

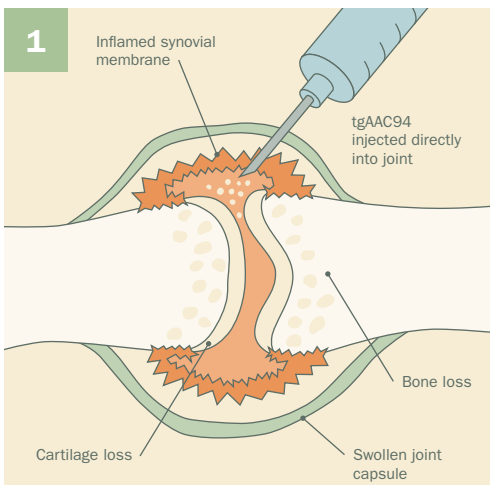
# DEVELOPING TARGETED LOCALIZED PROTEIN THERAPY FOR INFLAMMATORY ARTHRITIS



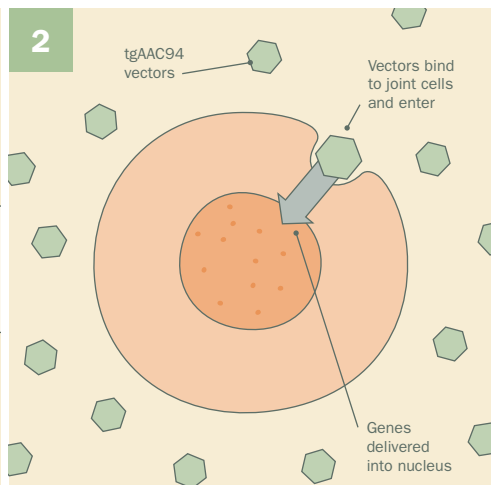
Targeted Genetics is advancing the company's lead clinical product candidate, tgAAC94, for inflammatory arthritis. tgAAC94 is an investigational therapeutic for local treatment of inflammatory joint diseases aimed at inhibiting the activity of the proinflammatory cytokine, tumor necrosis factor alpha (TNF $\alpha$ ). The diagrams below illustrate how tgAAC94 is designed to work.

TNF $\alpha$  is a key mediator of joint-related inflammation and damage to cartilage and bone. Systemic TNF $\alpha$  inhibitor therapies have been approved for treatment of inflammatory diseases, including rheumatoid arthritis. Though systemic TNF $\alpha$  therapies have a positive impact on arthritis symptoms, many patients continue to experience painful inflammation in one or more affected joints.

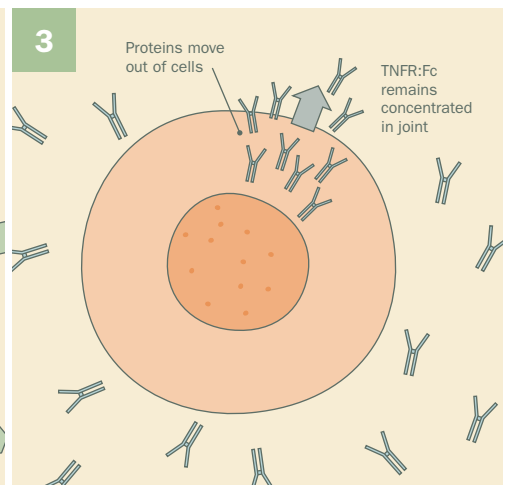
Currently in Phase I/II clinical trials, tgAAC94 is being developed to complement other anti-inflammatory therapies already on the market. Potential benefits may include relief in joints not responding to other therapies, long-term symptom reduction, reduction in progressive bone and cartilage loss, and improved quality of life.



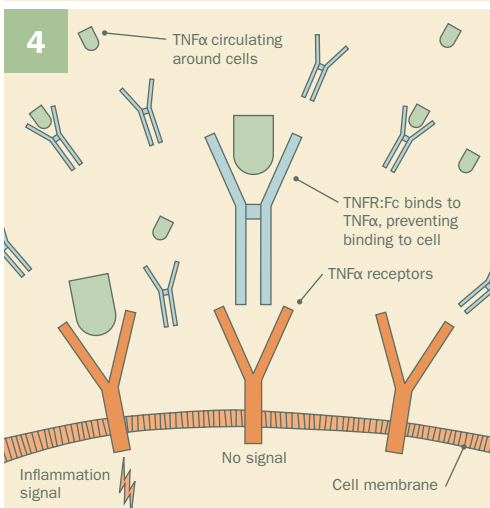
tgAAC94 is injected directly into the arthritic joint where TNF $\alpha$ , a proinflammatory cytokine, is implicated in disease-related inflammation that causes tenderness, swelling, and tissue damage.



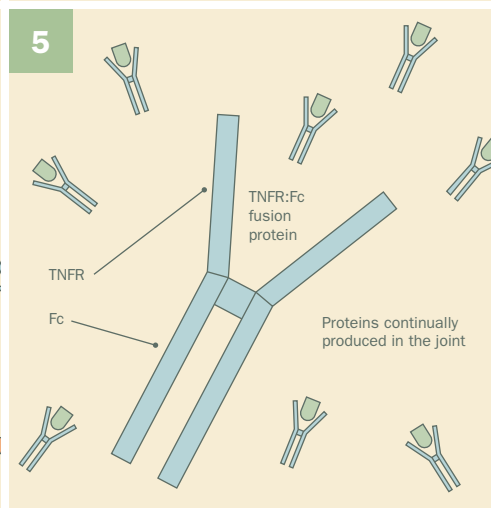
After injection, the tgAAC94 vectors bind to and enter joint cells, where they deliver genes into the nucleus. The nucleus then instructs the cells to produce TNFR:Fc (TNF $\alpha$  receptor: immunoglobulin [IgG1] Fc), a potent TNF $\alpha$  inhibiting protein.



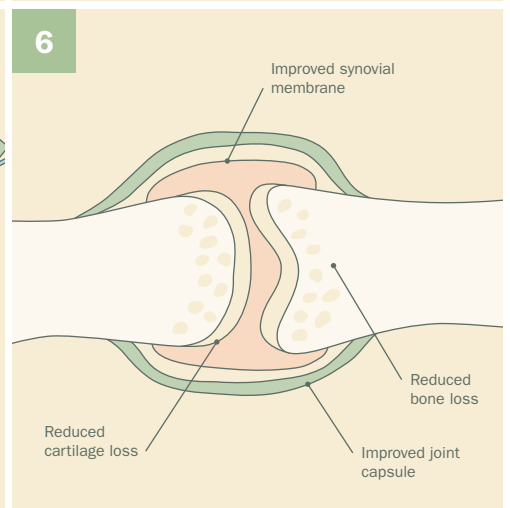
The TNFR:Fc proteins move out of the cells and concentrate within the joint, where they inhibit TNF $\alpha$  and reduce other proinflammatory cytokines.



The therapeutic benefits of TNFR:Fc proteins result when they bind to TNF $\alpha$  molecules, inhibiting them from binding with receptors in the cell membrane. Thus blocked, TNF $\alpha$  is unable to cause joint inflammation.



The joint cells produce an ongoing supply of the TNFR:Fc protein over a long period of time.



Following injection with tgAAC94, the patient may experience relief from tenderness and swelling, and reduced bone and cartilage loss, the most damaging effects of rheumatoid arthritis.