Background: Modic changes (MC) are inflammatory vertebral bone marrow lesions adjacent to degenerative intervertebral discs [1]. On MRI, three types can be distinguished: Modic types 1 – 3 changes (MC1, MC2, MC3). Especially MC1 are associated with low back pain (LBP), and the larger the lesion, the stronger is the association with pain [3]. However, in clinics, MC is often a binary (present/absent) observation with insufficient inter-observer reliability in identifying and classifying MC.

Objectives: The aim of our study was to find potential serum biomarkers for the presence or the extent of MC using data of the Northern Finland Birth cohort of 1966 (NFBC1966) [2].

Methods: We selected 103 participants of the NFBC1966 to form 4 groups: With and without MC, and with and without LBP. For each participant with MC, we had information about the type, number, location, height, and transverse area (TA) of the MC. Height was given in 4 groups: “along the endplate” > 25%; “25-50%”; and “<50%” of the height of the vertebral body/TA was measured in 1/9 parts of the vertebral endplate surface of a fictitious 3x3 grid (Fig. 1). We defined the MC load for each person and MC type as the sum of the product of height and TA of each MC.

The serum samples were subjected to a sequential window acquisition of all theoretical mass spectra (SWATH-MS) analysis. To find a potential biomarker for the presence of each MC type we compared serum concentrations of proteins identified by mass spectrometry between participants with and without MC using Mann-Whitney-U tests. Performance to predict MC was calculated with Receiver Operating Characteristics (ROC). A covariate analysis for significantly different proteins was done with an ANCOVA. To find a potential biomarker for the extent of MC, we searched for associations between serum concentration and MC-load with Spearman’s logistic regression. We corrected for multiple comparisons with False Discovery Rate (FDR).

Results: Of the 103 participants, 49 had MC, 54 had no MC (noMC). Of the participants with MC, 5 (10.2%) had only MC1, the others had multiple types of MC. 30 (61.2%) had MC1, 43 (87.7%) had MC2 and 40 (81.6%) had MC3. The average MC number per person was 3.0 (1 – 9). The MC load, calculated from number, area, and height of the MC-lesions, was on average highest for MC2 (7.0, 95% CI: 3.5 – 10.6). Serum Mass Spectrometry identified 1087 proteins. Of these, only the concentration of Apolipoprotein D (APOD) was significantly different between MC1 and noMC (Mann-Whitney-U-Test, FDR-adjusted p = 0.034). A covariate analysis with ANCOVA showed that this was independent of LBP. There was no significant result for MC2 or MC3 after correction for multiple comparisons. The ROC for APOD in MC1 had an area under the curve (AUC) of 0.79. As APOD is part of lipoproteins and involved in lipid transport, we hypothesised a disturbed lipid transport in patients with MC1 and tested if adding other proteins involved in lipid transport to the model could increase the AUC of the ROC. Adding Apolipoprotein C3 (APOC3) to the linear model increased AUC of the ROC to 0.83 despite not associating with MC1. Additionally, linear regression showed a correlation between serum APOD and MC load (ρ = 0.46, FDR adjusted p-value = 0.002).

Conclusion: The serum concentration of APOD is associated with the presence of MC1 and correlates with the load of MC1. Especially in combination with the serum concentration of APOC3, it is a potential biomarker for the presence of MC.

REFERENCES: