cells was evaluated in a cell proliferation assay. NF- κ B intracellular levels were determined by Western Blot. TNF- α production was measured in culture medium supernatants by ELISA.

Results: An enhancement in cell proliferation was found in CS+GLU treatments at a concentrations of 100 and 200 μ g/ml, increasing 1,60-fold ($p<0.01$) and 2,04-fold ($p<0.001$), respectively, compared to untreated cells. In addition, myoblasts were then incubated with IL-6 (50 ng/ml) for 72 hour in order to induce an inflammatory environment. The results showed an IL-6 induced-reduction on cell proliferation in all groups, although the data did not reach statistical significance. Therefore, an IL-6 inhibitory effect on cell proliferation in human muscle cannot be ensured. We also measured the effect of the combined treatment CS+GLU on NF- κ B activation and TNF- α production in human skeletal muscle cells in primary culture. Despite of TNF- α levels were undetectable in cell supernatants, preliminary data showed a slight reduction on NF- κ B signalling pathway. Global gene expression profiles, measured by microarrays and GeneChip Human Gene 1.0 ST Arrays (Affymetrix), will also be analysed.

Conclusions: The mechanisms of action involved in the potential therapeutic effect described in an *in vivo* injured muscle model seem to be related with an increase in muscle cell proliferation, together with blocking NF- κ B nuclear translocation and TNF α production. Although further investigation is required, these pre-clinical data suggests potentially positive effects of CS and GLU administration for the treatment of skeletal muscle injuries in sports medicine.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2942

AB0061

SERUM IL-37 AS AN EFFICIENT BIOMARKER OF DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: POST-HOC ANALYSIS OF PLANETAS STUDY

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Background: IL-37 is an anti-inflammatory cytokine which belongs to IL-1 cytokine superfamily. Patients with ankylosing spondylitis (AS) also had a higher serum IL-37 concentration than controls, and were also associated with other inflammatory markers such as CRP, ESR, and BASDAI levels.¹ However, the relationship between serum IL-37 and disease activity after anti-TNF treatment has not been reported.

Objectives: To investigate the association of serum IL-37 level with disease activity in AS patients who were treated with infliximab.

Methods: Patients were recruited from the PLANETAS study (NCT01220518). Patients with active AS were treated with CT-P13 or infliximab originator. The serum levels of IL-37 were measured at week 0 and week 30 with specific ELISA. Other demographic, laboratory and clinical variables were evaluated simultaneously.

Results: Fifty patients with active AS (BASDAI >4) were analysed. The median age of patients was 40 years old [Interquartile range (IQR), 33.8–49.5], and the median BASDAI score was 6.7 (IQR 5.3–7.9). Compared to baseline, all measured clinical and laboratory parameters and serum IL-37 were significantly reduced. There was a statistically significant correlation between IL-37 and CRP, BASDAI at baseline, but not at week 30. Additionally, the differences (Δ) of parameters at baseline and at week 30 were assessed on their associations with other disease activity parameters. Delta IL-37 was significantly correlated with Δ CRP, Δ BASFI and Δ BASDAI. The ROC curves of serum biomarkers for ASAS 20 achievement revealed that AUC value for Δ IL-37 (AUC=0.74) was similar with Δ ESR (AUC=0.71, $p=0.64$) and superior than Δ CRP (AUC=0.54, $p<0.01$). AUC value for Δ IL-37 of ASAS 40 achievement was 0.66, which was similar with Δ ESR (AUC=0.60, $p=0.38$) and superior than Δ CRP (0.46, $p<0.01$).

Abstract AB0061 – Table 1. Demographic & Clinical characteristics of analysed patients, comparing at baseline and at week 30.

Variables	At baseline	At week 30	P
Age	40.0 (33.8–49.5)	-	N/A
Female sex	7 (14%)	-	N/A
IL-37	105.1 (25.9–286.9)	44.5 (18.2–153.9)	<0.01
ESR	35.0 (28.0–41.3)	7.5 (5.0–16.0)	<0.01
CRP	158.1 (53.4–291.4)	20.0 (7.4–73.1)	<0.01
BASDAI	6.7 (5.3–7.9)	3.3 (1.9–4.5)	<0.01
BASMI	4.0 (3.0–5.0)	3.0 (2.0–4.0)	<0.01
BASFI	6.6 (5.3–8.1)	3.3 (1.6–5.9)	<0.01
PGD	70.5 (57.3–80.8)	33.0 (14.8–53.3)	<0.01

Abstract AB0061 – Table 2. Correlations between IL-37 and other disease activity markers; at baseline and the differences between baseline and at week 30.

	At baseline			Difference between baseline and week 30		
	IL-37	ESR	CRP	Δ IL-37	Δ ESR	Δ CRP
IL-37		0.14	0.39**	Δ IL-37	0.24	0.36*
ESR	0.14		0.57**	Δ ESR		0.50**
CRP	0.39**	0.57**		Δ CRP	0.36*	0.50**
BASDAI	0.31*	0.31*	0.23	Δ BASDAI	0.32*	0.25
BASMI	0.05	0.09	0.16	Δ BASMI	-0.05	0.06
BASFI	0.20	0.36**	0.25	Δ BASFI	0.34*	0.35*
PGD	0.25	0.10	0.06	Δ PGD	0.16	0.28
						-0.06

Abstract AB0061 – Figure 1. Figure 1 ROC Curves of disease activity markers of ASAS 20 and ASAS 40 achievement.

Conclusions: Serum IL-37 levels are associated with BASDAI, patient's pain score, and CRP in active AS patients. Change in serum IL-37 level may serve as an efficient biomarker predicting the improvement of BASDAI and the achievement of ASAS 20 and 40 after anti-TNF treatment in AS patients.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6488

AB0062

RECIPROCAL INTERACTION BETWEEN MACROPHAGE MIGRATION INHIBITORY FACTOR AND INTERLEUKIN-8 IN GOUT

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Background: Macrophage migration inhibitory factor is a proinflammatory, chemotactic, and tissue destructive cytokine.

Objectives: This study determined monosodium urate crystal-induced macrophage migration inhibitory factor production and its interaction with interleukin-8 in gout.

Methods: Peripheral blood, synovial fluid, and clinical data were obtained from 98 patients with gout. Synovial fluid and serum concentrations of macrophage migration inhibitory factor and interleukin-8 were measured. Synovial fluid monocytes and neutrophils were cultured with monosodium urate crystals and the cytokine production was determined. The signalling pathways involved were determined using signal inhibitors. The interaction between macrophage migration inhibitory factor and interleukin-8 was investigated.

Results: Synovial fluid macrophage migration inhibitory factor was higher in acute gout and that in serum was higher in patients with intercritical gout compared with controls. Synovial fluid macrophage migration inhibitory factor was positively correlated with synovial fluid leukocyte and neutrophil counts and interleukin-8. The expression of macrophage migration inhibitory factor was similar in synovial fluid neutrophils and monocytes, while interleukin-8 was higher in monocytes. Monosodium urate crystals induced macrophage migration inhibitory factor production in monocytes and interleukin-8 production in neutrophils. This effect was decreased by inhibiting Fc-gamma receptor 1 and toll-like receptor 4. Interleukin-8 increased macrophage migration inhibitory factor production in monocytes while macrophage migration inhibitory factor increased interleukin-8 production in neutrophils.

Conclusions: Macrophage migration inhibitory factor and interleukin-8 are highly produced in acute gout. Monosodium urate crystals induced macrophage migration inhibitory factor production in monocytes and interleukin-8 production in neutrophils with a reciprocal interaction between the two cytokines.

Acknowledgements: This work was supported by Konkuk University Medical Centre Research Grant 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2365

AB0063

HIGH-EFFICIENCY TRANSDUCTION OF MESENCHYMAL STEM CELLS BY AAV2/DJ VECTOR FOR THEIR POTENTIAL USE IN AUTOIMMUNE DISEASES

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Background: Mesenchymal stem cells (MSC), multipotential non-hematopoietic progenitors, can be isolated from various tissues and can modulate allogeneic immune cell responses. These properties make MSC as a promising potential treatment of autoimmune diseases.¹ Our previous studies have found that bone marrow-derived (BM)-MSC from systemic lupus erythematosus (SLE) patients are defective structurally and functionally,² treatment with modified and optimised MSC may bring a better effect on patients with autoimmune diseases. Most efforts have relied on adeno- and lentiviral vectors for delivering genes to MSC. Effective as these vectors may be, concerns regarding their immunogenicity and, in the case of lentivirus, the risk of insertional mutagenesis, have led to the pursuit of safer alternatives. Among these, adeno-associated virus (AAV) holds several advantages as a vector for human gene therapy. There are many serotypes of AAV available, and certain serotypes have been found to transduce specific cell types more efficiently than others.

Objectives: To determine the efficiency of different serotypes of AAV vectors for their ability to mediate transduction of different sources of MSC and assess whether AAV transduction affects MSC multipotentiality.

Methods: Serotypes 1, 2, 5, 6, 8, 9, PHP and DJ of AAV vectors were constructed in Viral Core, Boston Children's Hospital. The enhanced green fluorescent protein (eGFP) gene under transcriptional control of a CAG promoter was cloned into the AAV vector backbone. MSC derived from umbilical cord (UC), BM and amniotic fluid (AF) were isolated and approximately 1×10^5 MSC were used for transductions with AAV vectors. eGFP expression was evaluated 3 days after transduction by fluorescence microscopy and flow cytometry. The capacity of MSC to differentiate *in vitro* was assessed.

Fig1 A: the transduction efficiencies of AAVs (MOI=5:1) in AF-MSC, BM-MSC and UC-MSC. B: the transduction efficiencies of AAV/DJ in UC-MSC with different MOI.

Abstract AB0063 – Figure 1. A: the transduction efficiencies of AAVs (MOI=5:1) in AF-MSC, BM-MSC and UC-MSC. B: the transduction efficiencies of AAV/DJ in UC-MSC with different MOI.

Results:

- AAV serotype DJ vector was the most efficient in transducing MSC. AAV was added directly to the medium at 5 multiplicities of infection (MOI), 41% UC-MSC was transduced by AAV2/DJ, while the transfection is 0.47%, 0.3%, 10.5%, 0.3%, 1.84%, 0.06%, 0.16% by AAV2/1, AAV2/2, AAV2/5,

AAC2/6, AAV2/8, AAV2/9, AAV2/PHP (Fig 1A). Transduction efficiencies ranged from 73.5% for MOI 10% to 91.3% for MOI 320 in UC-MSC (Fig 1B).

- MSC derived from different tissues share a comparable level of transduction with the same AAV vector serotype. In our result, AAV2/DJ was the most efficient in transducing UC-MSC and AF-MSC.
- AAV2/DJ transduced MSC retained the same multipotential activity to differentiate into osteogenic and adipogenic lineage as comparable to untransduced cells.

Conclusions: AAV2/DJ vector can be used as a highly efficient tool to modify MSC *ex vivo* for therapeutic transplantation for autoimmune diseases.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5014

AB0064

ROLE OF IL-35 IN THE REGULATION OF IMMUNE RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Interleukin 35 (IL-35) is a recently identified member of the IL-12 family of cytokines and represents a novel target for therapies of autoimmune, inflammatory, and infectious diseases, including rheumatoid arthritis (RA). Choi et al. 2015

IL-35 is a heterodimer consisting of EBV-induced gene 3 (EBI3) and IL-12 α chain p35 (Nakano et al. 2015). In contrast to other IL-12 cytokine family members, IL-35 appears to have anti-inflammatory and immunosuppressive properties mediated by induction of regulatory T and B cells; (Choi et al. 2015. Huang et al. 2017). In particular, IL-35 may play an important role in suppressing the inflammatory response by expanding regulatory T cells and in dampening the differentiation of Th17 cells (Niedbala et al. 2007).

Objectives: This study was designed to analyse effects of IL-35 on stimulated peripheral blood mononuclear cells (PBMC) and their subpopulations in RA patients and healthy controls.

Methods: PBMCs of 10 RA patients and 10 controls as well as CD14⁺ and CD4⁺ cells isolated from PBMCs using magnetic separation were cultured for 24 hours, and subjected to three conditions: no stimulation, stimulation with LPS (PBMC and CD14⁺) or stimulation with anti-CD3/anti-CD28 antibodies (PBMC and CD4⁺), and stimulation with added IL-35 (100 ng/ml). A panel of nine cytokines (IL-1 β , IL-6, IL-8, IL-10, IL-12 (p70), IL-17a, IFN- γ , MIP-1 β and TNF) was analysed in the cell culture supernatants.

Results: RA patients had higher serum levels of IL-35 compared to healthy controls. A decreased secretion of IL-8 and increased secretion of TNF in the presence of IL-35 was observed *in vitro* in stimulated PBMCs of RA patients. In the control group, we observed an increased secretion of IL-6 by PBMCs and decreased secretion of IL-10 by T lymphocytes as a result of IL-35 addition to stimulated cells.

Conclusions: In this study, we found elevated serum levels of IL-35 in RA patients suggesting a possible involvement of IL-35 in the pathogenesis of RA. However, *in vitro*, the effect of IL-35 on stimulated immune cells was partially anti-inflammatory and partially pro-inflammatory, suggesting that the effect of IL-35 is pleiotropic and depends on the type and the state of the affected immune cell.

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