FROM A 2-YEAR MULTICENTRE CLINICAL TRIAL IN KNEE OSTEOARTHRITIS, A METABOLOMIC ANALYSIS REVEALS THAT OVER ACTIVATION OF THE CONVERSION PATHWAY OF PHOSPHATIDYLCHOLINE TO LYSOPHOSPHATIDYLCHOLINE IS ASSOCIATED WITH KNEE CARTILAGE VOLUME LOSS OVER TIME

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Background: While progression of osteoarthritis (OA) is variable, no tools yet exist to predict disease course.

Objectives: To identify, using a metabolomic approach, serum marker(s) for predicting knee cartilage volume loss over time measured by magnetic resonance imaging (MRI) in a 24 month Phase III clinical trial in patients with symptomatic knee OA.

Methods: 139 knee OA patients who completed the trial according to protocol were selected from a 24 month DMOAD trial studying the effect of licofelone treatment, and controls (non-OA) from individuals having a fracture (n=21; n=9, respectively) was done to further explore the potential metabolic pathway(s).

Results: Data revealed that the baseline ratio of the metabolite lysophosphatidylcholine 18:2 (lysoPC 18:2) to phosphatidylcholine 44:3 (PC44:3) was associated with the cartilage volume loss in the lateral compartment (univariable, \(b=0.01 \pm 0.04, p=8.53 \times 10^{-2}\); multivariable, \(b=0.18\pm 0.04, p=9.51 \times 10^{-6}\)). Further experiments demonstrated that the lysoPC 18:2/PC44:3 ratio was also significantly correlated with PLA2G5 (\(r=0.71, p=0.02\)).

Conclusion: Our data suggest that PLA2, PLA2 group 5 (PLA2G5), was markedly over-expressed in OA cartilage and subchondral bone compared to these non-OA tissues (445% and 158% increase, respectively, all \(p<0.02\)). Interestingly, in these tissues TNF-a was also upregulated (p=0.007; p=0.06, respectively), and positively correlated with PC44:5 (r=0.71, p=0.02).

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References:

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