Bone Marrow-Derived Mesenchymal Stem Cells Yield Greater Pain Relief and Tissue Protection than Umbilical Cord Tissue-Derived Cells in a Surgically Induced Instability Model of Osteoarthritis

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INTRODUCTION: Intra-articular mesenchymal stem cell (MSC) injections are rapidly increasing as a viable treatment option to relieve pain and slow disease progression of osteoarthritis (OA). Clinical and preclinical studies have demonstrated efficacious effects, yet variability in treatment protocols, donor source, and patient status have considerably slowed translation to a consistent therapy. Bone marrow (BM) and adipose tissue are the most common MSC sources currently in clinical use (typically as a heterogeneous cell mixture such as bone marrow aspirate concentrate (BMAC)), but require point-of-care harvest for autologous use that may have reduced quality in older and/or osteoarthritic individuals (1). Postnatal tissues, including the umbilical cord tissue (UCT), have gained popularity as an alternative, autologous MSC source due to their lack of ethical concerns, compatibility with manufacturing (high proliferation and cell line stability), and high transcriptional consistency (2). Variations in microenvironment, ontogenic age, and cell heterogeneity between sources could impact MSC efficacy for OA. In this project, we directly compared the therapeutic efficacy of human BM- and UCT-MSCs in relieving OA pain and slowing tissue degradation in a preclinical rat model. To investigate the potential role of cellular heterogeneity, we also evaluated BM-MSCs in a pilot experiment. We hypothesized that efficacy would differ between MSC sources, but that UCT-MSCs would provide a less variable source among donors.

METHODS: BMAC and UCT-MSCs were provided by our collaborators from an ongoing multicenter clinical trial (MILES; NCT03818737). BM-MSCs were generated by in vitro expansion of the MSC population in bone marrow aspirate concentrate (BMAC). UCT-MSCs were classified as adherent cells cultured from BMA aspirate concentrate (BMAC)). We assessed donor variability by including cells from three UCT donors (including one donor with t...