Application Forum

Using a cocktail of anti-collagen type II antibodies induces a synchronized model of arthritis in just a few days

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Introduction

The collagen-induced arthritis (CIA) model is mediated by autoantibodies that bind to a particular region of type II collagen (CII) and complement. Initial symptoms of inflammation occur at approximately day 21 with the model requiring 6–8 weeks to complete. These time requirements, along with variable disease onset, have caused researchers to look for more efficient and cost effective alternatives.

Research by Nandakumar and Holmdahl (1) has shown an antibody cocktail of collagen type II antibodies selected for their epitope specificity can induce rapid arthritis with 100% synchronicity. Evidence suggests that an antibody response to certain epitopes is better associated with arthritis than other epitopes.

MD Bioproducts ArthritoMab™ Antibody Cocktail (Cat. no. CIA-MAB) consists of four monoclonal antibodies to CII that bind to the well-defined epitopes C1, J1, D3, and U1. These epitopes are spread across the entire CII region, are found in mice immunized with CII and developing arthritis, and encourage better immune complex formation on the cartilage surface or in the synovium (1). These complexes can then activate, complement, and induce inflammation by both the classical and alternative pathways. Monocytes in the joint are also activated by these complexes via Fc receptors releasing pro-inflammatory cytokines, (i.e., TNF-α and IL-1β), which recruit neutrophils and macrophages.

Methods: induction of arthritis

Mice were injected with ArthritoMab™ Antibody Cocktail on day 0 (either IP or IV). LPS boost is administered on day 3. Inflammation develops within 24–48 h, and the model is terminated on day 10–12. If desired, the model can be extended to allow for a 6-day recovery phase, which can reveal the ability of a compound to promote arthritis resolution.

Results

BALB/c mice were administered ArthritoMab™ Antibody Cocktail on day 0 and boosted with LPS on day 3. Joints were isolated on days 0, 4, 7, and 12 from both a vehicle and dexamethasone-treated groups. Homogenized joints

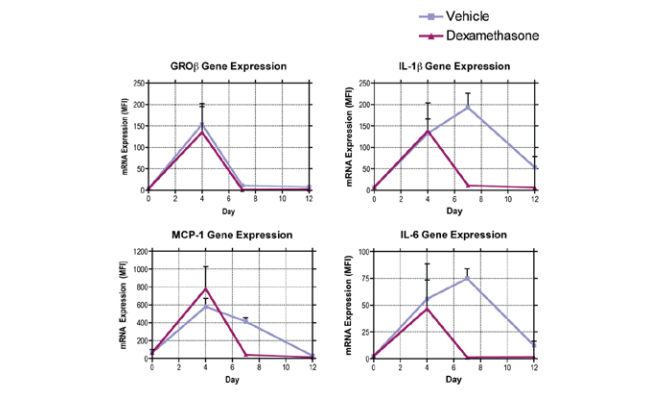

Figure 1.

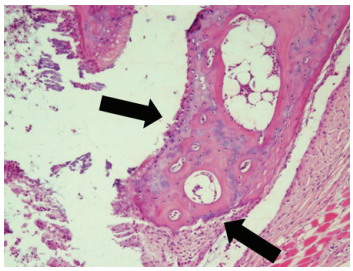

Figure 2.

were assayed for mRNA levels expressed as median fluorescent units (MFI). Mean values are shown for GROβ, IL-1β, MCP-1, and IL-6.Histology was performed on day 12, and data shows synovial hyperplasia in the knee joint (H&E, ×40 magnification).

Conclusion

The CIA model using ArthritoMab™ Antibody Cocktail is ideal for rapidly screening anti-inflammatory therapeutic agents in a variety of animal strains. For more information on the ArthritoMab™ Antibody Cocktail, please visit our web site (www.mdbioproducts.com) to download a full whitepaper with further data.

References

1. **Nandakumar, K.S., and R.J. Holmdahl.** 2005. J. Immunol. Methods. *304*:126-136.

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