Background: Our group have recently shown that Sema3B is reduced in RA patients and plays a protective role in an arthritis mouse model, through the reversion of inflammatory mediators and the synovial fibroblast invasiveness and was associated with a reduction of CD68 positive synovial macrophages (Igea, 2022). On the other hand, MerTK is a receptor protein kinase involved in the resolution of inflammation and plays a protective role in arthritis mice models (Waterborg, 2018).

A recent study has shown that a population of synovial tissue macrophages characterized by the expression of MerTK are associated with remission maintenance and with an anti-inflammatory phenotype of RA FLS (Alivernini, 2020). The aim of this study is to determine the role of Sema3B in the phenotypic characteristics of RA macrophages and the implication of MerTK.

Methods: Peripheral blood monocytes from RA patients (n=10) were differentiated into macrophages by culturing in the presence of IFN-γ (10ng/mL) for 6 days. Afterwards, macrophages were stimulated for 24h with LPS (10ng/mL), Sema3B (200ng/mL) or the combination of both mediators. The expression of pro-and anti-inflammatory mediators was determined by quantitative PCR (qPCR) and ELISA. The expression of MerTK and macrophage surface marker was measured by flow cytometry.

Results: Sema3B did not modulate the macrophage expression of pro-inflammatory mediators IL1B, IL6, IL12B, IL23, TNF, CCL2, CXCL10 and CD86, but significantly reduced the expression of lipid involved in resolution of inflammation (Figure 1B). Moreover, Sema3B reduced the expression of the M1 marker CD64, while induced the expression of the M2 marker CD163.

Conclusion: Our data demonstrate that Sema3B modulates the macrophage phenotype of RA macrophages, inducing a skewing towards an anti-inflammatory/pro-resolving phenotype, likely in a MerTK-dependent manner. Therefore, here we identified a new mechanism involved in the protective role of Sema3B in RA pathogenesis.

REFERENCES:

Acknowledgements: All patients involved in this study.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.5056