

**Project Title:** Temporal Understanding of the Conversion of Normal Synovial Fibroblasts into Osteoarthritic Fibroblasts.

### ***Project Description***

Osteoarthritis (OA) is the most common form of arthritis debilitating individuals all across the world. This disorder is characterized by severe inflammation of synovial joints, or joints distinguished by the presence of a fluid filled space, called an articular cavity. The articular cartilage, cartilage that protects the ends of bones forming joints, also faces gradual degradation as a result of this disorder. As OA progresses, all of the joint's components are involved in responding to inflammatory signals and in contributing to the destruction of the joint and its cartilage. The primary cellular components participating in this degradative process are synovial fibroblasts, cells involved in providing fluid and components of the extracellular matrix to the articular cavity; synovial macrophages, cells that work to remove undesirable molecules from the articular cavity and maintain a balance of pro-inflammatory and anti-inflammatory proteins, called cytokines; and resident chondrocytes, cells involved in maintaining and repairing articular cartilage (Figure 1).

Although information concerning late-stage OA and its effects on these components is abundantly available, there is a lack of information centered around the conversion of normal cells to diseased cells. Due to their role as mediators involved in carrying out messages from macrophages to chondrocytes when subject to inflammatory signals, we will choose to work with synovial fibroblasts. The focus of this investigation in turn, will be to better understand the conversion of normal fibroblasts to OA fibroblasts. Using sodium alginate hydrogels to encapsulate and simulate a 3D structure for the normal fibroblasts, we will investigate how placing these cells in an inflammatory environment can affect their potential to become osteoarthritic cells. As Interleukin 1-beta (IL-1 $\beta$ ) and Tumor Necrosis Factor-alpha (TNF- $\alpha$ ) have been shown to be pro-inflammatory cytokines released by macrophages and have been shown to be critical to the deterioration of chondrocytes and components of the extracellular matrix, they will be used to mimic an inflammatory environment.

### ***Project Impacts***

Through the results of this research, we will be able to interpret the impact inflammation could potentially have on the transformation of synovial fibroblasts to osteoarthritic fibroblasts. By performing this research, we would thus be able to obtain vital information that could bring us closer to improving upon the autologous chondrocyte implantation method as a means to enhance surgical treatment of cartilage damage induced by OA.

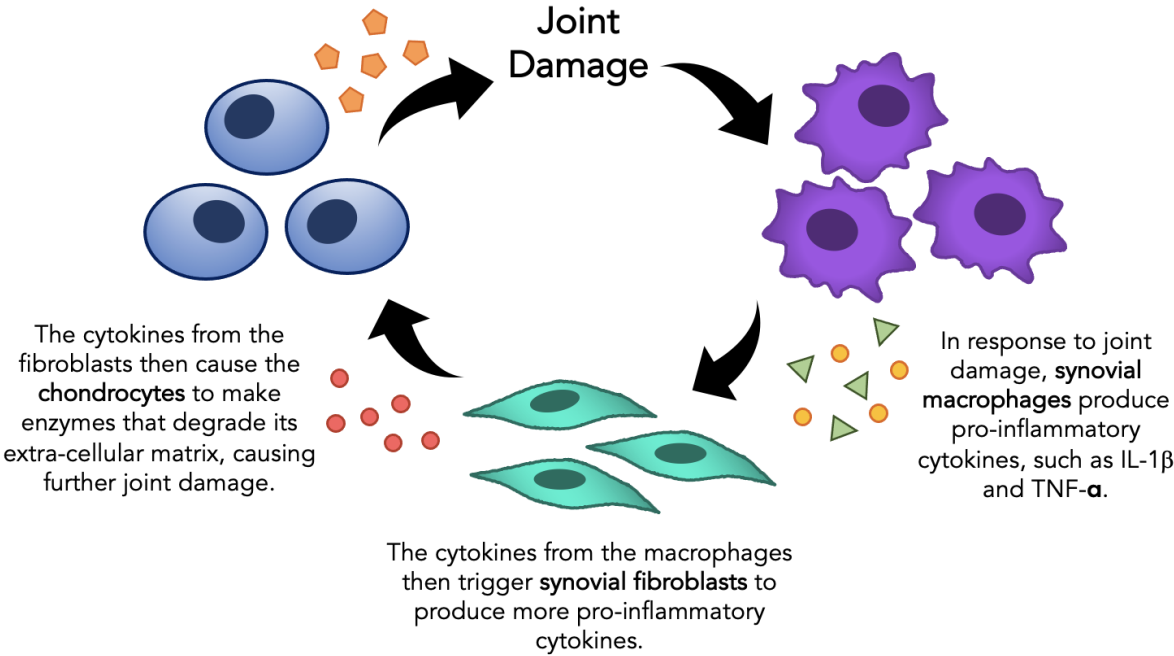
### ***Timeline***

12-week period from May 17, 2021 to August 3, 2021.








### ***Contingency Plan***

We will take all precautions and adhere to the posted UAH COVID guidelines. Wearing face masks, gloves, and lab coats will be strictly mandated. Work hours will be clearly posted. No more than two students will be allowed to work in a 600 square-foot laboratory and social distancing has to be practiced at all times. Most meetings will be via Zoom. In the event the laboratory has to scale-down due to unprecedented COVID rates, a staggered work schedule will be adopted to limit access to one student at a time.

**Figure 1.** Communication between synovial macrophages, synovial fibroblasts, and chondrocytes.



Key

- |   |                     |   |  |
|---|---------------------|---|--|
|  | Synovial Macrophage |  | Interleukin 1-beta (IL-1 $\beta$ )           |
|  | Synovial Fibroblast |  | Tumor Necrosis Factor-alpha (TNF- $\alpha$ ) |
|  | Chondrocyte         |  | Pro-Inflammatory Cytokine                    |
|   |                     |  | Degradative Enzyme                           |