of Anti-Modified Protein Autoantibody Reactivities in Rheumatoid Arthritis. *Arthritis Rheumatol.* 2020 Oct;72(10):1643-1657. PMID: 32501655

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POS0010 CD38+ MEMORY T CELLS ARE A FUNCTIONALLY DISTINCT SUBSET THAT IS EXPANDED IN SLE AND ASSOCIATED WITH LUPUS NEPHRITIS

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Background: We recently reported the beneficial clinical responses of the anti-CD38 monoclonal antibody daratumumab in two patients with systemic lupus erythematosus (SLE) [1]. While the primary rationale for its use was the depletion of autoantibody-producing long-lived plasma cells, daratumumab may promote additional therapeutic effects on CD38-expressing T cells, but their origin, lifestyle and role in lupus pathophysiology remains elusive.

Objectives: To investigate the phenotype, transcriptional program, functional properties and clinical associations of CD4+ and CD8+CD38+ memory T cells in SLE compared to healthy controls (HC).

Methods: CD38-expression on memory T cell subsets was measured by flow cytometry in 65 patients with SLE and 28 healthy controls. We investigated the functional capacity of CD38+ T cells using CFSE staining and intracellular cytokine staining after polyclonal stimulation. Additionally, we performed single-cell transcriptome and T-cell-receptor sequencing of 7 SLE patients and 7 matched healthy controls, including surface protein expression analysis using CITE-seq (RNA-barcoded) antibodies.

Results: Compared to healthy controls, the frequency of CD38-expressing memory T cells in SLE was significantly increased in both CD4+ and CD8+ T cells. SLE patients with a previous or current lupus nephritis had significantly increased levels of CD8+CD38+ memory T cells compared to those without

history of renal involvement. CD38+ memory T cells expressed increased levels of Ki-67 and displayed higher proliferative capacity upon polyclonal stimulation than their CD38- counterparts, both in SLE patients and HC, while they showed decreased ability to secrete IFN- γ , IL-2, GM-CSF and TNF- α . Single-cell transcriptome sequencing revealed that CD8+CD38+ memory T cells were enriched within terminally differentiated, cytotoxic CD8 T cells, and had reduced TCR repertoire diversity compared to their CD38- counterparts. CD8+CD38+ memory T cells from SLE patients had significantly higher expression of type I interferon associated genes, both compared to CD38- memory T cells from SLE patients and CD38+ cells from HCs.

Conclusion: CD38+ memory T cells with increased proliferative capacity but altered effector functions are significantly expanded in peripheral blood of SLE and correlate with the lupus nephritis. Although the factors mediating their generation and their precise role in the disease pathophysiology remain to be investigated, CD38-expressing T cells may be useful as a future biomarker for lupus nephritis.

REFERENCES:

- [1] Ostendorf L, Burns M, Durek P, Heinz GA, Heinrich F, Garantzotis P, et al. Targeting CD38 with Daratumumab in Refractory Systemic Lupus Erythematosus. *N Engl J Med.* 2020 Sep 17;383(12):1149-55.
- [2] Katsuyama E, Suarez-Fueyo A, Bradley SJ, Mizui M, Marin AV, Mulki L, et al. The CD38/NAD/SIRTUIN1/EZH2 Axis Mitigates Cytotoxic CD8 T Cell Function and Identifies Patients with SLE Prone to Infections. *Cell Reports.* 2020 Jan;30(1):112-123.e4.

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Epidemiology and treatment of pain in RMDs

POS0011

THE ASSOCIATION BETWEEN BARIATRIC SURGERY AND CARPAL TUNNEL SYNDROME: A COHORT STUDY FROM SWEDISH NATIONWIDE HEALTHCARE REGISTRIES

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Background: Carpal tunnel syndrome (CTS) is a chronic compression neuropathy caused by entrapment of the median nerve in the wrist causing pain and sensory loss. Prior observational research suggested that obesity increased the risk of CTS. However, the impact of weight loss among obese patients on CTS has not been assessed to date.

Objectives: To assess the association between bariatric surgery and CTS in a secondary care setting.

Methods: We performed a propensity score (PS)-matched cohort study using data from Swedish nationwide healthcare registries (patient registry [secondary care], causes of death registry, prescribed drug registry). Patients aged 18-79 years who underwent bariatric surgery between 2006 and 2019 were matched to up to 2 obese bariatric surgery-free patients (called unexposed patients) based on their PS. PS-matching was carried out in risk set sampling to reduce selection bias, within 4 sequential cohort entry blocks to account for time trend biases. The outcome CTS was defined as a diagnosis of CTS in secondary care or carpal tunnel decompression surgery. After a 1-year run-in period, patients were followed in an "as-treated" approach. We applied Cox proportional hazard regression to calculate hazard ratios (HR) with 95% confidence intervals (CIs) of CTS among bariatric surgery patients when compared to obese unexposed patients overall, and in subgroups of age, sex, bariatric surgery type, and by duration of follow-up.

Results: A total of 40 619 bariatric surgery patients were PS-matched to 63 540 obese unexposed patients. A total of 72.3% of bariatric surgery patients were women. Bariatric surgery patients had a mean age of 41.7 years and a mean follow-up of 6.8 years. All patient characteristics in obese unexposed patients were highly similar. We observed 1 356 and 1 938 severe CTS cases among bariatric surgery and obese unexposed patients, respectively. Bariatric surgery was not associated overall with CTS (HR of 0.98, 95% CI 0.91-1.05). However, the risk of CTS seemed to decrease with age at bariatric surgery – the lowest CTS risk was observed among bariatric surgery patients aged 18-34 years (HR of 0.87, 95% CI 0.74-1.01), when compared to obese unexposed patients. Sex did not modify the risk of CTS among bariatric surgery patients compared to obese