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APPLICATION OF TRANSGENIC TECHNOLOGIES ON TRANSGENIC ANIMALS: FOR PROVISION OF NEW AND IMPROVED PRODUCTS, DISEASE RESISTANCE, SELECTIVE BREEDING AND BIOPHARMING: REVIEW

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Abstract:
Modified animals play a significant role in the field of biomedicine especially in drug development, animal disease models, xenotransplantation, gene pharming, antibody production, and blood replacement. Pigs and transgenic animal products like milk and eggs seem to be promising in developments of therapeutic strategies. Advances in molecular biology have made it possible to develop traits in animals quicker with more precision and allowing them as an alternative means to increase yields and improve the nutritional value of food products. Likewise, increased disease resistance can be achieved by introducing resistance conferring gene constructs into animals or by depleting a susceptible gene or locus from the animal. Moreover, livestock health can also be improved through the advent of sensitive and specific diagnostic technologies and new generation vaccines through genomic sequence. Similarly, the DNA sequence of genomes provide data for animal breeding programs to select breeds with desired traits (meat quality, milk production) and increased disease resistance. However, there are also some limitations in producing transgenic animals, being not a perfect technique by itself; its difficulty, lengthy and expensiveness of the procedure with low success and survival rates of transgenic animals.

Key words: Animal Biotechnology; Bio-pharming; Selective breeding; Transgenic animals

Introduction

Globally livestock production is growing faster and is becoming the most important agricultural sector in terms of added value, and hence, referred to as 'livestock revolution'. Agricultural biotechnology is a source of innovation in production and processing of new and improved agricultural products. Transgenic animals and genetically modified organisms (GMOs) are organisms with a segment of foreign DNA incorporated into their genome, or with any modification introduced artificially in their genome sequence. With the advent of transgenic technology and its application in many laboratories around the world, there is an increase in the generation and use of genetically modified animals in biomedical, pharmaceutical research and improvement of animal health and production, in areas such as assisted reproduction, increased disease resistance, refined diagnostic techniques, and increasingly improved vaccines with effective delivery systems (Houdebine, 2009). Quantitative geneticists developed techniques to identify individual genes that influence complex traits. Quantitative traits loci (QTLs) have been identified and mapped on specific chromosomes in model organisms and/or animals such as fruit fly, mouse, pigs (for their fatness and growth rates) and cows (for milk production). Biotechnology is not a single technology; rather it is a group of technologies that share two (common) characteristics: working with living cells and their molecules having a wide range of practice that can improve our lives. One example of modern biotechnology is genetic engineering which is the technique of removing, modifying or adding genes to a DNA molecule in order to change the information it contains. Genetic engineering is used in the production of drugs, human gene therapy, and improved plants Faizi, (2013).

All organisms are made up of cells that are programmed by the same basic genetic material, called deoxyribonucleic acid (DNA). Each unit of DNA is made up of combinations of nucleotides (Adenine, Guanine, Thymine and Cytosine) as well as a sugar and a phosphate. The nucleotides pair up into strands that twist together into a spiral structure called a "double helix". Segments of the DNA so called genes tell individual cells how to produce specific proteins. It is the presence or absence of the specific protein that gives an organism a trait or characteristic Watson and Crick (1953). The objective of this review is to present the application of transgenic technologies on transgenic animals: for provision of new and improved products, disease resistance, selective breeding and biopharming.

Animal biotechnology

Animal biotechnology developed rapidly over the past 20-25 years. The production of genetically modified animals began in the early 1980s (Gjerris *et al.,* 2006). Most work within animal biotechnology has been carried out on laboratory mice, sheep and cattle, but more recently the technologies have been adapted to other species such as pigs, goats, horses and cats. However it should be noted that methodologies and success rates vary from species to species (Gjerris *et al.,* 2006). Animal biotechnology is used primarily for two purposes; to produce animals that can be employed in basic biological research for biological development and function, and to produce disease models that mimic human diseases and can therefore be utilized both in the study of disease (such as Parkinson's, cancer, cystic fibrosis, etc.) and to test new drugs (Gjerris *et al.,* 2006).

Application of Transgenic Technologies on Transgenic Animals

Developing of disease resistance transgenic animals

As described by Müller & Brem (1998) increased disease resistance can be achieved either by introducing resistance conferring gene constructs of that specific disease into the animal's DNA or by depleting a susceptible gene or locus from it.

The emerging biotechnology contributes much more for the livestock sector. Of these contributions, developing of disease resistance transgenic animals is the one. Currently, numerous studies are being performed to induce disease resistance in a variety of animals. Some of these diseases being studied include mad cow disease, foot and mouth disease (FMD), porcine reproductive and respiratory syndrome (PRRS), and avian influenza viruses (AIVs) (Houdebine, 2009).

Mad Cow disease /Bovine spongiform encephalopathy (BSE)

Bovine spongiform encephalopathy (BSE) is a specific type of a transmissible spongiform encephalopathy (TSE) caused by prions and mainly characterized by progressive and degenerative diseases of the brain, spinal cord, central nervous system and a long period of time between infection & detectable symptoms (Schook *et al.,* 2014).

Prion protein (PrP) is encoded by a single-copy host gene and is normally found at the outer surface of neurons (Basler *et al*.1986). The abnormal folding of PrP is thought to cause transmissible spongiform encephalopathy. Abnormally folded PrPs can be transmitted and cause host PrPs to adopt abnormal configurations (Wells *et al*., 1987). According to Scott (1995) speculation, histopathological changes which would rise to clinical disease of a spongiform encephalopathy of cattle are due to spontaneous prion mutation. But Andrews *et al.* (2004) put their idea far from the former one; they describe as whilst neurones and neurites develop there is formation of fine vacuolation of the ground substance resulting one or more well defined intra cytoplasmic vacuoles and this condition distends the cell body and processes which in turn resulting the disease. The primary method for inducing resistance is to silence the PRNP gene, which encodes for the normal PrP. These knock out studies, performed in cattle and mice, have shown that animals without PrP are unable to produce and transmit the infectious form of the protein (Richt *et al*., 2007).

Foot and Mouth Disease /FMD/

Foot and Mouth Disease is a highly contagious viral disease that infects cloven-hoofed animals. Its pathogen, foot and mouth disease virus (FMDV) is easily transmitted through direct contact, aerosols (air-borne), and ingestion. The virus also replicates rapidly once it gets inside the host and symptoms typically appear within 2–3 days (Andrews *et al.,* 2004).

Foot and Mouth Disease poses enormous economic losses on the global livestock and trade industries; for this reason researchers have been created entirely synthetic vaccines to protect animals against FMD. However, vaccines remain problematic for eradicating FMD because of the fact that; there are more than seven serotypes and more than sixty strains of the virus. This has sparked many studies that explore producing transgenic livestock that are resistant to FMD. Multiple studies have shown that RNAI is a viable antiviral strategy in vitro and in vivo, either through the use of small interfering RNAs (siRNAs) or short hair pin RNAs (shRNAs). In brief, when small hairpin RNAs (shRNAs) composed of gene sequences homologus to key gene sequences encoding the infectious agent are introduced into cells and/or embryos, these inhibit replication of the infectious agent by way of RNA interference (Grubman, 2005).

Porcine Reproductive and Respiratory Syndrome /PRRS/

It is a highly contagious disease of swine manifested by reproductive failure and respiratory disease in young pigs and is caused by porcine reproductive and respiratory syndrome virus (PRRSV). It is transmitted through direct contact, aerosol, semen, feces and discharges. It has different antigenic strains with variable virulence (Radostits *et al.,* 2006).

Vaccines have been developed to control the spread of PRRS, but the efficacy of the vaccines varies. The reason many vaccines are not effective is the virus's ability to generate a high degree of genetic diversity and its remarkable ability to evade host defenses. Owing to the unreliability of vaccines, other methods are being studied to control the disease. Some studies are focused on creating breeding programs that only breeds wine with a high resistance to PRRS. Other studies are focused on creating transgenic pigs that are resistant through RNAi (Schook *et al.,* 2014).

Avian Influenza Viruses /AIVs/

Avian influenza viruses are a very diverse group of viruses that infect a wide variety of birds. Moreover for their high rate of mutation, AIVs can also infect other species such as human beings. $H_5N_1$is One of the AIV strands that can infect humans and many other species (Schook *et al.,* 2014).

The human health risks have sparked research into creating disease resistant fowls. Transgenic studies are at the fore front of this field. Transgenic chickens that are unable to transmit AIVs to other birds have recently been produced. This is a monumental achievement for genome editing and disease resistance (Schook *et al.,* 2014).

Transgenic animals for provision of new and improved products

Selective breeding is used to increase desirable traits in animals. However, the possible increased production potential from traditional selective breeding practices is limited. Advances in molecular biology have made it possible to develop traits in animals quicker with more precision, allowing as an alternative means to increase yields and improve the nutritional value of food products. Some transgenic animals already have been approved by the US Food and Drug Aministration (FDA) for production of nonfood products. (Schook *et al.* 2014).

Pig: for production of organs, proteins and being less smelly

According to Bagle *et al.* (2013) description pig is one of the transgenic animals which were been used for development of organs for xenotransplantation, human hemoglobin and human protein C.

Less smelly pig: Production of transgenic farm animals that are more environmentally friend is one of the goals of biotechnology. Guelph University in Canada, have been developed transgenic pigs (EnviroPig) with the issue of manure related environmental pollution in mind. EnviroPig is capable of digesting phosphorus in plants more efficiently than conventional pigs. The EnviroPig contains a bacterial phytase gene controlled by a salivary gland specific promoter, which limits the production of phytase to the saliva. Phytase is an enzyme that releases phosphate from phytate, which accounts for up to 80% of phosphorus content in most feeds. The ability to digest plant phosphorus limits the need for costly feed supplements such as phosphate minerals or commercially produced phytase. In addition, the EnviroPig excretes 30–70% less phosphorus in its waste than conventional pigs. This is environmentally important, as excess phosphorus from manure alters the local water environment, causing increased algae growth, production of greenhouse gases, and the death of fish and aquatic animals. The lower levels of phosphorus in pig feces reduce water pollution (Schook *et al.,* 2014).

Cattle and pigs: for more and better meat production

The ability to produce transgenic pigs and cattle with enhanced muscle growth is an area of interest. Researchers have been studying the effects of targeting myostatin, the only secreted protein known to negatively affect muscle mass in vivo, as well as genes for growth related hormones and lean muscle mass (Long *et al.,* 2009). Transgenic myostatin knockout cows have been produced in the US; however, there are concerns regarding the increased neonatal morbidity that arises from giving birth to larger calves with increased fetal muscle mass (Tessanne *et al.,* 2012).

As Schook *et al.* (2014) described in their review, until 2014; no myostatin knockout pigs have been developed; however, transgenic pigs for growth related hormones have been produced. Although they show improvement in growth rate, feed conversion and body fat/muscle ratios, they also showed signs of fatigue, gastric ulcers, and low libido. Transgenic pigs containing insulin like growth factor1 and a desaturase gene from spinach have been shown to have increased growth rates and increased levels of polyunsaturated fatty acids, respectively.

As it was described by WU *et al*. (2012) omega-3 fatty acids are found mainly in fish oils and largely considered beneficial to human health. Conventional meat products contain large amounts of omega-6 fatty acids, and low levels of omega-3 fatty acids. And diets with a high omega 6/omega 3 fatty acid ratio are correlated with coronary artery disease, cancer, diabetes, arthritis, and depression. To try and create a healthier balance, researchers have developed transgenic pigs and cows containing high levels of omega-3 fatty acids in their tissue. This was done by inserting a gene encoding for an omega-3 fatty acid desaturase into the genome of the pig and cow. Omega-3 fatty acid desaturases are enzymes required for the conversion of omega-6 fatty acids to omega-3 fatty acids. The end result is an increase in omega-3 fatty acids and a decrease in omega-6 fatty acids, thus creating the potential for meat products with a healthier omega 6/omega 3 ratio.

Cow and pig: for Production of β-lactoglobulin lacking milk

Beta-lactoglobulin (BLG) is a whey protein which is expected to be the main cause of milk allergies in humans, and knocking out this gene could allow for the production of hypoallergenic dairy products. A team of scientists at University of Waikato in NewZealand has successfully produced a transgenic cow lacking β-lactoglobulin (BLG) (Jabed et al., 2012). The researchers use miRNA technology to silence the expression of BLG in the milk, making it potentially less allergenic. In addition, high casein levels were reported in the BLG-deficient milk. Casein makes up 80% of milk protein in conventional cows and is an extremely valuable component of milk because of its nutritional value and processing properties. The increased casein levels associated with this BLG knockout cow could also provide increased calcium levels and higher cheese yields. Rresearchers at the University of Illinois have produced transgenic pigs expressing bovine α- lactalbumin, which leads to an increase in milk production (Wheeler *et al*., 2001).

Similar to better meat production by transgenic animals by taking the consideration of omega 3 importance to the human being, researchers developed transgenic pigs and cows containing high levels of omega-3 fatty acids in their milk. This was done by inserting a gene encoding for an omega-3 fatty acid desaturase into the genome of the pig and cow (WU *et al*., 2012).

Cow and goat: for Production of kappa-casein and Silk in milk

Researchers in NewZealand have produced transgenic cows containing β and κ casein genes (Brophy et al., 2003). These cows have been shown to produce milk with a two fold increase in κ casein, and up to 20% increase in β-casein levels. The increase in κ-casein has been associated with improved heat stability and cheese-making properties, whereas increased β-casein has been associated with increased milk calcium levels and whey expulsion.

In addition to cows, there is much interest in producing transgenic goats to create healthier milk for human consumption. For instance, changes in the fatty acid composition of milk produced by goats containing a transgene encoding a stearoyl-CoA desaturase (SCD) enzyme has been reported (Reh *et al*., 2004). SCD works by converting saturated fatty acids into monounsaturated fatty acids. Saturated fatty acids can lead to increased blood cholesterol levels, leading to increased risk of atherosclerosis and coronary heart disease, the decreased level of saturated fatty acids in milk is an important heath

concern. The SCD transgenic goats were shown to have increased levels of monounsaturated fatty acids as well as decreased levels of saturated fatty acids, which could prove to have increased health benefits compared to milk from conventional animals.

Transgenic goats are also being produced for dragline silk in their milk. Dragline silk is made by orb spiders and is the strongest known material. Because of its strength as well as its elasticity, there is much interest in large-scale production of dragline silk for use in military uniforms, medical sutures, and tennis racket strings. After failing to produce the material in bacteria and mammalian cell culture, scientists in Canada have successfully inserted the spider silk genes into goat embryos. When the transgenic goats matured, the spider genes were expressed in the mammary glands of females, which began to secrete tiny strands of spider silk in their milk. Once protocols are in place for the purification and spinning, the resulting thread could be used for a number of commercial as well as medical applications (Schook *et al.*, 2014).

Sheep: for Production of improved wool

Increased wool growth in transgenic sheep has been achieved in New Zealand by introducing an insulin-like growth factor-1 gene associated with a keratin promoter. The keratin promoter allows production of the transgene in the skin and results in an increase in the production. Although no health issues were been observed in the transgenic sheep, the staple strength of the wool produced by the male transgenic sheep was lower than that of female transgenic and non-transgenic animals (Damak *et al*., 1996).

Other new products produced by different transgenic animals

In addition to the above specified new products developed by transgenic animals, Bagle *et al.* (2013) were described some of the transgenic animals and their products in development before some years back as noted here.

Cows: Factors VIII and IX, protein C, recombinant antithrombin III (rATIII) and recombinant HSA.

Sheep: human Factor VII, Factor IX, activated protein C and alpha-1-antitrypsin

Goats: Monoclonal Antibodies (MAbs), Ig fusion proteins, tPA (tissue Plasminogen Activator) and ATryn (recombinant human antithrombin III).

Chickens and Eggs: vaccines, interferons, cytokines, Human Serum Albumin (HSA), insulin and MAbs.

Mice: expression of malaria protein for vaccine development, MAbs, ATIII, beta interferon, cystic fibrosis transmembrane regulator; Factor X, HSA, tPA, myelin basic protein, prolactin, fibrinogen and antineoplastic urinary protein.

Rabbits: recombinant human C1 inhibitor, human erythropoietin, human alpha antitrypsin, human interleukin 2, tPA, alpha glucosidase, and human growth hormone.

Transgenic Animals for Enhancing and Advancing Selective Breeding

Genetics and breeding

Genetics is the science of heredity and it attempts to explain the similarities and the differences that occur among related organisms. Individuals in a population, have significant differences in their genetic composition. And this variation can be quantified by measuring the trait of individuals. http://www.eolss.net/Eolss-sampleAllChapter.aspx

Quantitative geneticists have developed techniques to identify individual genes that influence complex traits. Each gene occupies a specific position in the set of DNA molecules. These DNA molecules organized into discrete structures called chromosomes. A gene's position in a chromosome is call a locus (plural, loci), and the locus for a gene that influences a quantitative trait is called a quantitative trait locus (QTL). QTLs have been identified and mapped on specific chromosomes in model organisms and animals such as fruit fly, mouse, pigs (fatness and growth rates) and cows (milk production). http://www.eolss.net/Eolss-sampleAllChapter.aspx

Traditional animal breeding (TAB) has the potential to exploit variations that existed within breeds and animal populations to bring about genetic improvement in traits of economic importance such as milk yield, growth traits, and egg numbers. TAB has been very successful over the years by utilizing records of the phenotype of an animal and a number of its relatives to estimate the likelihood that an animal will pass on its good traits to its offspring. However, for traits those are difficult to measure such as disease resistance, fertility, and feed conversion efficiency, these traditional breeding methods have not been successful (Oltenacu and Broom 2010).

Use of marker-assisted selection (MAS) overcomes the short falls of TAB. MAS is the selection of traits of interest indirectly by selecting genetic markers associated with desired qualities, as opposed to traditional methods of finding desired qualities by observing phenotypic traits. By estimating breeding values based on marker, pedigree and phenotypic information, MAS can bring genetic improvement in traits of animals where TAB alone has failed.

Beginning in the late 1970's many molecular genetic markers were discovered and developed, including allozymes, restriction fragment length polymorphisms (RFLP), random amplified polymorphic DNA (RAPD), microsatellite DNA and SNPs. The ability to analyze these markers was developed over several decades and has made the mapping of quantitative trait loci (QTL) feasible on a large scale (Brumlop and Finckh, 2010). Out of these genetic markers, SNPs are currently the marker of choice because of their large numbers spaced across the genome.

A disadvantage in the implementation of livestock MAS is that population based, genome wide association studies are unable to detect SNPs associated with a trait if the desired allele has a frequency below 5% or 1% (Brookfield, 2010). Additionally, MAS requires prior knowledge of markers that are associated with traits. Many markers are now known across the genomes of many livestock species, including cows, sheep, and pigs. Genomic selection uses these markers to predict the genomic estimated breeding value (GEBV) for traits of animals (Meuwissen *et al*. 2001).

Bio-pharming: Transgenic Animal for development of medicine and research

With the advent of transgenic technology and its application, there is an increase in the use of genetically modified animals in biomedical, pharmaceutical research and safety testing. Transgenic technology has potential to influence the attrition rate in pharmaceutical research by increasing the quality of both targets and compounds (Bagle *et al.* 2013)

Complex Protein Production

For decades proteins such as insulin and human growth hormone have been produced in bacteria and yeast cultures. However, proteins such as blood clotting factors and monoclonal antibodies require complex folding patterns and additional sugar molecules to become biologically active. These sophisticated modifications require the proteins be produced in mammalian cells to be carried out properly, thus showing the limitations of in vitro bacterial culture techniques to be able to produce complex proteins. Milk-producing transgenic animals are especially useful for medicines. The milk of

transgenic cows, sheep and goats contain nutritional supplements and pharmaceuticals products such as insulin, growth hormone and blood anti-clotting factors .Transgenic milk used for treatment of devastating diseases such as phenylketonuria and cystic fibrosis (Rajesh, *et al.*, 2015). The first therapeutic protein produced in the milk of transgenic animals to be approved for human use was antithrombin, an anticoagulant protein that can treat patients with a congenital deficiency. The first transgenic cow was produced whose milk was enriched with the human protein α-lactalbumin. The transgenic milk, being more similar to human breast milk is more nutritionally balanced than natural bovine milk and could be given to babies or the elderly with special nutritional or digestive needs (Van Berkel *et al.* 2002).

Human disease models

There are around 20 000–25 000 human genes responsible for the formation and maintenance of human body (Human Genome Sequencing 2004). Thousands of human diseases are caused by genetic mutations already characterized in mice models by knockout through gene targeting. Those animals are valuable experimental models to study the symptoms and causes of a variety of human diseases, such as cancer. However, mouse anatomy, physiology and lifespan differ significantly from those of humans. Therefore, the use of mice as a genetic model has shown some limitations regarding the study of several human traits. Hence, farm animals, such as pigs, sheep or cattle, could be more appropriate models to avoid some problems, for example, the requirement of longer observation periods in studies of many human diseases. Conventional pigs are already used to study cardio vascular disease, athero sclerosis, cutaneous pharmacology, wound repair, cancer, diabetes and ophthalmology. Using transgenic technology, pig models are currently being produced for diseases of Alzheimer, cystic fibrosis, retinitis pigmentosa, spinal muscular atrophy, diabetes and organ failure (Aigner *et al*. 2010).

Xenotransplantation

Today more than 250,000 people are alive for the successful transplantation of an appropriate human organ (allotransplantation). The average survival rate of a heart, liver or kidney transplanted patient is about 10–15 years. However, progress in organ transplantation technology has led to an acute shortage of appropriate organs, and cadaveric or live organ donation does not meet the demand. To close the growing gap between demand and availability of appropriate human organs, porcine xenografts from domesticated pigs are considered to be the best alternative (Niemann et al., 2005).

Essential prerequisites for a successful xenotransplantation are: prevention of transmission of zoonoses, compatibility of the donor organs in anatomy and physiology and overcoming the immunological rejection of the transplanted organ (Niemann et al., 2005) and (Niemann and Kues 2003). Nonhuman primates such as chimpanzees are genetically closes to humans and reduce the chances of graft rejection. But primates are endangered in the wild to use as a source of replacement organs and the increased risk of disease transmission between such closely related species might face. For these reasons pigs serve as an alternative, for a source of organs because they have large litters, a short gestation time, anatomically and physiologically similar to humans, already produced in high volume as a food source, and are currently used to provide some replacement tissues such as heart valves (Schook *et al.* 2014).

Xenotransplantation would have to overcome many technical and ethical obstacles before it can become a reality. One of the first technical issues researchers have focused on is the antigens on the surface of pig cells. These surface antigens are similar to the ABO blood group antigens that trigger severe immune responses called hyper acute rejection. To address this, scientists have inserted

human genes into single-cell pig embryos in an attempt to make their cell surface proteins more similar to human ones, so the tissues are no longer antigenic. However, even if this procedure reduces the risk of hyper acute rejection, other immunological barriers to xenotransplantation, such as acute humoral xenograft rejection, thrombotic micro angiopathy, and coagulation dysregulation still exist. In addition, there are concerns of cross-species infections caused by exogenous viruses, such as porcine cytomegalovirus, present in the xenotransplanted organs (Fishman and Patience 2004).

In1997, Robin A., a virologist at University College London, discovered a new class of pig viruses called porcine endogenous retroviruses (PERVs) and determined that they have the ability to infect cultured human cells. The transplantation of a pig organ into a human host would therefore create the opportunity for the transmission of PERVs, potentially enabling such viruses to evolve into human pathogens. Retrospective studies of patients who received heart valves from pigs identified the DNA of PERVs in some recipients. Therefore there is real concern that xenografts from pigs could provide a path for the transmission of novel viruses from animals to humans.

Limitations of the Technology

Production of transgenic animal is a difficult, lengthy and expensive procedure and leads to breeding problems, mutagenesis and functional disorders. The technique is also not perfect; with low success and survival rates of transgenic animals. The joining efficiency of external genes at the determined site is low and unstable. One of the problems of transgenesis is the one which faces in xenotransplantation. For instance, the antigens on the surface of pig cells are similar to the ABO blood group antigens that trigger severe immune responses called hyper acute rejection. To address this, scientists have inserted human genes into single-cell pig embryos in an attempt to make their cell surface proteins more similar to human ones, so the tissues are no longer antigenic. However, even if this procedure reduces the risk of hyper acute rejection, other immunological barriers to xenotransplantation, such as acute humoral xenograft rejection, thrombotic micro angiopathy, and coagulation dysregulation still exist. In addition, there are concerns of cross-species infections caused by exogenous viruses, such as porcine cytomegalovirus, present in the xenotransplanted organs (Fishman and Patience 2004).

Conclusion

Different methods used for generating transgenic animals, each method have its own advantages and disadvantages. There are wide range of applications of transgenesis in different species like cattle, sheep, goat, pig, chicken, fish, mice and humans. Now days genetically modified animals play a significant role in the field of biomedicine especially in drug development, animal disease models, xenotransplantation, antibody production, gene pharming and blood replacement. Advances in molecular biology have made it possible to develop traits in animals quicker with more precision and allowing them as an alternative means to increase yields and improve the nutritional value of food products. Likewise, increased disease resistance can be achieved by introducing resistance conferring gene constructs into animals or by depleting a susceptible gene or locus from the animal. Moreover, livestock health can also be improved through the advent of sensitive and specific diagnostic technologies and new generation vaccines through genomic sequence. Similarly, the DNA sequence of genomes provide data for animal breeding programs to select breeds with desired traits (meat quality, milk production) and increased disease resistance. But there are also some limitations during production of transgenic animals. Transgenic by itself is not a perfect technique; it is a difficult, lengthy and expensive procedure with low success and survival rates of transgenic animals.

As a result considerations should be given to ethical concern regarding animal welfare, human health and environmental issues.

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