**Therapeutic Microparticles Functionalized with Biomimetic Cardiac Stem Cell Membranes and Secretome** Junnan Tang<sup>1,2,3,4\*</sup>, Adam Vandergriff<sup>2,3</sup>, Tyler A. Allen<sup>2,3</sup>, Michael Taylor Hensley<sup>2,3</sup>, Phuong-Uyen Dinh<sup>2,3</sup>, Jhon Cores<sup>2,3</sup>, Jinying Zhang<sup>1</sup>, Ke Cheng<sup>2,3,4</sup>

<sup>1</sup> Department of Cardiology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan 450052, China. <sup>2</sup> Department of Molecular Biomedical Sciences and Comparative Medicine Institute, North Carolina State University, Raleigh, North Carolina 27607, USA.

<sup>3</sup> Department of Biomedical Engineering, University of North Carolina at Chapel Hill & North Carolina State University, Chapel Hill and Raleigh, North Carolina 27599 and 27607, USA.

<sup>4</sup> Division of Molecular Pharmaceutics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA.

**Statement of Purpose:** Stem cell therapy represents a promising strategy in regenerative medicine. However, cells need to be carefully preserved and processed before usage. In addition, cell transplantation carries immunogenicity and/or tumorigenicity risks. Mounting lines of evidences indicate that stem cells exert their beneficial effects mainly through secretion (of regenerative factors) and membrane-based cell-cell interaction with the injured cells.

**Methods:** We fabricated a synthetic cell-mimicking microparticle (CMMP) that recapitulates stem cell functions in tissue repair. CMMPs carried similar secreted proteins and membranes as genuine cardiac stem cells did.

**Results:** In a mouse model of myocardial infarction, injection of CMMPs leads to preservation of viable myocardium and augmentation of cardiac functions similar to cardiac stem cell therapy. CMMPs (derived from human cells) do not stimulate T cells infiltration in immuno-competent mice.

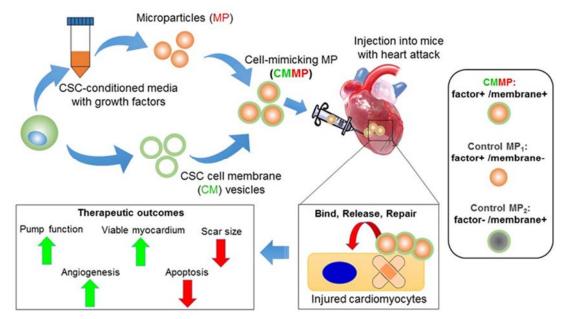


Figure 1. Overall biochemical design and study model of CMMPs.

**Conclusions:** CMMPs act as "synthetic stem cells" which mimic the paracrine and biointerfacing activities of natural stem cells in therapeutic cardiac regeneration. Although our first application targeted the heart, the CMMP strategy represents a platform technology that can be applied to multiple stem cell types and the repair of various organ systems.

## **References:**

- 1. Li TS. J Am Coll Cardiol. 2012; 59: 942-53.
- 2. Cheng K. JACC Heart Fail. 2014; 2: 49-61.
- 3. Cheng K. J Am Heart Assoc. 2014; 3, e001260.