

Abstract A6.8 Table 1

Patient	Sex	Age	Type	RF	ANA	Uveitis	Swollen joints
1	Female	10	Systemic	Negative	Positive	No	Knee
2	Female	13	Polyarticular	Negative	Negative	No	Knee and wrists
3	Male	10	Systemic	Positive	Positive	No	Knee and wrists
4	Female	10	Polyarticular	Negative	Negative	No	Temporomandibular and wrists
5	Female	11	Polyarticular	Negative	Negative	No	Wrists and metatarsophalangeal
6	Male	7	Oligoarticular	Negative	Negative	No	Ankles
7	Male	7	Oligoarticular	Negative	Negative	No	Knees
8	Female	5	Oligoarticular	Negative	Positive	Yes	Knees
9	Female	6	Oligoarticular	Negative	Negative	No	Ankles

from diagnosis to initiation of biological therapy was 3.94 ± 2.83 years. The disease characteristics are detailed in the table.

All the children had previously received DMARDs (66.6% methotrexate (MTX) and 33.3% MTX and sulfasalazine). Eight of the 9 patients (88.9%) were taking corticosteroids at baseline. Eight received etanercept (ETN) and one Adalimumab (ADA), with good outcomes in all the patients unless 1 that had to switch from ETN to ADA due to inefficacy, and improved after the change. The steroids were suspended in 75% of children (6). Differences between mean values of CRP, ESR, and platelets from baseline to actual moment were statistically significant.

The median biologic time is 4 (1.11) years.

Actually all the children are in remission, two of them (patients 1 and 4) without biological treatment or classic DMARDs (since 5 and 2 years respectively).

None of the children have had significant adverse effects nor required hospitalisation from the beginning of therapy.

Discussion ETN has proved its efficacy in JIA (regardless of the type of onset), as it has been reported in multiple efficacy and safety studies, including long term studies of up to eight years of continuous therapy. [1, 2]

We present our experience in children treated with up to 11 years, with good outcomes in terms of efficacy and safety in all the patients, and also 2 patients still in remission after 2 and 5 years without treatment.

References

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2. Pratsidou-Gertsis P, Trachana M, Pardalos G, Kanakoudi-Tsakalidou F. A follow-up study of juvenile idiopathic arthritis Patients with etanercept discontinued due to Who disease remission. *Clin Exp Rheumatol.* 2010 Nov–Dec, 28(6):919–22. Epub 2011 Jan 4.

A6.9

DIRECTED TRANSPORT OF MICRORNAs FROM APOPTOTIC CELLS TO PHAGOCYTES BY MEMBRANE-COATED VESICLES (MCVS)

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Background and Objectives A distinctive feature of cell activation and apoptotic cell death is the formation of MCVs. MCVs have previously been identified as mediators of cell-to-cell communication and are recognised as carriers of microRNA. An impaired clearance of apoptotic debris has been observed in SLE patients. This is caused by an increased rate of apoptosis and by a defect in phagocytic-cell clearance.

We investigated differences in the microRNA content of MCVs released by activated and apoptotic lymphoblasts from normal healthy donors (NHDs) and SLE patients. MicroRNA content of

lymphoblasts and MCVs and the effect of MCV uptake into monocytes were analysed.

Materials and Methods Activated lymphoblasts, UV-B irradiated lymphoblasts and corresponding MCVs of NHDs and SLE patients were compared in an Agilent microRNA array and validated by qPCR. MiR-155 expression was determined by qPCR in monocytes with engulfed autologous UV-MCVs. Western blot was performed to investigate the expression of the miR-155 target protein Tab-2.

Results MiR-155, miR-155*, miR-34b and miR-99a were significantly less expressed in UV-lymphoblasts compared to non-irradiated lymphoblasts. The effect was even more pronounced in staurosporine-treated lymphoblasts. In contrast, the expression of miR-34a increased after UV-B irradiation but decreased under staurosporine treatment. The comparison of viable and apoptotic MCVs showed a decrease of miR-155* in apoptotic MCVs. In UV-MCVs, the miR-99a level was higher compared to viable MCVs. MiR-155 was not altered in MCVs after apoptosis induction. MiR-34a was expressed at higher levels in viable SLE lymphoblasts and MCVs compared to NHDs. In contrast, miR-34b expression was decreased in UV-lymphoblasts and UV-MCVs of SLE patients. In functional assays we could demonstrate higher miR-155 levels and consecutively decreased target protein levels in monocytes after engulfment of autologous UV-MCVs.

Conclusions Our data show an unequal distribution of the content of different microRNAs within apoptotic cells and cell derived MCV. This suggests a directional transport rather than a random distribution. Thus, cells can regulate their microRNA as well as the microRNA content within released MCV. We could show that microRNA and protein expression changes in phagocytes after UV-MCV engulfment. Thus, our results suggest that MCVs could serve as a transport vehicle for microRNAs to mediate cell-cell communication and influence intracellular processes in the phagocyte. Disturbances of this system could contribute to the pathogenesis of SLE.

A6.10

HIGH DISEASE ACTIVITY AND EROSION RATE IN SUDANESE RHEUMATOID ARTHRITIS PATIENTS

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Background and Objectives Reports from Nigeria claim that rheumatoid arthritis (RA) in Western Africa has relatively low disease activity with a 29 occurrence of hand erosions. No data are published on RA in Sudan and our aim was to collect a first Sudanese RA cohort for comparative studies.

Materials and Methods 264 consecutive patients (87% females) with RA according to the 1987 ACR criteria attending two

rheumatology centres in Khartoum between December 2008 and September 2010 were included. Samples analysed in Uppsala for anti-CCP and IgM RF.

Results The mean age at inclusion was 48 years (range 14–80). Median disease duration was 3.8 years. ESR data was available for 113 patients, with a mean of 60.3 mm/1 h (range 10–140). Mean blood haemoglobin was 12.1 g/L. On clinical examination, 26% (68/264) had Z deformity, 14% (38/264) had Swan neck deformity and 9% (25/264) had Boutonniere deformity. X-rays of hands were available for 86 patients, with 49/86 (57%) showing erosions. 40% were treated with methotrexate, 7% with sulfasalazine 3% azathioprine, 2% with leflunomide and 2% with hydroxychloroquine in monotherapy. 41 (16%) were treated with steroids + DMARD monotherapy, 48 (18%) with DMARD combinations. Three % were treated with steroids only, and 9% with NSAIDs only.

52% were anti-CCP2 positive and 51% were IgM RF positive, corresponding to 97.6% specificity compared to the Sudanese healthy controls. Compared to Swedish RA patients (Rönnelid *et al*, *ARD* 2012) Sudanese patients had 270% higher mean ESR (55 versus 21 mm/h; $p < 0001$), and significantly lower age of disease onset (median 43 versus 56 years, $p < 0.0001$).

Conclusions RA as presented in an outpatient clinic in Khartoum is severe and with earlier RA onset than in Sweden. Sudanese patients show significantly higher ESR levels than Swedish patients, more Sudanese than Nigerian RA patients have radiological erosions, and the number of patients with classical hand deformities is substantial. Blood haemoglobin levels are rather well preserved. Immunological and genetic characterisation is now underway.

A6.11 INTRA-ARTICULAR OVEREXPRESSION OF INTERLEUKIN-10 DIMINISHES CARTILAGE PROTEOGLYCAN DEPLETION IN STREPTOCOCCAL CELL WALL ARTHRITIS: A PROMISING CONCEPT FOR DISEASE-REGULATED GENE THERAPY

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Background and Objectives Local gene therapy for arthritis, with the use of disease-inducible promoters, represents a promising alternative for coping with side effects of the conventional treatments. These disease-inducible promoters react to transcription factors that are released during inflammation and therefore only produce a therapeutic protein when necessary. Interleukin-10 (IL-10) could play an important regulatory role in streptococcal cell wall arthritis (SCW), and therapeutic effects are present when IL-10 was injected systemically (Lubberts *et al*, 1998).

In this study IL-10 was used to investigate the potential of intra-articular gene therapy in an acute model of arthritis.

Materials and Methods C57Bl6/N mice were injected intra-articularly in the kneejoint with lentivirus, expressing the therapeutic protein IL-10 or the luciferase reporter. Inducible promoters S100a8, Cxcl1, MMP13, Saa3, IL-1b, and TNFaip6, which were selected from endogenous genes differentially regulated in the inflamed synovium of collagen-induced arthritis mice, were used to express luciferase. The constitutive PGK promoter was used to express IL-10. Arthritis was induced by injection of 25 µg SCW into the knee joint cavity 4 days later. At 1, 4, and 7 days after arthritis induction, mice treated with PGK-IL10 were sacrificed, and knee joints were dissected for either histological analysis, or RNA isolation for qPCR analysis. At the same timepoints, in-vivo bioluminescent imaging was performed in mice treated with the inducible promoter reporter, using the IVIS Lumina system.

Results PGK-IL10 significantly decreased proteoglycan (PG) depletion at day 4 and 7 after arthritis induction, probably by inhibiting MMPs and upregulating TIMPs. No effects on inflammation were

seen histologically, but synovial IL-1, IL-6 and TNFa gene expressions were markedly decreased at day 1. The inducible promoters all showed a different activation profile during the course of inflammation, meaning they all react differently during the disease process. The Saa3 promoter showed the highest upregulation (120 fold) and was the only promoter which showed an early peak in activation at day 1 after arthritis induction, resembling neutrophil influx.

Conclusions Effects of IL-10 were seen on PG depletion and gene expressions, therefore IL-10 can be a feasible therapeutic protein to modulate SCW arthritis. On the other hand, the Saa3 promoter seems to be the best candidate for local intra-articular gene therapy with the use of disease-inducible promoters, because it showed a high and quick upregulation during disease activity. Hence, combining the Saa3 promoter with the therapeutic protein IL-10, can be a promising combination to modulate an acute model of arthritis using disease regulated gene therapy.

A6.12 LATERAL EPICONDYLE TENDON LESIONS TREATMENT WITH PLATELET GROWTH FACTORS

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Background Chronic painful tendon disorders are common and difficult to treat. Recently, research has focused on regenerative therapies based in the injections with autologous platelet growth factors (PGRF). Two randomised clinical trials involving patients with tendinopathy receiving autologous PGRF showed conflicting results. However, better outcomes were observed among individuals randomised to PGRF injections in the trial randomising patients with lateral epicondyle tendon lesion. The potential benefit of PGRF injections in patients without response to standard therapy is not established.

Objectives To evaluate the efficacy and safety of local injections with autologous PGRF to treat epicondylitis in patients refractory to standard therapy.

Methods Patients with epicondylitis who had received standard therapy including corticosteroid local injections and NSAIDs, with or without local ice or orthosis, were included in this prospective study. Patients being treated with physiotherapy were excluded. Patients were treated with one PGRF injection per month during three months. Symptoms, side effects of injections, visual analogic scale (VAS) were recorded in every visit. Fried man test was applied to compare VAS among visits.

Results 17 patients were included, 12 (57%) of whom were men. The median age was 52 (range: 42–61) years. 8 individuals have completed the scheduled therapy, 17 have reached 1 month. Median (RIQ) VAS were: at baseline 7 (6–9); at 1 month 6 (4–8); at 2 months 5 (3–9.5) ($p < 0.001$). An improvement in VAS was observed in 14 (82%) patients at 1 month, and 6 (75%) at 2 month. No significant side effects were observed.

Conclusions Local PGRF injections were efficacious to treat lateral epicondyle tendon lesions in patients without response to previous standard therapy. Local PGRF injections were well-tolerated.

A6.13 MINOR DISCREPANCY BETWEEN BMD OF SPINE AND HIP

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Background and Objectives Diagnostic discordance for osteoporosis is the observation that the T-score of an individual patient varies from one key measurement site to another, falling into two different diagnostic categories of minor and major discordances, identified by the World Health Organization (WHO) classification