Collagen Antibody Induced Arthritis (CAIA) mouse model for Rheumatoid Arthritis

Introduction

ModiQuest Research has developed an efficient mix of anti-collagen antibodies, for the generation of a Collagen Antibody Induced Arthritis (CAIA) mouse animal model. The ModiQuest Research CAIA model is ideal for rapidly screening novel arthritis therapeutics and to study the mechanisms involved in the development of arthritis.

The CAIA antibodies can be delivered directly to clients for in-house animal generation. Alternatively, under collaboration with third parties complete animal studies using these CAIA antibodies are offered by ModiQuest Research.
Collagen-induced arthritis

Collagen-induced arthritis is an antibody mediated disease. Therefore, type II collagen specific antibodies can be used to induce arthritis in mice. ModiQuest Research’s mixture of type II collagen specific antibodies (2.4-3.2 mg per animal) together with LPS (25µg/mouse) induces severe inflammation in the ankle and paws of DBA mice (Fig. 1), which resemble many aspects of arthritis. One of the biggest advantages of our monoclonal antibody-induced arthritis model is that arthritis is induced within 24-72 hours (Fig. 2) instead of the four weeks required to induce arthritis after immunization with type II collagen. ModiQuest Research recommends highly susceptible DBA/1 mice. Other strains may be used as well, however the amount of antibody cocktail required may vary.

Advantages of the MQR-Collagen Antibody Induced Arthritis model:

- **Short time frame:** Severe arthritis develops in mice typically within 24-72 hr, allowing the completion of a study within a few weeks, reducing the number of assessments and scoring periods.
- **LPS synchronization:** Onset of disease is synchronized between animals, simplifying treatment schedules.
- **Reduced animal use:** Rate of incidence is nearly 100%, depending on the strain used, allowing for smaller group sizes.
- **Ease of application:** I.P. injection instead of I.V. injection in other systems offered.

### Specifications:

#### Reagents provided

Mixture of 8 antibodies that recognize 7 different collagen type II epitopes (Isotypes IgG1, IgG2a, IgG2b). Antibodies have been lyophilized in a 10 mM ammonium bicarbonate buffer.

#### Procedure

1. On day 0 administer antibody cocktail intra-peritoneal (i.p.) between 2.4 mg and 3.2 mg per animal.
2. In-between day 3 and 7 LPS can be administered i.p (25µg/animal) to enhance and synchronize the inflammation.
3. Observe arthritis score throughout the study on a daily basis. Initial symptoms of arthritis typically appear on day 2.

#### TABLE 1

**Arthritis scoring method**

<table>
<thead>
<tr>
<th>Arthritis Score</th>
<th>0.25</th>
<th>1.50</th>
<th>1.75</th>
<th>0.5</th>
</tr>
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<tbody>
<tr>
<td>1-2 Swollen Toes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-4 Swollen Toes</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Slightly Swollen Footpad or Ankle</td>
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<td></td>
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<tr>
<td>Swollen Footpad or Ankle with</td>
<td></td>
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</tr>
<tr>
<td>1-2 Swollen Toes + Swollen Footpad or Ankle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swollen Footpad + Swollen Ankle + Swollen Toes</td>
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</tbody>
</table>

**FIGURE 1**

DBA/1 | BALB/c

Mice were injected i.p. with 2.6mg CAIA antibody mixture and followed during 7 days. Pictures were taken after 3 days of injection.

**FIGURE 2**

CAIA using 8 monoclonal antibodies. Arthritis incidence (A) and total arthritis score (B) are indicated. Groups of 6 DBA/1 mice were treated i.p. with 8 collagen specific monoclonal antibodies. Different concentrations of the antibody cocktail (0.8 mg, 2.4 mg and 3.2 mg) were used. An irrelevant control antibody (CTL) has been used at a 2.3 mg concentration. LPS (25 µg/mouse) was injected i.p. on day 7.