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THU0180

INFLUENCE OF BLUE MUSSEL (MYTILUS EDULIS) INTAKE ON FATTY ACID COMPOSITION IN ERYTHROCYTES AND PLASMA PHOSPHOLIPIDS AND SERUM METABOLITES IN WOMEN WITH RHEUMATOID ARTHRITIS

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Background: The positive effects of omega-3 on risk of cardiovascular disease, on inflammation and immune function are well established [1]. Unfortunately fish as a source of omega-3 is not economically or environmentally sustainable. In contrast, blue mussel farming is beneficial for the environment since excessive nitrogen is removed at harvest and eutrophication of the sea is reduced [2]. Blue mussels contain not only omega-3, but are rich in nutrients such as zinc, selenium, riboflavin and carotenoids. We have previously shown, in the randomized cross-over trial Mussels, Inflammation and RA (MIRA), that disease activity (DAS28-CRP), fatigue, pain and general health in RA is improved by a dietary intervention with blue mussels compared to control [3]. It is not clear what the mechanisms of the intervention were, and if the intake of omega-3 from the blue mussels plays a role.

Objectives: The aim of this study was to investigate if the intake of blue mussels in patients with RA lead to changes in fatty acid composition in plasma phospholipids and erythrocytes and/or in metabolites (detected by NMR-metabolomics), compared to a control diet, in an attempt to understand the health beneficial effects found in the MIRA study.

Methods: Twenty-three women completed the randomized 2 × 11-week cross-over dietary intervention, exchanging one cooked meal a day, five days a week, with a meal including 75 g blue mussels or 75 g meat. Fatty acid composition in erythrocytes and plasma and ¹H-NMR metabolomics data were analysed and multivariate data analysis; Orthogonal Projections to Latent Structures with Discriminant Analysis (OPLS-DA) and OPLS with effect projections (OPLS-EP) were performed to compare the two diets.

Results: Intake of the blue mussels led to a different fatty acid profile in erythrocytes, compared to control, and all samples could be correctly classified with OPLS-DA (figure 1). The changes included significant increases in omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The patterns for plasma phospholipids and ¹H-NMR serum metabolites were not as specific for the diets and metabolites were strongly influenced by body mass index (BMI) (figure 2).

Abstract THU0180 – Figure 1. A) Model prediction for all individuals in OPLS-EP models for erythrocyte fatty acids (%). B) OPLS-DA models showing separation for erythrocyte fatty acids (%). Black boxes = control diet, grey circles = blue mussel diet

Abstract THU0180 – Figure 2. Orthogonal Projections to Latent Structures (OPLS) for metabolites in relation to significant related factors (n=92). TAG= triacylglycerides, BMI= body mass index

Conclusion: To conclude, the change in fatty acid pattern in erythrocytes could be related to reduction in disease activity in the MIRA-study, although it cannot be excluded that other factors than omega-3 fatty acids potentiate the effect. Multivariate modelling of fatty acids in erythrocytes increased the precision for compliance, compared to evaluating EPA and DHA content alone.

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TREATMENT WITH UPADACITINIB RESULTS IN THE NORMALIZATION OF KEY PATHOBIOLOGIC PATHWAYS IN PATIENTS WITH RHEUMATOID ARTHRITIS: BIOMARKER RESULTS FROM THE PHASE 3 SELECT-NEXT AND SELECT-BEYOND STUDIES

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Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) with an inadequate response (IR) to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs) in the SELECT-NEXT¹ and SELECT-BEYOND² trials, respectively. The pivotal immune regulatory pathway targets served by JAK1 in patients have not been comprehensively explored.

Objectives: To investigate the mode of action (MoA) of UPA in patients with RA via a proteomic approach that evaluates a set of plasma proteins associated with inflammation.

Methods: Patients from the SELECT-NEXT and SELECT-BEYOND (PBO, n=167; UPA 15 mg QD, n=200) studies were randomly selected from the pool of patients with plasma samples available at baseline, Week 2, and Week 12. Samples from 24 age- and sex-matched healthy controls were included. The levels of 92 proteins were analyzed using the Olink[®] Inflammation Panel. Results from both studies were combined. Data were clustered using the Ward (unsupervised) method; correlations were calculated using the Pearson method; and multiple comparisons were corrected using the Benjamini-Hochberg method; all statistical analyses were performed in JMP 13.10 (SAS Institute). Pathway analysis was performed with Ingenuity[®] Pathway Analysis (Qiagen Inc.) version 45868156.