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Heart regeneration with cardiac progenitor cells and engineered ECM mimicking carriers in large animal models

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Cell-based therapy represents a highly promising approach for the treatment of heart diseases but its validation requires extensive preclinical studies. Major challenges include lack of clinically relevant large animal reporter models, the identification of ideal cell source, and the extremely low retention and survival rates of transplanted cells. To address these critical challenges in heart regeneration, we have generated stable and high-level expression reporter swine and rabbit animals. For the first time in the field, we characterized and targeted the porcine ROSA26 (pROSA26) locus and generated ROSA26-EGFP swine reporters readily inducible by Cre expression. These swine reporters will enable precise quantification of transplanted cells versus host cells. We also generated knock-in pigs containing Cre-T2A-tdTomato at endogenous ISL1 locus, which allow us to trace the specification and reactivation of ISL1+ CPCs in pig hearts. Meanwhile, we have established cutting-edge injectable cell microcarriers for tissue regeneration. In particular, we have developed new nanofibrous hollow microspheres (NF-HMS) that mimic the extracellular matrix architecture at the nanometer scale. Building on pioneering works in cardiac stem cell field, we are able to robustly generate embryonic cardiac progenitor cells (CPCs) from pluripotent stem cells for heart regeneration. Our results show that NF-HMS greatly enhances the CPC retention, survival, and integration in infarcted hearts of large animals. Our progress using these combined approaches in heart regeneration will be presented. Our integration of advanced cell source, biomimetic carrier, and large animal models for heart regeneration should provide general principles in developing an informative model system for regenerative medicine.

Biography

Zhong Wang has completed his PhD from Oregon Health and Science University and Post-doctoral studies from University of California, Berkeley. He was a Principal Investigator at Massachusetts General Hospital, Harvard Medical School and Harvard Stem Cell Institute before he joined the Department of Cardiac Surgery, University of Michigan, USA.

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