Food Control 84 (2018) 128–137

Contents lists available at ScienceDirect

Food Control

journal homepage: www.elsevier.com/locate/foodcont

Review

Risk analysis for genome editing-derived food safety in China

Wei Gao [a], Wen-Tao Xu [a, b], Kun-Lun Huang [a, b], Ming-zhang Guo [a], Yun-Bo Luo [a, b, *]

[a] Beijing Advanced Innovation Center for Food Nutrition and Human Health, College of Food Science and Nutritional Engineering, China Agricultural University, Beijing, 100083, China
[b] Key Laboratory of Safety Assessment of Genetically Modified Organism (Food Safety), Ministry of Agriculture, Beijing, 100083, China

ARTICLE INFO

Article history:
Received 4 May 2017
Received in revised form
23 July 2017
Accepted 24 July 2017
Available online 25 July 2017

Keywords:
Risk analysis
Genome editing
Food safety
Regulatory framework

ABSTRACT

Novel foods derived from genome-editing techniques call for an updated risk analysis of the use of plant produced by genome editing, especially in China. As a developing country with the largest population and limited arable land, China has invested intensively in genetically modified (GM) crops to improve agricultural productivity, which is aimed to secure food security and safety, the top priority for China. China has recently made great progress in genome-editing technology due to its powerful applications in the field of crop improvement such as rice and wheat. To ensure food safety and agricultural commodity trade, China has developed a regulatory system for the risk assessment and management of GM products, and the discussion on how to regulate products derived from genome-editing technology have also been initiated. A working group within National Biosafety Committee was established to provide technical assistance on risk assessment of new techniques including genome-editing. As GMO safety remains a public concern in China, genome-editing technology is in many ways even more precise and predictable than GM. From that perspective, genome-editing technology may be accepted by the public more easily with active communication with broad stakeholders, such as government, consumer, media, industry and others. This article reviews current developments in genome-editing technology and its applications in plant in China, regulatory status of genome editing-derived products around the world, and risk analysis framework for genome-editing derived food in China.

Contents

* Corresponding author. Beijing Advanced Innovation Center for Food Nutrition and Human Health, College of Food Science and Nutritional Engineering, China Agricultural University, Beijing, 100083, China.
E-mail address: lyb@cau.edu.cn (Y.-B. Luo).

http://dx.doi.org/10.1016/j.foodcont.2017.07.032
0956-7135/

1. Introduction

Like the search/replace function in Microsoft Word, genome-editing technology makes it possible to accurately edit genomes. Genome-editing technology has been widely used in medicine, animals and agriculture. For example, it has been applied in medicine to cure genetic diseases such as sickle-cell anemia (Gaj, Gersbach, & Barbas, 2013), in animal husbandry for the cultivation of hornless dairy cows (Carlson, Lancto, Zang, Kim, Walton, & Oldeschulte, 2016) and more widely in agriculture to produce disease-resistant rice (Li, Liu, Spalding, Weeks, & Yang, 2012), high-oleic soybeans (Haun, Coffman, Clasen, Demorest, Lowy, & Ray, 2014) and anti-browning mushrooms (Waltz, 2016a, 2016b), which could reduce food waste.

As a developing country with the largest population, China is making efforts to employ genetic-engineering technology to boost agricultural productivity even there are some challenges for adopting GM crops in developing world (Aghaee, Olkowski, Shelomi, Klittich, Kwok, & Maxwell, 2015). Chinese government has steadily increased the investment in agricultural since high-tech 863 program in 1986. In 2008, China launched the National Genetically Modified Organism (GMO) New Variety Breeding Program, one of the 16 National Science and Technology Major Projects from 2006 to 2020 (Li, Peng, Hallerman, & Wu, 2014). Since 2007, the No.1 Central Document issued by Central Committee of the Communist Party of China and the State Council has mentioned biotechnology 8 times, which requests to increase public awareness of and promote biotechnology. With more than 20 years of promotion of agricultural biotechnology, China has also developed a regulatory system for risk assessment and management of GM products to ensure food safety.

Based on those intensive investments, many new genetically modified (GM) crop traits and varieties have been developed in China with characteristics such as insect resistance, herbicide tolerance, and stress tolerance. However, only insect-resistant *Bt* cotton and disease-resistant papaya have been commercialized on a large scale (Li, Peng, Hallerman, & Wu, 2014). Biosafety certificates for commercial planting for two GM Bt rice lines and one GM phytase corn were issued in 2009 and renewed in 2015, but cultivation has not yet occurred.

In contrast to conventional genetic modification resulting from the insertion of large pieces of exogenous DNA, genome-editing techniques generate phenotypic variation that is indistinguishable from that generated by natural means or induced mutations. Given the debate and concern on GM food safety, it is important to get clarity on the regulatory status of genome-editing, which is the key to genome-editing techniques' application (Jones, 2015). With clear and science based regulatory path, it is possible for China to adopt the genome editing derived products easier because of less concerns and more advanced research and development in genome editing technology compared with GM.

2. Genome-editing technology development in China

Genome-editing techniques with sequence-specific nucleases (SSNs) creates DNA double-strand-breaks (DSBs) in the genomic target sites that lead to gene mutations, insertions, replacements or chromosome rearrangements by non-homologous end joining (NHEJ) or homology-directed repair (HR) mechanisms. NHEJ produces small insertions or deletions (indels) and is useful for disrupting gene function. HR can induce precise gene repair of one of thousands of base pairs in the presence of a homologous donor molecule to correct point mutations and introduce exogenous sequences (Fig. 1). There are four major SSNs: meganucleases, or homing endonucleases (HEs), zinc finger nuclease (ZFN), transcription activator-like effector nuclease (TALEN) and the clustered regularly interspaced short palindromic repeats/CRISPR-associated 9 (CRISPR/Cas 9) system (Gaj et al., 2013; Ménoret, Fontanière, Jantz, Tesson, Thinard, & Rémy, 2013; Smith, Grizot, Arnould, Duclert, Epinat, & Chames, 2006).

As Chinese scientists adopted genome editing as a powerful tool for crop improvement, functional genomics and drug discovery very quick, Chinese publications and patents in genome editing technology have been ranked 2nd in the world (Zhou, 2016).

2.1. Comparison of ZFN, TALEN, MegaN and CRISPR/Cas 9

ZFN, the first genomic-editing strategy, uses custom DNA endonucleases that are mostly based on the *Fok*I restriction enzyme fused to a zinc finger DNA-binding domain engineered to target a specific DNA sequence. But researchers must order reagents from Sigma Aldrich as ZFN technology is licensed to Sigma Aldrich for research applications by Sangamo Biosciences, the owner of this technology (Perkel, 2013), which makes zinc fingers relatively expensive. In addition, off-target effects created by site-specific nucleases are high and can be toxic to cells.

Similar to ZFNs, TALENs induce targeted DSBs that activate DNA damage response pathways and enable custom alterations. (Gaj et al., 2013). TALENs can perform most of the functions of ZFNs but provide high specificity and a low chance of off-target effects. However, the large size of TALENs may limit their delivery by size-restricted vectors, and construction is more complicated (Shan & Gao, 2015).

Mega Nucleases (MegaN) recognise DNA sequences of 12–40 bases by DNA-protein interaction, and contain nuclease activities. The recognition sites of natural MegaN are limited, while engineered MegaN could be constructed by introducing amino acids into recognition domain to create new MegaN (Ménoret et al., 2013; Smith et al., 2006). MegaN could be used in genome editing with high specificity and less toxicity to the cell. However, similar to