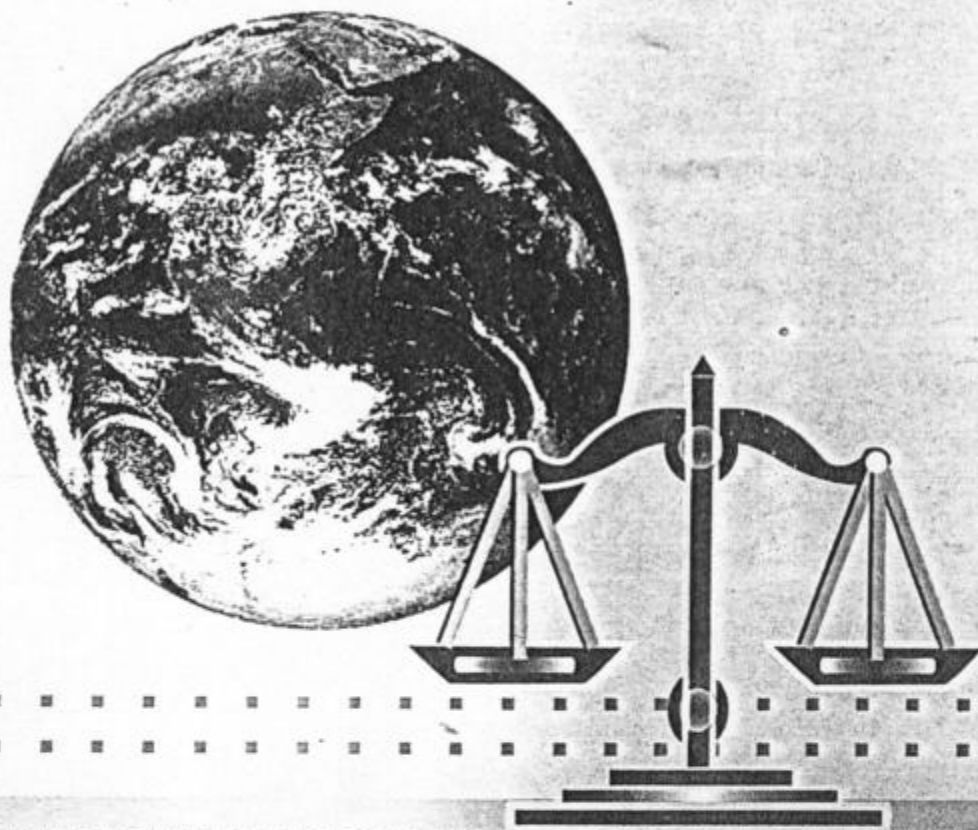




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ETHICAL ISSUES IN ANIMAL TRANSGENESES

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Abstract

The production and use of various kinds of the genetically manipulated (transgenic) animals has rapidly increased in biomedical and farm animal biotechnology. In this paper the moral aspects of animal genetic manipulation (animal transgenesis) according to the Iranian culture, moral, and religious values have been addressed. First the morally acceptable and objectionable issues in the process of animal transgenesis are discussed. The process of animal transgenesis is categorized into three phases of gene transfer into host embryo, transfer of genetically manipulated embryos into surrogate mother, and the evaluation of transgenic offspring. These three phases are outlined with an emphasis on the moral and cultural appropriateness of concepts like transfer of foreign genes into an organism, hormonal and surgical intervention of embryo donors and recipients, physical manipulation and selection of embryos as living entities, and the final selection of transgenic animals to choose the desirable modified genomes. Next, the potential benefits, harms, and also cultural and religious acceptability of various uses of transgenic animals have been outlined. Two main categories of utilization of transgenic animals, being beneficial for the life of just human, or for both human and animal lives are elaborated. In many cases transgenic animals are exploited to serve solely for human life, when they are used to advance our knowledge about the biological processes, when they are the donors of human-compatible organs, and when they make many pharmaceuticals as bioreactors. Enhancement of resistance to diseases, and protection of the endangered species from extinction are examples of the second category, where the transgenesis improves the life of the animals that are also valuable for human life. Finally, an emphasis has been put on the current status of animal transgenesis in Iran, and for the improvement and

future development of animal transgenesis some policies have been proposed. Implementation of globally-accepted laws, establishment of organizations that could act as the national references of all biotechnological acts, and raising the general public's awareness through educational programs are among these policies. A special reference has been made to the necessity of a balance among three elements of "demands", "expert opinion", and the "understanding of the general public", which seems necessary for a decision to be made at the level of government and society.

Keywords: Animal, Transgenesis, Bioethics

Introduction

GENERATION OF TRANSGENIC ANIMALS

The main objective of animal transgenesis is to have a genetically modified animal [1,2] which is able or unable to produce specific protein (s). Figure 1 summarizes the whole procedure which essentially is made of three steps.

1) The transgene is transferred into a host embryo using different methods of gene transfer. 2) The host embryo containing the transgene will be transferred into the uterus of a recipient female. 3) The surrogate mother gives birth to the transgenic offspring.

1. GENE TRANSFER INTO HOST EMBRYOS

In this step, the foreign DNA molecule (transgene) is transferred into the host embryo. For the production of host embryos, female donor animals are stimulated by different hormones to ovulate multiple oocytes. For the best results, usually the young females and even before their puberty are chosen for superovulation. The superovulated small donor animals are killed for the collection of oocytes. However, in large animals there is no need to kill the animal and the oocytes could be collected by flushing of the female reproductive system. Transfer of a foreign DNA molecule, hormone injection, embryo collection, and physical manipulation of host embryos are four stages of the host embryo production, which need to be examined ethically [3] (items shown by asterisks in Figure 1). As long as Iran's culture and national beliefs is concerned, to intervene in what might be thought of as "the fabric of life" ...

The transgene is transferred by completely different methods of retroviral transfer, pronuclear microinjection, using embryonic stem (ES) cells as packages to transfer the transgene, using adult cells nuclei as packages that transfer the transgene (cloning); and using sperm cells as packages that transfer the transgene (Figure 1). Since none of these methods are 100% efficient and as a matter of fact are very inefficient, the genetically manipulated embryos may not have the desired genetic makeup. Using ES cells and nuclear transfer (cloning) makes it possible to

select the desired embryos at this stage and before transfer to the surrogate mother; however, the outcome of transgenesis with other gene transfer techniques would not be possible until the birth of transgenic offspring. The unwanted embryos will be thrown away.

2. TRANSFER OF GENETICALLY MANIPULATED EMBRYOS —

The embryos containing the transgene for further growth will be transferred into the uterus of a pseudopregnant female. Pseudopregnancy is caused in a female by hormones and /or by mating the animal with a vasectomised male. Transfer of the embryo, necessitate s surgical operation on the pseudopregnant female. Here we need to emphasize on the morally objectionable aspects of pseudoprgnancy, vasectomy, and surgical transfer of embryos (items shown with filled rectangles in Figure 1).

3. TRANSGENIC OFFSPRING

As mentioned before, not all the embryos which are used in the process of gene transfer, would have the desired genetic makeup. Likewise, among those embryos which are transferred, not all of them could result into a desired transgenic animal. Thus, it would be necessary to take tissue samples from the potential transgenic animals and test them to determine transgency. Those animals that produce a negative test will be killed in a humane way or will be so -called "euthanized". Tissue sampling and killing the unwanted animals, are two more stages of the transgenesis process that need to be examined ethically (items shown with hollow rectangles in Figure 1). The subject of "respect for the life of animals" has been emphasized in both cultural and religious backgrounds of Iran. The famous Iranian poet, Ferdowsi, says: "don't hurt an ant that is carrying food because he has life and he likes his own dear life".

USE OF TRANSGENIC ANIMALS

In Figure 1 different uses of transgenic animals are outlined. There is no doubt that using transgenic animals have opened many new horizons in medicine, biology, and agricultural biotechnology [4]. However, what needs to be emphasized on here is the need for a balance of benefit over harm resulting from any intervention. In the following sections, the possible benefits and harms of different uses of transgenic animals will be addressed (Figure 2).

TRANSGENIC ANIMALS AS HUMAN DISEASE MODELS

TRANSGENIC ANIMALS AS DONORS OF HUMAN-COMPATIBLE ORGANS AND TISSUES

Another active area of research on transgenic animals is aimed at producing animals which

could be sources of organs and tissues for human transplantation (xenotransplantation) [5]. Pigs are the most noticed animals which could be used as organ and tissue donors in the near future. Besides the harm to the donor animal which is unavoidable, in Islam pigs are considered as ... animals. Another important subject lays in this context that whether or not human being has the moral and ethical right of killing other animals to keep himself alive. Moral perplexities often arise when there is a clash between two goals of human wellbeing and animal welfare [6].

USING TRANSGENESIS TO INCREASE GENETIC VARIANCE

Unlike its reputation of decreasing genetic variance, transgenesis might contribute to both increasing and decreasing genetic variance [7]. The key concept here is that we often forget to consider the "units of populations" when we think about genetic variance. In a given animal species, genetic variance could be considered in total world population, regional population, between herds, between individuals, and even within individuals. Transgenesis results in genetic variance by adding genes, even genes of other species or recombinant genes to an animal.

TRANSGENIC ANIMALS AS BIORACTORS

Today production of animals that can produce pharmaceuticals (recombinant proteins) is successfully established [8]. Milk, egg white, blood, urine, seminal plasma, and silk worm cocoon from transgenic animals are candidates to be the sources of recombinant proteins [9]. Productions of different proteins including Human growth hormone in cow's milk, and ... in egg white are examples of the efficiency of transgenic animals for being an invaluable source of rare proteins. From the point of animal welfare, aside from the process of transgenesis, the physiological changes which have been taken place in the transgenic animal bioreactors do not seem to cause any suffering.

TRANSGENIC ANIMALS WITH MORE AND BETTER QUALITY OF PRODUCTS

TRANSGENIC ANIMALS TO GAIN INSIGHT INTO GENE FUNCTION

USING TRANSGENESIS TO ENGINEER DISEASE RESISTANCE

Enhancing disease resistance in transgenic animals is another interesting application of transgenesis. These animals are able to produce recombinant antibodies and other proteins that make them and their offspring (through milk) immune to specific diseases. The animal does not suffer from the disease, and the human benefits from the better quality and more quantity of animal product.

CONCLUSION

Almost all of the steps used in transgenesis already occur in nature; identical twins are ultimate clones, fertilization is nuclear transfer, and retroviruses transfer genes between species.

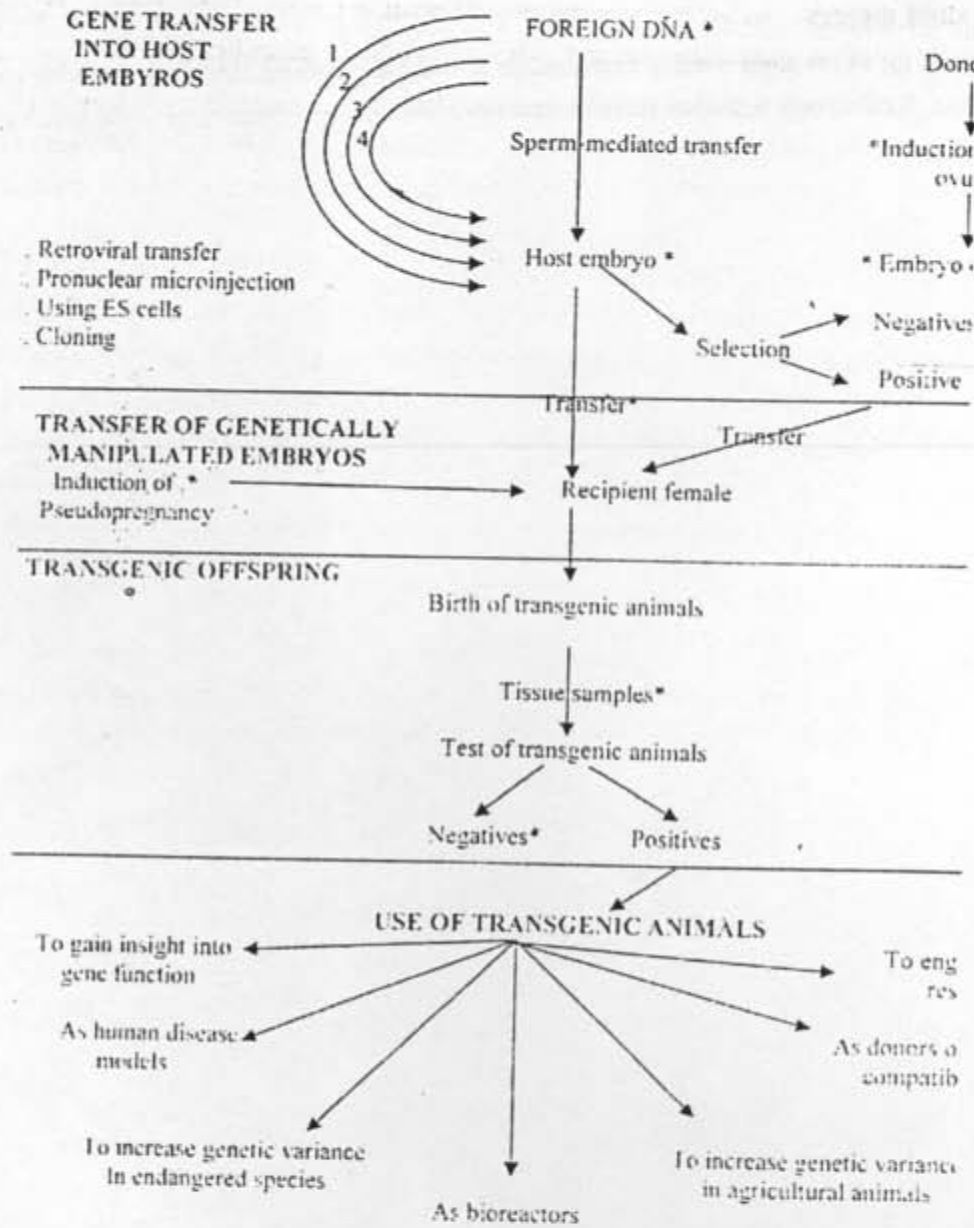


Figure 1. Transgenesis and use of transgenic animals
(Asterisks, show the possible places of harms to animals)

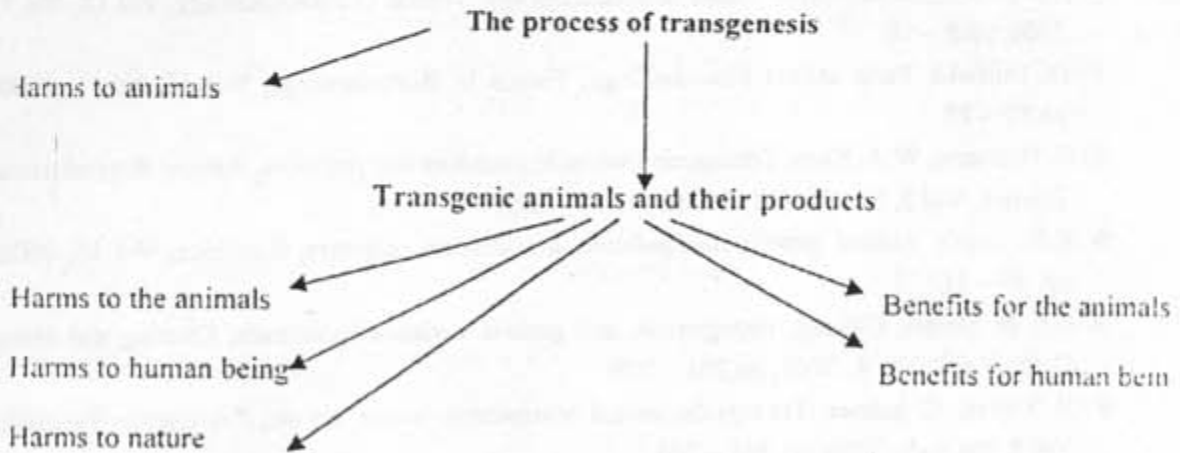


Figure 2. Harms and benefits of Transgenesis and transgenic animals

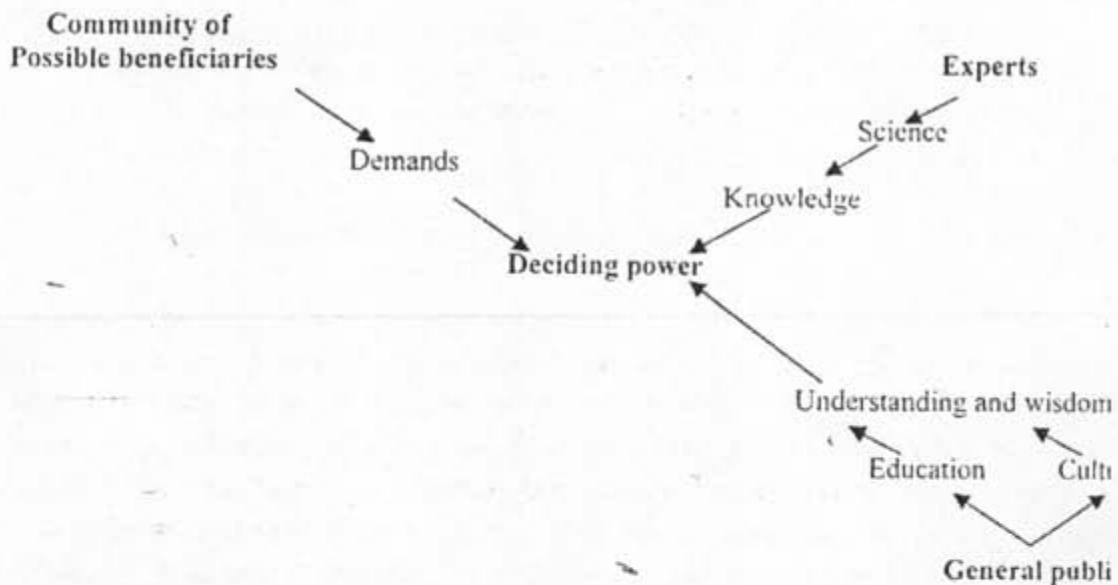


Figure 3. Different parties must be involved to make decisions on the ethical issues of animal transgenesis

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H. ten Have, Ph.D
Director, Division of Ethics
of Science and Technology, UNESCO

A handwritten signature in black ink, appearing to be "H. ten Have".

M. H. Sanati, Ph.D
Secretary of the Congress
Director of NRCGEB

A handwritten signature in black ink, appearing to be "M. H. Sanati".