CAIA: an induced arthritis model for the efficacy evaluation of arthritis therapeutics

Representative photos of CAIA arthritic paws.
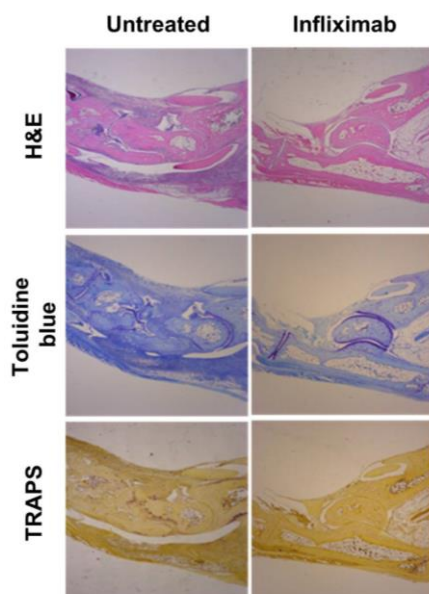
Microscopic images indicate the amelioration of arthritis pathology following anti-hTNF treatment (H&E:inflammation, Toluidine blue: Cartilage destruction, TRAPS: osteoclast activation)

The model

Collagen antibody-induced arthritis (CAIA) is a simple mouse model of rheumatoid arthritis that can be used to address questions relating to the pathogenic mechanisms of the disease and serves as a platform for the evaluation of candidate therapeutic agents.

CAIA is an extension of the classical collagen-induced arthritis (CIA) model, which has been used extensively in rats, mice and primates, and involves immunization with type II collagen in adjuvant. Although it is known that collagen-II- specific monoclonal antibodies bind to normal joint cartilage surface the precise mechanisms that lead to inflammatory arthritis in CAIA are unclear. Recent studies have demonstrated the involvement of both innate and adaptive immunity in CAIA.
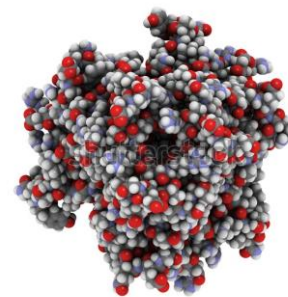
In the CAIA model, arthritis is induced by the systemic administration of a **cocktail of monoclonal antibodies that target various epitopes of collagen type II**, which is one of the major constituents of articular cartilage matrix proteins. The antibody cocktail is administered together with lipopolysaccharide (LPS) which serves to enhance the disease pathology. The pathogenic features of the CAIA model have striking similarities with human rheumatoid arthritis, including synovitis with infiltration of polymorphonuclear and mononuclear cells, pannus formation, cartilage degradation and bone erosion.

Biomedcode has standardized the model in
1. **C57BL/6** wild type mice,
2. Mice humanized for **hTNFR1**
3. **Tg1278TNFKO** human TNF transgenic mice
4. Mice humanized for **both TNF and TNFR1**

and developed platforms to allow the evaluation of different arthritis therapeutics.

As CAIA model is not fully TNF dependent, there is one clear therapeutic window for the evaluation of anti-TNF therapeutics that leaves place for a second one that can serve for the evaluation of combination therapies.

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The CAIA model offers several key advantages over conventional CIA:

☐ Arthritis is induced within only a few days rather than the several weeks that are required to induce arthritis by immunization with type II collagen in CIA.

☐ CAIA has 100% incidence therefore reducing the CIA requirement for large experimental groups.

☐ CAIA offers synchronized induction of the disease.

☐ CAIA develops fully within 2 weeks of induction allowing for the evaluation of therapeutics with a short half life as they can be administered as frequently as twice daily for this short time period

☐ Unlike the CIA model, CAIA can be induced in a wider spectrum of mice, including gene-deficient mice, transgenic mice and strains that are resistant to classic CIA.
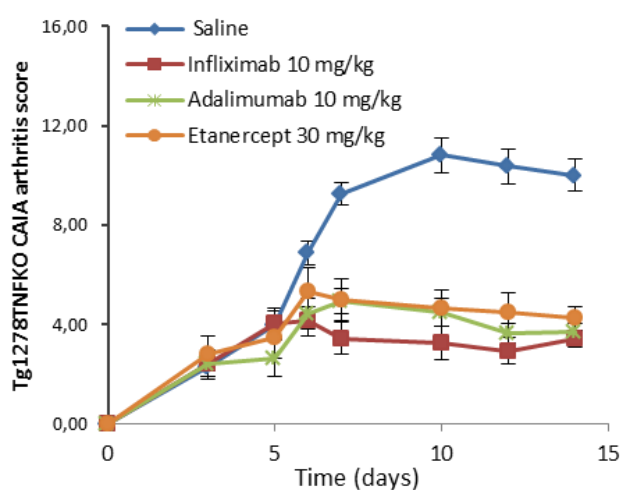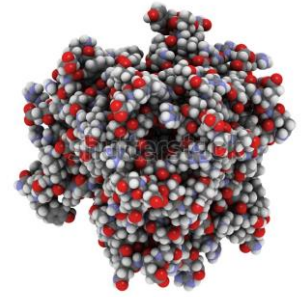

Representative CAIA in-vivo arthritis progression in Tg1278TNFKO animals treated prophylactically with anti-hTNF therapeutics.
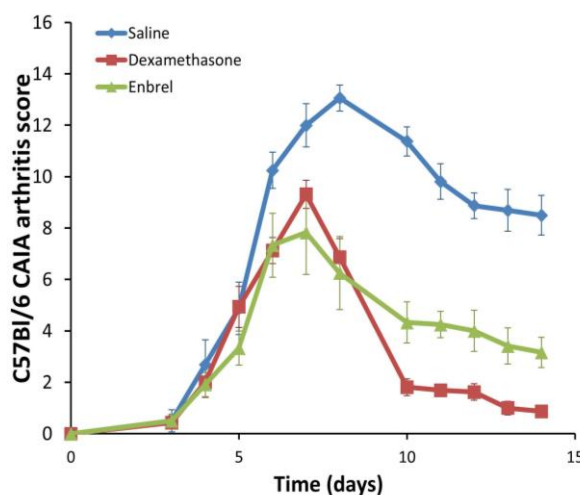
CAIA induced arthritis pathology in wild type animals (C57BL/6) can be reversed following anti-TNF treatment.

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REFERENCES

Moore A, Allden S, Bourne T, Denis MC, Kranidioti K, Okoye R, Sotsios Y, Stencel Z, Vugler A, Watt G, et al., 2014. "Collagen II antibody-induced arthritis in Tg1278TNFko mice: optimization of a novel model to assess treatments targeting human TNFα in rheumatoid arthritis". J Transl Med., 12(1):285

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