Conclusion: Using target proteome profiling technique, we demonstrated PON1 as a potential biomarker of D2T RA. However, these results have to be validated on a larger cohort.

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AB0064

EVALUATION OF QUALITY OF LIFE IN RHEUMATOID ARTHRITIS USING SF-36 AND HAQ SCALES

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Background: The assessment of health-related quality-of-life (HRQoL) in rheumatoid arthritis (RA) is becoming a common tool in clinical practice. The medical outcomes survey short form 36 (SF-36) is one of the most widely used tools for measuring HRQoL in RA as well as the HAQ scale.

Objectives: The aim of our study is to evaluate the impact of the RA in the quality of life (QoL) of our patients using the SF-36 and the HAQ questionnaires.

Methods: This is a cross-sectional study during a period of the year 2020, including 70 patients followed in the department of Rheumatology in Mahdia, Tunisia. All patients were diagnosed with RA based in ACR 1987/EULAR 2010. We evaluated for each patient, the mean global scale and the eight domains of SF-36 (physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), a social functioning (SF), role emotional (RE) and mental health (MH)), scored from 0 (worst) to 100 (best).

Results: Our study included 70 patients (59 females/11males) with an age ranged from 21 to 76 years. The mean age was 54 ± 12 years. The mean duration of the disease was 11 ± 10 years [1-40]. The mean number of tender joints was 9.7 ± 9.4 and swollen joints were 4.2 ± 6.1. The mean disease activity score (DAS28) was 4.6 ± 1.9 [1.2-8.4]. The mean HAQ score was 1.5 ± 1.3, 47.1% of patients had specific joint deformations, 82.9% had radiologic involvement and 31.4% had osteoporosis. The biologic analysis showed that the mean ESR was 46.7 ± 30.5 and the CRP was 15.8 ± 23.3. Rheumatoid factors were positive in 42.9% of cases, the ACPA were positive in 50% of cases. 84.3% of RA patients were treated by methotrexate, 4.3% were treated by salazopyrin and 11.4% were treated by biologic treatments.

The SF-36 global score was 50.4 ± 26.3 [15.3-92.8]. 46 patients (65.7% of cases) had impaired QoL (SF-36 < 66.7). The means of different domains (PF, RP, BP, GH, VT, SF, RE, MH) were respectively 51; 41.4; 51.4; 50; 51.2; 57.7; 41.9; 59.2. The most severely impacted domains were the RP and RE.

Our study showed a significant correlation between the SF-36 global score and the number of tender joints (p=0.002), the DAS28 (p=0.017) and the HAQ (p=0.000).

Conclusion: Our study showed that 65.7% of RA patients presented impaired QoL (SF-36 < 66.7), which is associated with high disease activity. So it's important to jugulate the disease, in order to ameliorate the quality of life of our patients.

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AB0065

HGF/C-MET SIGNALING PROMOTE ANGIOGENESIS THROUGH CXCL16 IN RHEUMATOID ARTHRITIS

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Background: Hepatocyte growth factor (HGF) binds to the receptor tyrosine kinase c-Met and is a multifunctional cytokine that promotes processes such as cell proliferation, survival, differentiation, migration and angiogenesis [1]. We previously reported that HGF is produced by inflammation in the RA synovium, and activates monocyte migration to the synovium and promotes bone destruction through its own chemotactic effect and enhanced chemokine production in the synovium [2].

Objectives: Therefore, we next aimed to determine the role of HGF in RA angiogenesis.

Methods: The expression of HGF / c-Met in the serum and synovial tissues (STs) of RA patients and controls and human umbilical vein endothelial cells (HUVECs) was evaluated by ELISA and immunostaining. The effect of HGF/c-Met signaling on the promotion of CXCL16 production from HUVECs and RA fibroblast-like synoviocytes (FLSs) was determined by ELISA. To examine the role of HGF in angiogenesis, we performed in vitro Matrigel assays using HUVECs treated with HGF.

Results: HGF in serum in treatment-naïve RA patients was significantly higher than that in controls and HGF in serum in treatment-resistant RA showed a significant positive correlation with CXCL16. c-Met were expressed on vascular endothelial cells of RA STs and HUVECs. Stimulation of HUVECs with HGF dose-dependently increased CXCL16 production. c-Met signal inhibition by SU11274 suppressed TNF- α stimulation-enhanced CXCL16 production by RA FLSs in a dose-dependent manner. Furthermore, HGF induced HUVEC tube formation by 1.8-fold.

Conclusion: HGF is produced by inflammation in the RA synovium, and activates angiogenesis through its own potent angiogenic effect and enhanced production of CXCL16 in the synovium. These results indicate that a strategy targeting c-Met signalling may be important for resolving treatment-resistant RA.

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AB0066

MECHANISMS OF TOTAL SAPONINS OF PANAX JAPONICUS MITIGATES COLLAGEN-INDUCED ARTHRITIS

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Background: Total saponins of *Panax japonicus* (TSPJ) are extracted from *Panax japonicus* (T.Nees) C.A.Mey and have achieved a good therapeutic effect in the treatment of rheumatoid arthritis (RA). Unfortunately, the mechanism of TSPJ acting on RA is not clear.

Objectives: To investigate the potential mechanisms and key targets of TSPJ on RA.

Methods: The raw data were downloaded from the Gene Expression Omnibus (GEO) database, and the RStudio3.6.1 software was used to identify differentially expressed genes (DEGs). The potential targets of active compounds from TSPJ were predicted by the PharmMapper and SwissTargetPrediction databases. Based on the overlapping genes, we used Cytoscape 3.7.2 software to construct a protein-protein interactions (PPI) network and to determine the mechanisms of the treatment by Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis. Collagen-induced arthritis (CIA) model was established and treated with different doses of TSPJ. Arthritis index (AI) and histology score were used to evaluate the symptoms of CIA. The levels of vascular endothelial growth factor (VEGF), hypoxia-inducible factor 1 (HIF-1), IL-1 β , and IL-17A tested by enzyme linked immunosorbent assay and real time-quantitative Polymerase Chain Reaction.

Results: A total of 2670 DEGs and 371 TSPJ targets were obtained, including 52 overlapping genes. 41 genes had protein interactions that are used to build the PPI network. The results of the KEGG enrichment analysis included VEGF and HIF-1 signaling pathway. Seven negative correlation genes and 16 positive correlation genes were obtained by correlational analysis of DEGs in VEGF and HIF-1 signaling pathway. SRC proto-oncogene, nonreceptor tyrosine kinase (SRC), and the signal transducer and the activator of transcription 3 (STAT 3) had a higher value of degree in PPI and showed a significant correlation in the pathways; they were regarded as key targets. Compared with the CIA model group, TSPJ significantly decreased the AI and histology scores. Moreover, the expression of VEGF-A, HIF-1 α , IL-1 β , and IL-17A in serum or spleens significantly reduced in a dose-dependent.

Conclusion: Present study show that SRC and STAT 3 may be the key targets of TSPJ acting on the VEGF and HIF-1 signaling pathways, thus inhibiting angiogenesis and improving RA.

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AB0067

RHEUMATOID ARTHRITIS IS DRIVEN NOT ONLY BY INFLAMMATION BUT ALSO BY FIBROGENESIS

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Background: Rheumatoid arthritis (RA) is a chronic, autoimmune disease characterized by inflammation of the synovium, cartilage and bone leading to joint swelling, tenderness, and dysfunction. The destruction of the joint tissue involves degradation of the extracellular matrix (ECM). The ECM consist of collagens and other connective proteins¹. Studies have shown that elevated levels of collagen metabolites, such as those of type I, II, III and VI, are highly elevated in RA, correlated to disease activity and modulated in response to, for example tocilizumab², baricitinib³ and methotrexate⁴. However, little is known about the formation of collagen, fibroblast activity, the fibrotic component of RA and how this influence likelihood of response to treatment.

Objectives: We investigated the level of active fibrogenesis in a population of moderate to severe RA patients (in contrast healthy controls) by assessing blood-levels of PRO-C3 and PRO-C6 (type III and VI collagen formation markers), which have been reported to be associated with the degree and extent of fibrosis⁵.

Methods: PRO-C3 and PRO-C6 was measured in serum of 166 RA patients (age; 54 (20-82), 83 % females, 91% white) at baseline and week 16 after treatment with an anti-IL6 receptor antibody in combination with MTX, as well as in serum of 77 donors (age; 42 (20-69), 51 % females, 66% white). Marker

data was LN transformed. A general linear model was used when comparing groups.

Results: The serum fibrogenesis marker PRO-C3, but not PRO-C6, was significantly elevated in RA compared to donors (2.1 vs. 2.4 $\approx$ 30% difference, $p < 0.0001$, fig. 1A). None of the markers were correlated with disease measures such as DAS28, CRP, VASpain. None of the markers were modulated significantly in response to treatment. Interestingly, PRO-C3 levels were significantly higher at in non-responders (resp.) at week 16 compared to resp. (2.8 vs. 2.4 $\approx$ 40% difference, $p = 0.0018$, fig. 1C). Similar trend was observed for PRO-C6 (2.2 vs. 2.0 $\approx$ 20% difference, $p = 0.061$ fig. 1D).

Conclusion: Active fibrosis, with activated fibroblasts, may play an unseen role in RA. Patients will elevated levels of the fibrosis markers PRO-C3 and PRO-C6 were less likely to respond to an anti-IL6R. This may also give clue why such treatment are less efficacious in diseases with a clear fibrotic component.

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AB0068

B- AND T- LYMPHOCYTE SUBSETS IN PATIENTS WITH EARLY AND PROGRESSED RHEUMATOID ARTHRITIS

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Background: Role of B- and T- lymphocytes is well established in pathogenesis of rheumatoid arthritis (RA). Self-containing activation of B-cells in ectopic germinal centers is followed by auto-activation of T-lymphocytes while T-cells themselves are antigen-presenting cells for B-lymphocytes [1-2]. As these processes continue with the duration of RA, different subsets of B- and T-cell might be prevalent at different stages of RA.

Objectives: Evaluate differences in dynamics of B- and T- cell subsets in early and progressed RA.

Methods: 53 patients with diagnosed RA (ACR/EULAR 2010 criteria) were included in research in October 2019 - May 2020. Age median 54.2 [47; 62] yrs. 2 groups were formed: 1st (n = 27 pts., 25 female and 2 male) with early arthritis, median duration of RA 6 [5; 12] months prior to therapy, mediane DAS28-CRP - 5.8 [5; 15-6.2]; and 2nd group (n=26 pts., 22 female and 4 male) - patients with progressed RA, duration of RA 84 [24; 121] months, on DMARDs (methotrexate 20 [15; 20] mg/week or leflunomide 20mg/day), mediane DAS28-CRP - 6.31 [5.64-6.88]. Control group included 29 individuals (23 female and 6 male), age median 58.5 [53; 62] yrs. Blood of all patients underwent standart flow cytometry with T- and B-cell immunotyping.

Results: B and C-cells subsets were studied. B-cells subsets are presented in table 1 below.

Conclusion: As disease activity was high in both groups, therefore therapy was ineffective, and results could be interpreted as natural progression of RA, resulting mainly in dynamics of switched B-memory cells, transitioning B-cells and plasmoblasts. These subsets might be indicating disease development patterns but further research is required.

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Fig. Difference in active fibrogenesis assessed by serum PRO-C3 and PRO-C6 between donors and RA patients at baseline (A,B) and between resp. and non-resp. at week 16 (C,D). Data is shown as back-transformed estimated marginal means (EMM) with 95%-CI adjusted for age, gender, and race (all), and BMI, disease duration and baseline marker level (C,D).