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Current scientific understanding of the environmental biosafety of transgenic fish and shellfish

A.R. Kapuscinski

Department of Fisheries, Wildlife and Conservation Biology and Institute for Social, Economic and Ecological Sustainability, 200 Hodson Hall, 1980 Folwell Avenue, University of Minnesota, St Paul, MN 55108, United States of America

Summary

A fluorescent zebrafish was the first genetically engineered animal to be marketed, and biotechnologists are developing many transgenic fish and shellfish. Biosafety science is not sufficiently advanced to be able to draw scientifically reliable and broadly trusted conclusions about the environmental effects of these animals. The science is best developed for identifying hazards posed by environmental spread of a transgenic fish or shellfish and least developed for assessing potential ecological harms of spread. Environmental spread of certain transgenic fish or shellfish could be an indirect route of entry into the human food supply. The management of predicted environmental risks is in its infancy and has thus far focused on the first step of the risk management process, i.e. risk reduction, via a few confinement methods. There is a critical need to improve scientific methods of environmental safety assessment and management and to gather empirical data needed to substantiate biosafety conclusions and to effectively manage transgenic fish and shellfish. Scientists and potentially affected parties should participate in prioritising the knowledge gaps to be addressed.

Keywords

Aquaculture – Aquatic animals – Biological confinement – Biological control – Biosafety research – Biosafety science – Ecological harm – Environment – Fish – Genetically engineered organism – Human food supply – Integrated confinement system – Invasive species – Ornamental fish industry – Risk assessment – Risk management – Shellfish – Transgene spread – Transgenic.

Introduction

Genetic engineers are inserting an increasing diversity of transgenes into an increasing diversity of aquatic animals (27, 44). In this paper, 'aquatic' refers to both freshwater and marine fish and shellfish and 'genetically engineered organism' (GEO) and 'transgenic organism' refer to organisms bearing man-made recombinant deoxyribonucleic acid genetic constructs (30, 42, 44, 54). Table I summarises representative examples of the growing diversity of fish and shellfish GEOs that are being engineered for aquaculture for a variety of purposes, e.g. for human food, for the biological control of nuisance species, for recreational markets, as water-quality monitors to detect contaminants that damage genes of living organisms, and even as bio-factories to produce commercially valuable compounds such as human pharmaceuticals. Growth-enhancement for human food production in aquaculture is the most common objective of current efforts but it may not remain so for much longer. Indeed, the first commercially marketed, genetically engineered animal in the United States of America (USA), and several other countries, was for the recreational, hobby aquarium market: the GloFish, a transgenic fish that 'glows' due to skeletal muscle expression of a fluorescent-protein genetic construct (16, 21, 49).

Table I
Examples of genetically engineered fish and shellfish under development (27, 45)

Species	Target engineered traits	Proposed application	Status of development
Finfish			
Mud loach	Increased growth rates, improved feed conversion after insertion of construct containing growth hormone gene driven by a strong promoter; construct is a novel recombination of mud-loach genes (39, 40)	Aquaculture (human food)	Research is ongoing
Channel catfish	Enhanced bacterial resistance after insertion of moth peptide antibiotic, cecropin B gene (14)	Aquaculture (human food)	Research is ongoing
Grass carp	Increased resistance to grass carp haemorrhage virus after insertion of human lactoferrin gene (63)	Aquaculture (human food)	Research is ongoing
Medaka	Transgenic fish serve as a detector of mutations (presumably caused by pollutants) that could affect aquatic animal or human health. After insertion of mutagenic bacteriophage vector, vector deoxyribonucleic acid (DNA) is removed and inserted into indicator bacteria to measure mutant genes (58, 59, 60, 61)	Industrial and environmental uses	Research is ongoing; a method has been patented
Atlantic salmon	Increased growth rate and food conversion efficiency by inserting Chinook salmon growth hormone gene and antifreeze gene promoter (9, 24)	Aquaculture (human food)	Seeking United States Federal Department of Agriculture approval for commercial use
Zebrafish	Fluorescent red or green body colour (21)	Hobby aquarium market	
Red sea bream	Increased growth rates after insertion of ocean pout antifreeze protein gene promoter and Chinook salmon growth hormone (62)	Aquaculture (human food)	Research is ongoing
Rainbow trout	Improved carbohydrate metabolism after insertion of human glucose transporter type I or rat hexokinase type II genes driven by viral or piscine promoters. Potentially allows higher plant-material content in fish feeds (48)	Aquaculture (human food); industrial uses	Research is ongoing
Trout	Increased growth rate and food conversion efficiency via insertion of sockeye salmon growth hormone gene (12)	Model transgenic fish line for public-domain research	Research is ongoing
Carp and medaka	Production of male-only offspring by insertion of gene construct that prevents the fish's aromatase enzyme from transforming reproductive hormone androgen into oestrogen; to prevent development of female fish (56)	Biological control of aquatic nuisance species, such as common carp	Research is ongoing
Goldfish	Increased cold tolerance after insertion of ocean pout antifreeze protein gene (57)	Aquaculture (human food)	Research is ongoing
Tilapia	Increased growth rate and food conversion efficiency after insertion of tilapia growth hormone gene (34)	Aquaculture (human food)	Preparing to seek regulatory approval
Tilapia	Production of clotting factor after insertion of human gene for clotting factor VII, for medicinal applications (5)	Pharmaceutical production	Research is ongoing
Tilapia	Increased growth rate, food conversion efficiency, and utilisation of protein after insertion of Chinook salmon growth hormone (52)	Aquaculture (human food)	Research is ongoing
Molluscs			
Surf clam and other species	Potential improved disease resistance and growth acceleration by harnessing altered genetic material from a virus to introduce foreign DNA (7)	Aquaculture (human food)	Research is ongoing; method patented
Oysters	Improved disease resistance by inserting retroviral vectors with disease resistance genes (31)	Aquaculture (human food)	Research is ongoing
Crustaceans			
Crayfish	Various aquaculture production traits by injection of replication-defective pantropic retroviral vector. Success in producing transgenic individuals shown by expression of marker gene (53)	Aquaculture (human food)	Research is ongoing; model for other research
Kuruma prawns	Various aquaculture production traits. Insertion of marker genes to confirm gene transfer method (50)	Aquaculture (human food)	Research is ongoing

This growing diversity of objectives, species, transgenes and target traits suggests that future requests for commercial approval of aquatic GEOs will also involve a growing diversity of species, transgenes and target traits. With this in mind, the author reviews the status of science needed to inform decisions about the environmental biosafety of transgenic fish and shellfish. This review refers primarily to fish because most studies to date involve transgenic finfish. Other publications address the role of biosafety science in informing regulatory policy and multi-stakeholder deliberations for governing transgenic fish and shellfish in a scientifically reliable and publicly trusted manner (26, 28, 42, 44, 47).

Biosafety science, policy and regulation must also address the food safety and human health safety issues of genetically engineered fish that could intentionally or unintentionally be introduced into the food supply. Although beyond the scope of this paper's focus on environmental biosafety, food safety was the focus of a recent expert consultation convened by the United Nations Food and Agriculture Organization and the World Health Organization. The final report of this consultation reviewed the status of the science for assessing the safety of foods derived from genetically engineered animals, including fish, and issued a number of recommendations (15). The report concluded that the spread and persistence of genetically engineered fish and shellfish – or their transgenes – in the environment could become an indirect route of entry of genetically engineered animal products into the human food supply, given that these animals could be caught by fishermen and unknowingly co-mingled with non-engineered fish products. The report thus recommended that risk and benefit assessments consider specific conditions of the local environment, farming system and human food system into which transgenic fish could be intentionally or unintentionally introduced.

Risk assessment and management

The risk assessment and management of GEOs should follow the kind of systematic processes that many long-existing industries routinely apply to assess and verify the safety of their various technologies (2, 3, 28, 33, 41). In the airplane construction industry, for example, system safety engineers have to predict the level of safety (or risk) resulting from complex interactions among numerous systems, such as electronic and mechanical parts of the airplane, weather in an airplane's flight paths and behaviour of pilots operating the plane. These system safety engineers apply a process of safety design and testing from the earliest stage of designing the airplane through rigorous pre-commercialization testing of fully assembled planes and follow-up testing after the plane is in commercial use. Practitioners in the animal health field have also recently adopted risk analysis processes (32). Risk assessment of complex technologies typically involves applying a mix of qualitative and quantitative methodologies (4, 6), as is needed to assess the environmental effects of GEOs (44). Assessing the environmental biosafety of an aquatic GEO requires integrating methods and knowledge from multiple fields, such as genetics, physiology, evolutionary biology, population biology and ecology, community ecology, ecosystem ecology, and system safety science (26).

Case-by-case approach

There is broad scientific agreement that risk assessment and management of GEOs should be case-specific. This idea is enshrined in the Cartagena Protocol on Biosafety (Annex III: Risk Assessment) (55). A case-by-case approach should consider the following:

– the characteristics of the non-engineered parental organism

– the inserted transgenes

– the altered traits of the GEO (including target and non-target traits)

– the intended uses of the GEO

– the accessible environments, i.e. environments that the GEO may enter accidentally or into which they may be deliberately introduced (1, 42, 44, 54).

Systematic steps of risk assessment and management

Table II summarises the systematic steps in risk assessment and management. Risk assessment involves hazard identification and risk analysis; risk analysis includes estimating exposure to the hazard, risk of harm given exposure to the hazard, and severity of harm. Risk assessment should also involve evaluating the extent to which the knowledge used for each of these steps is well established (44). This makes it possible to identify specific limits to quantifying risk, particularly those limits due to various types of uncertainty (6). The steps in risk management include risk reduction, risk monitoring and remedial action. Finally, risk communication should consider transparency, and participation by potentially affected and interested parties in all steps of risk assessment and management (41, 44).

Risk communication can be facilitated by presenting conclusions from quantitative risk assessment as a matrix of risk (likelihood of harm) plotted against severity of

Table II
Systematic steps in risk assessment and management (based on 26, 44)

Step	Key questions
Risk assessment	
Hazard identification	What event posing harmful consequences could occur?
Risk analysis	Estimate hazard exposure: how likely is the hazard? What harms could result from hazard exposure, and how severe would they be, taking into account social values? How likely is the harm, given hazard exposure? What are the conclusions of the quantitative risk assessment conclusions, presented as a matrix of risk (likelihood of harm) plotted against severity of harm? (Each cell of the matrix should be accompanied by a qualitative assessment of the response and a quantification of the assurance needed to reduce harm if the cell's conditions were to occur.) How well established is the knowledge used to identify the hazard, estimate its risk, and predict harms?
Risk management	
Risk reduction planning and implementation	What can be done (including bioconfinement and other confinement) to reduce risk, either by reducing the likelihood of the harm occurring or mitigating the potential effects in the event that it does occur? Are there steps that can be taken to prepare for remediation?
Risk tracking (monitoring)	How effective are the implemented measures for risk reduction? Are they as good as, better than, or worse than planned? What follow-up, corrective action or intervention will be pursued if findings are unacceptable? Did the intervention adequately resolve the concern?
Remedial action	What remedial action should be taken? What assurance is there that the action itself will not cause another environmental problem?
Risk communication	
Transparency and public participation	How transparent should the entire process be? How much and what type of participation should there be in all steps above by the public at large, by experts, and by interested and affected parties?

harm. Figure 1 depicts a simplified risk assessment matrix (35, 44). Depending on the quality of available information, the axes of a real risk matrix could consist of continuous values or more discrete categories. Social, economic and ecological considerations influence decision-making about acceptable levels of risk and severity of environmental harm. Great effort should be made to avoid approving cases with the highest risk and the most severe consequences (black area of Figure 1). Whether to make the next priority avoiding low risk of highly severe harm or avoiding high risk of less severe harm (grey areas in Figure 1) is a question that should be carefully considered by legitimate representatives of potentially affected and interested parties (28, 44). Multi-party deliberations should weigh both potential benefits and risks, as well as the credibility of such information, in order to decide whether to accept a proposed use of a GEO. The field of environmental conflict management offers various methodologies to guide such multi-party deliberations, such as a 'problem formulation options assessment' approach recently explored for genetically engineered crops in Kenya and Brazil (8, 45).

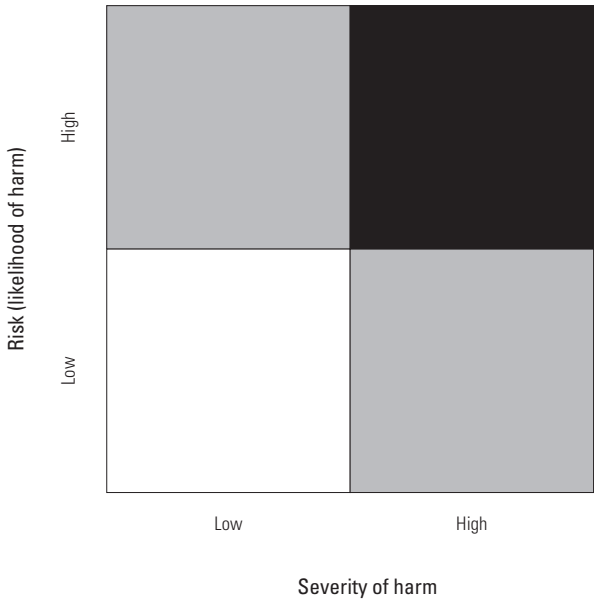

Fig. 1
A simplified risk assessment matrix (based on 35, 44)

Risk assessment of genetically engineered fish: current scientific knowledge

The scientific and regulatory communities are currently well equipped to identify hazards posed by escapes of aquatic GEOs, but lack the methods and empirical data required to reach reliable conclusions in all other stages of the risk assessment process.

Hazard identification

Detailed scenario trees have been developed through an interdisciplinary inductive process to identify hazards posed by escapes of aquatic GEOs into accessible ecosystems (1, 54). Some analysts consider escaping fish to be the hazard (42); but in these scenario trees a hazard consists of a problem that escaping fish can subsequently pose, including:

1) spread of transgenes to wild relatives of a native species

2) spread of transgenes to feral relatives of an alien species already established in the ecosystem

3) heightened invasiveness by an alien species due to one or more traits altered by transgenesis.

For aquaculture applications, assessors can predict unintended movements of transgenic fish into water bodies from empirical data sets on rates of escape of fish from different kinds of aquaculture operations, as well as practitioner knowledge (42, 43, 47). The first and third hazards listed above would be the main concerns in the case of the intentional environmental introduction of transgenic fish, such as for biological control of invasive species. In such cases, assessors should consider the spread of the transgenic fish beyond the targeted water body and to unintended water bodies, including all possible natural and human-mediated means of spread (54).

Estimating exposure to the hazard with the net fitness methodology

To quantify hazard exposure, risk-decision makers need a reliable, standardised and sufficiently confirmed methodology consisting of tractable and repeatable tests that can be conducted in confined settings and yield robust predictions. A methodology that meets all these criteria does not yet exist, but the net fitness methodology (37, 38) is a promising candidate for getting to this point (15, 23, 42, 44, 47).

The net fitness methodology involves the collection of fitness trait data on real transgenic individuals and their non-engineered counterparts, followed by input of these data into a mathematical model that predicts the fate of the transgene over multiple generations. Ideally the non-engineered counterparts should be from a truly wild population. The first step measures six fitness components (fecundity, fertility, juvenile viability, age at sexual maturity, mating success, and longevity) in order to cover critical points in the entire life-cycle of the organism and the second step quantifies the joint effect of all six fitness traits to predict transgene fate. To date, the methodology has been researched primarily for potential spread of transgenes to wild relatives or feral relatives (hazards 1 and 2, above) but it could also be used to estimate exposure to heightened invasiveness (hazard 3, above).

Studies with a growth-enhanced transgenic line of a model fish species, the Japanese medaka (*Oryzias latipes*) and model simulations in which transgenic fish escape into a population of wild relatives have shown that different combinations of values for six fitness traits could lead to three different predictions of transgene fate (25, 36, 38):

– purge scenario: purging of the transgene at some time after the initial escape of transgenic fish

– spread scenario: spread of the transgene through a wild population of relatives with no impact on the size of the introgressed population

– Trojan gene scenario: initial transgene spread that then triggers a decline in the size of the introgressed population; such a scenario occurs when the transgene has an antagonistic effect on different fitness traits.

Comparable scenarios for transgenic alien species would be (47):

– disappearance scenario: transgenic fish disappear from the environment when their net fitness is much lower than that of the parental species

– establishment scenario: transgenic fish establish a self-regenerating population when their net fitness is greater than or equal to that of the parental species.

Purging/disappearance

Gong *et al.* (21) modified the methodology for fitness trait measurements to generate data that suggested that transgenic zebra fish (*Danio rerio*) with strong expression of a fluorescent protein gene in their skeletal muscle would be no more invasive if they escaped into non-native habitats than conventional zebra fish. These findings were invoked in the recent commercial release of these transgenic zebra fish into the hobby aquarium market in the USA (20).

Transgene spread

Muir and Howard (37) suggested that age at sexual maturity has the greatest influence on the likelihood of

transgene spread through a population of wild relatives, followed by juvenile viability, mating advantage, female fecundity and male fertility. Some data consistent with predicted transgene spread were collected from studies of fast-growing transgenic lines of species relevant for food-production aquaculture. Coho salmon bearing a type-1 sockeye salmon growth-hormone gene driven by the sockeye salmon metallothionein promoter (pOnMTGH1) were, on average, eleven times heavier than conventional controls and had an earlier age at sexual maturity (11) (the most important fitness trait influencing transgene spread [37]). Larger size and younger sexual maturity were also found in one line of transgenic medaka bearing the psGH-hGH construct, consisting of a salmon growth hormone promoter linked to a human growth hormone gene (37). Devlin *et al.* (12) found that transgenic rainbow trout (construct pONMTGH1) started from a wild population had lower viability and were 37 to 83 times larger at sexual maturity than wild fish. Larger size at sexual maturity (the third most important fitness trait affecting transgene spread) could give these trout a large mating advantage (10, 17, 18). Transgenic tilapia bearing a Chinook salmon growth hormone gene driven by ocean pout antifreeze protein gene promoter (OPAFPcsGH) were three times larger than controls, both as juveniles and at sexual maturity (51). Predicting whether or not these transgenic fish lines fit the spread scenario requires obtaining complete net fitness measurements. So long as they exhibit earlier age at sexual maturity or larger size at maturity, these lines would have to exhibit severe reductions in viability to fit the safer, purging scenario.

Trojan gene effect

The growth-enhanced lines of transgenic salmon, trout and tilapia discussed in the above paragraph could perhaps fit the Trojan gene scenario if their viability is moderately reduced (36, 38). Howard *et al.* (25) documented that one of their growth-enhanced transgenic medaka lines exhibits reduced juvenile viability and a male mating advantage, with a mathematical prediction of the Trojan gene scenario.

Risk assessors will be reluctant to apply the net fitness methodology until it is confirmed by evidence that its predictions agree with relevant empirical data (29). The research laboratory of the author is addressing this problem by comparing model predictions to the observed fate of transgenes after releasing growth-enhanced transgenic medaka into contained mesocosms where they can interbreed with a naturally reproducing population of non-transgenic medaka. Substantial variation in transgene fate several generations post-release have been observed, both within and between two transgenic lines (data unpublished).

Several weaknesses of the net fitness methodology have been identified (23), all of which could be addressed by appropriate modifications. The present approach to measuring the six fitness traits ignores ecological, evolutionary and stochastic factors that could affect the fate of the transgene. It is not feasible to make the net fitness methodology perfectly mimic all ecological factors in nature, nor is this necessary to make it a powerful tool for risk assessment. It is important, however, to strategically identify those factors which, if included in the methodology, would have the greatest impact on improving the reliability of its predictions. A number of research teams are addressing these issues.

Assessing environmental harm and its severity

The scientific basis for assessing consequences of ecological spread of aquatic GEOs is the weakest of all steps in risk assessment. This step includes identifying possible environmental harm, estimating the risk (likelihood of harm given occurrence of a specific hazard), and assessing the severity of the harm, taking into account the social values for the affected part of the environment. Prior studies have identified numerous possible environmental harms (1, 42, 44, 54), but these can be grouped into three broad categories. They include possible harm to:

– gene pools in the affected species' centre of origin

– species of special concern, such as endangered species or economically or culturally important species

– ecological resilience of aquatic biological communities – their ability to recover from external disturbances such as floods, contaminants or climate change.

It is difficult to make reliable scientific assessments of these possible ecological harms; they are listed above in increasing order of difficulty, with harm to ecological resilience being the most difficult to assess.

Some decision-support tools can help identify case-specific issues to consider in assessing environmental harms, for example, the 'Manual for assessing ecological and human health effects of genetically engineered organisms' (54). There is a desperate need, however, to establish standardised, scientifically vetted methodologies for assessing different kinds of environmental harms. The assessment of environmental harm requires the combined expertise of professionals working together across numerous scientific fields, such as the following:

– population and conservation genetics

– evolutionary biology

– population biology

– ecology of populations, communities and ecosystems.

Environmental harm assessments should consider potential genotype-environment interactions, such as those that have been demonstrated in laboratory research on food competition between growth-hormone transgenic and unmodified coho salmon (13). For example, mixed populations of transgenic and non-transgenic salmon experienced population crashes or complete extinction under environmental conditions of low food-availability, but maintained a stable population size under conditions of high food-availability.

The hazard scenario, defined by the identified hazard and predicted transgene fate, determines the categories of ecological harm that should be assessed (Table III). The purging and disappearance scenarios are the environmentally safest options but they may not always be impact free. Purging of maladaptive transgenic fish by natural selection is not instantaneous but would occur over a number of generations depending on the degree of natural selection against the transgenic phenotypes. When potentially affected wild populations are already in decline, the potential for harm to these species of special concern should be assessed. It is relatively easy to predict effects of transgene spread on gene pools in centres of origin, somewhat harder to predict effects on species of special concern and extremely difficult to predict effects on resilience of fish communities. Assessing potential harm from the Trojan gene effect is more straightforward because its predicted population decline constitutes an environmental harm. Loss of a wild fish population would clearly lead to loss of unique genes. If transgenes conferring the Trojan gene effect spread through a threatened or endangered population, this would increase the chance of extinction. The loss of an entire population, in turn, might reduce the resilience of the aquatic biological community, for instance through simplification of the food web, unless the community contains other species that serve the same ecological function (46).

The potential effect of GEOs on ecological resilience has received little attention, but it could become a critical issue if GEOs come into widespread use. Other human causes of decline in ecological resilience have been characterised by long lag times before the harm was documented (19). For instance, loss of productivity and ecological resilience has occurred after long-term enhancement of the abundance of a single species in fisheries, for instance, by stocking large numbers of hatchery fish into natural waterbodies (22).

Risk management of genetically engineered fish: current scientific knowledge

Risk management in many technology industries entails risk reduction planning and implementation, post-release monitoring, and remedial action as outlined in Table II (27). To date, discussions about risk management of transgenic fish have focused on risk reduction and have largely ignored risk monitoring and remedial action. It is also unclear if regulatory agencies in different countries intend to require risk monitoring and remedial action plans as a condition of any approval they might give for the large-scale production of transgenic fish.

Discussions and proposals for risk reduction have focused on confinement methods that would reduce the environmental entry of transgenic fish and spread of their transgenes. A recent National Research Council (NRC) report on biological confinement of GEOs, commissioned by the Department of Agriculture in the United States of America (USDA), had a number of conclusions applicable to risk management of transgenic fish (44). Confinement of genetically engineered fish and shellfish can be

Table III
Environmental hazard scenarios for intentional and unintentional introductions of aquatic genetically engineered organisms (GEOs) and the categories of ecological harms that should be assessed for each scenario
Scientific difficulty of assessing harms increases going from the left to right columns

Hazard scenario	Predicted fate of transgene or transgenic individuals	Assess ecological harms			
		Ecologically safe?	Alter genetic diversity?	Harm species of special concern?	Reduce aquatic biotic community resilience?
Gene flow to wild relatives	Purging	Assess		Assess	
	Spread		Assess	Assess	Assess
	Trojan gene		Assess	Assess	Assess
Alien species invasion	Disappearance	Assess		Assess	
	Establishment			Assess	Assess

accomplished physically (e.g. by screens and other mechanical barriers to prevent escape from rearing tanks and ponds), physico-chemically (e.g. by lethal water temperatures or chemicals applied to water in existing fish tanks), or biologically (e.g. by rendering the organism incapable of reproducing or of surviving outside of the aquaculture system). It is unlikely that 100% confinement would be achieved by a single method.

The best developed and scientifically documented method for biological confinement of transgenic fish involves disrupting sexual reproduction by triploidy induction. The weaknesses of this method include incomplete success in producing triploids and the fact that the degree of functional sterility in triploids varies depending on the species and sex. Biotechnologists can increase the degree of functional sterility in some fish species, such as salmon, by combining triploidy with all-female lines. The environmental entry of large numbers of triploid transgenic individuals on a recurring basis would call for the assessment of two different scenarios that could potentially cause ecological harm, as follows:

– triploids of some species have enough sex hormones to stimulate them to engage in normal courtship and spawning behaviour, which could lead to losses of entire broods and lowering reproductive success of wild fish

– sterile transgenic adults could lead to heightened predation or competition if they survive and grow for an indeterminate period beyond the normal life span.

The NRC report includes a chapter on the biological confinement of animals which presents a case study of combining triploidy and all-female lines as well as applying mass screening methods to identify and remove non-triploids. The case examines the possibility of introducing transgenic Atlantic salmon into the existing salmon farms in Maine, which consist of floating cages in coastal waters. Salmon escape from such cages, sometimes in the order of thousands during storms or other catastrophic events. Many of the wild populations of Atlantic salmon in Maine are already threatened or endangered, with eight populations legally protected by the Federal Government, and expensive efforts are underway to recover these populations. For this scenario, individual screening to cull non-triploids is the more prudent choice before moving young salmon from more secure land-based hatcheries to floating cages. A conservative estimate indicates that the cost of screening individual salmon by flow cytometry would add US$0.02 to US$0.04 per 1 kg of fish to the market cost of farmed adult Atlantic salmon (26).

The report recommended an integrated confinement system approach for GEOs that warrant confinement. The stringency of the integrated confinement system should reflect the predicted risk and severity of harm of GEO escape. Elements of an integrated confinement system include:

– commitment to confinement by top management

– establishment of a written plan for implementing redundant (i.e. backup) confinement measures in case the first measure fails, including documentation, monitoring, and remediation (in case of complete failure of all confinement measures)

– training of employees

– dedication of permanent staff to maintain continuity

– use of standard operating procedures for implementing redundant confinement measures

– use of good management practices for applying confinement measures to pharmaceutical-producing GEOs or the equivalent

– periodic audits by an independent entity to ensure that all elements are in place and working well

– periodic internal review and adjustment to allow adaptive modifications of the system in light of lessons learned

– reporting to an appropriate regulatory body.

Finally, the report addressed a number of scientific and technical needs, the importance of transparency and public participation in the development and implementation of bioconfinement, and the need for international cooperation to adequately manage the confinement of GEOs.

Conclusion

Scientists are poorly equipped at present to provide decision-makers and other interested parties with the information needed for assessing and managing the biosafety of most genetically engineered fish and shellfish. Obstacles to providing this information include key gaps in the scientific knowledge about traits of aquatic GEOs, the ecology of natural environments these organisms might enter, and interactions between the two. These obstacles are sometimes compounded by a lack of understanding of the biology and ecological role of unmodified counterparts in the ecosystems that transgenic individuals might enter. Another considerable impediment is the lack of scientifically confirmed methodologies for obtaining empirical data needed to inform the risk assessment and management process. Current scientific methods and data are sufficient for hazard identification (the first step in risk assessment) but not adequately developed for the assessment of potential harms and their severity (the last

step in risk assessment). Risk management of aquatic GEOs is in its infancy, focusing so far on reducing risk by applying a few well-known biological and physical confinement methods. Virtually no work has been undertaken to design feasible and reliable safety monitoring and remedial action plans that could be implemented as part of possible future large-scale uses of transgenic fish or shellfish.

The development of a growing diversity of genetically engineered fish and shellfish is advancing in spite of these existing weaknesses in environmental biosafety science. A transgenic ornamental fish is already on the market; at least one company in the USA is known to be actively seeking commercial approval for growth-enhanced transgenic salmon and perhaps trout; and other labs in Cuba and the People's Republic of China are moving in this direction (Table I). There is thus a clear need to increase national efforts and international cooperation to improve the status of the biosafety science, risk assessment and management of aquatic GEOs. It will be important to prioritise the kinds of weaknesses discussed in this paper and then design and implement cooperative programmes to support research to redress them. Input into this process should come not only from the scientific community but from legitimate representatives of all potentially affected parties (28, 41).

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État actuel des connaissances scientifiques sur la biosécurité environnementale des poissons, crustacés et mollusques transgéniques

A.R. Kapuscinski

Résumé

Le poisson-zèbre fluorescent a été le premier animal produit par génie génétique à être commercialisé ; de nombreux poissons, mollusques et crustacés trangéniques sont désormais obtenus par les spécialistes des biotechnologies. Les connaissances scientifiques en matière de biosécurité ne permettent pas encore de tirer des conclusions fiables d'un point de vue scientifique et communément admises sur les effets produits par ces animaux sur l'environnement. La science parvient à identifier les dangers posés par la propagation dans l'environnement de poissons, de mollusques ou de crustacés transgéniques, mais les nuisances écologiques potentielles de cette propagation restent difficiles à évaluer. La dispersion dans l'environnement de certains poissons, crustacés ou mollusques transgéniques pourrait constituer un mode indirect d'introduction dans la chaîne alimentaire humaine. La gestion du risque dans le cadre de la science de la biosécurité n'en est qu'à ses débuts et a été jusqu'ici axée sur la première étape du processus de gestion du risque, à savoir la réduction du risque par l'application de quelques méthodes de confinement. Il est crucial d'améliorer les méthodes scientifiques d'évaluation de la sécurité de l'environnement et de collecter les données empiriques permettant d'établir le bien-fondé des mesures de biosécurité et d'élaborer des méthodes efficaces de gestion des poissons, crustacés et mollusques transgéniques. Les chercheurs et les parties potentiellement concernées devront se concerter sur les lacunes qu'il convient de traiter en priorité.

Mots-clés

Aquaculture – Animal aquatique – Aliment destiné à la consommation humaine – Confinement biologique – Contrôle biologique – Environnement – Espèce invasive – Évaluation du risque – Gestion du risque – Mollusque et crustacé – Nuisance écologique – Organisme produit par génie génétique – Poisson – Propagation transgénique – Recherche en biosécurité – Science de la biosécurité – Secteur de l'élevage des poissons d'ornement – Système de confinement intégré – Transgénique.

Estado de los conocimientos científicos sobre el nivel de bioseguridad para el medio ambiente que presentan los peces y crustáceos transgénicos

A.R. Kapuscinski

Resumen

Tras la primera comercialización de un animal genéticamente modificado (un pez cebra fluorescente), los especialistas en biotecnología están obteniendo un gran número de peces y crustáceos transgénicos. En materia de bioseguridad, la ciencia no está lo bastante avanzada como para poder extraer conclusiones fiables desde el punto de vista científico y comúnmente aceptadas acerca de los efectos que tienen estos animales sobre el medio ambiente. La ciencia es capaz de detectar los peligros derivados de la dispersión en el medio natural de peces o crustáceos transgénicos, pero no sabe cómo determinar los posibles perjuicios ecológicos que ello acarrearía. La dispersión en el medio de ciertos peces o crustáceos transgénicos podría constituir una vía indirecta de entrada en el aprovisionamiento alimentario del hombre. La rama de la ciencia que trata de la bioseguridad apenas empieza a ocuparse de la gestión de riesgos, y hasta ahora se ha concentrado en la primera etapa del proceso, a saber, la reducción de riesgos mediante unos pocos métodos de confinamiento. Es imperativo mejorar los métodos científicos de evaluación de la inocuidad para el medio ambiente, y también reunir datos empíricos que justifiquen las medidas de bioseguridad y que ayuden a elaborar procedimientos eficaces de gestión de los peces y crustáceos transgénicos. Los científicos y las eventuales partes afectadas deberían definir conjuntamente el orden de prioridades en que deben abordarse las incógnitas científicas en este terreno.

Palabras clave

Acuicultura – Alimento de consumo humano – Animal acuático – Ciencia de la bioseguridad – Confinamiento biológico – Control biológico – Crustáceo – Determinación del riesgo – Diseminación de transgenes – Especie invasiva – Gestión del riesgo – Industria de peces ornamentales – Investigación en bioseguridad – Medio ambiente – Organismo genéticamente modificado – Pez – Perjuicio ecológico – Sistema integrado de confinamiento – Transgénico.

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