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Biotechnology can help us save the genetic heritage of salmon and other aquatic species

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The use of gene editing to create genetic barriers between farmed and wild aquatic animals is emerging as the most effective way to preserve aquatic genetic diversity. Image credit: Shutterstock/Sekar B.

Salmon are iconic keystone species across the northern Pacific and Atlantic basins. Salmon is also a prized human delicacy. Wild salmon populations have been decimated by a combination of overharvesting, dams, and water diversions. Efforts to increase salmon abundance through fish farming and hatcheries have failed to stem the decline, instead exposing wild populations to diseases, pests, and the debilitating genetic effects of interbreeding with partially domesticated farm escapees and hatchery releases (1).

The plight of salmon is not unique. Preserving the genetic heritage of the many aquatic species now entering the food supply through aquaculture is a growing challenge. Breeding programs enhance commercially valuable traits but reduce genetic diversity. Yet the reservoirs of genetic diversity in wild aquatic populations become increasingly critical to their survival and adaptation as the warming climate alters oceans and resculpts rivers and coastal regions. We argue here that using gene editing to create genetic barriers between farmed and wild aquatic animals is emerging as the most effective approach to preserving aquatic genetic diversity. As such, it merits the strong support of the conservation community.

Conflicting Objectives

Aquaculture is the most rapidly growing food production sector and now accounts for a larger fraction of seafood consumption than wild fisheries. Both

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the continued growth of the human population and its increasing affluence drive up the demand for food in general and high-quality animal protein in particular. The Organisation for Economic Cooperation Development (OECD)–Food and Agriculture Organization (FAO) Agricultural Outlook 2019–2028 report predicts a 15% increase in demand for agricultural products in the next decade and projects that virtually all growth in the supply of fish and seafood will come from aquaculture due to limitations in capture fisheries (2).

Despite the antiquity of aquaculture, substantial domestication efforts date back less than half a century, as compared with the more than 10,000-year history of land-based agriculture (3). There are many more farmed aquatic than terrestrial animal species, all of which are in the early stages of domestication and hence have abundant genetic variation to support rapid progress in breeding programs for commercial aquaculture. The potential for progress is expanding markedly with the sequencing of aquatic genomes and the growing sophistication of genomics-based breeding methods (4).

Because of their high economic and cultural value, salmon are the focus of some of the most advanced breeding programs. Norwegian family-based selective breeding programs first focused on accelerating growth rates, later broadening to include disease resistance, maturation rates, and flesh quality (5). The recent adaptation of gene-editing techniques to aquatic species promises to further accelerate the development of economically valuable traits (4).

And yet, currently cultivated salmon species, as well as the many other farmed aquatic species, remain genetically very similar to their wild counterparts and fully capable of interbreeding with them (6). Domestication and breeding efforts inevitably reduce genetic variation and often render organisms less able to persist in the wild. Hence, it is increasingly important to consider the consequences of interbreeding between domesticated breeds and their wild relatives.

Even as the aquaculture industry expands, researchers and conservationists worldwide are actively promoting the preservation and restoration of natural ecosystems. Small-scale river restoration projects underway for many years have been buoyed by the recent broad agreements between environmental and conservation groups and the operators of U.S. hydropower dams to remove dams and restore habitats for wild fish populations (7). Success in repopulating restored aquatic habitats altered by climate warming will require substantial adaptation, which in turn depends on ample reservoirs of genetic variation in the reintroduced aquatic species.

Unfortunately, increasing aquaculture productivity through sophisticated breeding programs and preserving genetic variation in wild populations of aquacultured species are currently incompatible goals because the physical and biological barriers now used to separate farmed from wild populations are simply inadequate to prevent interbreeding.

Physical and Biological Barriers

Net pens, the physical barriers widely used in the marine phase of production, are breached regularly (6). Improvements in the reliability of open water systems will undoubtedly continue, yet they will remain vulnerable to some level of unintended release of farmed animals. Land-based recirculating aquaculture systems (RAS), which are growing in number, size, and sophistication, are the most reliable physical isolation technologies currently practiced for reducing the impact of aquaculture on natural ecosystems (8). RAS are used to decrease the time salmon spend in net pens, improving uniform growth and minimizing exposure to pathogens and sea lice (9). Fully land-based salmon farms are proliferating at a brisk pace, although their high capital cost and carbon footprint hinder their universal adoption.

Triploid sterility, although not foolproof, is the best biological barrier currently available to minimize interbreeding of wild and farmed aquatic animals. Sterility can be induced in many aquatic species by physical treatments, including pressure and temperature (10). Triploidization is presently used in trout management and oyster farming, but it is not widely used in commercial salmon farming and has even recently been prohibited in Norway (11).

Biotech in Aquaculture

Improving agricultural organisms by altering specific traits using genetic modification techniques became a reality during the late 20th century and constitutes a subset of the biology-based technologies encompassed by the term "biotechnology" or the more recently coined term "synthetic biology." Despite extensive use in research on aquatic organisms, gene transfer technology has yet to be integrated into commercial aquatic animal breeding programs.

An Atlantic salmon strain containing an added growth hormone gene remains the only example and illustrates both the benefits and the difficulties of commercialization. Called AquAdvantage salmon, it was developed by a Canadian group more than 30 years ago (12) and licensed shortly thereafter to AquaBounty Farms, Inc. (now AquaBounty Technologies, https://aquabounty.com). AquAdvantage salmon finally reached the commercial market in 2016 in Canada, with US market entry following in 2021 (13).

AquAdvantage salmon is Atlantic salmon (*Salmo salar*) modified by the introduction of a gene construct expressing an extra copy of a growth hormone gene from a different salmon species, Chinook salmon (*Oncorhynchus tshawhytscha*). The expression of the added gene is further modified by putting it under the control of a promoter sequence from a gene that codes for an antifreeze protein in the ocean pout, *Macrozoarces americanus*. The genetically modified (GM) salmon produce more growth hormone and produce it continuously, rather than seasonally, as do wild salmon (12).

The resulting GM AquAdvantage salmon grow faster during their first year, making it possible for the fish to reach market size almost twice as fast as their wild counterparts (12). Moreover, they are more efficient at converting feed to biomass and require up to 25% less feed than conventional Atlantic salmon (14). These characteristics make it economically feasible to raise them in high quality, fully land-based RAS facilities. Such facilities can be located close to inland markets, reducing transportation costs and improving market freshness.

AquAdvantage salmon pose no threat to wild salmon because of the redundant physical and biological barriers that isolate them from their wild counterparts. The production facilities are land-based, located far from wild salmon habitats, and use recirculated water. Such physical containment is further reinforced by reproductive containment through the use of only sterile triploid females (15).

Nonetheless, the journey of AquAdvantage salmon through the regulatory requirements imposed on genetically modified organisms (GMOs) has spanned two decades from first submission of regulatory inquiries to the US Food and Drug Administration (FDA) in 1995 to US and Canadian regulatory approvals for consumption in 2015 and 2016, respectively (16). Despite its long and difficult journey to market, AquAdvantage salmon is getting good reviews from food writers and should soon be more widely available in the United States (17).

Biological Barriers and Biotech

AquAdvantage salmon has been genetically modified to serve economic objectives, and the barriers that separate wild salmon populations from it are conventional, albeit high-quality, RAS and sterile animal production technologies. To date, both research and dialog in the aquatic conservation context have focused on using biotechnology to prevent the transfer of transgenic traits from farmed species to wild relatives or, more recently, to eradicate invasive species (18, 19). But progress in the understanding of the reproductive physiology of aquatic organisms is laying the groundwork for using biotechnology to create much more effective biological barriers between farmed and wild populations.

> **Our best chance of saving the genetic heritage of wild salmon—and of the many other aquatic organisms now being bred for farming—is to create genetic firewalls around the farmed animals, even as we seek to advance the productivity of aquaculture to meet the needs of the still-growing human population.**

For example, the results of recent studies using CRISPR/Cas gene-editing have demonstrated that knockout of the *dead end* (*dnd*) germ cell-specific gene in Atlantic salmon yields sterile animals that do not produce either gametes or sex steroids but grow normally (20, 21). The development of a new method of producing genetically sterile animals at scale is now possible and, indeed, proceeding apace (22).

Another potential approach is through the active creation of reproductive barriers. Relocation of centromeres is known to interfere with meiosis and is believed to be important in speciation (23). As such speciation mechanisms are better understood, it should become possible to establish hybrid incompatibility between farmed and wild aquatic strains by editing or relocating centromeres (24). Breeders will, of course, need to ensure that the behavior of such animals does not interfere with the reproductive success of their wild counterparts (25).

Consumer Acceptance

Despite early controversies, biotechnology has been widely adopted in medicine and in certain aspects of food production, such as in cheese-making and beverage fermentation. Consumer attitudes toward other types of GM ingredients, including corn and soybeans, remain divided, largely because of prolonged campaigns from anti-GMO groups and organic food marketers intent on vilifying these products for their own economic gain (26). The scientific consensus, based on more than four decades of studies, is that the GM food and feed ingredients in wide use today are as safe for humans and agricultural animals as their non-GM counterparts (27). Nonetheless, consumer attitudes toward foods constituting or containing GM ingredients remain mixed (28).

To date, AquAdvantage salmon is one of only three GM animals approved for human consumption by the FDA (29, 30). The results of recent surveys indicate that both US and Norwegian consumers recognize the importance of using biotechnology to improve farmed plants and animals and evince willingness to buy GM salmon (31). 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.

A Pressing Need

Wild salmon are in deep trouble. Increasingly, it's farmed salmon, selectively bred for traits of commercial value and reared in regularly breached open-water facilities, that are meeting growing consumer demand. But escapees interbreed with their wild cousins, producing offspring both less capable of survival in the wild and impoverished in the genetic diversity essential for adaptation to a rapidly changing climate. Similar pressures confront the wild populations of the many other aquatic species that are being bred and farmed. And yet, advances in both aquaculture technology and molecular techniques can reduce the threat to wild populations.

What's needed now is the strong backing of the broader conservation biology and environmental communities for the kinds of contemporary biotechnological approaches discussed here. 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 (32). By articulating such benefits, conservation experts can make modern molecular approaches more acceptable to a public increasingly cognizant of and concerned about the conservation of biodiversity and the environment. Our best chance of saving the genetic heritage of wild salmon—and of the many other aquatic organisms now being bred for farming—is to create genetic firewalls around the farmed animals, even as we seek to advance the productivity of aquaculture to meet the needs of the still-growing human population.

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