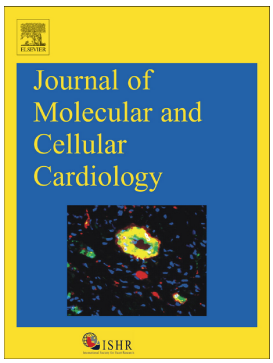


# Exosomal miR-21a-5p mediates cardioprotection by mesenchymal stem cells

Kristin M. Luther, Lauren Haar, Myc McGuinness, Yang Wang, Tom Lynch, Anh Phan, Yang Song, Zilong Shen, George Gardner, Gina Kuffel, Xiaoping Ren, Michael J. Zilliox, W. Keith Jones

PII: S0022-2828(18)30140-8
DOI: doi:10.1016/j.yjmcc.2018.04.012
Reference: YJMCC 8723

To appear in: *Journal of Molecular and Cellular Cardiology*

Received date: 7 November 2017
Revised date: 2 April 2018
Accepted date: 21 April 2018

Please cite this article as: Kristin M. Luther, Lauren Haar, Myc McGuinness, Yang Wang, Tom Lynch, Anh Phan, Yang Song, Zilong Shen, George Gardner, Gina Kuffel, Xiaoping Ren, Michael J. Zilliox, W. Keith Jones , Exosomal miR-21a-5p mediates cardioprotection by mesenchymal stem cells. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Yjmcc(2018), doi:10.1016/j.yjmcc.2018.04.012

# Exosomal miR-21a-5p Mediates Cardioprotection by Mesenchymal Stem Cells

Kristin M. Luther[a,b,1,*] kristin.luther@cshs.org, Lauren Haar[a,b,] Myc McGuinness[a,b] Yang Wang[a], Tom Lynch[a], Anh Phan[a,] Yang Song[a,] Zilong Shen[b,] George Gardner[b,] Gina Kuffel[a,] Xiaoping Ren[a,b,] Michael J. Zilliox[a,] W. Keith Jones[a,b,*] wjones7@luc.edu
[*]Corresponding author.

[a]Loyola University Chicago, Bldg 115, Health Sciences Campus, 2160 S. First Ave, Maywood IL 60153, United States

[b]University of Cincinnati, Cardiovascular Research Center, 231 Albert Sabin Way, Cincinnati, OH 45267, United States

**Abstract**

Though experimental, stem cell transplantation has the potential to improve the condition of the heart after myocardial infarction. It does so by reducing infarct size and inducing repair of heart muscle and its blood supply. Mesenchymal stem cells (MSC) have been found to be effective in pre-clinical animal models and clinical trials, but the mechanisms by which they induce cardioprotection and repair are still not fully understood. Small extracellular vesicles known as exosomes are now recognized to be key mediators of beneficial MSC paracrine effects, and the concept that they transfer miRNA to change gene expression in recipient cells is of current therapeutic interest. We present complete deep miRNA sequencing of MSC exosome cargo, and found that of several cardioprotective miRNAs, miR-21a-5p was the most abundant. Because miR-21a-5p is a well-known cardioprotective miRNA, we investigated the hypothesis that MSC exosomes can cardioprotect the heart by increasing the level of miR-21a-5p in recipient cardiac cells, thereby downregulating expression of the pro-apoptotic gene products PDCD4, PTEN, Peli1 and FasL in the myocardium. Using miR-21 mimic transfection and treatment with wild type and miR-21a knockout MSC exosomes, we confirmed that exosomal miR-21a-5p is transferred into myocardium and is a major cardioprotective paracrine factor produced by MSCs acting via synergistic activity on multiple pathways. The data supports that residual cardioprotective effect may be due

[1] Present address:
Capricor Therapeutics
8700 Beverly Blvd
Los Angeles, CA 90048