

# TGF-β Neutralization Therapy and Surgical Posterior Capsule Release Exhibit Similar Efficacy in a Rat Model of Knee Stiffness

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**INTRODUCTION:** Knee arthrofibrosis, characterized by excessive and dysregulated scar tissue formation under the influence of TGF-β, remains a debilitating complication that substantially limits postoperative range of motion after total knee arthroplasty (TKA). There are currently no widely used pharmacologic treatments to target TGF-β and prevent arthrofibrosis. In this therapeutic void, new pharmacologic approaches, as well as surgical interventions, such as posterior capsular release, have been explored to mechanically restore knee extension by excising the posterior capsule of the knee joint to release contractures. The efficacy of such interventions has been unclear. Furthermore, utilizing this surgical release in combination with emerging therapies remains unexplored.

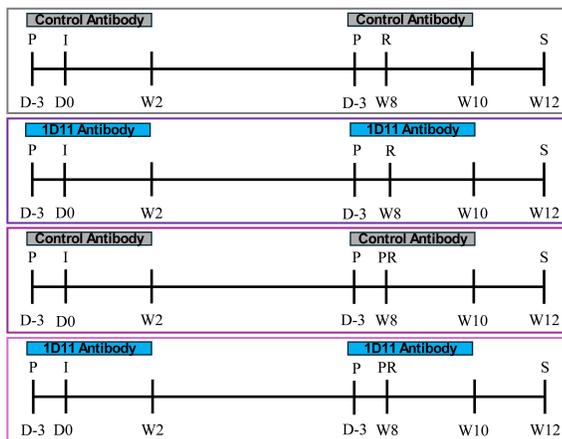
**METHODS:** This study was approved by our Institutional Animal Care and Use Committee (IACUC). A total of 40 female Sprague-Dawley rats were separated into groups of n=10. Rats either received TGF-β neutralizing antibody (1D11, neutralizes all TGF-β isoforms, including TGF-β1, TGF-β2, and TGF-β3) or isotype control antibody. The right hindlimb of rats were immobilized in knee flexion with a 2-0 stainless steel suture for 8 weeks. During the immobilization surgery, rats also had cortical defects drilled into their medial and lateral femoral condyles and their posterior capsule was disrupted via knee hyperextension. The rats were injected intraperitoneally with antibody or control 3 days before immobilization, at immobilization surgery, and every other day for 2 weeks. The same injection protocol was performed at remobilization surgery, where the steel suture was removed and the rats were allowed free movement for 4 weeks. At the remobilization surgery, two of the four experimental groups received a posterior capsule release by sharp dissection of the posterior capsule from the posterior aspect of the femoral condyles. After 4 weeks, the rats were sacrificed and their harvested knees tested on a load-cell based biomechanics device (Figure 1). The resulting angle and torque data were evaluated by Kruskal-Wallis with Dunn's Multiple Comparisons within a torque range of 1-10 N·cm.

**RESULTS SECTION:** At a torque threshold of 3 N·cm, the Control-Control group (received control antibody at all time points without posterior capsule release) was significantly more stiff than all other groups, including rats that received the 1D11 antibody at all time points with a posterior capsular release at the time of remobilization (1D11-PR group), rats that received the isotype control antibody with a posterior release (Control-PR group), and rats that received the 1D11 antibody at all time points without a posterior release (1D11-1D11 group). The mean increase in range of motion relative to the Control-Control group was 32.8 ± 6.5° for the 1D11-PR group, 21.2 ± 4.6° for the Control-PR group, and 18.0 ± 4.1° for the 1D11-1D11 group. The 1D11-1D11 group was not significantly different from either the 1D11-PR or Control-PR groups (Figure 2).

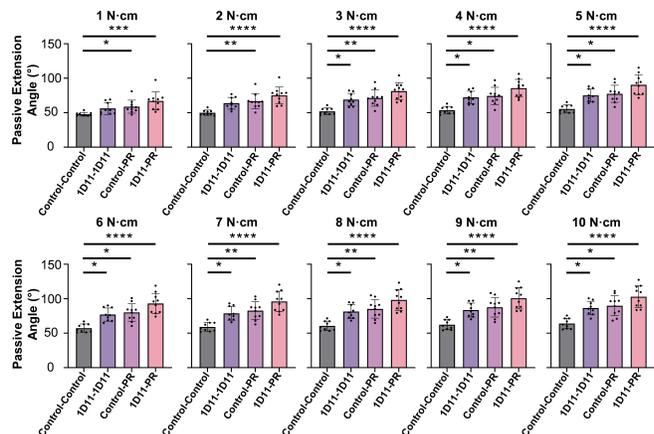
**DISCUSSION:** Posterior capsular release and TGF-β neutralization independently reduce joint stiffness in a rat model of knee stiffness. Rats receiving the combination of 1D11 antibody and posterior capsular release (1D11-PR group) yielded the greatest improvement. However, the lack of a statistically significant difference between the combination group and the monotherapy groups suggests that the effects of 1D11 and posterior release may not be additive, or that a therapeutic ceiling was reached. These findings underscore the mechanical benefit of posterior capsular release and reinforce the antifibrotic potential of TGF-β blockade, while also highlighting the need for further investigation into optimizing the timing and synergy of combined surgical and pharmacologic treatments.

**SIGNIFICANCE/CLINICAL RELEVANCE:** Arthrofibrosis remains a challenging complication following total knee arthroplasty, with current interventions limited to surgical procedures. This study provides evidence that posterior capsular release and TGF-β inhibition independently reduce postoperative knee stiffness and may serve as viable strategies, whether alone or in combination, to improve range of motion. These findings support a multimodal therapeutic approach and provide the basis for future translational studies aimed at integrating mechanical and biologic treatments for arthrofibrosis.

## IMAGES AND TABLES:



**Figure 1.** Experimental design. P = pre-treatment, I = index surgery, R = remobilization surgery, PR = posterior capsule release during remobilization surgery, S = sacrifice, D = day, W = week.



**Figure 2.** Biomechanical analysis comparing experimental groups with and without posterior capsule release. p\* = 0.01-0.04, p\*\* = 0.007-0.009, p\*\*\* = 0.0001, p\*\*\*\* = <0.0001.