## FR10024

# The role of microRNA-146a in inflammatory Arthritis

Saferding Victoria<sup>1</sup>, Puchner Antonia<sup>1</sup>, Goncalves Alves Eliana<sup>1</sup>, Melanie Hofmann<sup>1</sup>, Michael bonelli<sup>1</sup>, Silvia Hayer<sup>1</sup>, Hans P. Kiener1, Smolen Joseph S.<sup>1</sup>, Redlich Kurt<sup>1</sup>, Blüml Stephan<sup>1</sup> <sup>1</sup>Medical University of Vienna Internal Medicine III, <sup>2</sup>Medical University of Vienna Department of Physiology



## miRNA mRNA Background MicroRNA (MiR-) 146a plays an important role in the regulation of the innate immune response and has also been shown to suppress

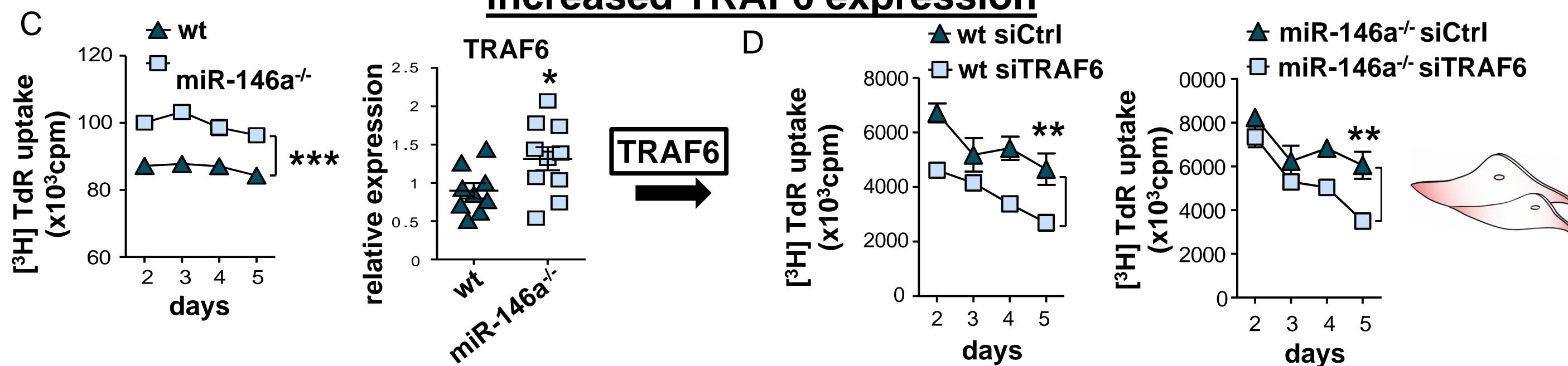
arthritis is still elusive.

miR-146a IRAK1 TRAF6 cancer development in myeloid cells. Elevated expression of miR-146a has been detected in synovial tissue of rheumatoid arthritis patients, NF-kB but its role in the development of inflammatory Inflammation Survival

Proliferation

bone marrow synovial RNA sequencing analysis cells fibroblasts hematopoietic mesenchymal cells B, RNA sequencing analysis from bone marrow cells and synovial fibroblasts. Volcano plots showing differentially expressed genes from wt versus miR-146a<sup>-/-</sup> animals. miR-146a<sup>-/-</sup> miR-146a<sup>-/-</sup> wt

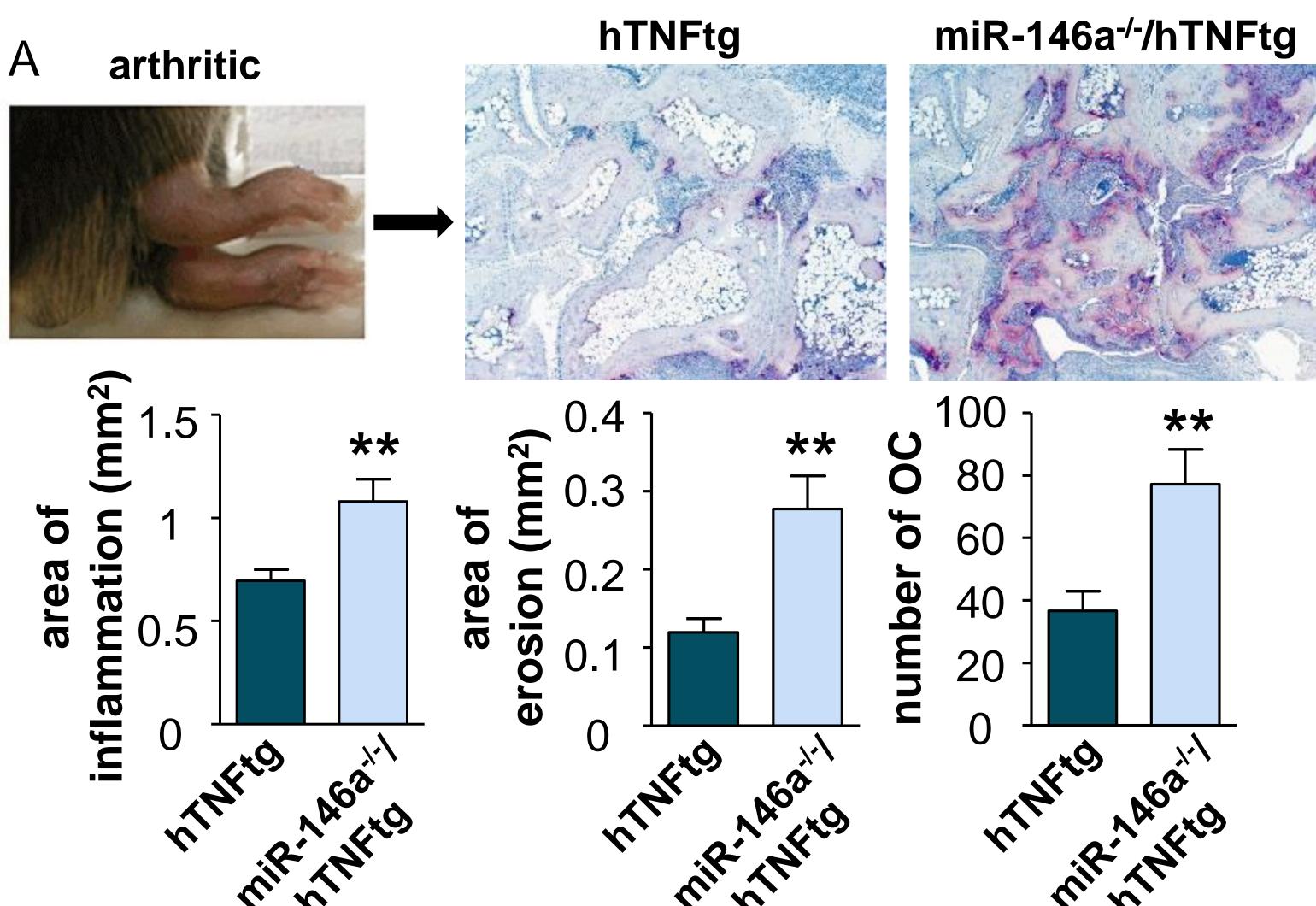
#### Fibroblasts lacking miR-146a display elevated proliferative capacity linked to increased TRAF6 expression



C, Proliferation of synovial fibroblasts from wt and miR-146a<sup>-/-</sup> animals was measured by [3H]Thymidine incorporation. The relative mRNA expression of TRAF6 was measured by Q-PCR in synovial fibroblasts from wt and miR-146a<sup>-/-</sup> animals.

D, Proliferation of synovial fibroblasts from wt and miR-146a-/- animals after siRNA mediated knock down of TRAF6 was measured by [3H]Thymidine incorporation.

#### Increased severity of arthritis in hTNFtg animals lacking miR-146a

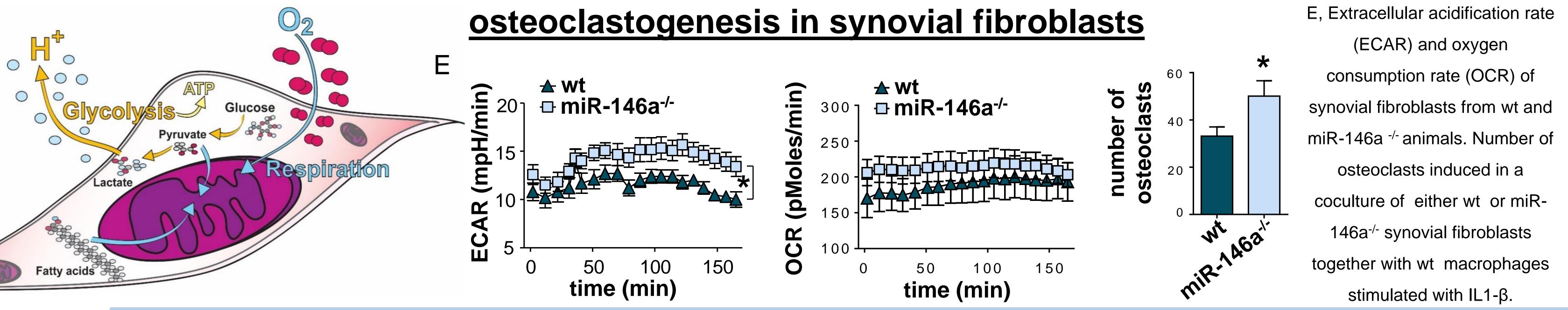


Histological assessment of inflammation, erosion and number of osteoclasts (OC) in the tarsal area of the

hind paws from 10 weeks old hTNFtg and miR-146a<sup>-/-</sup>/hTNFtg mice.

A, TRAP stained histological sections of the hind paws from hTNFtg and miR-146a<sup>-/-</sup>/hTNFtg mice.

Deficiency of miR-146a leads to increased metabolic activity and capacity to induce



## Conclusion

These data demonstrate an important mitigating role of miR-146a in inflammatory arthritis, most importantly in local bone destruction, by controlling mesenchymal expression of osteoclastogenic factors. This shows an important anti-inflammatory role of miR-146a, which might possibly be exploited for therapeutic purposes.