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Drug Discovery for Rheumatoid Arthritis
## Proven Disease Models for Translational Research

Drug discovery for rheumatoid arthritis (RA) is vital, as many patients remain unresponsive to current treatments. Inotiv advances this research by providing validated RA models and conducting contract studies to assess the efficacy and safety of new therapies.

Models of RA

Choosing the best RA model for evaluating a novel drug is challenging due to the disease's complexity and the diversity of symptoms. No single model fully replicates human RA, which can lead to discrepancies between preclinical and clinical results. Inotiv's scientists specialize in modeling RA joint damage with various induction techniques, offering multiple options to help you select the most suitable model for evaluating your novel therapeutic.

- Adjuvant arthritis (AIA) in rat
- Antigen-induced knee and/or footpad arthritis in mouse
- Collagen antibody-induced arthritis (CAIA) in mouse
- Collagen-induced arthritis (CIA) in mouse and rat

**Figure 1** Effect of CIA on Ankle Diameter in Rats Over Time
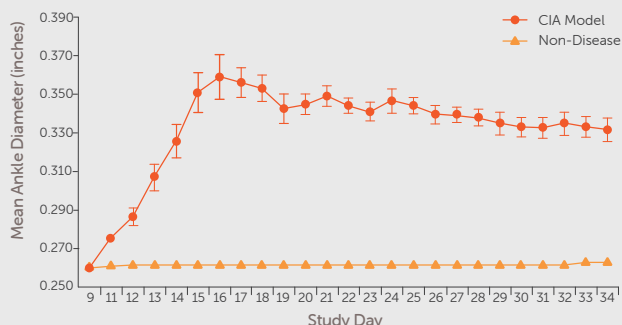
CIA was induced in female Lewis rats by immunization with porcine type II collagen in incomplete Freund's Adjuvant. Caliper measurements of ankle diameter of CIA rat models (red circles) and non-disease control animals (orange triangles) were taken daily starting study day 9 through termination. $p \leq 0.05$ ANOVA to non-disease animals.

Figure 2 Anti-Type II Collagen Antibodies in CIA Rat Models
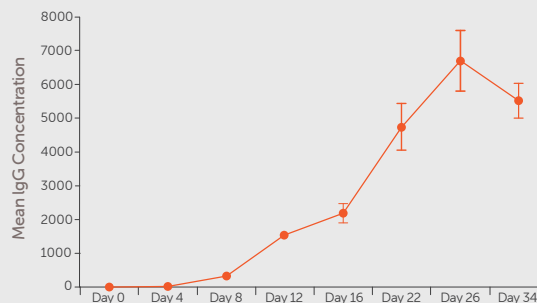
Concentration of autoantibodies to rat type II collagen, which induce arthritis, in terminal serum samples from a CIA rat model.

**Figure 3** Effects of Dexamethasone on Clinical Arthritis Scores in a CAIA Mouse Model
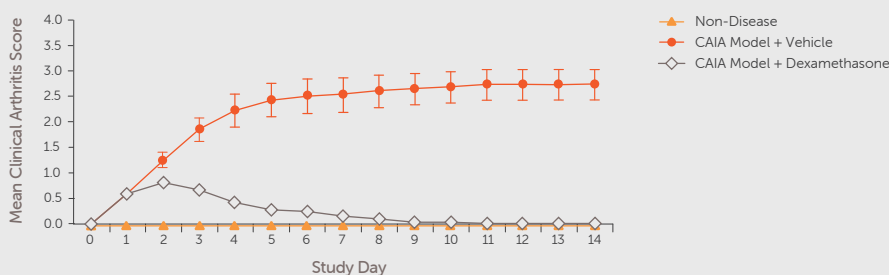
CAIA was induced in DBA/1OlaHsd mice. Clinical arthritis scores were recorded from CAIA mice, treated with dexamethasone (0.2 mg/kg, PO, BID; (grey diamonds) or vehicle (red circles) on study days 3-14, and non-disease animals (orange triangles). $p < 0.05$ ANOVA to CAIA Model + Vehicle.

Histopathological Assessment of RA Models

Inotiv offers advanced capabilities for histopathological assessment of joint tissue from RA animal models, conducted by ACVP board-certified pathologists. Our specialized histology and pathology methods allow for a detailed understanding of key RA pathological features, delivering the insights you need to make informed decisions in your therapeutic development process.

Figure 4 Effects of Baricitinib on Histopathological Features of Arthritis in a CIA rat Model
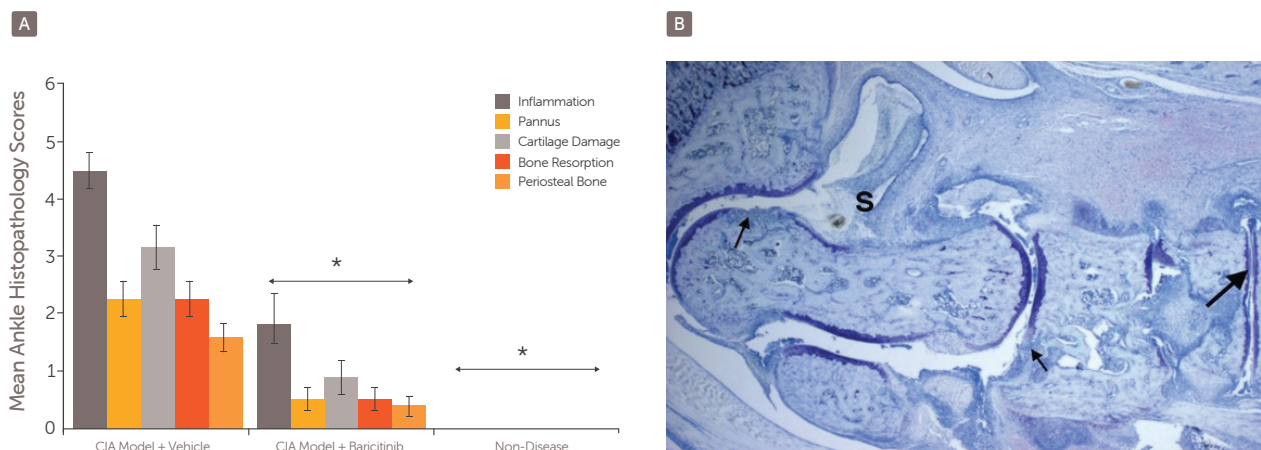
(A) Mean histopathology scores for inflammation (dark grey bars), pannus formation (yellow bars), cartilage damage (light grey bars), bone resorption (red bars) and periosteal bone formation (orange bars) in the ankle of CIA rat models, treated with baricitinib (3 mg/kg, PO, QD) or vehicle on study days 6-18, and non-disease animals. *$p \leq 0.05$ ANOVA to CIA Model + Vehicle. **(B)** Representative photomicrographs of an ankle joint from a CIA rat model stained with toluidine blue. Histology reveals marked synovitis (S) and periarticular inflammation with moderate cartilage damage (large arrow) and mild pannus and bone destruction (small arrows).

Figure 5 Effects of Dexamethasone Histopathological Features of Arthritis in a CAIA Mouse Model
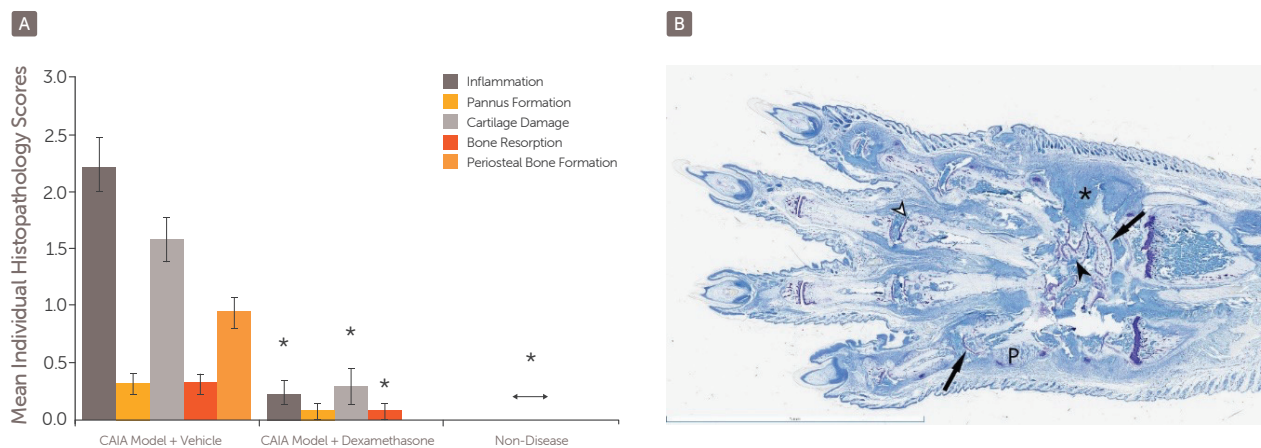
(A) Mean histopathology scores for inflammation (dark grey bars), pannus formation (yellow bars), cartilage damage (light grey bars), bone resorption (red bars) and periosteal bone formation (orange bars) in the fore paw of CAIA mouse models, treated with dexamethasone (0.2 mg/kg) or vehicle, and non-disease animals. *$p < 0.05$ ANOVA to CAIA Model + Vehicle. **(B)** Representative photomicrographs of a fore paw from a CAIA mouse model stained with toluidine blue. Histology reveals inflammation (*), cartilage damage (arrow), periosteal bone formation (P), bone resorption (black arrowhead) and pannus formation (open arrowhead).

Demonstrating efficacy of novel therapeutics can require assessing additional endpoints.

Contact us at **inotiv.com/contact** to discuss the data you need to assess your therapeutic and how our models and services can support your RA drug development program.