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EDITORIAL

Highlights for special issue on "Large Animal Stem Cells"

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Biological techniques such as stem cell culture, somatic cell reprogramming and gene editing are important for the large animal breeding. Also, these techniques can produce large animal models, which hold great potential for developing disease treatment and clinical applications, especially pigs given their high degree of physiological similarity to humans. However, research on large animals, including pigs and cattle, has been challenging for decades due to the lack of knowledge of regulatory pathways, and mechanisms involved in embryogenesis and physiological process. Studies using large animals take much longer than the commonly studied small animals, for example mice and zebrafish. Considerable effort has gone into developing innovative operating techniques for gene editing, stem cell derivation, and understanding the relevant signaling pathways that regulate cell differentiation and the maintenance of pluripotency in large animals. This special issue of *Frontiers of Agricultural Science and Engineering* (*FASE*) features 10 articles covering a wide range of current research topics on large animal somatic cell reprogramming, stem cell culture and gene editing, which mainly focus on research progress of stem cell derivation from different large animal species and technology improvement related to embryo manipulation and cryopreservation.

Somatic cell nuclear transfer (SCNT) has been widely used for the generation of different types of genetically-engineered and gene-knockout animal models. To improve the success rate of SCNT, Jin et al. studied the effects of donor cell characters (type, culture time, confluence degree and cell passage), the culture interval of SCNT embryos, selection and chemical treatment of breed recipient on cloning efficiency in pigs, which provided valuable suggestions for further optimization of current SCNT protocols. Throughout the process of SCNT, oocyte enucleation is a crucial step. Zhao et al. compared the pig cloning efficiency of four enucleation methods and demonstrated that spindle imaging system-assisted and blind aspiration plus post-enucleation staining-based had distinct advantages in severals aspects compared to the standard aspiration-based enucleation method. However, the mortality rate of SCNT is still higher than other embryo manipulation techniques. In their study, Ao et al. speculated the low survival rate of SCNT piglets was associated with abnormal umbilical cord and placenta development by comparing with artificial insemination-generated piglets. Chen et al. reported the construction of a vector with shRNA to successfully generate SCNT porcine embryos resistant to pathogens of porcine epidemic diarrhea virus and transmissible gastroenteritis virus, providing a new pathogen-free model for future application.

Culture and cryopreservation of embryos are also two indispensable parts of embryo manipulation. Dang and Zhang reviewed the factors affecting early embryonic development in cattle and emphasized the importance of treatment with epigenetic modifiers to cloned bovine embryos. Huang et al. reviewed the impressive progress achieved in cryopreservation for animal embryos and gametes as well as existing problems.

The remaining four articles focus on pluripotent stem cells. Wang et al. proposed a negative feedback regulation between SALL4 and OTX2, that SALL4 maintains self-renewal of porcine pluripotent stem cells through downregulation of OTX2. Han et al. and Tian reviewed the recent progress and future prospect of porcine pluripotent stem cells and bovine pluripotent stem cells, respectively. Finally, Lei et al. reviewed the main steps in the reprograming of primordial germ cells to pluripotent stem cells.

Although major breakthroughs have been made in recent years, there are still many mysteries waiting to be

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unraveled. Finally, as the Guest Editor, I wish to express my great appreciation to all the authors and reviewers who have contributed to this collection, and of the unfailing support and behind-the-scenes work of the *FASE* editorial team.

Jianyong Han, Professor from College of Biological Sciences, China Agricultural University, received his PhD degree in Biochemistry and Molecular Biology from China Agricultural University in 2006. From 2006 to 2011, he was engaged in stem cell and developmental biology researches in Genome Institute of Singapore, and was promoted as a Research Scientist in 2010. Dr. Han joined China Agricultural University in 2011 as distinguished Professor. Since 2011, he has been selected into the “Thousand Youth Talents Plan”, the “New Century Excellent Talents in University” and the “Youth Science and Technology Innovation Leader Project” of the Ministry of Education and Ministry of Science and Technology. His research focuses on regulation mechanisms of early embryo development and somatic cell reprogramming, derivation of naive embryonic stem cells from pig and other large animals; animal model for human diseases, and new techniques for stem cells and development, such as self-assembled embryo-like structure using blastocyst-derived stem cells. His works have been published in *Nature*, *Cell Stem Cell*, *Nature Communications*, *Cell Research* and other international academic journals.