

Application Forum

Monoclonal Antibody Induced Arthritis: a shorter, more synchronized alternative to the classic CIA model

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INTRODUCTION:

Collagen-induced arthritis (CIA) in mice is widely used as an experimental model for rheumatoid arthritis. Initial symptoms of inflammation in the CIA model occur at approximately day 21-24 with the model requiring 6-8 weeks to complete. The induction of the disease is typically at 80% of the animals and varies from laboratory to laboratory and with the use of different collagen sources. The disease symptoms also appear at slightly different times in different animals, making therapeutic administration protocols more demanding technically. With the long study length, significant amounts of compounds are required to be prepared for use over the study duration. Furthermore, the lengthy study period also requires increased number of measurements and scoring periods, increasing the cost of the study further. These points illustrate some of the key issues in running a typical CIA model. The monoclonal antibody induced arthritis model (mAb-induced RA, AIA or CAIA) is ideal for rapidly screening and evaluating anti-inflammatory therapeutic agents providing more information in a shorter amount of time. The flexibility of the system means it is applicable to the wide range of transgenic strain bred on the C57Bl background. It is also relevant for studying inflammatory mediators such as cytokines, chemokines, matrix metalloproteinases and other factors such as the role of bacterial flora and their by-products in triggering and exacerbating arthritis.

MATERIALS AND METHODS:

Collagen induced arthritis model was run using DBA/1 mice. Bovine Collagen Type II (2 mg/mL, Cat# 804001, MD Biosciences, Inc) was emulsified in Complete Freund's adjuvant (4 mg/mL), MD Biosciences, Inc and administered to each animal on day 0. Collagen boost was performed on day 21.

Antibody-Induced arthritis model was run using Balb/c mice. ArthritoMab™ Antibody cocktail (2 mg/mL, Cat #

CIA-MAB-50, MD Biosciences) was administered to animals on day 0. LPS boost was performed on day 3. Scoring for both models was on a scale of 0-4 based upon the number and severity of arthritic joints .

RESULTS AND DISCUSSION:

The ArthritoMab™ cocktail of four monoclonal antibodies binds to the well-defined epitopes C11b, J1, D3 and U1, which are all major epitopes in mice immunized with CII and developing arthritis. These epitopes are also spread across the entire CII region (CB8, CB10, and CB11 fragments) possibly encouraging better immune complex formation on the cartilage surface for the initiation of arthritis. The ability to induce arthritis using an antibody cocktail to CII provides an efficient protocol as an alternative to the lengthy CIA protocol. Results can be obtained

Figure 1

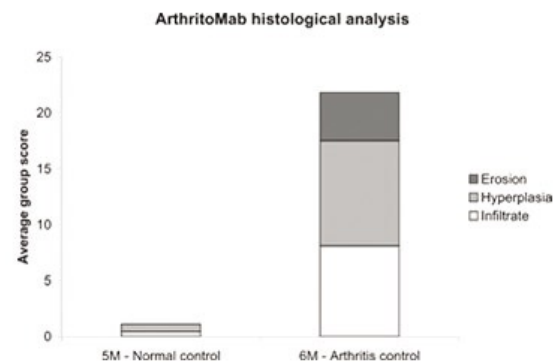


Figure 2 - Control

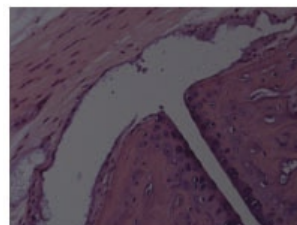
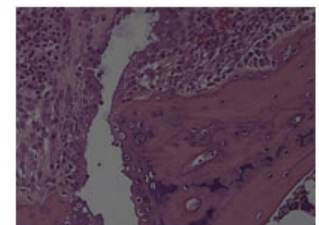


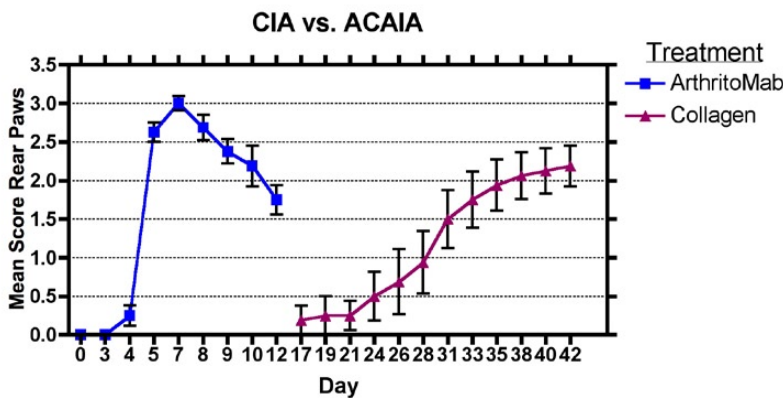
Figure 3 - Erosion



in as little as 7 days with significant histology results indicating the degree of erosion, hyperplasia and infiltration in the joint of the arthritis group as compared to the control group in less than 18 days (figure 1-3).

Figure 4 shows the ArthritoMab™ in the antibody-induced arthritis model in comparison to the CIA model. Not only is the length of the model greatly improved, all animals develop disease on the same day making therapeutic administration schedules more manageable than in the CIA in which animals will develop disease at different rates. Incidence in ACAIA goes from 0 to 100% within 48h of giving LPS but incidence in CIA does not reach 100% until 10 days after collagen boost. The antibody-induced arthritis model may also be used in many different strains of mice including DBA/1, B10.RIII, Balb/c and C57Bl animals.

Figure 4



CONCLUSION:

The monoclonal anti-collagen antibody induced model presents a real alternative to the CIA, significantly reducing the study duration and cost while increasing disease induction and synchronicity among individual animals.

For further information download our whitepaper from the website or contact us:

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The ArthritoMab™ (Cat # CIA-MAB-50) antibody cocktail is supplied as a kit that includes LPS. MD Biosciences also performs the antibody induced arthritis model for contract research. To order or inquire, please visit our website at www.mdbiosciences.com