Developmental and Comparative Immunology 43 (2014) 300–312

Contents lists available at ScienceDirect

Developmental and Comparative Immunology

journal homepage: www.elsevier.com/locate/dci

Review

Fish immune responses to parasitic copepod (namely sea lice) infection

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ARTICLE INFO

Article history:
Available online 31 August 2013

Keywords:
Parasitic copepod
Inflammation
$T_{H1/2}$-like response
Eosinophil
Immunostimulation

ABSTRACT

Parasitic copepods, in particular sea lice, have considerable impacts upon global freshwater and marine fisheries, with major economic consequences recognized primarily in aquaculture. Sea lice have been a contentious issue with regards to interactions between farmed and wild populations of fish, in particular salmonids, and their potential for detrimental effects at a population level. The following discussion will pertain to aquatic parasitic copepod species for which we have significant information on the host-parasite interaction and host response to infection (Orders Cyclopoida, Poecilostomatoida and Siphonostomatoida). This review evaluates prior research in terms of contributions to understanding parasite stage specific responses by the host, and in many cases draws upon model organisms like *Lepeophtheirus salmonis* and Atlantic salmon to convey important concepts in fish responses to parasitic copepod infection. The article discusses T_H1 and T_H2-like host responses in light of parasite immunomodulation of the host, current methods of immunological stimulation and where the current and future work in this field is heading.

Contents

1. Parasitic copepod importance

Parasitic copepods have considerable impacts upon global freshwater and marine fisheries, with major economic consequences recognized primarily in aquaculture. Within this large and diverse group of parasites, sea lice, the common name used for several species of marine ectoparasitic copepods of the family Caligidae (Order Copepoda: Suborder Siphonostomatoida), are the most commonly reported and best studied (reviewed in Johnson et al., 2004; Wagner et al., 2008). Most recent estimates of sea lice (mainly *Lepeophtheirus salmonis*) disease-related economic losses to marine salmoniculture exceed 430 million USD worldwide per annum (Costello, 2009). Of particular concern at present is that there are few treatments available for the therapeutic control of these infections, and multiple species of sea lice (*Caligus rogercresseyi* and *L. salmonis*, etc.) have populations that exhibit resistance to the compounds available (reviewed by Burka et al., 2012; Horsberg, 2010). Furthermore, sea lice have been a contentious issue with regards to interactions between farmed and wild populations of fish, in particular salmonids, and their potential for detrimental effects at a population level (Finstad et al., 2011; Krkosek et al., 2007, 2009). Although, less intensively studied, other groups of parasitic copepods and the interactions they have with their hosts can provide further insight into the evolutionary relationships between parasitic copepods and their fish hosts. The following discussion will pertain to aquatic parasitic copepod species for which we have significant information on the host-parasite interaction and host response to infection (Orders Cyclopoida, Poecilostomatoida and Siphonostomatoida; Table 1A–C).

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http://dx.doi.org/10.1016/j.dci.2013.08.019

1.1. Parasitic copepod biology

Although the copepod Orders Cyclopoida, Poecilostomatoida and Siphonostomatoida are quite diverse, they share some basic life history traits. For example, these groups have the same basic body form at the copepodid stage (Fig. 1). Although there are variations in the number and naming of the developmental stages, members of these groups share a similar life cycle that includes up to 6 naupliar and metanaupliar stages followed by up to 5 copepodid stages prior to development into the adults stages (Huys and Boxshall, 1991), with all species exhibiting 8 different life stages in total, separated by a moult (Maran et al., 2013). Nauplii may be planktotrophic, feeding on other planktonic organisms, or lecithotrophic, relying on yolk stores for their energy source. In the Siphonostomatoida the number of naupliar stages is reduced and there is a single infectious copepodid stage, which is followed by a series of attached copepodid/chalimus stages on the host. The chalimus stages are easily distinguished by attachment to their host by a thread-like frontal filament produced from a frontal gland. Some families such as Lernaeaopodidae (i.e. *Salmincola* spp.) escape their egg sac directly as copepodids and other species within the family Caligidae (e.g. *Lepeophtheirus* spp.), have pre-adult stages between the chalimus and adult stage (Kabata, 1970). Pre-adults are free-moving on the host with the exception of short periods at the moult when temporary frontal filaments are produced. In all species there is a single adult stage, which does not undergo any further moulting.

Upon maturation, adult males will mate with virgin adult females, with multiple matings possible within less than 48 h in some species, e.g. *L. salmonis*, (Pike and Wadsworth, 1999). Despite extensive mate guarding and deposition of spermatophores on females by males, polyandry can occur in *L. salmonis*, as in other Crustacea. This can lead to multiple paternal gamete contribution to female clutches (Todd et al., 2005). Following copulation, egg strings are produced in pairs by females of all species of parasitic copepods, but egg number and size can range from an average of 285 eggs/egg string for *L. salmonis* (Heuch et al., 2000) to as few as 29 eggs/egg string for *C. rogercresseyi* (Bravo, 2010). One Caligid female can produce 6–11 pairs of egg strings in a lifetime of approximately 7 months and these can be longer, contain more eggs and have differing viability depending on environmental salinity, temperature and whether on wild or farmed hosts (Heuch et al., 2000; Mustafa et al., 2001; Bravo, 2010). Life spans of other parasitic copepods, have been estimated to be even longer (greater than 2 years), such as *Lernaeocera branchialis* on Atlantic cod, *Gadus morhua* (Khan, 1988).

Parasitic copepods also differ in the number of hosts needed for development. The life cycle of *Lernaea cyprinacea* begins with 3 naupliar non-feeding stages, prior to seeking a host upon which it undergoes its first copepodid moult (Grabda, 1964). This stage is followed by three subsequent moults through copepodid stages before leaving the host as a sexually mature cyclopoid adult in search of another host upon which to reproduce (Shields and Goode, 1978). Lernaeaocerids also require an intermediate host in their life cycle (Kabata, 1970). Unfortunately, for many more species, details of their life cycles are, as yet, unknown (Kabata, 1970). What is, however, certain is that the rate of development of parasitic copepod life stages is largely dependent upon water temperature and, to a lesser extent but still important, the host species (i.e. relative resistance vs. susceptibility) upon which they develop (Johnson, 1993).

Most parasitic copepods first attach to their hosts via a modified second antennae and maxillae (Fig. 2), which can be reduced and even lost in some species (Kabata and Cousens, 1977; Bron et al., 1993; Paterson and Poulin, 1999; Roubal, 1999; Bennett and Bennett, 2001). *Lernaea* spp. attach to the host skin and then penetrate the tissue with the anterior-cephalic region of their body. After penetration, the cephalic region elongates and undergoes metamorphosis to produce an anchor process, which solidifies attachment to the host. The mechanism by which penetration is achieved has not been fully described, but may occur through mechanical disruption (Shields and Goode, 1978). Penetration into the host results in extravasated blood occurring between the parasite cuticle and the epidermal sheath that covers the parasite (epithelial cover). Substantial compression and necrosis adjacent to the developing horns of the anchor process (Shields and Tidd, 1974) also occurs. Similarly, the siphonistomatoid families, Lernaeaoceridae and Pennelidae, undergo cephalothoracic expansion and development of antlers anterior to the swimming legs, which anchor the parasite to host tissue (Kabata, 1969; Radhakrishnan and Nair, 1981a). Lernaeopodidae differ from these groups in that they remain outside the host and only the inserted bulla (attachment structure) remains within the host. The process is best described for *Salmincola californiensis* and involves the excavation of an implantation cavity, insertion of a frontal filament which later becomes associated with the second antennae and fuses with it to form the bulla. The implantation cavity is then further enlarged through inflation of the bulla (Kabata and Cousens, 1972). In the

Table 1A
Histopathological examination of parasitic copepod infections.

Copepod family	Parasite species	Host species	Observed host responses (to adult parasites unless otherwise stated)	References
Order Cyclopoida				
Lernaeidae	*Lamproglena clariae*	*Clarias gariepinus*	Penetration resulting in acute inflammation characterized by haemorrhage, edema and neutrophilia; hypertrophy and hyperplasia of epithelial and mucous cells. Connective tissue compressed in vicinity of the maxillipeds	Tsotetsi et al., 2005
	Lernaea cruciata	*Micropterus salmoides*	No signs of inflammation against older females; recently metamorphosed females stimulated inflammation. Inflammation was associated with expulsion and consisted of EGCs	Noga, 1986
	L. cruciata	*Morone chrysops*	Thickened epithelial collar near copepod penetration; the anterior thoracic region of parasite may become encapsulated. Large numbers of leucocytes (neutrophils) along the margins of penetration	Joy and Jones, 1973
	L. polymorpha	*Aristichthys nobilis*	Neutrophils around the periphery of the lesions; only EGCs observed in immune fish	Shariff and Roberts, 1989
	L. cyprinacea	*Oncorynchus mykiss,* *Carassius auratus,* *Helostoma temmincki*	Copepodid development and attachment produces minimal response, anchors surrounded by fibrous tissue (thick collar) and leucocyic responses below dermis	Berry et al. 1991; Shields and Goode, 1978; Shields and Tidd, 1974; Woo and Shariff, 1990
	L. piscinae	*A. nobilis*	Mainly neutrophils observed in eye pathology	Shariff, 1981

EGCs = eosinophilic granule cells.