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. **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.