Washington University in St. Louis
Office of Technology Management

# EXOSOME-BASED THERAPY FOR TENDON INJURIES AND OTHER SOFT TISSUE REPAIR

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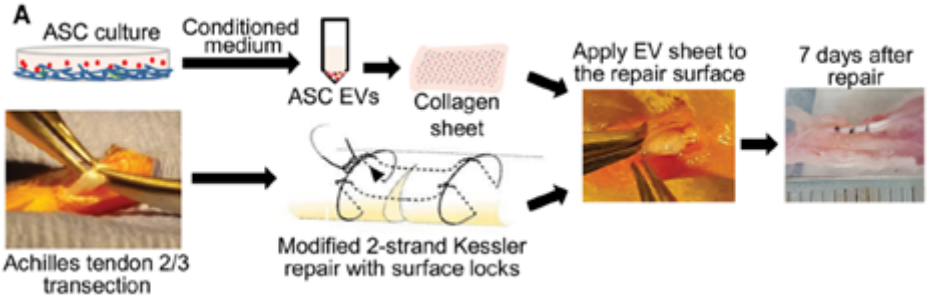
## Technology Description:

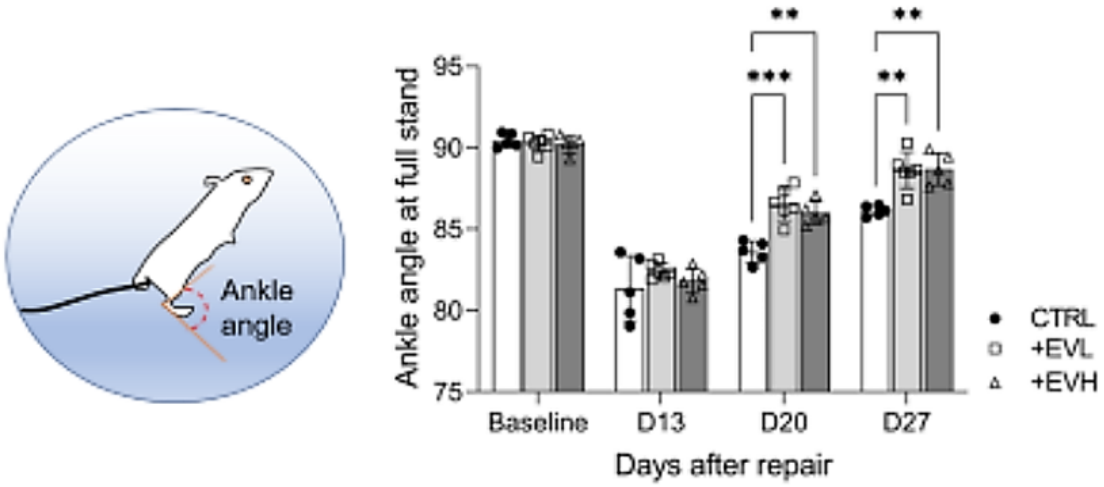
A team of researchers at Washington University has developed a cell-free, nano-sized extracellular vesicle (EV/exosome) system to enhance repair of soft musculoskeletal tissue. This technology leverages the natural anti-inflammatory effects of adipose-derived stem cells (ASCs) through derived exosomes and includes a local delivery mechanism that promotes healing.

The underlying cause of poor outcomes following many soft tissue injuries (Achilles tendon rupture, rotator cuff tear, flexor tendon injury) is inflammation triggered by macrophages. ASCs can be used to curb inflammation, but they have safety concerns and are hard to deliver to the repair site. Exosomes secreted by the ASCs provide an alternative approach by mimicking the anti-inflammatory function of ASCs but avoiding some safety concerns and offering improved features.

These exosomes can be delivered locally via a collagen sheet and can penetrate the injured tissue because they are nano-sized. In addition, they have the potential to be selectively enriched with active molecules (e.g., miRNA) to further enhance healing.




*Schematic illustration of process and preparation of delivering adipose-derived stem cell (ASC) extracellular vesicles (EV's, also known as exosomes) to a mouse model of Achilles tendon transection and repair.*




*Mice who received ASC exosomes recovered range of motion more quickly following Achilles tendon repair*

**Stage of Research:**

The inventors have used a mouse model of Achilles tendon injury to demonstrate the effects of primed ASC exosomes in modulating tissue inflammatory response, promoting tendon matrix regeneration, and reducing post-operative rupture/gap formation. The priming effect is likely associated with selective enrichment of certain regulator miRNA cargos within the exosomes.

**Applications:**

- Exosome therapy for soft tissue injury – enhance healing after tendon, ligament or cartilage injuries

**Key Advantages:**

- **Nano-sized and cell-free –** ASC-derived exosomes mimic the function of ASC's to modulate inflammatory response with improved features:
  - readily deliverable in large quantities to full thickness tissue through biological barriers
  - eases safety concerns of stem cell therapy
  - potential to enhance effects by loading with therapeutic cargo such as miRNA or other agents
  - stable membrane lipid composition that could protect, carry and delivery a variety of functional agents)
- **Targeted and local delivery**
  - exosomes have cell surface markers that could enable cell-specific interactions and delivery of therapeutic cargo
  - collagen sheet can be used for local and retained delivery of exosomes to site of surgical repair

**Publications:**

- Shen, H., Yoneda, S., Abu‐Amer, Y., Guilak, F., & Gelberman, R. H. (2019). Stem cell‐derived extracellular vesicles attenuate the early inflammatory response after tendon injury and repair. *Journal of Orthopaedic Research*.

**Patent Application:** WO2020102684

**Related Web Links:** Shen Profile