Effect of Shh Signaling on Neonatal Cardiomyocyte Proliferation

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Regenerative medicine is seen as the future for cardiovascular health. Adult human cardiomyocytes have very little proliferative capacity. However, neonatal mice have shown very high levels of cardiomyocyte proliferation. Other studies have shown that the Shh signaling pathway is integral in many areas of cardiac regeneration. Therefore, the researcher hypothesized that neonatal mouse ventricle cardiomyocytes would have increased proliferation if exposed to a Shh agonist and decreased proliferation if exposed to a Shh inhibitor. Additionally, the researcher hypothesized that if Shh signaling does cause a proliferative response, then the TAZ protein modulates this response. To carry out the experiment, first the researcher determined the best culture conditions in order to obtain 90% pure neonatal cardiomyocytes. Then the cardiomyocytes were cultured in the media containing a Shh agonist, antagonist, or control in order to find the proliferative index. After culturing the cardiomyocytes were analyzed with Western Blotting and immunohistochemistry in order to investigate the mechanism of proliferative response. Immunohistochemical analysis showed that activation of the Shh pathway increased cardiomyocyte proliferation, as well as the percentage of cardimyocytes in the sample, while inhibition of the pathway decreased proliferation. This proved the first two hypotheses. Western blotting analysis showed increased concentration of the TAZ protein in Shh activated samples, and decreased concentration in Shh inhibited samples, proving the researcher's third hypothesis to be correct.