

Conditioned Medium from Adipose-Derived Mesenchymal Stem Cells: A Promising Strategy for Treating Diabetic Tendinopathy

Gabriele Martin, Annalisa Iтро, Gianluca Conza, Niccolò Garofalo, Maria Consiglia Trotta, Adriano Braile, Marina Russo, Giuseppe Toro

INTRODUCTION: Tendinopathies are musculoskeletal conditions that cause persistent pain, particularly in athletes, due to structural tendon alterations. Their management is often difficult, with conventional treatments such as NSAIDs and corticosteroids offering limited and inconsistent benefits. Regenerative medicine, particularly cell-based therapies using adipose-derived mesenchymal stem cells (ASCs), presents a promising alternative for tendon repair. To mitigate potential risks linked to ASC use, extracellular vesicles and ASC-conditioned medium (CM) are being investigated. However, the underlying mechanisms of chronic tendinopathy—especially in diabetic conditions—are not yet fully understood. This study explores the effects of ASC-CM on diabetic tenocytes subjected to scratch wound injury, focusing on the modulation of the TGF- β 1 signaling pathway, which is often impaired in diabetic tendons and contributes to hyperglycemia-induced changes.

METHODS: Human tenocytes (HTCN) were cultured in normal (5 mM) or high glucose (25 mM) conditions for 7, 14, and 21 days. For the final 24 hours, cells were treated with ASC-CM obtained from ASCs isolated from microfragmented adipose tissue of patients with early osteoarthritis. Cell viability, morphology, and scratch wound closure were assessed. TGF- β 1 pathway activity was analyzed using ELISA, qRT-PCR, and immunofluorescence.

RESULTS: HTCN exposed to high glucose (HG) showed reduced viability at 7 days ($72 \pm 2\%$, $p < 0.01$ vs. normal glucose, NG), with further declines at 14 and 21 days ($60 \pm 4\%$ and $60 \pm 5\%$, both $p < 0.01$ vs. NG and HG7). HG-HTCN also developed a more rounded, less fibroblast-like morphology. Treatment with ASC-CM significantly improved viability, restored cell morphology, and enhanced wound closure in HG conditions across all time points. Moreover, ASC-CM increased TSP-1 and TGF- β 1 levels, along with upregulation of collagen I (Col I) and VEGF.

DISCUSSION AND CONCLUSION: ASC-CM appears to improve tenocyte function in high-glucose conditions by enhancing cell structure and viability and restoring TSP-1 and TGF- β 1 levels. These results support its potential as a therapeutic approach for diabetic tendinopathy, although clinical trials are necessary to confirm efficacy.