Healing a Broken Heart: Examining the Role of Polycomb Group Protein Asxl2 in Cardiomyocyte Proliferation

Gunderson, Rachel (School: Breck School)
Agyeman-Mensah, Boatemaa (School: Breck School)

Heart disease is the number one killer worldwide, resulting in 800,000 American deaths annually. Scarring of the heart, due to cardiomyocyte death during myocardial infarctions, compromises the muscles' capability to pump blood in a normal rhythm. Cardiomyocytes turnover at a rate of less than 1% per year making natural proliferation of cardiomyocytes insufficient when it comes to regenerating the human heart. Although there are currently no approved treatments to enhance the low proliferative capabilities of cardiomyocytes, a number of genes are known to affect cardiomyocyte proliferation. Preliminary work on the gene Asxl2 reported improved proliferation and de novo cardiomyocyte formation in a knockout mouse model. As a first step to studying the underlying mechanism of Asxl2 mediated inhibition of cardiomyocyte proliferation, we attempted to validate these published results in an Asxl2 knockout mouse model. Tissue samples from wild type and knockout mice were stained on sites positively possessing EdU, a synthetic thymidine analog which marked replicating cells. Immunohistochemistry with cardiomyocyte marking antibodies was used to identify cardiac muscle cells. Images were taken on a fluorescent microscope and quantified to compare cardiomyocyte size, the number of EdU+ cardiomyocytes, and the number of EdU+ non-cardiomyocytes between the knockout and wild type models. The average number of proliferative cardiomyocytes was higher in Asxl2 knockout mice, although this did not reach statistical significance. Further examination regarding the mechanism of Asxl2-dependent gene and chromatin regulation in relation to cardiomyocyte proliferation is warranted in hopes of developing a therapeutic treatment for cardiovascular disease.

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