

Vium Arthritis Index



Automated Index to Track Disease Progression

INTRODUCTION

Animal models of arthritis are routinely used to evaluate the efficacy of therapeutics for Rheumatoid Arthritis (RA). A variety of pharmacologically induced and transgenic animal models have been developed, each capturing a different facet of human pathophysiology (1-3). As a result, researchers must select the model that is best suited to the disease mechanisms targeted by their therapeutic candidates. Metaanalysis of animal studies has revealed that drugs displaying therapeutic efficacy in both Collagen Induced Arthritis (CIA) and Adjuvant Induced Arthritis (AIA) models are most successful in the clinic (1).

VIUM ARTHRITIS INDEX

The Vium Arthritis Index™ enables researchers to evaluate the efficacy and safety of therapeutic interventions in rodent models of RA through near realtime measurements and data analysis. Our use of physiological measurements combined with advanced analytics provides a highly sensitive readout of arthritis induction, as well as clinically relevant measures of therapeutic response. The net result is that researchers can non-invasively assess treatment effects during the course of the study, and make on-the-fly decisions about which treatment arms are worth continuing.

BIOMARKER VALIDATION

We have conducted a series of experiments demonstrating 1) that we are able to induce arthritis using standard models such as rat CIA and 2) that the Vium Arthritis Index accurately tracks disease severity and prophylactic treatment efficacy when compared to conventional measurements.

METHODS

The rat CIA model was conducted according to standard protocols (4,5). Briefly, Lewis rats were inoculated with Porcine collagen type II (2 mg/mL) in Incomplete Freund's Adjuvant (IFA). Control animals were induced with IFA only. On study day 0, rats were given 200 µl intradermal injections on the back at 2 sites, and a single 100 µl booster injection was given on day 7. Test compound administration began on day 9 and continued according to the following dosing regimens:

- Vehicle (daily)
- Methotrexate (MTX, 0.075 mg/kg, daily PO)
- Ibuprofen (18 mg/kg, daily, PO)
- Enbrel (10 mg/kg q3d SC)
- Dexamethasone (DEX, 0.075 mg/kg, daily PO)

The Vium Arthritis Index and daily joint size measurements were made for the duration of the study, with organ weight (spleen, liver) and ankle joint histopathology determined after study termination.

Preclinical Researchers Use This Biomarker to:

- **Improve Flexibility:** Use standard rat CIA or AIA models or customize study designs.
- **Collect data in the home cage non-invasively and reduce extraneous variables and labor involved in animal handling and observation.**
- **Conduct adaptive preclinical studies using digital endpoints that closely track with conventional methods.**
- **Automated sensors are on 24/7, giving researchers access to additional general health biomarkers.**

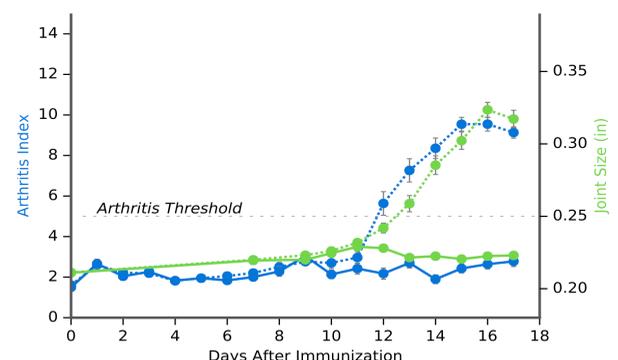


Fig. 1. Vium Arthritis Index tracks with conventional joint measurements.

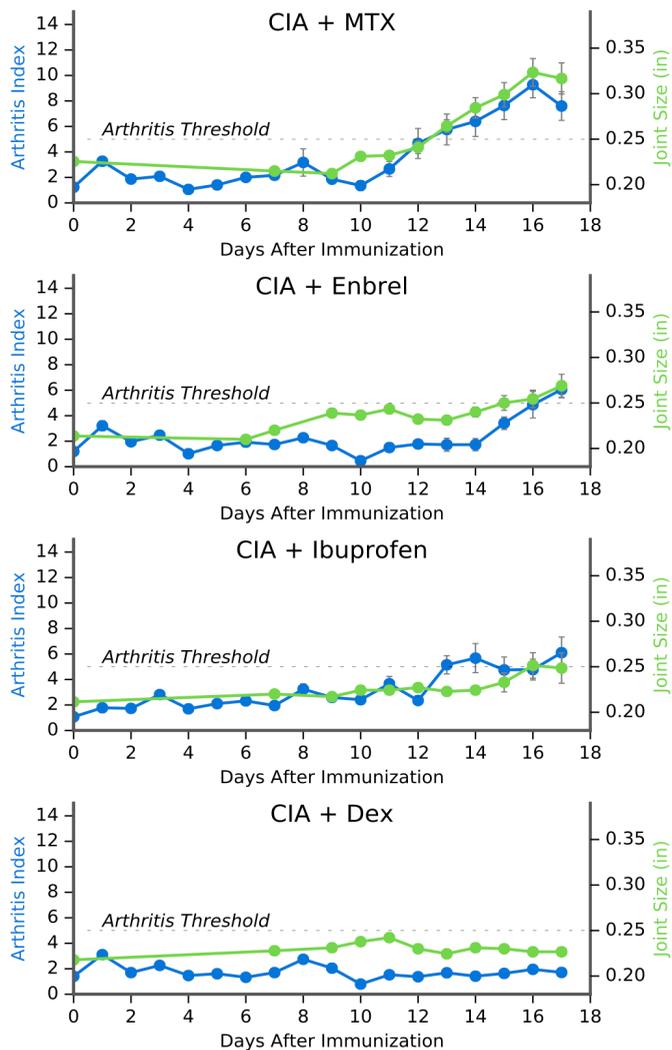


Fig. 2. Vium Arthritis Index tracks with conventional joint measurements with standard of care drugs

RESULTS

Arthritis developed in collagen-induced animals within the expected time window of 11 – 13 days as measured either by joint size or the Vium Arthritis Index (Fig. 1). The Vium Arthritis Index tracked with joint size measurements for each of the drugs tested (Fig. 2). Furthermore, the data mirrored the rank ordering of the three standard of care drugs as determined by ankle joint histopathology, indicating that the Vium Digital Platform can be used to determine the relative efficacy of test articles. In a follow-on study, we tested 9 compounds at 3 doses each in the CIA model. Using the Vium Arthritis Index, we ranked the compounds by therapeutic efficacy to rapidly identify high performing compounds.

REFERENCES

1. Hegen M, Keith JC Jr, Collins M, Nickerson-Nutter CL. (2008) Utility of animal models for identification of potential therapeutics for rheumatoid arthritis. *Ann Rheum Dis.* 67: 1505-15.
2. Bevaart L, Vervoordeldonk MJ, Tak PP. (2010) Evaluation of therapeutic targets in animal models of arthritis: how does it relate to rheumatoid arthritis? *Arthritis Rheum.* 62: 2192-205.
3. Bendele A. (2001) Animal models of rheumatoid arthritis. *J Musculoskelet Neuronal Interact.* 1: 377-85.
4. Trentham DE, Townes AS, Kang AH. (1977) Autoimmunity to type II collagen an experimental model of arthritis. *J Exp Med.* 146: 857-68.
5. Courtenay JS, Dallman MJ, Dayan AD, Martin A, Mosedale B. (1980) Immunisation against heterologous type II collagen induces arthritis in mice. *Nature* 283: 666-8.