

Nile tilapia Toll like receptors

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Abstract

The fish immune system structure and function are not well studied like mammalian models and recent researches showed that a lot of factor not common between freshwater and other fish and there are many disease and microbes affect some fish and cause a sever effect where other fish resist it. Our review focused on Nile tilapia as a model for freshwater bony fishes, where Nile tilapia consider one of the major massive culture fish all over the world and little is known about is immune system from the structure and functional point of view. Hence, interest is growing regarding comparative aspects of innate and adaptive immune defense mechanisms between lower vertebrates and mammals. Considering these reasons, new models are required to verify the universal validity of the results obtained in human and mice, so Nile tilapia as suitable models to represent the freshwater fish.

Key words: Toll like receptor-Innate immunity – Nile tilapia- PRRs- fish

Pathogen-associated molecular patterns, or PAMPs, are molecules associated with several pathogens which recognized by immune system cells. These molecules can be described as small molecular motifs conserved within microbes' classes. They are recognized by Toll-like receptors (TLRs) and other pattern recognition receptors (PRRs) in both animals and plants. The PRRs have different families and each one has different structure and different domain with various distribution, the PRRs families and subfamilies and its domain structures, while the position of the receptors and its natural ligand and adaptor as a general for each main family. They activate innate immune responses, protecting the host from infection, by identifying some conserved non-self-molecules. The receptor named, Toll protein, came from the *Drosophila* where the first TLR member has been identified in *Drosophila*, vertebrates has

around 13 members placed into two main categories according to its localization to cell-surface receptor and cytoplasmic receptors, 13 members have been reported in mammalian till now while there is 12 members reported in avian, where TLR8, 9, 10,11,12,13, absent in birds(Takeda, Kaisho et al. 2003, Akira and Takeda 2004, Takeuchi and Akira 2009). classified the vertebrate TLRs into 6 major families (based on mice model): TLR1 (TLR1, TLR2, TLR6 and TLR10), TLR3, TLR4, TLR5, TLR7 (TLR7, TLR8 and TLR9), and TLR11 (TLR11, TLR12, and TLR13 in mice). Meanwhile, TLRs have been described from a many different vertebrates. Bacterial Lipopolysaccharide (LPS), an endotoxin found on the bacterial cell membrane of a bacterium, is considered the prototypical PAMP. Every TLR receptor mainly specialized in recognizing one or more pattern. LPS is specifically recognized by

TLR 4, a bacterial flagellin recognized by TLR. lipoteichoic acid from Gram positive bacteria and peptidoglycan recognized by TLR-2, and nucleic acid variants normally associated with viruses, such as double-stranded RNA dsRNA recognized by TLR 3(Baoprasertkul, Peatman et al. 2007, Baoprasertkul, Xu et al. 2007, Avunje, Kim et al. 2011, Chang, Collet et al. 2011, Anandhakumar, Lavanya et al. 2012, Blum and Begemann 2012, Breau, Wilson et al. 2012, Aoki, Hikima et al. 2013) or unmethylated CpG motifs, recognized by TLR 15, 21(REHAM R. ABOUELMAATTI 2013). Although the term "PAMP" is relatively new, the concept that molecules derived from microbes must be detected by receptors from multicellular organisms has been held for many decades, and references to an "endotoxin receptor" are found in much of the older literature(Elfeil, Soliman et al. 2011, Elfeil, Abouelmaatti et al. 2012, Elfeil 2012, Abouelmaatti, Elfeil et al. 2013, REHAM R. ABOUELMAATTI 2013). Toll-like receptors (TLRs) are the basic components of the vertebrate pathogen recognition system. Despite uniform general structure, remarkable variability in domain composition can be found in individual TLRs among species. TLRs are typical type I transmembrane proteins, and contain three major domains: a tandem repeat leucine-rich repeat (LRR) motif which identifies PAMPs, a transmembrane region and an intracellular Toll/IL-1 receptor (TIR) domain which transmits signals(Akira and Takeda 2004, Diebold, Kaisho et al. 2004, Coban, Ishii et al. 2005, Akira, Uematsu et al. 2006, Beutler, Eidenschenk et al. 2007, Choi, Wang et al. 2009, Coban, Igari et al. 2010). Knowledge of inter-specific differences is of particular importance to our understanding of selective pressures on TLRs. Toll-like receptors (TLRs) are membrane-bound sensors of the innate immune system that recognize invariant and distinctive molecular features

of invading microbes and are also essential for initiating adaptive immunity in vertebrate(Hemmi, Takeuchi et al. 2000, Coban, Ishii et al. 2005). The genetic variation at TLR genes has been directly related to differential pathogen outcomes in humans and livestock. Nonetheless, new insights about the impact of TLRs polymorphism on the evolutionary ecology of infectious diseases can be gained through the investigation of additional vertebrate groups not yet investigated in detail. Toll-like receptors (TLRs) are a member of the pattern recognition receptors (PRRs) which detect pathogen-associated molecular patterns (PAMPs) and have a role in initiating the innate as well as adaptive immune defense(Kaisho and Akira 2006, Kato, Takeuchi et al. 2006). They play a vital role in host immune responses through the recognition of lipopolysaccharides (LPS), lipopeptides, flagellins, dsRNA or CpG DNA motifs. TLR system is part of ancient machinery that is evolutionary conserved with homologs present in insects, nematodes, plants, fish, mammals and birds(Akira and Takeda 2004). A range of TLR genes has been identified in non-mammalian vertebrates including Birds and fish. The numbers of TLR genes vary among various organisms. Thirteen TLRs (TLR 1–13) have been identified in mammals, and functionally these receptors recognize and respond to a wide range of exogenous as well as endogenous ligands. Of the 13 mammalian TLRs, TLR 11, 12, and 13 were identified only in the murine genome. In teleost fish, orthologs of TLR 1–5, 7–9 have been identified, while various reports indicated that TLR 6 and TLR 10 do not exist in teleost fish(Ishii and Akira 2006). In addition to the orthologs of TLRs in mammals, 'fish-specific' TLRs have been reported including TLR 18, TLR 19, TLR 20, TLR 21, TLR 22, and TLR 23. However, all these fish TLRs and their signaling

cascade factors represent high structural similarity to the mammalian TLR system (Buwitt-Beckmann, Heine et al. 2005). Currently, most TLRs are characterized only in a limited number of model species, including Salmon fish, according to our knowledge there is almost no data about the Nile tilapia toll like receptors which consider one of the most common farm fish and has a great economic important all over the world. Here we want to describe the TLRs in Nile tilapia. The research dedicated to the description of the enormous diversity of molecules involved in pathogen recognition is of vital importance in human and veterinary medicine. It is equally important to the evolutionary biology of host– parasite interactions. Much effort has been devoted to the characterization of immune system components in human and mouse models, while much less is currently known about the architecture of the immune system in other species (Akira, Uematsu et al. 2006). Information concerning any one of the wealth of living species may bring new insights into the principles of vertebrate immune function. Aiming to describe general patterns of immune system evolution in terrestrial vertebrates, the investigation of the fish clade may be particularly useful. Fish form a well-diversified taxon with origin distinct to mammals but with physiology comparable to them. However, in contrast to mammals, our knowledge of the molecular structure of the fish immune system is limited. Meanwhile, TLRs have been described from a many different vertebrates. The first piscine member of the interleukin-1/Toll-like receptor superfamily was characterized in 2000 from an isolated cDNA sequence of an interleukin-1 receptor from *Oncorhynchus mykiss* lacking a cytosolic signal-transducing domain, then Subramaniam et al. described the IL1R

cDNA in Atlantic salmon (*Salmo salar*) comprising also a C-terminal TIR domain. Ever since, 17 TLR types (TLR1, 2, 3, 4, 5, 5S, 7, 8, 9, 13, 14, 18, 19, 20, 21, 22, 23) were identified in more than a dozen teleost species. Key features of piscine Toll-like receptors and factors involved in downstream signaling are structurally related to those of the mammalian TLR activation pathways (Hemmi, Takeuchi et al. 2000, Hayashi, Smith et al. 2001, Takeda, Kaisho et al. 2003, Akira and Takeda 2004, Takeda and Akira 2004, Ishii and Akira 2006, Kawai and Akira 2006, Loo, Fornek et al. 2007, Sasaki, Kataoka et al. 2010). The structural conservation of the archaic TLR system suggests that also the regulation of the immune response might be similar in fish and mammals. Nevertheless, remarkably distinct features of teleostean TLR cascades have been discovered. Teleosts occupy a key position in the evolution of innate and adaptive immunity. Hence, interest is growing regarding comparative aspects of innate and adaptive immune defense mechanisms between lower vertebrates and mammals. Considering these reasons, new models are required to verify the universal validity of the results obtained in human and mice, so Nile tilapia as suitable models to represent the freshwater fish.

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