

# Targeting oxMIF with antibody ON104 ameliorates clinical signs of arthritis by preventing tissue injury and reducing synovial macrophage infiltration

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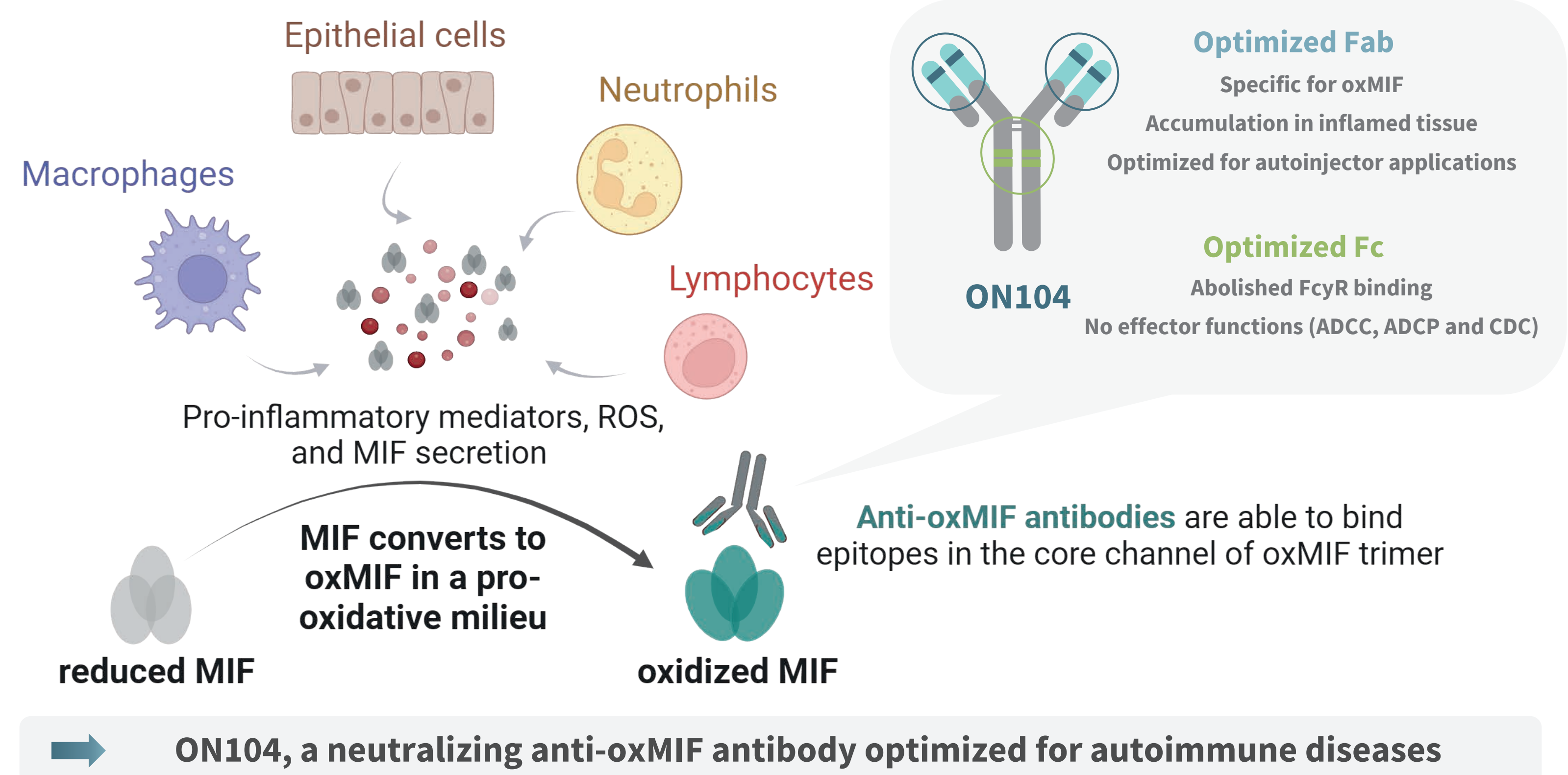
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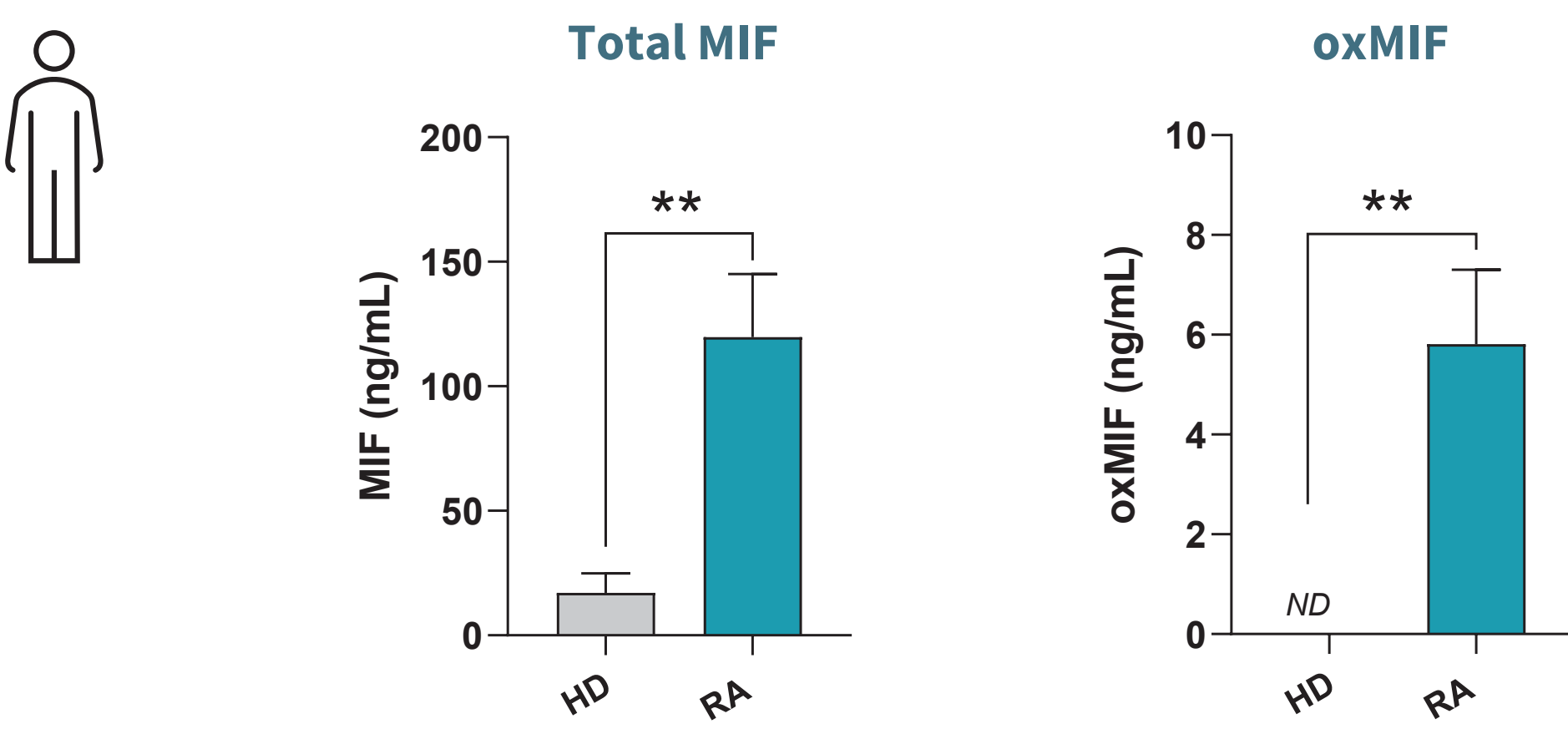
## 1 Oxidized Macrophage Migration Inhibitory Factor (oxMIF)

**Macrophage Migration Inhibitory Factor (MIF)** is a multifaceted inflammatory cytokine involved in the pathogenesis of various inflammatory diseases, including rheumatoid arthritis (RA). MIF exists in different, redox-dependent isoforms namely redMIF and **oxMIF**. OxMIF is generated in inflamed tissues and can be neutralized with isoform-specific antibodies that effectively inhibit the pathological functions of MIF.

Herein, we demonstrate the presence of oxMIF in the circulation of human RA patients and therapeutic efficacy of anti-oxMIF antibody ON104 during Collagen-Induced Arthritis (CIA), a well-established model of RA. At disease onset, arthritic DBA/1j mice were treated with ON104 twice a week for three weeks. ON104 effectively reduced paw thickness and the overall disease score compared to control mice. Furthermore, ON104 substantially attenuated both synovial and cartilage damage and markedly reduced F4/80-positive macrophages within the joints. These findings highlight the importance of oxMIF in RA pathogenesis and suggest that targeting oxMIF with human monoclonal antibody ON104 offers a promising and innovative treatment approach for RA and other MIF-related autoimmune-disorders.



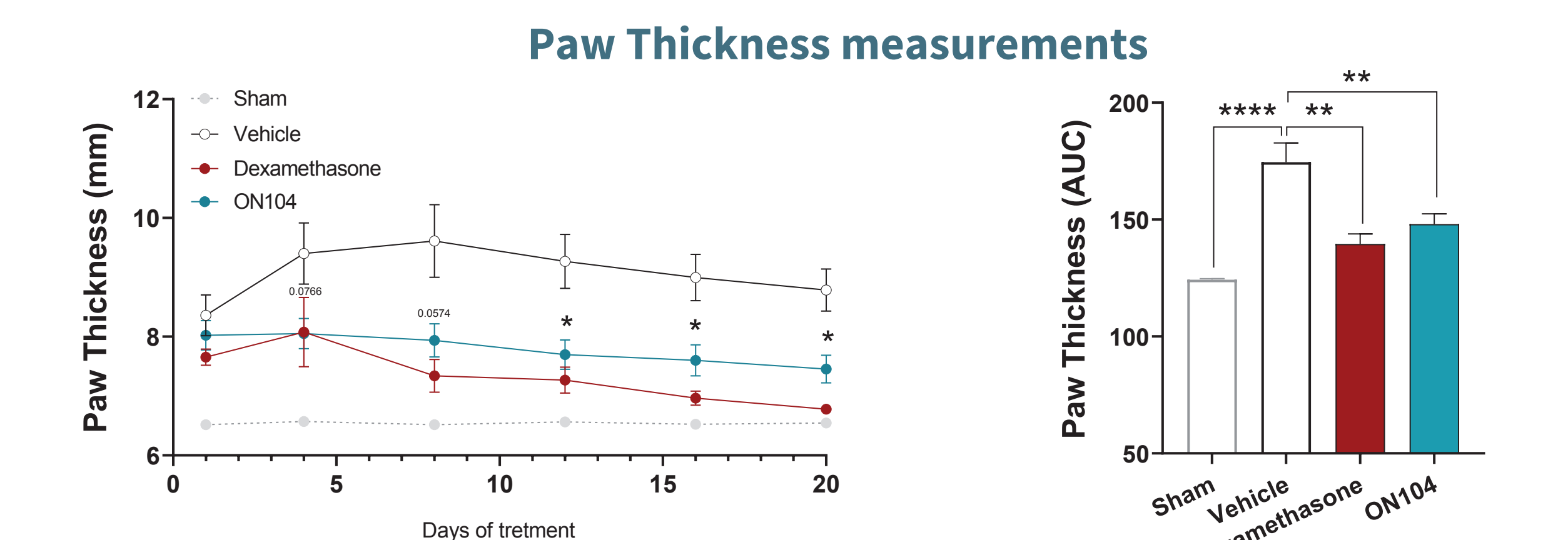
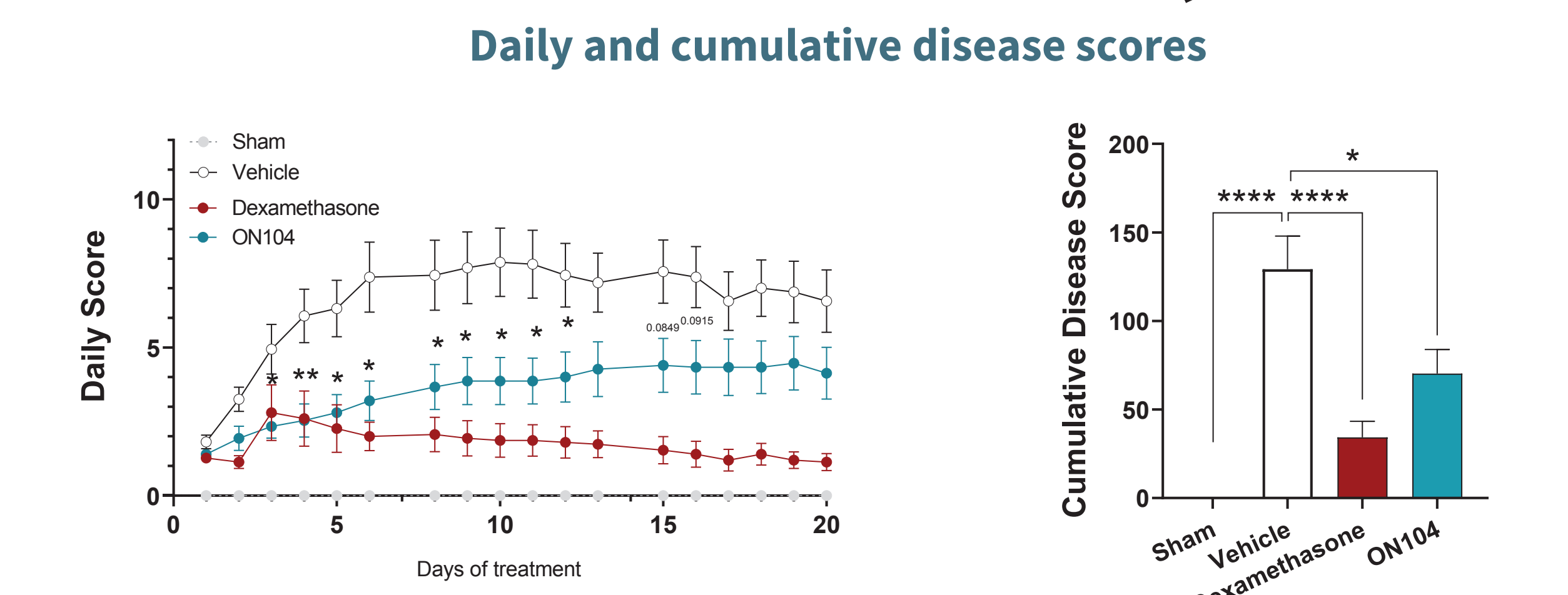
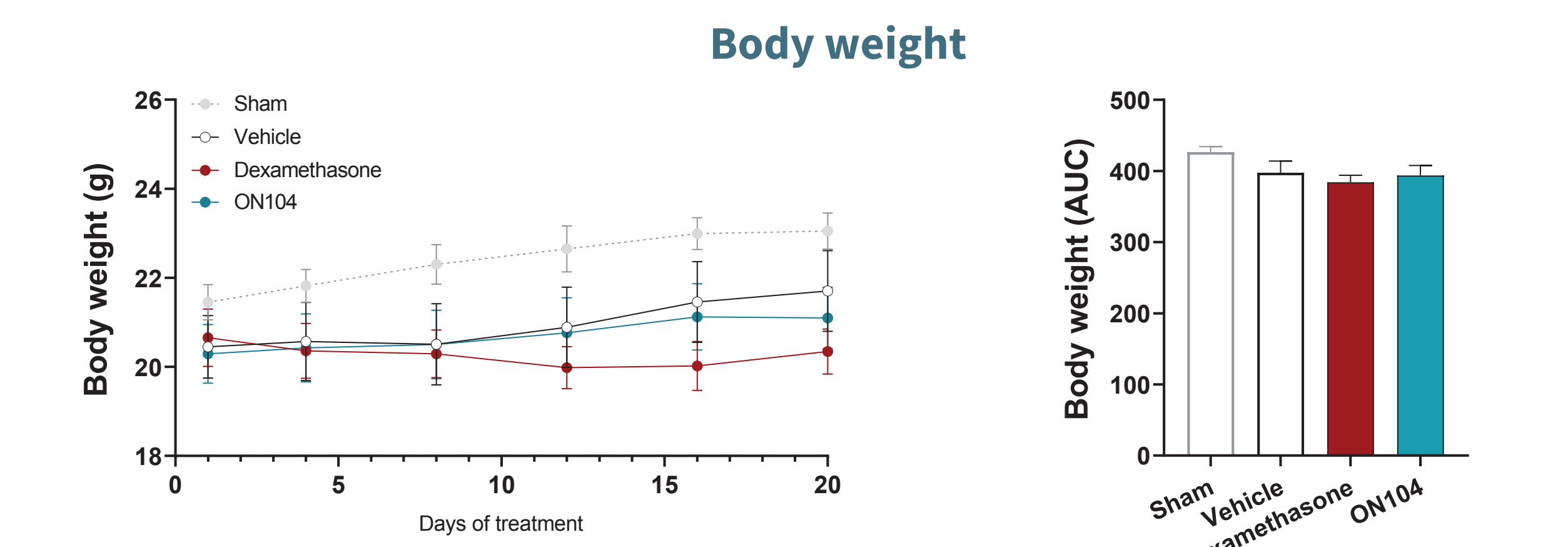
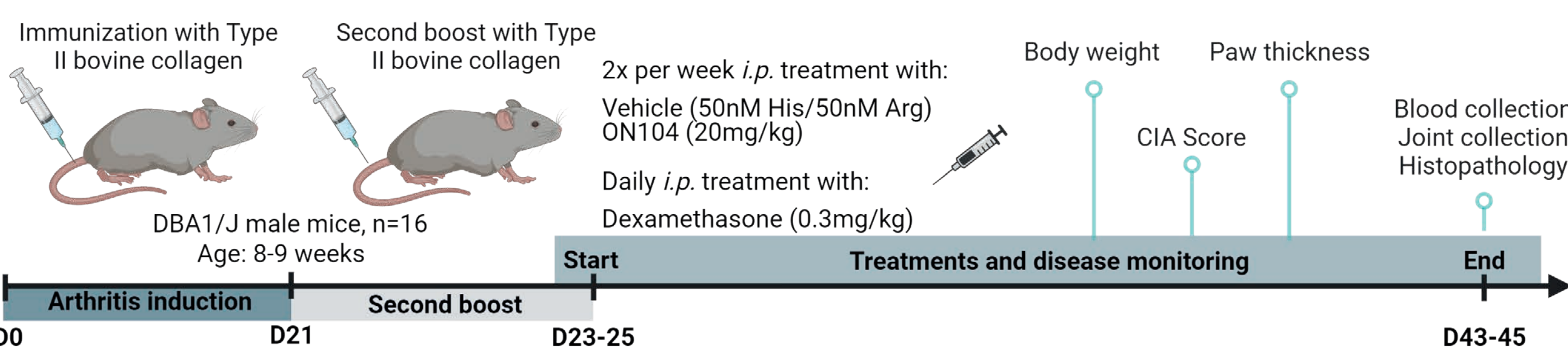
## 2 Circulating oxMIF expression in patients with RA



Data are expressed as mean ± SEM and analyzed by Mann-Whitney test. \*\*p < 0.01. HD for Healthy Donors (n=9); RA for Rheumatoid Arthritis (n=15).

oxMIF is present in the circulation of patients with rheumatoid arthritis (RA) and not detectable in healthy donors (HD) in contrast to MIF that is present in HD and upregulated during RA.

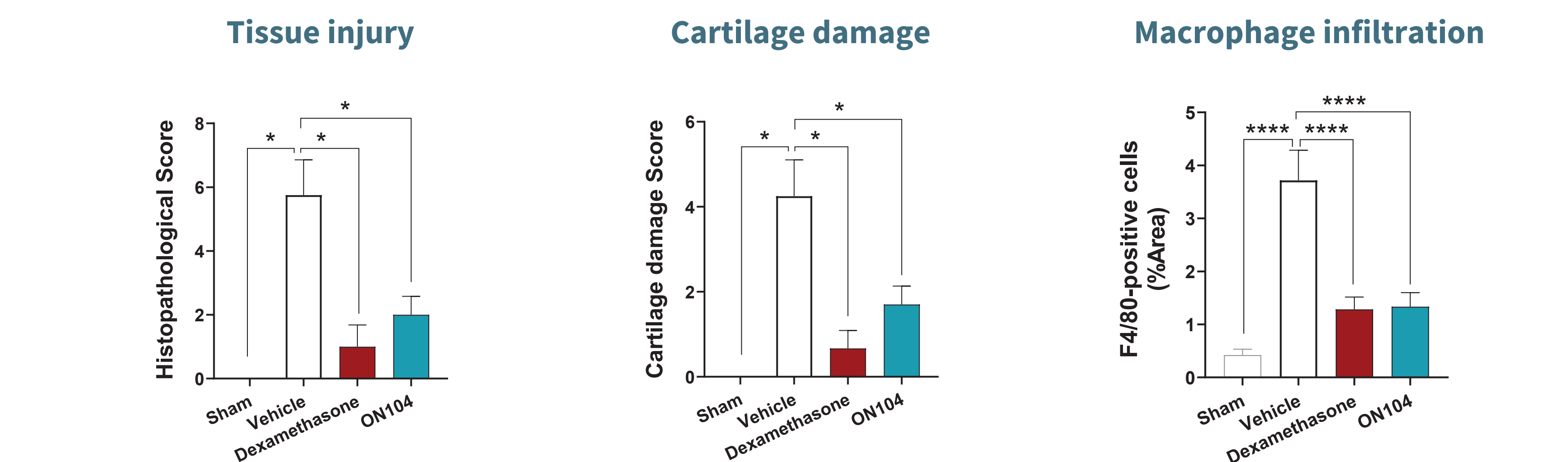
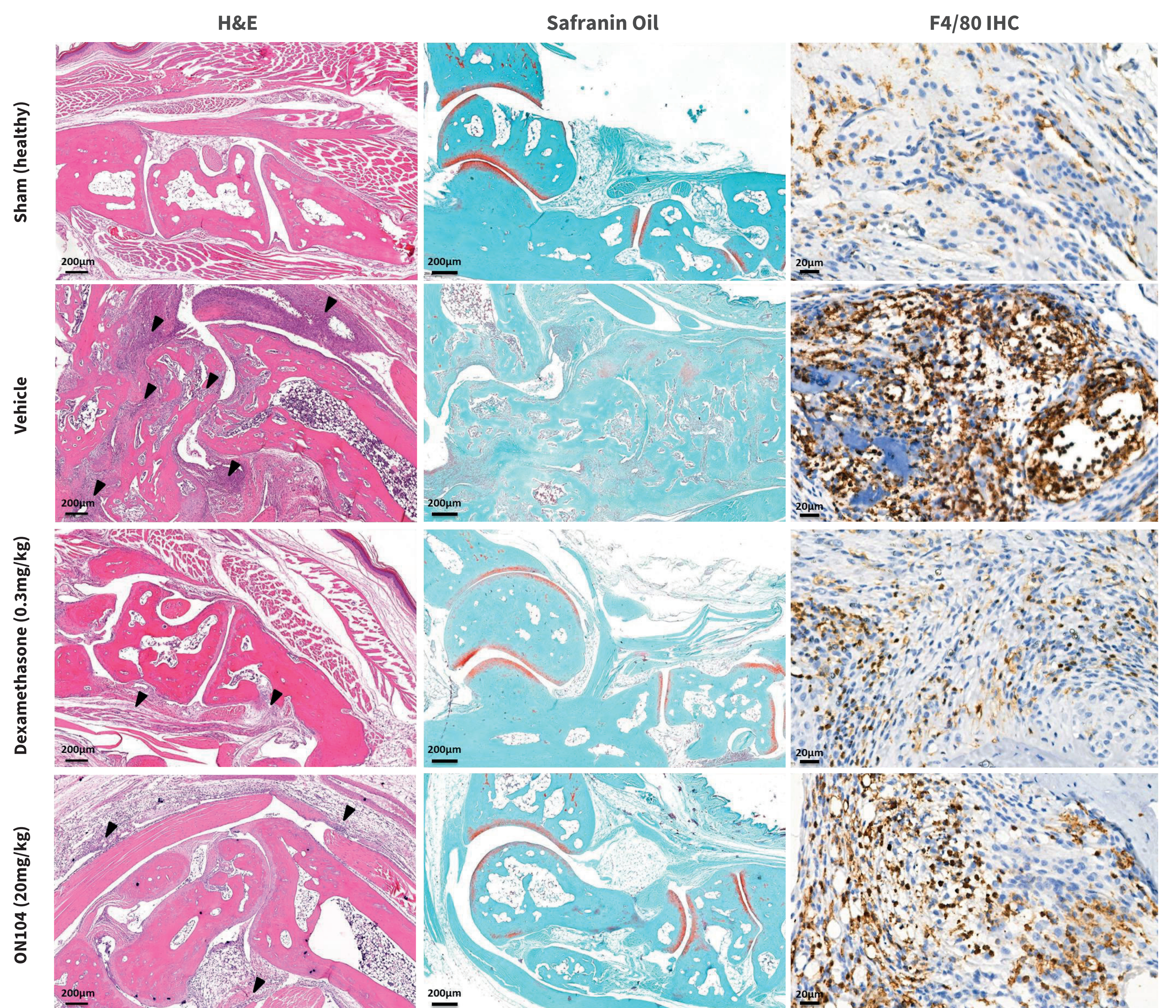
## 3 Effect of ON104 on clinical signs of *in vivo* arthritis



Disease severity, paw oedema and body weigh were periodically monitored. All data are expressed as mean ± SEM and analyzed by Two-way ANOVA for multiple comparison and Mann-Whitney test for paired comparison. \*p < 0.05; \*\*p < 0.01; \*\*\*\*p < 0.0001.

ON104 significantly reduced disease severity and reduced paw thickness during experimental arthritis.

## 4 Effect of ON104 on tissue damage and inflammation in experimental arthritis



Histology was performed on paraffin-embedded tissues (n=4-6 animals/group). IHC evaluation was performed using ImageJ software and an average of 160 picture per animal was evaluated. Data are presented as mean ± SEM and analyzed by Mann-Whitney test. \*p < 0.05, \*\*\*\*p < 0.0001.

ON104 significantly prevents tissue injury, cartilage damage, and reduces immune cell infiltration within the inflamed joints.

## 5 Conclusion & Outlook

- ON104 significantly ameliorates clinical signs of arthritis
- ON104 inhibits key pro-inflammatory activities of oxMIF mediated by macrophages
- ON104 has a high potential as anti-rheumatic therapeutic - either as monotherapy or in combination with standard-of-care *i.e* glucocorticoids



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