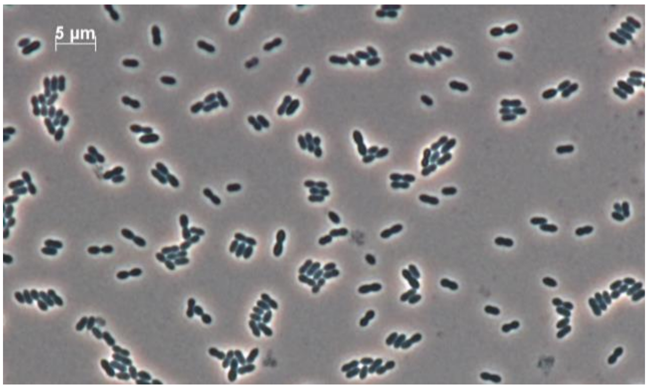
GM bacteria: potential uses and concerns



Recent developments in scientific understanding and technology mean that GM bacteria have great potential for benefit to human health and nutrition. GM crops have been a subject of widespread public debate (POSTnote 386), whereas there is far less public awareness about the uses for and issues surrounding GM bacteria, particularly in regard to use outside of agriculture. When discussing the release of GM bacteria, similar considerations must be made about the environmental and health risks, as well as philosophical and religious concerns.

Background

Genetic modification (GM) refers to the process by which either a pre-existing gene is modified or a new gene (a transgene) is inserted, in such a way that would not occur naturally. This was first achieved in 1973 when *E. coli* was engineered to carry a resistance gene to the antibiotic kanamycin[1]. Since then, GM bacteria have been used extensively in research and industry, often for the production of compounds and proteins, but under strict containment protocols.

Current regulation

The current framework regulating the release of GMOs in the UK is Directive 2001/18/EC. GM for food and feed is also regulated by Regulation 1829/2003. These regulations are extensive enough so as to effectively entirely prohibit the release of GMOs, and no GMO has been approved for release in the UK since they came into effect. This prevents any commercialisation of live GM bacteria for use in medicine or agriculture. A recent European Commission study found these regulations no longer fit for purpose[2].

Overview

- Genetically modified (GM) bacteria have been used in industry and research for many decades, but under strict controls that prevent their release
- Naturally occurring bacteria are often used in agriculture and medicine
- New technologies and understanding mean there is potential to use GM bacteria to improve agricultural yields and human health
- Currently, no GM microorganisms are authorised within the UK or EU for use in food or medicine
- There are specific considerations involved in the release of GM bacteria that differ from those relating to plants
- Each genetically engineered bacterial product has its own associated risks and benefits, depending on the function and the bacteria and technology used in its creation

Box 1: Biocontainment mechanisms

A variety of tactics have been used to limit the proliferation of GM bacteria into the environment. Many of the genes that are inserted into bacteria come at a fitness cost, meaning that the presence of the transgene makes the bacterium less able to compete against non-modified bacteria, and therefore these bacteria are unlikely to thrive outside of controlled conditions. Bacteria used in industry are often stripped of non-essential genes that are required to grow competitively in complex environments but are unnecessary in single culture. In addition to this, bacteria are often engineered to lack key genes in such a way that prevents them from surviving without the supplementation of key nutrients. However, it has been shown that bacteria are able to overcome this containment through horizontal gene transfer[3] (Box 2).

Another strategy is the use of 'kill switches' whereby the antibiotic susceptibility of the GM bacterium is characterised and then these antibiotics are used to kill the bacteria. Due to the antimicrobial resistance concerns involved in the wide-scale use of antibiotics, this would only be feasible for the use of GM bacteria in humans and not in agriculture. The risk of the bacterium acquiring genes for antibiotic resistance and therefore not being able to be killed can be reduced by using bacteria that are susceptible to a wide range of antibiotics[3].

Potential uses

Agriculture

Naturally occurring bacteria have been used in agriculture to protect crops from damage, for example from pathogens, frost, or pests, or to improve yield by enhancing nutrition. These are generally derived from bacteria with pre-existing evolutionary relationships with crops. Genetic engineering has the potential to make these bacteria more effective, combine several activities into one strain, and aid tracing of bacteria to monitor their success and potential harms. This creates the potential to increase crop yields without the use of chemicals that have adverse effects on the environment and ecosystems[5].

Medicine

Genetically engineered bacteria have been used in medicine since 1978 when bacteria were first engineered to produce insulin, but their use up until now has been limited to the production of biological products. When these products are purified, the bacteria are removed and therefore not released into the environment.

In recent years, there has been an increased appreciation for the role of the microbiome, particularly the gut microbiome, in human health. This has led to interest in the development of Live Biotherapeutic Products (LBPs) in the form of bacteria. These differ from probiotics, which are bacterial products for the benefit of human health but are not permitted to be labelled with any claim of efficacy against disease. Engineered live bacterial therapeutics could continually deliver drugs and have the potential to detect and respond to biological signals in the body. GM LBPs are currently in development to target diseases such as cancer, diabetes, and phenylketonuria[4].

Currently, most LBPs require continual delivery and cannot colonise the human body long-term. Long-term colonisation would enable more continuous delivery and better patient compliance, but also increase risk. More study is required to understand the dynamics of GM LBPs in patients.

The UK is in a good position to become a leader in the development of GMOs due to our existing scientific expertise.

Box 2: Horizontal gene transfer

Bacteria can share DNA in many ways. Not all bacterial species are capable of these processes and they are more likely between, but not entirely confined to, bacteria of the same species[6]. It is also more likely in environments densely populated with bacteria, such as soil or the human gut. Whether the gene is retained by the bacterial population and spreads more widely is determined by the fitness advantage provided by the gene[8]. Most engineered genes come at a fitness cost, which limits their spread.

In addition to this, genetic recombination allows genes to move around the bacterial chromosome and between the chromosome and mobile genetic elements. These phenomena create the possibility of transgenes spreading to different species of bacteria but the likelihood depends on properties of parent species, the technology used to modify it, and the transgene itself.

Concerns

The spread of GM bacteria and genes outside of their intended use is not in itself a hazard, but they may have unintended effects that do constitute hazards.

Risks to the environment

Depending on the species and inserted genes, GM bacteria can survive and proliferate in soil anywhere from a few weeks to several years. Farming practices may spread bacteria between fields[5]. Prior knowledge of the species in question can be used to assess how long it is likely to persist and any impact it may have, including on native microorganisms, larger organisms, and ecosystem processes. Organic farmers are also concerned about the widespread use of GMOs as they are required to show the absence of GM DNA in their products for some certifications[10].

Risks to health

The risk to health posed by a GM bacterium can be assessed using prior knowledge of the characteristics of the parent organism and the inserted transgene. “Qualified Presumption of Safety” is a framework used for the safety assessment of microorganisms. If the parent bacterial species has a known QPS status, the only further safety assessment required is of the effect of the genetic modification[8]. This includes any changes to the ability of the organism to cause infection, or produce toxins or allergens, whether these changes are intended or unintended. Where the GM bacterial treatment is intended for use by the vulnerable, for example in cancer treatment, the risk may be higher due their weaker immune systems. The risk profile of the transgene can be assessed through knowledge of its properties in the ‘donor’ organism, or if the gene is synthetic, through its homology to known genes.

Antimicrobial resistance

During the genetic engineering of bacteria, antibiotic resistance genes are often used to select for successful transformants. Given the current threat of antimicrobial resistance and the potential for these resistance genes to be passed to pathogenic bacteria, it has been suggested by some that any antimicrobial resistance genes are removed from GM bacteria before their release[9].

Intellectual property

The issue of patents for GMOs is complex. GM bacteria are mobile, and this may cause issues of ownership if they spread. There are also concerns that patenting naturally occurring genes will limit scientific research.

Tracing GMOs

The ever-reducing cost of genetic sequencing and improved tools for environmental monitoring will make tracing easier in the future. GM bacteria can also be engineered with marker genes that enable easier tracing[3]. Surveillance can be used to monitor for any detrimental effects to the environment following the release of GM bacteria.

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