Detecting Extracellular Matrix Turnover in axSpA Patients with concomitant Inflammation on MRI and Normal CRP

Frederik Gillesberg[1,2],René Østgård[3], Joachim Høgh Mortensen[2], Martin Pehrsson[2], Signe Holm Nielsen[2], Bent Deleuran[1,4], Anne-Christine Bay-Jensen[2], Tue Kragstrup[1,3,4]

[1]Aarhus University, Department of Biomedicine, Aarhus, Denmark; [2]Nordic Bioscience, Immunoscience, Herlev, Denmark; [3]Regional Hospital Silkeborg, Diagnostic Center, Silkeborg, Denmark; [4]Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark

Correspondence to: frg@nordicbio.com

AARHUS UNIVERSITY

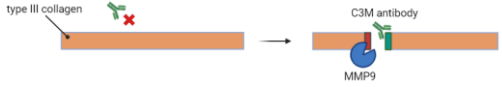
BACKGROUND

- Many axial spondyloarthritis (axSpA) patients present normal CRP levels despite having inflammation in the axial skeleton.
- Erosions and new bone formation are hallmarks of axSpA.
- The disease is characterized by aberrant neutrophil activation.
- We hypothesize that mechanistic biomarkers reflecting axial skeleton inflammation *in situ* may be superior to CRP for assessing disease activity.

- Objective: To investigate the association of the soluble biomarkers Cpa9-HNE, C3M and PRO-C3 with MRI inflammation in the sacroiliac joint (SIJ) and spine of axSpA patients.

METHODS

Biomarkers for neutrophil activity (Cpa9-HNE), type III collagen degradation (C3M) and type III collagen formation (PRO-C3) were measured in plasma samples from axSpA patients (n=21) in the INTASAH cohort[1]. EDTA plasma samples collected at baseline (week 0) and after 12 and 52 weeks of adalimumab treatment were measured. Changes in biomarker levels were analyzed using linear mixed models. MRI scoring of active inflammatory and chronic changes in spine and sacroiliac joints (SIJ) at weeks 0, 20 and 52 were published previously[1]. Spearman correlations were used to compare MRI scores and biomarkers at week 0 and 52. ROC analysis was used to investigate the sensitivity of biomarkers to indicate columna inflammation at week 52.



C3M neo-epitope generation through cleavage of type III collagen, mechanistically reflecting inflammatory tissue turnover

CONCLUSIONS

- CPa9-HNE, C3M and CRP correlated significantly with spine MRI inflammation at baseline
- CPa9-HNE and C3M had superior sensitivity over CRP to indicate spine MRI inflammation at week 52
- Cpa9-HNE and C3M may be useful to detect disease activity changes in AxSpA with normal CRP

References: 1. Østgård, R. D. et al. Faecal calprotectin detects subclinical bowel inflammation and may predict treatment response in spondyloarthritis. Scandinavian Journal of Rheumatology 47, 48–55 (2018).

Disclosures: Joachim H. Mortensen, Martin Pehrsson, Signe Holm Nielsen and Anne-Christine Bay-Jensen are employees of Nordic Bioscience, a biotech company. Anne-Christine Bay-Jensen owns stock in Nordic Bioscience. Frederik S. Gillesberg, Tue W. Kragstrup and Bent W. Deleuran have nothing to disclose in relation to this work.

RESULTS

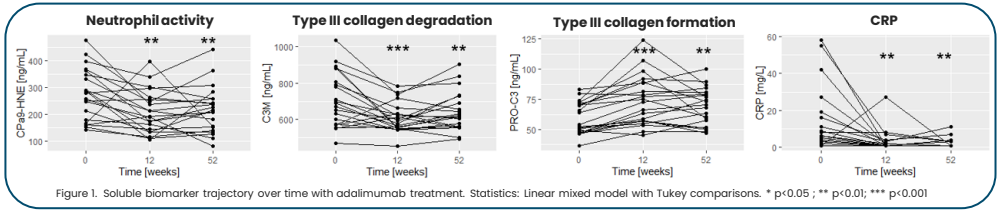


Figure 1. Soluble biomarker trajectory over time with adalimumab treatment. Statistics: Linear mixed model with Tukey comparisons. * p<0.05 ; ** p<0.01; *** p<0.001

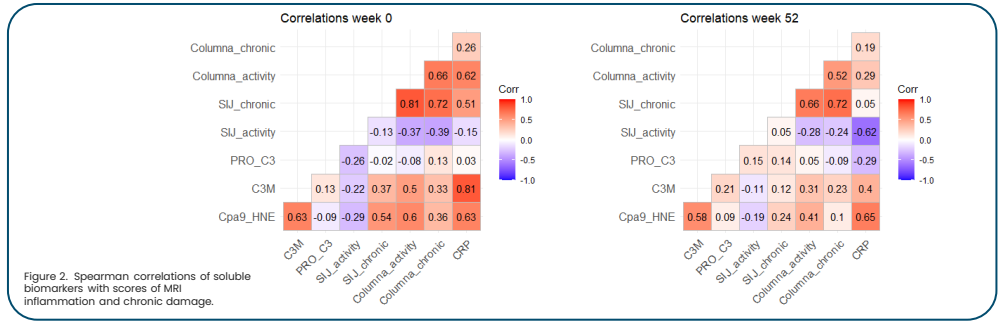


Figure 2. Spearman correlations of soluble biomarkers with scores of MRI inflammation and chronic damage.

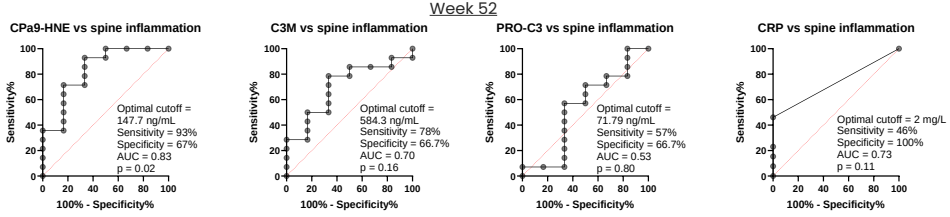


Figure 3. ROC analysis of biomarkers in detecting spine inflammation at week 52. Statistics: Mann-Whitney test.