

# Studies of Unique Immune Systems of Teleost Fish and Development of Vaccine against Fish Diseases

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Japan is one of the advanced country for fish culture, and the amount of production reaches 4 million tons per a year. However, pathogenic bacteria, viruses and parasites affect many fish species and the infectious diseases are one of the major facts of the loss of fish production in the aquaculture. To control infectious diseases in fish, inactivated vaccines are available in aquaculture, too. In 2000, vaccines against major infectious diseases, vibriosis and streptococcosis have been available in aquaculture in Japan. The vaccines achieved great success and dramatically reduced the economic damage and the amount of antibiotics usage. Recently, infection of intracellular parasitic bacteria such as *Mycobacterium* sp., *Nocardia seriolae* and *Photobacterium damsela* subsp. *piscicida* causes severe economic damage in Japanese aquaculture instead of the diseases which can be prevented by inactivated vaccines. Since these intracellular parasites can survive and propagate in host phagocytes, antibodies induced by the inactivated vaccines cannot access to the pathogens. Therefore, cell mediated immune responses by CD4<sup>+</sup> Th1 cells and cytotoxic T lymphocytes are necessary to be induced to eliminate the intracellular parasites. To develop vaccines against intracellular parasites in teleost fish, it is important to know unique immune systems in teleost fish. Teleost fish has two CD4 molecules: CD4-1 with four Ig domains and CD4-2 with only two Ig domains. However, little is known about the role of both CD4s in fish cell mediated immunity. We have shown that mammalian live attenuated vaccine, *Mycobacterium bovis* BCG, confers protective efficacy and specific cell mediated immunity against fish mycobacteriosis [1]. In addition, we found that tuberculin response also occurred in BCG-vaccinated fish after injection of purified protein derivative (PPD) [2]. So, we aimed to reveal gene expression pattern of CD4-1 and CD4-2 during fish tuberculin response, to investigate the role of the CD4<sup>+</sup> cells in teleost fish. Fluorescent *in situ* hybridization detected CD4-1 mRNAs on melano-macrophage centers and CD4-2 mRNAs at some cell clusters located near the melano-macrophage centers [3]. CD4-2 mRNA, but not CD4-1 mRNA increased in the kidney during tuberculin response in teleost fish [3]. These results suggest that CD4-1 and CD4-2 are expressed in different cells and that CD4-2-positive cells, rather than CD4-1-positive cells, have a main role in Th1-related immune responses in teleost fish.

## References

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