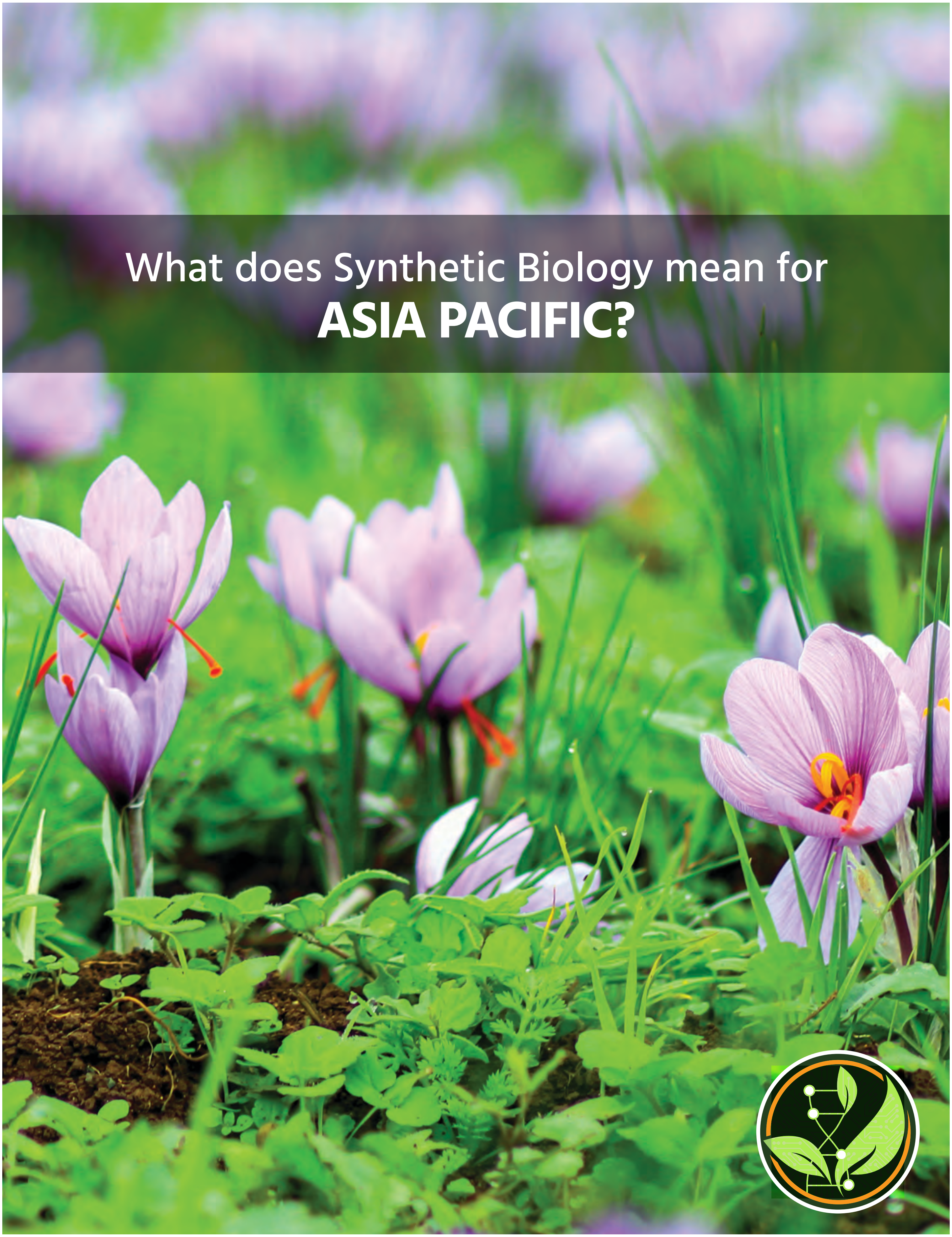
What does Synthetic Biology mean for **ASIA PACIFIC?**



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Layout: Cheri Johnson

Building International Capacity
in Synthetic Biology Assessment
and Governance

What does Synthetic Biology mean for Asia Pacific?

Introduction

After twenty years of 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 engineered 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 the Asia-Pacific region. Governments and civil society are now urgently attempting to identify and assess the potential impact of this new syn bio wave before it breaks.

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 Asia Pacific 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

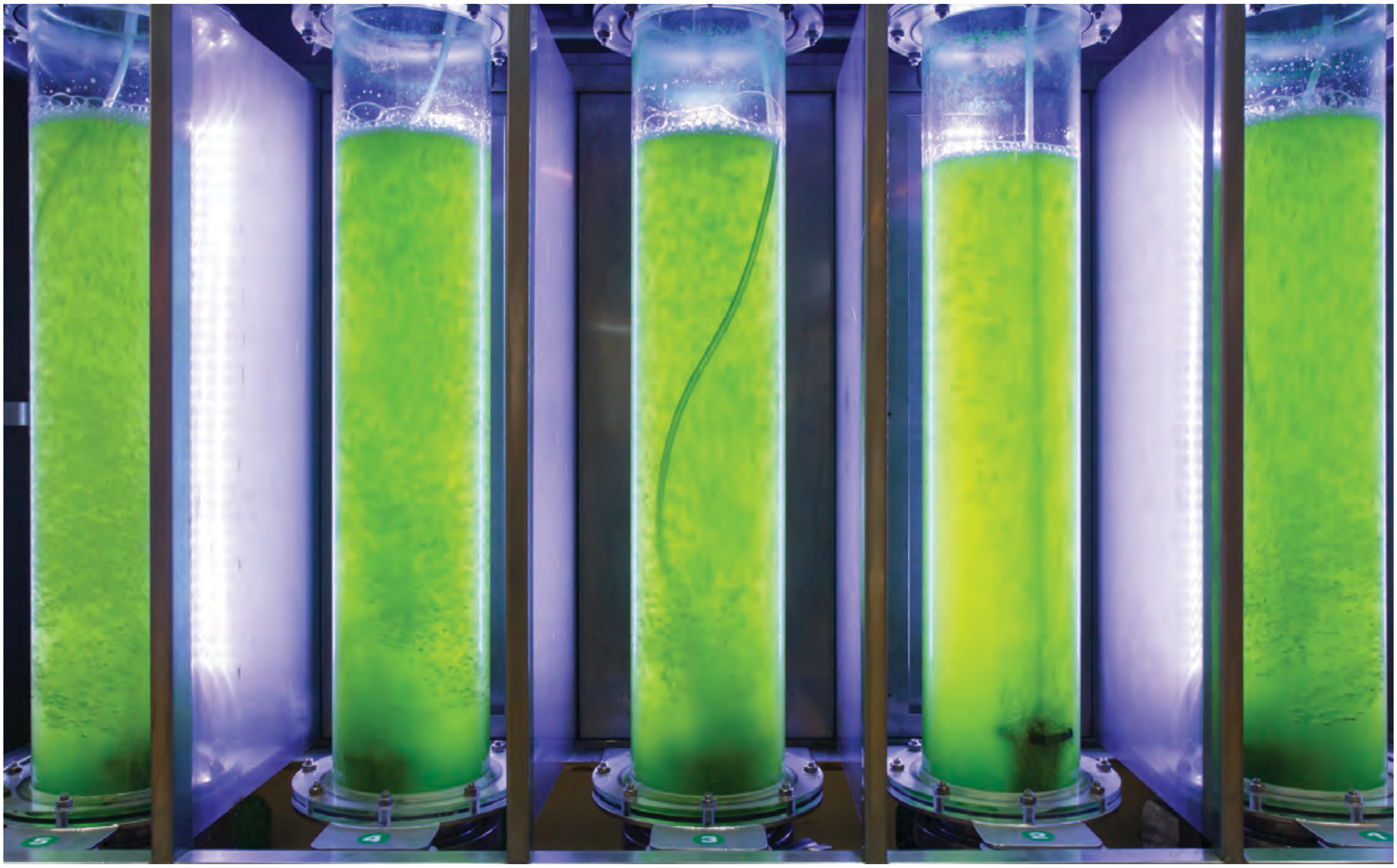
The Asia-Pacific region is extremely diverse and so are its attitudes to genetic engineering. In terms of commercialisation of genetically modified (GM) crops, there are several countries in the region which have approved cultivation for some time already – Australia (canola, cotton), China (cotton, poplar), India (cotton) and the Philippines (maize). More recently, Bangladesh (brinjal), Myanmar (cotton), Pakistan (cotton) and Vietnam (maize) have joined the ranks of countries growing GM crops. Other countries, such as Malaysia, have not allowed commercial cultivation of GM crops, but have approved GM crops for food, feed and for processing.[1]

At the same time, several countries in the region remain deeply sceptical and concerned by GM crops. Japan and Korea are particularly precautionary about GM food, and Bhutan has prohibited the import, transit, intentional introduction

into the environment, use (including contained use) and research and development of any GMO capable of reproducing.[2] As of February 2016, the total area of GMO-free zones in Japan was estimated at 87,167 ha.[3] Even in countries where commercial cultivation of GM crops is allowed, opposition to GM crops remains strong. Several states in Australia maintain legal moratoriums on planting GM crops and several provinces and municipalities in the Philippines have ordinances banning GM crops. China has also been cautious when it comes to growing GM food crops, with consumers raising an increasingly active voice on the issue.

The lessons from India's 15 years of experience growing Bt cotton are particularly challenging. Bt cotton was engineered to produce an insecticidal toxin, yet farmers have faced increasing pest attacks, both from the target pest, bollworm, which has developed resistance, and from secondary pests. Insecticide use on cotton more than doubled from 2006-2013. After being grown on 12.85 million hectares in 2014-15, Bt cotton areas declined to around 10.5 million hectares by 2016-17.[4] For farmers, rising costs – in the form of pesticides – have not matched returns, pushing many to the brink, financially and otherwise, and leaving a tragic legacy of suicides among Bt cotton farmers. In 2015, state governments began actively urging farmers to switch away from Bt cotton and have revived efforts to promote native *desi* cotton. A moratorium on the commercial release of Bt brinjal, a crop for which India is a centre of diversity, was established in 2010,[5] and in 2017 the commercial release of GM mustard was also shelved.

Nonetheless, Bangladesh is already growing Bt brinjal and the Philippines may begin soon. Field trials have been conducted on Vitamin A-enriched Golden Rice in Bangladesh, and approval is being sought for field trials in the Philippines. Indonesia has reportedly approved a domestically-developed drought-tolerant sugarcane, although it has not yet been cultivated.



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 grown in Asia-Pacific. 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 affects 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 most likely acquired through expanded methane fracking or coal bed mining, with negative implications for land, ecosystems and biodiversity.

Producing these ingredients via synthetic biology also poses economic and social risks that may significantly affect Asia Pacific 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 flavours, 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 in development or on the market found over 350 different projects to produce biosynthesized compounds, many of them already in foods, cosmetics and dietary supplements.[6] See *Synthetic Biosynthesis Primer* for more background on this industry.

Asia Pacific as a natural products source

There are several key commodities grown in Southeast Asian countries for which synthetic biology replacements are being developed or are already released commercially. These include:

- Coconut
- Patchouli oil
- Shea, cocoa butter, other cocoa butter equivalents
- Vetiver
- Agarwood
- Sandalwood
- Vanilla
- Artemisinin
- Ginseng
- Stevia
- Silk

Saffron

Known for its rich scent and brilliant red and orange hues, saffron is the world's most expensive spice by weight. Saffron itself is the stamen (the part where grains of pollen germinate) of the flower *Crocus sativus*. It is used in a variety of dishes, baked goods and liquors. Due to its high labour requirement, saffron is known to employ on average 200 persons per day per hectare, employing a large percentage of women (80%). Its production involves more than 150,000 farmers in Iran, 16,000 in Kashmir and 6,000 in Afghanistan. Good quality saffron sells from US$2,000 to US$10,000/kg or more. Annual worldwide sales of saffron are an estimated US$660 million.

Evolva, a Swiss synthetic biology company, has successfully created bioengineered yeast that produce the key chemical compounds in saffron that create its colour and flavour. Evolva is now able to make these compounds through fermentation of engineered yeast, bypassing the need to grow crocus flowers. Seeking imminent commercialization, Evolva claims that its saffron will not so much replace existing saffron markets as open new uses for saffron as a flavour, since it will be affordable for use in processed snacks and other low-priced products as well as saffron extracts for medicinal use. However, if Evolva's saffron is sold as "natural" (because it is derived from fermentation) then it will be going head-to-head with current saffron markets, and at a much lower price, potentially threatening the livelihoods of thousands of farmers.

Patchouli oil

Patchouli, or *Pogostemon cablin,* is a perennial species of the mint family that thrives in the wild in warm tropical climates. Patchouli oil is important for a class of perfumes and is widely used in laundry detergents, air fresheners, candles, soaps, baby wipes and other household scented products. It is also commonly used in pharmacy and cosmetics as an antimicrobial ingredient. Indonesia is the world's largest producer of patchouli, accounting for over 80% of the global market. Current annual production of patchouli oil is around 1,000-1,200 metric tonnes, with market demand around the same. Secondary suppliers are China, India and Malaysia. Patchouli oil can fetch US$40-70 per kg. A typical patchouli farming family in Indonesia owns between 0.25 and 1 hectares of land and produces 25 to 100 kg of patchouli oil per year. Around 12,000 farming families are involved in cultivation (supporting 50,000 individuals). A further 2,000 people are employed in distillation and 300 in the collection trade.

The key constituent of patchouli oil is patchoulol, which has now been produced using synthetically engineered yeast by California-based biotech company Amyris, in partnership with Firmenich, a Swiss purveyor of perfumes and flavours. Their patchouli ingredient is trademarked Clearwood™ and is already incorporated into leading fragrances. A Dutch synthetic biology company, Isobionics, is also planning commercialize a syn bio form of patchouli oil. The production of patchouli oil, like other essential oils, is dominated by small farmers, and as such makes an important contribution to incomes and livelihoods. Small farmers will inevitably be affected by Clearwood™ and forthcoming products from Isobionics. With Clearwood™, Amyris can replace the lengthy cultivation and extraction process with a single manufacturing process that produces patchouli oil in about two weeks. Even if the resulting product may not possess the same qualities as the natural oil, the ease of production undercuts farmers' efforts tremendously and will also impact consumers' future ability to get true patchouli oil.

Artemisia-Artemisinin

Artemisinin, the active ingredient in the Chinese herbal shrub *Artemisia annua*, or sweet wormwood, is the principal ingredient in a range of effective anti-malarial drugs authorized by the World Health Organization. *Artemisia* is also widely used in herbal tea as a traditional protection against malaria, and whole powdered versions of the leaf also appear to be effective. *Artemisia* is grown primarily as a cash crop for sale to pharmaceutical companies. Until as recently as 2013, natural artemisinin was sourced entirely from an estimated 100,000 small farmers in Asia and Africa, as well as wild harvesters of the crop in China. Currently, 80% of all artemisinin derived from *Artemisia* is produced in China. Vietnam is second (around 10%), with the remainder coming from Madagascar, Kenya, Tanzania and Uganda. A small amount is grown in India. The average crop area per farmer in China and Africa is around 0.2 hectares.

In April 2013, a "semi-synthetic artemisinin" (SSA) entered the market, produced via synthetic biology. This synthetic version was created by Amyris Biotechnologies in collaboration with Sanofi Aventis, using US$64 million of funds from the Bill & Melinda Gates Foundation. It was initially supposed to replace one third to half of global supply, although key researchers expressed their ambition to take over the entire global market. However, Sanofi was unable to sell its first run of SSA to any manufacturer because their price was above market cost; and in 2015 they produced no SSA at all. Upon the arrival of the syn bio version, 2014 prices of botanical artemisinin dropped to a decade low; and subsequent plantings reportedly fell by two-thirds. The price fell so low that even SSA was overpriced (which is why Sanofi was unable to sell). SSA may therefore have helped fuel price volatility and undermined a valuable income source for tens of thousands of farmers. The state of the future supply of this important and much needed antimalarial compound is now unclear – and so are the livelihood implications for the farmers who grow it.

Agarwood

Agarwood oil (Gaharu or Oud oil) is the fragrant resinous heartwood found in trees from the genus *Aquilaria*, native to southeast Asia. This highly-prized but endangered aromatic, resinous wood is only formed inside the tree if it becomes damaged or diseased. Agarwood is used to make essential oils for perfumes and wood chips for incense. The trees traditionally grow throughout South and Southeast Asia, and Malaysia is the major producer of high-quality agarwood. It is not known how many people earn their livelihoods from collecting and processing agarwood, especially because most of the trade is illegal. According to industry sources, the estimated value of global trade in agarwood is US$6 to 12 billion. High-quality agarwood essential oil – priced wholesale at US$15,000 per litre – has been dubbed “liquid gold.” The retail value is often triple that amount. The price of agarwood oil ranges from US$100/kg for lower quality material up to US$100,000/kg for superior, high-purity oil. In 2013, global trade in agarwood chips and powder was 4.7 million kg – agarwood chips price from US$20 to 6,000 per kg; high quality wood sells for up to US$30,000 per kg.

Unfortunately, the wild collection of this expensive oil is endangering the species and so trade in wild agarwood is now illegal. In response, *Aquilaria* plantations are being established to farm agarwood more sustainably. Two biotech companies (Evolva and Efflorus) have made it known that they are trying to produce the main components of agarwood through synthetic biology. At this point, neither has a timeline for commercialization, methodology or product names. While a compelling case can be made that biosynthesis of agarwood’s aromatic compounds offers a more sustainable approach than illegal cutting of endangered trees, it remains to be seen if Efflorus or Evolva can produce a commercially viable product via biosynthesis, and how that might affect the global market. There is not yet a meaningful discussion about the impact that the transition from wild harvesting and plantation production to synthetic production may have on traditional collectors or plantation workers.

Ginseng

The hairy root of the ginseng plant (*Panax ginseng*) has been used for over 4,500 years in eastern medicine to counter stress, disease and exhaustion. It is especially highly prized in South Korea. Since the 19th century, a North American variety (*Panax quinquefolius*) is also widely grown and used and is also eaten as a food. Ginsenosides are active compounds only found in ginseng that have several health-related effects. Approximately 40 ginsenoside compounds have been identified and approximately 72,600 tonnes of botanical ginseng are produced annually worldwide, with China, South Korea, Canada and the US accounting for over 99% of the global ginseng harvest. China is the world’s largest producer with annual production of 40,596 tonnes. It is followed by South Korea (24,929 tonnes), Canada (5,884 tonnes) and the US (956 tonnes). Culturally, ginseng is most significant for South Korea, which is also the world’s largest consumer. The world ginseng market – including ginseng root and processed products – is estimated to be worth US$2.1 billion; the size of the Korean market alone is US$1.1 billion. Growing a ginseng root for harvest takes 4-6 years and successful ginseng farming is difficult and requires skill.

There are active research projects in Belgium and China successfully using synthetic biology to produce some of these 40 ginsenosides in engineered yeast and in other plants. Additionally, Swiss synthetic biology company Evolva has confirmed that it is targeting ginseng as a commercial product. Currently, there is no concrete evidence that a synthetic biology version of ginseng is poised to enter the market. However, with several teams working to create such a product it is likely that a synthetic biology ginseng could soon emerge that might impact the market for this iconic crop and the farmers who grow it.

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.

There has been debate in some countries as to whether organisms produced through gene editing are GMOs. In New Zealand at least, this issue has been resolved: New Zealand's Hazardous Substances and New Organisms Act (1996) covers all types of modern biotechnology. In addition, any organism not present in the country on 29 July 1998 is deemed to be a new organism and is also covered by the Act. This means that all gene editing and other new techniques of synthetic biology are covered by the Act, and their products are regulated as GMOs. This was confirmed by the High Court in New Zealand in 2014[7] and subsequently affirmed following a government review of the regulations in 2016.

Under the New Zealand Act, risk assessment and prior regulatory approval are required for field trials and any release of gene edited organisms and products of synthetic biology from laboratory containment. Field trials must be contained so that heritable genetic material does not leave the site during the trial and is removed after the trial. All applications must be publicly notified, subject to public consultation, open to submissions by any stakeholder, and involve a public hearing. In its assessment, the regulator must consider economic impacts (costs and benefits) of the proposed use, in addition to scientific, ethical and social matters. The Act tries to incentivise the consideration of alternatives, by asking for comparisons to be made to the best practicable alternative. - The scope and features of the Act are therefore important elements for good governance of GMOs, gene editing and synthetic biology[8].

Off-target effects

Gene editing with CRISPR is not as well-understood or 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, allergens or altered/compromised nutritional value.[9]

Climate Smart Agriculture: Photosynthesis Engineering of Rice

One popular application of synthetic biology involves changing the underlying mechanism of photosynthesis. Photosynthesis is the core process by which crops turn sunlight and atmospheric carbon dioxide into oxygen and plant matter. Synthetic biologists are designing new enzymes that would more efficiently convert solar energy to biomass in a plant and bioengineering the leaves of plants to collect more light. This approach is promoted not only as a potential strategy to increase yields, but also to sequester more greenhouse gases, thus qualifying as 'Climate Smart.' The International Rice Research Institute (IRRI) in the Philippines is part of a consortium funded by the Bill and Melinda Gates Foundation that is trying to change the photosynthetic properties of rice from C3 to C4. Rice is categorized as a C3 plant based on the way it converts carbon dioxide to carbohydrates (C3 refers to 3 carbon atoms), but if it can be upgraded to a C4 crop it would fix more atmospheric carbon, use water and nitrogen more efficiently, and better adapt to hotter and drier climates. Similar work is underway by another consortium of public and private researchers called the C4 Rice Project, funded by the European Union. This consortium includes Bayer CropScience and Biochemtex.[10]

Fundamentally altering the core metabolism of a staple food crop like rice is no small matter and would require extensive ecological and food safety evaluation, and so far, looks likely to extend industrial high input rice production. It also risks distracting from other agroecological approaches to increase rice production that reduce chemical use and put breeding in the hands of farmers instead of high-tech companies. People in Southeast Asia consume an average of 2.5 times more rice than elsewhere in the world. More than a fifth (22%) of global rice consumption occurs in Southeast Asia and over half (53%) of net rice exports are from Southeast Asian nations, particularly Indonesia, Vietnam, Thailand, Philippines and Cambodia. Anything that alters rice in such fundamental ways has huge implications for Southeast Asia's biodiversity and food systems.

Gene drives

One of the more novel applications of synthetic biology and gene editing is known as an engineered 'gene drive.' This is where an organism is gene edited with a carefully designed set of 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 engineered 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” for more information).

Several organizations are working to prevent the release of organisms containing engineered gene drives in the Asia Pacific region. Civil society groups such as the Sustainability Council of New Zealand and Friends of the Earth Australia have been particularly active, as some of the first field trials of such gene drive organisms for conservation purposes are proposed in those countries.

Gene Drive promoters target Islands

Several teams are now working on systems to introduce engineered gene drives into wild populations of invasive species that will have the effect of eradicating those species. They present this as a potential conservation tool. One international organization, Island Conservation, funded largely by the US military, is working with US and Australian scientists on a ‘daughterless mouse’ project – introducing CRISPR gene drives into mice populations that cause all offspring to be male. This could have the effect of crashing the mouse population. Island Conservation argues that if used on islands this could theoretically help protect birds whose eggs are destroyed by mice.[11] In Hawai’i, proposals are being advanced to release gene drive equipped mosquitos to eradicate invasive mosquitoes who carry an avian form of malaria that is endangering rare honeycreeper birds.[12] Proposals are being advanced in Guam to release gene drive snakes to counteract invasive brown tree snakes while Australian researchers have been working for some time to develop gene drives in carp (fish) to eradicate invasive carp[13] and are discussing putting gene drives in feral cats. It is likely that some of these applications will be presented to Asia-Pacific governments by these researchers as potential silver bullets – especially for countries with islands – e.g. Indonesia, Philippines, Malaysia. While each of these applications are proposed for specific locations, there is a risk 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. Carp, for example, is an important food and livelihood source in the Asian region. If a gene drive carp was to reach Asia and jump into common native carp species it could wreak havoc with local populations and undermine food security and livelihoods.

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 the Cayman Islands, Malaysia, Brazil and Panama. 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, without 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 suppress the mosquito population, 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 effective in the dry season, when numbers are low, and when combined with spraying.[14] Meanwhile, large numbers of biting female mosquitoes, which may transmit disease, have been released, despite assurances to the contrary.[15] There is no evidence that releasing the engineered mosquito reduces the incidence of dengue, or other diseases such as zika or chikungunya. The situation is compounded by the immaturity of international and national regulatory and risk assessment frameworks governing genetically engineered mosquitoes.[16] In the US for example, there was discussion about which agency should regulate the proposed release of the mosquitoes because the regulatory system was unfamiliar with this area of biotechnology. In fact, the first release of these engineered mosquitoes, in the Cayman Islands, was conducted in the absence of a biosafety law.[17] This meant that specific biosafety questions may not have been fully considered or evaluated and that public information, consultation and participation were lacking. In 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 does not once mention that the mosquitoes are genetically engineered.

CRISPR Bananas

The Southeast Asian region is a major global producer of bananas, with Philippines, Indonesia, Vietnam, Thailand and Laos leading the region's production of this popular fruit. However, a new strain of virulent soil fungus TR4, known as panama disease, has severely affected production of the popular Cavendish variety of bananas with tens of thousands of hectares of Cavendish plantations wiped out in China, Indonesia, Malaysia and the Philippines. In response, 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,[18] while Taiwanese scientists have successfully begun to engineer bananas using CRISPR with a view to make TR4-resistant varieties.[19] Unfortunately, engineering with CRISPR is still poorly understood and appears to create unexpected changes elsewhere in an organism's genome (so-called "off target" effects). Other non-engineered approaches to the TR4 problem include simply diversifying away from planting monoculture Cavendish varieties.[20] Moreover, 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."[21]

Sequence Information

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 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.

A controversial series of patent applications on gene sequences, or "traits," recently claimed by the International Rice Research Institute (IRRI) in the Philippines, illustrate the potential problems sequence information poses for benefit sharing. First made public in March 2017,[22] IRRI's claims include the sequence of a gene from an Indonesian farmers' variety. The claim (and several others) rely on farmers' varieties of rice held by IRRI in-trust under the International Treaty on Plant Genetic Resources for Food and Agriculture. The claims raise the spectre of IRRI and perhaps soon other Consultative Group on International Agricultural Research (CGIAR) centres mining their own gene banks for profitable sequences.

While IRRI tried to respond to the controversy by changing its intellectual property policy to say that any licenses that it concludes with seed companies for the patents will include an obligation for the licensee to pay into the Treaty's Benefit Sharing Fund, critics maintain that this does not sufficiently address the issue. Farmers in particular question IRRI's right to lodge the patent claims at all – after all, the plants that are the source of the gene sequences came from farmers' fields. Also, IRRI plans to collect royalties from its patents above and beyond what is paid into the multilateral system of access and benefit sharing under the Treaty, meaning that it will also generate benefits for itself from its patents, and these may be substantially larger than what goes to the multilateral system. Some of the claims cover yield-increasing gene sequences, and potential financial gain from the patents could be substantial. There is concern that IRRI is becoming intent on transforming itself into a patent powerhouse, and that this will come to impair its mission to serve developing countries and farmers, turning IRRI into an institution intent on generating license income from seed multinationals rather than focused on supporting public research systems. It was also widely rumoured that other CGIAR centres are looking to copy IRRI's approach, meaning the problem is poised to grow larger.

Accessing sequence information increasingly satisfies many of the same purposes previously served by accessing material, including use in the creation of new commercial products that may be placed under patent and other intellectual property rights claims. Because sequences are used this way, and will increasingly be used this way, the access and benefit sharing rules that apply to physical material should also apply to sequences. Malaysia's Access to Biological Resources and Benefit Sharing Act 2017 may offer a good example for the region. Its definition of 'biological resources', to which access and benefit sharing rules apply, includes:

(a) the genetic resources, organisms, microorganisms, derivatives and parts of the genetic resources, organisms, microorganisms or derivatives;

(b) the populations and any other biotic component of an ecosystem with actual or potential use or value for humanity; and

(c) any information relating to paragraphs (a) and (b).

Furthermore, the Act's definition of 'derivative' includes a naturally occurring biochemical compound derived, developed or synthesized from a biological resource or resulting from the genetic expression or metabolism of the biological or genetic resource, or part, tissue or extract, whether it contains functional units of heredity or otherwise, and information in relation to derivatives.

Conclusions and Next steps

The potential adverse effects of synthetic biology on the Asia-Pacific 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 organisms containing engineered gene drives should be treated with precaution, with no releases into the region's biodiverse environment given the irreversible nature of the technology. The regulatory environment, including for contained use, needs to be strengthened, so that 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 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 "Synthetic biology, biodiversity and farmers":

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/

Third World Network's Biosafety Information Centre, webpage on emerging trends/techniques: https://www.biosafety-info.net/subsection.php?ssid=5

Endnotes

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3 https://www.gmo-free-regions.org/gmo-free-regions/asia/japan.html

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