DIVISION OF RHEUMATOLOGY

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The role of microRNA-146a in inflammatory Arthritis

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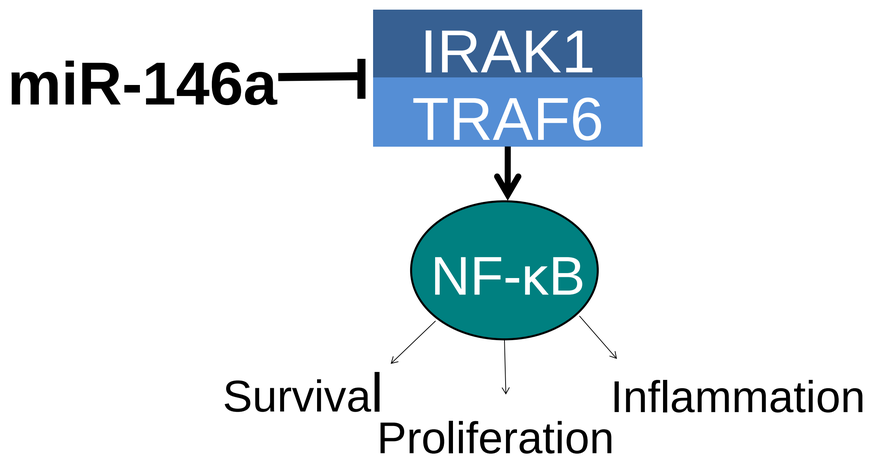
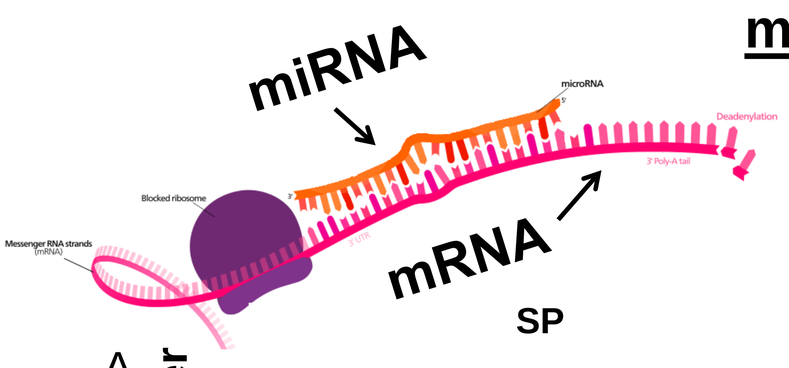
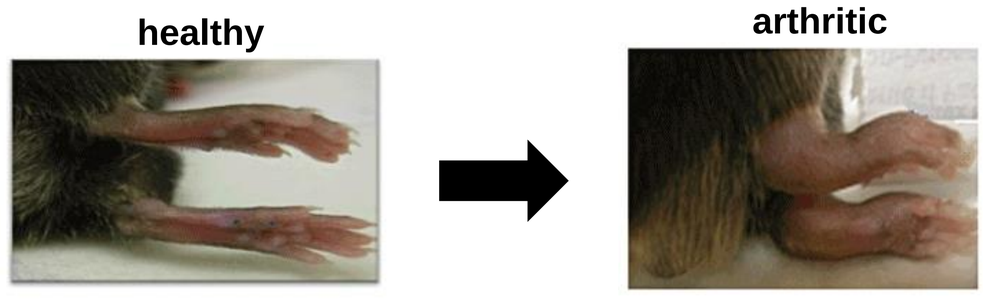
Background:

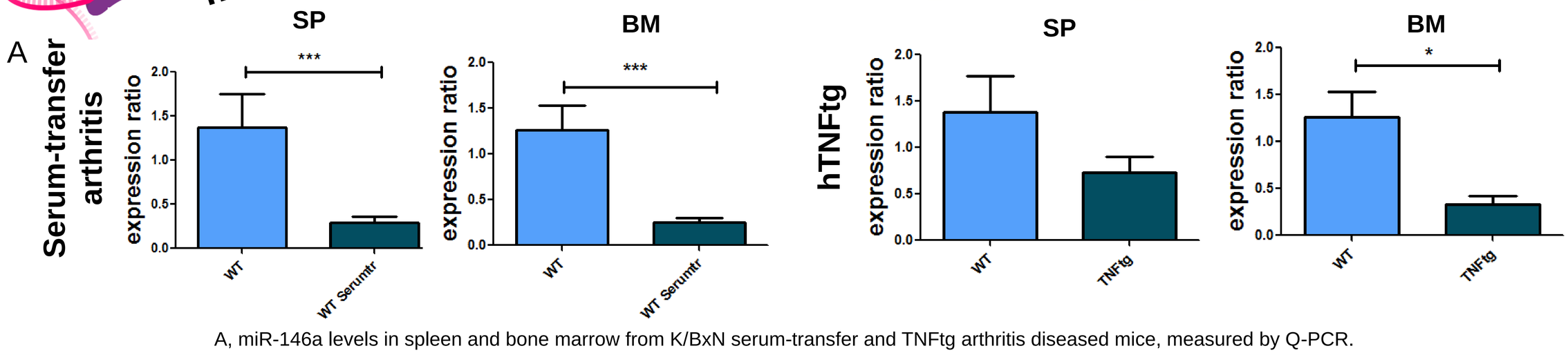
MicroRNA (MiR-) 146a is a key regulator of the innate immune response and has also been shown to suppress cancer development in myeloid cells. Elevated expression of miR-146a has been detected in synovial tissue of rheumatoid arthritis patients, but its role in the development of inflammatory arthritis is yet unknown.





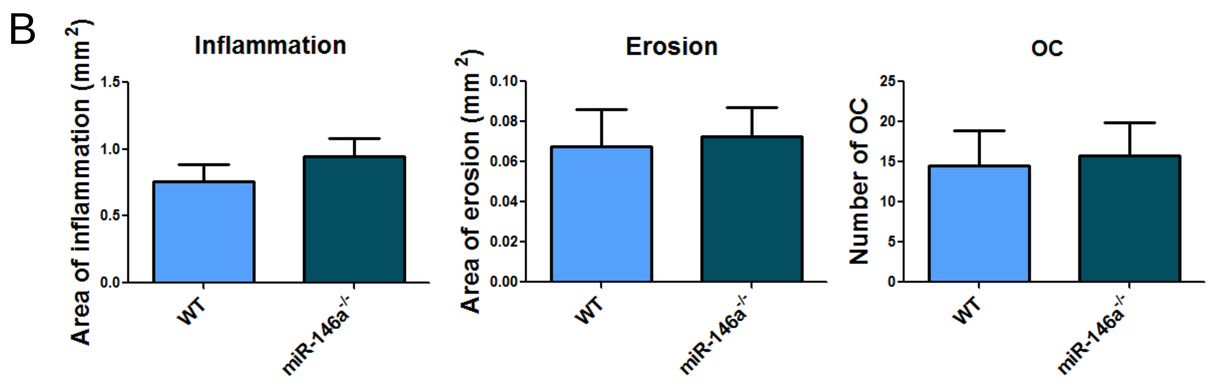
miR-146a level in arthritis disease models



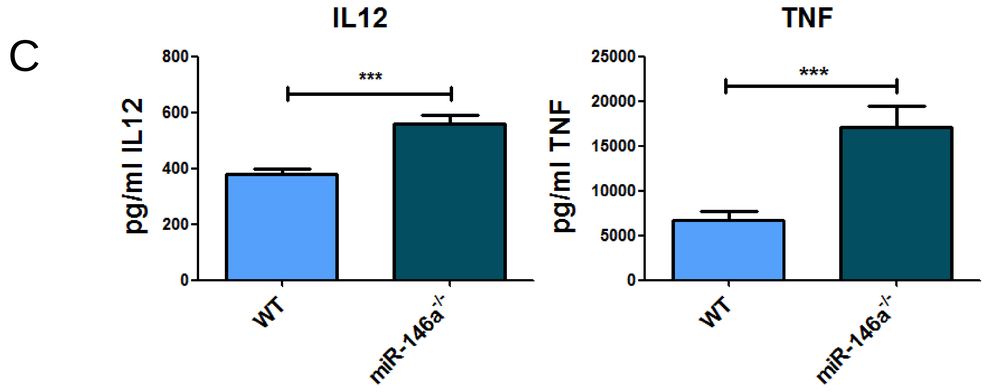


A, miR-146a levels in spleen and bone marrow from K/BxN serum-transfer and TNFtg arthritis diseased mice, measured by Q-PCR.

K/BxN serum-transfer arthritis

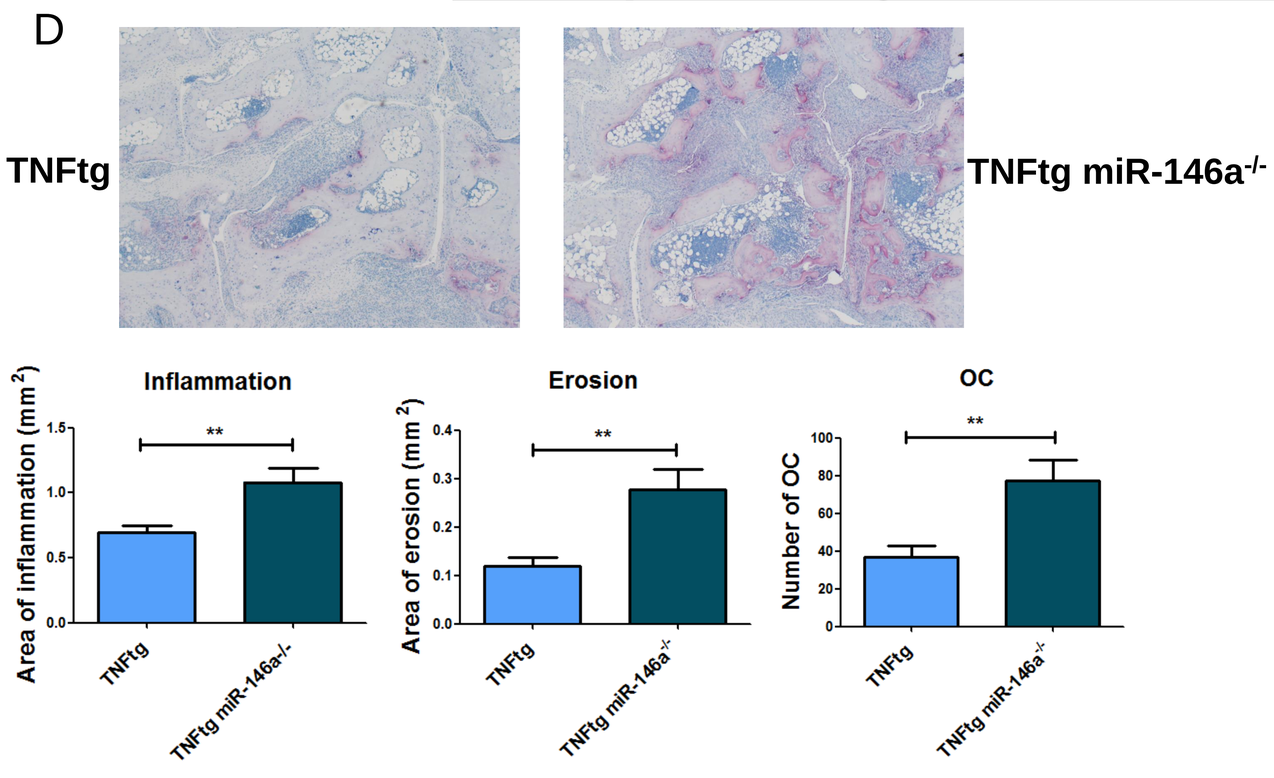


B, Histological assessment of inflammation, erosion and number of osteoclasts (OC) in the tarsal area of the hind paws 12 days after induction of serum-transfer arthritis.

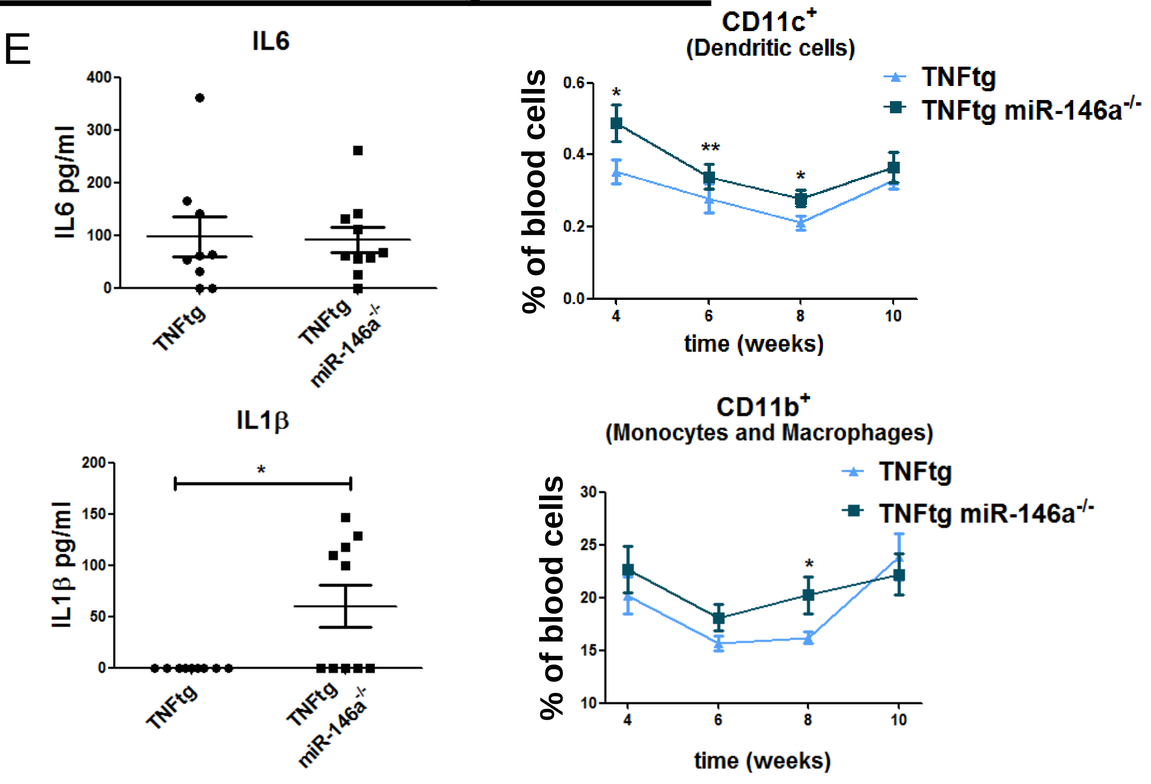


C, Serum Cytokine levels after the induction of serum-transfer arthritis in wild-type and miR-146a$^{-/-}$ mice, measured by Elisa.

TNF-alpha transgenic mouse model of inflammatory arthritis



D, Histological assessment of inflammation, erosion and number of osteoclasts (OC) in the tarsal area of the hind paws from 10 weeks old TNFtg and TNFtg miR-146a$^{-/-}$ mice. Images of the TRAP stained tarsal area of the hind paws from TNFtg and TNFtg miR-146a$^{-/-}$ mice.



E, Serum Cytokine levels from 10 weeks old TNFtg and TNFtg miR-146a$^{-/-}$ mice measured by Elisa. Amount of myeloid cells, measured in the blood from 4 to 10 weeks old TNFtg and TNFtg miR-146a$^{-/-}$ mice analysed by flow cytometry.

Conclusion:

These data clearly demonstrate a negative regulatory role of the miR-146a in inflammatory arthritis. During arthritis, miR-146a is centrally involved in the regulation of proinflammatory cytokines as well as local bone destruction. These results identify an important anti-inflammatory role of miR-146a, which might possibly be exploited for therapeutic purposes.