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Osteoarthritis Drug Discovery

Validated Translational Disease Models and Histopathology Services

Preclinical osteoarthritis (OA) research is challenging as its onset is driven by different mechanisms, resulting in diverse array of symptoms such as joint pain, inflammatory flares, and cartilage lesions. Additionally, choosing the best OA model is difficult as there is not a single model which encompasses all sequelae of this disease. Inotiv's scientists are experts in modeling OA joint damage using a variety of induction techniques, giving you a range of options for choosing the best model to assess your novel therapeutic.

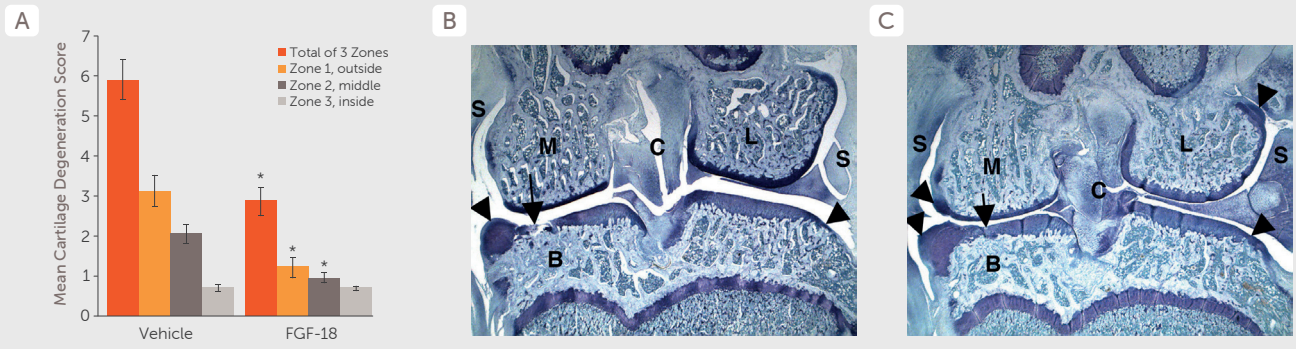
Models for Post-Traumatic Osteoarthritis

A key feature of post-traumatic OA (PTOA) is the active degradation of cartilage, specifically its main components, following injury to the joint. Rodent models with surgically induced localized lesions in the knee offer researchers a translational model that mimics PTOA and are powerful tools that enable scientists to investigate the mechanism, evaluate factors, and screen novel therapies for preserving cartilage and initiating regeneration.

Models

- Rat Medial Meniscal Tear
- Mouse Destabilization of the Medial Meniscus
- Rat Destabilization of the Medial Meniscus

Figure 1 Evaluation of FGF-18 Treatment on Cartilage Repair in the Rat Medial Meniscal Tear Model



Rats with meniscal tear-induced OA in one knee received weekly injections, starting 7-days post injury (dpi), of FGF-18 (3 µg) or vehicle into the operated knee. At 28-dpi, the damaged knee joints were isolated, fixed and stained with toluidine blue for histological analysis of medial tibial cartilage degeneration. (**A**) Mean cartilage degeneration scores for three equally spaced regions across the medial tibial plateau surface, Zone 1 (outside region, orange bars), Zone 2 (middle region, dark grey bars), Zone 3 (inside region, light grey bars), along with the sum of the three areas (red bars). **P<0.05 FGF-18 treated versus vehicle for respective zone.* (**B-C**) Photomicrographs of toluidine blue-stained sections of knee joints from rat medial meniscal tear OA models treated either with vehicle (**B**) or FGF-18 (**C**). Arrowheads indicate proliferative changes in the marginal zone and "S" indicates synovial thickening with proteoglycan deposition. M = medial, C = cruciate ligament, L = lateral, B = bone, S=synovium.

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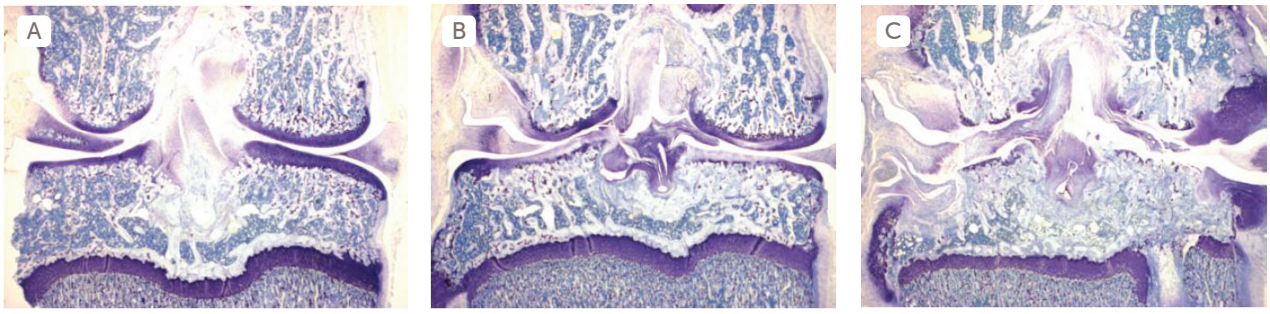
Models and Assays for Osteoarthritis Pain

OA is a major source of chronic pain, and the pharmacological options currently available to treat OA pain have several limitations, including inadequate relief and potential toxicity. Chemically induced OA rodent models are valuable tools for researching OA pain as the injected agents cause chondrocyte death, resulting in inflammation and subsequently joint damage.

Models

- Rat Monoiodoacetate-Induced Osteoarthritis
- Rat Peptidoglycan Polysaccharide-Induced Osteoarthritis

Figure 2 **Histological Evaluation of Knee Joint in Rats Injected with Monoiodoacetate**

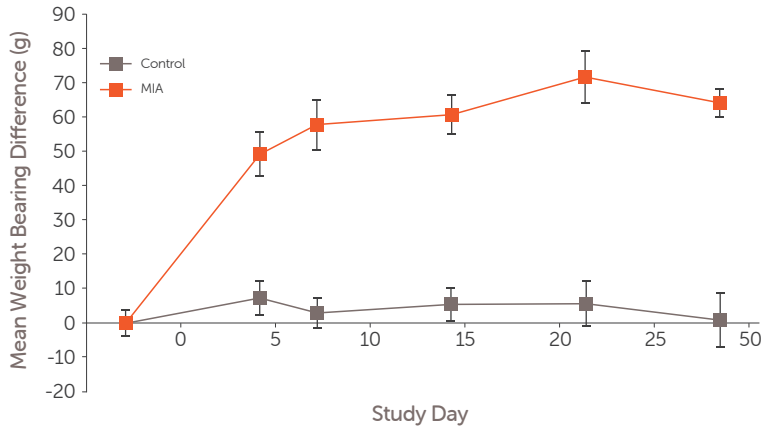


Rat knee joints, stained with toluidine blue, from rats injected intra-articularly with saline (**A**), 0.5 mg of monoiodoacetate (MIA, **B**) or 2.0 mg of MIA (**C**). The lower dose of MIA results in milder, more variable lesions whereas the higher dose of MIA results in severe, more consistent lesions.

Assays for Evaluating Pain and Inflammation

- Gait Analysis
- Knee Swelling
- Inflammatory Pain Assessment
- Bone Pain Assessment
- Von Frey Analysis
- Weight Bearing Analysis

Figure 3 **Analysis of Hind Paw Weight Bearing in Rat Model of Monoiodoacetate-Induced Osteoarthritis**



Weight bearing asymmetry, a translatable measure of joint pain, was assessed in a rat model of MIA-induced OA (red boxes) and control animals (grey boxes). Rats treated with MIA exhibited differences in weight exerted by its hind paws, with the untreated (left) limb wielding more weight than the treated (right) limb. There was little difference in weight exerted by the hind paws of the control rats.

Demonstrating efficacy of novel therapeutics can require assessing additional endpoints. Contact us at **inotivco.com/contact** to discuss the data you need to assess your therapeutic and how our models and services can support your OA drug development program.