

Preclinical Studies

Challenge: identify methods for testing interventions in mice

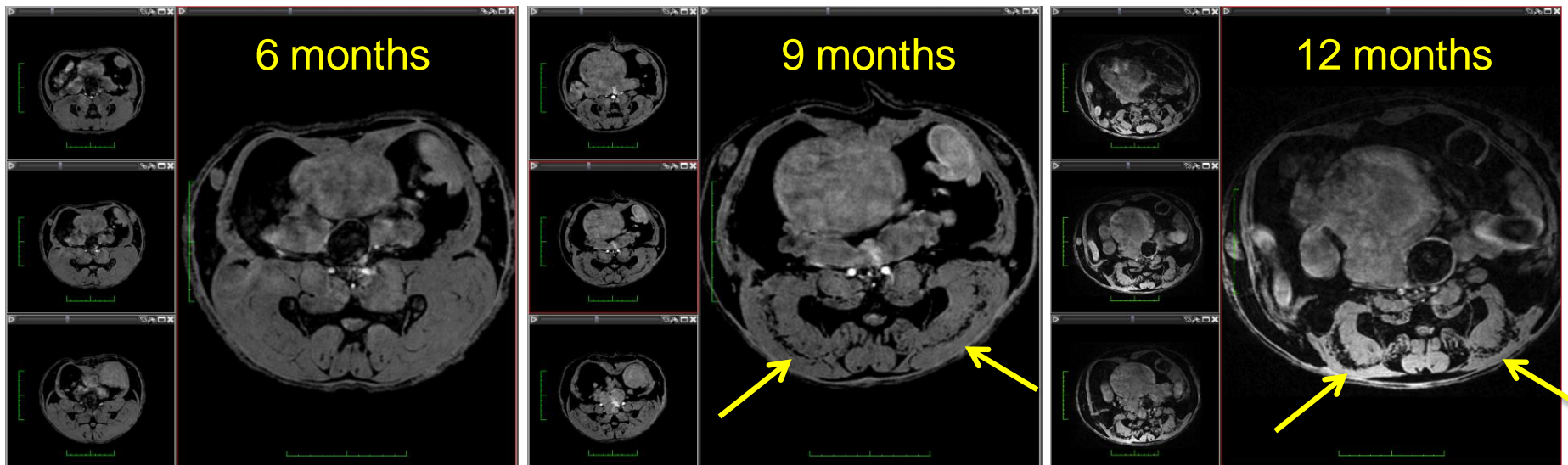
Behavioral changes - not apparent until 9 months +

Histological changes - detected by 6 months

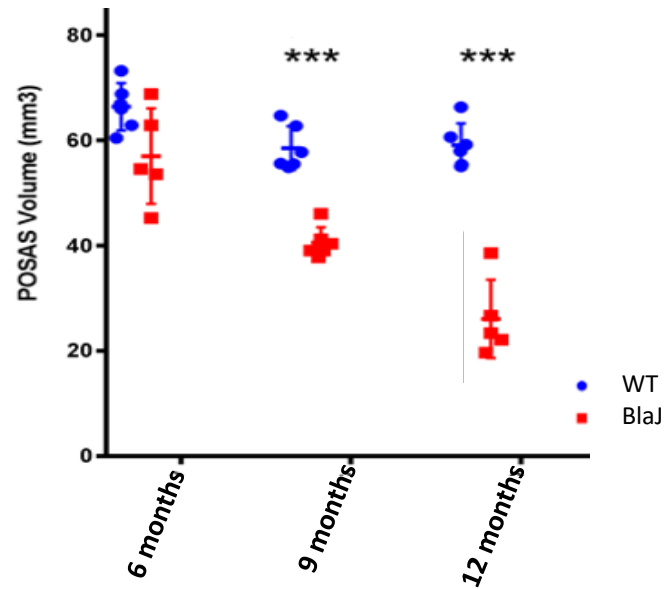
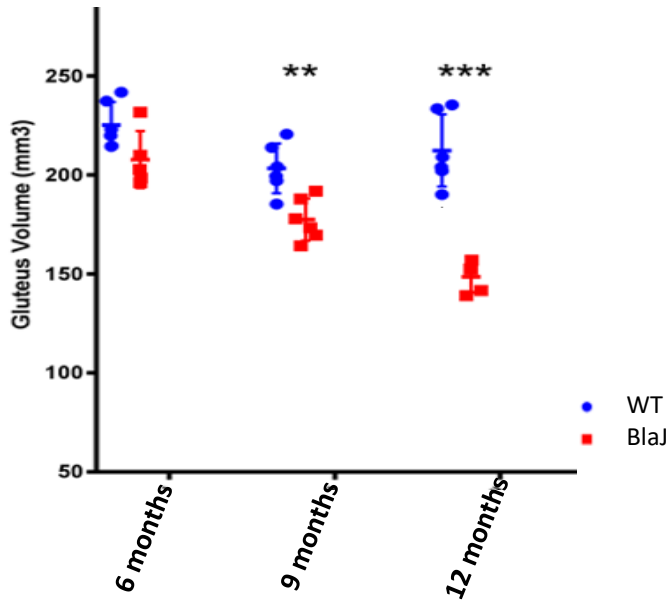
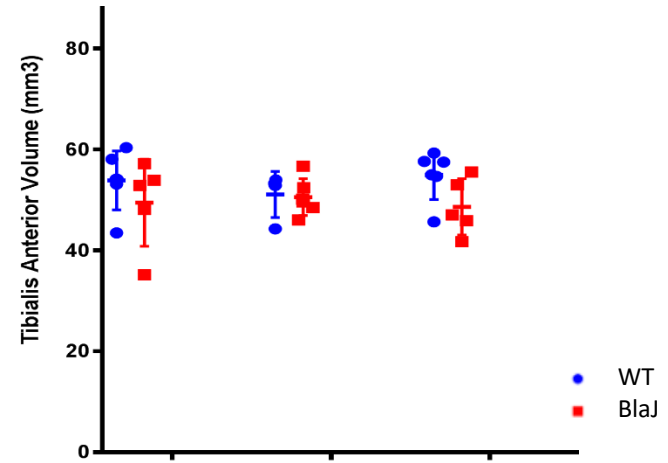
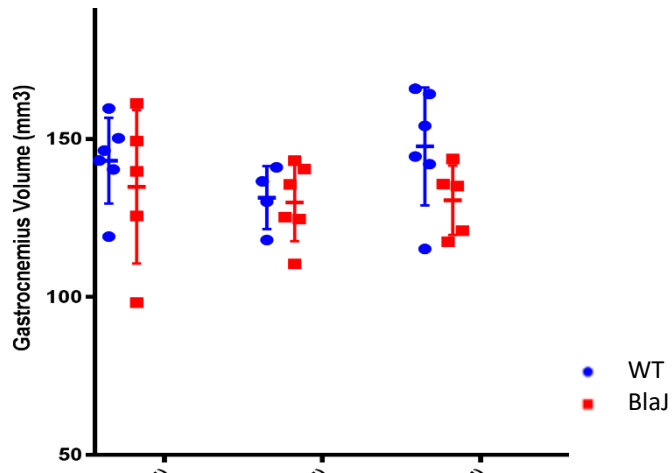
- Differences are slight
- Methods time consuming/costly

Goal: Establish methods for robust comparison of interventions

Hip Muscle Deterioration in BLAJ Mice

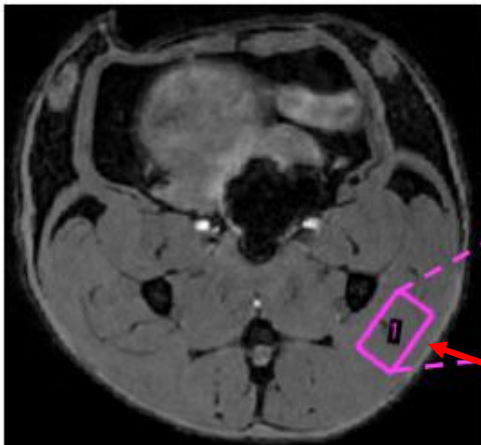
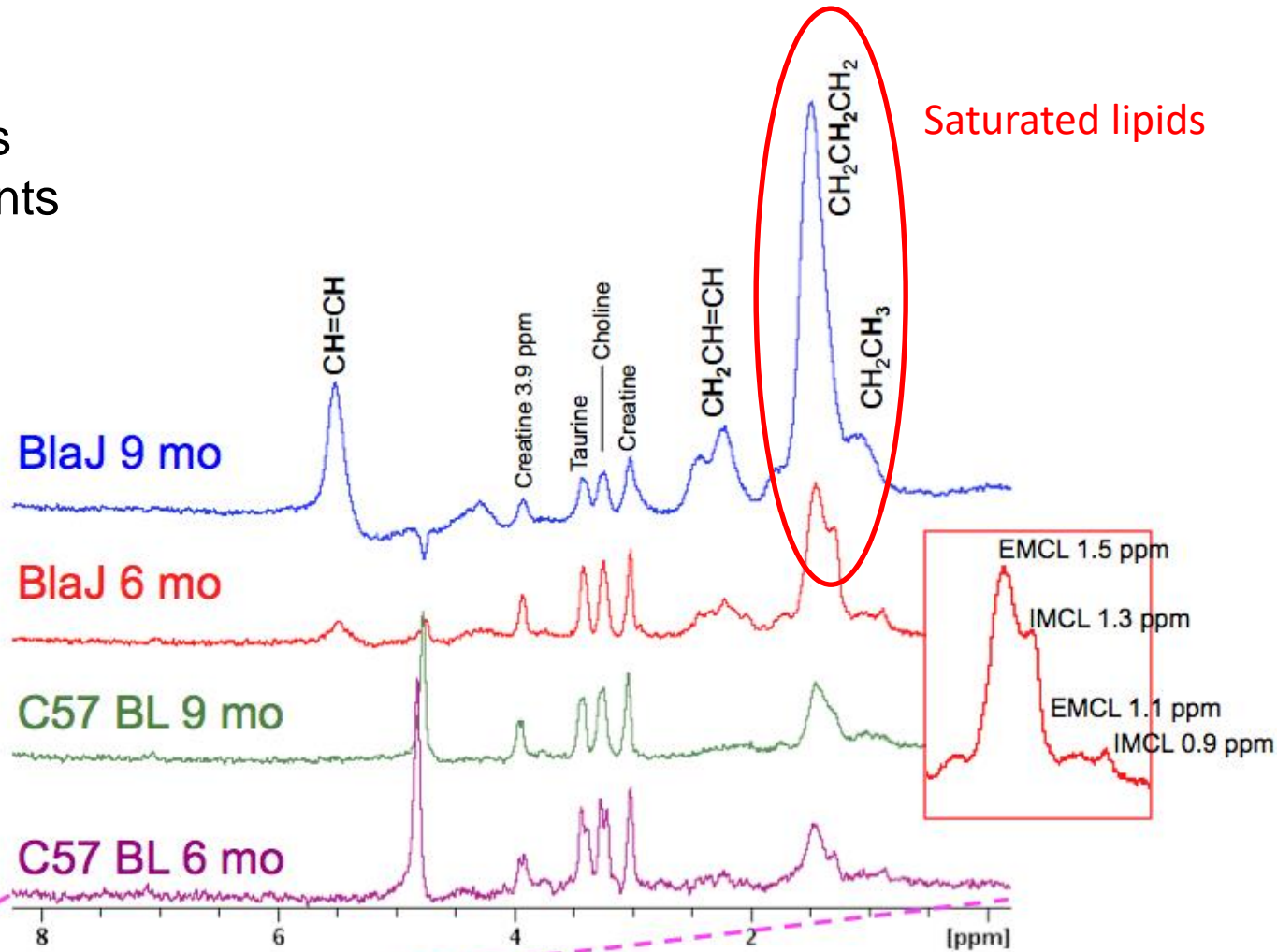


Muscle volumes in BLAJ, and C57BL/6J mice



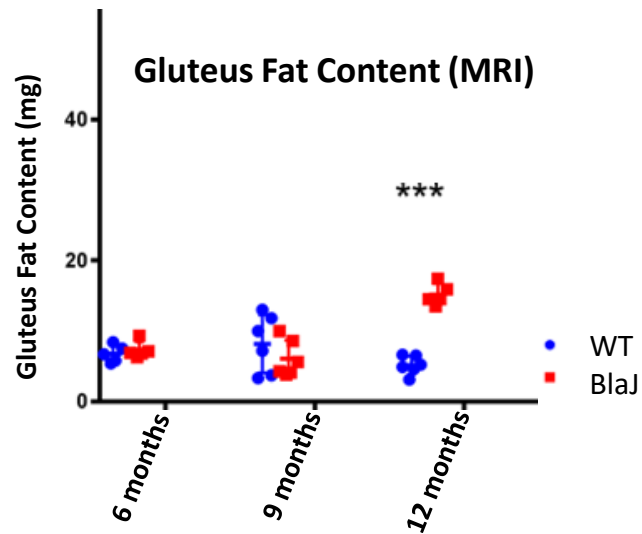
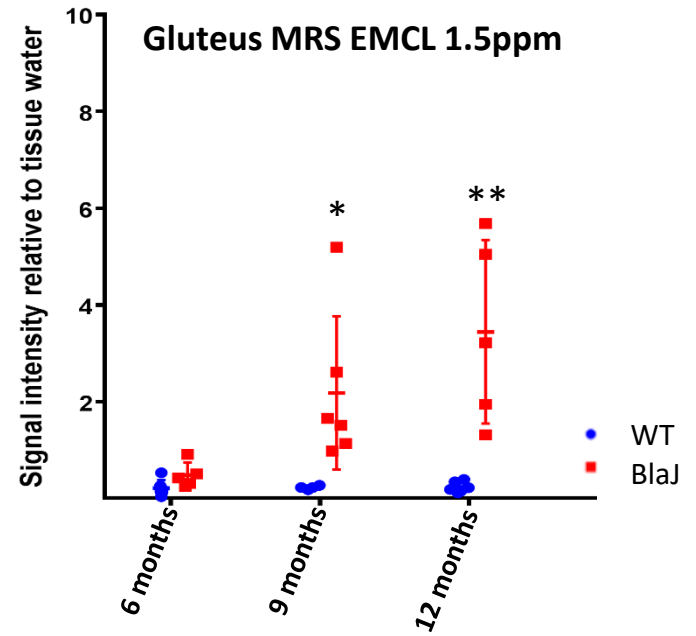
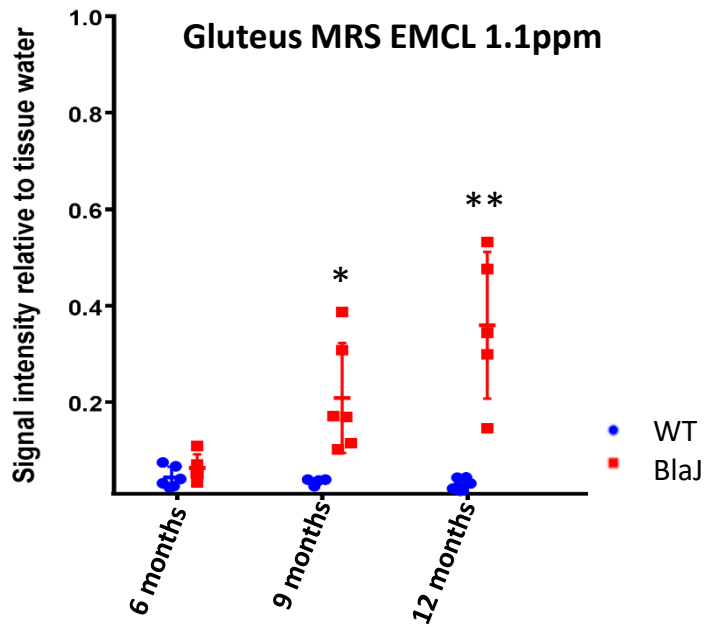
Magnetic Resonance Spectrum

Metabolites and lipids peaks at different points of the spectrum

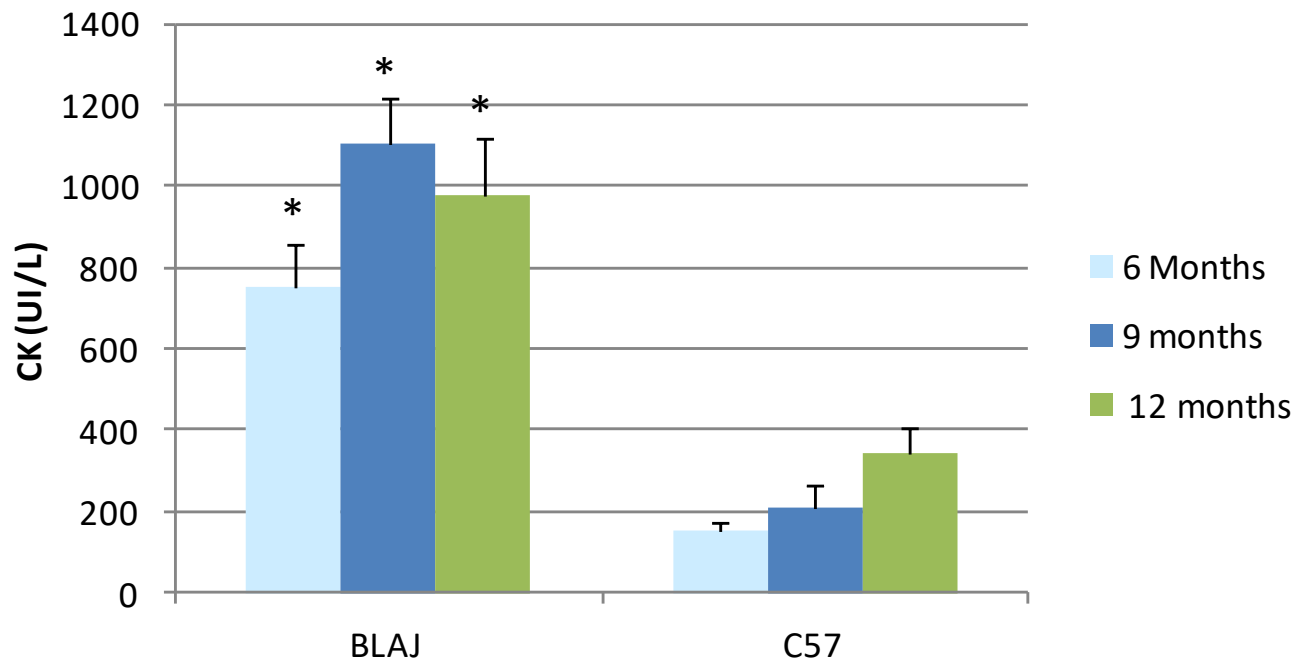


“Voxel”

MRS lipid quantitation

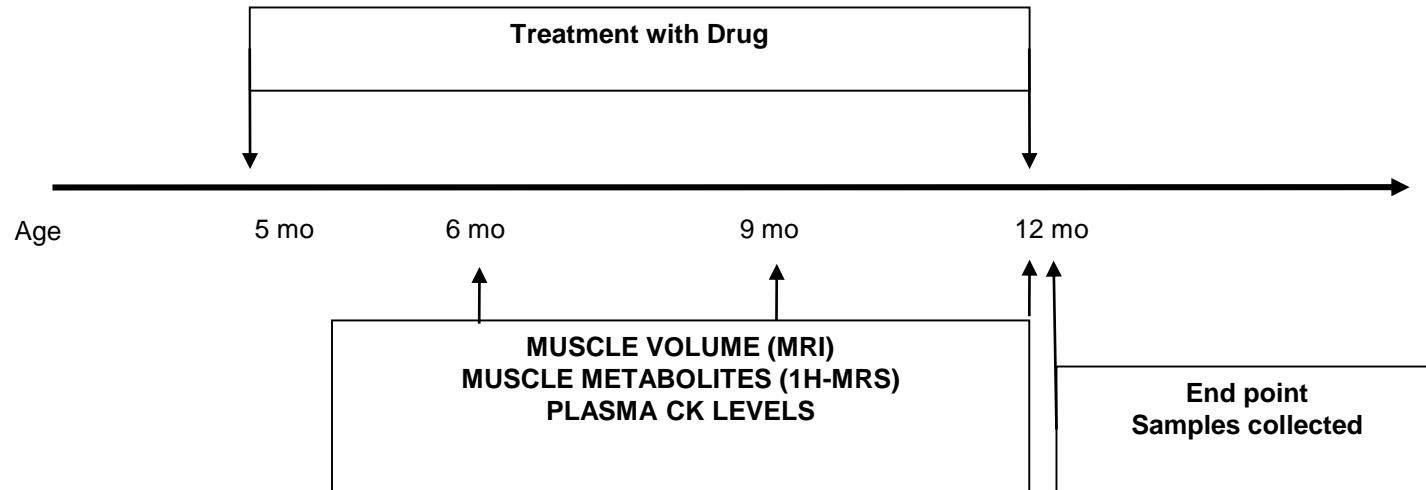


CK in BLAJ, and C57BL/6J mice



* $p < 0.05$, BlaJ versus C57

Study Design



- BLAJ mice (*A/J backcrossed 10x to C57BL/6J*)
- C57BL/6J from Jax production colony
- 20 mice/group equal genders or 10 mice/group single gender

Study Trends

Studies completed: 18

Mice analyzed ~ 426 BlaJ, 113 Wt,

Muscle loss very consistent across studies

- ✓ 30% reduction in glute volume at 12 months
- ✓ 50% reduction in psoas volume at 12 months

Fat accumulation (MRS and MRI)

- reliably elevated at 9 months (MRS)
- High (MRI), unmeasurable (MRS) at 12 months

Slight Gender differences

- Males frequently have 15-40% higher CK values
- Males have slightly earlier muscle loss
- Females have slightly more fat accumulation

Revised study design – n = 10 single gender

Phenotype confirmed in KI32 mice n=13 KI32

Collaborations - 7 different pharma companies
- 6 different academic labs

Psoas Volume

