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Characterization of six IL-17 family genes in miiuy croaker and evolution analysis of vertebrate IL-17 family



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Qiong Yang ^{a, 1}, Yuena Sun ^{a, b, 1}, Xiurong Su ^b, Taiwu Li ^b, Tianjun Xu ^{a, *}

^a Laboratory of Fish Biogenetics & Immune Evolution, College of Marine Science, Zhejiang Ocean University, Zhoushan, 316022, China ^b School of Marine Sciences, Ningbo University, Ningbo 315211, Zhejiang Province, China

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ABSTRACT

Interleukin-17 (IL-17) family is a cytokine family which is one of the major signaling molecules family involved in immunity. Six member of IL-17 family cytokines (IL-17A-F) were found in mammals. In fish, all IL-17 family genes except IL-17B and IL-17E have been isolated and identified. Besides, IL-17N is uniquely found from teleosts. IL-17 family genes are widely studied in mammals, but have not been widely reported in lower vertebrates. In this study, we identify six IL-17 family genes (IL-17A/F1-3, IL-17C, IL-17D, IL-17N) from miiuy croaker, using LPS and poly (I:C) to infect miiuy croaker in order to analyze the expression response to bacteria and virus and expression in normal tissues. Challenge experiment showed that miiuy croaker IL-17 family genes exhibited more sensitive response to the poly (I:C) than the LPS. The expression of IL-17 in un-stimulated tissues showed that different gene has expressed in different tissues. Through the analysis of IL-17 family members exist in various representative species to study the evolution of the IL-17 family, and the result showed IL-17A/F, IL-17B, IL-17C, and IL-17D should be present in early gnathostomes species.

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1. Introduction

Cytokines play a significant role in immune-regulation which are broad and loose category of small proteins. The interleukin-17 (IL-17) family is one of the most ancient cytokine families comprise of six cytokines, IL-17A to IL-17F. IL-17A was first identified and named CTLA8 [1] that is produced by activated T cells [2]. And then the other five members of IL-17 family, namely IL-17B, IL-17C, IL-17D, IL-17E (IL-25) have been reported [3]. In this family, the degree of homology among IL-17A and the other members was only 16%-50% [4]. IL-17F shared the highest amino acid sequence similarity with IL-17A and acts as an proinflammatory cytokine as well as IL-17A that can promote the release of immune-related molecules (proinflammatory cytokines, chemokines and antimicrobial peptides) [5,6]. And these two genes are known produced by Th17 cells, CD⁸⁺cells, gdT cells and NK cells [7–9] and have been considered can be share the similar biological functions. IL-17A also can up-regulated expression many target genes like IL-6 by synergizing with TNF-α [10]. IL-17B and IL-17C have been reported

¹ Contributed equally.

have the similar function in inducing the mRNA expression of inflammatory cytokines such as IL-1β, IL-6, and IL-23 in the 3T3 cell line and peritoneal exudate cells with IL-17A [11]. Compared with IL-17A and IL-17F, these two IL-17 family members just expression promote monocytic cell line THP-1 to release TNF- α and IL-1 β which IL-17A has a small effect [12]. IL-17D was deemed to be prior and variously expressed in tissues and also be reported as the most evolutionary conserved one in the IL-17 family [13,14]. And IL-17D was found can be adjust the production of cytokines in endothelial cells and performed an hold-up effect on hemopoiesis in vitro [15]. Although it can not stimulate the prolif-eration of immune cells all by itself, it is capable to stimulate the production of other cytokines from target tissues. IL-17E which is also named as IL-25 had close homology to the rest of IL-17 family members is principally expressed by Th2 cells. IL-17E stimulate Th2 cytokines (IL-4, IL-5 and IL-13) to generate their production and augmenting the expression of eotaxin and tissue eosinophilia [16,17].

As an important significant cytokine which activates downstream pathways to induce the expression of anti-microbial peptides, cytokines and chemokines through their correspondent receptors, many studies have investigated IL-17 family members in mammals, but still have not been widely reported in lower vertebrates. In 2006, five IL-17 members (IL-17A/F1-3, IL-17C and IL-17D)

^{*} Corresponding author.

E-mail address: tianjunxu@163.com (T. Xu).





IL-7C



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