



A Monthly e Magazine
ISSN:2583-2212

March 2024 Vol.4(3), 1035-1038

Popular Article

Transgenic Animals: Application and Ethical Issues

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<https://doi.org/10.5281/zenodo.10842781>

Introduction

During the 1980s, with considerable effort, the idea of genetically manipulating animals by introducing genes into fertilized eggs was converted into a reality. An animal whose genetic composition has been altered by the addition of exogenous DNA is said to be transgenic. The DNA that is introduced is called a transgene, and the overall process is called transgenesis or transgenic technology.

Transgenic Methodology

For transgenesis, DNA can be introduced into mice by (1) retroviral vectors that infect the cells of early-stage embryo prior to implantation into a receptive female (2) microinjection into the enlarged sperm nucleus (male pronucleus) of a fertilized egg and (3) introduction of genetically engineered embryonic stem cells into an early stage developing embryo prior to implantation into a receptive female.

Retroviral Vector Method

This method has got the advantage of being an effective means of integrating the transgene into the genome of a recipient cell. However, they can only transfer small pieces (~8 kb) of DNA which, because of the size constraint, may lack essential adjacent sequences for regulating the expression of the transgene. Another drawback of retro viral method is that although the vector is designed as replication defective, the genome of the retroviral strain (helper virus) that is needed to create large quantities of the vector DNA can be integrated into the same nucleus as the transgene.

DNA microinjection

It involves the direct introduction of foreign genetic material, typically DNA, into the nucleus of a target cell. Using a fine-tipped glass micropipette, the genetic material is carefully injected into the chosen cell or nucleus, ensuring its integration into the host genome. The cell is then allowed to develop, with the introduced genetic material replicating along with the host DNA. After development, screening techniques are employed to identify individuals that have successfully incorporated the foreign DNA. Those individuals can be bred to establish a stable line of genetically modified organisms. DNA



microinjection has played a crucial role in various fields, including biomedical research, agriculture, and biotechnology, allowing scientists to study gene function and create organisms with specific traits for scientific and practical applications.

The engineered embryonic stem cell method

Cells from the blastocyst stage of a developing mouse embryo can proliferate in cell culture and still retain the capability of differentiating into all other cell including germ line cells- after they are reintroduced into another blastocyst embryo. Such cells are called pluripotent embryonic stem cells (ES) cells. When in culture, ES cells can be readily engineered genetically without altering their pluripotency. With this system, for example, a functional transgene can be integrated into a specific site within a dispensable gene in the genome of ES cells. Then the genetically engineered cells can be selected, grown, and used to generate transgenic animals. In this, the randomness of integration that is inherent with the DNA microinjection and retroviral vector systems is avoided.

The CRISPR-Cas9 system has revolutionized genetic engineering across diverse fields, including stem cell research. This technique leverages a guide RNA (gRNA) that directs the Cas9 protein to a specific DNA sequence, enabling precise modification. Cas9, acting as a molecular scissor, cleaves the DNA at the targeted site. Its remarkable specificity and versatility make CRISPR-Cas9 a preeminent method for gene editing in embryonic stem cells. Researchers utilize it to effectuate gene knockouts, insertions, or other modifications with unparalleled precision.

Transgenic animals have a wide range of applications across various fields.

Biomedical Research

Transgenic animals are engineered to carry specific genetic mutations associated with human diseases. This allows scientists to study the underlying mechanisms, progression, and potential treatments for conditions like cancer, Alzheimer's disease, cystic fibrosis, and diabetes. The efficacy and safety of new drugs, providing valuable information before moving to human clinical trials are also carried out using transgenic animals. Transgenic rats, pigs, rabbits, zebrafish and even yeast have been developed for carrying out various levels of drug human testing. Researchers can also use transgenic technology for studying biological processes. Genes can be manipulated to understand fundamental biological processes, such as development, aging, and immune response. Transgenic animals are used in educational settings to help students understand genetic principles, biological processes, and the impact of genetic modification.

Medicine and Therapeutics

Transgenic animals, like goats or rabbits, can be engineered to produce human proteins or antibodies in their milk or blood. These proteins can then be harvested for use in medications and supplements. Pigs have been genetically modified to potentially serve as donors for human organ transplants (xenotransplantation), although this is an area still under development.

Agriculture

Transgenic animals can be engineered for traits such as faster growth, improved feed conversion efficiency, and disease resistance, which can enhance agricultural productivity. Animals can also be



modified to produce nutrient-rich products, such as milk with enhanced protein or vitamin content.

Biotechnology and Industry

Transgenic animals can be used to produce industrial enzymes, which are valuable in various manufacturing processes, including food processing and textiles. Animals can be engineered to produce complex pharmaceuticals, such as vaccines or therapeutic proteins.

Environmental Applications

Certain transgenic animals, like bacteria-eating fish, have been engineered to help clean up polluted environments by metabolizing or neutralizing contaminants. These augment the bioremediation efforts to a great extent. Transgenic animals can be used to develop pest-resistant or drought-tolerant crops, contributing to sustainable agriculture.

Conservation and Endangered Species

Transgenic techniques can potentially be used to assist in the preservation of endangered species by addressing genetic diversity or infertility issues. Modification of phenotypically relevant genes in an extant species to reflect what existed in the closely related extinct species (or trait resurrection) can be carried out to help survive the varying environmental conditions that we are experiencing presently.

Vaccine Production

Transgenic animals, particularly rodents, have been used to develop viral vector vaccines, which have shown promise in fighting diseases like Ebola and COVID-19. Recombinant vaccine production has been successfully biopharmed in milk of transgenic mice. Transgenics can thus help in the production of easily available vaccines in the future.

Transgenic animals, while holding significant potential for scientific advancement and various industries, also raise several ethical concerns and considerations. Concerns related to transgenic animals encompass a range of ethical, environmental, and safety considerations.

Ethical Considerations

Creating transgenic animals can raise concerns about the well-being and quality of life of these organisms. Some worry about potential harm or stress caused by the genetic modification process or the expression of foreign genes. There is debate about whether altering an animal's genetic makeup infringes upon its intrinsic value or natural state. Some argue that manipulating an animal's genome may compromise its identity or integrity.

Environmental Impact

There is a potential risk of transgenic animals interacting with wild populations if they were to escape into natural environments. This could lead to unforeseen consequences for ecosystems, including competition with native species or genetic contamination. The release of transgenic animals into the wild may have unpredictable effects on biodiversity, food chains, and ecosystems.

Human Health and Safety

There are concerns about potential allergenic reactions or the production of harmful substances in products derived from transgenic animals. These concerns relate to unintended consequences of genetic modification. The introduction of transgenic animals into agricultural or research settings may



raise concerns about the potential transmission of diseases from animals to humans.

Regulation and Oversight

In some regions, there may be inadequate regulatory frameworks or oversight mechanisms for the creation and use of transgenic animals. This can lead to uncertainties about safety and ethical practices. Ensuring that transgenic animal research projects undergo rigorous ethical scrutiny is essential to address concerns about potential harm and ethical implications.

Long-Term Implications

The release of transgenic animals into the environment could have long-term effects on wild populations if they were to interbreed with native species. This could potentially alter genetic diversity and adaptation abilities.

Social and Cultural Concerns

Public acceptance of transgenic animals can vary based on cultural, religious, and societal norms. Some may have ethical or moral objections to altering the genetic makeup of animals. Concerns about transgenic animals may also extend to consumer preferences, potentially affecting markets for products derived from these organisms.

Transgenic animals find applications in biomedical research, agriculture, biotechnology, and more. Techniques like DNA microinjection, viral vectors, and CRISPR-Cas9 are used for genetic engineering. Ethical concerns involve animal welfare, environmental impact, and human health risks. Regulation and oversight, as well as public perception, are crucial factors. Despite these concerns, transgenic animals have significantly advanced various fields, including medicine, agriculture, and biotechnology, with proper oversight and ethical considerations being essential.

References

- Houdebine LM. Transgenic animal models in biomedical research. *Methods Mol Biol.* 2007;360:163-202. doi: 10.1385/1-59745-165-7:163. PMID: 17172731
- Yin, H, Xue, W, Chen, S, Bogorad, RL, Benedetti, E, Grompe, M *et al.* (2014). Genome editing with Cas9 in adult mice corrects a disease mutation and phenotype. *Nat Biotechnol*32: 551–553.
- Bikard, D, Euler, CW, Jiang, W, Nussenzweig, PM, Goldberg, GW, Duportet, X *et al.* (2014). Exploiting CRISPR-Cas nucleases to produce sequence-specific antimicrobials. *Nat Biotechnol*32: 1146–1150.
- Maksimenko OG, Deykin AV, Khodarovich YM, Georgiev PG. Use of transgenic animals in biotechnology: prospects and problems. *Acta Naturae.* 2013 Jan;5(1):33-46. PMID: 23556129; PMCID: PMC3612824.
- Holt, N, Wang, J, Kim, K, Friedman, G, Wang, X, Taupin, V *et al.* (2010). Human hematopoietic stem/progenitor cells modified by zinc-finger nucleases targeted to CCR5 control HIV-1 in vivo. *Nat Biotechnol*28: 839–847.

