by developing embryos (Arukwe and Goksøyr, 2003; reviewed in Finn and Fyhn, 2010). Vg was initially regarded as a female-specific protein (Pan et al., 1969); however its synthesis, albeit in smaller quantities, has been shown to occur in male and sexually immature animals (reviewed in Engelmann, 1978; Piulacks et al., 2003). These suggest that Vg may, in addition to being involved in yolk protein formation, play a role independent of gender. Recently, Vg has been shown to be an immune-relevant molecule involved in the defense of host against the microbes including bacterium (Zhang et al., 2005; Shi et al., 2006; Li et al., 2008, 2009; Liu et al., 2009; Tong et al., 2010; reviewed in Zhang et al., 2011) and virus (Garcia et al., 2010).

Pv and Lv, that both are proteolytically cleaved products of Vg, are naturally transferred from mother to eggs in fish. They are traditionally considered as the yolk reserves of nutrients essential for growth and development (reviewed in Finn and Fyhn, 2010). As Vg has been demonstrated to be an immune-relevant molecule, we thus hypothesize that its derived proteins, Pv and Lv, may also play an immunological role in developing embryos and larvae. As expected, Pv was proven to possess an antimicrobial activity in zebrafish embryos and larvae (Wang et al., 2011). In line with this, chicken egg yolk Pv was also shown to be able to inhibit the growth of the Gram-negative bacterium *Escherichia coli* (Sattar Khan et al., 2000). Similarly, fish native Lv was associated with the immune defense of rosy barb embryos and larvae (Zhang and Zhang, 2011). All these demonstrate that Pv and Lv are maternally-transferred proteins involved in both nutritional supply and immune defense in embryos and larvae in fishes (Fig. 1).

### 2.2. Complement components

Complement system consisting of approximately 35 plasma and membrane-bound proteins comprises one of the first lines of