Changes in Left Ventricular Circumferential Strain in the African Spiny Mouse following Myocardial Infarction

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Introduction - Peak circumferential strain (ε_{cc}%) as measured by cardiac magnetic resonance imaging (cMRI) has been shown to be a reliable tool to monitor cardiac remodeling due to myocardium insult in various heart conditions and also the effect of the therapeutic intervention in these pathologies[1-3]. Myocardial infarction (MI) is one of the leading causes of fatal cardiac remodeling in humans leading to necrosis of myocytes and replacement by non-contractile scar tissue. At present, different therapeutic strategies have been targeted to reduce damage to cardiac myocytes following this devastating injury. The African spiny mouse (acomys cahirinus) (AS) has been shown to have a remarkable ability to regenerate following an injury completely. Recent studies have shown that these animals completely regenerate their skin, hair follicles, sebaceous glands, skeletal muscle without the development of scarring[4,5]. We hypothesized that based on their regenerative capacity, AS will show rapid improvement in peak circumferential strain when compared to control wild-type mice post MI.

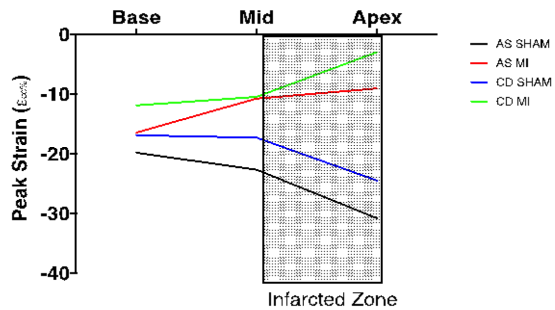

Fig.1 Peak circumferential strain (ε_{cc}%) measured in different regions of left ventricle of the heart using MRI either following control operation (SHAM) or myocardial infarct (MI) in wild type (CD) or African spiny (AS) mice .

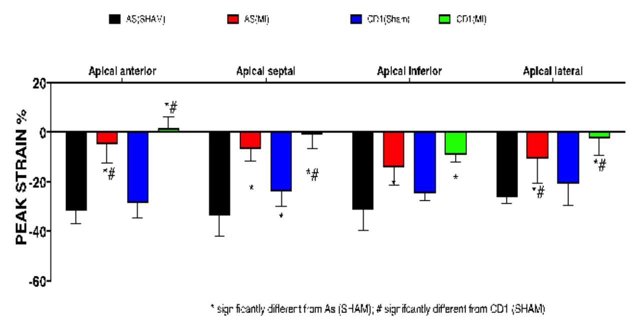

Fig.2 Peak segmental strain of four apical segments in the most distal slice of the apex.

Experimental - Wild-type (CD1) and African spiny (AS) mice aged 3-6 months were divided into four groups: CD1 sham (n=3), CD1 MI (n=4), AS sham (n=3), AS MI (n=3). Left anterior descending (LAD) artery occlusion was performed in the mice to induce MI while sham-operated mice went through the similar surgical procedure without LAD occlusion (SHAM). Thirteen weeks following surgery mice underwent cMRI on 4.7T Oxford Magnet with an Agilent operating system (AMRIS). A quadrature birdcage volume coil was used to acquire ECG triggered short axis CINE images of the left ventricle (LV) from base to apex (6-8 slices; 1mm thick; 12-14 cine frames through the cardiac cycle; spoiled GRE cine sequence; TR=110ms; TE=1.37ms; Flip angle =15^{o}; FOV=25x 25 mm^{2}; matrix=128x128). Composite ε_{cc}% was calculated for the base, mid and apex (region of infarction) of LV and also 4 apical segments as defined by American Heart Association (AHA) using feature tracking module of Segment software (Medviso). At the completion of the study, high resolution imaging of remaining myocardium was performed ex vivo using MRI 17.6T and the vasculature by microCT.

Results and Discussion - In comparison to CD1 mice, AS mice showed higher composite ε_{cc}% production for apex, base and mid regions of the heart (Fig 1). Following MI, ε_{cc}% changed by 70% in the AS and 88% in CD1 within the infarcted zone (Apex of LV) (Fig 1). When strain was compared in the four apical segments from the most distal slice of the apex (Fig 2), all the segments of AS showed greater strain production and less decline in comparison to CD1 mice after MI (apical anterior- AS=-85%, CD1=-106%; apical septal- AS=-79%, CD1=-95%; apical inferior- AS=-55%, CD1=-63%; apical lateral- AS=-60%, CD1=-87%).

Conclusions - This study shows that cMRI can be used as a non-invasive tool to detect changes in cardiac muscles of murine models of MI. These findings also suggest that similar to other tissues, the AS myocardium experiences accelerated regeneration as was evident by greater preservation of circumferential strain post MI. Future studies will build upon these results to better understand the physiological process governing enhanced regenerative capacity in the heart muscle of these mice and potentially help in the development of therapeutic targets of MI infarction in humans.

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References - [1] Hung C,et al. *J Am Coll Cardiol.* 2010;56(22);[2] Hor K et al. *J Vis Exp*. 2011;(48)[3] Hor K., et al. P*ediatr Cardiol.* 2014;36(1):111-9;[4] Seifert A. et al. *Nature*. 2012;489(7417):561-5.;[5] Maden M, et al. *Sci Rep*. 2018;8(1):8920.