Objectives: The aim of this study was to determine LV systolic and diastolic function and their association with circulating inflammatory markers in CIA.

Methods: Male Sprague Dawley rats were randomly divided into two groups: a control group (n=12) and a collagen-induced arthritis group (CIA, n=21). Rats in the CIA group were immunised with 0.2 ml type-II bovine collagen emulsified in incomplete Freund's adjuvant at the base of the tail followed by a 0.1 ml booster injection 7 days later. Eight weeks post-immunisation, markers of LV systolic function and geometry including ejection fraction (EF), fractional shortening (FS), stroke volume (SV) and LV end systolic diameter (ESD) were assessed echocardiographically using two-dimensional directed M-mode imaging. Markers of LV diastolic function including the early-to-late diastolic filling velocity ratio (E/A), the lateral (Lat e') and septal (Sep e') wall myocardial tissue lengthening at the mitral annulus and the ratio between early mitral inflow velocity and mitral annular early diastolic velocity (E/e') were assessed using pulsed Doppler and tissue Doppler echocardiography. Serum concentrations of interleukin 6 (IL-6), interleukin 1 β (IL-1 β), tumour necrosis factor alpha (TNF- α) and C-reactive protein (CRP) were determined by an enzyme-linked immunosorbent assay.

Results: No significant differences in markers of systolic function or geometry (EF, FS, SV and ESD) were observed between the groups ($p>0.05$). Compared to the control group, E/A (control=2.17 $\pm$ 0.39; CIA=1.46 $\pm$ 0.46; $p=0.0001$) and Sep e' (control=3.75 $\pm$ 0.69; CIA=3.23 $\pm$ 0.47; $p=0.04$) were lower in the CIA group. By contrast, E/e' (control=29.94 $\pm$ 6.99; CIA=24.17 $\pm$ 8.49; $p=0.13$) and Lat e' (control=3.99 $\pm$ 0.43; CIA=3.79 $\pm$ 0.78; $p=0.31$) did not differ amongst the two groups. IL-6 (115 $\pm$ 70.09 versus 365.3 $\pm$ 88.96 pg/mL; $p<0.0001$), IL-1 β (14.1 $\pm$ 55.7 versus 238.6 $\pm$ 49.01 pg/mL; $p<0.0001$), TNF- α (293.5 $\pm$ 87.16 versus 626.0 $\pm$ 119.7 pg/mL; $p<0.0001$) and CRP concentrations (0.23 $\pm$ 0.34 versus 0.97 $\pm$ 0.35 ng/mL; $p<0.0001$) were higher in the CIA compared to control group. A lower E/A was associated with TNF- α ($r=-0.63$; $p=0.0003$), IL-6 ($r=-0.56$; $p=0.0001$), IL-1 β ($r=-0.48$; $p=0.001$) and CRP concentrations ($r=-0.60$; $p=0.001$) in the total sample. Lower TNF- α ($r=-0.39$ $p=0.04$) and IL-1 β ($r=-0.47$, $p=0.01$) levels were associated with E/e' in the total sample.

Conclusions: Diastolic function is impaired in male Sprague Dawley rats with CIA. Our results indicate that exposure to high grade inflammation can reduce LV relaxation without impairing systolic function in CIA. Markers of inflammation were also associated with increased filling pressures in this animal model. Systemic inflammation may directly impact myocardial diastolic function in CIA.

REFERENCE:

- [1] Liang KP, Myasoedova E, Crowson CS, et al. Increased prevalence of diastolic dysfunction in rheumatoid arthritis. *Ann Rheum Dis*. 2010;69:1665–1670.

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THU0083 CD30 APTAMER-SLAT-SHRNA CHIMAERAS INHIBIT TH17 DIFFERENTIATION BY ROR γ T IN RHEUMATOID ARTHRITIS

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Background: T helper 17 (Th17) cells play a central role in rheumatoid arthritis (RA) via the production of pro-inflammatory cytokines interleukin (IL)-17. SWAP-70-like adapter of T cells (SLAT) has recently emerged as an important regulator of Th17 differentiation. Aptamer-facilitated cell specific delivery of shRNA represents an attractive novel approach for efficient RNAi delivery. However, the role of CD30 aptamer-SLAT-shRNA chimaeras in regulating Th17 differentiation in patients with RA is unclear.

Objectives: SLAT play a crucial role in regulating Th17 cell differentiation and function. This study was undertaken to investigate the role and mechanism of SLAT in Th17 cells differentiation in patients with RA.

Methods: Peripheral blood CD4⁺ T cells and synovial fluid CD4⁺ T cells derived from RA patients and healthy controls were used to test the effect of SLAT *in vitro*. CD30 aptamer-SLAT-shRNA chimaeras were generated *in vitro* and transfected into CD4⁺ T cells. The effect of CD30 aptamer-SLAT-shRNA chimaeras on Th17 production and differentiation was detected.

Results: SLAT was expressed mostly in cytoplasm and cell membrane of CD4⁺ T cells. The protein levels of SLAT in peripheral blood and synovial fluid CD4⁺ T cells of RA patients were higher than that of healthy controls. The effect of CD30 aptamer-SLAT-shRNA chimaeras on Th17 differentiation was due to its ability to sequester SLAT and prevent it from targeting the transcription factor ROR γ T.

Abstract THU0083 – Figure 1. A. SLAT was expressed mostly in cytoplasm and cell membrane of CD4⁺ T cells. D. CD30 aptamer-SLAT-shRNA chimaeras reduced the percentage of CD4⁺ROR γ T⁺T cells and CD4⁺IL-17⁺T cells.

Conclusions: This study reveals new evidence of the role of SLAT in Th17 differentiation in CD4⁺ T cells of RA patients.

REFERENCES:

- [1] Park H, Li Z, Yang XO, et al. A distinct Lineage of CD4⁺ T cells regulate tissue inflammation by producing interleukin 17. *Nat Immunol* 2005;6 (11):1133–1141.
- [2] Gupta S, Lee A, Hu C, et al. Molecular cloning of IBP, a SWAP-70 homologous GEF, which is highly expressed in the immune system. *Hum Immunol* 2003;64(4):389–401.
- [3] Canonigo-Balancio AJ, Fos C, Prod'homme T, et al. SLAT/Def6 plays a critical role in the development of Th17 cell-mediated experimental autoimmune encephalomyelitis. *J Immunol* 2009;183(11):7259–7267.
- [4] Binder N, Miller C, Yoshida M, et al. Def6 Restrains Osteoclastogenesis and Inflammatory Bone Resorption. *J Immunol*. 2017;198(9):3436–3447.
- [5] Wheeler LA, Trifonova R, Vrbanc V, et al. Inhibition of HIV transmission in human cervicovaginal explants and humanized mice using CD4 aptamer-siRNA chimaeras. *J Clin Invest*. 2011;121(6): 2401–2412.
- [6] Takahashi M, Burnett JC, Rossi JJ. Aptamer-siRNA chimaeras for HIV. *Adv Exp Med Biol*. 2015;848:211–234.
- [7] Zhang P, Zhao N, Zeng Z, et al. Combination of an aptamer probe to CD4 and antibodies for multicolored cell phenotyping. *Am J Clin Pathol* 2010;134(4): 586–593.
- [8] Song P, Chou YK, Zhang X, et al. CD4 aptamer-ROR γ shRNA chimera inhibits IL-17 synthesis by human CD4⁺ T cells. *Biochem Biophys Res Commun* 2014;452(4):1040–1045.

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THU0084 HISTONE DEACETYLASE 1 (HDAC1): A NOVEL THERAPEUTIC TARGET IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Despite enormous efforts to develop new therapeutic strategies for treatment of rheumatoid arthritis (RA), the large number of non responding