OPEN ACCESS Freely available online

Journal of Developing Drugs

ISSN: 2329-6631

Commentary

Non-Cardiomyocytes in Process of Remodeling Chronic Heart Failure

Pragya Srivastava*

Department of Cardiology, University of Medical Center, Maastricht, The Netherlands

DESCRIPTION

Non-Cardiomyocytes (non-CM) play an important role in the process of cardiac remodeling in chronic heart failure. The mechanisms of transit and interaction between non-CMs are largely unknown. Here, we attempt to characterize the cellular landscape of non-CM in chronic heart failure mice by Single-Cell RNA Sequencing (scRNA-seq) and provide potential therapeutic avenues. Cellular and molecular analyzes revealed that the most affected cell types were primarily fibroblasts and endothelial cells. Notably, the fibroblasts cluster, the most abundant cluster in fibroblasts, was the only cluster enriched for collagen synthesis genes such as adamts and Crem, which may be responsible for fibrosis in cardiac remodeling. Clusters of endothelial cells are also the most common and only increased, affecting vascular morphogenesis. Cellular communication further confirmed that fibroblasts and endothelial cells are driving nodes in chronic heart failure. Furthermore, using fibroblasts and endothelial cells as entry points for his CMap technology, Histone Deacetylation (HDAC) inhibitors and HSP inhibitors were identified as novel heart failure therapeutics that may be evaluated in the future. The combined application of scRNA-seq and His CMap could be an effective way to achieve drug repositioning.

After an infarct occurs, the injured heart often undergoes a series of delicate and coordinated events to compensate for the dysfunction. But over time, or as the disease worsens, these finely-tuned specific responses gradually shift toward chaos and imbalance, ultimately progressing to congestive heart failure. Cardiomyocytes cannot be the sole participants among the several pathological conditions that occur in. On the contrary, many non-cardiomyocytes, including fibroblasts, endothelial cells, etc., serve as key functional components of the heart. Various stimuli inevitably lead to a series of changes in chain-like molecule composition and biological function. In particular, the excessive activation or infiltration response of specific cells favors scar formation, leading to decreased compliance throughout the tissue, leading to a vicious cycle of decompensation. Therefore, the development and exacerbation of heart failure may be partially attributed to non-CM pathological responses. On the other hand, we suggest that these cells can be functionally reprogrammed in a damaged environment and replace necrotic or apoptotic cardiomyocytes, potentially contributing significantly to myocardial repair. Therefore, improving our understanding of non-CM also provides an opportunity to find attractive alternative treatment strategies for heart failure.

For complex multicellular tissues such as the heart, single-cell RNA-seq provides a powerful tool to accurately characterize cell population changes and internal heterogeneity between normal and disease states. In recent years, describing gene expression patterns in individual cells has allowed researchers to reveal in greater detail the cellular composition and behavior of the heart, particularly the unexpected role of fibroblasts and immune cell populations. Applying this technology to the study of end-stage heart failure is also essential to fully understand changes during the disease and to develop treatment strategies. Based on the aberrant properties of the transcriptome reflected by cells in disease states, the rapid search for effective restorative drugs can be achieved by Connectivity Maps (CMaps). These agents are inversely related to disease stimuli, inversely regulating aberrantly expressed genes. This strategy does not require detailed mechanisms of action or drug targets to predict therapeutic potential, allowing researchers to communicate drug, gene, and disease relationships without prior knowledge.

Therefore, in this study, we used single-cell sequencing techniques to systematically investigate pathways and intrinsic regulatory responses of non-cardiomyocyte lineage changes in tissue systems affected by chronic heart failure (8 weeks LAD). Our data showed that cardiac fibroblasts and endothelial cells are major non-cardiomyocyte components of cardiac tissue. At the same time, ischemia-induced chronic heart failure increases the number of specific marker genes in cardiac fibroblasts, endothelial cells and their subsets. Most strikingly, the Adamts marker gene, which is differentially expressed by the fibroblast subtype cluster, is predicted by CMap subjects as well as the pathological state of fibroblast internal heterogeneity and fibrosis. It also effectively reflects potential drug HDAC inhibitors. In general, these data provide a basis for further understanding of phenotypic changes in non-CM and help achieve accurate and rapid phylogeny of disease states. Importantly, drug repositioning based on new data and techniques is increasingly worthy of reconsideration, and our strategy of combining single-cell sequencing could be applied to many research areas of cardiac biology and disease.

Correspondence to: Dr. Pragya Srivastava, Department of Cardiology, University of Medical Center, Maastricht, The Netherlands, Tel/Fax: +31 300 019 6; E-mail: pragyasristava@gmail.nl

Received: 05-Sep-2022, Manuscript No. EOED-22-19697; **Editor assigned:** 09-Sep-2022, Pre Qc No. EOED-22-19697(PQ); **Reviewed:** 23-Sep-2022, Qc No. EOED-22-19697; **Revised:** 30-Sep-2022, Manuscript No. EOED-22-19697 (R); **Published:** 07-Oct-2022, DOI: 10.35248/ 2329-6631.22.11.182.

Citation: Srivastava P (2022) Non-Cardiomyocytes in Process of Remodeling Chronic Heart Failure and Drug Targets. J Develop Drugs.11:182.