

Protecting wild salmon and other aquatic species: Success of AquaAdvantage salmon shows sustainable aquaculture will lean heavily on advanced breeding and biotechnology

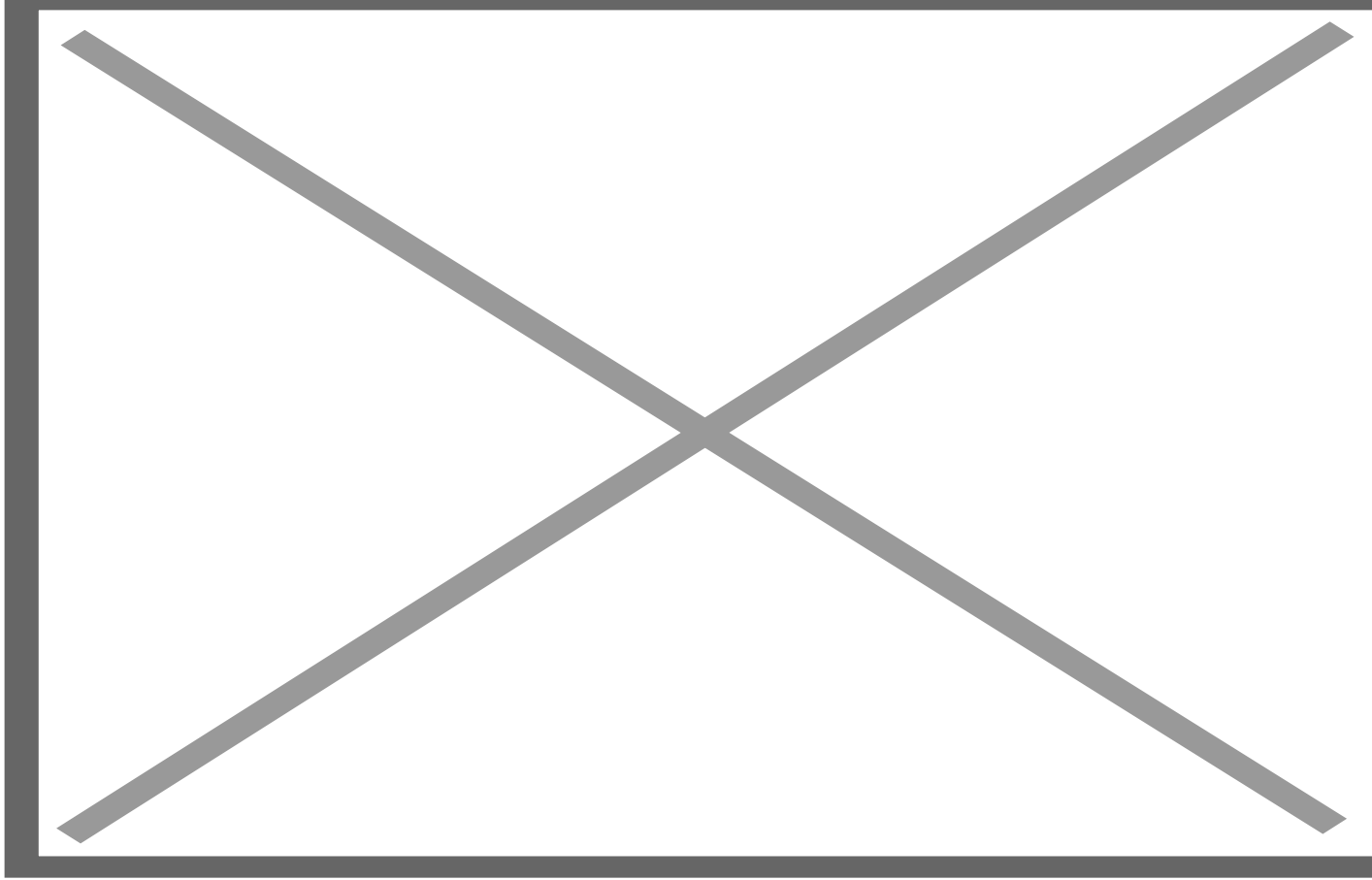
Wild salmon are in trouble worldwide. Many [Pacific](#) and [Atlantic](#) populations have disappeared or [declined](#) to record lows. But as we and a group of other colleagues argue [in the *Proceedings of the National Academy of Sciences*](#), recent advances in biotechnology can play an important role in conserving wild salmon while simultaneously increasing the availability and quality of farmed salmon—an important and valued food for humans with enormous [cultural significance](#).

We know [why](#) salmon are in trouble. It started with impacts from overfishing, habitat fragmentation and destruction by dams, and unsustainable agriculture and forestry practices, followed by competitive and inbreeding interactions with hatchery fish, and disease and parasites from [sea pen](#) escapees. Along with [climate change](#), all these have combined to cause massive crashes in wild salmon numbers.

Modern biotechnology can not only help wild salmon, but also other aquatic species and ecosystems. One would think developments that could eliminate at least some of these threats would be universally welcomed, yet [opponents claim](#) they bring all manner of dangers and threats to wild fish. An interdisciplinary group of scientists ([we are among them](#)) has taken a closer look. The facts are worth examining.

In the autumn of 1805, as Lewis and Clark [passed through the confluence](#) of the Snake and Columbia rivers on their way to the Pacific, they “were [astonished](#) at the numbers of salmon in the river... the water was so clear that no matter how deep the river, the bottom was clearly visible.” Historical accounts indicate salmon runs on the Columbia [averaged](#) 11 to 16 million fish, of which as many as half may have been [harvested](#) by Native Americans. Wild salmon numbers have [declined](#) since by 95 to 98 percent and continue their [downward trajectory](#).

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Lewis and Clark journal drawing of white salmon. Credit: The Granger Collection

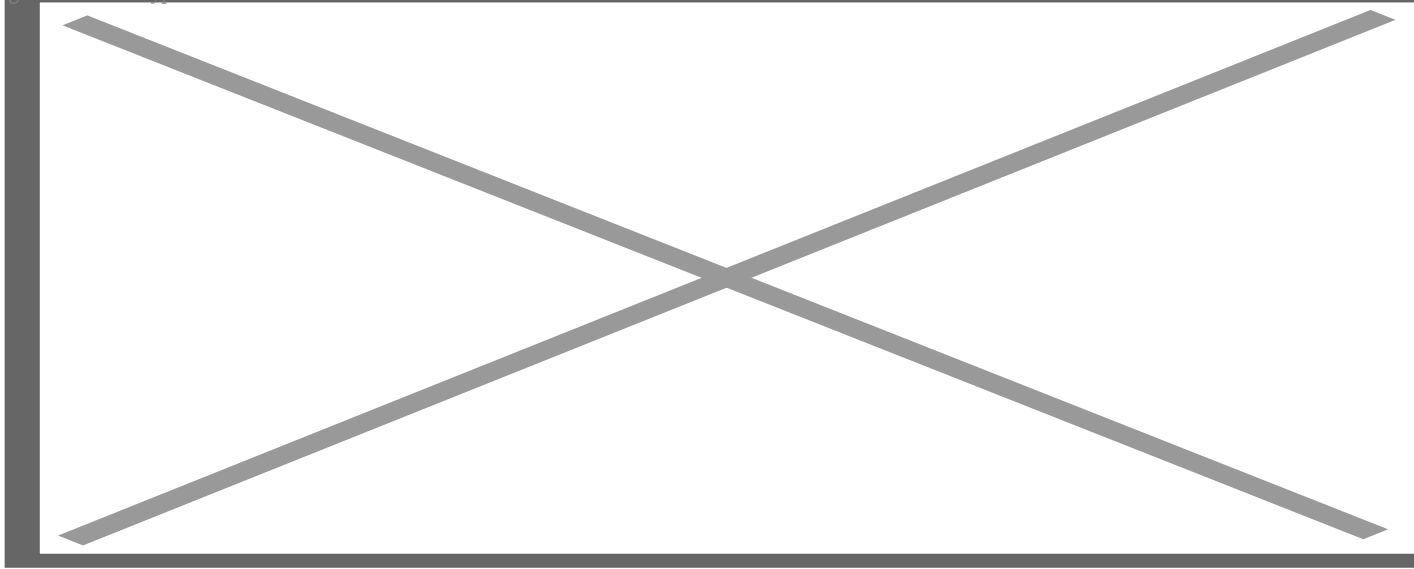
The [declines began](#) more than two centuries ago, fueled by overharvesting, habitat degradation and fragmentation, then exacerbated by dam construction throughout the 19th century, first for irrigation, then for hydroelectric power, that [increased pressure](#) on salmon numbers, escalating through the 20th century with the building of huge [federal hydropower dams](#) commencing in the 1930s. Dams block or restrict access of salmon to historical spawning grounds and profoundly alter water quality and riparian (riverside) ecology, commonly obliterating spawning habitats and favoring introduced nonnative competitors. Mitigation strategies such as fish ladders and hatcheries have [failed](#) to [stem](#) the decline.

The rapid growth of salmon farming at the end of the 20th century aimed to increase the supply of salmon for human consumption but presented new threats for wild salmon populations. By the beginning of the 21st century, farm escapees constituted a [significant fraction](#) of the commercial salmon catch, particularly in the Atlantic basin. [Interbreeding](#) between wild and escaped farmed salmon is [well-documented](#) and the hybrids exert a further downward pressure on wild populations because of their [lower survival and reproduction rates](#) in the wild.

Aquaculture has grown explosively worldwide since the early 1970s. It now accounts for a [larger fraction](#) of seafood consumption than wild fisheries, which have [plateaued](#) globally and are declining for many

species. Indeed, for decades aquaculture has been the most rapidly growing food production sector, providing an ever-increasing fraction of the animal protein consumed by people and contributing to food security on a global scale.

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The harvest of coho and chinook salmon has dropped since the mid-1970s. Credit: Washington State Governor's Salmon Recovery Office

Aquatic animals are much more [efficient](#) at converting food to body mass than terrestrial animals. Consequently, shifting human diets toward more seafood can reduce pressure on land use, yet aquaculture, as presently practiced, often has negative [impacts](#) on aquatic biodiversity and on wild populations of farmed species, as seen with salmon. Restructuring aquaculture systems to reduce such impacts is necessary, if aquaculture is to continue growing as [climate change](#) increases storm severity, warms and acidifies oceans and resculpts coastal regions.

Developing aquaculture systems that produce more and do less damage to biodiversity and aquatic ecosystems demands major technological and biological [innovations](#). Recent [comprehensive overviews](#) identify the many challenges posed by the diversity of aquaculture systems practiced around the world today. Land-based [recirculating aquaculture systems](#) (RAS) are the most reliable physical isolation measures for [reducing the impact](#) of aquaculture on natural ecosystems. RAS are being used with salmon to deliver more consistent growth and a reduction or elimination of exposure to pathogens and sea lice, compared to ocean net-pen salmon farms. Fully land-based salmon farms are [proliferating](#) briskly, although they are costly and unlikely to [fully displace](#) coastal net pens.

Improving agricultural organisms through genetic modification techniques became a reality during the late 20th century and provides a subset of the technologies encompassed by the term “[biotechnology](#)” or the more recently minted term “[synthetic biology](#).” Gene transfer was the first such biotechnology to be widely adopted and has been used primarily to improve commodity crops, such as corn, cotton, and soybeans, by making them biologically resistant to insect pests and tolerant to herbicides for weed management.

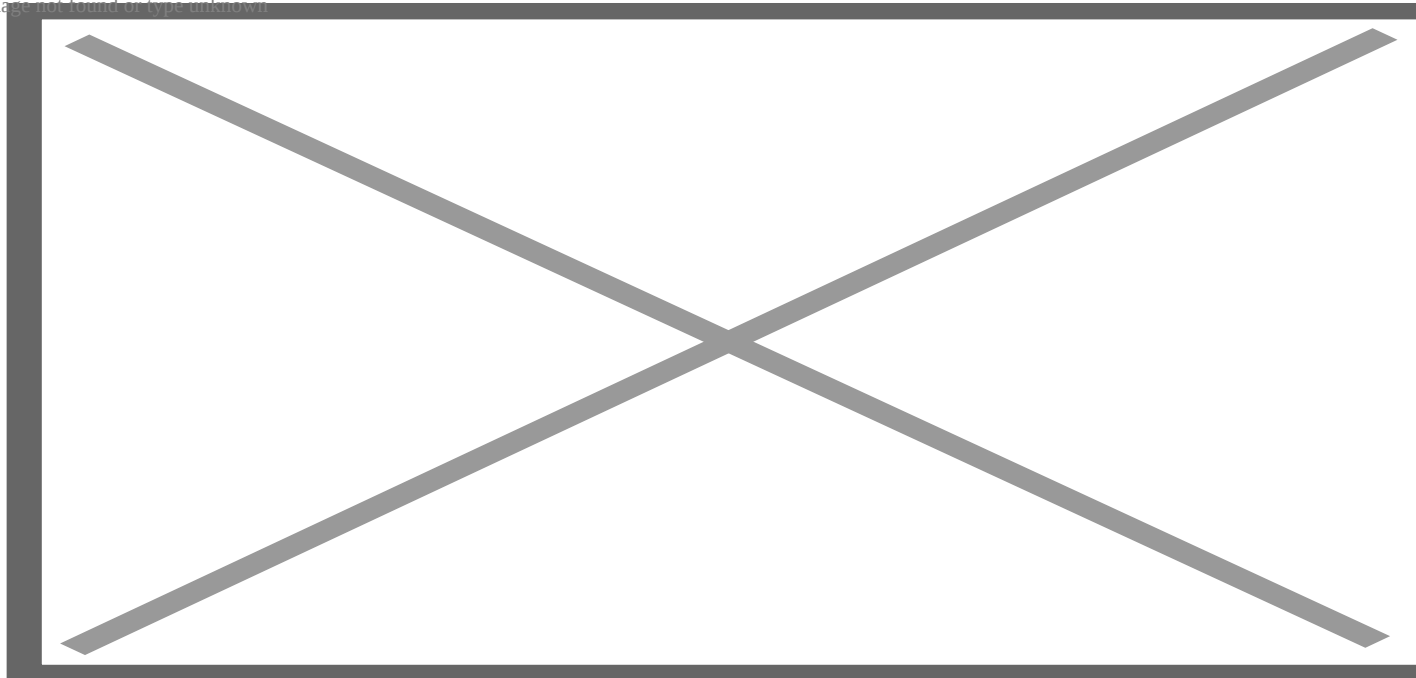
Introduced commercially in 1996, such “genetically modified” (GM) crops have been extremely successful in [more than 30 countries](#) that permit their cultivation, dramatically increasing [farmer incomes](#) and decreasing insecticide use, as well as [reducing carbon emissions](#) and contributing to soil conservation.

Despite extensive use in research and commercial crops, gene transfer technology has been slower to be integrated into commercial agricultural animal breeding programs, including those of aquatic organisms, because of outmoded and unjustified regulatory barriers, organized special-interest opposition, and a perception of consumer reluctance. AquAdvantage salmon, containing an added growth hormone gene, is to date the only example, illustrating both the benefits and the difficulties of commercializing transgenic organisms. It was developed by a [Canadian group](#) more than 30 years ago and licensed to AquaBounty Farms, Inc. (now [AquaBounty Technologies](#)). It finally reached the commercial market in 2016, in Canada, and in the U.S. in [2021](#).

AquAdvantage salmon is Atlantic salmon (*Salmo salar*) modified by the introduction of a chimeric gene construct expressing a cDNA copy of the Chinook salmon (*Oncorhynchus tshawytscha*) growth hormone gene expressed through the promoter of an ocean pout (*Macrozoarces americanus*) gene encoding an [antifreeze protein](#). The resulting continuous expression of the chimeric growth hormone gene results in [substantially faster growth](#) of the salmon during the first year, making it possible for it to reach market size in about of [half the time](#) as its wild counterpart.

This more rapid growth makes it economically feasible to raise AquAdvantage salmon in land-based RAS facilities located close to inland markets, reducing transportation costs (and carbon

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Wild salmon versus farmed salmon capture. Credit: FAO

emissions) and improving market freshness. Extensive studies have shown that AquAdvantage salmon

are [more efficient](#) at converting feed to biomass and require up to 25 percent less feed than conventional net-pen reared Atlantic salmon. They also do well on a diet containing plant-based replacements for some of the traditional fish meal, further reducing both the cost and environmental impact of production. They are free of [parasites and pathogens](#) that are common in the coastal net pens. The physical containment facilities are extraordinarily stringent, further reinforced by reproductive containment through the use of [only sterile triploid females](#).

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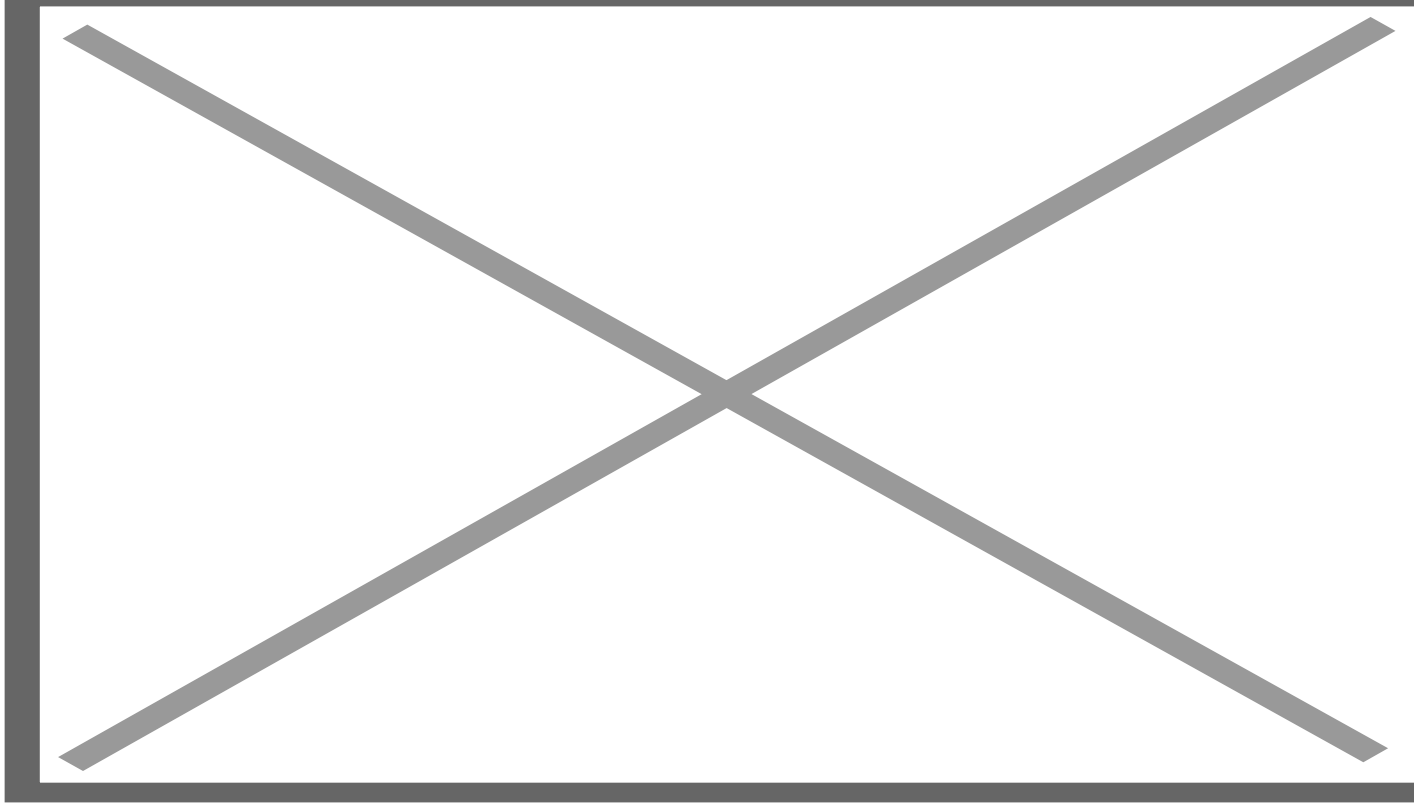
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The journey of AquAdvantage salmon through the regulatory gauntlet imposed on GM organisms (GMOs) has been long and twisting. Despite its difficult journey to market, AquAdvantage salmon is getting good reviews from food writers and is [now available](#) in the US. Assuming it achieves market success, it will have paved the way for acceptance of other GM aquacultured species by producers and consumers.

The kinds of physical and biological containment implemented around AquAdvantage salmon will become increasingly valuable to the conservation of aquatic biodiversity and the preservation of natural ecosystems. Modern animal breeders are now able to develop much stronger reproductive barriers around domesticated aquatic organisms, even as they seek to improve economically important traits. Growing recognition by conservation biologists and environmentalists of the value of erecting reproductive barriers as genetic firewalls between wild and domesticated organisms will encourage development of such mechanisms, and should be viewed favorably by consumers, who are increasingly conservation conscious.

Progress in aquaculture breeding programs has expanded dramatically with the sequencing of genomes of commercially important species, the growing sophistication of genomics-based breeding methods, and the [recent adaptation of genome editing techniques](#) to aquatic species. There are many more farmed aquatic than terrestrial animal species, but all are in the early stages of domestication and retain abundant genetic variation to support rapid progress in breeding for economically valuable traits. Farmed aquatic species will quickly diverge genetically from wild species increasing the potentially greater deleterious impacts on wild populations from interbreeding with escapees from aquaculture facilities.

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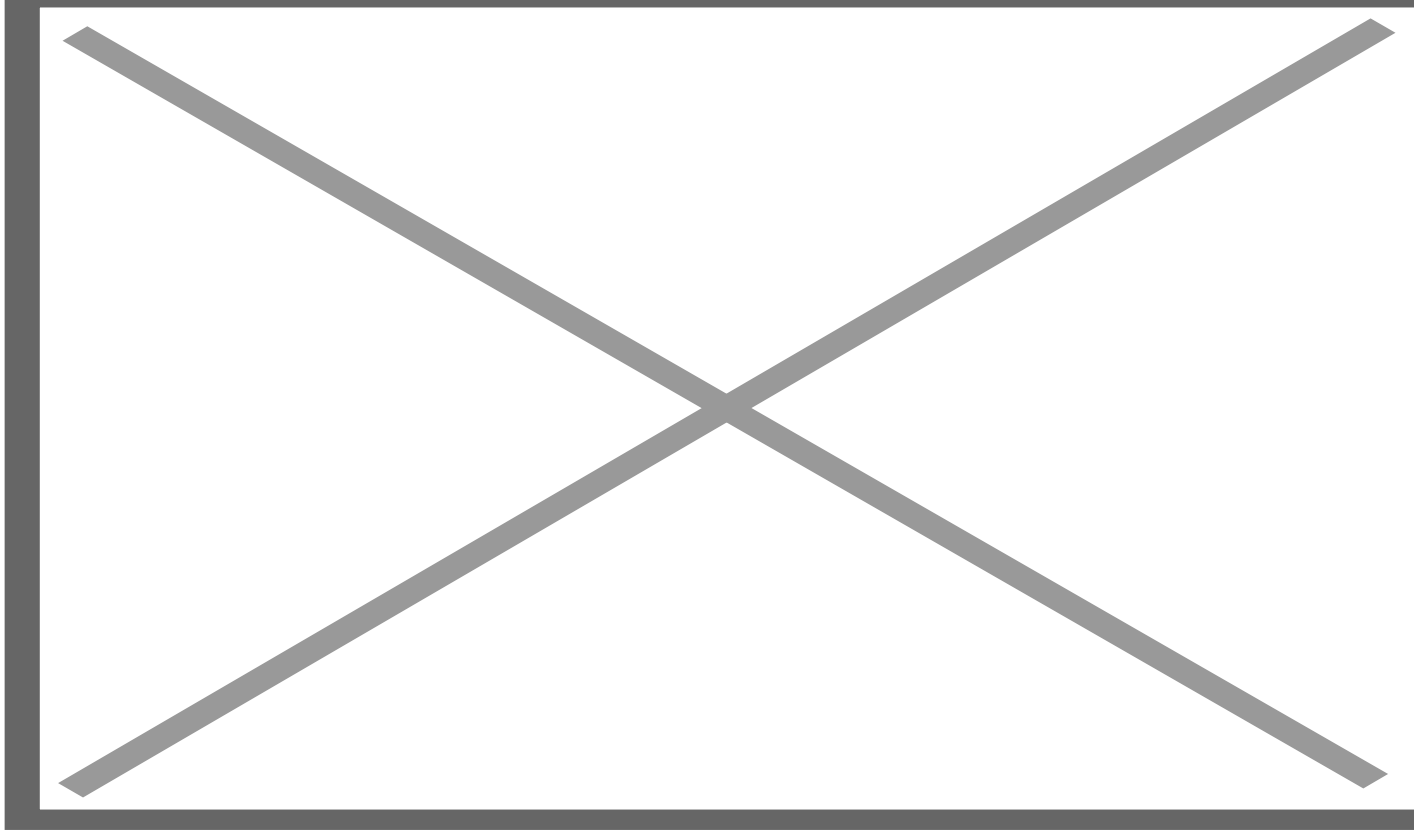


An artificial salmon run in Juneau, Alaska. Credit: MacAulay Salmon Hatchery

For salmon, the most stringent isolation approach currently in practice is the combination of land-based RAS and triploidization sterility of all-female stock already proven in AquAdvantage salmon. Although land-based RAS provide the most reliable physical containment currently available, their high capital costs likely precludes their universal adoption. Open water systems will continue to remain vulnerable to some level of [unintended release](#) of farmed animals. Coupling the advantages of isolation offered by the RAS approach and an increased reproductive barrier between farmed and wild populations will aid in further preserving important indigenous aquatic biodiversity.

Improved understanding of the molecular mechanisms of reproductive physiology makes it possible to strengthen genetic isolation using [genome editing](#) techniques. Recent studies using CRISPR/Cas genome-editing have [demonstrated](#) that knockout of the *dead end (dnd)* germ cell-specific gene in Atlantic salmon yields sterile animals that have neither gametes nor sex steroids, but still grow normally, knowledge which lead to producing genetically sterile animals at scale. Triploid sterility, although not totally foolproof, offers the best option currently available for implementing a stronger reproductive barrier between farmed and wild salmon.

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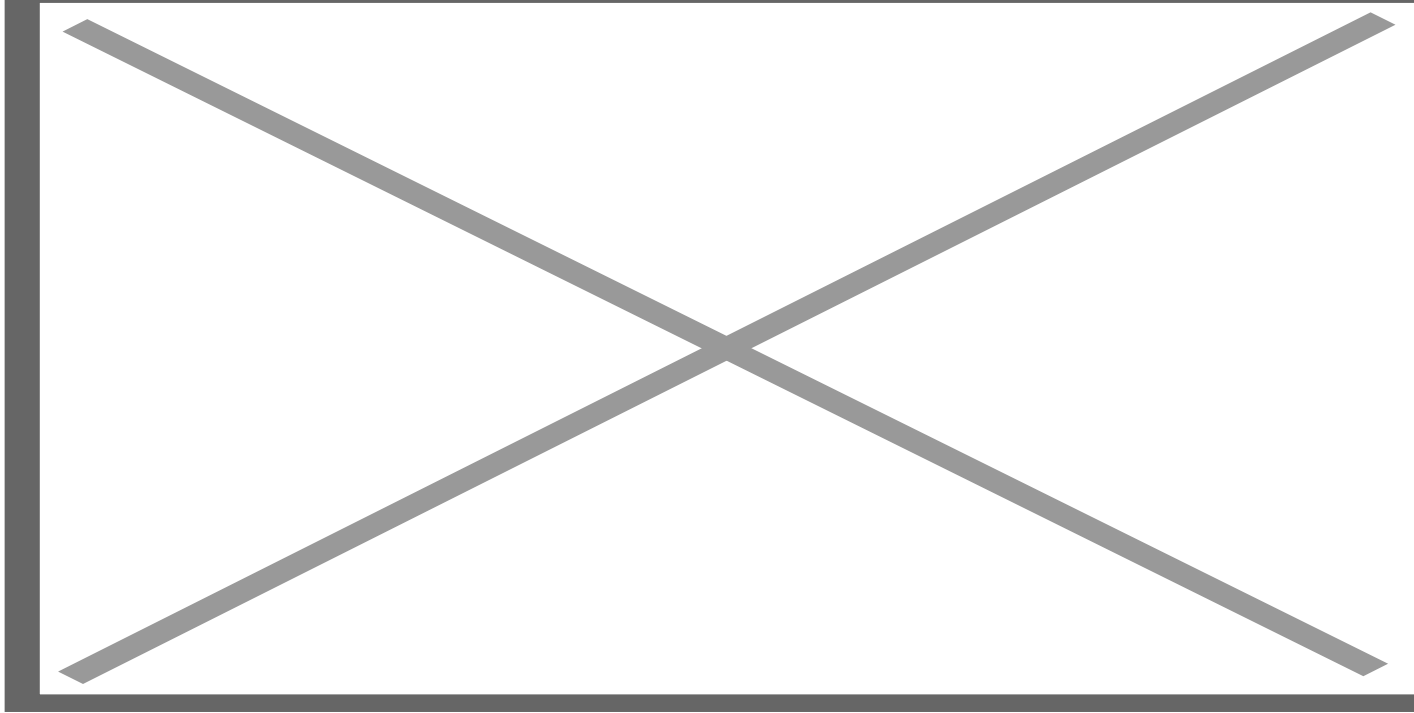


Each of the salmon eggs must be individually altered. Credit: Erlend A. Lorentzen via Institute of Marine Research

Despite early controversies, biotechnology has been widely adopted in medicine and in certain aspects of food production. Nevertheless, consumer attitudes toward GM foods or ingredients remain mixed, with some [continuing](#) to harbor concerns about the impact of GM foods on health. Yet such products have enjoyed wide market success, and the [scientific consensus](#), based on more than two decades of studies, is that the GM food and feed ingredients in wide use today are [as safe, or safer](#) for humans and agricultural animals as their non-GM counterparts.

AquAdvantage salmon is the first GM animal approved for human consumption, paving the way for by [pigs](#) in 2020 and [beef](#) in 2022). Recent surveys indicate that consumers recognize the importance of using biotechnology to improve farmed plants and animals and evince [willingness to buy](#) GM salmon. While anti-GMO special interest groups continue to pressure retailers to boycott it, grocers are likely to bend to consumer demand if AquAdvantage salmon proves [popular](#).

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Salmon filets are a source of protein and healthy fats. Credit: IntraFish

The OECD-FAO Agricultural Outlook 2019-2028 [report](#) predicts a 15 percent increase in demand for agricultural products just in the next decade. Anticipated increases in crop output will come from technology-driven yield improvements and intensification of production practices, rather than from a net increase in farmed land. Growth in the supply of fish and seafood is anticipated to come from aquaculture because of limitations in capture fisheries.

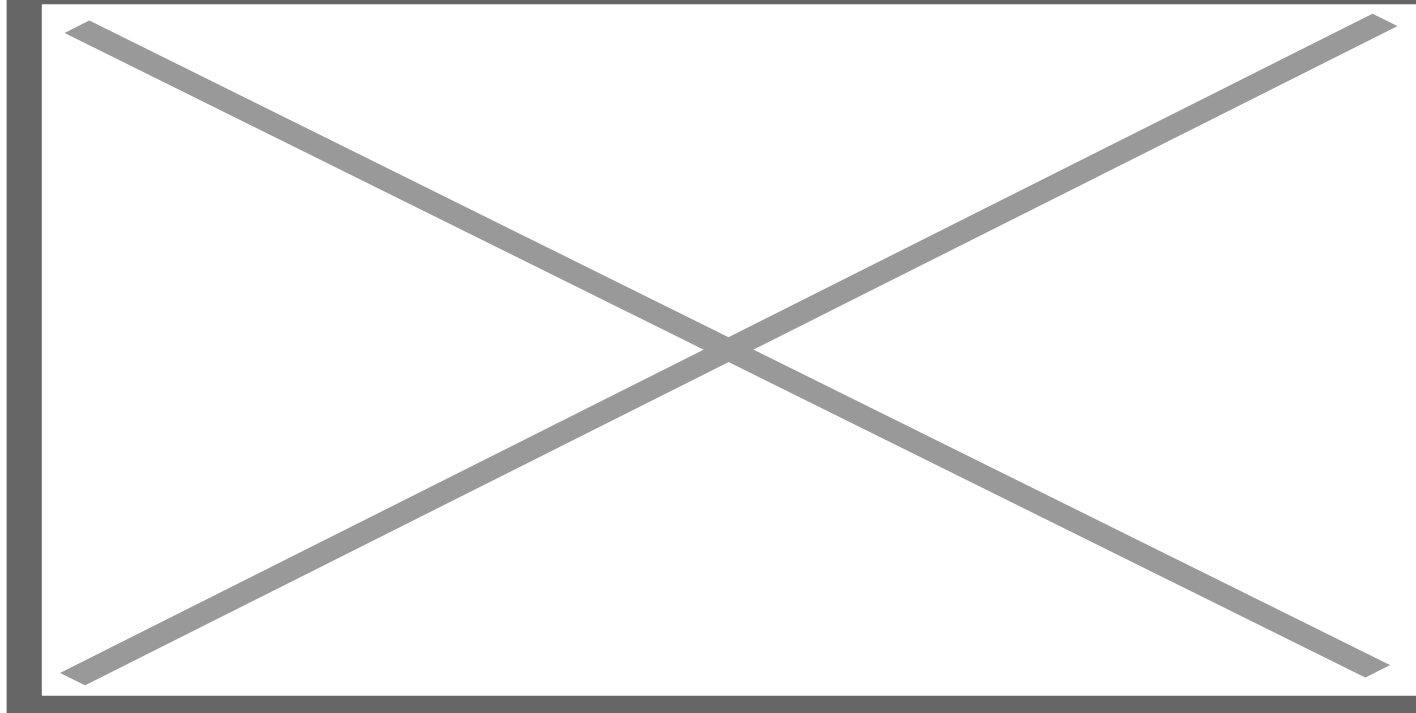
Intensification of land-based agriculture through innovation [spares marginal land for biodiversity conservation](#). Advanced breeding methods and [biotechnology](#) contribute to [increasing crop yields](#), while [precision agriculture](#) promotes crop intensification through computer-controlled farm machinery and algorithms for remote imaging-based optimization of irrigation, fertilization, and pest control.

Aquaculture is poised to make major gains through the application of advanced breeding strategies and biotechnology. Breeding for traits valuable in the human food chain, such as size, flesh quality, and rapid growth rate, is inevitable. Maintaining aquatic biodiversity will therefore depend on improvements in both the genetic and physical isolation of farmed aquatic species from wild populations, as well as on the restoration of damaged natural ecosystems.

Oregon, California, and the utility PacifiCorp have recently jointly [created](#) the Klamath River Renewal Corporation to fund the removal of 4 large hydroelectric dams, reopening many miles of salmon habitat in the Pacific Northwest. While this is the largest dam removal project to date, more than 1500 [dams have been dismantled](#) in the US since 2012 and 26 states embarked on such projects in 2019. There is

optimism that the recent broad agreement between environmental and conservation groups and the operators of U.S. hydropower dams will result in a [nationwide effort](#) to remove aging dams and restore habitats for wild fish populations where such opportunities exist—as recently (2014) happened in the [Elwha River](#) in Washington’s Olympic Peninsula, where two 100-year old dams were removed and native salmon and steelhead populations are rebounding.

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These indigenous constructed logjam tree dams can also be helpful for salmon populations. Credit: John Gussman

The prospect of habitat restoration further emphasizes the importance of erecting substantial genetic barriers between farmed and wild populations. Calls for [deeper dialog](#) between conservation biologists and environmentalists with biotechnologists and [synthetic biologists](#) have grown more insistent over the past decade, resulting in an extensive recent [assessment](#) of the pros and cons of biotechnological approaches by the International Union for the Conservation of Nature (IUCN). However, both [research](#) and [discussion](#) in the aquatic conservation context have focused primarily on using biotechnology and [synthetic biology](#) to eradicate invasive species or [prevent](#) the transfer of transgenic traits from farmed species to wild relatives.

Efforts to restore aquatic ecosystems and the growing awareness of the deleterious impacts of climate warming underscore the need to protect remaining wild ecosystems and the genetic diversity of wild aquatic species. Indeed, the importance of protecting this genetic heritage grows as sophisticated breeding techniques accelerate domestication of derived lines as important sources of high-quality dietary animal protein with a favorable environmental footprint. The genetic approaches we describe here can play a positive role in reducing the threats to wild salmon from net-pen aquaculture escapees and

hatchery fish.

Used as elements in a portfolio of management tools including dam removal and spawning habitat restoration, such measures offer hope for reversing the trajectory of decline in wild salmon, restoring them to prominence as a keystone species in their natal ranges. The strong backing of conservation biologists and environmentalists for the kinds of contemporary approaches discussed here that limit genetic exchanges between farmed aquatic organisms and their wild relatives would support efforts to perfect and implement them in farmed species. The results of a recent in-depth [survey](#) of consumer acceptance of gene-edited food revealed greater acceptance of the technology when respondents were provided with information about its benefits. Articulation of such benefits by experts in the conservation community would make modern molecular approaches more acceptable to a public increasingly cognizant of and concerned about the conservation of biodiversity and the environment.

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