

# Meloxicam sustained release injection site reactions in male and female mice

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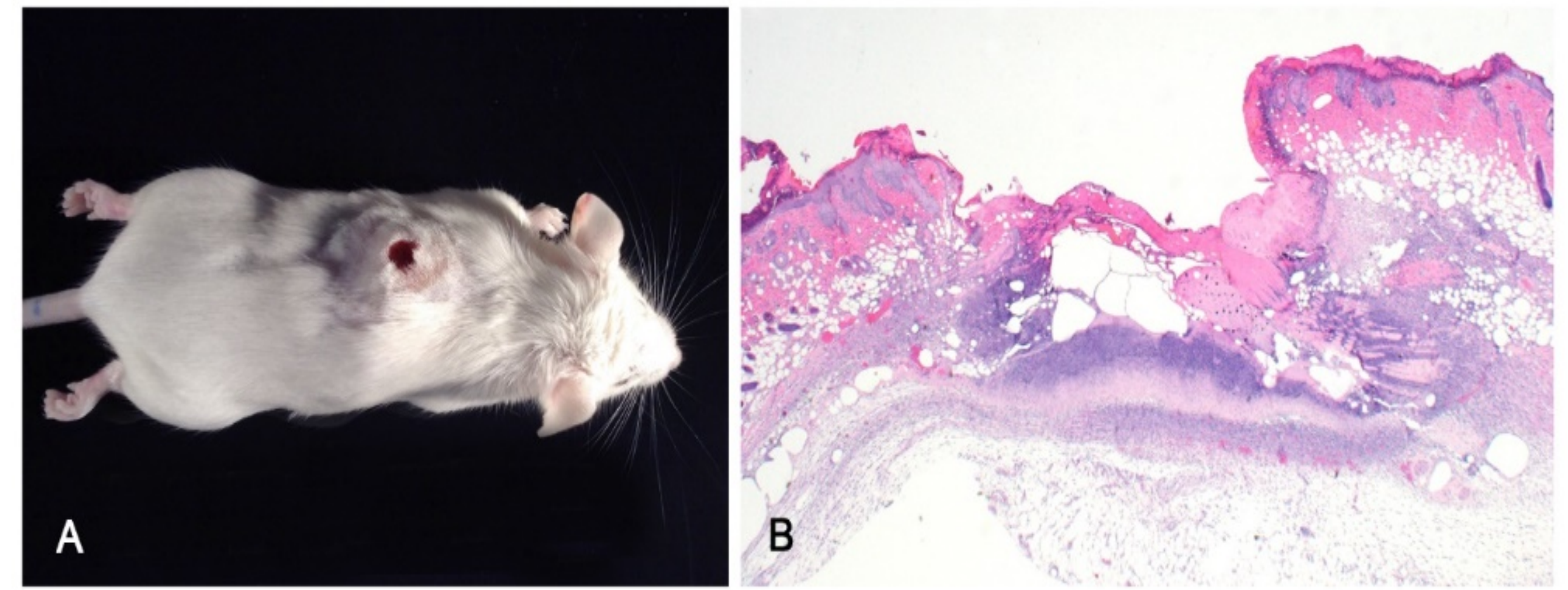
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## Why are we interested in Meloxicam Sustained Release (MSR)?

- Meloxicam (an NSAID) provides up to 12 hours of analgesia<sup>1,3</sup>
- MSR provides up to 72 hours of analgesia
  - Reduce animal handling to minimize stress<sup>1,2,3</sup>
  - Efficacy established, but full MSR formulation not tested for safety
  - Some treated animals developed skin lesions, granulomas, or open draining tracts
- Reactions can lead to:
  - Interference with study objectives
  - Premature loss of study animals
  - Welfare concerns



**Figure 1.** Male CD-1 mouse with 0.5 cm diameter mass at the injection site 1 week post MSR subcutaneous administration. **A.** Ulcerated lesion **B.** Haired skin and subcutis: Severe, chronic, regionally extensive, necrotizing dermatitis and panniculitis with granulation tissue and intralesional basophilic foreign material with moderate, regionally extensive, chronic acanthosis and hyperkeratosis.

## Hypotheses

Treatment of mice with injectable meloxicam sustained release results in:

- Greater lesion incidence and severity than control treatments
- Strain differences in reactions
- Sex differences in reactions

## Materials and Methods

### Animals

- 9 weeks old, age and sex-matched; 36 Balb/cJ, 36 C57BL/6J, 36 ICR(CD1)
- Ad libitum rodent chow and water
- Communal housing in a temperature and humidity controlled room

### Treatments

- Single subcutaneous injection of MSR (4 mg/kg), Meloxicam (4 mg/kg), OR saline (MSR volume)

Mouse Strain	Saline		Standard Meloxicam		MSR	
	7 days	14 days	7 days	14 days	7 days	14 days
Balb/cJ	4 (2M/2F)	4 (2M/2F)	4 (2M/2F)	4 (2M/2F)	10 (5M/5F)	10 (5M/5F)
C57BL/6J	4 (2M/2F)	4 (2M/2F)	4 (2M/2F)	4 (2M/2F)	10 (5M/5F)	10 (5M/5F)
ICR(CD1)	4 (2M/2F)	4 (2M/2F)	4 (2M/2F)	4 (2M/2F)	10 (5M/5F)	10 (5M/5F)

### Data Collection

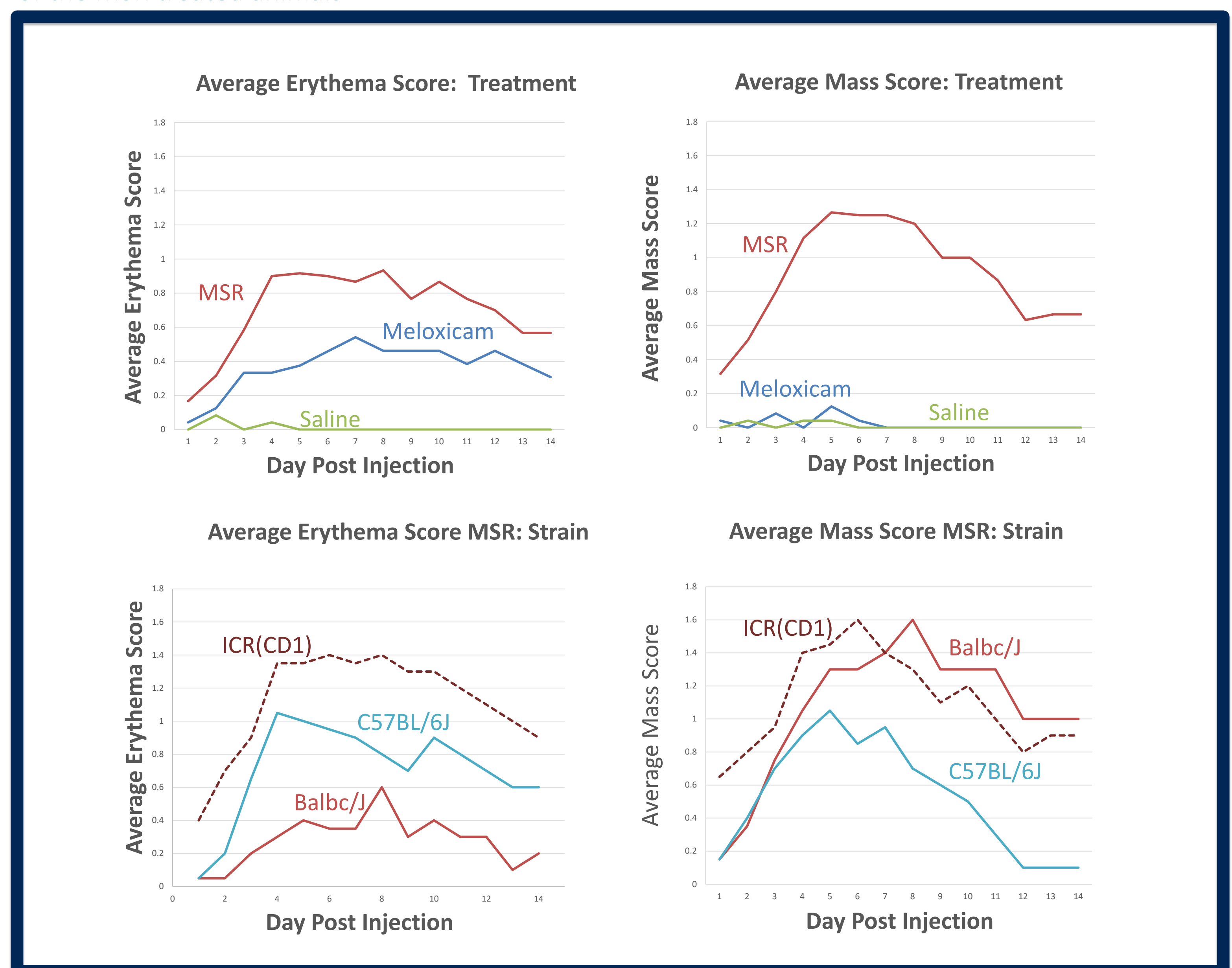
- Erythema and mass scores measured daily by treatment blinded researcher
- Animals were submitted for necropsy at day 7 or 14, and histology interpreted by a Veterinary Pathologist

Score	Erythema	Mass
0	No visible reaction	No palpable thickening or mass
1	Mild alopecia or erythema, scabs are no larger than 1 mm diameter	Palpable thickening, borders undefined, cannot measure
2	Moderate alopecia or erythema, skin intact, if present scabs are greater than 1 mm	Palpable mass, borders defined, measurable, overlying skin and hair intact
3	Moderate alopecia or erythema with PARTIAL thickness ulceration	Palpable mass, borders defined, measurable, with alopecia and PARTIAL thickness ulceration
4	Moderate to Severe alopecia or erythema with FULL thickness ulceration	Palpable mass, borders defined, measurable, with FULL thickness ulceration

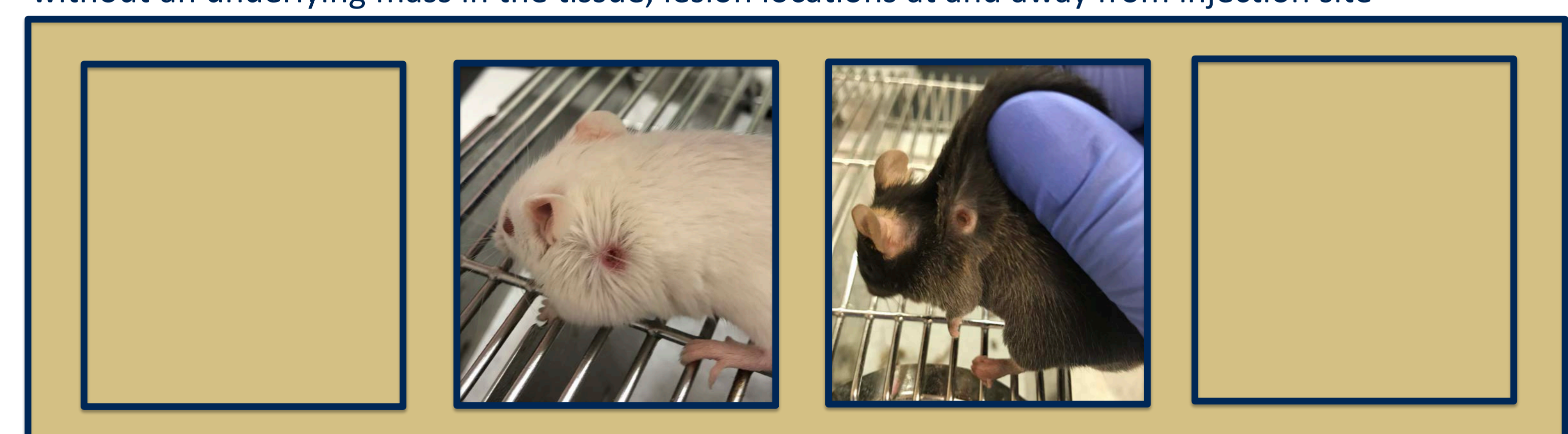
## Results

### Trend Considerations

Average scores for erythema and mass are represented by treatment group and also for each strain of the MSR treated animals



**Variation of Lesion Characteristics:** Scabs, soft to firm masses, alopecia, outside lesion with and without an underlying mass in the tissue, lesion locations at and away from injection site



### Analyses to Come

- Mixed analysis of variance: patterns of reactions, reaction resolution, time/group interactions
- Histological interpretations

## Results

### Frequency Data

- MSR increased lesion incidence** for erythema and mass scores in all groups (Fisher's Exact for Erythema, P=0.00018, and mass P=5.49\*10<sup>-12</sup>)
- There were no difference for Meloxicam and MSR in erythema scores, but both were statistically greater than saline
- There were **no sex differences** in erythema or mass of any scores
- Among MSR treated mice; there were **significant strain differences** in erythema scores, but not mass scores (Fisher's Exact for Erythema 1+, P=0.018)

## Discussion

- Observable characteristics varied, histology findings may provide additional insights
- Lesions often occurred away from the injection site: on the sides, near the arms, behind the neck
- Lesions could be missed or mistaken for dermatitis or as a bite wound
- ICR(CD1), the only outbred strain represented, had the greatest frequency and most severe lesions
- Potential side effects and animal welfare should be considered when choosing this drug

### Acknowledgements

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### References

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