

P032

SIALIC ACIDS INHIBIT NEUTROPHIL EXTRACELLULAR TRAP FORMATIONAK Molhoek*, MM van Gool, RE Li, M van Egmond, SJ van Vliet, Y van Kooyk. *Molecular Cell Biology and Immunology, Amsterdam UMC, Amsterdam, Netherlands*

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Career situation of first and presenting author Student for a master or a PhD**Introduction** In rheumatoid arthritis (RA) activated neutrophils produce neutrophil extracellular traps (NETs), which provide a source of autoantigens that drives the autoimmune process.¹ To identify novel immune processes that dampened neutrophil activity, we investigated a family of inhibitory glycan-binding receptors (Siglecs) that bind a specific type of glycan; called sialic acids.² We hypothesize that sialic acid-mediated triggering of siglecs on neutrophils, which express siglec-5, -9 and -14, will reduce their activation. In this study we focused on dampening the activity of neutrophils and thereby NET formation.**Methods** Polymorphonuclear cells (PMNs) were isolated from healthy donors. Neutrophil binding of sialic acid-containing glycoconjugates was assessed by flow cytometry. Neutralizing antibodies for siglec-5/14 and -9 were used to block the interaction with the sialic acid glycoconjugates. For functional assays a branched synthetic molecule containing sialic acids (sialic acid dendrimer) was used. PMNs were rested for 1 hour at 37°C followed by stimulation of sialic acids dendrimers for 30 min. Subsequently, IgA coated beads were added for 30 min to activate the neutrophils. NETosis was quantified via Sytoxgreen and visualised via microscopy, and phagocytosis was measured by flow cytometry.**Results** Binding of sialic acid glycoconjugates was observed on neutrophils. Neutralizing siglec-5/14 and -9 receptor almost completely abolished sialic acid glycoconjugate binding to neutrophils. Neutrophils activated with IgA beads released NETs, as confirmed via microscopy. Triggering neutrophils with sialic acid dendrimer reduced this process of NETosis. The capacity to engulf IgA beads was not affected by sialic acid dendrimer stimulation.**Conclusions** Neutrophils stimulated with sialic acid dendrimers show reduced activation. Patients with RA might benefit from treatment with sialic acid to dampen neutrophil-mediated autoimmune response.**REFERENCES**

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2. Macauley MS, Crocker PR, Paulson JC. Siglec-mediated regulation of immune cell function in disease. *Nat Rev Immunol* 2014;**14**(10):653–66.

Disclosure of Interest None declared.

P033/O31

CD38-EXPRESSING MEMORY T CELLS ARE EXPANDED IN PERIPHERAL BLOOD, CONTAINED IN INFLAMED TISSUE AND REPRESENT A POTENTIAL TREATMENT TARGET IN SYSTEMIC LUPUS ERYTHEMATOSUS^{1,2}L Ostendorf*, ^{2,3}P Enghard, ^{1,2}F Hiepe, ^{1,2}T Alexander. ¹Rheumatology, Charité Universitätsmedizin; ²Deutsches Rheumaforschungszentrum; ³Nephrology, Charité Universitätsmedizin, Berlin, Germany

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Career situation of first and presenting author Student for a master or a PhD.**Introduction** The unresponsiveness of long-lived plasma cells (PC) to immunosuppressive and B cell depleting therapies represents a therapeutic challenge in systemic lupus erythematosus (SLE) and other immune-mediated diseases. Novel potential targets such as CD38 have emerged.¹**Objectives** Here, we aimed to analyze expression levels of CD38 on circulating plasmablast and peripheral blood and tissue residing lymphocyte subsets in SLE to estimate the therapeutic potential of CD38-targeting therapies.**Methods** Multicolor flow cytometry was performed to investigate the CD38 expression on peripheral blood mononuclear cells (PBMCs) of SLE patients (n=36), healthy controls (HC, n=20) and multiple myeloma (MM, n=10) patients. In addition, kidney-infiltrating T cells isolated from urine were analyzed in patients with lupus nephritis (LN). To investigate the cytokine secreting potential, cytokines were analyzed intracellularly in CD38-expressing T cells after polyclonal stimulation *in vitro* with PMA/Ionomycin.**Results** Circulating CD19⁺CD24^{neg}CD27^{high} plasmablasts are more frequent in SLE and MM patients and display higher mean fluorescence intensity for CD38 compared to HC. In SLE, CD38 is significantly higher expressed in both CCR7⁺ central and CCR7^{neg} effector memory CD4 and CD8 T cells compared to HC. Such cells co-express other markers of T cell activation and recent proliferative history such as HLA-DR and Ki-67, and are preferentially negative for FoxP3 and Helios. CD38 is most exclusively expressed on CXCR3⁺ memory T cells isolated from urine of patients with LN in contrast to their CXCR3^{neg} counterparts. Upon polyclonal stimulation, cytokine (IFN- γ , IL-17, TNF α , IL-2) secreting cells were confined to memory T cells lacking CD38 expression.**Conclusions** Expression levels of CD38 are significantly higher in peripheral blood memory B- and T-cell subsets from patients with SLE compared to HC. CD38^{pos} T cells co-express markers of recent activation and proliferative history, are confined to conventional memory T cells and contained in inflamed tissue, suggesting a pathogenic role of a chronically activated memory T cell compartment in SLE. The lack of effector cytokine secretion of such cells is unexpected and merits further investigation. PC depleting therapies targeting CD38 may represent a promising treatment option in SLE given their potential therapeutic effect on activated memory T cells in inflamed tissue.**REFERENCE**

1. Hiepe F, Radbruch A. *Nat Rev Nephrol* 2016.

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P034

PRESENCE OF A SPECIFIC DEFECT IN M2 POLARIZATION OF BLOOD MONOCYTES FROM PATIENTS WITH RHEUMATOID ARTHRITIS, ASSOCIATED WITH INCREASED MICRORNA-155A Paoletti*, J Rohmer, B Ly, J Pascaud, E Riviere, G Nocturne, X Mariette. *U1184 INSERM IMVA, le Kremlin bicetre, France*

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Career situation of first and presenting author Post-doctoral fellow.**Introduction** Macrophages contribute *in situ* to the rheumatoid arthritis (RA) pathogenesis. Two distinct states of