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Application of recombinant DNA technology (genetically modified organisms) to the advancement of agriculture, medicine, bioremediation and biotechnology industries

Abstract

Genetic engineering has always been a topic of controversy as the balance it aims to reach between the benefits accrued to humans and attendant ethical considerations is open to debate. In each of the diverse fields of agriculture, medicine, bioremediation and biotechnology concerns vary in a discipline-specific manner. However, the principal source of apprehension often involves the ecological impact, real or perceived, of the use of recombinant DNA technology, in particular the release of genetically modified organisms into the environment. In this short review, pressing issues are highlighted, the potential severity of the negative effects is addressed, and methods for overcoming these are indicated.

Keywords: biotechnology, genetic engineering, genetically modified organism, recombinant DNA, transgenic

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Introduction

History

The use of recombinant (r-)DNA technology to produce genetically engineered organisms started in the early 1970s with the pioneering transfer of genes between bacteria of the same *Escherichia coli* species.[1] Following these successful pilot experiments, in 1978 Cohen and colleagues progressed to transfer an insulin synthesis gene into a plasmid of *E. coli*, with that producing the first genetically modified organism (GMO).[2] By 1982 this protocol received full approval from national drug regulatory authorities, notably the US Food and Drug Administration, thereby enabling the economically viable mass production of human insulin, a hormone that regulates blood sugar levels and is made naturally by beta cells in the pancreas. This facilitated the widespread commercial availability of insulin at a price affordable to patients with the metabolic disorders types 1 and 2 diabetes mellitus, who either fail to produce or to metabolize sufficient insulin.[3]

This proof of principle demonstration of the translational medical benefits of genetic modification pioneered a trend in biotechnology for molecular cloning methods to transfer genes expressing desirable traits into another host organism thereby producing favourable characteristics. This now involves both prokaryotes such as bacteria (comparatively routine to modify genetically by r-DNA technology) and eukaryotes including yeast, plants, insects and mammals (comparatively complex to manipulate via r-DNA technology).

Range of uses

r-DNA technology has been exploited in order to provide selective improvements in various specialties that include crop agriculture, pharmaceutics, gene therapy, vaccine design and bioremediation. The latter is a waste management technique that deliberately introduces GMOs into a site to neutralize environmental contaminants (breaking down hazardous substances into less toxic or non-toxic compounds) with the aim of cleansing thoroughly, quickly and cheaply polluted soil or water. For each use there will be costs as well as benefits, all of which should be considered rationally when coming to an informed decision whether to use genetic modification on an industrial scale.

Agriculture

In agriculture development of genetically modified crops with a purpose to improve both yield and resistance to plant pests or herbicides seems to have gained a degree of public acceptance and is already practised in a commercial context in several countries.[4] The genetically modified tomato CGN-89564-2 was the first commercially grown, genetically engineered crop product to be granted a licence for human consumption. This was developed in 1994 to express the trait of delayed softening of tomato flesh as a practical means to minimize post-harvest crop losses.[5] Ironically given its brand name of 'Flavr Savr', this failed in the marketplace due not to public apprehension over eating a genetically altered food *per se* but to an apparent lack of taste. Nevertheless, the introduction of a genetically modified fruit paved the way for use of GMOs in food and today genetic modification is widespread. In the US, 88% of corn and 93% of soybeans are genetically altered and much of this finds its way unlabelled into processed foods.[6]

The introduction of pest-resistant brinjal (also known as eggplant or aubergine) was met with criticism in some countries, in contrast to the concurrent popularity of pest-resistant cotton. Both attempts at implementation followed incorporation of the identical crystal protein gene (*Cry1Ac*) from the soil bacterium *Bacillus thuringiensis* (Bt) into the genome of the host plant expression of which synthesizes so-called Bt toxins that confer resistance to predation by lepidopteran insects. However, of the two uses as a food and as clothing the one which caused anxiety among the general public involved human consumption. The benefits to humans of using Bt toxin should

be stressed in an attempt to overcome the initial unpopularity of consuming Bt-brinjals in developing countries such as India,[7] Bangladesh[8] and Philippines.[9] This would reduce public scepticism founded on the misperception that eating a plant product containing a 'toxin' is in fact toxic to humans irrespective of its unrelated target and benign mechanism of action.

Medicine

Drug delivery systems in medicine that are based on bacterial or viral hosts could prove hazardous if either the organism is genetically unstable and converts to a pathogenic type or if purification is incomplete.[10,11] In an analogous proof of concept from the agricultural sphere, use of the soil bacterium *Agrobacterium tumefaciens* as a vehicle for gene transfer is very effective and has become widely adopted despite its tumorigenicity, causing crown gall disease of dicotyledonous plants.[12] Genetic reversion is also a major concern regarding the experimental technique of gene therapy to treat or prevent otherwise incurable genetic disorders and acquired diseases, research into which was slowed in the early 2000s due to cases of viral vector instability. Consequently, identification of a preferred system to safely and efficiently deliver an altered gene of choice has become a priority as the technology advances from development and laboratory research to clinical translational trials.[13,14]

Bioremediation

Pseudomonas putida and *Nitrosomonas europaea* are the organisms which are typically utilized in bioremediation. The objective is to isolate the original genes located in these bacteria that promote bioremediation, then modify and incorporate them into a suitable host to be used as a bioremediation agent usually *E. Coli*.[15] This may, however impact normal ecosystems as well; for example, bacteria that have an improved ability to digest petroleum could, if exposed, cause destruction of important petroleum products. Hence, stringent monitoring of *in situ* bioremediation is essential.[16] In producing genetically modified bacteria the simplest way of screening is to incorporate a marker gene, which typically is one that confers antibiotic resistance. This achieves the purposeful generation of antibiotic-resistant organisms which, if mishandled, could become problematic under natural conditions.[17]

Biotechnology

An appreciable biotechnological success and novel commercial application is the production of genetically modified fluorescent zebrafish, *Danio rerio*, and similar species using genes encoding glowing characteristics. This is marketed under the GloFish® patent in the US where fish coloured bright red, green, orange-yellow, blue and purple are sold as pets to be kept in the controlled environment of an indoor aquarium. In the event of release, inadvertent or deliberate, into the environment the survival capacity of these constantly fluorescent fish is markedly reduced due to increased vulnerability to predation compared to wild type fish; thus, the risk of sustained ecological impact is considered to be marginal.[18] However, in-depth research to confirm or refute this notion is currently not possible because of insufficient understanding and a lack of technology to study the nexus of evolutionary biology and ecology with specific reference to the introduction of a novel species into, and its subsequent migration from, an ecosystem.[19]

Ethics

In evaluating eukaryotic organisms as suitable for genetic engineering, there are ethical issues to be considered, such as the possibility of GMOs released into the environment as bio-controlling agents becoming pathogenic to non-harmful organisms. Notably, this occurred for the entomopathogenic hyphomycetous fungi *Lagenidium*, *Coelomomyces* and *Culicinomyces* used to kill *Anopheles* and *Aedes* mosquito larvae as a supposedly environmentally friendly means to combat the major vector-borne diseases malaria and dengue.[20]

In choosing to exploit r-DNA technology for developing novel GMOs public education should be an important consideration. A high level of acceptance is required in order to attain societal trust in and use of a given product and thereby to achieve its economic success.[21] Ethical concerns should be addressed by rolling out effectively communicated information campaigns and by designing strategies for stronger community engagement.

Regulation

On an industrial scale, use of GMOs is gaining recognition as a technologically feasible means to obtain desired agricultural, biological and biomedical products. For the most part, manufacture is carried out in bioreactors under tightly controlled conditions the use of which minimizes the possibility of inadvertently producing an environmental hazard. During the development process, the effect that a GMO has on the ecosystem into which it is released should be investigated thoroughly in a series of controlled trials prior to progressing to industrial production. Selection of a non-pathogenic organism is also important to ensure operator safety of handling during purification, processing and distribution. There have been attempts to make 'marker-free' transgenic plants in order to diminish these risks.[22]

Controversy

Matters of contention surround such fundamental aspects as the creation of organisms containing an altered genome and the inheritance of modified genes by the offspring of such animals or plants.[23] These should be addressed in greater detail and with considerable circumspection since there may be robust counter arguments regarding each issue. In agriculture, for example, these include the possibility of elimination of wild type plant cultivars in the absence of insect pest resistance, insects developing resistance, elimination of organisms which consume modified plant material, and existing non-target secondary pests becoming primary pests.[24] The ethical right of humans to intervene with nature through 'artificial selection' by altering genomes has been questioned, eliciting a critical outcry in Europe during the introduction of GMOs.[25] Hence, it is important to determine the possibility of modified genes being passed to future generations as well as their effects on the ecosystem.[26]

Discussion

Ultimately, the prospect of exploiting r-DNA technology to create humans with apparent superior characteristics, thus afforded an enhanced capacity to perform various (gene-determined) tasks, has been of significant concern to the general public ever since this became a reality with farm animals and pets.[27] The selective incorporation of pathogen-resistance genes into the human genome, via gene therapy, has the potential to improve dramatically public health and to reduce greatly the need for drug treatment.[28] This would herald an age of personalized medical care, with ramifications for the pharmeutical industry. However, such a vision is still futuristic since at present r-DNA technology remains a hugely debatable concept based on what we know of safety and ecological concerns. Nevertheless, the trialling

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of essentially the same genetic modification techniques in plants and animals other than humans has made significant progress which, from an ethical perspective, only heightens the surrounding debate.

Conclusion

The utilization of genetic engineering in the production of transgenic organisms is a recent major development in the agriculture, medicine, bioremediation and biotechnology industries. In spite of the now widespread use of GMOs the potential for less obvious long-term ecological impacts is acknowledged. The acceptance by the lay public of genetically engineered products appears to be affected by perceived increased risk to personal health and to the environment, especially when relating to food production and consumption. Ecological impacts observed to date have proved much less threatening and occurred with less frequency than public perception would suggest. However, in some notable cases GMOs have had an adverse impact on wildlife due to both determined and undetermined changes.

In summary, it is reasonable to assert that the use of GMOs in a diverse range of fields is safe within carefully selected and strictly controlled environments. Nonetheless, given our incomplete understanding of the impact of applying currently available r-DNA technology more widely and over longer periods continued vigilant monitoring is necessary. This is in order to observe for any possibility of unforeseen side effects in the environment and then as required to take action to mitigate against any adverse events.

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Conflict of interest

The author declares no conflict of interest.

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