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A life with transgenics in 21st century

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Abstract

A transgenic organism is one that contains a new gene or genes from another species. Because of the important and very exciting benefits of transgenics in agricultural, medical and industrial areas, we are going through a new revolution called "Transgenic Revolution". However, they have also brought many risks and controversies with them. In this paper, benefits and risks of transgenic animals and plants, which mark this century and take part in our life, and also concept of biosafety were discussed in a broad spectrum.

Key Words: Transgenic organism, transgenic revolution, biosafety, risk assessment, risk management.

21. Yüzyılda transgeniklerle bir yaşam

Özet

Diğer bir organizma orijinli ve doğal olarak taşımadıkları yeni bir gen veya genleri taşıyan organizmalar transgenik olarak adlandırılmaktadırlar. Transgeniklerin tarım, tıp ve endüstri alanlarında ortaya koydukları önemli, heyecan verici ve gelişmeye açık yararlar nedeniyle "Transgenik Devrim" olarak nitelendirilebilecek yeni bir döneme doğru gidilmektedir. Ancak, transgenikler, pekçok riski ve tartışmayı da beraberlerinde getirmişlerdir. Bu makalede, çağımıza damgasını vuran ve kaçınılmaz bir şekilde hayatımıza giren, transgenik hayvan ve bitkilerin yararları ve riskleri ve ayrıca biyogüvenlik kavramı geniş bir yelpazede ele alınmıştır.

Anahtar Sözcükler: Transgenik organizma, transgenik devrim, biyogüvenlik, risk değerlendirme, risk yönetimi.

Introduction

Genetically modified organism (GMO) is operationally defined as an organism whose hereditary traits have been modified by human intervention using any method that results in the introduction, rearrangement or removal of genetic material from the genome of it (Egypt Biosafety Regulations and Guidelines). A transgenic organism is one that contains a new gene or genes from another species.

Since the 1970s, it has been possible to introduce DNA fragments into prokaryotic and eukaryotic cells in vitro and to induce the expression of the foreign DNA in these cells (Charles River Laboratories, 1991).

Transgenic Animals

Transgenic animal systems combine the virtues of cell culture and congenic breeding strategies while avoiding the negative aspects of each system (Charles River Laboratories, 1991). Many uses of non-human vertebrate transgenic animals have been developed and many more are forecast. These uses can be classified mainly in four areas:

Uses in research and testing

By far the most common use of genetically modified animals is in biomedical research. Such as, fundamental and applied research into human and animal development, gene function and regulation, brain receptor chemistry, genetic disorders and development of human gene therapy (The Boyd Group, 1999).

The predictability of many transgenic phenotypes permits the innovative testing of diagnostic and therapeutic agents while using a reduced population of experimental animals. The generation of novel cell lines from transgenic organs also promises to reduce the number of research animals required to evaluate a therapeutic compound (Charles River Laboratories, 1991).

Transgenic rodent models have been characterised for several human diseases including cardio-vascular disease (Walsh et al. 1989), cancer (Sinn, 1987), autoimmune disease (Hammer et al. 1990), AIDS (Vogel et al. 1988), sickle cell anemia (Ryan et al. 1990) and neurological diseases (Small et al. 1986).

Use in targeted production of pharmaceutical proteins

Another use of transgenic animals involves the biological production of valuable human enzymes, hormones and growth factors. The use of transgenic animals, particularly larger mammals, as bioreactors (pharmaceutical pharming) is a cost-effective alternative to cell culture methods. Transgenic animals are not only cost-effective bioreactors but, with the complex secretary cell types and organs of the mammalian organism, can perform much more complicated protein modifications than simply cultured cells (Charles River Laboratories, 1991). Sheep, cattle and goats have all been modified to produce pharmaceutically important proteins for human use.

Use in developing animals which might, in future, be used as sources of organs and tissues for xenotransplantation

Researches aimed at developing xenotransplantation generally involve genetically modified pigs as sources of organs, and some use of non-human primates as recipients. There is much on-going debate about the issues posed by such uses of animals (The Boyd Group, 1999).

Use in modification of animal anatomy and physiology

These researches mainly centre around the attempts to get animals growing faster, using less food, putting on more or less fat, proteins etc., resisting infections better, having increased speed, giving higher yields of meat or milk etc. In these type of studies most often, foreign genes are added to the host genome, but selective deletion of specific genes or DNA regions has been attempted. It has become apparent that merely adding genes for growth factors or hormones to the genome is a simplistic approach to altering the complex multigenic physiology of the mammal (Charles River Laboratories, 1991).

Alongside the potential benefits, genetic modification of animals raises a variety of concerns:

Concerns about safety

Production and usage of genetically modified animals must take into account potential risks to human and other animals, as well to the wider environment that they interact. The Boyd Group (1999) categorises the concerns about risks to safety need to be considered as follow:

1. concern that modified animals might 'escape' and breed with other domestic or wild animals, so transferring the new gene(s) to these other populations;
2. concern about risks from the use of retroviruses as DNA vectors during production of genetically modified animals: e.g. risks that genes might inadvertently be transferred to other individuals or species, or that retroviruses might infect other organisms;
3. concern about possible risks to human and animal health from consumption of genetically modified animals and their products;
4. concern about risks that drug resistance gene markers used in some genetic engineering procedures might inadvertently be transferred and expressed;
5. 'ecological' concerns, e.g. about the wider effects of producing disease-resistant animals;
6. in xenotransplantation, concern about risks that human recipients of animal organs might

become infected with animal viral diseases, which might then infect the wider population.

Concern about animal welfare

From the point of animal welfare there are two main aspects need to be considered:

1. The harms that can be caused during the production of genetically modified animals: In general, there is a of published data on mortality rates and ages at which death occurs during production of genetically modified animals, and there is a need for more detailed analysis of the full range of welfare problems caused during such production (The Boyd Group, 1999).
2. The welfare of the resulting modified animals: In some cases, genetic modification appears to have no impact on the welfare of resulting animals; in theory, it might in some cases benefit animal welfare; and in other cases there are certainly adverse welfare effects, which encompass a range of severities (Moore and Mepham, 1995; VanZutphen and Van den Meer, 1996). Many of genetic manipulations prove fatal to the developing embryo. When the effect is not lethal, the welfare of the resulting animal can be seriously compromised (mice have been born with deformed limbs or kidney malfunction, for example) (Mepham et al. 1998; Moore and Mepham, 1995).

In addition to the concerns mentioned above, genetic modification of animals resulted in some moral objections. The base of these objections are that genetic engineering is 'unnatural', that it amounts to 'playing God', and that it 'debases animals' by treating them as 'commodities'.

Transgenic plants

It has become possible about the past twenty years to isolate genes from any class of living organism and introduce them into most of plants, especially crop plants. Because of the nature of crops, transgenic crop studies found more diverse application areas than animals. Transgenic technology provides a wider choice of genes for crop improvement than is available by conventional plant breeding. Crop varieties developed by genetic engineering were first introduced for commercial production in 1996. According to the data collected by International Service for the Acquisition of Agri-Biotech Application (ISAAA, 2004), in 1996 4.2 million acres in six countries were planted with GM crops. By 2003, the numbers had grown to 167.2 million acres in 18 countries on six continents – a 40-fold increase in eight years. The estimated global area of approved GM crops for 2004 was approximately 200 million acres, up from the 167.2 million acres in 2003. So, the increase in GM crop area between 2003 and 2004 is 32.9 million acres or 47-fold since 1996.

The adoption of GM crops has been the most rapid in the United States, where there has been a 29-fold increase in the area of GM crops planted during the same eight year period (3.7 million acres in 1996 to 105.7 million acres – (63.2 %) in 2003). Argentina is the next largest producer, with 34.4 million acres (20.6 %), followed by Canada with 10.9 million acres (6.5 %), Brazil with 8.4 million acres (5.0 %), China with 6.9 (4.1 %) million acres, and South Africa with 1.0 million acres (0.6 %) in 2003 (ISAAA, 2003). Together, these six countries grew 99 percent of the global GM crop area last year. Australia, Mexico, Romania, Bulgaria, Spain, Germany, Uruguay, Indonesia, the Philippines, India, Columbia, and Honduras also planted significant acreage in GM crops in 2004. The number of farmers planting GM crops has also increased. In 2000, 3.5 million farmers planted GM crops. That number has nearly doubled, to an estimated total of seven million farmers planting GM crops in 2003. 8.25 million farmers in 17 countries planted GM crops in 2004. Notably, 90 % of the beneficiary farmers were resource-poor farmers from developing countries, whose increased incomes from these crops contributed to the alleviation of poverty (ISAAA, 2004).

Four commodities dominate GM crop market today. These are: Soybean (102.5 ma, 61 %), corn (38.4 ma, 23 %), cotton (17.8 ma, 11 %) and canola (8.9 ma, 5 %). The other GM crops occupy less than 1 % (ISAAA, 2003).

Main application areas and potential benefits of transgenic crops can be summarized as follow:

1. Resistance to biotic stress factors, mainly to diseases (fungi, bacteria, viruses) and pests (insects, mites, nematodes).
2. Resistance to abiotic stress factors (such as cold, drought, salinity, herbicides, etc.).

3. Modifications in fruit ripening and tuber storage; research in potatoes is likely to reduce dependence on anti-sprouting compounds.
4. Enhancement of vitamins, minerals and anticancer substances (such as vitamin A and iron).
5. Reduction in seed shedding at harvest time.
6. Elimination of allergens from certain crops (such as rice).
7. Changes in plant architecture (e.g. dwarfing) and flowering (e.g. flowering time).
8. Modification of oil, starch and protein to provide sustainable supplies of raw materials for food, biodegradable plastics, detergents, lubricants, paper making and packaging.
9. Increase in the ability of certain plants to remove toxic metals from soils (bioremediation).
10. Production of pharmaceutical substances (e.g. edible vaccines).

Among these application areas herbicide tolerance is the most dominant trait for transgenic crops, accounting for 77 % of soybeans, corn and cotton. In 2003, herbicide resistant crops made up 73 % of the total GM crop growing area, while insect resistant crops constituted 18 %. GM crops containing genes for both herbicide resistance and insect resistance comprised 8 % of the total GM crop growing area (Mayer et al., 2004).

For many years, transgenic technologies for plants were restricted to manipulations of nuclear genome. More recently, a second genome of the plant cell has become amenable to genetic engineering: The prokaryotically organized circular genome of the chloroplast (Bock, 2001). The possibility to directly manipulate chloroplast genome-encoded information has paved the way to detailed in vivo studies of virtually all aspects of plastid gene expression. Moreover, plastid transformation technologies have been intensively used in functional genomics by performing gene knockouts and site-directed mutagenesis of plastid genes. These studies have contributed greatly to our understanding of the physiology and biochemistry of bioenergetic processes inside the plastid compartment (Bock, 2001).

Although transgenic crops have very useful and exciting application areas mentioned above, which are open to develop, they have also many potential risks to concern.

Environmental risks

Although there are serious considerations about the environmental effects of transgenic crops, the knowledge on this area is still not enough. According to Ervin et al. (2003) the of knowledge on potentially significant environmental effects of transgenic crops raises three risks: First, there may be serious environmental damage from accumulating pressures that trigger threshold effects, such as depleting populations of certain non-target organisms. Second, without improved monitoring and science, the potential environmental benefits of some transgenic plants may be underestimated, making the technology vulnerable to inappropriate restrictions. Third, the long-term potential of transgenic crops or alternative agricultural technologies to reduce or solve genuine environmental problems will not be fully exploited.

According to NRC (2002) transgenic crops do not present new categories of environmental risks compared to conventional methods of crop improvement, but specific traits introduced by either approach can pose unique risks. The nature of the risks vary depending on the transgenic crop's characteristics, the ecological system in which it is grown, the skill with which it is managed, and the private and public rules governing its application (Ervin et al., 2003).

There is ample evidence that transgenic crops and their genes, through pollen dispersal, can spread (Brookes 1998) even between species that are mainly inbreeders (Cavan, et al., 1998). The effects of such "genetic pollution" on the environment are still uncertain (Robinson, 1999) but the certain thing is the most probable dangerous effects of this new intense pollution on the complex ecological balances.

Although there is some concern that transgenic crops themselves might become weeds, a major ecological risk is that large scale releases of transgenic crops may promote transfer of transgenes from crops to other plants, which may than become weeds (Darmency, 1994). Evidence indicates that such genetic exchanges among wild, weed and crop plants already occur. The incidence of shattercane (*Sorghum bicolor*), a weedy relative of *sorghum* and the gene

flows between maize and teosinte demonstrates the potential for crop relatives to become serious weeds (Altieri, 2001).

In this respect the most important thing is the potential transfer of genes from herbicide-resistant crops (HRCs) to wild or semi-domesticated relatives thus creating "superweeds". In actuality the use of herbicide-resistant transgenic crops is likely to increase herbicide use as well as production costs. It is also likely to cause serious environmental problems ((Altieri, 2001).

Total weed removal via the use of broad-spectrum herbicides may lead to undesirable ecological impacts, given that an acceptable level of weed diversity in and around crop fields has been documented to play important ecological roles such as enhancement of biological insect pest control, better soil cover reducing erosion, etc. (Altieri, 1994). HRCs, through increased herbicide effectiveness, could further reduce plant diversity, causing shifts in weed community composition and abundance, favoring competitive species that adapt to these broad-spectrum, post emergence treatments (Radosevich et al., 1996).

Also some types of herbicides, for example glyphosate, has been reported to be toxic to some non-target species in the soil-both to beneficial predators such as spiders, mites, carabid and coccinellid beetles and to detrivores such as earthworms, as well as to aquatic organisms, including fish (Pimentel et al., 1989).

At this point, it is very important to notice that at least 27 corporations have initiated herbicide-tolerant plant research, including the world's 8 largest pesticide companies Bayer, Novartis, Zeneca, Rhone-Poulenc, Dow/Elanco, Monsanto, Hoescht and DuPont, and virtually all seed companies, many of which have been acquired by chemical companies (Gresshoft, 1996).

An additional area where serious considerations are relevant to a discussion of transgenic crops is that of genetic diversity and its possible erosion. Some argue that development of transgenic crops will enhance biodiversity by creating an increased need for exotic genes. On the contrary, it is obvious that transgenic crops promote monoculture for the reason of uniformity. Although a certain degree of crop uniformity may have certain economic advantages, it has two ecological drawbacs: First, history has shown that a huge area planted to a single cultivar is very vulnerable to a new, matching strain of a pathogen or pest. And, second, the widespread use of a single cultivar leads to a loss of genetic diversity (Robinson, 1996). Evidence from the Green Revolution leaves no doubt that the spread of modern transgenic varieties has been an important cause of genetic erosion (Tripp, 1996).

Pest and disease resistance is a further area of transgenic crops that has to be considered carefully.

The microbial insecticides most widely used since the 1960s are preparations of the bacterium *Bacillus thuringiensis* (Bt). The best known types of these insecticides are pathogenic and toxic only to larvae of the butterflies and moths (Lepidoptera). The promise of transgenic plants containing Bt genes is the replacement of synthetic insecticides now used to control insect pests (Altieri, 2001). Since most crops have a diversity of insect pests, insecticides will still have to be applied to control pests other than Lepidoptera not susceptible to the endotoxin expressed by the crop (Gould, 1994). On the other hand, several Lepidoptera species have been reported to develop resistance to Bt toxin in both field and laboratory tests, suggesting that major resistance problems are likely to develop in Bt crops which through the continuous expression of the toxin create a strong selection pressure (Tabashnik, 1994). Given that a diversity of different Bt-toxin genes have been isolated, biotechnologists argue that if resistance develops alternative forms of Bt toxin can be used (Kennedy and Whalon, 1995). However, because insects are likely to develop multiple resistance or cross-resistance, such a strategy is also doomed to fail (Alstad and Andow, 1995).

Moreover, Bt plants might poison non-target organisms. Evidence from studies conducted in Scotland suggest that aphids were capable of sequestering the toxin from Bt crops and transferring it to its coccinellid predators, in turn affecting reproduction and longevity of the beneficial beetles (Birch et al., 1997). Bt toxins can be incorporated into the soil through leaf materials, where they may persist for 2-3 months, resisting degradation by binding to soy clay particles while maintaining toxin activity (Palm et al., 1996). Such Bt toxins that end up in the soil and water from transgenic leaf litter may have negative impacts on soil and aquatic invertebrates and nutrient cycling process (James, 1997).

Bt crops may have also some downstream effects. Such as, a major environmental consequence resulting

from the massive use of Bt toxin in cotton or other crop occupying a larger area of the agricultural landscape, is that neighboring farmers who grow crops other than cotton, but that share similar pest complexes, may end up with resistant insect populations colonizing their fields (Altieri, 2001). As Lepidopteran pests that develop resistance to Bt cotton, move to adjacent fields where farmers use Bt as a microbial insecticide, may render farmers defenseless against such pests, as they lose their biological control tool (Gould, 1994). "Who will be accountable for such losses?" is the appropriate question asked by Altieri (2001).

One another important attempt of scientists is to engineer plants for resistance to pathogenic infections. Two serious ecological risks of this attempt are: 1) Vector-mediated horizontal gene transfer and recombination to create new pathogenic bacteria; 2) Vector recombination to generate new virulent strains of viruses, especially in transgenic plants engineered for viral resistance with viral genes.

Risks related to human health

In May 1999, the British Medical Association published a statement on GMO addressing three areas over potential health effects of GM foods (BMA Science Department, 1999). It focused on the transfer of antibiotic resistance, toxicity, and allergenicity.

As it is well known that transgenic crops contain risky genes including for example, antibiotic resistance genes used as markers and promoter sequences derived from viruses. The obvious fear is that antibiotic resistance marker genes could be recruited into humans and domestic animals rendering antibiotics ineffective in curing bacterial infections (Robinson, 1999). In recent years, growing public concern regarding the spread of antibiotic resistance has limited consumer acceptance of genetically modified plants, especially in Europe (European Federation of Biotechnology (EFB), 2001).

Also, these genes could spread from the plants into which they were inserted to wild plant populations and to bacterial populations that would than be advantaged in their natural environment. There is evidence that gene escape can arise as a result of transformation using *A grobacterium* as the gene vector (Barrett et al., 1997; Mogilner et al., 1993). On the other hand, Thompson (2000) points out that antibiotic resistance markers are widely distributed in nature and the possibility of increasing the reservoir of antibiotic resistance through horizontal gene transfer from plants is extremely remote. Kurtland et al. (2003) suggest that genes transferred by horizontal gene transfer would be quickly eliminated from the genome particularly in the absence of selection pressure.

Approximately fifty marker genes used for transgenic and transplastomic plant research or crop development have been assessed for efficiency, biosafety, scientific applications and commercialization (Miki and McHugh, 2004). The World Health Organization (WHO) has judged antibiotic resistance marker genes to be safe (WHO, 1994), but the outcome of their use might be hazardous if they represent a major source of resistance to a wide class of antibiotics (Robinson, 1999). Although, there is no evidence to suggest that the currently used antibiotic resistance markers, such as *npt II,* pose any risks to humans, animals or the environment, to alleviate public concerns recommendations have been made to eliminate all antibiotic resistance genes from GM plants as new technologies become available (FAO / WHO, 2000; EFB, 2001).

An area of research that is growing rapidly but is still in its infancy is the development of strategies for eliminating selectable marker genes to generate marker-free plants (Miki and McHugh, 2004). Among the several technologies described, two have emerged with significant potential. The simplest is the co-transformation of genes of interest with selectable marker genes followed by the segregation of the separate genes through conventional genetics. The more complicated strategy is the use of site-specific recombinases, under the control of inducible promoters, to excise the marker genes and excision machinery from the transgenic plant after selection has been achieved (Miki and McHugh, 2004). Scutt et al. (2002) describe and compare the different techniques that have been tested for the removal of marker genes from transgenic plants, concentrating particularly on the more recent and promising innovations in the field.

Other principle concerns are that food from transgenic crops could be toxic or allergenic. There are two issues from an allergic standpoint: First, there is the potential to transfer a known allergen into a target crop. The second possibility is to create a new allergy to a neoallergen (Lack, 2002). The probability of allergenicity is thought to be increased by some

defense proteins of plant origin which are cloned to render plants more pest or disease resistant. Defense proteins like proteinase inhibitors or lectins are thought to be more likely to cause allergies than other plant proteins because of known adverse effects, or because of sequence similarities with known allergens (Franck-Oberaspach and Keller, 1996). Side effects of the transformation might alter the allergenic properties of the known allergenic food or might induce allergenicity in a hitherto non-allergenic food. These issues would be easily clarified if there were tests which could demonstrate the food allergenicity of a given food protein. However, this is only possible for known allergens which can be tested with the serum from people with antibodies to known allergens. How allergenicity of new allergens is to be tested is the real question (Weber, 1997).

An experiment carried out in Scotland, where rats fed for ten days on transgenic potatoes containing a lectin gene from snowdrops appeared to develop internal organ damage, is often cited in support of health hazard caused by transgenic plants, although this particular study has been widely criticized by other scientists as being too small-scale and inconclusive (Ewen and Pusztai, 1999). As an other example, a project to insert a brazil nut protein gene into soybean was halted when early tests showed that people allergenic to nuts reacted to the modified soy products (Nordlee et al., 1996). BMA Science Department (1999) highlighted the importance of further research on the potential allergenicity of GM products.

It is very important to note that, it is not clear who is legally responsible for future cases of adverse health effects.

Socio-economic impacts

Weil (1996) stated that large-scale farmers will be favored by transgenic technologies. This will adversely affect the socio-economical balances especially in developing countries.

A particularly controversial transgenic technology has been described recently and has become commonly known as "Terminator Technology" (Service, 1998; Crouch, 1998). "Terminator", "Traitor" or "Gene Use Restriction Technology (GURT)" are names given to a range of technologies which create sterile seeds, or prevent a plant from growing successfully without the application of an external influence, such as a chemical. In general, it involves three steps:

1. Scientists add terminator genes to a crop.
2. The seed company initiates the terminator process before selling the seeds by adding an inducer.
3. Farmers plant seeds, grow plants, and harvest mature, but sterile seeds.

As it is obvious, this would potentially put the farmers very firmly under control of the company providing the seeds. On the other hand, what poor farmers need is inexpensive, locally adapted seeds that can be easily saved, not sterile seeds that must be repurchased every year. Therefore, this technology has very troubling implications for the developing countries where seed saving is more widely practised than in some developed countries.

Advocates of the technology claim however to be able to revolutionize farming, save environment and make money (Anon, 1997), and thereby address the humanitarian, environmental and business ethic simultaneously (Robinson, 1999).

Ethical issues

An area of study that is often not explicitly stated but influence the acceptability of biotechnology may be called ethic (Shelton et al., 2002). The insertion of human genes into animals and plants is the main ethical rejection arose by the transgenic technology. The insertion of the genes of certain animals may also be unacceptable to certain religions.

Biosafety

In late January 2000, after 5 years of negotiations, The Extraordinary Conference of the Parties to the Convention on Biological Diversity (CBD) adopted the so-called "Cartegena Protocol on Biosafety" (Kathen, 2000). This protocol is the first international legally binding agreement on biosafety and ratified by 75 countries including Turkey by the date of September 2000 (Kılınçarslan, 2000).

The Cartagena Protocol on Biosafety aims: *"to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the*

conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements" (Anonymous, 2000).

"Risk assessment" and "risk management" are the two main provisions that the term "biosafety" expresses. Risk assessment refers to all the available scientific evidence in order to identify and evaluate the possible adverse effects of living modified organisms on the conservation and sustainable use of biological diversity, taking also into account risks to human health (Anonymous, 2000). Risk management refers to all appropriate mechanisms, measures and strategies to regulate, manage and control risks identified in the risk assessment provision of this protocol associated with the use, handling and transboundary movement of living modified organisms (Anonymous, 2000).

The development of new technologies opens up a series of questions on risk for which there is limited or no data to help in its evaluations (Egypt Biosafety Regulations and Guidelines). A definition that was suggested for risk is:

Risk = Probability of Hazard x Magnitude of Hazard

If there is any increase in risk, it has to be balanced against the benefits which would accure from using that transgene and we should consider redefining risk as "acceptable risk" (Egypt Biosafety Regulations and Guidelines).

$$\text{Acceptable Risk} = \frac{\text{Probability of Hazard x Magnitude of Hazard}}{\text{Benefits from Product}}$$

After a slow start many developing countries are now investigating in agricultural biotechnology. There is however a major debate towards the development of biotechnology, especially GM organisms, in the developing countries and there is a need for them to address biosafety issues and proper monitoring systems (Dookun, 2001).

Conclusion

Because of the important and very exciting benefits of transgenics in agricultural, medical and industrial areas, we are going through a new revolution called "Transgenic Revolution" which seems to mark this century. It is a part of the larger revolution in genetics, which has been proclaimed as the third technological revolution following the Industrial and Computer Revolutions (Abelson, 1998).

The prodigious yield increases seen in the major world crops during the Green Revolution, which was only four decades ago, were achieved at a high cost to the environment (Kappeli and Auberson, 1998). This negative experience gained from Green Revolution and the negative impacts of Industrial Revolution have been transferred to the safety and risk discussion in the "Transgenic Revolution". Seeing this awareness is hopeful, because otherwise the consequences of this revolution will obviously be much more effective and irreversible than Green and Industrial Revolutions.

A major problem in risk assessment of transgenic organisms in general is that the outcome of transformations can not be fully foreseen and we have to deal with uncertainties in this field (Weber, 1997). These uncertainties are mainly caused by pleiotropy of genes and gene silencing. As Weber (1997) states that "A gene is usually cloned because of an effect which the gene shows in the donor organism, but it may have additional unwanted effects which were overlooked in the donor organism. The genetic background too of the recipient may influence effects of the cloned genes. More research in this field could help to detect some of the problem. Nevertheless, long term environmental and health effect can not be completely foreseen. The side effect of transformations can not be predicted at all. These are generated by undirected random integration of sometimes several copies of the transgene into the recipient's genome. Thus the question is: How should we deal with those uncertainties?"

By 2030 the world's population is expected to top eight billion. Can the world produce enough food to meet global demands? The answer is "yes", according to a report from the UN's Food and Agriculture Organization's (FAO) Global Perspective Studies Unit completed in April 2001 and released at the end of July 2001. This report reveals transgenic crops not needed to feed the world. So, from another point of view, what we actually need is better food distribution,

other than taking unnecessary risks of transgenics discussed throughout in this paper.

On the other hand, in order not to reject the important benefits of transgenic technology in medicine and industry, it is very important to make objective judgments considering acceptable risk and benefit(s) of the end product.

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