Popular science summary of the PhD thesis

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Title of the PhD thesis	**Vaccination of European Sea Bass (*Dicentrarchus labrax*) against Viral Nervous Necrosis and Characterization of Protective Immunity**
PhD school/Department	DTU Aqua

Science summary

European sea bass (*Dicentrarchus labrax*), one of the main cultured fish species in the Mediterranean, are affected by viral nervous necrosis (VNN) which can result in great losses compromising both fish welfare and the economy of the production. The disease is caused by nervous necrosis virus (NNV), a small RNA virus belonging to the genus *Betanodavirus.* The virus infects many marine and fresh water species and thus circulate both in farmed and wild fish. Vaccination, breeding towards resistant lines of fish and biosecurity measures seems to be the most promising management tool available. This thesis investigates the first two, through vaccination and challenge experiments of European sea bass.

Natural immunity in three different populations of sea bass was investigated through experimental challenge of naïve fish from the three populations. An experimental vaccine based on a virus like particle (VLP) resembling the nervous necrosis virus, although not infectious, was also tested experimentally in different formulations and in different sizes of sea bass. The efficacy of the vaccine was evaluated in terms of vaccine-induced immune response and protection in experimental challenge with live virus at several time points after vaccination. Furthermore, the safety of the vaccine was evaluated.

The population of sea bass originating from the eastern Mediterranean seemed to have a natural resistance to the virus used in the challenge. The VLP-based vaccine showed very good protective effect after intraperitoneal injection. It induced a dose-dependent response of neutralizing antibodies and provided significant protection in experimental intramuscular challenge after a single dose of ≥20 µg/fish, even in small fish (~ 5 g). Following a single injection of the VLP-based vaccine, both the innate and adaptive immune system were activated in a well-balanced pattern, which might explain the high efficacy. The vaccine provided protection for at least 7.5 months (4500 degree days). Furthermore, fewer VLP-vaccinated survivors were positive for virus, indicating not only protection from disease but also inhibition of infection. The formulation with an adjuvant did not enhance the survival, and since the pure VLP was so immunogenic in itself, it seems that adjuvants are redundant in the formulation. The VLP was safe to administer, as it had no negative influence on the performance of the vaccinated fish.

In conclusion, the NNV VLP harbor great potential in the prevention of VNN in sea bass. VLPs have several advantages compared to traditional inactivated vaccines making them ideal candidates for prophylaxis of disease. These advantages include, but are not limited to; no need for laborious inactivation of virus and no remnant from the chemicals used to inactivate, very immunogenic and often no need to add adjuvant and they are easier to modify to match new emerging strains. Future studies could be aimed at investigating alternative delivery routes and testing the already effective IP delivery route in a field trial. The protective effect against other strains of NNV and in other NNV susceptible fish species could also be investigated.