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Horizontal gene transfer: the hidden health risks of genetic engineering

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ABSTRACT: **Horizontal or lateral gene transfer involves to the movement of genetic material between organisms in a manner that is not associated with traditional reproduction. This process can occur through direct methods or via vectors, and it contrasts with vertical gene transfer, where genes are passed to offspring. Genetic engineering often utilizes artificial constructs to cross species barriers and integrate in to genomes, facilitating unregulated horizontal gene transfer. These constructs which typically include genetic elements, can naturally mediate horizontal gene transfer. This can lead to the spread of diseases, antibiotic resistance, and even cancer in mammalian cells. Given these risks, it is crucial to establish effective regulatory measures to prevent the release of these constructs into the environment and to consider the continuation of potentially hazard experiments. This review aims to highlight the current status and implications of horizontal gene transfer facilitated by genetic engineering, emphasizing the need for stringent regulatory measures to mitigate associated risks.**

KEYWORDS: **Antibiotic resistance, artificial vector, dormant viruses, CaMV promoter, naked DNA, transgenic DNA**

INTRODUCTION

Genetic material is typically inherited from parents and ancestors through both sexual and asexual reproduction. This process, known as vertical gene transfer (VGT), occurs within species or between closely related species [1]. In contrast, horizontal gene transfer (HGT) involves the exchange of genetic information between contemporary organisms, bypassing the parent-offspring route [2].

A unique instance of HGT includes the transfer of DNA between chloroplasts, mitochondrial, and nuclear genomes. Not only entire genes but also parts of genes, such as exons or introns, can be transferred in this manner [3]. While horizontal transfer is more successful between closely related species, it can also occur between vastly different species, even those in different domains of life [4]. Traditionally, HGT was thought to be limited to bacteria and unicellular eukaryotes. However, recent studies suggest that lateral gene transfer may play a significant role in the evolution and development of animals, including humans [5, 6].

The concept of horizontal gene transfer (HGT) was first demonstrated by Frederick Griffith in 1928 through the transfer of virulence determinants between bacteria, a process later known as transformation. The HGT can occur between closely or distantly related organisms within the same kingdom or even between different kingdoms.

Horizontal gene transfer can happen through direct pathways, where genes are exchanged directly between donor and recipient organisms [7] or through vector-mediated pathways. Vector-mediated transfer involves vectors like pollen, fungi, bacteria, viruses, plasmids, transposons, or insects, facilitating gene transfer without direct contact between the organisms. Mobile genetic elements such as plasmids, viruses, and transposons primarily drive vector-mediated HGT [8, 9].

The transfer of foreign genes, whether transgenic or non-transgenic, into recipient organisms can have both positive and negative effects. However, genetic engineering poses inherent risks, as it often involves genetic material from bacteria, viruses, and other genetic parasites. These materials can cause diseases, spread drug and antibiotic resistance genes, and potentially create new pathogens, making infectious diseases untreatable. Given

these risks, it is crucial to establish effective regulatory measures to prevent the release of these constructs into the environment and to reconsider the continuation of potentially hazardous experiments [8, 10].

HORIZONTAL GENE TRANSFER MAY SPREAD TRANSGENIC TO THE ENTIRE BIOSPHERE.

Horizontal Gene Transfer in Bacteria

Horizontal gene transfer (HGT) occurs throughout the entire biosphere, with bacteria serving as intermediaries for gene trafficking and as reservoirs for gene multiplication and recombination. Bacteria can adapt to new environments and respond to selective pressures by acquiring new genetic traits through mutation, gene function modification, and HGT, which involves acquiring new genes from other bacteria [11] . Bacteria acquire foreign genes horizontally, in addition to vertical gene transfer, either directly or via vectors. HGT significantly enhances the genetic diversity of bacteria. In bacteria, there are three main mechanisms mediate HGT: transformation (uptake of free DNA), conjugation (plasmid-mediated transfer), and transduction (phage-mediated transfer) [12-14].

Transformation

Bacterial transformation is a process of horizontal gene transfer by which some bacteria take up foreign genetic material (naked DNA) from the environment. Such bacteria are termed as competent cells. Transformation is a form of genetic recombination in which a DNA fragment from a dead, degraded bacterium enters a competent recipient bacterium and is exchanged for a piece of DNA of the recipient. Transformation usually involves only homologous recombination, a recombination of homologous DNA regions having nearly the same nucleotide sequences. Typically this involves similar bacterial strains of the same species, and also it is a process in which a competent bacterial cell takes up naked DNA released by other bacteria in environment [15]. Transformation has been shown to occur in many natural ecosystems ranging from soil microcosms to river or spring water and has been reported in Achaea as well. Transformation may also be used to describe the insertion of new genetic material into nonbacterial cells, including animal and plant cells; however, because "transformation "has a special meaning in relation to animal cells , indicating progression, the process is usually "transfection." .A gene from bacterial cell 1 is moved from bacterial cell 1 to bacterial cell 2. This process of bacterial cell 2 taking up new genetic material is called transformation [16].

Conjugation

Conjugation is a direct transfer of DNA (plasmid and chromosomal DNA) from a donor (+) bacterial cell to a recipient (-) bacterial cell through F pilus plasmid mediated contact. That means conjugation requires physical contact between a donor and a recipient cell via a conjugation pilus, through which genetic material is transferred [13]. The donor and recipient strains need to be in the same environment to allow for the creation of the conjugative machinery between the donor and recipient cells. Conjugation is canonically restricted to bacterial cells as the donor and recipient however, *Agrobacterium* spp. is an exception and uses its conjugation machinery for HGT into plant cells [17].

The plasmid genes in question need to be transferable to mediate the movement of DNA within genomes. The transported DNA has to avoid the restriction nucleases of the recipient and this recipient to be recombined efficiently in order for effective future persistence. The recipient has the more active role that promotes the uptake of exogenous DNA in transformation but with conjugate transformation, the donor is the more active participant in the DNA transfer process. Conjugation mainly involves the transfer of plasmids both fertility and replace plasmids, conferring fertility. In some o-conveying fertility plasmid (F-plasmid) becomes integrated into the host (bacterial) cell, genome, and the resulting cell is referred to as a high frequency of recombinant cells (HFR) cell because such cells are cells able to transfer chromosomal genes to recipient cells at high frequency [18].

Transduction

Transduction is the transfer of DNA from a donor bacterial (first host) cell to a recipient bacterial cell (second host) by a bacteriophage (bacteria eater virus) infection. The principle is that during the maturation stage of viral replication with in a donor bacterial cell, a portion of DNA from the bacterium is wrongly or unknowingly assembled with virus DNA within the capsid. When the virus is released and infects the second host, the wrongly assembled DNA of the first host is incorporated into the genome of the second host [13]. There are two types of transduction: generalized, in which a random piece of the host DNA is incorporated into the recipient cell as a result of wrong packing; and specialized, which occurs when lysogenic viruses are the lytic cycle; prophage imprecisely excise themselves from a host genome and incorporate only specific genes of host DNAs.Transduction in the environment was thought to be unlikely due to the highly specific nature of the host range of bacteriophage.

Some bacteriophage can exist as lysogens, where the phage DNA integrates with the host DNA and lies dormant as a part of the host genome until induced back to the infective lytic cycle by some environmental signal. These lysogenic phages are protected from degradation by the host cell in which they reside. The DNA protection offered by the phage protein coat in lytic phages also confers relative stability from environmental degradation. Phages have been known as mediators of environmental gene exchange, and they also play an integral role in the evolution of new food borne pathogens [19].

HORIZONTAL GENE TRANSFER IN HIGHER ORGANISMS (PLANTS AND ANIMALS)

Horizontal gene transfer is extensive in prokaryotes and within the past 10 years it has been has increasingly recognized as a genomic conduit among eukaryotes even in humans [20]. Thus, horizontal gene transfer has the potential to occur across the entire biosphere, with bacteria and viruses acting as intermediaries for gene trafficking and as reservoirs for gene multiplication and recombination, which is the process of creating new combinations of genetic material [21].

Route of horizontal gene transfer in plants and animals

In prokaryotes, we have a relatively clear understanding of a number of HGT pathways, such as transformation, conjugation, and transduction. However, HGT processes in eukaryotes are much more underestimated. There are many potential routes for HGT to plants and animals, which can be via vector or direct methods [20].

Direct HGT methods

Accumulating evidence suggests that two organisms are likely to undergo HGT when they are in contact; however this is less dangerous and common in eukaryotes. Whereas vector mediated HGT occurs more frequently and is dangerous. The most common mechanisms of HGT are transformation. If a variety of 'bare' genetic material is administered in solution to the eye, rubbed into the skin, injected, breathed, or eaten, it can be readily absorbed by various cells. Frequently, these alien gene constructions end up being integrated into the genome. However, since plant cells typically have a protective cell wall, direct transformation might not be as important [22]. In plants, direct HGTs have been observed in association with grafting or parasitism by endophytes and epiphytes, where plants were not only the donors but also the recipients of horizontally transferred genes. Grafting creates an opportunity for cell-to-cell contact between distantly related plant species [22, 23].

A) Vector mediated HGT: Vector-mediated horizontal gene transfer (HGT) involves the transfer of genetic material between organisms using vectors such as viruses, bacteria, fungi, parasite, and transposable elements. This process allows genes to move across different species without direct contact between the donor and recipient organisms [24].

1) Transduction (virus-mediated HGT): transduction is expected to be a main route, as there are many viruses that infect plants and animals. Viruses have an extremely strong ability to capture genes from host genomes, including bacteria, fungi, and eukaryote genomes. Thus, viruses are an important vector for HGT. DNA viruses, can, for instance, capture host genes and integrate these genes into their own DNA, subsequently infecting other organisms such as plant parasitic insects and transferring this captured DNA [25] .

2) Bacteria-mediated: Bacterial pathogens that enter plant and animal cells may take up foreign genetic material and carry it into the cells, thus serving as vectors for horizontal gene transfer. Bacteria comprise a vector for gene transfer between plants, with a well-known example of this found in the bacteria species tumefaciens. *Agrobacterium tumefaciens.* Evidence has also been provided in transplastomic tobacco that naked DNA from degraded plant tissue in the environment can be transferred to bacteria [26].

3) Fungi-mediated HGT: Fungi often have the ability to infect other organisms, providing a possible pathway for HGT. Many land plants have obtained the biosynthesis of aromatic compounds for carbohydrate metabolism from symbiotic fungi via horizontal gene transfer. Fungi also reported genes from plants to other organisms, such as aphids [27] .

4) Parasite-mediated HGT: Parasitic can also be a vector for horizontal gene transfer. For instance, cellulose genes were found to have been transferred to nematodes from bacteria, fungi, and other plant parasites, including other nematode species and HGT from endosymbiotic bacteria to their host mosquitoes (*Wolbachiapipientis*) have also been documented [28].

5) Transposable elements-mediated HGT: Transposable elements (TEs) are important vectors for the horizontal movement of genes between eukaryotic genomes. Transposons, with their inherent ability to mobilize, proliferate, and integrate into genomic DNA, generate HGTs with ease. Transposons have been demonstrated to capture and transduce genomic DNA sequences in both *Daphnia pulex*and *Drosophila* species [29].

Types of vector in HGT

Natural vectors

Natural vectors are virus, plasmid, transposons, fungi, and insects. Transfer genetic materials from one cell to another cell naturally. Natural vectors regulated by regulated factors:

1) Species barriers or donor-recipient dissimilarity barrier: HGT naturally occurs between closely related species from the same taxonomic group. A graphical representation of the network with species colored by their genomic GC content reveals that clusters of densely connected donors and recipients are very similar in their genomic GC content. Furthermore, the difference in genomic GC content between donors and recipients is <5% for most (86%) of connected pairs. This suggests that there exists a biological barrier for gene acquisition from donors of dissimilar genomic GC content. And it is known that, for instance, viruses that infect pigs cannot infect human beings due to host specificity. Plasmids and transposons typically target a limited range of host species, though there are exceptions [30].

2) Restrictions as a barrier: DNA that is recognized as foreign because it does not have the same sequence-specific chemical signatures can be broken into pieces by restriction endonucleases. For small plasmids and individual genes, there is a significant chance that they might not contain some of the rarer restriction sequences and therefore avoid the effect of enzymatic cleavage. In addition, the fact that DNA entering through conjugative transfer or natural transformation is single-stranded instead of double-stranded might provide some protection, and indeed, comparison with transformation frequencies of double-stranded DNA does confirm a greater ability to avoid destruction through the former mechanism [31].

3) Functional barrier: Once imported and integrated into the genome, acquired genes still have to adapt within the genome in order to be retained during evolution. Microbes tend to delete nonfunctional or otherwise unneeded DNA from their genomes. Therefore, the fixation of the acquired DNA within the genome is highly dependent on its functionality or utility to the recipient under selectable environmental conditions. In order to be expressed, the gene has to be either inserted near a recognized promoter, bring one with it, or be acquired together with the corresponding regulator [32].

Artificial vectors

Genetic engineers have created artificial vectors to overcome natural species barriers that restrict gene transfer and maintenance, enabling the transfer of genetic material across different species. These vectors are constructed by combining parts of the most infectious natural vectors, such as viruses, plasmids, and transposons from various sources, and are designed to cross wide species barriers. Consequently, a single vector may transfer genes to the genomes of all organisms, greatly enhancing horizontal gene transfer. Genetic engineering involves laboratory techniques to isolate and combine the genetic material of any species and to multiply the constructs in convenient cultures of bacteria and viruses. These techniques allow the transfer of genetic material between species that would never interbreed in nature, using artificial vectors. Artificial vectors significantly enhance horizontal gene transfer for several reasons:

1. They are derived from natural genetic parasites that mediate horizontal gene transfer most effectively.
2. Their highly chimeric nature means they have sequence homologies (similarities) to DNA from viral pathogens, plasmids, and transposons of multiple species across kingdoms, facilitating widespread horizontal gene transfer and recombination.
3. They routinely contain antibiotic resistance marker genes, enhancing horizontal transfer in the presence of antibiotics, either intentionally applied or present as environmental pollutants.
4. They often have 'origins of replication' and 'transfer sequences', signals that facilitate horizontal gene transfer and maintenance in cells to which they are transferred. Genes are transferred in unit constructs known as 'expression cassettes'. Each gene is accompanied by a promoter, which signals the cell to turn the gene on, transcribing the DNA gene sequence into RNA, and a terminator, which ends the transcription and marks the RNA for further processing and translation into protein.
5. Chimeric vectors are known to be structurally unstable, with a tendency to break and rejoin incorrectly or join with other DNA, increasing the propensity for horizontal gene transfer and recombination.
6. They are designed to invade genomes and overcome mechanisms that break down or disable foreign DNA, thus increasing the probability of horizontal transfer [34].

HORIZONTAL TRANSFER OF RECOMBINANT DNA

Transgenic DNA has been found to transfer from transgenic organisms to non-transgenic organisms in the biosphere through HGT. Recombinant DNA (from different sources) can be transferred using genetic engineering intentionally in the laboratory or in other confined places of field experiments in one hand. On the other hand, it can transfer from the intentionally or unintentionally released GMO to other non-GMOs unintentionally in the environment. Hence, for the sake of understanding, horizontal transfer of recombinant DNA is categorized into intentional genetic engineering and unintentional transgenic DNA HGT [35] .

Intended/ GE horizontal transfer of transgenic DNA

Intentional HGT is the insertion of defined DNA fragments into the target unrelated organism using artificial vectors. Transfer non-transgenic DNA or transgenic DNA from one or more organisms to another organism (which is intended to be modified) using artificial vectors in the laboratory. It is artificial horizontal gene transfer after the notification of unintended horizontal transfer of transgenic DNA; intended horizontal gene transfer is called primary horizontal transfer of transgenic DNA [36]. Intended horizontal gene transfers facilitate unintended horizontal transfer of genes, including recombinant DNA; from genetically modified organisms to different organisms since artificial vectors are vectors greatly unstable. The intended horizontal transfer and recombination of genetic material across species barriers is thought to be of little concern by many scientists active in genetic engineering, as genes are considered to be mechanistic entities or modules that can function equally well in many organisms, regardless of their historical and evolutionary context [37, 38].

Unintended horizontal transfer of transgenic DNA

There was an argument on whether transgenic DNA may transfer horizontally from GMO to non GMO or not in the environment. Supports of the biotechnology industry are often argued that transgenic DNA, once incorporated into the transgenic organism, will be just as stable as the organism's own DNA. Others argue that transgenic DNA transfers horizontally more likely than non-recombinant DNA, however the transfer is not intentional [39]. Genetic engineering has effectively created pathways for unintended horizontal gene transfer and recombination. The broad sense of unintended horizontal gene transfer is about the transfer of recombinant DNA from GMOs to other organisms in the environment in an unintentional way .It occurs naturally and it is random. It is called secondary horizontal transfer (since it is transferred from GMO, which is transferred primarily, to another organism for the second time). Unintended horizontal gene transfer of recombinant DNA is receiving more attention now a days due to the wide and unregulated release of artificial vectors (there is still no legislation in any country to prevent the escape and release of artificial vectors and other artificial constructs into the environment) and due to its impact on health and the environment [34, 39].

TRANSGENIC AND NON-TRANSGENIC DNA IN HORIZONTAL GENE TRANSFER

Genes are never transported in isolation; instead, they are transferred in "expression cassettes," which are unit structures. The promoter, gene, and terminator are usually the three parts of the construct that originate from separate sources. Additionally, the gene itself might be a combination of components from many sources. Since viral promoters continuously over express the genes they control, they are the most often utilized promoters. These promoters are generated from viruses linked to significant disorders. All genetic engineering applications, whether in agriculture or medical, use this fundamental foundation, which carries the same risks [40]. Transgenic DNA is thought to have a far higher horizontal spread rate than native DNA from an organism. First of all, vectors and artificial constructs are made to break through species barriers and infiltrate genomes; because they are physically unstable, they are all vulnerable to horizontal transfer and recombination. Second, foreign gene constructs may be able to extract and reintegrate at other locations or in different genomes thanks to the same mechanisms that allow them to integrate into the genome. As an example, the enzyme integrase, which facilitates the insertion of viral DNA into the host genome, may also catalyze the opposite reaction by acting as a disintegrase [39]. All genomes, from bacteria and viruses to higher plants and mammals, contain integrase, which are members of a super family of related enzymes. The third reason is that the integration sites of most commonly used artificial vectors for transferring genes are' recombination hotspots' and may therefore have an increased tendency to transfer horizontally. Moreover viral promoters, such as those from the cauliflower mosaic virus (CaMV) widely used to make transgenes over express contain recombination hotspots, and may further enhance horizontal gene

transfer [41][3].The metabolic stress on the host organism due to the continuous over-expression of the foreign genes linked to aggressive viral promoters may also contribute to the instability of the transgenic DNA. Lastly, transgenic DNA is typically a mosaic of DNA sequences from many different species and their genetic parasites; that means they have sequence homologies with the genetic material of many species and their genetic parasites, thus facilitating wide-ranging horizontal gene transfer and recombination [42].

EVIDENCE FOR HORIZONTAL TRANSFER OF TRANSGENIC DNA

It is often argued that transgenic DNA, once incorporated into the transgenic organism, will be just as stable as the organism's own DNA. But there is both direct and indirect evidence against this supposition. Transgenic DNA is more likely to spread and has been found to spread by horizontal gene transfer [43].

Transgenic lines are notoriously unstable and often do not breed true. There is a lack of molecular data documenting the structural stability of the transgenic DNA, both in terms of its site of insertion in the genome and the arrangement of genes, in successive generations. Instead, transgenes may be silenced in subsequent generations or lost altogether [44]. An herbicide tolerance gene, introduced into *Arabidopsis* by means of a vector, was found to be up to 30 times more likely to escape and spread than the same gene obtained by mutagenesis. One way this may have happened by means of horizontal gene transfer via insects visiting the plants for pollen and nectar. The reported finding that pollen can transfer transgenic genes engineered into transgenic plants has been transferred via pollen to bacteria and yeasts living in the gut of bee larvae. In turn, this is supported by the fact that the fact that the persistence of DNA is not rapid in the gut. After being exposed to human saliva for 60 minutes, a genetically modified plasmid showed a survival rate of 6% to 25% [34]. A bacterium that typically inhabits the human mouth and throat, *Streptococcus gordonii*, was able to undergo transformation by the partially broken plasmid DNA. After ten minutes, the frequency of transformation was still measurable, but it reduced dramatically with the amount of time spent in saliva. It has been discovered that viral DNA given to mice can enter the intestinal wall and enter the spleen, liver, and white blood cells, where it can integrate into the genome of the mouse cell. The viral DNA enters the cells of the fetuses and the newborn animals when given to pregnant mice, suggesting that it has also crossed the placenta [45]. In experimental conditions, transgenes and antibiotic resistance marker genes from genetically modified crop plants have been shown to secondary horizontally transfer into soil bacteria and fungus. Transfer to bacteria was verified by comparing re-isolated transgenic DNA with total transgenic plant DNA, whereas transfer to fungi was accomplished by straightforward co-cultivation. Total DNA extracted from homogenized plant leaves from a variety of transgenic plants, such as Solanum tuberosum (potato), *Nicotiana tabacum* (tobacco), *Beta vulgaris* (sugar beet), *Brassica napus* (oil-seed rape), and *Lycopersicon esculentum* (tomato), was used to successfully transfer a kanamycin resistance marker gene to the soil bacterium Acinetobacter [46]. German researchers started tracking field releases of transgenic sugar beets (Beta vulgaris) that were resistant to rhizomania and carried the kanamycin resistance marker gene in 1993. They looked studied the horizontal gene transfer and persistence of transgenic DNA in soil microorganisms. After the transgenic crop was planted, they discovered that the transgenic DNA remained in the soil for as long as two years. Furthermore, between 1.5 and 2 years, the percentage of kanamycin-resistant bacteria in the soil rose noticeably, possibly as a result of the antibiotic resistance marker gene being horizontally transferred to soil bacteria [47].

The researchers also carried out microcosm experiments in which total transgenic sugar-beet DNA was added to non-sterile soil with its natural complement of microorganisms. The intensity of the signal for transgenic DNA decreased during the first days and subsequently increased due to the fact the fact that the transgenic DNA has been taken up by bacteria and becomes replicated as the bacteria multiply. They conclude that transgenic DNA is found to persist in all environments and not rapidly break down as previously supposed. In parallel, soil samples were plated, and the total bacterial lawn allowed growing for 4 days. After that, DNA was extracted and probed for transgenic DNA; several positive signals were found, 'which might indicate uptake of transgenic DNA by competent bacteria [48].

HAZARDS OF HORIZONTAL GENE TRANSFER

The HGT and recombination have been responsible for problems. Indeed, the evolution of virulence and the spread of drug and antibiotic resistances are now linked to the extensive horizontal gene transfer and recombination events among bacteria and viruses, many of which may have occurred in recent years. There is already strong evidence that recombination and horizontal gene transfer have produced novel infectious bacterial and viral strains and promoted antibiotic and drug resistance in these pathogens. From 1988 to 1996, new viruses were discovered

[49].Recombination with dormant, inactive, or inactivated viral genetic material found in the genomes of all plants and animals is one method by which new viral diseases can be produced. The majority of artificial vectors are made to penetrate genomes and cross species boundaries; they are either derived from viruses or include viral genes. The genetic material of other viruses may recombine with these vectors, reactivating old viruses and producing new infectious viruses and bacterial strains that are capable of overcoming species boundaries [50]. One major issue with human gene therapy is the possibility of reactivating proviral sequences, which are often dormant copies of viral genomes found in all plant and animal genomes.

Viral vectors have to be 'packaged' in human cell lines, and replicating viruses are often generated by the viral vector recombining with proviral sequences in the cells .A new bacterial strain responsible for the cholera outbreak in India in 1992 and for the *Streptococcus* epidemic in Tayside in 1993. The *E. coli* 0157:07 strain involved in the recent outbreaks in Scotland is believed to have originated from horizontal gene transfer from the pathogen, *Shigella* [51]. The antibiotic resistance genes carried by artificial vectors have been transferred horizontally and have recombined with one another to generate multiple antibiotic resistances throughout the bacterial populations. Antibiotic resistance genes spread readily between human beings and from bacteria inhabiting the gut of farm animals to those in human beings. Antibiotic-resistant strains of pathogens have been endemic in many hospitals for years and are making infections untreatable [52]. Moreover, HGT is responsible for various health and food safety problems. Random insertion of transgenic DNA into the genomes of cells results in harmful effects, including cancer. Transgenic DNA can spread to farm workers and food processors via dust and pollen. DNA is not readily degraded during food processing nor in the silage; hence, can transgenic DNA in animal feed spread to bacteria in animals. Generally, HGT involves spreading new genes and gene constructs that have never existed and multiplication of ecological impacts due to all of the above negative impacts [39, 53].

CONCLUSIONS AND RECOMMENDATIONS

Horizontal gene transfer (HGT) has been a part of our evolutionary history and continues to occur naturally today. This process is typically regulated by species barriers and mechanisms that degrade foreign genetic material. However, genetic engineering has introduced numerous artificial constructs designed to bypass these barriers and integrate into various genomes. Some of the most hazardous constructs may originate from the waste produced by laboratories working with transgenic organisms, including cancer genes from research labs and virulence genes from pathology labs. Consequently, the biosphere is now exposed to novel genetic constructs and combinations that would not have naturally occurred. To address these risks, it is imperative to implement stringent regulatory oversight to prevent the release of these dangerous constructs into the environment. Additionally, it is essential to evaluate whether certain high-risk experiments should be permitted to continue. Transparent communication of the current scientific understanding of HGT, the data used for risk assessment, and the identification of knowledge gaps are necessary to build public confidence in the regulatory process and guide future HGT research.

DECLARATIONS

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Correspondence and requests for materials should be addressed to Eden Woldegerima; E-mail edengem14@gmail.com: ORCID: https://orcid.org/0009-0002-7704-6341 We authors declare that agree to its publication after any amendments arising from the peer review, agree to the posting of the full text of this work on the web page of the journal and to the inclusions of references in databases available on the internet

Data availability

Data is available upon the request to the corresponding author.

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Authors' contributions

Eden Woldegerima designed, edited, performed literature revision and wrote the review; Birhanu Andualem critically read, modified the final revision of review; and took care of the editing.

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