therefore also our hypothesis¹ that BSSL is a novel target for treatment of inflammatory diseases.

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AB0133

HUMAN UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS AMELIORATE COLLAGEN-INDUCED ARTHRITIS VIA IMMUNOMODULATORY EFFECT ON T LYMPHOCYTES

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Background: Rheumatoid arthritis (RA) is an autoimmune disease that results in cartilage and bone destruction. Overactivation of T lymphocytes and imbalance of T lymphocyte subsets are closely related to the occurrence and development of RA. These have become important mechanisms of inflammation, immune activation, and bone destruction. RA treatment ideally involves regulation of immune abnormalities and maintenance of immune homeostasis. Mesenchymal stem cells (MSCs) are multipotent adult stem cells with high proliferation, multi-differentiation, and immune regulation. They exert immunoregulatory effects on T lymphocytes to improve RA symptoms, inhibit synovial hyperplasia, and reduce cartilage and bone erosion. However, the specific molecular mechanisms have not been fully elucidated.

Objectives: This study investigated the effect of human umbilical cord mesenchymal stem cells (hUCMSCs) on collagen-induced arthritis (CIA) in rats in comparison with that of methotrexate (MTX), a classical drug for RA. It evaluated T lymphocyte proliferation, apoptosis, differentiation, and associated inflammatory factors, further explored the regulatory mechanism of T lymphocyte differentiation at the gene transcription level. This study elucidated that hUCMSCs play an immunoregulatory role in T lymphocytes of CIA rats through multiple pathways and explored the possible mechanism of hUCMSCs in RA treatment via the immunomodulated T lymphocyte pathway.

Methods: The effects of hUCMSCs on arthritis, radiological and synovial pathological changes in CIA rats were assessed. Flow cytometry was conducted to detect T lymphocyte proliferation, apoptosis, the ratio of Th17 and Treg cells in the spleen, and IL-17 and TGF- β levels in the sera from CIA rats. Further, Foxp3 and ROR- γ T expression in the spleen were assessed by immunohistochemistry, Foxp3 mRNA and ROR- γ T mRNA expression were assessed by reverse transcription-polymerase chain reaction (RT-PCR).

Results: hUCMSCs inhibited proliferation and promoted apoptosis of T lymphocytes, up-regulated Foxp3 mRNA and protein expression, increased the proportion of Treg cells, down-regulated ROR- γ T mRNA and protein expression, and decreased the proportion of Th17 cells in the spleens of CIA rats. Correction of the Foxp3/ROR- γ T imbalance to regulate the Treg/Th17 ratio, promoted anti-inflammatory factor TGF- β expression and inhibited pro-inflammatory factor IL-17 expression, thereby improving arthritis in CIA rats, delaying radiological progression, and inhibiting synovial hyperplasia. This effect was similar to that of MTX.

Conclusion: hUCMSCs exert immunoregulatory effects on T lymphocytes in CIA rats through many pathways and are expected to become a new immunoregulatory therapy for RA.

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AB0134

ANALYSIS OF INTESTINAL MICROBIOME PROFILE OF PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

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Objectives: Describe the intestinal microbiome profile in RA patients and analyze the mechanisms through which intervenes in the pathogenesis RA.

Methods: **Design:** Controlled, observational, cross-sectional study of established RA cohort. **Patients:** Forty consecutive RA patients (ACR/EULAR 2010 criteria) >16 years, selected from a prospective inception cohort (2007-2011) and 40 sex-age matched healthy controls. **Protocol:** Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity were collected during the follow-up and analytical values were determined. Fecal samples were frozen within 24 hours of collection. **Main outcome:** Fecal samples exam. Microbial DNA was extracted from fecal samples using QIAamp DNA stool Mini kit. The concentration and quality of DNA was determined by Nanodrop. **Secondary Other variables:** Demographic, clinical-analytical and therapies (DMARDs). **Statistical analysis:** Analysis of microbiota profile: UniFracPCoA (Principal Coordinate Analysis) was performed with the abundance data of operational taxonomic units (OTU) by means of the variancecovariance matrix implemented in Quantitative Insights Into Microbial Ecology (QIIME). The relative abundance of each OTU (taxa) was compared using a Wilcoxon test. The variations of abundance and diversity were compared by ANOSIM pathway. The calculation of α and β -diversity was carried out using QIIME.

Results: Most of subjects were women (75%) (table). In RA patients, the average DAS28 was 3.6. β -diversity data showed that patients tend to differ from healthy subjects according to their microbiota ($p = 0.07$). Patients with RA exhibited decreased gut microbiome diversity compared with controls, although was not statistically significant. Regarding in species richness, the analysis suggested an increase of the *Collinsella aerofaciens* species and *enterococcus* genera in patients compared with controls. Likewise, an increase of arginine deaminase activity was observed, which belonged, in approximately 90%, to the RA genes of the genus *Collinsella*. The multivariate analysis identified ACPA positive (β [95% CI], 0.33 [27.4-390]), smoking (0.3 [8.8-256.4]) and age (-0.3 [27.4-390.0]) as factors associated with *Collinsella*. Also, we observed a decrease in other bacterial lineages. On the other hand, RA patients showed an altered metabolic capacity for the transport of zinc and copper.

Conclusion: These observations suggest a dysbiosis in RA patients, resulting from the abundance of certain bacterial (i.e. *Collinsella*) and decrease of other bacterial lineages. These alterations could influence in a significant way in the perpetuation of the autoimmunity of the disease.

VARIABLE	RA n=40	Control n=40	P - VALUE
Age (years), mean (SD)	58,5 (9,4)	58,5 (9,4)	0,998
Sex (female), n (%)	30 (75,0)	30 (75,0)	1,000
Rheumatoid factor, n (%)	32 (80,0)	2 (5,0)	<0,001
Anti-cyclic citrullinated peptide, n (%)	28 (70,0)	0 (0,0)	<0,001
DAS28 average value, mean (SD)	3,6 (0,5)	-	-
Metotrexato (%)	72,5	-	-
biologic disease-modifying antirheumatic drugs (%)	37,5	-	-

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AB0135 LEVELS OF MYOKINES AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Myokines, such as irisin and myostatin, are cytokines and growth factors mainly expressed in skeletal muscle, which is also their primary target tissue. They are released into circulation and exert a variety of systemic effects promoting crosstalk among different tissues [1]. Irisin is known to retrieve disuse-induced bone loss by stimulating the osteoblast pathways, while myostatin was demonstrated to be highly expressed in the synovial tissues of rheumatoid arthritis (RA) subjects, with direct role in osteoclastogenesis [2, 3].

Objectives: To investigate whether myokines serum levels can predict one-year radiographic progression in patients with RA.

Methods: Forty female patients with RA, according to ACR/EULAR 2010 classification criteria, were included in the study. Blood samples were collected, and ELISA was used to measure serum levels of irisin and myostatin. Radiographs of hands and feet, taken within three months of the blood collection and a year later, were evaluated using the Sharp-van der Heijde (SvH) score to verify the one-year radiographic progression. The RA activity was assessed by disease activity score based on evaluation of 28 joints (DAS28-ESR). Statistical analysis included Mann-Whitney U test and Spearman correlation. A value of $p < 0.05$ was considered significant.

Results: The mean age of RA patients was 53 years old, mean DAS28-ESR was 4.09, mean disease duration was 11.2 years and mean BMI was 27.33 kg/m². The mean serum levels of irisin and myostatin were respectively 25.61 $\pm$ 8.25 ng/ml and 3011.28 $\pm$ 1271.11 pg/ml. Considering radiographic progression, the mean values of SvH score were 28.3 and 31.3 in the baseline and after one year, respectively, resulting in a mean Δ SvH of 3. Over one year, 89.2% of the patients presented radiographic progression (Δ SvH score > 0), and 10.8% presented rapid progression (Δ SvH score > 5).

SvH score	Irisin (ng/ml)	Myostatin (pg/ml)
Δ SvH = 0	31.66 $\pm$ 10.66	2943.94 $\pm$ 719.96
Δ SvH > 0	26.67 $\pm$ 7.28	2996.90 $\pm$ 1356.66
Δ SvH > 5	31.61 $\pm$ 8.31	3255.81 $\pm$ 975.68

Conclusion: The serum levels of irisin and myostatin were not correlated with one-year radiographic progression. There was a tendency of increased myostatin levels in patients with rapid progression compared to patients with no progression. More studies are needed to investigate whether the myokine levels in the joint environment differ from the circulating concentration.

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AB0136 EVALUATION OF ANALGESIC ACTIVITY OF ALLOPURINOL AND FEBUXOSTAT IN EXPERIMENTAL ANALGESIC MODELS IN MICE

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Background: Allopurinol and febuxostat are xanthine oxidase inhibitor which are used in the treatment of hyperuricemia and gout. Pain is one of the important symptoms in gout patients.

Objectives: The present study is to evaluate the analgesic activity of allopurinol and febuxostat in two analgesic models in mice.

Methods: The analgesic activity of allopurinol (39 mg/kg) and febuxostat (15.6 mg/kg) was evaluated by using central analgesic model of Eddy's hot plate and peripheral analgesic model of acetic acid induced writhing. Both drugs were compared with the positive control, pentazocin for hot plate method & aspirin for the Writhing method. Also both allopurinol and febuxostat were compared with each other.

Results: Both allopurinol and febuxostat showed significant increase in reaction time at various time periods in hot plate method & also showed significant delay in onset of writhing as well as decrease in number of writhes in writhing method. As compared to positive control result allopurinol and febuxostat result were lower. Febuxostat shows better analgesic activity as compared to that of allopurinol.

Conclusion: Allopurinol and febuxostat exhibited analgesic activity in both central and peripheral models of pain.

Disclosure of Interests: None declared

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AB0137 ROLE OF VIMENTIN AS A TARGET OF ANTIBODIES AGAINST CARBAMYLATED PROTEINS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Patients with Rheumatoid Arthritis (RA) have an increased risk of cardiovascular diseases (CVD). Inflammation and autoantibodies independently promote endothelial dysfunction, which is the earliest, reversible stage of atherosclerosis. *In vitro* studies have demonstrated that antibodies against carbamylated proteins (anti-CarP), recently described in RA patients, can induce the production of proatherosclerotic molecules like Vascular Cell Adhesion Molecule (VCAM-1) and activate Interleukin-1 Receptor-Associated Kinase (IRAK-1), Nuclear Factor κ B (NF- κ B), inducible Nitric Oxide Synthase (iNOS) in endothelial cells (1,2). Moreover, anti-CarP are associated to endothelial dysfunction and subclinical atherosclerosis in RA patients (3).

Objectives: Aims of the present study were: 1) to analyze the role of vimentin as a target of autoantibody response in the serum of patients with RA and 2) investigate the expression of vimentin and carbamylated proteins in endothelial cells.

Methods: Consecutive RA patients were enrolled in this study. Vimentin was carbamylated and used as an antigen for the detection of anti-Vimentin Carbamylated antibodies (CarVim), through immunoenzymatic methods. Cells were incubated with anti-vimentin and carbamylated antibodies. The presence of vimentin and carbamylated proteins was investigated by immunofluorescence on the immortalized endothelial cell line EA.hy 926.

Results: Eighty-eight (88) RA patients were enrolled in this study (F:M = 79:9, mean age = 56 $\pm$ 13 years). Anti-CarVim antibodies were present in 9% of the patients with a mean titre of 442 aU/ML (IQR 303 aU/ml). Vimentin and carbamylated proteins were detected in the endothelial cells by immunofluorescence (Figure 1).