What does Synthetic Biology mean for LATIN AMERICA AND THE CARIBBEAN?

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Building International Capacity in Synthetic Biology Assessment and Governance

What does Synthetic Biology mean for Latin America?

Introduction

After twenty years of real world experience with transgenic genetically modified organisms (GMOs), the global biotechnology industry is now pushing forward a platform of novel genetic engineering techniques. These are addressed by the UN Convention on Biological Diversity (CBD) under the term synthetic biology.

These new techniques of synthetic biology or "syn bio" include gene synthesis, genome editing and gene drives. Some are resulting in organisms and products that are already moving into commercial use – first for the artificial production of flavours, fragrances and ingredients in closed vats and soon for the release of novel genetically engineered (or gene-edited) organisms to change agriculture or wild ecosystems.

Touted by OECD governments as 'disruptive innovation,' this "GMO 2.0" wave (as with the first wave of GMOs) will have real environmental, social and cultural impacts on the peoples and biodiversity of Latin America and the Caribbean. Governments and civil society are now urgently attempting to identify and assess the potential impact of this new syn bio wave before it breaks on Latin American and Caribbean shores.

The synthetic biology industry threatens traditional economies and livelihoods that depend on natural products, challenges fragile biosafety regimes and opens new paths to digitally-driven biopiracy. This briefing reflects on lessons learned by Latin American and Caribbean countries from the first wave of GMOs and identifies some emerging issues for the continent as the synthetic biology wave comes to the fore.

From GMO 1.0 to GMO 2.0: History of first generation genetic engineering in the region

As Latin American and Caribbean society and policymakers begin to comprehend and assess synthetic biology, there is already significant experience with the first generation of genetic engineering to draw upon, and important precautionary lessons to learn. Today, the continent is the second largest global producer of Genetically Modified Organisms (GMOs) in agriculture (after North America), concentrated in Argentina, Brazil and Paraguay, Uruguay and Bolivia. Other countries, such as Mexico, Colombia, Honduras and Panama have also approved some commercial planting of GM crops, and Chile and Costa Rica allow GM seed production for export, but not for domestic planting. Significantly, however, 27 countries in Latin America and the Caribbean have chosen not to allow commercial planting of GMOs.

This caution by most countries in the region is probably founded on the experience of observing their neighbours. From first generation GMOs, pesticide tolerant soybeans and stacked traits maize (pesticide tolerance + Bt) are by far the dominant crops, followed by GM cotton and canola. There have been minor trials of other crops, such as alfalfa, wheat and pineapple. Brazil has also approved GM trees and, along with Panama and Cayman Islands, has had trials of GM mosquitoes.[1] The planting of glyphosate tolerant soybeans dominates: this first and largest GM crop at the global level emerged during the 1990s and quickly had a major impact in the Southern Cone of Latin America, with 54 million hectares planted in five countries. In most of these cases, the GMO was first introduced illegally, without biosafety considerations – companies and big farmers smuggling GM seeds to force "de facto" situations, in what Syngenta dubbed "the United Republic of Soybeans."[2] As predicted at the time by critics, the use of agrochemicals in this region increased 10 to 20-fold after the first planting of GMOs in 1996. Today, Brazil and Argentina are among the top five global users of agrochemicals in the world, a development linked to herbicide-tolerant GMO cultivation. Currently, 550 million litres of glyphosate (now classified by the World Health Organization as "probably carcinogenic to humans") are applied annually to transgenic soy.[3] Virtually all of these GM soybeans and maize are devoted to animal feed, and the vast majority are for export.

The downstream effects have also become clear. Both in Argentina and Brazil, studies have found glyphosate residues in drinking water, mothers' milk and citizens urine and blood, particularly in rural areas and cities close to plantations.[4] In Argentina, multi-year evaluations of public health in the most intensive GM production areas has shown a surge of neonatal deformities, abortions and cancer cases.[5] In all five countries, there has been a significant increase of land concentration into fewer hands linked to GM cultivation, along with the disappearance of tens of thousands of small farms and thousands of displaced peasants. GM cultivation is the main driver of deforestation in the region.[6]

Despite 20 years of industry promises of ‘public benefit’, all planted commercial GM crops in the region are proprietary seeds from a few transnational companies (Monsanto-Bayer, Syngenta, DuPont-Dow). This has precipitated changes in seed and international property right laws in each country to protect the commercial interests of these players. These companies also have achieved, through the dependency that GMOs have created in key agricultural sectors, a large influence on public agricultural policies and on biosafety regulations: “dangerous liaisons” that have been documented in several cases.[7] In Brazil, there have been repeated attempts to legalize suicide seeds (also called “Terminator” technology) that would make farmers completely dependent on companies.

In the case of GM maize, an additional concern has been the transgenic contamination of peasant and traditional maize varieties in its center of origin in Mesoamerica. Once again, such contamination was foreseen but dismissed. In Mexico, there has been a broad, sustained public opposition from many sectors (scientists, indigenous and peasant farmers, artists, environmentalists, consumers) to GM maize. Following collective action against it, planting GM maize has been legally suspended for four years by a court order that is still on trial.

Lessons learned and implications of the first wave of GMOs

Despite promises to improve nutrition and solve hunger, the first generation of GMO production in Latin America and the Caribbean was not developed for food but largely for feed, and overwhelmingly for export. The benefits most clearly went to transnational companies and big landowners, but had significant negative impacts on public health, environment, small farmers and consumers. In the five countries with large biotech presence, the pressure from these economic interests has shifted the focus of biosafety regulations away from precautionary protection of consumers, environment or biodiversity. This has set a poor precedent and weak foundation for regulating the next set of emerging biotechnologies. Countries in the region should reflect critically on the promises now accompanying the second wave.

Synthetic biology and biosynthesis

As the next wave of biotechnology arrives, the first commercial fruits of synthetic biology are not fruits at all – they are engineered single-molecule ingredients produced in large vats of microbes. These, in turn, carry large risks for regional economies and sustainable use of biodiversity thousands of miles away. A growing number of corporations and researchers are using the tools of synthetic biology to produce artificial replacements for ingredients formerly derived from natural products. Their goal is to produce high-value flavours, fragrances, oils and sweeteners by using bio-engineered microbes instead of costly botanical imports or conventional chemical synthesis. To manufacture the desired compound, companies engineer new genetic pathways into microorganisms like yeast or algae.

They alter the DNA so that when the microorganism feeds on sugar or natural gas it excretes the compounds that were previously extracted from plants. In basic terms, by producing the compound in an industrial fermentation vat there is reduced need for the botanical plant or natural substance to produce the desired ingredient. This impacts sustainable use of biodiversity.

Currently, the organisms used to produce synthetic biology replacements are fed by sugar or other biomass. Switching at scale from agricultural-derived ingredients to syn bio production will require feedstock crops cultivated in large-scale monoculture agriculture, or cheap methane acquired through expanded methane fracking or coal bed mining, with negative implications for land, ecosystems and biodiversity.

The production of these ingredients via synthetic biology also poses economic and social risks that may significantly affect Latin American and Caribbean countries and economies by replacing livelihoods dependent on high-value commodities, reducing demand for naturally-derived products from the export market, and relocating production of high-value natural products from agriculture-dependent economies to industrialized countries.

There are already dozens of syn bio-produced compounds in products that are on or nearing the market, including versions of flavors, fragrances, fuels, pharmaceuticals, textiles, sweeteners, industrial chemicals, cosmetic and food ingredients that taste, smell, and behave like compounds derived from nature. A database of ingredients being developed or on the market found over 350 different projects to produce biosynthesized compounds, many of them already in foods, cosmetics and dietary supplements.[8] See Synthetic Biosynthesis Primer for more background on this industry.

Latin America as a natural products source

Latin America and the Caribbean is rich with biodiversity. The region has historically been a source of many valued botanical natural products, including spices, flavours, cosmetic ingredients and essential oils. Spices in particular need very specialized processes and knowledge to both grow and process. To harvest a crop like vanilla or vetiver requires navigating weather, altitude, isolation, and even political ups and downs. The artisanal extraction of oils, fragrances and medicines often relies on well-kept forests.

The production of spices is currently particularly relevant in Central America, the Caribbean and other tropical regions. The collection and/or production and processing is done mostly by peasant and indigenous communities, generally women, for whom these activities are often their only cash income, allowing them to stay on their territories and continue their important historical role as biodiversity maintainers. Some products that may be replaced by synthetic biology are of economic importance, such as cacao butter and cacao butter equivalents (including coconut oil) for the Caribbean and some areas of Brazil, Mexico and Ecuador, and vetiver in Haiti. All are of significant cultural, environmental and social importance for indigenous and small farmers producers.

All countries in Latin America and the Caribbean produce **cocoa** butter and/or cocoa butter equivalents (CBE) or substitutes (CBS) including coconut oil, except for Argentina, Chile, Paraguay and Uruguay. For several countries, these are very significant economic productions. Mesoamerica is the center of origin of cacao, but recent studies also attributes it to some Amazon regions. Small farmers in six countries produce **Stevia**: Paraguay, México, Colombia, Argentina and Uruguay. Paraguay is the center of origin of Stevia. **Vanilla** has center of origin in Mexico and it is produced in Mexico, Costa Rica and Guadalupe as well as on Caribbean Islands. **Vetiver** is a key economic production in Haiti, is being planted elsewhere in the Caribbean and is also produced in Brazil and Paraguay. **Squalane** derived from olives or amaranth is produced in Argentina and Chile. Two countries in the region harvest **sandalwood**: Costa Rica and Haiti. Mexico has a significant industry of **rose oil** and Dominica of **patchouli**.

1. Cocoa butter and Cocoa Butter Equivalents (CBE)

Cocoa Butter is part of a class of vegetable fats used for both food and cosmetics. Made mostly from the oilseeds of the cacao beans grown across the tropics, other less common butters in this class include murumuru, mango, coconut and palm grove butters. Cacao's use is particularly targeted towards chocolate, while other butters have food uses but are also commonly used in cosmetics as moisturizers. All Latin American countries – except Chile, Uruguay, Paraguay and Argentina – harvest and collect cocoa butter and/or CBEs.

In Latin America, nine countries represent 80% of the global "prime" production (the best quality cacao and cacao butter, sustainably produced). For more than 3 million peasants in Latin America and the Caribbean, this high-quality cacao is the center of their livelihoods.[9] Cacao's world production is growing at a fast rate (10 percent annually)[10] due to the increasing demand from Europe and United States.

Replacing Cacao Butter and CBEs with Algal Butter

On 13 April 2017, the synthetic biology enterprise TerraVia (formerly Solazyme) announced that their Algal Butter had been granted "Generally Recognized as Safe" status by the Food and Drug Administration. According to their information, "Algae Butter is a revolutionary new structuring fat for use in bakery, spreads, and confectionery,"[11] aiming directly to replace the use of cacao butter from Latin America and other regions in the world.[12] Their April 2017 news release informs: "Algae Butter is exclusive to TerraVia and Bunge. The production would be done by the Bunge-Terravia joint venture SB Oils aiming to replace a market valued more than 2 billion dollars.[13] Although Terravia went bankrupt at the end of 2017, their assets were purchased by ingredient producer Corbion and it appears that Corbion and Bunge intend to continue with their plan to place syn bio algal butter on the market as a cocoa butter replacement.[14]

2. Babassú and coconut oil

Babassú or babaçú is a palm tree that originates in the Amazons and grows widely in the Brazilian states of Tocantins, Maranhão and Piauí. Its nut kernels are the source of babassu oil, similar in properties and uses to coconut oil. Most Babassu oil is used in the soap and cosmetic industries, although it can be used in cooking. The press cake that remains after oil is extracted from the kernels is used as animal food. Babassú-related production is crucial for the livelihoods of peasants of the Northeast of Brazil, especially for women. Removing Babassú kernels is labour-intensive, and is traditionally carried out by women. More than 400,000 women and their families process the palm for oil, soaps, flour and animal feed.[15]

Coconut oil is produced in several countries in Latin America and the Caribbean, and has significant production in Brazil, Mexico, Dominican Republic and Venezuela.

Replacing Babassú and Coconut oil with Algal Butter

Terravia, (formerly Solazyme) has engineered algae to create oils that are "genetically tailored" to express fatty acids such as lauric and myristic acids that could replace coconut and babassú oils. Solazyme/Terravia has partnered, among others, with Unilever, ADM and Bunge, and as mentioned above, it made the joint venture SB Oils with Bunge.

Some of Unilever's well-known soap brands are now being produced with Terravia's engineered algal oils instead of the natural sources they previously used.

3. Stevia

Stevia refers to a shrub with sweet-tasting leaves. Its center of origin is the region that is now eastern Paraguay and Brazil's southwestern state of Mato Grosso do Sul. The region's indigenous Guaraní people, who refer to stevia as *Kaá he'é*, have used its leaves in foods and medicines for hundreds of years. Currently, the use of Stevia as a non-glycemic sweetener is very popular and has motivated its cultivation by small farmers, often organically, in several countries in Latin America, including Paraguay. The replacement of Stevia by synthetic biology extracts would compete with these cultivations. It also constitutes a form of biopiracy against the Guaraní Peoples.

Chemists are interested in the plant's *steviol glycosides* – the 40+ compounds that are responsible for the leaves' sweetness – some of which are 300 times sweeter than cane sugar. The global market value of stevia, most of it in the form of powdered extract, exceeded US$400 million in 2016.[16] The Swiss company Evolva collaborates with agribusiness giant Cargill on a sweetener produced via syn bio fermentation, a combination of two steviol glycosides, Rebaudioside D and M. In 2015, the companies branded their next-generation sweetener "EverSweet," and the product was set to launch in 2016. Early in 2017, however, Evolva reported a forced delay due to a "complex combination of factors, including strain characteristics; fermentation and downstream processing costs; facility conversion costs, production scale [and] customer indications on pricing."[17] The launch is now set for 2018 although rumours are that Cargill may launch their own syn bio Stevia extract without Evolva. Ingredients giant DSM is also planning to sell a fermented syn bio stevia extract.

4. Vanilla

Natural vanilla is derived from the cured seed pod of the vanilla orchid, which grows as a vine in tropical climates. Vanilla production is very labour intensive, requiring cultivators to hand-pollinate vines dispersed in forested areas. The pods take about five months to mature, after which they are collected by hand and cured. The forests must be in good health for the vanilla orchids to thrive, so caring for the forest is also part of the work of the vanilla producers. An estimated 200,000 people are involved in the annual production of cured vanilla beans. Globally, Madagascar is the biggest producer, but Mexico, its center of origin, also maintains natural vanilla production which has an important cultural and economic value for indigenous and peasant communities.

In Mexico, vanilla is pollinated manually in March and April, when unemployment in communities is on the rise. Because of this, cultivating vanilla represents the possibility of avoiding a greater number of emigrants from communities and therefore prevents further family disintegration. Manual pollination of vanilla is a moment of assembly and celebration. Keeping the traditional ways of cultivating this orchid keeps cohesion among communities and families. During pollination, children learn their culture, the elders feel included and valuable, and the young men remain in the community. Important community matters are addressed together during that time.

At the consumer end, natural vanilla sells for thousands of dollars per kilogram, while synthetic "vanillin" sells for about ten times less. In 2014, Evolva, a Swiss syn bio company, and US industry giant International Flavors & Fragrances (IFF) commercialized a bio-synthesized vanillin flavor which is now sold as part of IFF's "Always Vanilla" line. Evolva brands its syn bio vanillin as "natural," so it directly competes with peasant production.

5. Vetiver

Vetiver is a perennial, densely tufted grass. It is planted in many places because its very efficient root system prevents erosion and filters water. Vetiver oil made from its roots is a high value cosmetic ingredient. It may be used in 90% of all Western perfumes, and also in lotions, air fresheners, household products and food preservation, among other uses. In Haiti alone, vetiver oil is the country's single most valuable agricultural export and supports around 60,000 people. In the Southwest of Haiti, it provides job for 27,000 farm families. Besides the much-needed cash income for farmers, vetiver cultivation provides many side benefits: vetiver grass thrives in harsh environments and it can be planted on steep hillsides and used for landslide control. In coastal areas it is grown for tidal flood control and in marshes it aids fish production.

The syn bio company Evolva has patents on vetiver and aims to produce compounds that are structurally related to vetiver and could be used by cosmetic industry, among others. However, Evolva reported that they are not intending to pursue this for the moment.[18]

However, the cultivation and production of essential oils in Haiti is an important economic activity, and is the means of survival for tens of thousands poor farm families. Vetiver is only one of the essential oils that syn bio industry aims to replace and is a very clear example of how biosynthesized products could have devastating impacts on the subsistence of poor farmers.

6. Squalane

Squalane is a high-end, "oil-free" moisturizing ingredient, found in nature and used in many cosmetics. Until recently, it was extracted from the livers of deep sea sharks, but the Squalane used today is derived largely from botanical sources, mostly olive oil and amaranth. Argentina and Chile have successfully developed botanical Squalane production.

Since 2010, leading synthetic biology firm Amyris Biotechnologies has been marketing its so-called "sugar-derived" Squalane as Neossance™.[19] Amyris' squalane is produced by bioengineered yeast fed on Brazilian sugarcane, and has gained a significant hold in the cosmetics market, used today by a wide variety of brands. It is also sold by Amyris' in-house cosmetics brand Biossance™.

Brazilian sugarcane as feedstock for syn bio microbes

Brazil is by far the largest producer of sugarcane and the biggest exporter of sugar in the world. It is also home to several synthetic biology production facilities, for which the underlying sugar production entails significant environmental and human rights impacts. In 2016, a UN report that analyzed the human rights abuses in countries that grow sugarcane found that in many cases the plantations are fraught with violations, including slave-like work conditions, deadly conflicts over land, fraudulent land acquisitions that led to forced evictions of communities and loss of hunting and grazing lands, and deforestation that has increased food insecurity and malnutrition.[20]

Gene editing

A handful of molecular genetic techniques allow synthetic biologists to quickly alter the DNA of crops and animals. These are now being applied for both agricultural and conservation purposes. The most famous of these techniques is known as CRISPR (Clustered Regularly Interspersed Palindromic Repeats) and it has been used to make hornless cattle, mushrooms that never brown, and new 'waxy' varieties of corn. Similar gene-editing techniques have been used to make herbicide resistant canola and engineered insects and mice.

Gene-edited crops involve altering the genetic makeup of organisms just as any other form of genetic engineering does, although some biotech companies are trying to argue that they should not be treated as GMOs because they may only involve small changes. However, even small changes in the gene sequence can have large impacts on the organism and the ecosystem, and gene editing appears to also give rise to unintended 'off target' changes. This is where additional unexpected changes occur elsewhere in the genetic code than intended that may or may not have significance for how the organism develops and behaves.

The History of gene editing and 'new GMOs' in Latin America and the Caribbean

There are not adequate biosafety regulations in Latin America and the Caribbean for new GMO techniques or for the experimental or commercial release of organisms modified with CRISPR-Cas9 and other gene editing technologies. In Argentina, the Ministry of Agriculture, Livestock and Fisheries issued a resolution in 2015 (173/2015) that could allow some new biotechnologies, including gene editing, to avoid biosafety evaluation and requirements if their biosafety commission considers they are not GMOs on a case by case consideration. Brazil had claimed until 2018 that new genetic engineering techniques could be covered by their current biosafety laws.

On this assumption, Brazil approved, for example, the experimental release of GM mosquitoes and the use of a synthetic biology modified yeast for the production of farnesene. In January 2018, the Brazilian CNTBio took a resolution that implies that New Breeding Techniques and Precision Breeding Innovation would follow a procedure that is similar to the Argentinian 2015 resolution. The Brazilian resolution raises significant concerns. It not only allows an exemption of biosafety risk assessment to some organisms and products of new biotechnologies, but it also, for the first time globally, includes organisms containing non-natural gene drives to be considered for environmental release under minimal or non-existent biosafety regulations.

These precedents, along with the recent US approval of some genome-edited crops without requiring them to go through the biosafety provisions for transgenics, may influence some of the other governments that have a heavy presence of transnational agribusiness companies in their country.

Another concern is the agreements between CIMMYT (International Maize and Wheat Improvement Center) with DuPont and Monsanto to develop CRISPR-Cas9 applications in maize, especially because CIMMYT is located in Mexico, the center of origin of the crop. These agreements have been strongly questioned by civil society.[21]

All the Latin American and Caribbean countries that have large GM plantations also have some degree of research applying new gene editing and synthetic biology techniques, but none has yet sought to update their biosafety laws to address the novel risks posed by the new techniques. On the contrary, some of them have even less requirements than the previous generation of genetic modified organisms.

Off-target effects

Gene editing with CRISPR is not as well-understood nor as precise as claimed. The 'editing' process appears to routinely create unintended additional changes at other parts of the organisms' genomes (so-called "off-target effects"). The frequency of these off-target effects undermines the assumption that new gene editing techniques like CRISPR are predictable and precise. Such unexpected changes in the genome may lead to surprising unintended effects on how the gene-edited organism functions or doesn't function. In plant foods, for example, "off-target effects can lead to unexpected toxins or allergens, or altered or compromised nutritional value[22]

Case study: CRISPR Bananas

The Latin American and Caribbean region is the major global producer of bananas, with Ecuador, Guatemala, Costa Rica, Colombia, Dominican Republic, Honduras and Mexico leading the region's production of this popular fruit. Together these countries produce 58% of the global supply. In other countries such as Panama, Saint Lucia, Grenada, San Vicente, St. Kitts-Nevis and Jamaica, banana production is an important component of the economy.

The main disease in Latin America for uniform large-scale banana plantations is Black Sigatoka, caused by the fungus *Mycosphaerella fijiensis*, which has been combated with a range of agrochemicals and lately, with better results and less health and environmental impacts, by improved soil management. There have also been several attempts to make transgenic bananas tolerant to Black Sigatoka infections, but they haven't been successful.

Globally, the perceived major current threat for large scale uniform banana production is a new strain of the virulent soil fungus TR4, known as Panama disease. Despite its name, TR4 has not spread in Latin America, but has nonetheless raised alarm in the region, as it has severely affected tens of thousands of hectares of the Cavendish variety of bananas (the most commercially common variety globally), in South East and Central Asia, Oceania, Middle East and Africa.

Synthetic biologists are attempting to use CRISPR gene editing to develop TR4-resistant varieties. Australian banana scientists have been re-engineering both Cavendish and Gros Michel bananas to resist different strains of TR4[23] while Taiwanese scientists have begun trying to engineer TR4-resistant bananas using CRISPR.[24]

As an alternative to risky and poorly-understood gene editing fixes, other non-engineered approaches to the TR4 and Black Sigatoka problems include simply diversifying away from planting monoculture Cavendish and Gros Michel varieties and improved soil management. From the demand side, it doesn't seem that consumers are ready for their bananas to be bioengineered. As a Chiquita spokesman told *the New Yorker*, "In our core markets, in America and Europe, a genetically modified banana would never be marketable. At the end of the day, we're interested in continuing to sell bananas."[25]

Gene drives

One of the more novel applications of synthetic biology and gene editing is known as a 'gene drive.' This is where an organism is gene edited with a carefully designed set of engineered instructions that force it to reliably pass on the engineered change to each of its progeny, overcoming normal processes of natural selection. In this way a single trait (e.g. determining that a mouse will be a male) will spread through an entire population or species and could eventually lead to that entire species changing or becoming extinct (e.g. if all mice are born male or sterile). Some conservation NGOs have advocated the use of gene drives to wipe out invasive species such as mice or snakes on islands or to eradicate mosquitoes that might carry vector borne diseases. Since gene drives work by changing (or eliminating) a population's structure through an unstoppable genetic cascade from generation to generation, a gene drive constitutes a very significant intervention into evolution and into an ecosystem. It initiates a genetic chain reaction that currently cannot be recalled once it starts.

Synthetic biology enables researchers and companies to create organisms that will differ fundamentally from naturally occurring ones. In the case of gene edited crops and animals, especially gene drives, these organisms are intended for release into the environment. The potential consequences on biodiversity from novel syn bio organisms that may escape from contained facilities or be intentionally released are unknown. (See "Gene Drives Report" [placeholder name] for more information).

Gene drives and agriculture: the case of the Amaranthus in Latin America

The US National Academy of Sciences report on Gene Drives considered one agricultural case study: engineered pigweed (amaranthus).[26] One species of Amaranthus has become a glyphosate resistant and therefore a "superweed." The report noted that if pigweed in North America was suppressed by a gene drive it could inadvertently end up reducing harvests of amaranth, an important traditional food source in Latin America. The report didn't consider it, but this a clear case where gene drives would transform agriculture and food systems, favouring increased seed and chemical monopolies and impacting Farmers' Rights and Food Sovereignty. Some species of Amaranth have many nutritional properties and the plant has multiple traditional food uses many Latin American and Caribbean countries, which would be lost if gene drives to suppress pigweed were applied.

Gene Drive promoters target islands

Several teams are now working on systems to introduce gene drives into wild populations of invasive species in order to eradicate those species. They present this as a potential conservation tool. It is likely that some of these applications will be presented to Latin American and Caribbean governments by these researchers as potential silver bullets – especially for countries with islands. While each of these applications are proposed for specific locations, the risk exists that gene drive equipped insects, fish and animals could unintentionally move beyond the place of release (e.g. carried by predators, weather, currents or human transport) and as a result, the gene drive could go 'global,' causing wider species extinctions.

In some cases, this would impact pollination (e.g. insects), harm food webs and potentially even human food security.

Oxitec Mosquitoes

Using synthetic biology-based genetic engineering techniques, mosquitoes have been engineered with a dominant lethal gene and released in large numbers (up to millions in some cases) in field trials in Brazil, Panama, the Cayman Islands and Malaysia. The release of these mosquitoes is being considered in the Florida Keys in the US. The engineered mosquitoes were developed, and the associated technology patented, by the UK-based company Oxitec, now owned by Intrexon Corporation, which pitches itself as a "leader in synthetic biology." The genetic engineering targets *Aedes aegypti*, commonly known as the yellow fever mosquito, which is a vector of dengue fever and other diseases. It involves a genetic regulation that, in the absence of the antibiotic tetracycline, causes death at the larval stage of the offspring. The release of mainly male mosquitoes carrying this lethal gene is intended to result in mosquito population suppression, with the aim of reducing the incidence of dengue fever and other diseases transmitted by *Aedes aegypti*.

However, the release of these engineered mosquitoes into the environment raises many scientific, social, ethical and regulatory concerns. For example, the releases in the Cayman Island have been found to only be relatively effective in the dry season, when numbers are low, and when combined with spraying. Meanwhile, large numbers of biting female mosquitoes which may transmit disease have been released, despite assurances to the contrary. There is no evidence that the engineered mosquito releases reduce the risk of transmission of dengue, or other diseases such as zika or chikungunya. The situation is compounded by the fact that the international and national regulatory and risk assessment frameworks governing genetically engineered mosquitoes are still immature. In the US, for example, there was discussion as to which agency should regulate the proposed release of the mosquitoes, since this is a completely new area which the regulatory world is unfamiliar with. In fact, the first release of these engineered mosquitoes, in the Cayman Islands, was conducted in the absence of a biosafety law. This meant that specific biosafety questions may not have been fully considered or evaluated. Public information, consultation and participation have also been lacking. In the case of the Cayman Islands, while it was claimed that adequate information was provided to the public prior to the release of the mosquitoes, the outreach video to the public does not once mention that the mosquitoes are genetically engineered.

Digital sequences

Gene segments, genes and, indeed, entire organisms of high economic value (e.g. vaccine viruses) are now synthesized from sequence information that may be exchanged electronically, meaning that organisms and genetic variants can effectively cross borders without physical biological material changing hands. It is not necessary to synthesize an entire genome in order for sequence information to generate benefits. Individual genes synthesized from sequence information and inserted into living organisms can be of enormous value, particularly in industrial, agricultural and medical applications. For example, the gene(s) encoding a valuable industrial enzyme or therapeutic component of a medicinal plant may be synthesized from sequence information and inserted into microbes for production in fermentation vats (see biosynthesis section above). Unlike in the past, such uses of sequence information may increasingly be accomplished without accessing the microbe (or plant, animal, etc.) itself or obtaining prior informed consent (PIC) and mutually agreed terms (MAT) from the originators of the genetic resources and knowledge holders.

As many access and benefit sharing (ABS) laws, policies, and agreements are predicated on physical transfers of material, these may not be applicable to sequence information in their current forms. This is a large problem for ensuring fairness and equity in use of genetic resources that is poised to grow as the cost of sequencing diminishes and tools for storage and manipulation of sequence information are further developed.

History of biopiracy in Latin America and the Caribbean

Latin America and the Caribbean are composed of very rich biodiversity areas, including mega biodiverse countries, such as Brazil, Bolivia, Costa Rica, Colombia, Ecuador, México and Venezuela, which have made the region attractive for biopiracy. Additionally, it is important to consider that many species were taken from Latin America and the Caribbean into gene banks and botanical gardens prior to the CBD. In the past two decades, some governments have entered agreements with transnational companies to conduct bioprospecting activities, in most cases without any Free, Prior and Informed Consent (FPIC) from the indigenous peoples who have nurtured and created those resources, and who are the main caretakers of biodiversity. An early example that unfortunately set the stage for other countries is the 1991 contract agreed between the national institute INBio in Costa Rica and the pharmaceutical company Merck. Merck paid a modest sum to INBio that allowed them to access up to ten thousand plant species in Costa Rica that were also present in many other Latin American countries.[27] Other governments, including Mexico, Colombia, Ecuador have also allowed similar bioprospecting contracts, different in formulation and scope. The result is that thousands of Latin American biodiversity species ended in private or public collections in Northern universities and companies, including many in the US (which is not Party to the CBD) where they can and have been accessed and patented by companies. Even the collected seed samples at the CGIAR gene banks have sometimes been transferred to private companies without a Material Transfer Agreement. Examples from CIMMYT and ICARDA were described by ETC Group in 2012.[28]

Conclusions and Next steps

It is clear that the potential adverse effects of synthetic biology on the Latin American and Caribbean region would be wide-ranging and include risks to the environment, human and animal health, as well as impacts on livelihoods. In particular, any consideration of research or deployment of organisms containing gene drives should be treated with extreme precaution, with no field releases of any kind, and particularly not into the region's biodiverse environment given the irreversible nature of the technology. The regulatory environment, including for contained use, must be reviewed and strengthened so the organisms, components and products of synthetic biology are robustly regulated, and the technology appropriately assessed for risks and socio-economic considerations. Identification, detection, risk management and monitoring measures are also needed and should be provided by the developers to enable close tracking.

Further information

A database of ingredients produced through synthetic biology biosynthesis techniques: http://database.synbiowatch.org

Online Map showing natural product growing regions threatened by synthetic biology replacements: http://www.synbiowatch.org/commodities/natural-products-map/

ETC Group's report, "Biología sintética, biodiversidad y agricultores" (Synthetic biology, biodiversity and farmers):

Spanish: http://www.etcgroup.org/es/content/biologia-sintetica-biodiversidad-y-agricultores

English: http://www.etcgroup.org/content/synthetic-biology-biodiversity-farmers

Friends of the Earth Australia webpage of its Emerging Technology Project, including synthetic biology: http://emergingtech.foe.org.au/synthetic-biology/

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