In spring of 2014 the Dean of OSU's College of Agricultural Sciences charged a faculty committee to review and summarize key considerations related to genetically engineered (GE) organisms. The committee chose five topics that engaged faculty expertise and that reflected public interest regarding GE organisms in agriculture.

Committee members drafted these white papers as a service to the public for the purpose of providing information from several scientific perspectives. These papers have been reviewed by all committee members and are intended to help inform public conversations about genetically engineered organisms in agriculture.

DEFINING GENETICALLY ENGINEERED ORGANISMS IN AGRICULTURE

OSU-CAS Committee
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September 30, 2014

INTRODUCTION

GMO stands for 'Genetically Modified Organism.' However, this is a somewhat flawed designation, since virtually all farmed and domesticated organisms (plants, animals and our pets) have been genetically modified for thousands of years. In our current usage, genetically engineered (GE) refers more precisely to an organism whose genetic material has been altered by means of genetic engineering. Therefore, a GE organism is defined based on the way in which it was originally produced (genetic engineering), and not on the characteristics (or 'traits') it shows. The traits of a genetically engineered organism can vary dramatically – from herbicide tolerance to vitamin fortification – much as genetic material can vary dramatically among different organisms.

WHAT IS GENETIC MATERIAL?

All organisms harbor genetic material within their genome. A genome is composed of extraordinarily long molecules of DNA, which are organized into series of building blocks of four different chemical types (often designated A, C, G or T). The *sequence* of these chemical types provides the information that allows an organism to grow and reproduce – just as the sequence of letters in this paragraph conveys information to the reader. DNA sequence can also strongly influence an organism's traits, such as eye color, height, seed size, or ability to resist disease. Advances in biology have allowed scientists to link some traits to distinct stretches of DNA sequence called genes. This knowledge helps predict the biological function of many genes, enabling, for example, genetic testing for inherited disorders in humans, or genetic engineering to produce genes that alter a particular trait in a crop plant.

WHAT IS GENETIC ENGINEERING?

In *civil engineering,* scientific knowledge is used to design and construct bridges or buildings. By analogy, *genetic engineering* uses knowledge of genetics and biology to design and construct DNA sequences, in order to generate particular traits in an organism. Inside an organism, DNA is synthesized biochemically by its cells. However, because it is a chemical, DNA can also be synthesized and/or manipulated outside an organism, in a test tube. Typically, genetic engineering involves assembling distinct stretches of DNA, sometimes derived from different organisms (bacteria, plants, animals), to create a new gene in a test tube. Such a gene is designed with particular characteristics in mind. The newly assembled gene is introduced back into an organism, where it becomes part of that organism's genetic material. Thereafter, it is copied and passed on to offspring (now categorized as 'genetically engineered') through the regular biological processes of growth and reproduction. Because the new gene is present in these GE offspring, they show the trait associated with that gene. In crop plants, genetic engineering is usually followed by use of more traditional breeding techniques, which help bring the GE trait into conventional plant varieties.

HOW HAVE GENETICALLY ENGINEERED ORGANISMS BEEN USED COMMERCIALLY?

In use since the 1980s, genetic engineering is now widespread in many biologically based commercial applications, due to its ability to generate organisms with desirable traits. In many cases, these traits are unlikely to be found in existing populations. For example, current treatment of diabetes generally uses human insulin – but this insulin has been produced by GE bacteria that have been genetically engineered to produce it, rather than being extracted from human or animal cells. Another example involves cheese: up to 80% of cheese is made with extracts ('FPC rennet') from a GE microbe that produces an enzyme originally from calf stomachs. Using FPC rennet is less expensive than rennet from calf stomach, and reduces the need to slaughter calves (Johnson and Lucey 2006).

Many foods categorized as 'GMO' are produced by plants that have been genetically engineered to express agriculturally beneficial traits. In plants, the most widespread GE traits are currently herbicide tolerance and insect resistance (EFSA 2008). These traits are dependent on the production, in the engineered plants, of proteins originally found in bacteria. However, other GE traits are present in agricultural production on a smaller scale, or are currently in development. For example, a current GE papaya variety is resistant to a viral disease because it is 'immunized' by producing a viral protein itself (Fermin et al 2011). The Golden Rice project has engineered two genes for production of beta-carotene (a precursor for Vitamin A), generating GE rice plants that produce an enriched yellow grain. This enhances the nutritional quality of the engineered rice (Tang et al 2009), and is targeted towards malnourished people in developing countries.

A key point: due to the variety of engineered traits and genes in genetic engineering, it is challenging to develop broadly applicable principles for predicting how a particular genetically engineered organism will affect the environment or the food supply. This is an underlying reason for testing each GE organism separately prior to commercial release, based on the specific concerns associated with each engineered gene and trait (see accompanying paper, "Food Safety Issues with Genetically Modified Foods").

IS GENETIC MODIFICATION ASSOCIATED WITH NON-GENETICALLY ENGINEERED PLANT VARIETIES?

Genetic modification, or alteration of DNA sequences, happens continuously and throughout nature, in many different ways. The genetic modification that occurs in wild and cultivated plants was used by ancient cultures to generate the progenitors of modern crops. For example, bread wheat evolved from the crossbreeding of a primitive wheat with a wild goatgrass species (Shewry 2009). Maize (corn) differs dramatically from its wild, weedy ancestor (teosinte) due to ancient mutations that alter many of its growth traits (Carroll 2010; Doebley 2004). The advent of modern plant breeding in the last century accelerated the use of genetic modification to generate useful traits, and to incorporate them into commercial plant varieties. Plant breeding methods that cause genetic modification include not only crossbreeding (hybridization) between different varieties within a crop species, but also 'wide crossing' with more distantly related and wild plant species; and stimulating mutation with chemicals or radiation (mutagenesis). One common food developed using mutations and plant breeding is sweet corn, in which the sugar content in the seed has been increased (Grubinger 2004).

Some of these traditional approaches introduce more genetic modification than does genetic engineering, and with less predictable results. However, none of these methods generates plant varieties that are categorized as GMOs, even though some traits associated with such breeding techniques are similar to those in genetic engineering. For example, herbicide tolerance is present naturally in certain plant species, or has been generated via mutational approaches (Darmency 2013; Jones et al 2014); insect and disease resistance and nutritional fortification are also traits of commercial interest that have been developed in non-genetically engineered plant varieties.

WHAT DISTINGUISHES GENETIC MODIFICATION IN TRADITIONAL BREEDING FROM GENETIC ENGINEERING?

There are two major distinctions between the genetic modification associated with traditional plant breeding and genetic engineering. First, in genetic engineering, genes are designed and constructed to generate or improve particular traits, using information regarding DNA sequences and their function. Such constructed genes can be designed to incorporate unique combinations of DNA that lead to specific and novel functions. In traditional breeding, choice of genes and traits is limited to those that are present, or have been generated randomly (through mutagenesis), in species that can be crossbred with crop species. Increasingly, traditional breeding is being guided by knowledge of plant genomes and of the DNA sequences associated with useful genes and traits. Traditional breeding can be used to combine traits (initially derived from genetic engineering, mutagenesis, or breeding populations) in the seed stocks that are ultimately released as commercial varieties.

Second, because genetic engineering assembles a gene in a test tube, and then introduces the gene back into an organism, the DNA sequences that are used to build that gene could (theoretically) be derived from any species, including bacteria, animals, or plants. Thus, traits of agricultural value that have been found, for example, in bacteria – such as herbicide tolerance, insect resistance, production of nutrients – can be moved into plant species via genetic engineering. Traditional breeding is limited to working with genes and traits that are present, or have been generated, in species that can be crossbred with crop species. However, it should be noted that genetic engineering does not necessarily involve DNA sequences from widely different species. So-called 'cisgenic' plant varieties are under development that use genetic material that is moved within a species via genetic engineering techniques (e.g., a disease resistance gene from a wild potato to a cultivated potato; Jones et al 2014).

DO 'GENETIC ENGINEERING' TYPES OF GENETIC MODIFICATION OCCUR WITHOUT HUMAN INTERVENTION?

Recent advances in DNA sequencing technologies have given biologists an unprecedented view into the processes that have altered genomes over the course of evolution. These data support the idea that genetic changes similar to those present in genetically engineered organisms (i.e., new combinations of DNA sequences resulting in appearance of novel genes and traits) do appear in natural populations on occasion. There are numerous examples in bacteria, plants, and animals of the formation of a new gene (called a 'chimera') in a genome by joining two distinct, and formerly separate, stretches of DNA. The movement of DNA from one species to another distantly related species is very rare, but has also been observed (e.g., from bacteria to arthropods; Wybouw et al 2014). One of the most notable movements of DNA sequences across species occurred between bacteria and the ancestors of animals and plants, forming mitochondria (the 'powerhouses' of the cell) that allow efficient use of oxygen for biological energy generation. Due to this event, the human genome includes an estimated several hundred mitochondrial genes that originated in bacteria (Timmis et al 2004).

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