CHRD 2022: Abstract & Poster Submission Form

Submitter Name

Jessica McBride

Submitter Email

mcbridej@myumanitoba.ca

Presenter Status

- ◉ Undergraduate Students
- ○ Masters Student
- ○ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ○ Non-Trainee

Research Category

- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

Role in the project

- ☑ Design
- ☑ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Title

Deciphering the Roles of Zinc Finger E Homeobox Binding-1 (ZEB1) and ZEB2 in Cardiac Fibroblast Activation

Background

Congenital heart defects (CHDs) are the main cause of infant death in North America but 80% of genetic mechanisms underlying CHDs are understood, including congenital valve defects (CVDs). CVDs may be caused by dysregulation of a hypersecretory cardiac fibroblast (CF) phenotype, the myofibroblast, which causes excess protein secretion and impaired heart function. Transcription factors ZEB1 and ZEB2 likely have roles in activating CFs because they are downstream targets of TGFb, a known CF activator.

Objective

My project aims to understand the roles ZEB1/2 play in CF activation to increase the knowledge on CVD formation.

Methods

Zeb1 and Zeb2 were overexpressed and knocked down in NIH3T3s (a common embryonic fibroblast model) and primary rat CFs (PRCFs). Secondly, ZEB1 and ZEB2 protein expression patterns during activation of PRCFs isolated from male and female rat ventricles were observed. PRCFs were mechanically activated by plating on hard tissue culture plates which was validated by α-smooth muscle actin (α-SMA) expression. Western blot was used to analyze protein levels.

Results

Western blot analysis demonstrated negative autoregulation of ZEB1 by ZEB2 in PRCFs during overexpression and knockdown studies. ZEB1 and ZEB2 also showed different protein expression patterns during PRCF activation: ZEB2 peaked during the myofibroblast stage while ZEB1 peaked during the intermediate CF activation. ZEB1 levels were considerably greater in quiescent CFs compared to ZEB2. Lastly, ZEB1 levels were much lower at the myofibroblast stage in female versus male PRCFs.

Conclusion

Based on protein expression patterns, ZEB1 may have a larger role in initiating CF activation while ZEB2 maintains the myofibroblast phenotype long-term. ZEB2 also negatively autoregulates ZEB1 protein expression in PRCFs. Future research will determine if ZEB1 exhibits negative autoregulation. The specific roles of ZEB1 and ZEB2 in CF activation will also be determined through functional assays and knockdown of Zeb1 and Zeb2 in disease and development models.

Do you have a table/figure to upload?

○ Yes ⊙ No

Authors

- For each author, please click "**[+] Add Item**" and provide the author's information

Name	Email	Role	Profession
Jessica McBride	mcbridej@myumanitoba.ca	Presenting Author	Student

Rohini Suresh	rsuresh@sbrc.ca	Co Author	Graduate Student
Jeffrey Wigle	jwigle@sbrc.ca	Co Author	Full Professor