Abstract: P282

High throughput screen to identify EMT-inducing compounds in human epicardial cells

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Topic(s):
Ischemia, Infarction, Cardioprotection

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S72

Background
Since the adult heart has only limited capacity to repair itself, myocardial infarction often leads to cardiac remodeling and consequently the development of heart failure. The epicardium, a single cell layer enveloping the heart, has been shown to have regenerative potential by providing cells and paracrine factors to the myocardium. To be able to aid the heart, epicardial epithelial-to-mesenchymal transition (EMT) is an essential step.

Purpose
The aim of this study is to find an activator of epicardial EMT using a high-throughput compound screen to ultimately improve the regenerative response of the epicardium after cardiac injury.

Methods and Results
A phenotypic screen was performed using the LOPAC1280 small molecule library (concentration=5 and 10 μM) on primary human epicardial cells derived from heart auricles. EMT was defined using aSMA immunostaining. The top 22 ranked compounds were validated in multiple epicardial cell lines using aSMA immunostaining and qRT-PCR for EMT related genes. With the two highest responders, concentration-response experiments are currently being conducted to determine the optimal dosage.

Conclusion
It is feasible and effective to perform high-throughput experiments using human primary epicardial derived cells to identify EMT activators. Furthermore, two compounds were found that can induce EMT in epicardial derived cells and may therefore serve as a potential therapeutic to improve the epicardial regenerative response. In the future, my research will focus on optimizing strategies to deliver these EMT-inducing compounds to the epicardium of the infarcted heart.