



## Review

## A short history of research on immunity to infectious diseases in fish

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## ARTICLE INFO

## Article history:

Available online 27 August 2013

## Keywords:

Immunology  
Vaccination  
Diseases  
Fish  
History  
Biography

## ABSTRACT

This review describes the history of research on immunity to infectious diseases of fish in the period between 1965 and today. Special attention is paid to those studies, which are dealing with the interaction between immune system and invading pathogens in bony fish. Moreover, additional biographic information will be provided of people involved. In the 1960s and 1970s the focus of most studies was on humoral (Ig, B-cell) responses. Thorough studies on specific cellular (T-cell) responses and innate immunity (lectins, lysozyme, interferon, phagocytic cells) became available later. In the period between 1980 and today an overwhelming amount of data on regulation (e.g. cell cooperation, cytokines) and cell surface receptors (e.g. T-cell receptor; MHC) was published. It became also clear, that innate responses were often interacting with the acquired immune responses. Fish turned out to be vertebrates like all others with a sophisticated immune system showing specificity and memory. These basic data on the immune system could be applied in vaccination or in selection of disease resistant fish. Successful vaccines against bacterial diseases became available in the 1970s and 1980s. Effective anti-viral vaccines appeared from the 1980s onwards. There is no doubt, that Fish Immunology has become a flourishing science by the end of the 20th century and has contributed to our understanding of fish diseases as well as the success of aquaculture.

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## 1. Introduction

This review describes the history of research on fish immunity to infectious diseases during the last 50 years. Special attention is paid to those studies, dealing with the interaction between the immune system and invading pathogens in bony fish. It is not the intent of this review to evaluate the scientific merit of the work discussed, but to provide the reader with an idea how our present knowledge did develop over the years and to give biographic information on the people behind these studies.

A historical review on fish health research in the USA was published by Mitchell (Mitchell, 2001). This extensive report covers a period of almost 3 centuries between 1609 and 1969! Another review focusing on the history of fish vaccinology was published by Evelyn (Fig. 1) (Evelyn, 1997). He describes, that initially the diseases in aquaculture were treated with “chemotherapy”, because of the relative low price of antibiotics and other drugs. It was only in the mid to late 1970s that the attention turned to the possibility



**Fig. 1.** From left to right George W. (Bill) Klontz (1929–2000), Michel Dorson and Trevor T.P. Evelyn at the symposium “Fish biologics: serodiagnostics and vaccines”, Leetown (WV), USA, 1981. *Bill Klontz* received his doctor of veterinary medicine degree from Washington State University, Seattle (WA, USA) in 1963. He was first employed by the US Fish & Wildlife Service and the Texas A&M University. From 1972 onwards he joined the University of Idaho as professor at the Fisheries department till his retirement in 1994. He developed the concept of fish health management, which concentrates on the importance of the environment of the fish in the disease response. His worldwide contributions were recognized by the American Fisheries Society, who awarded him the Snieszko Distinguished Service Award in 1994. *Michel Dorson* received his doctor of Microbiology degree from the Université Paris 7, Paris (France) in 1985. He joined the Institut National de la Recherche Agronomique (INRA) after finishing his MSc degree in Biology (1967). He was director of the Fish Pathology Laboratory (INRA) from 1981 to 1985 and director of the Experimental Fish Facilities (INRA) at Jouy-en-Josas (France) from 1986 till his retirement in 2004. He is an internationally recognized expert on antiviral responses and vaccination of rainbow trout. *Trevor Evelyn* received his doctor of Microbiology-Biochemistry degree from the University of British Columbia (BC, Canada) in 1963. He was research scientist and head of the Fish Health and Parasitology Section, Biological Sciences Branch, Pacific Biological Station, Nanaimo (BC, Canada) from 1964 to 1997. Now he is scientist emeritus of the same institute in Nanaimo. He was president of the Fish Health Section of the American Fisheries Society (FHS/AFS) in 1983 and honoured by the FHS/AFS with the Snieszko Distinguished Service Award in 1992. He wrote >85 scientific papers on bacterial diseases (e.g. *Renibacterium salmoninarum*) and vaccination of salmonids. Photographs in this review were made by the 1st author unless otherwise mentioned.

of vaccination in fish farming. A 3rd review on the early days of fish immunology and vaccination describing the period between 1850 and 1965 appeared a few years ago (Van Muiswinkel, 2008). Only after 1940 the 1st researchers can be found, who were devoting their career mainly to fish immunology and/or comparative immunology, e.g. Gongarov, Cushing, Fänge, Ambrosius, Hildemann, Sigel, Clem, Lukyanenko, Anderson and Marchalonis. For more information on these early pioneers see previous review (Van Muiswinkel, 2008).

For practical reasons we have limited ourselves in this publication to the period from 1965 till present. Taking into account, that recent technical and scientific progress (gene cloning, genome sequencing) is amazingly fast, it implies that this historical review offers only a limited picture of the past. The other contributions to this special issue of *Developmental & Comparative Immunology* provide us with an overview of recent developments in this field. We will refer to these publications in our introductory paper, when appropriate.

## 2. Innate and acquired immunity

### 2.1. Epithelial barriers

The skin, gills and gut are examples of these epithelial barriers. It is of prime importance for fish to maintain the integrity of covering epithelia because they are important in defense and for osmoregulation. Normal epithelia are covered by a mucus layer, which is secreted by goblet cells. It has been shown, that an increase of bacterial load in the surrounding water is stimulating the production and release of high molecular weight glycoproteins



**Fig. 2.** Thelma C. Fletcher obtained her PhD degree on mucus of fish at the University of Aberdeen (Scotland, UK) in 1968. Her publication on the immunoglobulins in the serum and mucus of plaice (Fletcher and Grant, 1969) was first in describing the presence of IgM-like molecules in this fish species. Fletcher wrote more than 100 papers in total and edited at least 6 books. Today she is honorary research fellow at the School of Biological Sciences, University of Aberdeen. Picture was taken during the “Fish Biologics: serodiagnostics and vaccines” symposium, Leetown (WV), USA, 1981.

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