Title: *Slc39a8*, a zinc importer, is essential for cardiac ventricular compaction

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Abstract (upto 300 words)
Left ventricle non-compaction (LVNC), the third most common cardiomyopathy, is resulted from failure of myocardial development during embryogenesis and is characterized by excessive trabeculation and ceased compaction. Extracellular matrix (ECM) that fills the interlayer space between endocardium and myocardium plays a critical role in ventricular trabeculation and compaction. However, it is not well understood how ECM is regulated in this process. *SLC39A8*, a zinc ion importer, has been implicated in ECM degradation through the Zn-Metal Regulatory Transcription Factor 1(MTF1) axis, which promotes the expression of ECM degrading enzymes including an Adamts metalloproteinase. We discovered that Slc39a8 is expressed in the heart during development and that it is critical for maintaining cellular zinc level. *Slc39a8* null hearts exhibited hallmarks of LVNC including ventricular hypertrabeculation and noncompaction. Mechanistically, *Slc39a8* null hearts had marked ECM accumulation and reduction of several Adamts metalloproteinases. Consistent with the in vivo observations, knocking down *SLC39A8* in Human Umbilical Vein Endothelial Cells (HUVECs) decreased Adamts1 transcription by decreasing cellular Zinc uptake and MTF1 transcriptional activity. Our study thus identified a novel gene underlying ventriclular trabeculation and compaction development and a novel pathway regulating ECM during myocardial morphogenesis.

Keywords—*ECM, heart development, ventricular compaction, Zinc*

Recent Publications (up to 5)

1. Ramjee V*, **Li D***, Manderfield LJ, Liu F, Engleka KA, Aghajanian H, Rodell CB, Lu W, Ho V, Wang T, Li L, Singh A, Cibi DM, Burdick JA, Olson EN, Jain R, Singh MK, Epstein JA. Epicardial Yap/Taz Orchestrate an Immune Suppressive Response following MI. **J Clin Invest.** 2017 Mar 1;127(3):899-911. doi: 10.1172/JCI88759. (*co-first author)
2. Zhang W, Qu X, Chen B, Snyder M, Wang M, Li B, Tang W, Chen H, Zhu W, Zhan L, Yin N, **Li D**, Li X, Liu Y, Zhang JJ, Fu XY, Rubart M, Song LS, Huang XY, Shou W. Critical Roles of STAT3 in beta-Adrenergic Functions in the Heart. **Circulation** 2016;133*:*48–61*.* doi: 10.1161/CIRCULATIONAHA.115.017472.
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Biography (upto 150 words)

Deqiang Li completed his PhD from Indiana University in 2009. He is an assistant professor of University of Maryland Baltimore, USA. He has over 12 first-author publications that have been cited over 200 times, and he has been serving as an ad hoc reviewer for several reputed Journals.

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