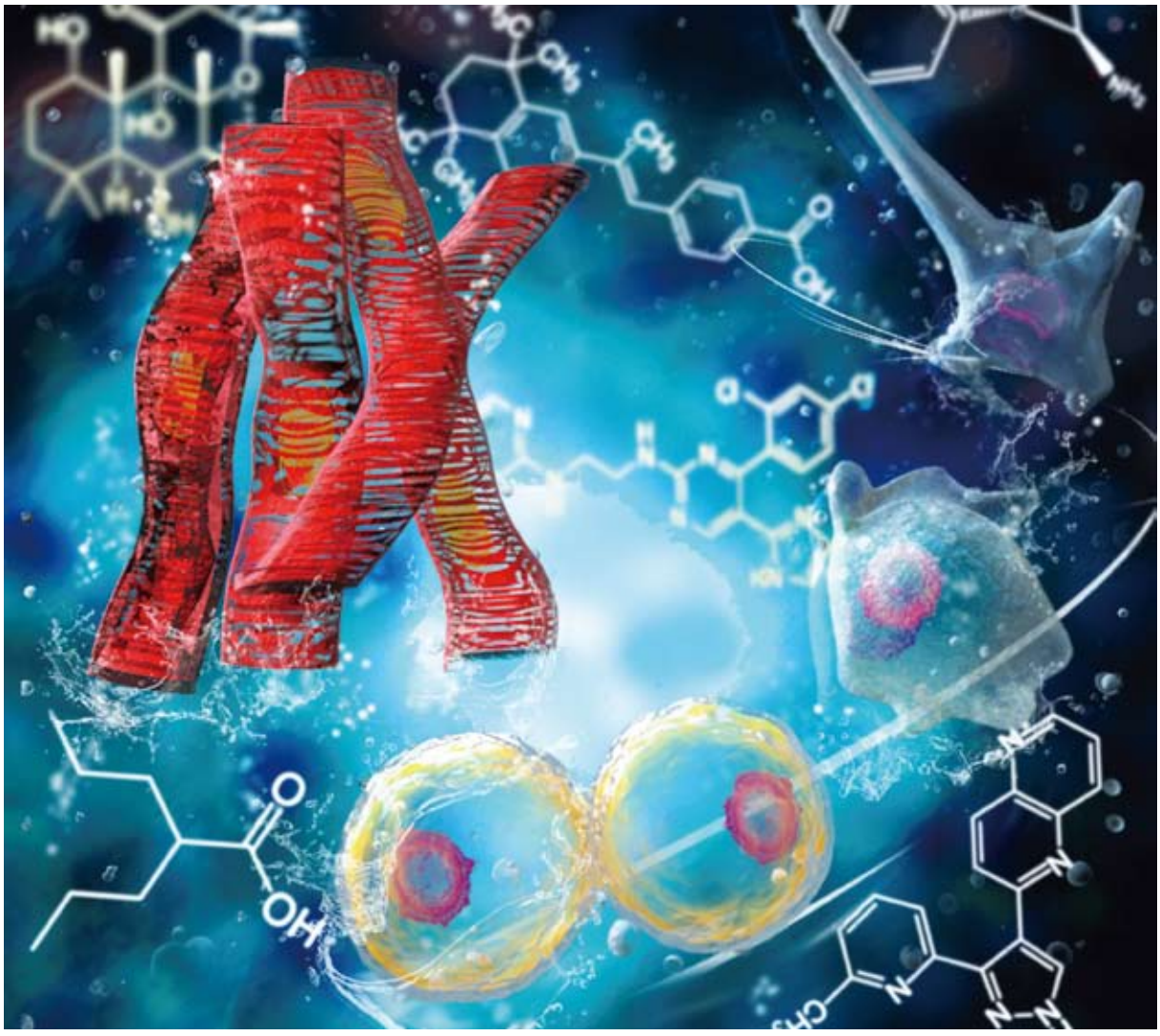
Chemical Induction of Cardiac Reprogramming of Fibroblasts

Heart failure caused by the loss or dysfunction of cardiomyocytes affects millions of people and is the leading cause of mortality. Adult heart has limited regeneration capacity. Transplantation of cardiac progenitor cells generated from embryonic stem cells or induced pluripotent stem cells (iPSCs) is one theoretically plausible way to improve cardiac functions.

The direct conversion, or transdifferentiation, of non-cardiac cells into cardiomyocytes by forced expression of transcription factors and microRNAs provides another approach for cardiac regeneration. However, genetic manipulations raise safety concerns and are thus not desirable in most clinical applications.

Prof. XIE Xin's group from the Shanghai Institute of



Chemical Induction of Cardiac Reprogramming of Fibroblasts (Image by courtesy of XIE's group)

Materia Medica (SIMM), CAS has dedicated themselves to research on chemical-induced somatic cell reprogramming and transdifferentiation. Earlier this year, they reported in *Cell Research* that a chemical cocktail containing bromodeoxyuridine (BrdU) can generate iPSCs without any genetic factors (*Cell Research*, doi: 10.1038/cr.2015.96). More recently, they succeeded in generating spontaneously beating cardiomyocyte-like cells from mouse fibroblasts by using only 3-6 small molecule compounds, and published their results online in *Cell Research* on August 21 this year (*Cell Research*, doi:10.1038/cr.2015.99).

These chemical-induced cardiomyocyte-like cells (CiCMs) express cardiomyocyte-specific markers, exhibit sarcomeric organization, and possess typical cardiac calcium flux and electrophysiological features. Genetic lineage tracing confirms the fibroblast origin of these CiCMs. Further studies show that the generation of CiCMs passes through a cardiac progenitor stage instead of a pluripotent stage. Bypassing the use of viral-derived factors, this proof of concept study lays a foundation for *in vivo* cardiac transdifferentiation with pharmacological agents and possibly safer treatment of heart failure.

FU Yanbin, HUANG Chenwen, both Ph.D. candidates from Tongji University, and Dr. XU Xinxiu, an SIMM staff, shared the first authorship. This work was supervised by Prof. XIE Xin, Principal Investigator of SIMM, and Deputy Director of the National Center for Drug Screening. XIE also works as an Adjunct Professor of Tongji University. Her research is mainly focused on GPCR-based drug discovery and chemical biology of stem cells.

Dr. YANG Huangtian from the Institute of Health Sciences (HIS) and Dr. GAO Zhaobin from SIMM also contributed to the work by offering their advice and technical support on electrophysiology study.

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