NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

BIOLOGY COLLOQUIUM

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Hosted by A/P Liou Yih Cherng

"Artificial spermatid"-mediated genome editing

Jinsong Li is a professor and director of State Key Laboratory of Cell Biology, Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences. He obtained his PhD from Institute of Zoology, Chinese Academy of Sciences, in 2002 and followed by postdoctoral training at Rockefeller University before joining SIBCB in 2007. His research is to establish high-efficient reprogramming strategies, generate high-quality reprogrammed cells, as well as to elucidate molecular mechanism of epigenetic reprogramming. He has made fundamental contributions to the establishment of androgenetic haploid embryonic stem cells ("artificial sperm") and haploid cell-mediated semi-cloned technology. Dr. Li has published extensively in numerous peer-reviewed journals includin Dr. Li has published extensively in numerous peer reviewed journals including Cell, Nature, Cell Stem Cell, PNAS, and Cell Res.

By **Li Jinsong**

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From androgenetic haploid blastocysts derived by injection of sperm into enucleated oocytes, we generate mouse androgenetic haploid embryonic stem cells (AG-haESCs) that can support full-term embryonic development upon injection into oocytes, leading to the generation of semi-cloned (SC) mice (semi-cloned technology). However, one major drawback of this technology is the very low birth rate of healthy SC mice (2% of total SC embryos). Recently, we establish AG-haESCs carrying H19-DMR and IG-DMR deletions (DKO-AG-haESCs) that can efficiently support the generation of SC pups at a rate of 20% ("artificial spermatid"). Importantly, "artificial spermatid"carrying CRISPR-Cas9 library can produce biallelic mutant mice in one step, thus enabling functional mutagenic screening at organism level in mice. Moreover, artificial spermatid-mediated SC technology enables efficient generation of mouse models carrying defined point mutation; one-step generation mouse models that mimic multiple gene dosage effect in human Myotonic Dystrophy type 1 (DM1); identification of novel mutations involved in human neural tube defects; medium-scale targeted screening of critical factors involved in bone development; and efficient generation of mice carrying tagged proteins at genome-scale (genome tagging project, GTP). Interestingly, we demonstrated that parthenogenetic haESCs derived from oocytes, after removing H19-DMR and IG-DMR, can also support the high-efficient generation of SC mice by injection into oocytes, thus enabling high-efficiency bi-maternal development in mammals. Furthermore, we establish haploid ESCs from monkey parthenogenetic embryos and human parthenogenetic haESCs. In summary, haESCs provide powerful tools for genetic analyses in mammals at both the cellular and organismal levels.

Artwork by Ann Nee, DBS, NUS