

Collagen Induced Arthritis Monkey Model

Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory disorder characterized by chronic inflammation of the synovial membrane, which over time results in damage to the joints and leads to pain and disability. It occurs in approximately 1% of adults, and approximately 2.5 times more women than men are affected. Rodent models with collagen II induced arthritis (CIA) have been extensively used in academic research and pharmaceutical industry for investigating rheumatoid arthritis (RA) and its treatments. However, an RA model in non-human primate (NHP) is particularly useful because of the close phylogenesis that provides the cross-reactivity to human for medical product development with most modern drug manufacturing technologies. Contrary to the successful RA modeling in rodents, NHP RA model has been reported extremely difficult because of the low and inconsistent disease incidence in both Rhesus macaques and Cynomolgus macaques, the most commonly used NHP for medicinal research. To resolve this issue, scientists at PharmaLegacy experimented type II collagen induced arthritis in Cynomolgus monkeys, and successfully established a reliable NHP arthritis model that can be used in rheumatology studies, as well as inflammation related anemia or pain studies, etc.



PharmaLegacy Models and Research Tools

Pharmacology Model

CIA NHP Model:

- * Bovine type II collagen induced arthritis in Cynomolgus monkey

Model Characteristics:

- * Disease moderate-to-severe, similar to human RA;
- * Poly-arthritis, persistent joint swelling, joint destruction and bone resorption;
- * Synovial membrane hyperplasia, inflammatory cell infiltration;
- * Pannus formation and cartilage damage

Primary Endpoints for Evaluating Arthritis:

- * Disease incidence;
- * Arthritic incidence of proximal interphalangeal joints;
- * Measurement of joint swelling;
- * Arthritic score;
- * Animal body weight

Available Endpoints for Monitoring Immune Response and Disease Progression:

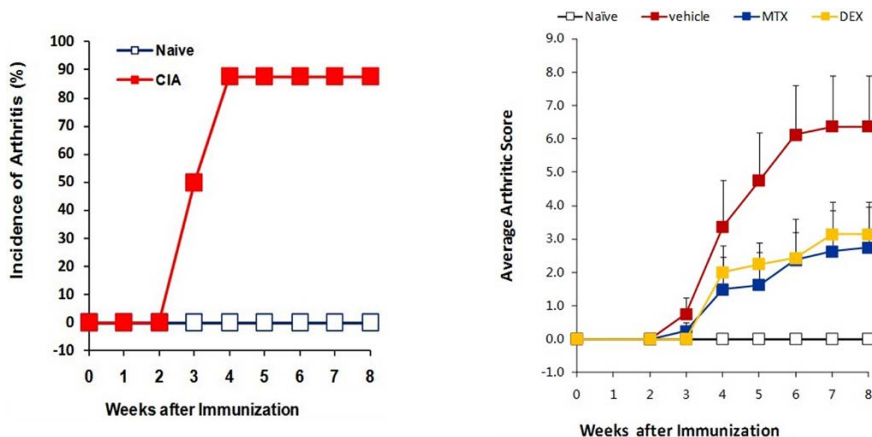
- * Hematology analysis;
- * Serum biomarkers (C-reactive protein, alkaline phosphatase, albumin, etc.);
- * Monkey anti-type II collagen IgG ELISA;
- * Antigen-specific T cell and B cell responses;
- * Cytokines

Additional Endpoints for Assessing Bone Histopathology and Histomorphometry:

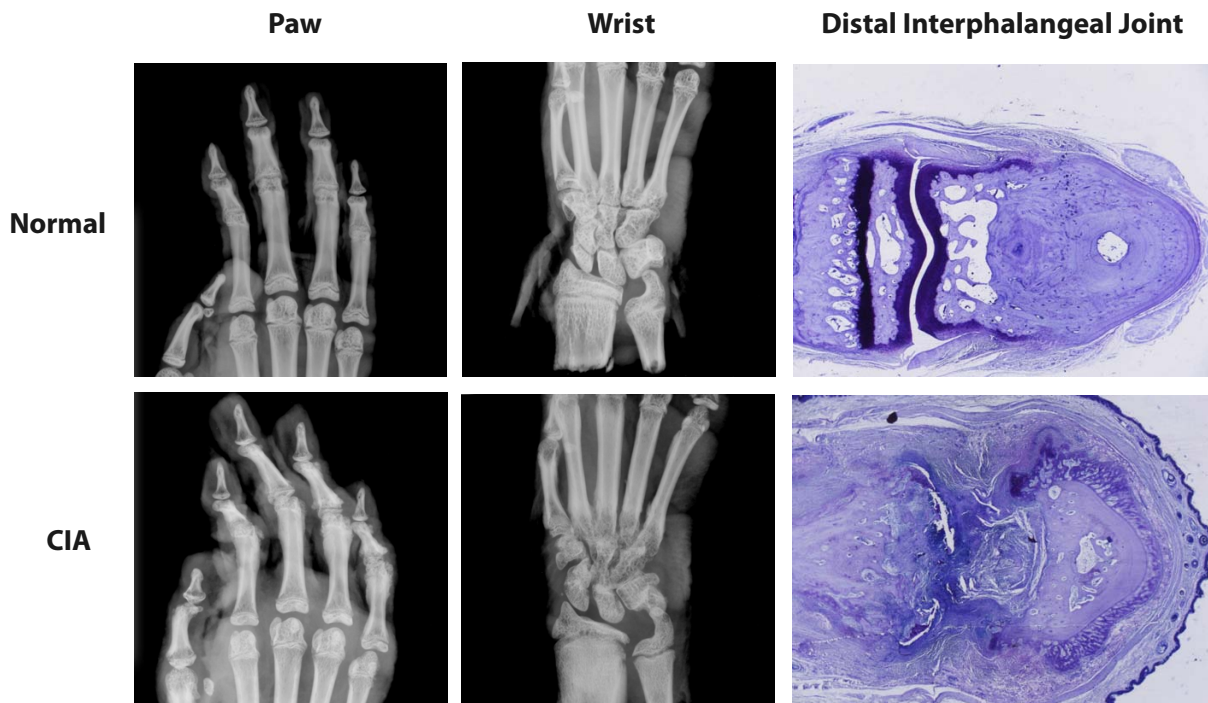
- * Radiology of arthritic joints and radiological image scoring (joint destruction, bone resorption and abnormal growth, lose of articular cavity);
- * Qualitative histopathology;
- * Quantitative histomorphometry (OsteoMeasure software system)
- * Immunohistochemistry

Case Study - Modeling Human Rheumatoid Arthritis in Cynomolgus Monkeys

Bovine type II collagen induced arthritis was established in Cynomolgus monkeys with an overall ~87% of disease incidence, which was significantly higher than that in the previous reports. The average arthritic score was reduced by 55% with the treatment of reference drugs comparing with the vehicle treated group.



Representative X-ray graphs of monkey joints and Toluidine blue staining of joint sections:



Complete loss of articular structure and significant numbers of infiltrated cells in CIA monkey joint.

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- World-class quality with increased speed and output at competitive cost.
- International GLP and QA-based operation.
- Electronic data management system (BioBook) for quality execution and maximum IP protection.
- AAALAC accredited large capacity to house over 10,000 animals under SPF and conventional conditions.
- Availability of 10000 non-human primates for research use.