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Assessment of modern biotechnologies

The IAASTD concluded that biotechnology was an essential part of transitioning agriculture from either subsistence or industrial (or other high input) to sustainable and productive. Biotechnology refers to the manipulation of living organisms through activities as diverse as breeding and fermentation to the use of tissue culture, irradiation, genomics and genetic engineering. The significant and ongoing contribution of biotechnology to the improved genetics and performance of plants, animals and microorganisms used in agriculture has altered the need for and type of inputs into agroecosystems, making enormous impacts on both productivity and social structure.

The most contentious biotechnologies are of the category called 'modern biotechnology'.[1] Modern biotechnologies including genetic engineering have made profound contributions to fundamental genetic science and medicine, at least as a research tool. However, in agriculture in particular, there has been a large scale although globally asymmetric adoption of GMOs, almost exclusively plants, too.

Most traits of agricultural importance are multigenic. For example, drought stress changed expression of over 10,000 genes in sorghum plants.

The use of GM plants in agriculture remains a small proportion of world agriculture and a minority proportion of the agriculture in all countries except for a few in South America. Adoption of GM agriculture globally as well as the number of GM plants that are commercially available, has increased in the last decade, but modestly. In some places, it has also disappeared. The assessment of the IAASTD was that such forms of modern biotechnology were highly specialised. This made them of limited value to small-scale farmers especially in developing countries, and these are the farmers that are the major food producers.

The IAASTD acknowledged that prevailing GM plants had benefits. However, these were mainly observed when comparing their use to other high input mainly monoculture agroecosystems and ongoing uncertainties of sustainability and safety confined their adoption to mainly commodity crop plants for industrial systems of feed, fuel and fibre and mainly countries in the Americas with large commodity crop monocultures and short or no rotation cycles.

Meanwhile, newer tools of gene technology have become available. These tools include, among others, regulatory RNA molecules, site-directed nucleases (SDN) and chemical and mechanical vectors that efficiently transport RNA, DNA and protein molecules into cells and organisms.

Regulatory RNA

Regulatory RNA molecules alter the expression of genes. The most common type of regulatory RNA molecule is a double-stranded RNA (dsRNA). Nearly all organisms so far tested use dsRNA gene regulatory pathways. In eukaryotic organisms, such as fungi, plants and animals, dsRNA molecules cause RNA interference (RNAi). Most often this causes gene silencing. RNAi may be reversed within a generation, or in some cases leads to intergenerational effects (Heinemann 2019).

New regulatory RNAs may be introduced into an organism by introducing into a cell a fragment of DNA that is transcribed within the organism with the resulting product forming a dsRNA. This strategy is the same as creating GMOs using recombinant DNA techniques. The first such commercial pesticidal plant has been approved for use in the United States. In addition, new chemistries and mechanical methods in research and pre-commercial stages allow the dsRNA to be directly introduced into cells or organisms at concentrations that are sufficient to initiate RNAi in the exposed organism or cause dsRNA-mediated epigenetic changes that are intergenerational (Heinemann 2019).

Site-directed nucleases

SDNs are commonly known for procedures referred to as gene/genome editing. SDNs have the potential to increase the rate at which intended modifications are created at intended locations. SDNs such as ZFNs or TALENs may be constructed to recognise a target sequence of nucleotides in a DNA or RNA molecule, or as in the case of CRISPR/Cas, the SDN recognises its target using an oligonucleotide (DNA or RNA) co-factor.

SDNs may be used to break the phosphodiester bonds between nucleotides in DNA, resulting in the initiation of repair of the damage and a high rate of mutation at the repair site. The outcome may be a change as small as a single nucleotide substitution to as large as a significant deletion or insertion of new nucleotide sequences. The repair mechanisms may make use of any available DNA to repair the damage, resulting in insertion of intended fragments of DNA or DNA from other sources, such as contaminants in the reagents (Ono et al. 2019).

Genome editing techniques are not new (Itakura and Riggs 1980), but the SDNs have made it possible to apply the techniques to a wider range of species with a greater target flexibility. Applied as an engineered gene drive, an SDN has a level of automation that was not available to earlier tools.

Environmental transformation technologies

Gene technologies are inseparable from the technologies that move nucleic acids, such as dsRNA and guide oligonucleotides for SDNs, and sometimes proteins, such as SDNs, into cells and organisms. The flexibility and proposed power

behind the capacity to alter traits using RNA and SDNs comes from a codeveloping revolution in chemistry and mechanical manipulation that increases the scale of application. The technology for transferring RNA, DNA and proteins into living tissues and cells has advanced to the stage where genetic engineering can now be done using topical or "spray-on" agents at landscape scales, with rapid repeat exposures or manipulation of multiple targets (for a large list of examples, see Heinemann and Walker 2019).

Evaluation

Fundamentally, the IAASTD saw that the contribution of modern biotechnologies to agriculture was out of balance with approaches that emphasised the multifunctionality of the agroecosystem. The new capacities also have not eliminated socio-economic, environmental or human health concerns, though they may shift the risk to hazards that have not been considered for older products (CBD 2017).

It is unlikely that the new modern biotechnology tools that have become more widely available for commercial deployment in agriculture will significantly alter the conclusions of the IAASTD. Core choices made by developed economies to increasingly devolve research and development to the private sector, and therefore to the structures and incentives that drive the private sector (Quist et al. 2013), are expected to groom applications of these new tools in the same way as the previous ones. The ultimate market concentration that results, reduces options for agriculture in both developed and developing countries because modern biotechnology has mainly served green revolution-type demands on breeding to fit high input and uniform agroecosystems.

There is no convincing evidence that the new generation of tools will change the role of modern biotechnology. However, some of the advances in related technologies, such as in "omics technologies" used to survey the changes introduced into organisms made using gene technologies, could help to advance characterisation of GMOs intended for use in the environment (NASEM 2016). The traits that are being developed for commercial release so far are either minor variants (e.g. non-browning apple and potato) or relevant to pesticide use (e.g. environmental transformation technologies). The interest in applying the techniques to improved nitrogen fixation in non-legumes, drought and other abiotic stress tolerances and climate change mitigation through animal genetics is high, but the evidence of significant progress is no greater than with the recombinant DNA techniques.

The underlying challenge to accelerating trait development through gene technology is that most traits of primary agricultural importance are multigenic and/or quantitative and responsive to the environment. For example, expression of over 10,000 genes, >40% of the genome, changed when sorghum plants were drought stressed (Varoquaux et al. 2019). The change is dynamic, occurring

at time scales of only days. Moreover, the changing environmental conditions alter the associated microbiota (Xu et al. 2018). Even though the new tools can be applied to multiple targets at once, or applied in serial applications or in the environment on multiple species simultaneously, they do not have the ability to cause the intended and only intended changes in the function and expression of many genes in crops and livestock at relevant time scales, much less the genes of the many microorganisms associated with them.

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Breeding is a foundational tool for agriculture that can be assisted by the tools of modern biotechnology without relying upon GMOs (Gilbert 2016). Breeding alone does not address the diversity of needs of farmers, especially subsistence farmers who may use modern elite varieties but have lower yields because of the environmental, social and economic constraints on them and their agroecosystems (Leakey 2019). While maximising potential yield is often the focus of discussions on biotechnology, social and environmental constraints determine actual yield in farmers' fields (Leakey 2019). The multifunctionality of agriculture requires policy approaches that also address poverty and livelihoods reaffirming the IAASTD conclusion that an integrated agroecological approach is the most promising for climate change mitigation and improving sustainability.

Abbreviations

CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
dsRNA	double-stranded RNA
GM	Genetically Modified
GMO(s)	Genetically Modified Organism(s)
DNA	Deoxyribonucleic Acid
RNA	Ribonucleic Acid
RNAi	RNA interference
SDN	Site Directed Nuclease
TALEN(s)	Transcription Activator-Like Effector Nuclease(s)
ZFN	Zinc Finger Nuclease

Endnote

1 For definitions please refer to the Convention on Biological Diversity, Cartagena Protocol on Biosafety and Codex Alimentarius.

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