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Do cisgenic plants warrant less stringent oversight?

To the editor:

While the debate continues on the appropriate level of regulatory oversight for transgenic plants, we believe there are strong reasons for legislators to differentiate cisgenic from transgenic plants. A cisgenic plant is a crop plant that has been genetically modified with one or more genes (containing introns and flanking regions such as native promoter and terminator regions in a sense orientation) isolated from a crossable donor plant. In contrast, transgenic plants contain genes from noncrossable organisms (e.g., a selection marker gene originating from a microorganism), synthetic genes or artificial combinations of a coding gene with regulatory sequences, such as a promoter, from another gene.

To date, the majority of established regulations on genetically modified organisms (GMOs) worldwide have not discriminated cisgenic from transgenic plants. This may be because until now cisgenic plants have been almost absent in applications for approval of deliberate release of transgenic plants into the environment. Only in Canada, which has a product-based regulation rather than a process-based regulation, might cisgenic plants be treated less stringently than transgenic plants.

In our view, cisgenic plants are fundamentally different from transgenic plants. In the case of transgenesis, a foreign gene is introduced into a plant. A transgenic plant may have a phenotypic trait that did not occur before in that species and its crossable relatives. Such a novel trait can affect fitness in ways new to the species. Gene flow to wild relatives could potentially extend this fitness effect. This may lead to increased invasiveness of the transgenic crop or its relatives.

In contrast, for cisgenesis, the introduced gene of interest with its native promoter has already been present in the species or in crossable relatives for centuries. Therefore, cisgenesis does not add an extra trait. It does not invoke a fitness change that could not also occur through traditional breeding or in nature. The same holds true for other environmental risks, such as effects on nontarget organisms or soil ecosystems, and for usage in food or feed. As a result, deliberate release of cisgenic plants into the environment is as safe as the deliberate release of traditionally bred plants.

As the process of genetic modification itself may lead to mutations and rearrangements, cisgenic plants should be screened for unwanted changes in a similar way as plants derived from mutagenesis are screened and selected. Mutation breeding has led over the past 70 years worldwide to more than 2,250 plant varieties, derived either as direct mutants or from their progenies[1]. Mutagenesis has led to undirected mutations and translocations. Release of mutation-derived varieties does not require molecular characterization of the mutations involved. Although these numerous mutation-derived plant varieties have been produced and used for food, feed or as ornamentals in more than 30 countries for several decennia[1], we are not aware of indications that the underlying but unknown mutations, after selection of the variety, have caused damage to the environment or have caused adverse effects on consumers or livestock[2]. This provides circumstantial evidence that the phenotypic screening and selection, which are the rule in plant breeding programs, in combination with other conventional selection procedures before introduction of varieties onto the market, have been sufficient to reduce risks of unknown mutations in plants to an acceptable low level. The same process of screening and selection will be the rule for development of cisgenic varieties.

Considering the equivalence of products resulting from cisgenesis and traditional breeding including mutation breeding, we propose that cisgenic plants should be excluded from GMO regulations. Cisgenic plants should in our view be handled at the regulatory level like traditionally bred plants (that is, those created via long-standing cross breeding, *in vitro* fertilization, polyploidy induction, protoplast fusion between crossable species and mutagenesis with chemicals or irradiation). Given that an increasing number of functional genes from crops and their crossable wild relatives are being isolated and can readily be used to create cisgenic plants, the time to act is now.

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