Rheumatoid Arthritis

Progress RA drug development with validated *in vivo* models

Improve selection of your RA lead agent through our preclinical inflammation drug development platform. Use validated mouse models, combined with expert consultation, to better understand the efficacy of your RA therapeutics.

- Select preclinical models with diverse mechanisms that capture many of the key characteristic clinical and pathologic features of RA including:
  - collagen-induced arthritis (CIA)
  - collagen antibody-induced arthritis (CAIA).
- Determine efficacy and response to treatment.
- Select qualified rheumatoid arthritis lead agents.

At a microscopic level joint cartilage destruction and bone loss are associated with an inflamed synovial lining that results from chronic activation of both innate and adaptive immune cells and stromal cells in the joint.

**Collagen antibody-induced arthritis – CAIA**

- Rapid onset of disease.
- Induction through administration of commercially available antibodies targeting Type II collagen.
- Major endpoints:
  - swollen joint count
  - assessment of inflammatory mediators/cytokines.
- Histopathological assessment:
  - Board Certified Veterinary Pathologist.

**Collagen-induced arthritis – CIA**

- DBA/1 mice immunized with Type II collagen in CFA and boosted with IFA.
- Peak disease (swollen joints) occurring 8–15 days post IFA boost.
- Major endpoints:
  - swollen joint count
  - assessment of inflammatory mediators/cytokines.
- Histopathological assessment:
  - Board Certified Veterinary Pathologist.

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**CAIA Model + Dexamethasone**
Representative Forepaw Histology Photomicrographs

Non-lesioned paw. A distal phalangeal bone (P), carpal bone (C), and proximal interphalangeal joint (J) are indicated.

Marked inflammation (*) of the intra- and peri-articular tissues, affecting the interphalangeal joints (phalangeal bone, P) and carpal (C) joints is noted. Cartilage damage (black arrows), bone resorption (black arrowheads), pannus (blue arrowheads), and periosteal new bone (NB) are indicated.

Forepaw lacks lesions associated with arthritis. Interphalangeal joint (J), proximal phalangeal bone (P), and carpal bone (C) are indicated.

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**CAIA Model + Anti-TNF mAb**
Representative Forepaw Histology Photomicrographs

Marked infiltration of neutrophils (*) into the intra- and peri-articular tissues of forepaw. Areas of cartilage damage (black arrows) and bone resorption (black arrowheads), along with periosteal new bone (NB) are present. Proximal phalangeal bone (P) and carpal bone (C) are indicated.

Minimal neutrophilic infiltration (inflammation; *) in the synovium of one interphalangeal joint (J) and the carpus (C). A proximal phalangeal bone (P) is indicated.