Zsófia Pethő: None declared, Szilvia Szamosi: None declared, Attila Hamar: None declared, Anita Pusztai: None declared, Emese Balogh: None declared, Nóra Bodnár: None declared, Levente Bodoki: None declared, Agnes Szentpetery: None declared, Harjit Pal Bhattoa: None declared, György Kerekes: None declared, Katalin Hodosi: None declared, Andrea Domjan: None declared, Sándor Szántó: None declared, Gabriella Szűcs: None declared, Hennie Raterman Grant/research support from: UCB, Consultant of: Abbvie, Amgen, Bristol-Myers Squibb, Cellgene and Sanofi Genzyme, Willem Lems Grant/research support from: Pfizer, Consultant of: Lilly, Pfizer, Zoltán Szekanecz Grant/research support from: Pfizer, UCB, Consultant of: Sanofi, MSD, Abbvie, Pfizer, Roche, Novartis, Lilly, Gedeon Richter, Amgen

DOI: 10.1136/annrheumdis-2020-eular.2462

FRI0374

PLASMA LEVELS OF 14-3-3 PROTEIN, S100A8/S100A9-PROTEIN, INTERLEUKIN-6, INTERLEUKIN-18, INTERLEUKIN-4, INTERLEUKIN-17, INTERLEUKIN-1B AND TUMOR NECROSIS FACTOR- α IN CHRONIC NON-BACTERIAL OSTEOMYELITIS AND NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

M. Kostik^{1,2}, M. Makhova³, D. Kozlova^{4,5}, D. Vasilyev^{4,6}, L. Sorokina^{2,7}, E. Isupova^{1,8}, A. Maletin⁹, A. Mushkin⁹. ¹Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russian Federation; ²Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation; ³Saint Petersburg State Pediatric Medical University, Saint-Petersburg, Russian Federation; ⁴LLC Scientific and Production Company "ABRIS+", Saint-Petersburg, Russian Federation; ⁵Sechenov Institute of Evolutionary Physiology and Biochemistry, Saint-Petersburg, Russian Federation; ⁶Sechenov Institute of Evolutionary Physiology and Biochemistry, Saint Petersburg, Russian Federation; ⁷Leningrad Regional Children's Hospital, Saint Petersburg, Russian Federation; ⁸Saint Petersburg, Saint Petersburg, Russian Federation; ⁹Science Research Institute of Phthisiopulmonology, Saint Petersburg, Russian Federation

Background: Chronic non-bacterial osteomyelitis (CNO) is an immune-mediated disease associated with cytokine dysbalance.

Objectives: The aim of our study was to evaluate the cytokines levels in CNO and compare to juvenile idiopathic arthritis (JIA) – disease with immune-mediated mechanism.

Methods: The diagnosis of CNO made with criteria, proposed by Jansson (2007, 2009), after the exclusion of other causes of bone disease [1]. We included 42 patients with NBO, 28 patients with non-systemic juvenile idiopathic arthritis (JIA). We evaluated plasma levels of 14-3-3 protein, S100A8/S100A9-protein, interleukine-6 (IL-6), interleukine-18 (IL-18), interleukine-4 (IL-4), interleukine-17 (IL-17), interleukine-1 β (IL-1 β) and tumor necrosis factor- α (TNF α) in 2 groups by the ELISA. Statistical analysis was carried out with Statistica 10.0 software. We utilized descriptive statistics (Me; IQR), Mann-Whitney tests.

Results: We have found differences in the proinflammatory biomarkers between CNO, JIA. Patients with NBO had lower levels of studied cytokines, exclude 14-3-3-protein, S100A8/S100A9 and interleukin-6 compare to JIA patients (table 1).

Table 1. Comparison the cytokine levels between CNO, JIA N

Parameter	NBO (n=42)	JIA (n=28)	p
Hemoglobin, g/l	112 (104; 124)	120 (114.5; 126.0)	0.02
WBC $\times 10^9/l$	7.9 (7.0; 10.5)	8.0 (6.7; 10.0)	0.86
PLT $\times 10^9/l$	347 (259; 408)	336.5 (274.0; 390.5)	0.98
ESR, mm/h	25.0 (9.0; 46.0)	8.5 (2.5; 13.0)	0.013
CRP, mg/l	6.1 (0.6; 2.4)	1.8 (0.4; 11.9)	0.027
14-3-3, ng/ml	21.4 (18.5; 27.1)	19.9 (18.0; 27.8)	0.77
S100A8/S100A9, ng/ml	5.9 (5.2; 6.5)	5.9 (5.0; 6.2)	0.76
IL-6, ng/ml	126.2 (112.8; 137.5)	132.4 (117.4; 142.9)	0.16
IL-18, ng/ml	270.1 (200.1; 316.1)	388.3 (373.9; 405.1)	0.0000001
IL-4, ng/ml	15.3 (11.5; 18.2)	18.7 (16.2; 20.2)	0.003
IL-17, ng/ml	83.1 (71.1; 97.3)	99.2 (87.3; 115.8)	0.003
IL-1b, ng/ml	47.4 (42.0; 51.3)	70.8 (65.3; 73.6)	0.0000001
TNF α , ng/ml	19.4 (17.8; 21.3)	23.1 (20.2; 25.9)	0.0006

Conclusion: Patients with CNO had less proinflammatory activity then JIA patients, besides IL-6 and S100A8/S100A9. Further investigations required for finding new more precise biomarkers and finding possible molecular targets for treatment.

This work supported by the Russian Foundation for Basic Research (grant № 18-515-57001)

References:

[1] Jansson AF, et al. Clinical score for nonbacterial osteitis in children and adults. *Arthritis Rheum.* 2009;60(4):1152-9.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6469

FRI0375

VISFATIN EFFECTS ON MSCS DURING OD VIA DIFFERENTIAL REGULATION OF LNCRNA H19 AND MICRO RNA 675-3P

D. Küppers¹, L. Tsiklauri¹, M. Hülser¹, K. Frommer¹, S. Rehart², C. Ospelt³, U. Müller-Ladner¹, E. Neumann¹. ¹Justus-Liebig-University Gießen, Dept. of Rheumatology and Clinical Immunology, Campus Kerckhoff, Bad Nauheim, Germany; ²Agaplesion Markus Hospital, Dept. of Orthopaedics and Trauma Surgery, Frankfurt am Main, Germany; ³University Hospital of Zürich, Dept. of Rheumatology, Center of Experimental Rheumatology, Zürich, Switzerland

Background: Long non-coding (lnc-)RNA are regulatory molecules transcribed from DNA similar to mRNA and interact directly with DNA, RNA and proteins. Some lncRNAs have been shown to contain micro (mi-)RNAs in their sequence that can be released by splicing and lead to active miRNA molecules, e.g. lncRNA H19 includes two miRNAs 675-3p and -5p in its sequence.

Adipose tissue derived factors (adipokines) are involved in inflammation processes and osteoarthritis (OA) development. The proinflammatory adipokine visfatin has been shown to alter osteogenic differentiation (OD) of pluripotent mesenchymal stem cells (MSCs) and reduces elastic fiber expression, increases matrix mineralization and proinflammatory cytokine and chemokine production⁽¹⁾.

Objectives: We evaluated a novel effect of visfatin on lncRNA H19 in MSCs during OD. The goal was to explore the kinetics of the visfatin effect during OD with regard to H19 regulation and to investigate H19 downstream mechanisms leading to the observed altered MSC differentiation and osteoblast activity.

Methods: MSCs isolated from OA hip or knee bone (phMSC) and commercially obtained healthy human (h-)MSCs were differentiated towards osteoblasts with/without visfatin, resistin, leptin, TNF and Wnt/TGF β 1 pathway inhibitors. Supernatants were collected at days 2, 7, 9, 14 and 21 of OD, cell lysates at day 2, 7, 9, 14 and matrix mineralization assays conducted at day 21. H19 and miRNA expression was evaluated by real-time PCR after mi-RNA isolation. IL-6 was analyzed by ELISA.

Results: H19 was continuously upregulated in unstimulated controls as expected during OD but also when stimulated with other adipokines. In contrast, stimulation with visfatin significantly decreased H19 (day 2 to 14 of OD, hip-phMSCs: $p = 0.0097$, knee-phMSCs: $p = 0.0075$, h-MSC: $p = 0.044$). Visfatin increased matrix mineralization and IL-6 production as expected (hMSC: $p = 0.03$, phMSC: $p = 0.013$)⁽¹⁾. TNF stimulation during OD did not lead to a downregulation of H19 nor increased matrix mineralization, thus showing that the effects were visfatin-dependent. H19s endogenous miRNA 675-5p was changed in parallel with H19, increased during control OD and significantly down-regulated by visfatin (e.g. day 14 $p = 0.015$). However, H19s endogenous miRNA 675-3p was inversely regulated, downregulated during control OD while visfatin stimulation attenuated this effect (e.g. day 14 $p = 0.025$). Altered Wnt-signaling and involvement of the TGF β 1 pathway could not be observed.

Conclusion: H19 is upregulated during OD and may therefore play a regulatory role in the process of osteogenesis. Visfatin stimulation of MSCs during OD showed pro-inflammatory effects, increased matrix mineralization while reducing elastic fiber production⁽¹⁾. These effects were associated with a downregulation of H19, a specific visfatin effect not triggered by other adipokines or TNF. The H19 sequence includes two endogenous micro-RNAs 675-3p and 5p. We demonstrated miRNA 675-5p to be regulated in parallel to H19, whereas miRNA 675-3p was inversely regulated and increased continuously upon visfatin stimulation. Based on these results, we hypothesize that visfatin provides a specific stimulus for the splicing of miRNA 675-3p from H19, in turn leading to H19 reduction. miRNA 675-3p thus represents an effector mechanism of visfatin that contributes to the observed functional effects in differentiating MSCs.

References:

[1] Tsiklauri, L. et al. Visfatin alters the cytokine and matrix-degrading enzyme profile during osteogenic and adipogenic MSC differentiation. *Osteoarthritis Cartil.* 26, 1225–1235 (2018).

Disclosure of Interests: Dennis Küppers: None declared, Lali Tsiklauri: None declared, Marie Hülser: None declared, Klaus Frommer: None declared, Stefan Rehart: None declared, Caroline Ospelt Consultant of: Consultancy fees from Gilead Sciences., Ulf Müller-Ladner Speakers bureau: Biogen, Elena Neumann: None declared

DOI: 10.1136/annrheumdis-2020-eular.1512

FRI0376

EFFECT OF CARBAMYLATED LOW-DENSITY LIPOPROTEINS ON BONE CELLS HOMEOSTASIS

B. Lucchino¹, M. Leopizzi², T. Colasanti¹, V. Di Maio², C. Alessandri¹, G. Valesini¹, F. Conti¹, M. Di Franco¹, F. R. Spinelli¹. ¹Sapienza University of Rome, Dipartimento di Scienze Cliniche Internistiche, Anestesiologiche e Cardiovascolari, Roma, Italy; ²Sapienza, Dipartimento di Scienze e Biotechnologie Medico-Chirurgiche, Rome, Italy