BMB
Reports

BMB Rep. 2024; 57(1): 1
www.bmbreports.org

Editorial

Current status of genome editing technologies: special issue of BMB Reports in 2024

Since the identification of DNA as a genetic material, manipulating DNA in various organisms has been a long standing dream of humanity. In pursuit of this objective, technologies to edit genome have been extensively developed over the recent decades. The emergence of zinc finger nuclease (ZFN), transcription activator-like effector nuclease (TALEN), and clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated (Cas) systems enabled site-specific DNA cleavage in a programmable manner. Furthermore, the advent of base editors (BEs) and prime editors (PEs) has enabled base conversion and insertion/deletion with a high accuracy. In addition to the editing of genomic DNA in the nucleus, attempts to manipulate circular DNAs in organelle are currently ongoing. These technologies are bringing major progress in diverse fields including the engineering of cells, livestock, and plants as well as therapeutic gene correction in humans. In this special issue, we aim to cover the recent advances in genome editing technology and its applications in therapeutics, breed improvement in plants and livestock, RNA recording, and protein evolution.

In recent years, substantial progress has been made in CRISPR genome editing technology and treatment of genetic diseases that were once considered incurable. Dr. Junho K. Hur and colleagues provide general reviews for molecular mechanisms of CRISPR-mediated DNA cleavage and repair, and recent applications in gene and cell therapy for human genetic diseases. Off-target editing is one of the major side effects of genome editing technologies. Dr. Seung Hwan Lee and colleagues provide reviews on the efforts for verifying bona fide off-target sites and recent strategies for improving target specificities in CRISPR technologies. In addition to mutations on genomic DNA, mitochondrial DNA (mtDNA) mutations can also result in severe genetic diseases. Dr. Kayeong Lim's review focuses on the strategies, challenges, and potential applications of mtDNA editing technologies including ZF- and TALE-based base editors. Genome editing technologies have also brought advances in the field of directed evolution of desired genes. Dr. Jae-Yean Kim and colleges covered technologies for CRISPR base editor-based targeted random mutagenesis (BE-TRM) for generating novel genetic variations with enhanced functions. CRISPR technology originates from the adaptive immune system of bacteria, while the CRISPR-Cas adaptation process serves as the initial phase. Dr. Sungchul Kim and colleges summarized the function and mechanisms of Cas1-Cas2 complex and reverse transcriptase (RT) as a molecular recorder in the process of CRISPR-Cas adaptation. Furthermore, they highlight the potential application of RT-Cas1-Cas2 to directional RNA recording tool in cells. Genome engineering in livestock presents opportunities for enhancing productivity and disease resistance of livestock, as well as offering genetically modified animal models for biomedical research. Dr. Goo Jang and colleges summarized technical advances of genome engineering in livestock, *in vitro* animal production, and its applications. Genetically engineered mesenchymal stem cells (MSCs) holds a great potential as a resource for regenerative medicine. Dr. Youngsub Kim and colleges established B2M knock-out MSCs by Cas9 ribonucleoprotein, which showed reduced T-cell differentiation and MSCs cell death with lower cytotoxicity. Based on the demand for *in-locus* tagging in plant genome, Dr. Pil Joon Seo and colleges demonstrated HA epitope tagging at desired sites via PEs in plants. To facilitate genome-wide *in-locus* epitope tagging, they also established prime editing guide RNA (pegRNA) database for all the *Arabidopsis* genes.

In conclusion, through recent years, substantial advancements have been achieved in the field of genome editing and the latest approval of the Exa-cel (also named as CASGEVY) in 2023, the first-in-kind CRISPR gene therapy by Vertex and CRISPR Therapeutics, signaled the entrance of genome editing technologies into our daily life. Of course, genome editing technologies are not currently perfect and complete. Although deleterious side effects of genome editing technologies (e.g., generating DNA large deletion, P53 activation, chromosomal rearrangements, and genome- and transcriptome-wide off-target edits) are huddles that need to be addressed, continuous progress of these technologies is expected to open new era for genetic engineering of diverse organisms on the Earth.

Ju-Chan Park[1], Ph.D. & Sangsu Bae[1,2,3,4,*], Ph.D.
[1]Medical Research Center of Genomic Medicine Institute, Seoul National University College of Medicine, Seoul 03080, [2]Cancer Research Institute, Seoul National University College of Medicine, Seoul 03080, [3]Institute of Molecular Biology and Genetics, Seoul National University, Seoul 08826, [4]Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul 03080, Korea
E-mail: sbae7@snu.ac.kr

https://doi.org/10.5483/BMBRep.2023-0248

Received 20 December 2023

ISSN: 1976-670X (electronic edition)