BDR SEMINAR in Kobe

"CDB SEMINAR" and "QBiC SEMINAR" have been renamed "BDR SEMINAR".

Yuka Morikawa

Texas Heart Institute

Tuesday, May 22, 2018

16:00-17:00, Seminar Room A7F

The Hippo Pathway and Heart Regeneration

Summary

Regeneration of the postnatal mammalian heart is limited due to the extremely low renewal rate of cardiomyocytes. Mammalian hearts do possess regenerative capacity during development, however after birth, when cardiomyocytes exit the cell cycle, their proliferative capacity is rapidly repressed. Our goal is to repair heart damage by reactivating the endogenous regenerative capacity of cardiomyocytes. Our approach is to uncover and reverse the mechanisms responsible for the repression of cardiomyocyte proliferation.

Our previous studies showed that deletion of the Hippo pathway component Salv results in heart repair after myocardial infarction. We found that repair in Hippo-deficient hearts is through enhanced cardiomyocytes proliferation and protrusion promotion of border zone cardiomyocytes that fill the injury induced scar. Heart deficiency of Salv results in activation of the transcription co-regulator Yap resulting in positive regulation of cytoskeletal and cell cycle genes. In addition, we found that the components of the dystrophin-glycoprotein complex (DGC) are Yap targets. DGC is essential for anchoring the cytoskeleton to the extracellular matrix and muscle maintenance. Surprisingly, the DGC feeds back to the Hippo pathway by sequestering Yap to the cell membrane repressing its transcriptional function including promoting proliferation. Our findings are providing new insights into the mechanisms underlying how heart repairs itself through enhancing regenerative capacity of adult cardiomyocytes.

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