The slippery slope of cisgenesis

To the Editor:

Your September Editorial[1] highlighted the negative public perception of genetically modified (GM) food. This unfortunate situation has certainly contributed to the current regulatory system in the European Union (EU; Brussels) that singles out GM products on the basis of technology rather than trait. In a creative attempt to get some GM crops into commercialization 'through the backdoor', several research groups are lately promoting the concept of cisgenesis as an alternative to transgenesis[2]. We would counter that there are no scientific indications of either risk or unpredictability associated with the phylogenetic distance between the DNA donor and recipient. The only raison d'être for this conceptual diversification is thus a somewhat arbitrary notion of unnaturalness in the mixing of unrelated genetic material in a fashion that cannot occur without human assistance. We would further point out that the idea of naturalness in plant breeding became obsolete already at the turn of the 19th century when scientific progress and particularly Mendelian genetics, rather than farm-based bulk selections, were adopted as the main drivers of crop improvement. The exploration of heterosis enabled an agronomically superior mix of alleles, and the introduction of induced mutations as an approach later created a vast wealth of novel genetic variation.

Cisgenesis started gaining a reputation following a number of publications in 2006 (refs. 3–5) where it was defined as the transfer of the full coding DNA sequence of a gene, including introns, together with the gene's own promoter and terminator, originating from the sexually compatible gene pool of the recipient plant. This concept was introduced as a smokescreen to counter one of the major public concerns about GM crops, namely the combination of genetic elements derived from species that cannot be crossed by natural means. In the words of Schouten *et al.*[3], cisgenesis therefore respects species barriers, and in this sense differs fundamentally from transgenesis.

Advancements in tissue culture and cytology paved the way for wide crosses through embryo rescue, protoplast fusion and chromosome doubling techniques. The advent of recombinant DNA technology in the 1970s spurred the era of molecular plant breeding which presented a virtually unlimited source of genetic variation: the entire clade of life. We must not forget that the essence of modern plant breeding is the steady increment of genetic variation available for crop improvement. Seen from this perspective, the promotion of cisgenesis as a replacement for transgenesis is nothing less than a giant leap backwards in the historical progress of plant breeding.

What may or may not be considered as 'natural' among the public is highly subject to change over time. Whereas we do acknowledge that public acceptance of scientific endeavors is essential in a democratic society, we argue here that rather than blunt appeasement, rational information is the key to moving the public debate forward. A recent study in Denmark indicated that a higher level of scientific knowledge generally makes people less likely to care whether a plant is cisgenic or transgenic[6]. Rather than giving in to public misconceptions of naturalness, it is therefore more important than ever that researchers engage in educating the public about the latest scientific advancements. About a decade ago, substantial research investments were dedicated to develop plant transformation systems free from selectable marker genes[7]. The focus then was on removing superfluous genetic elements after transformation. In the meantime, a multitude of reports have continued to confirm that plants containing every known and used selectable marker gene to date pose no greater risk than plants bred by conventional means[8].

At least part of the rationale for the cisgenic approach's focus on the origin of the genetic material appears to be to sidestep the burdensome regulatory pathway in the EU, thereby facilitating commercial release of a subset of transgenic products[9]. However, even if cisgenics would deliver this proposed benefit, the strategy also poses risks and additional costs.

First, the adoption of a cisgenic strategy over a transgenic one will involve the need to invest yet more resources (purely for the purpose of circumventing discriminatory regulations). The expertise and time needed to create case-specific genomic clones that include endogenous promoters and terminators, free from selectable marker genes and vector backbones, should not be underestimated.

Second, rather than promoting public understanding of scientific principles, adoption of the approach may be seen as tacit agreement with the nonscientific view that there is something inherently unnatural and risky with the cross-kingdom transfer of genetic material. This strictly philosophical notion is not based on current scientific knowledge. As a consequence, it reinforces prejudice and discrimination against transgenic crops. Therefore, if the postulated cisgenesis concept alone is exempted from the regulation that currently applies to GM crop plants, we would enter a slippery slope that inexorably leads away from objective and unbiased scientific principles.

Finally, there is a danger that the promotion of cisgenesis would result in a backlash in the trust that the public places in its scientific institutions. If cisgenic plants are really less risky than transgenic plants, people may start to ask, why have scientific institutions consistently made a stand for several decades that transgenic crops are no more inherently risky than conventionally bred crops?

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The authors declare no competing financial interests.

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