Food and Agriculture Organization of the United Nations

# GENE EDITING IN AQUACULTURE



*Farmed fish that have had their genes edited using the CRISPR tool are now available at retail outlets in Japan. The tool is showing promise for producing desirable traits – from disease resistance to improved fillet yields – in a range of species.*

Breeding programmes for aquatic species have advanced considerably in the last few decades, with an evolving variety of techniques – from mass selection to genomic selection – leading to major improvements in performance and health of stocks.

Breeders initially tended to focus on improving two specific traits – growth rates and yields. However, as aquaculture has expanded and intensified, so has the range of issues facing the sector. As a result, breeding programmes – particularly for high-value species – have become more complex and target many traits to meet producers' increasingly varied and subtler demands.

In the salmonid sector, which has some of the most advanced and established breeding programmes in aquaculture, family selection has been used to achieve incremental improvements in growth rates, fillet size and quality, as well as disease resistance. More recently, marker-assisted and genomic selection have led to more rapid improvements in on-farm performance and health, including – notably – conferring marked improvements in resistance to the infectious pancreatic necrosis (IPN) virus (Norris, 2017).

While selective breeding has been successful, it is limited by the heritability of the trait, the generation interval of the species and the genetic variation which exists within the farmed stocks. Gene editing holds significant potential to enhance selective breeding for key production, health and sustainability traits via specific targeted changes in the animals' DNA.

Successful projects have tested gene editing in a wide range of aquaculture species. In Atlantic salmon (*Salmo salar*), for example, the use of this tool has enabled researchers in Norway to produce sterile fish. This is seen as desirable to prevent interbreeding with wild salmon should they escape from a marine farm, while also offering the potential for improved growth rates and fewer downgrades by attenuating maturation prior to harvest.

However, there are still constraints to be resolved for practitioners of gene editing – including regulatory hurdles, issues of cost and ethical concerns – before it can make a significant impact on the commercial aquaculture sector.

# TECHNIQUE AND APPROACH USED

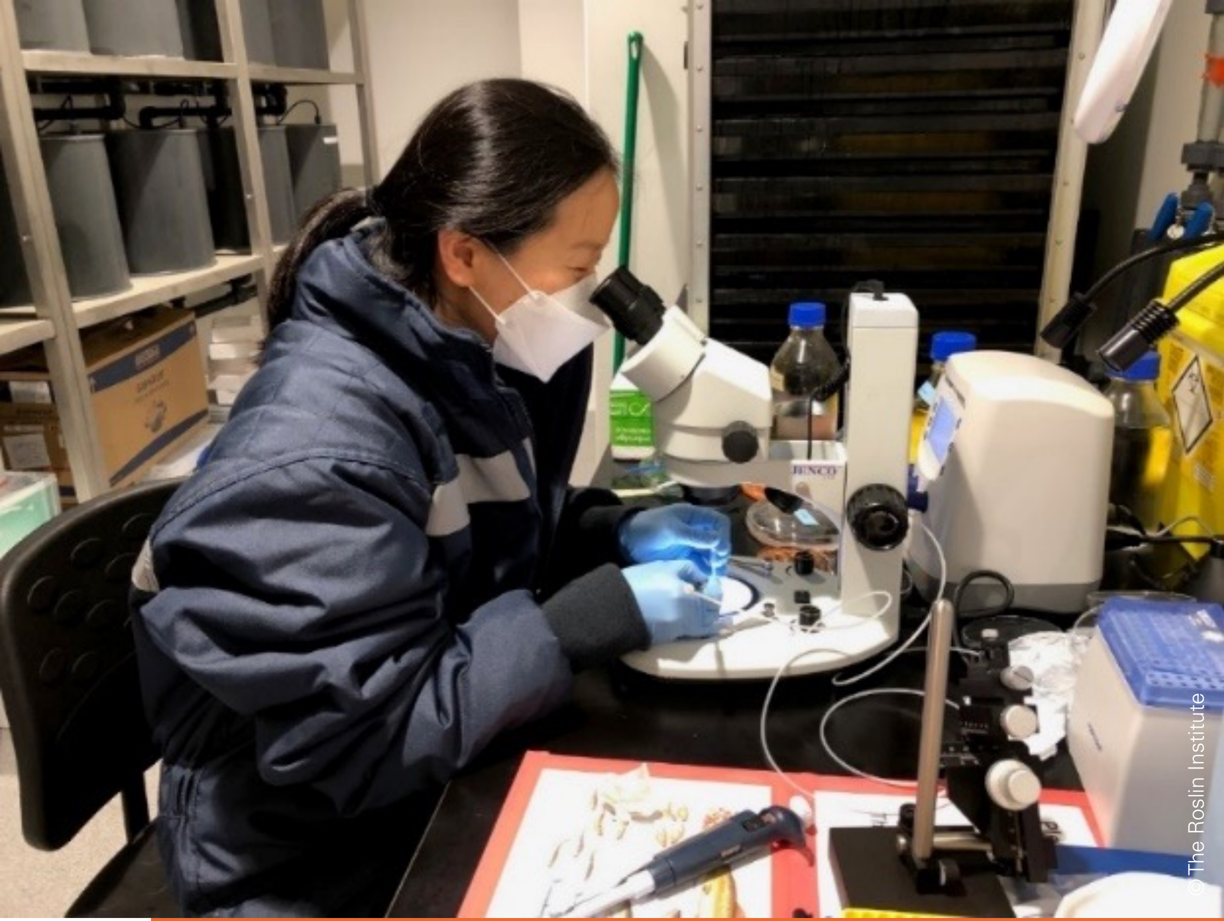
Unlike transgenesis, which involves the transfer of a gene from one organism to another and is highly contentious, genome editing allows specific, targeted and typically minor changes to the genome of the species of interest (Gratacap *et al.*, 2019).

One of the most popular gene-editing tools is clustered regularly interspaced short palindromic repeats (CRISPR). It was initially used by scientists to target specific points on DNA strands to knock out certain genes and the tool can be applied to almost any organism. Not only have researchers refined their techniques and the range of organisms that have had their DNA sequences expanded but this also applies to the gene-editing options available to study.

In order for any modifications made by tools such as CRISPR to be heritable they need to take place when the organism is at a very early stage in its embryonic development, so that they can be incorporated into its gametes once it matures. This process is generally done by micro-injection into the ova in fish species like salmon.

Through advances in genetics and genomic research, it is possible to identify specific genes where CRISPR editing is expected to give a significant boost to performance or health. For example, CRISPR was used to identify a gene affecting resistance to IPN in salmon in a recent study (Pavelin *et al.*, 2021).

The use of CRISPR to bring in desirable traits from other strains or species is also possible. For example, a major international project called CrispResist aims to understand the genes causing differential resistance to sea lice in salmonid species, and then to use CRISPR to edit Atlantic salmon to show a response similar to other resistant salmonid species.




Dr Yehwa Jin, postdoctoral research fellow at the Roslin Institute, performing salmon egg micro-injection at the University of Edinburgh's aquaculture genetics research facility.

# SCOPE AND SCALE OF APPLICATION

The mass use of CRISPR to edit individual production animals is unlikely to be feasible. However, editing broodstock populations or use of emerging methods of reproductive biotechnology including surrogate broodstock may offer avenues for commercial application. This could be relevant for a wide range of aquaculture species, as their high fecundity and external fertilization can facilitate genome editing at a scale that is not possible in farmed terrestrial animals.

Current peer-reviewed studies into gene-editing projects cover a growing range of aquatic species – including various salmonids, roho labeo (*Labeo rohita*), grass carp (*Ctenopharyngodon idellus*), common carp (*Cyprinus carpio*), channel catfish (*Ictalurus punctatus*), Pacific cupped oyster (*Magallana gigas*), Nile tilapia (*Oreochromis niloticus*) and red seabream (*Pagrus major*).

Eyed salmon eggs


# ACCESSIBILITY

The cost of using gene-editing tools has decreased dramatically in the last few years, but it is still a process that requires some specialist facilities and equipment. For example, it is necessary to have access to reproducing broodstock, micro-injection and molecular biology equipment, and a suitably biosecure hatchery facility. However, the reagents themselves are relatively cheap, perhaps only a few hundred dollars, and it is a technique that shows plenty of promise for a range of aquatic species and geographies.

Recently, one of the most significant projects relating to the use of CRISPR in aquaculture involved researchers from the Kyoto-based Regional Fish Institute, who partnered with Kyoto University and Kindai University to develop a red sea bream with 20 percent more meat (Kishimotoa *et al.*, 2018). They succeeded by knocking out a protein that suppresses muscle growth. While genetically modified food that contains foreign genes must undergo safety screening in Japan, gene-edited products do not face the same rules, allowing the fish to be harvested and sold to Japanese consumers.

However, many countries are yet to pass legislation related to the sale of gene-edited animals for human consumption, and the position of the European Union to date is to consider gene-edited animals in the same manner as genetically modified organisms. Such restrictions are likely to drastically limit the possibility for the industry to benefit from the improvements in animal production, health and sustainability which CRISPR has to offer. Therefore, it is important that informed dialogue continues about the techniques and a reasoned risk–benefit pragmatic approach is taken for its regulation.

# OUTCOME AND BENEFITS

Gene editing has the potential to improve a range of issues that currently affect aquaculture that include improving animal welfare, reducing environmental impact and increasing efficiency – and therefore the profitability – of production.

As some of the examples listed above illustrate, researchers have already shown the huge potential of gene editing for improving the performance of a wide range of traits in a growing selection of farmed aquatic species. It is a technique with huge promise, should regulations allow it to take place on a commercial scale.

Whether, when and how widely this is permitted remains to be seen. But given the raft of potential benefits, and that gene-edited red sea bream have already been legitimately sold for consumption in Japan, those involved in gene-editing projects believe that it is only a matter of time before it is widely adopted in commercial aquaculture production.

# REFERENCES


**Gratacap, R.L., Wargelius, A., Edvardsen, R.D. & Houston, R.D.** 2019. Potential of genome editing to improve aquaculture breeding and production. *Trends in Genetics*, 35(9): 672–684.

**Kishimoto, K., Washio, Y., Yoshiura, Y., Toyada, A., Ueno, T., Fukuyama, H., Kato, K. & Kinoshita, M.** 2018. Production of a breed of red sea bream *Pagrus major* with an increase of skeletal muscle mass and reduced body length by genome editing with CRISPR/Cas9. *Aquaculture*, 495: 415–427.

**Norris, A.** 2017. Application of genomics in salmon aquaculture breeding programs: Who knows where the genomic revolution will lead us?. *Marine Genomics*, 36: 13–15.

**Pavelin, J., Jin, Y.H., Gratacap, R.L., Taggart, J.B., Hamilton, A., Verner-Jeffreys, D.W., Paley, R.K., Rubin, C., Bishop, S.C., Bron, J.E., Robledo, D. & Houston, R.** 2021. The nedd-8 activating enzyme gene underlies genetic resistance to infectious pancreatic necrosis virus in Atlantic salmon. *Genomics*, 113(6): 3842–3850.

# ACKNOWLEDGEMENTS

This brief was prepared by Rob Fletcher (FAO consultant) and Ross Houston (Chair of Aquaculture Genetics at the Roslin Institute, University of Edinburgh).

**Required citation:** FAO. 2022. *Gene editing in aquaculture*. Bangkok.

FAO Regional Office for Asia and the Pacific
FAO-RAP@fao.org
www.fao.org/asiapacific/en/

**Food and Agriculture Organization of the United Nations**
Bangkok, Thailand


CC0581EN/1/06.22