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SPECIAL TOPIC: Genome editing in genetic therapy and agriculture
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Anything impossible with CRISPR/Cas9?

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Since the adaptation of the bacterial CRISPR/Cas9 system to eukaryotic cells, this "magic" tool has now been dramatically modified and applied to all kinds of biomedical research, clinics and agriculture (Jiao and Gao, 2016). The system was first reported to rapidly, specifically and effectively target genomic sequences in human cells (Cong et al., 2013; Jinek et al., 2013). Since then it attracted scientists' attention from every corner of the biological and related sciences, and it is emerging as the best genetic manipulation method, being used in almost all organisms. In this special topic of "Genome editing in genetic therapy and agriculture", nine new articles are published with a focus on two major areas: genetic therapy and agriculture.

The clustered regularly interspaced short palindromic repeats (CRISPR)-associated protein 9 (CRISPR-Cas9) system provides a novel genome editing technology that can precisely target a genomic site to disrupt or correct a specific gene. Taking advantage of non-homologous end-joining (NHEJ) and homology directed repair (HDR)-mediated DNA repair, studies have recently reported the use of CRISPR/Cas9 to successfully correct disease-causing alleles ranging from single base mutations to large insertions (Men et al., 2017). New Cas9 systems have been extensively applied for identifying therapeutic targets, developing gene therapies. They are also being used to partially or completely alleviate disease symptoms by mutating or correcting related genes. Safe, efficient, and reproducible delivery systems for Cas9 mRNA, Cas9 protein, or vectors encoding the Cas9 gene and corresponding sgRNA are being developed (He et al., 2017). Despite an increasing number of reports of CRISPR/Cas9-mediated genome editing as a powerful technology for gene therapy, challenges still remain (Zhang et al., 2017). Model organisms continue to contribute to the developing field of CRISPR/Cas9-based genetic therapy. *Drosophila* has been and is still one of the leading model organism system for such purpose (Ren et al., 2017b). Delivery of the genome engineering reagents into plant cells is still the major barrier to the use of these technologies for creating novel traits (Ran et al., 2017).

Four original research papers on plant genome editing are among the nine articles of this special topic. Two research papers demonstrate that precise base editing in plants with a Cas9-cytidine deaminase fusion is a powerful tool to generate known and novel inheritable mutations that bear great values and interests for basic research and crop improvement. Ren and colleagues from Huanbin Zhou's and Honghui Lin's labs report a highly efficient toolkit comprising rBE3 and rBE4 for generating gain-of-function alleles at defined loci in cultivated rice. Several rice genes were selected to test the base editing efficiency of rBE3, the rBE3/sgRNA converted cytosine to all other nucleotides at frequencies of 38.9% in T0 transgenic plants (Ren et al., 2017a). Similarly, Chen and colleagues from Linjian Jiang's and Qi-Jun Chen's labs describe that CRISPR/Cas9-mediated base-editing system efficiently generates gain-of-

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functions in *Arabidopsis*. They generated point mutations on ALS gene conferring herbicide resistance in *Arabidopsis* and showed base-edited T1 lines, harboring known and novel herbicide resistant (HR) mutations at the desired position, survived herbicide treatment (Chen et al., 2017). Wang and colleagues from Yi Lin's and Rui Zhang's labs report the first success in achieving knock-out upland cotton mutant using CRISPR/Cas9-mediated genome editing. By engineering GhARG genes on both the A- and D-chromosomes in T1 plants, the CRISPR/Cas9-mediated mutations significantly improved lateral root system development under both high- and low-nitric conditions (Wang et al., 2017). Shen and colleagues from Changjie Yan's and Kejian Wang's demonstrate the potential of the CRISPR/Cas9 system for rapid introduction of genetic diversity during crop breeding (Shen et al., 2017).

It is exciting to witness the rapid advances of gene modification and related technologies, especially its applications in genetic therapy and agriculture. In this process, biosafety and ethical issues have drawn particular attention, which are something not to be neglected by scientists in the field and government officials. Further efforts are needed to establish specific safety and ethical guidelines for all scientists working in this field.

Compliance and ethics *The author(s) declare that they have no conflict of interest.*

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Biographical Sketch

Dr. Renjie Jiao, born on the 30th of Jan., 1965 in Jiangsu, graduated from Peking University in 1987, received his Master's degree in 1991 before employed as a teaching assistant and a lecturer two years later in Peking University. He obtained his Ph.D. from the Institute of Molecular Biology at University of Zurich in 1999. He established his own group in 2004 at the Institute of Biophysics, Chinese Academy of Sciences, where he had been working on *Drosophila* development, with a central question of what are the mechanisms of cell proliferation and differentiation. Since 2017, Dr. Jiao moved to Sino-French Hoffman Institute, Guangzhou Medical University, where he continues to work on *Drosophila*, aiming to construct a genome-wide *Drosophila* mutant library with the CRISPR/Cas9 system, in addition to the scientific research projects in his own lab.

Prof. Caixia Gao is Principal Investigator of the Institute of Genetics and Developmental Biology (IGDB), Chinese Academy of Sciences. Prior to joining IGDB in 2009, she served as Research Scientist (Plant Genetic Transformation) of DLF-Trifolium's biotechnology group in Denmark. Dr. Gao completed her Ph.D. in Plant Genetics from China Agricultural University, Beijing, and her M.Sc. and B.S. degrees in Agronomy from Gansu Agricultural University, Lanzhou. Her extensive research and professional experience has been in plant genome engineering, crop molecular breeding and plant genetic transformation.