

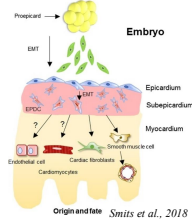
# Intramyocardial Injection of Human iPSC-Cardiomyocytes/Proepicardial-like Cells Enhances Vascularization and Salvages Myocardial Thickness in Cryoinjured Rat Hearts

Fatin Fazrina Roslan<sup>1</sup>, Yuexin Yu<sup>1,2,3</sup>, Jer Ping Ooi<sup>1</sup>, Yaping Xu<sup>1,2,3</sup>, Yoke Keong Yong<sup>4</sup>, Chun Chen Chung<sup>1</sup>, Nurul Ain Nasim Mohd Yusof<sup>5</sup>, Catherine Hong Huan Hor<sup>6</sup>, Mohd Nor Azim Ab Patar<sup>7</sup>, Jun Jie Tan<sup>1</sup>

<sup>1</sup>USM-ALPS Laboratory for Heart Research, Advanced Medical and Dental Institute, Universiti Sains Malaysia, 13200 Bertam, Kepala Batas, Malaysia, <sup>2</sup>Henan Key Laboratory of Medical Tissue Regeneration, Xinxiang Medical University, Henan, China, <sup>3</sup>Henan Key Laboratory of Cardiac Remodelling and Transplantation, Zhengzhou Seventh People's Hospital, Henan, China, <sup>4</sup>Department of Human Anatomy, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia, <sup>5</sup>Hematology Unit, Cancer Research Centre, Institute for Medical Research, Block C, National Institute of Health (NIH) Malaysia, 40170, Setia Alam, Selangor, Malaysia <sup>6</sup>Department of Chemistry, Faculty of Science, Hong Kong Baptist University, Kowloon Tong, Hong Kong SAR, <sup>7</sup>Department of Neurosciences, Universiti Sains Malaysia 16150 Kubang Kerian, Kelantan, Malaysia

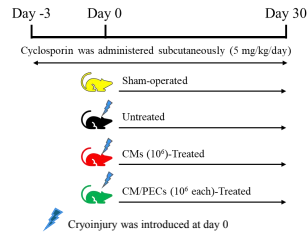
## Introduction

The proepicardial organ derives cells which forms the epicardium for heart development but ceases after birth. A prior study demonstrated that proepicardial-like cells (PECs) from human induced pluripotent stem cells (hiPSCs) resemble embryonic epicardial cells. This study explored PEC functions in cardiomyocyte therapy for cryoinjured rat hearts.



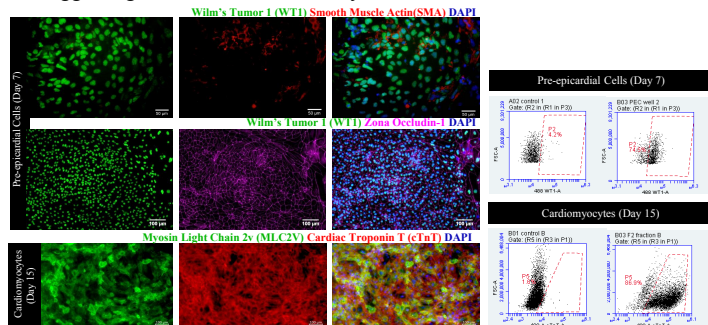
## Methods

- HiPSCs were reprogrammed from frozen cord blood. CMs and PECs were differentiated based on Tan et al. (*Nat. Commun.*, 2021).
- PECs at 7 days of differentiation and CMs at day 15-20 and were used in the in vivo experiment. CMs were purified using Percoll-gradient centrifugation before use.
- Sprague Dawley rat hearts were cryoinjured for 30 sec twice prior to injecting PBS, CM or CM/PEC into the infarct region. Millar Pressure Volume System was used to measure cardiac hemodynamics after 30 days post cell injection.



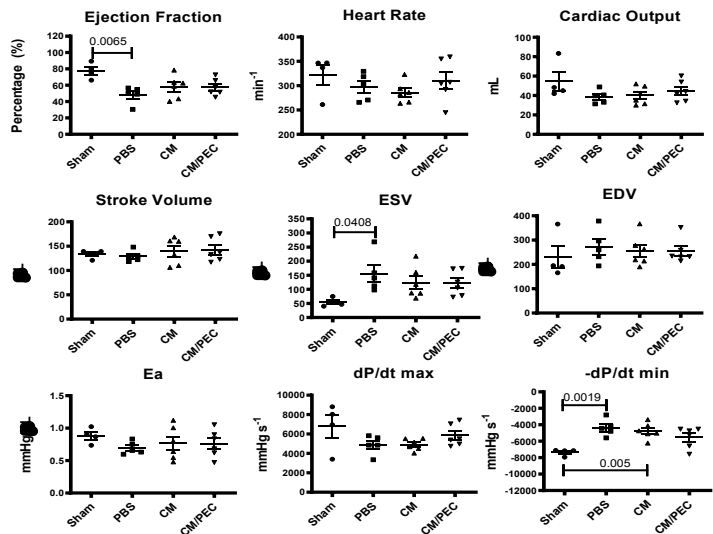
## Results

- Majority WT-1<sup>+</sup> PECs co-expressed zona occludin-1 (ZO-1) at day 7, and very few express smooth muscle actin.
- Percoll gradient separation of differentiated CMs yielded 85±1.9% cTnT<sup>+</sup> cells, majority of which also co-expressed MLC2v, suggesting their ventricular identity.

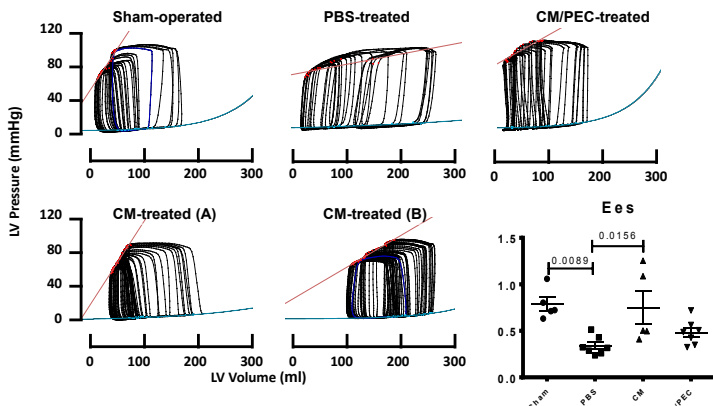


## Result

- After 4 weeks, the functions of CMs and CM/PECs-treated hearts did not show significant differences compared to those of PBS-treated cryoinjured rat hearts.

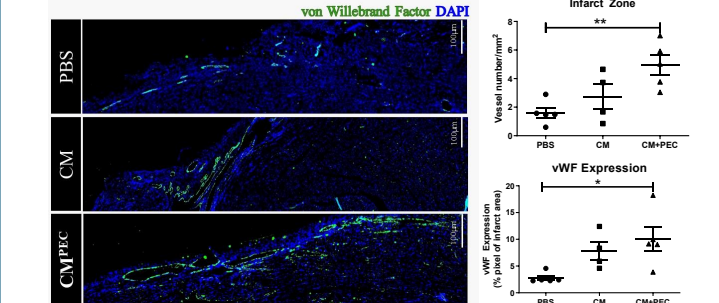
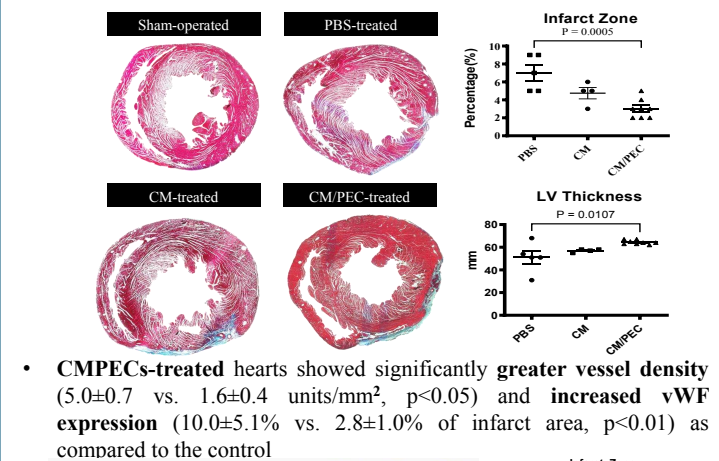


- Intramyocardial co-injection of CM/PECs preserved ventricular compliance as compared to CMs alone treatment.
- Cryoinjury significantly reduced ventricular elastance (Ees). CM only treatment significantly improved Ees of cryoinjured hearts.



## Result

- Cryoinjury successfully produced a necrotic lesion on the epicardial surface, as evidenced by the presence of fibrosis
- CMs and CM/PECs-treated hearts showed reduced infarct size and preserved the myocardial wall thickness.



## Conclusion

- In conclusion, CMPECs preserved myocardial wall thickness by promoting vascularization within the infarct region

## Acknowledgment

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