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Establish cardiac stem cell tracking and lineage tracing system in the farming animal swine for preclinical studies

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Abstract

Cardiovascular disease is the leading cause of death in the world today, and the mortality rates have remained virtually unchanged in the last twenty years, highlighting a critical need for developing novel therapeutic strategies. Understanding the specification, proliferation and differentiation of diverse cardiovascular stem cell lineages during normal development and heart injury is a critical step toward cell-based therapies for heart diseases.

To fulfil this goal, it is essential to establish large animal models whose physiology and cardiogenesis are very similar to humans because (1) it is very challenging to fully characterize human cardiac stem cells and examine their potential therapeutic roles during heart injury due to the difficulties in obtaining human embryos and the infeasibility of in vivo lineage-tracing technology and (2) the development of cardiac stem cells in fetal hearts appears rather different in humans than in mice. In this regard, the farming animal swine (Sus scrofa) are arguably the most attractive model species because of their remarkable anatomic and physiological similarities with humans. Using TALEN-mediated homologous recombination and somatic nuclear transfer, we have generated Cre-mediated EGFP reporter swine lines. More importantly, we are well on our way to generate knockin swines containing Cre-T2A-tdTomato at endogenous cardiac progenitor marker gene loci.

We are highly enthusiastic that this study will promote both basic and preclinical research in the scientific community. This study will facilitate systematic studies of cardiac pregenitor lineage tracing in first heart field, second heart field, and epicardium development. With these models, cell-based therapy and in vivo delivery of various drug candidates can be performed to explore their effect on promoting endogenous CPC regeneration and contribution to injured hearts.

Biography

Dr. Zhong Wang obtained his Ph.D. from Oregon Health and Science University in 2000, and pursued his postdoctoral research at University of California, Berkeley before he became a faculty member at Massachusetts General Hospital, Harvard Medical School and Harvard Stem Cell Institute. Dr. Wang moved to University of Michigan in 2013. His major interest is epigenetic regulation of embryonic and cardiac stem cell differentiation and regeneration.