



## Editorial

## Preface to the special issue ‘targeting fish vaccination’



Fish farming in Aquaculture employs some 100,000 people and with an annual turnover of 7 billion euros in Europe alone, is the world's fastest growing industry within animal food production. However, the outcome can be severely affected by outbreaks of infectious diseases among the farmed fishes, not only costing the sector up to 20% of its production value on average, but also having a significant impact on individual fish health and welfare, as well as on the environmental footprint of the industry, aspects which cannot be directly expressed in euros. When disease resistant fish are not available, the most appropriate method for controlling disease problems, both from a production and welfare point of view is often to vaccinate the fish in order to prevent these diseases from occurring in the first place. This is also in accordance with the EC-adapted strategy of prevention being better than cure in terms of husbandry animal health. The EU-funded TARGE-TFISH project (2012–2017) was thus set out to not only lay the fundamentals of how fish can establish an adequate memory response through vaccination able to confer them with a long term protection, but also to generate practically-relevant knowledge regarding, for example, safer and cheaper antigen formulations, novel types recombinant vaccines, different routes of vaccine administration suitable for mass vaccination or the development of adequate adjuvants. This special issue provides a glance of the diverse approaches taken within the project and provides interesting insights into a number of relevant issues fundamental to the success of fish vaccination.

Specifically, this special issue includes fundamentally important issues such as the mechanisms of immunological memory [1], essential for the duration of protection and underpinning the success of fish vaccination. Further related to vaccine induced immune mechanisms, Granja and Tafalla [2] studied the peritoneal responses of B cells in vaccinated fish, while Wangkahart et al. [3] established the immune pathways involved in the response to a highly protective vaccination against ERM.

Further, the use of (novel) adjuvants remains a continuing topic of interest [4] for many antigenic formulations not able to provide a full protection on their own, exemplified by the use of a non-mineral oil adjuvanted vaccine to induce a protective immune response against one of the most important bacteria causing disease in salmonid fish, namely *Flavobacterium psychrophilum* [5]. Other studies specifically include attempts of vaccine delivery by oral route, not always successful but nonetheless (and maybe even more so) informative [6–8,11]. Along this line, the protection of antigens from degradation in the gastro-intestinal tract is an issue of importance when oral vaccination routes are preferred as addressed by several authors [6,8,11]. Often, different forms of antigen protection can indeed lead to a strong uptake of antigen and subsequent immune responses in the gut which, regretfully, are not always fully protective upon challenge. Yet, tailoring to individual diseases might be required, and better protection rates may be expected

in the future when formulations, doses and distribution regimes of oral vaccines are optimized. Related to tailoring of vaccines against viral diseases studies of both protein and DNA based vaccines are included [6,8–12]. Recognizing that the latter type of recombinant vaccine, after having been used commercially for a decade in Canada, was recently approved by EMEA for protection of Atlantic salmon against pancreas disease and hereby becoming a practical reality also in Europe, a review of the history and perspectives of DNA based vaccines for aquacultured fish is also included [13].

Last but not least, articles within this issue have focused on generic aspects related to vaccine development such as optimizing the sampling strategy during challenge trials [14] as well as identification of correlates of protective immunity following vaccination [15]. These aspects have high practical relevance in terms of defining reliable read-outs of successful vaccines and vaccinations without use of large numbers of experimental animals. Currently, vaccine batch potency testing thus typically relies on vaccination-challenge trials comparing mortality in groups of vaccinated and control fish.

While vaccination of aquacultured fishes has expanded very significantly since the early 1980's, the most commonly used vaccines are still the traditional bacterin-based formulations for immersion or intraperitoneal delivery. However, these largely empirically-based vaccines are limited to a certain type of bacterial infections, and as illustrated by the papers in this issue and also exemplified by the new DNA vaccines, dedicated research combining both basic and applied aspects of fish immunology and vaccinology is needed to further explore the potential of disease prophylaxis by vaccination in the modern expanding aquaculture production.

## References

- [1] Takuya Yamaguchi, Edwige Quillet, Pierre Boudinot, Uwe Fischer, What could be the mechanisms of immunological memory in fish? <https://www.sciencedirect.com/science/article/pii/S1050464818300354>, (2018).
- [2] Aitor G. Granja, Carolina Tafalla, Different IgM+ B cell subpopulations residing within the peritoneal cavity of vaccinated rainbow trout are differently regulated by BAFF, <https://www.sciencedirect.com/science/article/pii/S1050464817306034>, (2018).
- [3] Eakapol Wangkahart, Christopher J. Secombes, Tiehui Wang, Dissecting the immune pathways stimulated following injection vaccination of rainbow trout (*Oncorhynchus mykiss*) against enteric redmouth disease (ERM), <https://www.sciencedirect.com/science/article/pii/S1050464817304503>, (2017).
- [4] Jorge Galindo-Villegas, Alicia García-Alcazar, José Meseguer, Victoriano Mulero, Aluminum adjuvant potentiates gilthead seabream immune responses but induces toxicity in splenic melanomacrophage centers, <https://www.sciencedirect.com/science/article/pii/S1050464818301153>, (2018).
- [5] R. Hoare, S.-J. Jung, T.P.H. Ngo, K. Bartie, J. Bailey, K.D. Thompson, A. Adams, Efficacy and safety of a non-mineral oil adjuvanted injectable vaccine for the protection of Atlantic salmon (*Salmo salar* L.) against *Flavobacterium psychrophilum*, <https://www.sciencedirect.com/science/article/pii/S1050464817306058>, (2018).
- [6] Carmen W.E. Embregts, Felipe Reyes-Lopez, Adina C. Pall, Ansgar Stratmann,

<https://doi.org/10.1016/j.fsi.2018.09.048>

- Luis Tort, Niels Lorenzen, Kirsten Engell-Sorensen, Geert F. Wiegertjes, Maria Forlenza, J. Oriol Sunyer, David Parra, Pichia pastoris yeast as a vehicle for oral vaccination of larval and adult teleosts, <https://www.sciencedirect.com/science/article/pii/S1050464818304315>, (2018).
- [7] Rzgar M. Jaafar, Azmi Al-Jubury, Inger Dalsgaard, Asma MohammadKarami, Per W. Kania, Kurt Buchmann, Effect of oral booster vaccination of rainbow trout against *Yersinia ruckeri* depends on type of primary immunization, <https://www.sciencedirect.com/science/article/pii/S1050464817306563>, (2018).
- [8] C.W.E. Embregts, D. Rigaudeau, L. Tacchi, G.P. Pijlman, L. Kampers, T. Veselý, D. Pokorová, P. Boudinot, G.F. Wiegertjes, M. Forlenza, Vaccination of carp against SVCV with an oral-based vaccine or an insect cells-based subunit vaccine, <https://www.sciencedirect.com/science/article/pii/S1050464818301451>, (2018).
- [9] Francesco Buonocore, Noelia Nuñez-Ortiz, Simona Picchiatti, Elisa Randelli, Valentina Stocchi, Laura Guerra, Anna Toffan, Francesco Pascoli, Anna Maria Fausto, Massimo Mazzini, Giuseppe Scapigliati, Vaccination and immune responses OF European sea bass (*Dicentrarchus labrax* L.) against BETANODAVIRUS, <https://www.sciencedirect.com/science/article/pii/S1050464817307167>, (2018).
- [10] Francesco Pascoli, Andrea Guazzo, Alessandra Buratin, Marica Toson, Francesco Buonocore, Giuseppe Scapigliati, Toffan Anna, Lack of in vivo cross-protection of two different betanodavirus species RGNNV and SJNNV in European sea bass *Dicentrarchus labrax*, <https://www.sciencedirect.com/science/article/pii/S105046481730640X>, (2018).
- [11] Carmen W.E. Embregts, Roni Tadmor-Levi, Tomáš Veselý, Dagmar Pokorová, Lior David, Geert F. Wiegertjes, Maria Forlenza, Intra-muscular and oral vaccination using a Koi Herpesvirus ORF25 DNA vaccine does not confer protection, <https://www.sciencedirect.com/science/article/pii/S1050464818301530>, (2018).
- [12] Dagoberto Sepúlveda, Ellen Lorenzen, Jesper Skou Rasmussen, Katja Einer-Jensen, Bertrand Collet, C.J. Secombes, Niels Lorenzen, Time-course study of the immune protection induced by an interferon inducible DNA vaccine against viral haemorrhagic septicaemia in rainbow trout, <https://www.sciencedirect.com/science/article/pii/S1050464818303978>, (2018).
- [13] Catherine Collins, Niels Lorenzen, Bertrand Collet, DNA vaccination for the finfish aquaculture, <https://www.sciencedirect.com/science/article/pii/S1050464818304108>, (2018).
- [14] L. Malcolm Hall, Catherine Collins, Bertrand Collet, The potential benefits of repeat sampling experiments for fish disease-challenge host-pathogen investigations, <https://www.sciencedirect.com/science/article/pii/S1050464818300330>, (2018).
- [15] Hetron Mweemba Munang'andu, Øystein Evensen, Correlates of protective immunity for fish vaccines, <https://www.sciencedirect.com/science/article/pii/S1050464818301840>, (2018).

Niels Lorenzen

Danish Technical University (DTU), Lyngby, Denmark

E-mail address: [nilo@aqu.dtu.dk](mailto:nilo@aqu.dtu.dk).

Carolina Tafalla

Fish Immunology and Pathology Laboratory, Center for Animal Health

Research (CISA-INIA), Madrid, Spain

E-mail address: [tafalla@inia.es](mailto:tafalla@inia.es).

Geert F. Wiegertjes\*

Cell Biology and Immunology Group, Wageningen University, the

Netherlands

Aquaculture and Fisheries Group, Wageningen University, the Netherlands

E-mail address: [geert.wiegertjes@wur.nl](mailto:geert.wiegertjes@wur.nl).

\* Corresponding author.