

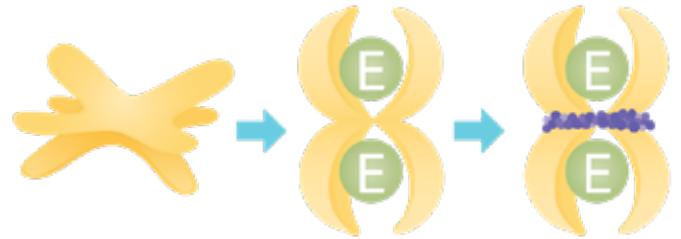
## THE POWER OF ALPHA-2-MACROGLOBULIN

Alpha-2-Macroglobulin (A2M) is a naturally occurring and abundant molecule found in blood. A2M has a broad-spectrum inhibiting activity against many enzymes, including those that are involved in inflammation and cartilage breakdown. This unique protein is quite large, therefore, it is not abundantly found in the joints. Research identified that patients affected by osteoarthritis have lower levels of A2M in the synovial fluid of the affected joints [1]. Hence, it is believed, that by administering supraphysiological concentration of A2M to a joint affected by inflammation and/or cartilage degradation, it can halt these negative events and thereby provide a potential therapeutic relief.

The therapeutic potential of A2M has been shown in a study for patients affected by lower back pain due disc degeneration [2]. The administration of A2M biologic in the disc was associated with improved pain scores and increased back functionality that lasted up to 24 weeks. This effect was likely to be present in response to A2M injection when participants tested positive for a unique biomarker associated with cartilage breakdown known as Fibronectin-Aggregan Complex (FAC). Overall, 77% of participants that tested FAC positive and 27% that tested FAC negative had a significant clinical improvement in their scores.

### References

- 1 Identification of Alpha 2 Macroglobulin (A2M) as a master inhibitor of cartilage degrading factors that attenuates post-traumatic osteoarthritis progression. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4187342/>
- 2 Intradiscal Injection of an Autologous Alpha-2-Macroglobulin (A2M) Concentrate Alleviates Back Pain in FAC-Positive Patients. <https://juniperpublishers.com/oroaj/pdf/OROAJ.MS.ID.555634.pdf>
- 3 Fibronectin–aggregan complex as a marker for cartilage degradation in non-arthritis hips. <https://www.ncbi.nlm.nih.gov/pubmed/24477496>
- 4 Identification of a novel fibronectin-aggregan complex in the synovial fluid of knees with painful meniscal injury. <https://www.ncbi.nlm.nih.gov/pubmed/21325584>
- 5 Early supplemental α2-macroglobulin attenuates cartilage and bone damage by inhibiting inflammation in collagen II-induced arthritis mode. <https://www.ncbi.nlm.nih.gov/pubmed/30609267>



High FAC levels were also found to be present in painful knees with meniscal injury as well as in non-arthritis hips with cartilage degradation [3,4]. Therefore, administration of A2M can potentially alleviate the symptoms and improve functionality of the joint affected by cartilage breakdown and inflammation [1,5]. However, conducting a formal clinical study is necessary to demonstrate this effect on large scale population.

The ALPHA2ACTIVE™ system (formerly APIC-A2M™) is a patented and proprietary process that concentrates A2M from blood to supraphysiological levels that can be administered as an injection into the tissue at the injury site. The ALPHA2ACTIVE™ system is an FDA 510(k) cleared device. Determination of FAC levels are performed using a laboratory developed test in a CLIA certified laboratory at the request of a licensed physician.