

# Use of natural immunity for controlling red mark syndrome in farmed rainbow trout

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Like the name suggests, red mark syndrome (RMS) is a disease that causes red wound-like marks on farmed rainbow trout. The disease does not kill the fish, but makes them less attractive for human consumption and thus lowers their value.

## What is the problem with RMS?

RMS is a relatively benign disease, as it is usually not associated with mortality. Nonetheless, for some fish farmers RMS is very problematic due to the appearance of conspicuous large red skin marks (see figure 1). Usually, RMS affects large fish – often when ready for the market. Although the disease in most cases does not affect the muscle to any significant extent and the sensory and nutritional quality of the meat therefore is unaffected, the fish do not look very appetizing.



*Figure 1. A rainbow trout with two large and a few smaller prototypical red mark syndrome lesions.*

This is not a problem if the fish are used for filets, fish cakes or similar processed products. However, the majority of the Danish rainbow trout production is of high quality and is sold as whole fish, and here the red marks result in downgrading and thus become a serious problem for the farmers who is left with the options of either accepting a reduced price or keeping the affected fish until the disease symptoms disappear. The latter leads to management challenges as it disrupts the planned flow of fish on the farm. On top of this put consumer dissatisfaction and loss of market shares.

Experiments at DTU have shown that the red marks, depending on water temperature, may be present on the fish for several weeks. Red mark syndrome is a cold-water disease, and symptoms are generally not observed above 16°C. At 12°C it takes about a month from early appearance of the marks until they start to heal. Even then, lack of scales at the affected sites influences the perception

of quality. The scales do regenerate after the inflammation is resolved, but this may take several weeks (see figure 2).



Figure 2. Images showing the typical progression (from left to right) of an RMS lesion. The fish in the images was kept at 12°C. At this temperature the first early symptoms typically appear after 6-7 weeks, then get progressively more severe over the next 4 weeks after which healing starts.

All together the effects of RMS may be visible on the fish for several months. On top of that, the disease usually does not affect all the fish in the pond or raceway simultaneously, and may thus affect a cohort of fish for many months.

#### Could a vaccine be the solution?

Vaccines have been developed to tackle a number of fish diseases. However, no vaccines exist for red mark syndrome. In order to produce a vaccine against a disease, the organism causing the disease needs to ideally be isolated and characterized.

Although we are getting more and more confident that the disease is caused by a bacterium, which we provisionally call *Midichloria*-like organism (MLO), we only know the bacterium from a short piece of its DNA. We can detect this genetic “footprint” in fish affected by red mark syndrome, but more information is needed for vaccine production, and we have not been successful in isolating and culturing the bacterium. We thus have to look into other preventive strategies for RMS.

#### What about treatment with antibiotics?

We have previously shown that RMS can be treated with antibiotics. However, there are several problems with this approach.

First and foremost, the use of antibiotics should be a last option in order to avoid the development of antimicrobial resistance.

Secondly, in organic trout farming the use of antibiotics is restricted by the legislation.

Thirdly, the disease is not lethal and even does not seem to affect the welfare of the fish to a large extent as no changes in behavior are observed in affected fish. Since antibiotics should be used to avoid pain, suffering and even death, it is ethically difficult to argue for the use of antibiotics for treatment or prevention of RMS.

Finally, antibiotics are usually given in-feed for ten days, after which there is a retention period of 500 degree-days (i.e. the water temperature in centigrade multiplied by the number of days must be at least 500) before the fish can be sold for consumption. Thus, depending on the water temperature this approach may take a couple of months, and thus there may be only marginal benefits compared to letting the disease run its course. Hence, treatment with antibiotics is not a good option either.

### What to do then?

Since the behavior and welfare of the fish appears relatively unaffected by the disease we wondered whether an option could be to deliberately expose the fish to RMS at a young age in order to establish natural immunity against later outbreaks. It can perhaps best be compared to taking your toddler to visit a friend with chickenpox – just to get it over with and establish immunity before adulthood, where the implications of the disease are more severe. Such an approach was previously common in fish farming even for more serious diseases where mortality in smaller, less valuable fish was preferred over risking loss of large valuable fish at a later stage.

In collaboration with fish farmers, we established that the optimal time to infect the fish would be when the fish were moved to ponds or raceways for on-growing – typically at a size of 5-50g.

### Promising – so far!

For this approach to work as intended we firstly needed to consider unknown properties of red mark syndrome:

First of all we did not know if fish of 5-50g could get the disease, as this had never been reported. Conversely, it was important to establish that the disease did not affect the small fish too much.

Secondly, it was essential to determine whether the fish would mount a long lasting immune response preventing RMS throughout the remainder of the production cycle. As humans, if we are sick with a given disease or if we are vaccinated against one, we expect our immune system to protect us from reinfection for years or even for our entire life. Although the immune system of a rainbow trout does not differ that much from ours, fish do not always produce robust and lasting adaptive immune responses the way humans do – especially not if they are infected or vaccinated at early life-stages.

Most of the trout produced in Denmark are sold as portion-sized trout of typically 3-500g. This size is typically reached after 6-9 months. We thus needed to show that the early induction of RMS would protect the fish from re-infection for at least 9 months. To be on the safe side we waited a whole year before we re-exposed our fish to red mark syndrome.

So far, we have successfully infected fingerlings: The fish did get the prototypical red marks of RMS without associated mortality. So we could tick the first of our two prerequisites. Currently, we are re-exposing the fish along with similar control fish, which have never encountered RMS.

If we find that the pre-exposed fish do not get RMS a second time, the next step will be to develop a strategy for efficient implementation into practice on the trout farms.

