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Pluripotent Stem Cells: A New Approach To Tendon Therapy

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Tendons are the white connective tissue, which connect the bones to muscles and are majorly (90-95%) constituted by tenoblasts and tenocytes (Sharma and Maffulli, 2005). Its overuse can injure it, as in runners almost the 30% injuries are due to its overuse, while in tennis players nearly 40% injuries are of elbow-tendons. The term tendinopathy is also used for tendon injury and patients usually recovered from it after several months, it can also cause morbidity (Sharma and Maffulli, 2006). The late recovery of patients is due to tendon's slow metabolic rate, as they use less oxygen than other tissues and involve anaerobic pathway. Moreover, the recovered tends can never behave and function like the normal ones. Its course of pathogenesis includes both inflammation and degeneration of tendon tissues, but it is difficult to differentiate them as major or minor contributors (Abate *et al*., 2009). It can be treated through the use of Mesenchymal Stem Cells (MSCs) of bone, which were previously used to heal bone fractures (Chong *et al*., 2009; Kraus and Kirker-Head, 2006). But this technique is under development as mechanisms of its action is yet unknown. Moreover, the survival rate of MSCs is less than 5% and their number decreases with time (Guest *et al*., 2010). Today many other techniques e.g., surgical, injection-based and shock waves are also used to treat tendinopathy, but they have non-scientific significance (Gaida and Cook, 2011). Thus, the pathogenesis and treatment of tendinopathy needs critical investigation and there should be more reliable technique to treat tendon injury.

Kim *et al*. (2010) observed that some genetic changes in induced pluripotent stem cells could modify their functions. This newly incorporated information would retain in them forever and can be changed when needed, thus may be used to treat various diseases. Recently Watts *et al*. (2011) conducted a research on large animal model (horse) to find out the significance of pluripotent cells in reducing the tendon lesions. They incorporate the male fetal cells line OK-100™ (fetal derived embryonic-like stem cells (fdESC)) in female's collagenase-induced tendon lesions and compare it with placebo control group. The implemented fdESC treatment brought many histological modifications in this tissue, like it reduced the lesion cross sectional area and irregularity of tendon fibers. Both these parameters were significantly different from the control group and the treatment proved its efficiency shortly after the application. This was confirmed by the time based analysis of the tendon injury through magnetic resonance imaging. In these images, the fdESC treated tissues were more regularly organized than the control group and the lesions were restricted to only small areas. The other significant improvements in the injury accessed by pluripotent cell treatment include improved cell shape, reduced inflammation and minimized peritendinous reactions. Although the externally supplemented cells actively grow, there was no tumor formation, thus it was safe treatment. This may be due to non-cellular behavior of these cells as only fewer DNA and RNA were found in these cells. However, these cells were normal and more active in reducing the disease symptoms. But the new generated tendon cells showed small lives in female receiver, which might be the result of immunogenic reactions against the Y-chromosome of male cells. Another important thing observed during the study was the invisibility of disease-injection needle tracts in the fdESC treated muscles, which were apparent in control group. This result verified the significance of treatment in tendon injuries as it reduced the disambiguated tissue structure. Thus, pluripotent cell treatment was a remarkable treatment for tissue injuries as it induced many histological improvements in tendon tissue. But there's need of further research accompanying the biochemical analysis of tendon cells to fully explore the significance of the used treatment. Furthermore, a large time based study with more parameter and animals should be conducted, as in this experiment only seven animals were examined for eight weeks. However, it was a noble experiment, as it explored the significant beneficial effects of fdESC in short time-based study.

Thus, tendons being the important part of human body are often severely injured by overuse. Although, various treatments are applied to deal with its injuries, every technique has its own limitation. But the research conducted by Watts *et al*. (2011) provided a base line for reliable treatment of tendon injuries. They use fetal pluripotent cells (fdESC) to treat the collagenase-induced tendon lesions in horse model, which showed significant positive results. These cells have the capability to reduce the lesions and structural incompatibility of tissues, without causing any signs of teratoma. So, the fdESC can be used to treat the tendon lesions, but its biochemical behavior needs more investigation.

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