TGF-ß3–Driven Reversal of Mesenchymal Stem Cell Senescence for Improved Regenerative Medicine Applications

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Mesenchymal stem cells (MSCs) have differentiation and anti-inflammatory properties, making them effective treatments for diseases including diabetes and osteoarthritis that affect approximately 1.2 billion people. Treatments are currently limited by senescence, which is permanent cell cycle arrest often resulting from oxidative stress accumulation due to repeated culturing. This project aims to reverse MSC senescence, restoring safe proliferation. Transforming growth factor beta 3 (TGF-beta3) was used to activate Akt, which can expel oxidative stress. First, a molecular dynamic simulation supported the feasibility of Akt activation. Afterwards, in-vitro, four 75cm2 flasks were prepared, by inducing senescence in two of them through hydrogen peroxide, then culturing one hydrogen-peroxide-treated and one untreated flask with TGF-beta3 followed by cell counting. The same was done for four 6-well plates, which would be used to stain for senescence and proliferation markers beta-galactosidase and Ki-67. Lastly, immunoblotting was run for further robustness. Cell counting shows that TGF-beta3, over 24 hours, increased senescent MSC count from ~820,000 to ~960,000, and healthy MSC count from ~2,020,000 to ~2,320,000. Immunoblotting for Ki-67 aligns with these results, as upon visualization, Ki-67 is most clearly detected in the control, completely undetected in the senescent group, and considerably visible in the senescent TGF-beta3-treated group, meaning that the treatment restored proliferation to a large extent. This study supports TGF-beta3 as a potential treatment for senescent MSCs to facilitate safe, sustainable manufacturing of MSC treatments, making them more effective in treating the billions of patients that need them.

Awards Won:
King Abdulaziz &amp
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