

Mid1 is a novel mediator of subchondral bone resorption in antigen-induced arthritis



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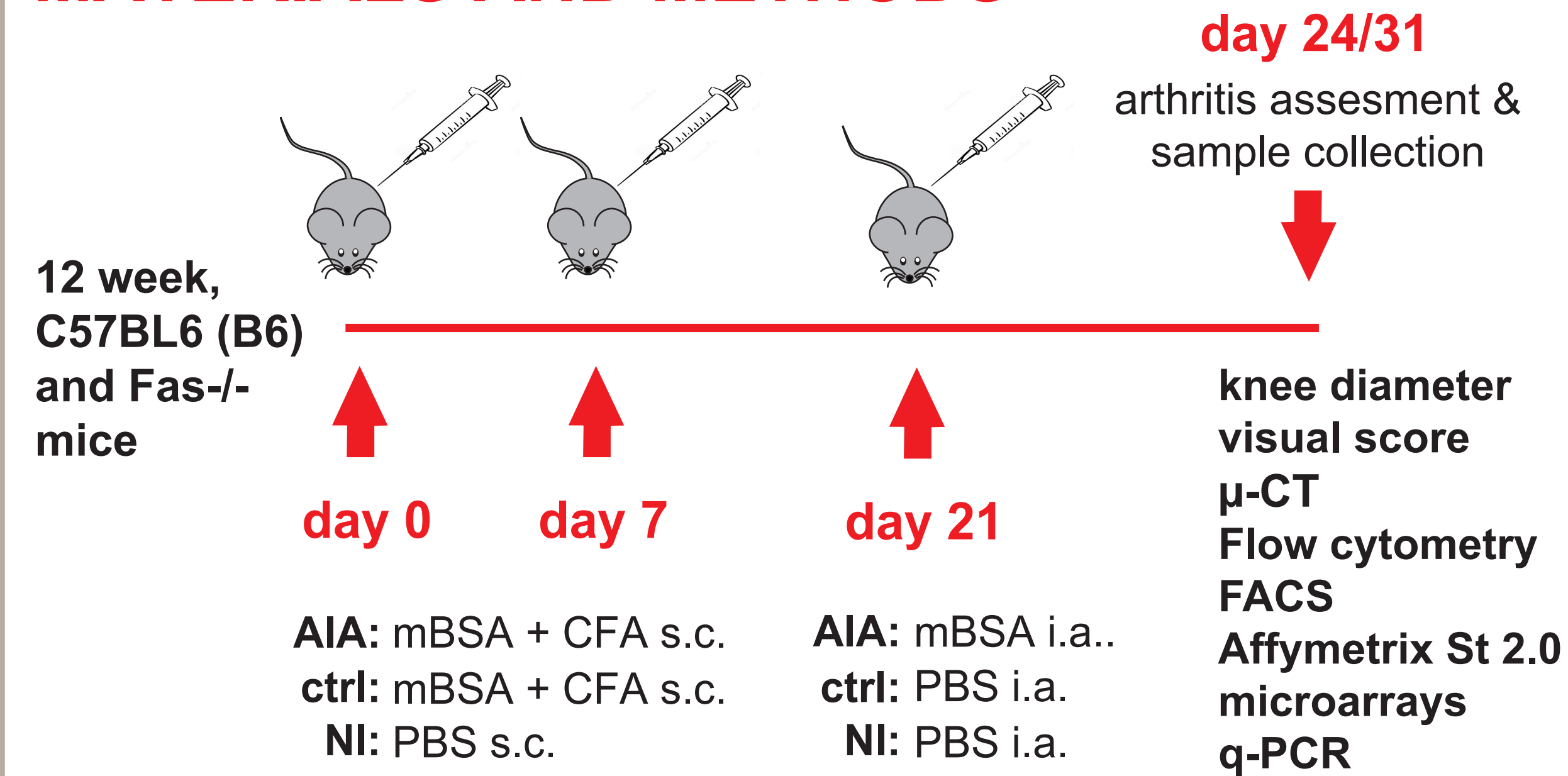
INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune joint disease characterized by subchondral bone destruction, irreversible by currently available therapeutics. We have shown that mice deficient for Fas gene (*Fas*^{-/-}) are protected from local bone resorption in antigen-induced arthritis (AIA), a murine model of RA, lack accumulation of synovial myeloid cells, which down-regulate *Mid1* gene.

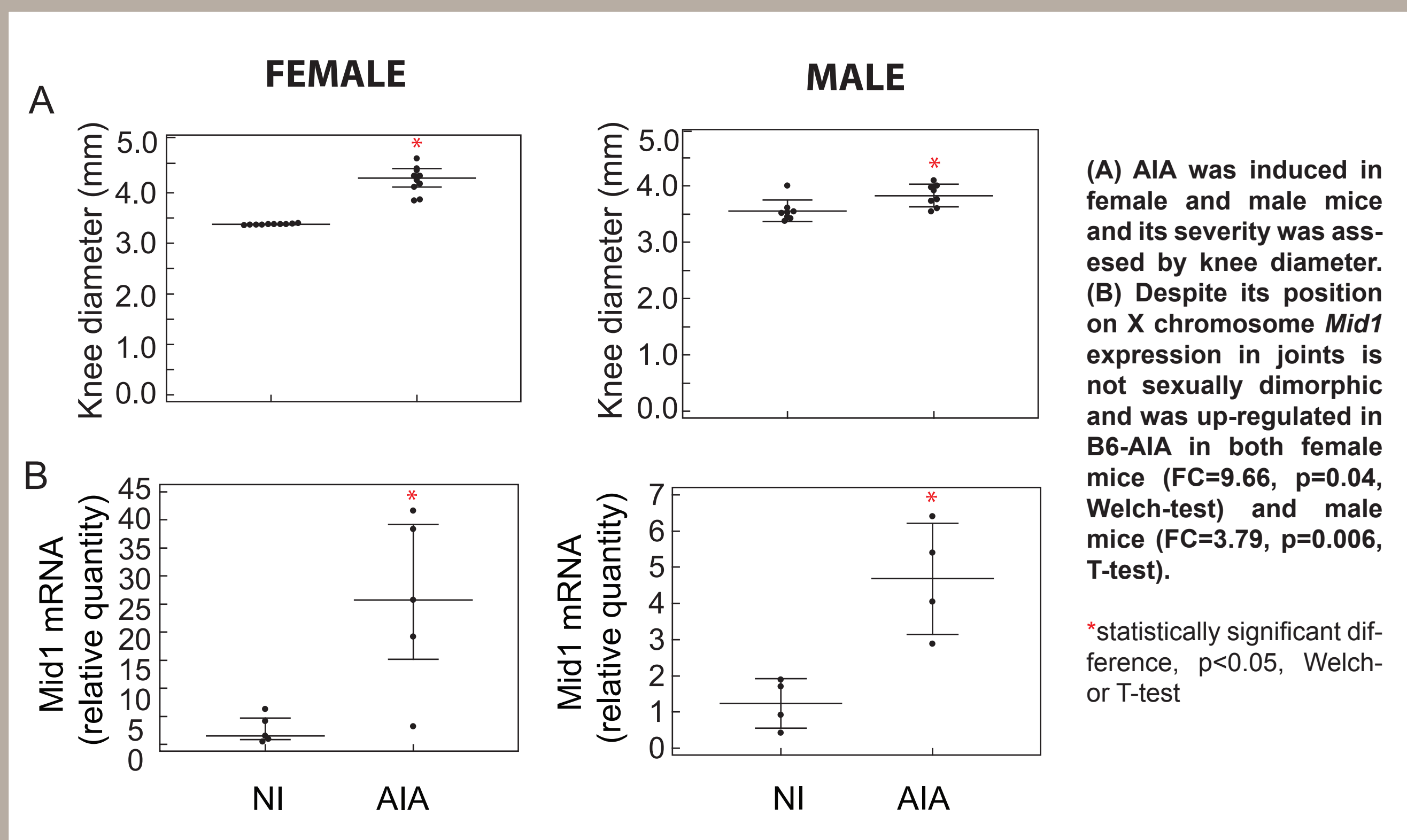
AIM OF THE STUDY

The objective of the study was to evaluate the expression and function of *Mid1* during AIA.

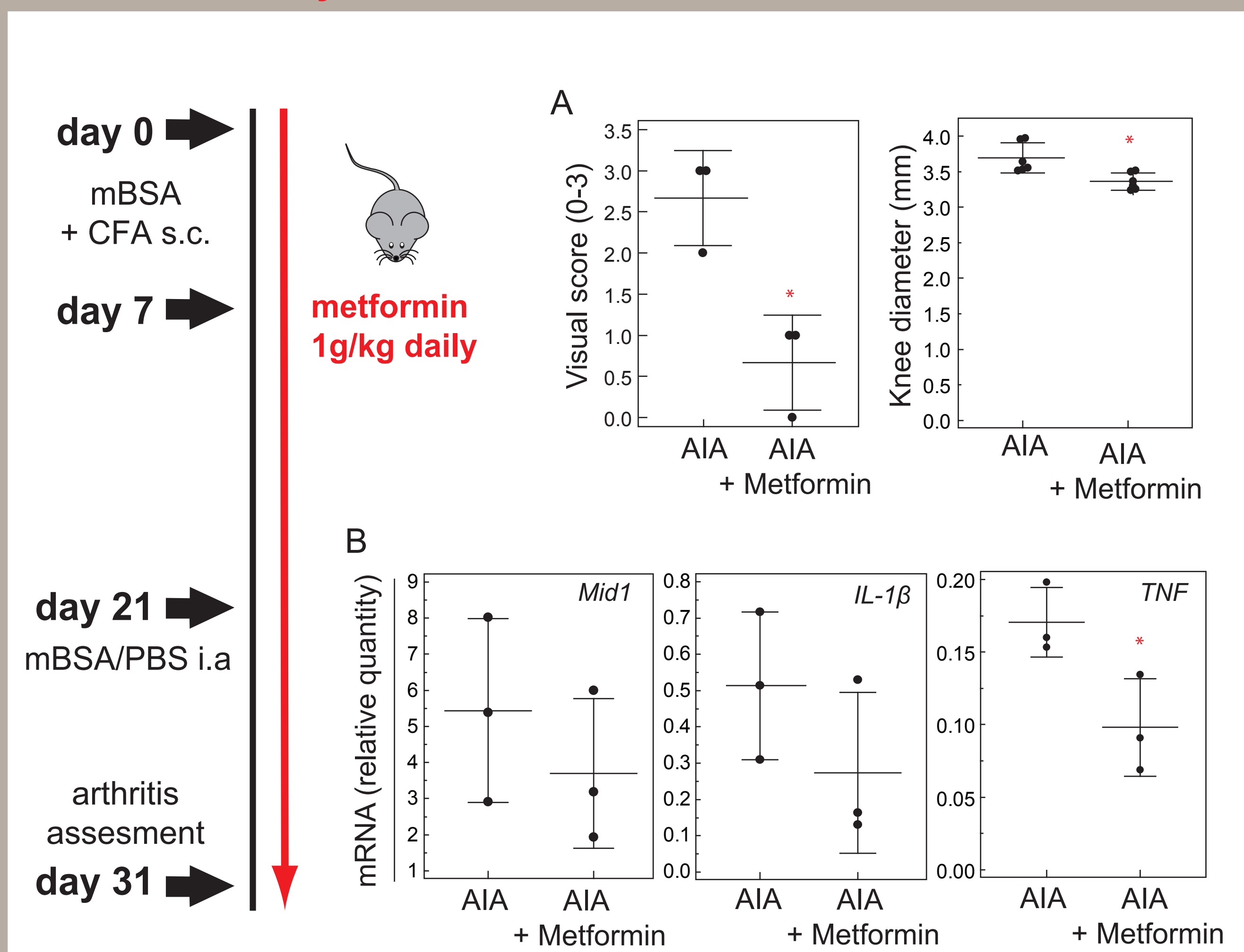
MATERIALS AND METHODS



3. Upregulation of *Mid1* in B6-AIA is not sexually dimorphic

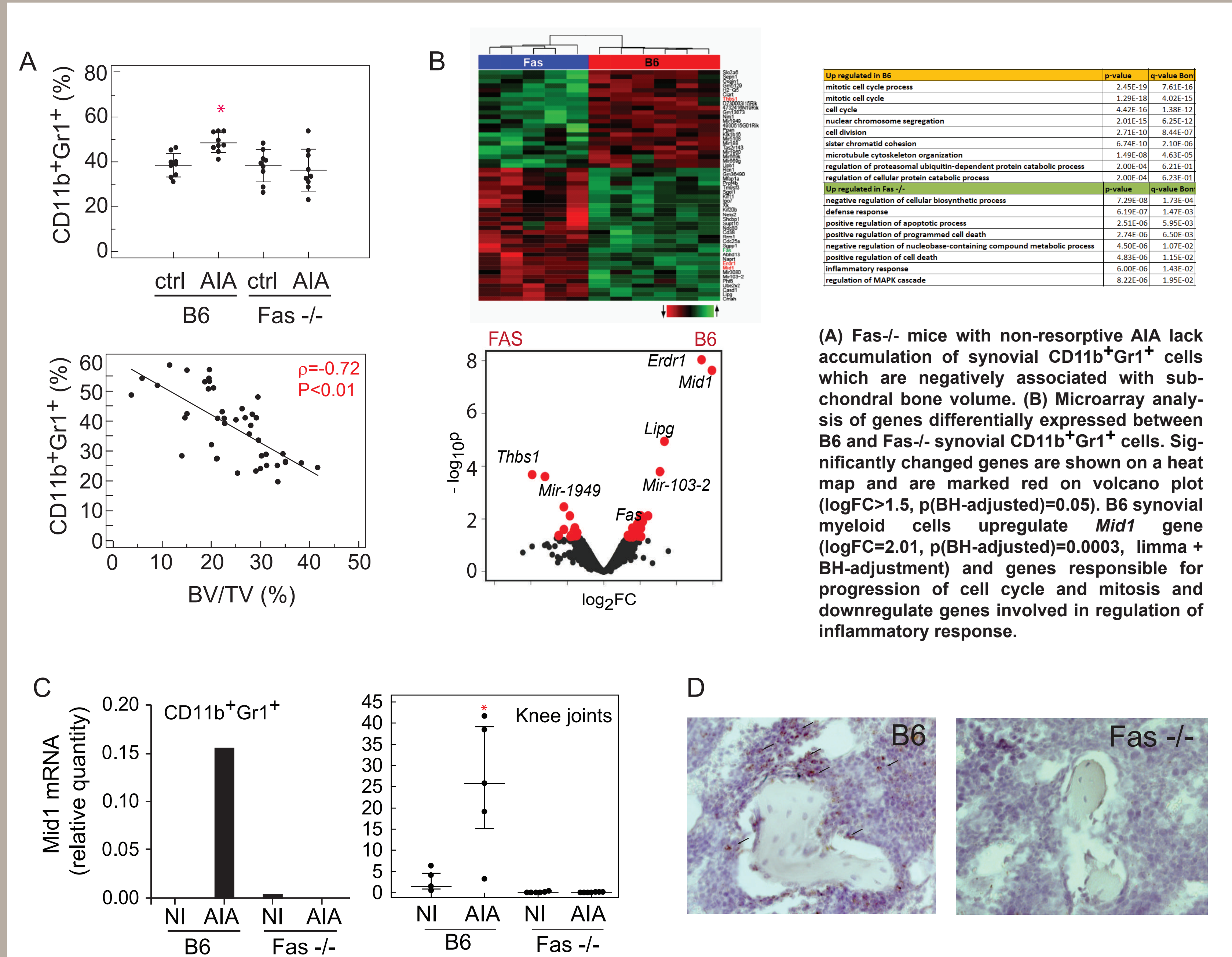


4. Metformin, which inhibits *Mid1*-PP2A interaction, ameliorates arthritis severity in B6-AIA mice

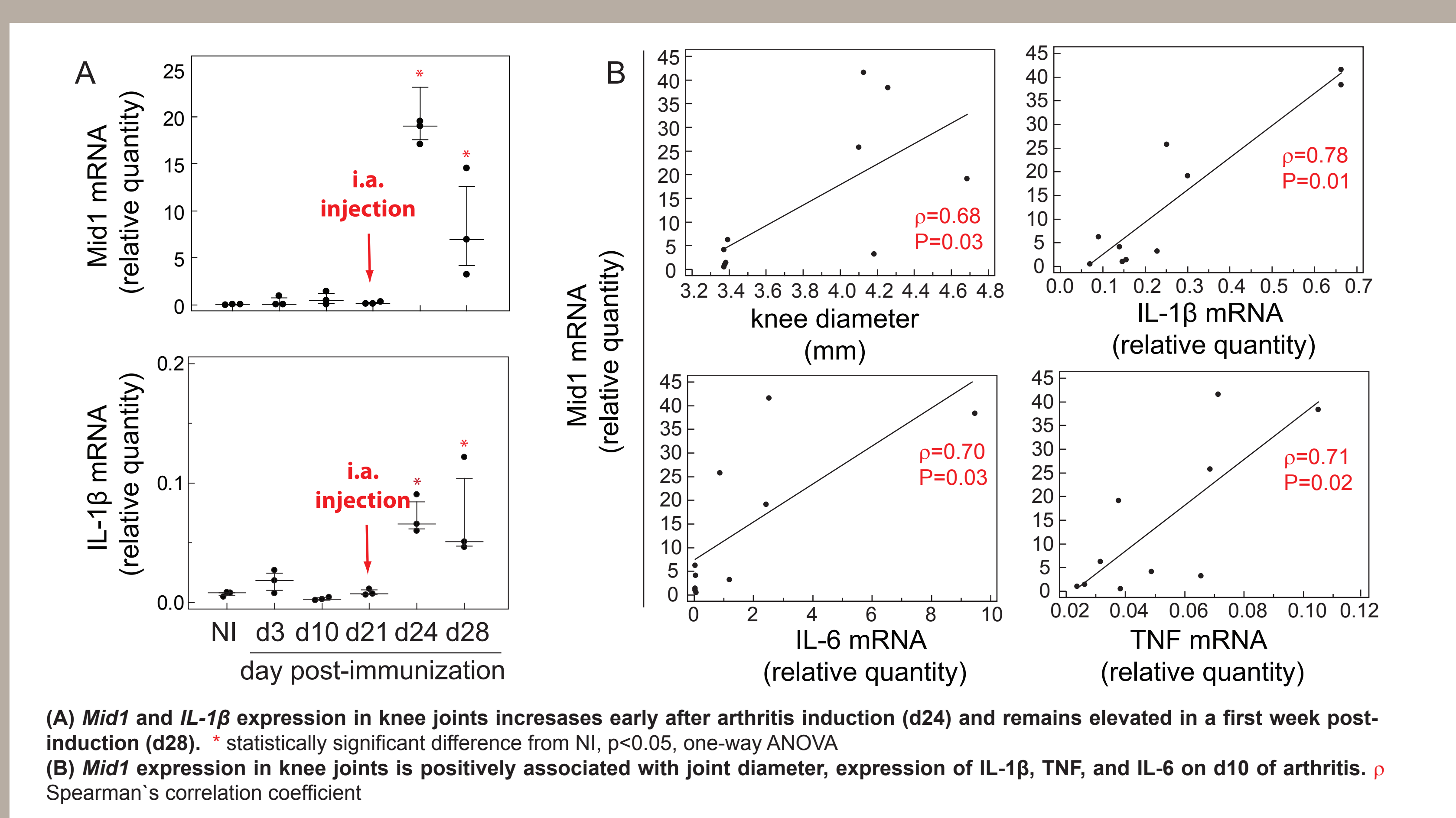


RESULTS

1. *Mid1* gene is upregulated in synovial CD11b⁺Gr1⁺ cells and bulk joint tissue in resorptive AIA in B6 mice



2. *Mid1* expression is upregulated early after arthritis induction and correlates with local proinflammatory cytokine expression



CONCLUSIONS

- Inflammatory response in resorptive AIA is marked by higher myeloid proliferation potential
- *Mid1* expression is upregulated in synovial myeloid cells and bulk knee joint tissue of B6 mice with resorptive arthritis
- *Mid1* expression is upregulated early after arthritis induction and correlates with expression of local markers of inflammation
- Despite its position on X chromosome *Mid1* expression in joints is not sexually dimorphic
- Metformin, which inhibits proinflammatory effects of *Mid1* by interfering with *Mid1*-PP2A interaction, ameliorates arthritis severity
- *Mid1* inhibition might present a new therapeutic target for inflammation-mediated joint destruction



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