



# CBI

# Murine collagen-induced arthritis

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COMPARATIVE BIOSCIENCES, INC.  
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

# Murine Collagen-Induced Arthritis

- Standard CBI model of rheumatoid-like or immune mediated arthritis in DBA1 mice
- Induced with collagen in Freund's adjuvant
- Duration is about 2 months
- In life parameters include clinical observational scoring, and body weights
- Necropsy with histology and immunohistochemistry
- Steroids and Enbrel are established positive control drugs



# Basic Study Design

- 10-15 mice per group, males, 7-8 week-old DBA/101aHsd (“DBA/1”) mice
- Sensitized with two systemic administrations of collagen in Freund’s adjuvant at Day 0 and 21.
- Brisk peri-arthritis swelling develops with subsequent arthritic changes over about 1 week and continues for up to 4 weeks.
- Scoring begins on Day 22. Animals may be synchronized with LPS
- Treatment as per protocol. Dexamethasone or Enbrel as positive control drug
- Weekly body weights
- Histopathology
- Complete report



# Clinical Lameness Scoring

- Clinical lameness scoring is conducted 2-3 x a week
- There are several methods that are useful
- Scoring each toe as normal (0) or affected (1) and totaling the score is a robust and reproducible method and has minimal subjectivity



# Histopathology

- Limbs fixed in NBF or paraformaldehyde
- Decalcified, processed, embedded and cut
- Stained with HE, and a cartilage stain such as toluidine blue or Movat's penatachrome
- Immunohistochemistry as relevant
- Scored for inflammation, cartilage damage, pannus formation, bone loss, synovial changes



# Histopathology Scoring

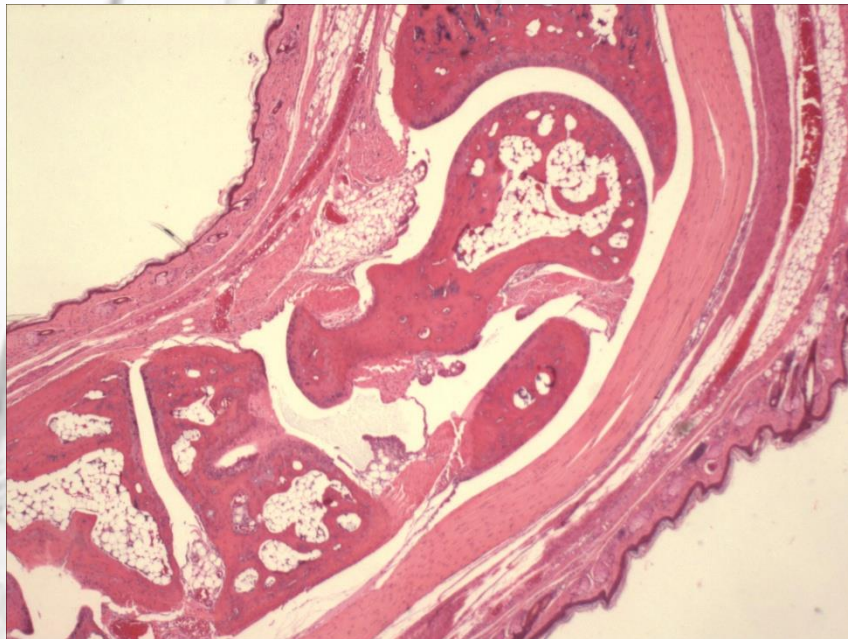
Group	Treatment	Inflammation Index	Force Rank
1	Vehicle	4.73 ±0.04	3
2	Enbrel	2.72* ±0.92	2
3	Dexamethasone	0.25* ±0.02	1(least severe)

Histopathology scoring: Marked inflammation in vehicle alone with significant reduction in inflammation in Enbrel and Dexamethasone treated animals. \*The decrease was statistically significant with both positive control groups ( $p < 0.001$ ).

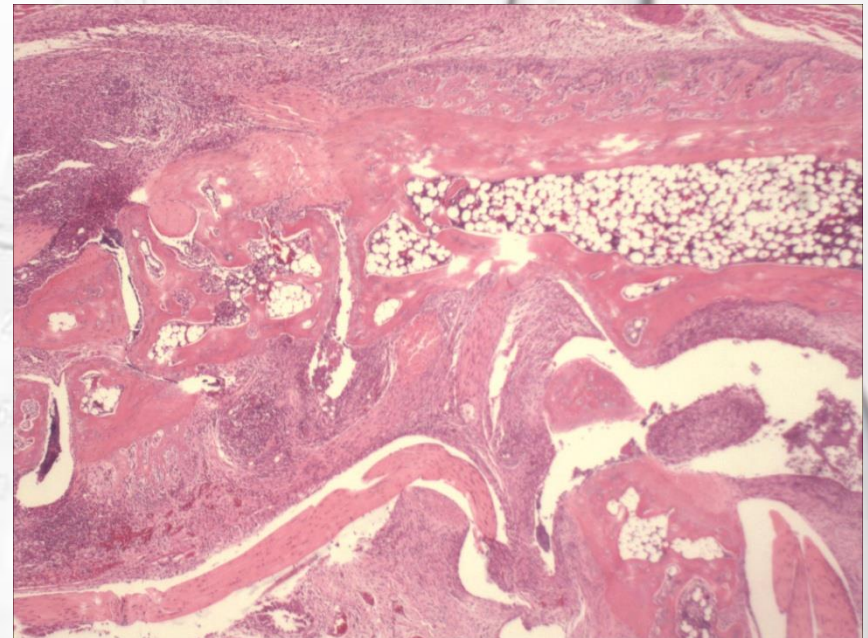


# Histology

Normal Leg

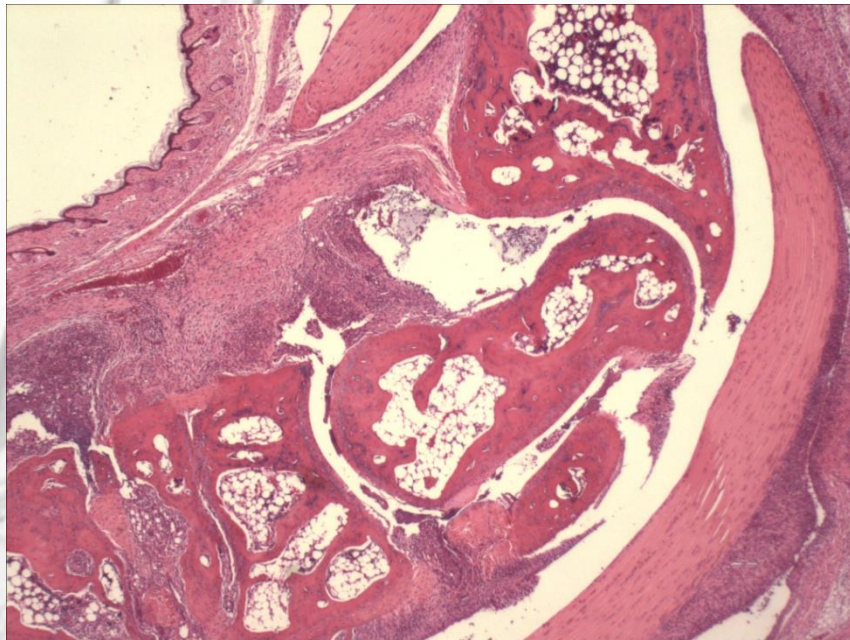


Collagen-induced arthritis with severe inflammation and joint destruction at 2 months

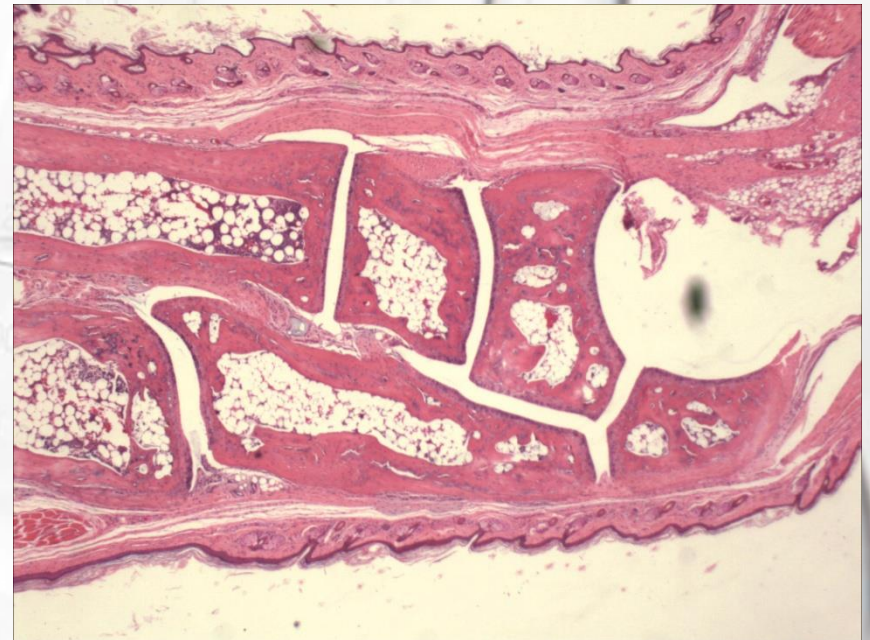


# Histology

Collagen-induced arthritis with moderate inflammation and joint destruction at 2 months



Dexamethasone treated leg-there is only mild inflammation





## Summary

- Induction with collagen and Freund's adjuvant produces a consistent brisk, arthritis in DBA1 mice between Day 22 and 50
- Dexamethasone and Enbrel induce statistically significant inhibition of inflammation.
- This is a suitable, conventional rheumatoid model in mice

