**IMMUNE RESPONSES TO BACTERIAL INFECTION IN ZEBRAFISH JUVENILES WITH DIFFERENT EARLY-LIFE INFECTIOUS HISTORIES**

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ABSTRACT

Early-life adversity has an important influence on immune responses during the lifespan development. In mammals, early-life stress was related to long-term consequences on immune functions. In fish, the exposure to a brief handling stressor or xenobiotics during early-life influenced the stress sensitivity and immunity in adulthood. So, it seems that challenges of various natures (e.g. social, chemical, physical or biological) during early-life can impact or shape an individual physical and mental’s health across the lifespan in fish. Bacterial infections during early life (embryonic and/or larval) stages are very common in fish, long before the attainment of immunocompetence, when the immune system is still developing. Zebrafish larvae only possess a fully developed immune system by 4-6 weeks post fertilization. During the first weeks of life, zebrafish larvae simply rely on efficient components of the innate immune system, most of which are already functional at the first day of embryogenesis. In this study, we aimed to evaluate the effects of different bacterial challenges during early development on zebrafish and on its immune system later in its life, notably for genes involved in immune responses against pathogenic infection. Thus, four histories of infection with a virulent strain of *Aeromonas salmonicida achromogenes* were tested in the first month post-hatching: control group without any infection, zebrafish exposed to an early infection at 15 days post-hatching (dph), zebrafish chronically exposed to bacteria, from 15 to 32 dph, and zebrafish exposed later at 32 dph. Then, all groups were maintained in tanks and exposed to the same pathogen at 58 dph. Fish were sampled before infection, and at 6h and 24h post-infection. The age of first infection was shown to influence both level and timing of the immune gene expressions, especially for inflammation-related genes. Besides, *il6* expression analysis suggested a pleiotropic activity of this cytokine that would exert anti-inflammatory activity in larvae and a pro-inflammatory activity at 61 dpf.Finally,evidences of an innate immune memory in zebrafish primarily infected with the pathogen at 35 dpf and re-infected at 61dpf provide new insights to consolidate the concept of “trained” innate immunity in fish.

KEYWORDS

Zebrafish; bacterial challenge; early infection; long-term effects; molecular analysis.

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