an origin for new highly improved treatment strategy of sJIA. As rat monocytes exhibited CD163 expression in a similar level with that shown for peritoneal macrophages [1], we decided to use CD163 as a key factor indicating cell reprogramming in the study.

Objectives: To investigate the dynamical changes in subpopulations of peripheral blood mononuclear cells (PBMC) and to assess doxycycline and dexamethasone effects in a model of arthritis with the systemic manifestations.

Methods: Animal model [2] was adapted in 24 Wistar rats (males, 6 month old). On the day of the last stimulation all the rats were divided into 3 equal groups and additional subcutaneous (s.c.) injections were performed as follows: DOXY-group – doxycycline (50 mg/kg, Saratov, Russia), DEXA-group – dexamethasone (4 mg/kg, KRKA, Slovenia), control group – 0,9% sodium chloride solution (Belarus). The s.c. injections were repeated on Day 54. Time points were 0, 21, 41, and 55 Days. PBMC were assessed by flow cytometry (BD FACSCanto II, USA) according to manufacturer's instructions. Staining was performed with FITC Anti-Rat CD11b (BD Pharmingen), anti-rat CD68 RPE (Serotec, UK), anti-rat CD163 ALEXA FLUOR 647 (Serotec, UK). CD11b+CD68+ and CD11b-CD68+ cells were regarded as monocytes and circulating dendritic cells consequently. At the termination animal organ masses were measured.

Results: Up to Day 55 proportions of CD163+ in CD11b+CD68+ population changed synchronically in all groups. On Day 55 the proportions (in comparison with the data of Day 41) were significantly higher in DEXA-group ($p<0,05$) but didn't change in DOXY- and control groups ($p>0,05$). Cell reprogramming was also observed in population of CD11b-CD68+. So, on Day 41 the proportions of CD163+ cells in CD11b-CD68+ population were significantly increased (in comparison with the data of Days 0 and 21) in DOXY- and DEXA-groups ($p<0,05$) but not in control group ($p>0,05$). Mentioned changes were subsequent with other parameters of inflammation. We observed significantly lower heart masses in DOXY- and DEXA-groups (median=0,63 and 0,635g consequently) in comparison with control group (median=0,74g) ($p<0,05$), but no difference between DOXY- and DEXA- groups ($p>0,05$).

Conclusions: In a model of arthritis with the systemic manifestations in Wistar rats we demonstrated that subpopulations of PBMC (CD11b-CD68+ and CD11b+CD68+) underwent reprogramming. Doxycycline and dexamethasone modyfied the dynamics of the reprogramming. In DOXY- and DEXA-groups there were lower heart masses than in the control group, the last fact is subsequent with the data by De P. et al. [3]. We can speculate that monocytes and dendritic cells undergo reprogramming (CD163neg and CD163+) in a similar way with M1 and M2 macrophages.

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AB0106 EFFECT OF SERUM CYTOKINES ON COLLAGEN INDUCED ARTHRITIS RATS AFTER INTRA-ARTICULAR INIECTION OF OZONE

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Background: Ozone is a new treatment method, study confirmed that the ozone intra-articular injection can reduce the level of TNFR II CIA in rat synovial TNF-a, synovial tissue, the regulation of rat apoptosis inhibiting gene Bcl-2 decreased expression of proapoptotic gene Bax expression increased, thereby promoting apoptosis of synovial cells. However, there are few reports on the effects of ozone on the inflammatory cytokines such as serum TNF-a in the pathogenesis of RA.

Objectives: To observe the effects of intra-articular ozone iniection on the contents of tumor necrosis factor-α(TNF-α),Interleukin-6 (IL-6), IL-17A,and vascular endothelial growth factor (VEGF)in the serum of rats with collagen-induced arthritis (CIA) and explore the therapeutic mechanism of ozone in RA treatment.

Methods: Thrity-two Wistar rats were randomized into 4 groups,including ozone groups receiving intra-articularinjection of 40 μg/ml ozone (O_3 group), Ca blank control group (normal group), a methotrexate group (MTX group) and a collagen-induced arthritismodel (CIA group). All the rats, except for those in the blank control group, were subjected to hypodermic iniection of bovine collagen II and complete Freund'S adiuvant to induce CIA. DOzone treatment was administered once weekly for 3 weeks starting at 14 days after the modeling.MTX group of 0.9 mg/kg, once a week, a total of three weeks.The swelling degree of the foot were observed,the serum contents of TNF-α,IL-6,IL-17A and VEGF were detected. One-way analysis of variance or Kruskal-Wallis test was used to evaluate the experimental data.

Results: At the end of treatment,the foot swelling degree was reduced significantly in rats with O_3 group compared with that in the CIA group [4.21±0.14 ml and 9.12±0.17 ml, t=8.43, P=0.023]. The serum contents of TNF-a, IL-6 and VEGF showed significant difference between the CIA group and O_3 group [93.86±12.49 pg/ml and 14.33±1.85 pg/ml, c^2=6.216, P=0.002; 189.12±164.62 pg/ml and 5.84 (5.47,15.93) pg/ml, c^2=13.136, P=0.00451.56 (46.09,74.10) pg/ml and 37.77±7.88 pg/ml, c^2=3.732, CP=0.002, there was no statistically significant difference between the O_3 group and MTX group [14.33±1.85 pg/ml and 12.45 (11.8,15.6)) pg/ml, c^2=0.243, P>0.05; 5.84 (5.47,15.93 pg/ml, vs 9.59±5.13 pg/ml, c^2=0.058, P>0.05; 37.77±7.88 pg/ml and 41.99±8.78 pg/ml, c^2=0.516, P>0.05]. The serum contents of IL-17A showed no significant difference between the normal group,CIA group,MTX group and the O_3 group (F=1.827, P=0.165).

Comparison of serum levels of inflammatory cytokines in each group rats

	TNF-α (MFI)	IL-6(pg/ml)	IL-17A(pg/ml)	VEGF(pg/ml)
control group	11.21±1.44	10.23±3.18	0.49±0.34	27.65±9.84
CIA group	93.86±12.49[a]	189.12±164.62[a]	0.77±0.18	51.56(46.09,74.10)[a]
MTX group	12.45(11.8,15.6)[b]	9.59±5.13[b]	0.49±0.32	41.99±8.78[a]
O_3 group	14.33±1.85[b]	5.84(5.47,15.93)[b]	0.64±0.27	37.77±7.88[b]
χ^2/F	23.148	17.116	1.827	12.574
P	0.000	0.001	0.165	0.006

Note: [a] indicated that P<0.05 was compared with the control group; [b]indicated that P<0.05 was compared with CIA group;

Conclusions: Intra-articular iniecfion of 40 ug/ml ozone Can attenuate svnovitis in rats with CIA, the mechanism of which may involve the inhibition of TNF-a, IL-6 and VEGF in the serum.

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AB0107 THE MODULATION OF MACROPHAGE POLARIZATION BY SIRT1 MAYBE NEW TARGET THERAPY IN RHEUMATOID ARTHRITIS

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Background: The polarization of macrophages was the expressed to M1/M2 phenotype by various stimuli or environment signals. The M1 macrophage was pro-inflammatory phenotype and was key effector cells in the immune response of rheumatoid arthritis (RA). So, M1 macrophage influenced the inflammation of RA synovial membrane and joint destruction in RA, whereas M2 macrophage was anti-inflammatory phenotype and could down-regulate the production of proinflammatory cytokines in RA. The SIRT1 attenuated the RA inflammation via down-regulation of NF-κB signaling. However, the effect of SIRT1 on macrophages polarization remained uncler.

Objectives: We aimed to check out that activated SIRT1 modulated macrophages polarization into M1 phenotype and controlled the inflammation of RA.

Methods: Monocytes from synovial fluid of RA patients, bone marrow–derived monocytes (BMDCs) from mice were studied. monocytes were cultured with M-CSF for 7days to differentiate into M0 macrophages (monocyte-derived mature macrophages M0 phenotype). M0 macrophages were incubated with LPS and IFN-gamma in order to obtain M1 macrophages. M1 macrophage markers were detected by real-time PCR.

Results: Activation of SIRT1 was achieved by Resveratrol, activated SIRT1 attenuated M1 macrophage phenotypes and pro-inflammatory cytokine expression. macrophages obtained from SIRT1-tg mice, which were overexpression of SIRT1, exhibited decreased M1 markers in association with enhanced activation of AMPK/ACC compared with macrophage from control C57BL/6 mice. In addition to SIRT1 activation, M1 polarizing signal, acetylation of NF-κB p65, was suppressed. In SIRT1-deficient macrophages, resveratrol fail to increase AMPK activity and to decrease the expression M1 markers owing to enhanced acetylation of NF-κB p65.

Conclusions: SIRT1 maybe an important modulator of M1 macrophages polarization and increased AMPK activity, which suppressed acetylation of NF-κB p65 during inflammation of RA. so, modulation of SIRT1 maybe a new target in RA treatment.

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