

3. NON-TECHNICAL ABSTRACT

Degenerative arthritis is the most frequently encountered orthopedic disease associated with cartilage damage. Almost every joint in the body, such as the knee, the hip, the shoulder, and the wrist, is susceptible to cartilage damage. If the degenerated cartilage could be replaced, most patients would be able to function without debilitating pain. A cell-mediated cytokine gene therapy approach for cartilage regeneration, such as that proposed with TissueGene-C, does not require an operation nor a lengthy rehabilitation time, whereas the autologous cell-based therapy and cytokine protein-based therapy involves at least one operation and a substantial rehabilitation time.

The purpose of this study is to see if we can safely regenerate cartilage without invasive surgery using a biologic product called TissueGene-C. TissueGene-C is human chondrocytes, some of which have been modified with DNA that contains the gene for transforming growth factor beta 1 (TGF- β 1). TGF- β 1 has been shown in laboratory testing to stimulate chondrocytes to form cartilage. In addition to its stimulatory action on chondrocytes, TGF- β has been shown to possess anti-inflammatory and immune suppressive properties, which has led to recent reports on the therapeutic value of the TGF- β protein in orthopedics. However, widespread clinical applications of this protein have been limited due to its short-term effects as a result of a short half-life. By delivering cells that express TGF- β 1, longer-term effects of TGF- β 1 can be realized. TissueGene-C is intended to promote the formation of new cartilage via stimulation of both endogenous cells and exogenous chondrocytes administered as part of the TissueGene-C treatment.

This proposed initial study is intended to assess the safety of TissueGene-C when injected into the knee joint. The patients selected for this study will have degenerative arthritis of the knee that requires surgical replacement of the knee joint. TissueGene-C will be administered four weeks prior to surgical replacement of the knee joint. The patients will receive TissueGene-C by local injection to the knee joint cavity. Groups of patients will receive increasing doses of TissueGene-C. Because of this, the first patients to be treated in this study will receive lower doses of TissueGene-C than the later patients, watching for side effects to be sure that it is safe to give the higher doses. Four weeks after injection the patient will undergo knee replacement as scheduled, thus removing the TissueGene-C cells and minimizing the risk to the patient.