domain protein-1/hypoxia-inducible factor-2 α (EPAS-1/ HIF-2 α) is a catabolic transcription factor that regulates osteoarthritis (OA) cartilage destruction.

Objectives: In this study, we examined whether microRNA-365 (miR-365) affects interleukin (IL)-1 β -induced expression of catabolic factors in chondrocytes via regulation of HIF-2 α .

Methods: Total RNA was isolated from normal and OA cartilage tissues and human chondrocytes. miR-365 expression was quantified by TaqMan assay. The effects of miR-365 on HIF-2 α and HIF-2 α -modulated genes were assessed by quantitative real-time reverse polymerase chain reaction (qRT-PCR), Western blot analysis, and enzyme-linked immunosorbent assay (ELISA). Direct interaction of miR-365 with the 3' untranslated region (UTR) of HIF-2 α mRNA was examined using a luciferase reporter assay. Nitrite concentration was measured in culture medium using a Griess assay.

Results: miR-365 levels were significantly decreased in human OA cartilage relative to normal cartilage. Overexpression of miR-365 significantly suppressed IL-1 β -induced expression of HIF-2 α in human articular chondrocytes. Pharmacological inhibition of various IL-1 β -associated signaling pathways revealed mitogen-activated protein kinase and nuclear factor- κ B as the primary pathways driving IL-1 β -mediated decreases in miR-365 and subsequent increase in HIF-2 α expression. Using a luciferase reporter assay encoding the 3'UTR of human HIF-2 α mRNA, we showed that overexpression of miR-365 significantly suppressed IL-1 β -induced up-regulation of HIF-2 α . Furthermore, miR-365 overexpression significantly suppressed IL-1 β -induced expression of catabolic factors, including cyclooxygenase-2, inducible nitric oxide synthase, and matrix metalloproteinase-1, -3 and -13, and nitric oxide (NO) production in chondrocytes.

Conclusions: MiR-365 regulates IL-1 β -stimulated catabolic effects in human chondrocytes by modulating HIF-2 α expression.

References:

- [1] Yang et al. Hypoxia-inducible factor-2 α is a catabolic regulator of osteoarthritic cartilage destruction, *Nat. Med.* 16 (2010) 687–693.
- [2] Akhtar et al. Haqqi, MicroRNA-27b regulates the expression of matrix metalloproteinase 13 in human osteoarthritis chondrocytes, *Arthritis Rheum.* 62 (2010) 1361–1371.
- [3] Park et al. MicroRNA-558 regulates the expression of cyclooxygenase-2 and IL-1 β -induced catabolic effects in human articular chondrocytes, *Osteoarthritis Cartilage* 21 (2013) 981–989.

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THU0051 ASSOCIATION BETWEEN BIOACTIVE TNF AND EULAR RESPONSE TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS

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Background: ROC study provided data to manage rheumatoid arthritis (RA) treatment after a failure to a first TNF blocker (1). We previously reported that high circulating TNF bioactivity was associated with good clinical response (2).

Objectives: To explore ability of TNF bioactivity to predict response to second TNF blocker.

Methods: Here, we assessed TNF bioactivity in 130 RA patients from the group rotation to a second TNF blocker at the time of randomisation and after 6 months. Clinical and biological data were recorded at baseline and 6 month with Eular response assessed at 6 month.

TNF bioactivity was assessed with HEK-Dual TNF cells adapted from our previous work (2). Due to non-normalised distribution, non parametrical analysis were performed.

Results: Baseline circulating TNF bioactivity was similar according to Eular response. However, circulating TNF bioactivity at 6 month was associated

with clinical response with low TNF bioactivity in responders. A ROC analysis suggested a cut-off at 0.320 with a sensitivity at 92% and a specificity at 41%.

Conclusions: After a failure of a first TNF blocker, circulating TNF bioactivity is not able to predict response to a second TNF blocker despite a lower level in responders compared to non-responders.

References:

- [1] Gottenberg J-E, Brocq O, Perdriger A, Lassoued S, Berthelot J-M, Wendling D, et al. Non-TNF-Targeted Biologic vs a Second Anti-TNF Drug to Treat Rheumatoid Arthritis in Patients With Insufficient Response to a First Anti-TNF Drug: A Randomized Clinical Trial. *JAMA.* 2016 Sep 20;316(11):1172–80.
- [2] Marotte H, Maslinski W, Miossec P. Circulating tumour necrosis factor- α bioactivity in rheumatoid arthritis patients treated with infliximab: link to clinical response. *Arthritis Res Ther.* 2005;7(1):R149–155.

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THU0052 LEVELS OF INFLAMMATORY SEROLOGIC BIOMARKERS IN HLA-B27 AND HLA-B15 POSITIVE PATIENTS WITH SPONDYLOARTHRITIS

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Background: A main challenge in spondyloarthritis (SpA) management was the availability of reliable biomarkers related with disease activity, or predicting joint damage and the response to treatment. Although erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are currently used as biomarkers for disease activity, they lack sensitivity, specificity and reproducibility. With the understanding of SpA pathogenesis, additional biomarkers like metalloproteinase 3 (MMP-3), interleukin (IL)-1 α , IL-6, lipopolysaccharide-binding protein (LBP), tumour necrosis factor α (TNF α), macrophage colony stimulating factor (M-CSF), interferon gamma (INF-g), IL-17 and IL-23, had been proposed

Objectives: We aimed to evaluate the associations of MMP-3, IL-1 α , IL-6, M-CSF, LBP, IL-17 and IL-23 levels in SpA patients positive for HLA-B27 or HLA-B15

Methods: 178 patients (100 men and 78 women) with SpA according to ASAS criteria were included in the study. HLA typing was performed by PCR using the Biorad® HLA-GSP ABDR plates. The levels of TNF α , IL-1 α , IL-6, INF-g and IL-17 were measured by a cytometric bead-array (CBA Flex Set) using a FACS Canto II Flow Cytometer. Enzyme-linked immunosorbent assay (ELISA) was used to determine serum levels of IL-23, M-CSF and MMP-3. CRP and LBP levels were measured by chemiluminescence. Statistical analysis was made with SPSS v19. For comparison of quantitative variables with a normal distribution we used the Student's *t*-test. Categorical variables were presented in frequency charts and percentages, and the Chi-squared test and Fisher's exact test were used when necessary, for comparing groups. Two-tailed P-value <0.05 was considered statistically significant

Results: Of the 178 patients, 70 were positive for HLA-B27, 34 for HLA-B15 and 74 had other HLA-B. According to ASAS classification criteria, 152 patients had axial SpA (axSpA) manifestations, 161 had peripheral SpA (pSpA) manifestations, and 148 patients had mixed axial and peripheral manifestations. Figure 1 shows the mean levels of inflammatory serologic biomarkers in these subgroups of patients

Figure 1. A. Mean activity biomarkers (CRP, C-reactive protein; LBP, lipopolysaccharide-binding protein) in axial spondyloarthritis (axSpA) and peripheral spondyloarthritis (pSpA); B. Cytokines (INF-g, interferon gamma; IL-1 α , interleukin; M-CSF, macrophage colony stimulating factor; TNF α , tumour necrosis factor α); C. ESR, erythrocyte sedimentation rate; D. CRP, C-reactive protein; E. IL-23, interleukin 23; F. IL-17, interleukin 17; G. IL-6, interleukin 6; H. IL-1 α , interleukin 1 α ; I. LBP, lipopolysaccharide-binding protein; J. TNF α , tumour necrosis factor α . *P < 0.05, **P < 0.01, ***P < 0.001.

Conclusions: High levels of IL-17 and IL-23 were associated with the presence of HLA-B27, which mainly correlates with an axial presentation of the disease as