

Effects of Genetically Modified Animals on Human Activities and Ecosystem

ABSTRACT: *The first transgenic animals was mice which are now still the transgenic organisms most commonly used. There are various strategies in place for transferring foreign genes to the specific organisms. Transgenic organisms were used to study the gene and biological functions primarily for basic research. Transgenic animals may also be important models for researching human and animal diseases, and for developing new medicines. Transgenics can also be the source of both human and medicinal organs and cells. Transgenesis' effect on developing animals for both the production of food and feed is still non-existent but is anticipated to become a fact in the coming months. A few transgenic animals were obtained and marketed. The use of the transgenic animals poses some welfare issues, and the EU has established specific regulations. Transgenesis in animals already impacts human activities and people's perception of the living organisms. The techniques accessible make it possible for transgenic human generation. Until now, this was not done or suggested. The human effects of transgenesis may be enormous. There are theoretical and ethical discussions under way on this subject.*

KEYWORDS: *Human Activities, Medicines, Pharmaceutical Proteins, Transgenic Animals, Transgenesis.*

INTRODUCTION

Transgenic animal processing has raised concerns about its possible ecological effects should they escape or be introduced into the natural environment. This problem emerged primarily from work on animals raised in laboratories and experiments in theoretical modelling[1]. Transgenes with a number of roles have been introduced into a broad range of animals with potential applications from low-scale fundamental laboratory research and applied medicine to huge-scale disease control and industrial meat processing[2]. In particular, the above application raised questions about the possible adverse effects that transgenic animals could have on the natural world, whether they escape from raising facilities or are intentionally released into the wild[1], [2].

In 1980, genetic engineering of animals for producing transgenic animals began. The first transgenic animals was mice which are now the transgenic organisms most commonly used[1]. Approximately 20 transgenic organisms have been obtained, and are usually used more or less. There are various strategies in place for transferring foreign genes to the specific organisms. Transgenic organisms are used to study gene and biological functions primarily for basic research[3]. Transgenics can also be the source of both human and medicinal organs and cells. Transgenesis 'effect on developing animals for the production of the food and feed is still non-existent but is anticipated to become a fact in the coming months.

Many animal species were domesticated by humans in order to acquire food, gain energy for various tasks and as companions. Breeding possibly helped expose the reproductive processes of humans including their own. Human beings actually separated themselves from animals long ago, while acknowledging their similarity to animals[4]. More recent humans have proposed incorporating certain animals' biological properties with their own. They had imagined the existence of human and bull or goat chimeras. They identified these chimeric species and they represented them but could not generate them. Therefore, genetic selection has become much

more effective but still relies entirely on natural and random mutations[1], [3]. To expand the variety of plants and animals, humans started using mutagenic chemical compounds. They introduced the mutagens to micro-organisms, then to the plants and animals. By that point, the mutations were more common, but still totally unpredictable and unknown. A collection helps new interest lines to emerge. Thus, more than 3000 varieties of plants have been collected and validated and are used as food[2], [4].

So transgenesis is a modern and complementary genetic selection process. The advantages and disadvantages of transgenesis over traditional genetic selection are as follows: modern genetic selection is based on the spontaneous dispatch in the same species of the different variants of the parental genes[1]. This gene transfer happens during the formation of gamete (sperm and oocyte). Therefore, the efficacy is limited by the fact that the natural selection evolution infrequently creates the new genes. Obtaining a maize variety resistant to insects by traditional selection may take many years, or may never even happen at all. Any such variety can also have poor genetic properties, too (low yield, toxin presence, etc.)[1], [2], [4].

Additionally, traditional genetic selection is focused on the chromosome rearrangements that pick a large number of unidentified genes around the gene (usually also unknown) responsible for the genetic improvement. Transgenesis can be very successful when a gene with a beneficial effect that is powerful enough has been established. It is true of the growth hormone gene that accelerates the development of salmon[5]. Conventional genetic selection remains important when a role depends on many genes which have not been established. Therefore, modern selection and transgenesis complement each other and are not really in competition. Nevertheless, it is now accepted that environment-induced epigenetic pathways have a significant effect on gene expression. It is especially true of the cloning technique presently used to produce transgenic large farm animals[1], [2], [5]. The errors in the reprogramming of genomes in clones and their possible deleterious consequences are unpredictable.

1. Major Uses Of Transgenic Animals

Through the genomics research it has become possible to classify all the genes in a variety of organisms. Any given genetic message can be read and the chemical structure of the respective protein predicted. In certain instances, this does not offer any insight as to how the protein acts in cells and entire species[6]. One way to cross this gap is by over- and under-expressing the gene at issue in mice. Another option is for the gene in mice or any other animal to be inactivated selectively. In particular, these genetic variations correlate with changes in the animal phenotype. An in-depth analysis of modifications may disclose the function of the gene as well as the protein in question[2]. For these basic studies, more than 90 per cent of transgenic animals are produced. The best way to research gene functions under natural conditions is to conduct transgenesis: that is, in living organisms.

In this form of research, the mouse is the most commonly used animal species for many reasons: mice are mammals including humans, mice are small but not too costly to breed and mice are scientifically one of the greatest-understood creatures. Genetic modifications in mice are pretty simple too[3], [5]. Mice are not regular pets, but instead animals with certain harmful human impacts. Mice may not be suitable models to study any of the human genes and biological functions. Many species of animals are also used: rodents, rabbits and pigs in the majority[4].

Basic studies to decode their unique biological properties are also performed in many organisms. The fruit-fly (*Drosophila*), fish (zebra fish and medaka) and a batrachian (*Xenopus*), are the same. For such cases, the results of transgenesis are by definition unpredictable[1], [6]. Many of such consequences for animals can be deleterious.

1.1. Generation of models for the biomedical studies

It is probable that animal models are used for researching human diseases. Spontaneous mutations may create lines of laboratory animals that mimic human diseases. Naturally this only happens occasionally and transgenesis is of utmost importance in the development of specific models. That implies the identification of genes potentially involved in a disease[7]. The transfer of genes that then generate transgenic animals that mimic or are immune to a disease. Transgenic animals that are immune to a disease can be used for testing of experimental medicines. A variety of models of cancer are mainly studied in mice and rats. Rodents are not suited for treating other diseases, like cystic fibrosis and cardiovascular disorders[8]. In such cases Rabbits are favored. Pigs are being more and more used as templates. Related models are difficult to obtain since some remain too distant from the human pathologies. That is the case with especially complicated Alzheimer's disease. Zebra fish, while not a mammal, is a valid model for the study of highly conserved mechanisms of growth[7], [8]. The use of these models is undoubtedly a cause of certain (hopefully minimal) animal suffering[5].

1.2. Adaptation of animal cells and organs for humans

The lifespan of humans is becoming prolonged and medical professionals are becoming increasingly willing to transplant the cells and organs into the patients. The number of patients requiring transplants is rising however the number of donors of organs is that much slower[3], [4]. This has generated an organs shortage and the deaths of rising numbers of the patients waiting for donations. One common procedure is to replace human organs with artificial organs (allotransplantation). Last attempted a century ago was to replace human organs with animal organs (xenotransplantation)[2], [5].

While the surgical component of the transplant has often been successful, in all instances the transplanted foreign organs have been firmly rejected and destroyed. Consequently, this method was slowly discarded until a potent immunosuppressor, cyclosporine A, was discovered[1], which led to greater acceptance of human organs transplanted in the patients. It soon became obvious that this medication, and others, did not enhance patients' protection of animal organs. Clearly, the mechanisms of rejection which triggered the destruction of grafted animal organs were different from those involved in rejecting human organs.[3]

Some animal components, such as cardiac valves, are presently being incorporated into humans. Valves hold no cells and are inactive, and thus are not rejected. The same wouldn't extend to organ transplants. This caused unexpected concern from patients who had been candidates for pig organ grafting (heart, kidney, etc.)[9]. Others asked if they should turn their movements and behaviors into pigs. Others considered what transgenic pigs would be like in wildlife. He felt the introduction of human genes would humanize the pigs and wondered how many human genes is enough to make a humanized pig. Clearly the reason is that increasing the numbers of human genes transmitted to pigs won't make them human. In the contrary, adding greater and greater human genes will only slowly alter the function of pigs, perhaps not making them viable any

more. The definition of xenotransplantation explicitly poses basic concerns about the properties of the living organisms[1], [9].

Many complications occurred when the pig pancreases were grafted into diabetics. Such patients have been warned that the grafting may not substitute insulin injections in all cases and they will be immunosuppressed to avoid rejection. It will mean patients who do not live in sunshine to prevent skin cancer[3], [4]. In addition, patients were told that the pancreas cells that had been grafted could be damaged in time. This will require a new transplant. Several patients opted instead for insulin injections. Several researchers discarded this path, given that the patients' future benefit was unclear.

1.3. Pharmaceutical proteins production by the transgenic animals

Proteins are the main molecular actors in living organisms, while DNA is the library of genes. When a cell or organism requires a protein, a message is then sent to the corresponding gene that is activated, as well as the protein in question is synthesized. Natural mutations could inactivate a gene, or corresponding protein, resulting in a disorder[1]. The gene coding for the coagulation factors is one example. The active corresponding factor could no longer be synthesized when one of them becomes mutated and the individual suffers from hemophilia. This genetic disorder can be treated in different ways. Many coagulation factors could be derived from the human blood to be injected when required into patients.

Hemophilia A and B are also treated with Factors VIII and IX removed, respectively[10]. Factor VII is not present in the human blood sufficiently to be removed and used as a medication. Hence, it must be generated using other methods. In addition, it was agreed globally to limit as far as possible the use of human blood as just a source of the pharmaceutical proteins[10], [11]. In reality, obtaining blood samples from humans can cause ethical issues, and pathogens can contaminate the blood. Utilizing transgenic animals to produce pharmaceutical proteins is a recent idea that is generally embraced by patients who someday will need such drugs and who have faith in the methods because these products are still under pharmaceutical agencies' scrutiny[11]. Transgenic plants also aim to produce specific recombinant proteins.

2. Use of transgenic animals for improving breeding and food

The first transgenic animal, mice, was born in 1980, and they produced the first transgenic plants in 1983[12]. But transgenic food plants only started to be marketed in the early 1990s and were produced on a high-scale basis from 1996 onwards, although no transgenic animal food is available on the market. The delay in the use for food of the transgenic animals (also known as GMA: genetically modified animals when it is used as a source of food)[13] is attributable to the fact that it is easier and less expensive to manufacture and sell transgenic plant products. Plants are also the first species in the food chain and the transgenic animals have been, and still are, primarily used in basic and medical studies[4]. The issues that the use of transgenic animals can theoretically address are not that different from those of plants.

2.1. The struggle against diseases

Combating disease is a priority because this will minimize herd losses and the number of pharmaceutical treatments in livestock, promote breeders' activities and reduce the risk of transmission of the animal pathogen to humans[1]. Using different methods, in other projects, cat

fish susceptibility to bacteria could be reduced; mice resistant to pig Aujeszki disease could be generated; chicken lines resistant to influenza virus H5N1 could be established; and cows potentially resistant to the mad cow disease. Three proteins are known to bear antibacterial activity: human lysozyme (hLys), human lactoferrin (hLf), and lysostaphin[12]. Both three, and particularly the third, raising mastitis incidence. In human milk hLf and hLys prevail, but not in ruminant milk. These human proteins are found in the milk from transgenic cows and goats. This milk can help protect the consumers from bacterial infections. Thus, milk can also be the transmitter of other proteins, including monoclonal antibodies with anti-pathogenic activity[13].

2.2.Improvement of food quality

Milk and meat enriched with polyunsaturated fatty acids, called omega-3, were obtained that are supposed to improve human health. A research has currently been published revealing transgenic cow's milk depleted of its main allergen, beta-lactoglobulin[12].

2.3.Growth acceleration

A simple examination of the domesticated plants and animals to use as food source reveals remarkably that one of the main goals of genetic selection over past 10,000 years has been to increase production[9], [10]. Nonetheless, domesticated plants and animals are sometimes greater than their wild counterparts, or grow faster. Why our ancestors decided to increase the agricultural yields to get some more food is easy to understand. This goal remains a concern with a few species currently domesticated and inappropriately selected for increased growth. It is particularly true of aquaculture. Some numbers of fish are rising over their entire lives[11]. In salmon this is the case. Huge quantities of salmon are produced, and it has been demonstrated that their growth can be significantly accelerated (but still not enhanced) by administering the growth hormone (sGH) experimentally[2], [9]. This method appears not to be feasible on a wide scale as sGH has a short half-life and it has to be injected for months numerous times a week to increase efficiency[5].

3. Social aspects of GM animals

During the past 15 years GM plants have achieved unparalleled progress in seed history. GM plants in all regions are cultivated but only slightly in the EU[1]. Yet in Spain and Portugal, Bt maize is increasingly cultivated. The decision to oppose GM plant culture in the EU is generally recognized as not focused on strong logical arguments. The first GM animals were about to be released into the market, salmon with rapid production. Specific guidelines have been developed in different countries, and also ethical and societal analyzes of GM animals[2].

3.1.Safety of food from GM animals

Guidelines for the use of GM plants have been in place for 15 years. It would appear appropriate considering that no adverse effects were found in humans and animals. When required these guidelines are updated to improve biosafety[14]. Previously, the guidelines of the EFSA (European Food Safety Authority) have established more precise criteria for carrying out the 90-days toxicity tests and analyze data using the most applicable statistical analysis methods. The various toxicity tests are similar in nature to those applied to GM plants[3]. On some different points, the animals vary from the plants. In certain cases, plants produce toxins which are in fact natural pesticides. Plants don't typically be immune to their own toxins[4]. Our ancestors have

chosen and picked the plants kept by humans for use as food in such a way as to pose no health concerns for consumers. Animals used in the food are assumed not to contain chemicals that are potentially harmful to humans. In fact, GM species are vertebrates, and even primates, that are biologically similar to humans[14]. Therefore GM animals are also outstanding laboratory animals for the identification of harmful substances. Nonetheless, any toxic compound found in GM animals but not in controls would also have obvious harmful effects on the animals that would in turn be eliminated and are not included in the food chain[1], [14].

Plants are deemed unable to transmit infectious diseases to humans, while the transmission of animal diseases to humans occurs rarely. It is possible that GM animals are more likely to infect customers, for reasons not generally understood[14]. The currently in place veterinary procedures are sufficient to adapt successfully to GM animals.

3.2. Environmental impact of GM animals

The great awaited environmental concern that emerges from GM animals is their potential escape. The threats depending on the species as well as the transgene are significantly different. Farm animals are restricted and, in wild conditions, some cannot survive. Cows, horses, pigs and goats will survive[3], [5], [14]. Pigs should be able to jump boars. Bred rabbits likely wouldn't have lasted for more than a couple of days because most are albinos and not suited to wide spaces. Foxes and dogs will track them down very soon. For the period of pregnancy and lactation, a female fertilized by a wild male would need to stay alive to disseminate its transgenes[4]. It certainly isn't going to happen. A male rabbit may live long enough to fertilize and transfer its genes to a wild female. The animals that fly and swim may usually flee, more or less endure and cross with the wild relatives[12].

The transgene function is essential, too. The escaped fish, with a higher survival capability (more resistant to microorganisms) and reproduction, could contribute by establishing a colonization of a given area. This situation does occur regardless of transgenesis[9], [11]. The mixing of regular escaped pigs with the boars creates hybrids that are both abundant and well suited to the wild. This form of occurrence should not be more common and riskier for genetically modified animals. On the opposite, GM pigs should not be bred in facilities of low quality thereby reducing their chances of escape. In fact, most of the transgenes were selected to enhance life in herds, not wildlife[9], [12]. The decision to breed a new product line of GM animals must take into account the potential environmental effects.

CONCLUSION

It is necessary to use genetically modified organisms in order to meet that demands and enhance existing conditions that are prevalent in our climate. Regulations related to the use of GMOs provide a wider framework for decision taking. International regulatory mechanisms for biosafety are sufficiently strict to protect against real, ascertainable threats, as well as the capacity of decision-makers to determine the acceptability of the data required to perform a risk assessment appropriately, both of which have major implications. Consideration needs to be considered of social, economic and ethical problems. Usage of the precautionary approach offers avenues for the future genetic engineering production and use. To humans another opportunity is to improve their natural environment. In reality, the human body is so complex that anyone can imagine slowing, but not stopping, deterioration and death. All the components (cells and

organs) cannot be easily replaced at any lifespan. The theme of the science fiction at the moment is improving human life, making people less violent, less nervous, and more intelligent and so on. Controlling brains by molecules or nanoparticles seems to be more practical, better or worse.

REFERENCES

- [1] A. Lievens, M. Petrillo, M. Querci, and A. Patak, "Genetically modified animals: Options and issues for traceability and enforcement," *Trends in Food Science and Technology*. 2015.
- [2] T. L. of Congress, "Restrictions on Genetically Modified Organisms," 2015, 2015.
- [3] K. Shankar and H. M. Mehendale, "Transgenic Animals," in *Encyclopedia of Toxicology: Third Edition*, 2014.
- [4] O. G. Maksimenko, A. V. Deykin, Y. M. Khodarovich, and P. G. Georgiev, "Use of Transgenic Animals in Biotechnology: Prospects and Problems," *Acta Naturae*, 2013.
- [5] J. D. Murray, "TRANSGENIC ANIMALS IN AGRICULTURE," *Reprod. Fertil. Dev.*, 2013.
- [6] B. Petersen and H. Niemann, "Molecular scissors and their application in genetically modified farm animals," *Transgenic Research*. 2015.
- [7] C. Xinaris, V. Brizi, and G. Remuzzi, "Organoid Models and Applications in Biomedical Research," *Nephron*, 2015.
- [8] B. Ellenbroek and J. Youn, "Rodent models in neuroscience research: Is it a rat race?," *DMM Dis. Model. Mech.*, 2016.
- [9] L. M. Houdebine, "Impacts of genetically modified animals on the ecosystem and human activities," *Glob. Bioeth.*, 2014.
- [10] L. M. Houdebine, "Production of pharmaceutical proteins by transgenic animals," *Rev. Sci. Tech.*, 2018.
- [11] L. R. Bertolini *et al.*, "The transgenic animal platform for biopharmaceutical production," *Transgenic Research*. 2016.
- [12] P. Ahmad *et al.*, "Role of transgenic plants in agriculture and biopharming," *Biotechnology Advances*. 2012.
- [13] G. Laible, J. Wei, and S. Wagner, "Improving livestock for agriculture - technological progress from random transgenesis to precision genome editing heralds a new era," *Biotechnology Journal*. 2015.
- [14] A. S. Bawa and K. R. Anilakumar, "Genetically modified foods: Safety, risks and public concerns - A review," *Journal of Food Science and Technology*. 2013.