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THE EFFECT OF ORGANOSULPHUR-ENRICHED DIET ON ENDOGENOUS METHANE PRODUCTION AND ETHANOL-INDUCED LIVER DYSFUNCTION IN MICE

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Keywords: Methanogenesis, Organosulphurs, Oxido-reductive, Ethanol, Liver

Aims: The anti-inflammatory properties of exogenous methane (CH₄) in ischemia/reperfusion model experiments are established (Boros, 2012; Li, 2017), and in vitro studies demonstrated the role of organosulphur compounds in CH₄ formation (Althoff, 2014). We aimed to investigate the methanogenic potential of a diet rich in organosulphur moieties and to study the biological consequences of the pre-feeding in a mouse model of ethanol-induced liver dysfunction.

Methods: Hairless mice were fed with standard- or 10% mustard-seed containing laboratory chow for 14 days (n=7, each group) and then the animals were allocated into control or 12% ethanol-consuming groups for further 7 days. The whole-body CH₄ emission was recorded using photoacoustic spectroscopy. Liver NADPH oxidase activity was determined to monitor the progress of oxidative stress. Repeated measurements ANOVA and Kruskal-Wallis followed by Dunn's test were used for statistical analysis.

Results: The organosulphur diet resulted in prompt CH₄ generation after the start of alcohol input at day 1 (p<0.001), which was followed by slight increase. Without the diet, this effect appeared only from the fifth day of ethanol intake (p<0.001) and it was kept up thereafter. Alcohol consumption led to a significant increase in the liver NADPH oxidase activity which was reduced by the diet significantly (p<0.05 vs. ethanol).

Conclusions: Mustard seed-containing pre-feeding caused an immediate endogenous CH₄ formation following ethanol intake. This CH₄ release protected the liver during the ethanol challenge and potentially contributed to a maintained oxido-reductive balance.

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DETERMINING THE EFFECT OF STEROLS AND POLYUNSATURATED FATTY ACIDS ON THE MAGNITUDE OF DIPOLE POTENTIAL WITH A NOVEL HIGH-THROUGHPUT FLOW CYTOMETRIC METHOD

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Keywords: dipole potential, F66, cholesterol, omega-3, omega-6

Aims: Dipole potential (DP) is an intramembrane potential with a magnitude of ~+300 mV, which greatly affects the function of transmembrane proteins. The magnitude of the DP is mainly determined by the lipid composition, especially the sterol concentration of the membrane. Thus, diseases characterized by elevated

cholesterol or 7-dehydrocholesterol (7DHC) levels, such as hypercholesterolemia (HC) or Smith-Lemli-Opitz syndrome (SLOS), can be associated with elevated DP, which may play a role in their pathophysiology. In such cases decreasing the DP could be beneficial, however, no known physiological method to lower DP has been described. Measurement of the DP, especially in living cells, is difficult, yet we were able to develop a novel flow cytometric method to study the DP in models of such diseases.

Methods: We have measured the magnitude of DP in models of HC and SLOS with our novel emission ratiometric (Rem) approach using the environment sensitive fluorophore F66 and flow cytometry. The models were created in JY lymphocytoid, THP-1 monocytoïd and HEK-293-T human embryonal kidney cell lines treated with methyl-beta-cyclodextrin/sterol complexes. The effects of omega-3 (alpha-linolenic-acid), omega-6 (gamma-linolenic-acid) fatty acids and stearic acid on DP were also determined in disease models.

Results: In models of HC and SLOS loading the cells with cholesterol and 7DHC resulted in dose-dependent increases in DP ($\Delta\text{Rem}_{\text{max}}$ -14%, -8%, respectively). Demonstrating the importance of a diet rich in polyunsaturated fatty acids, ω -3 fatty acid decreased, while ω -6 or saturated fatty acid increased the magnitude of DP ($\Delta\text{Rem}_{\text{max}}$ +10%, -5%, respectively). In combined treatments ω -3 fatty acid attenuated, while ω -6 fatty acid amplified the effects of cholesterol on DP.

Conclusions: The results of our novel flow cytometric method confirmed the positive effect of ω -3 fatty acid in reducing the adverse membrane biophysical alterations observed in HC and proposed ω -3 fatty acids as physiological DP lowering agents.

INVESTIGATION OF THE RELATIONSHIP BETWEEN CARDIOLIPIN AND PREDIABETES INDUCED CARDIAC DAMAGE

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Keywords: cardiolipin, remodeling, prediabetes, OGTT, mass-spectrometry

Aims: Prediabetes is a symptomless disease that mostly remains unrecognized. Prediabetes induces cardiac damage, which involves mitochondrial dysfunction. One of the main components of the mitochondrial inner membrane is cardiolipin. The cardiolipin level decreases in diabetes mellitus correlated to diabetic myocardial damage. Our work aimed to examine the relationship between prediabetes induced cardiac damage and cardiolipin levels.

Methods: We used 16 male Wistar rats. The rats were divided into two groups. The control group received a normal diet while the fructose-fed group received a 60% fructose-supplemented chow for 24 weeks. During the experiment, we measured fasting blood sugar levels and oral glucose tolerance (OGTT). In the 24th week, animal hearts were isolated and cardiac functions were examined by working heart perfusion. With mass-spectrometry, we determined cardiolipin levels in the myocardium.

Results: The results of fasting blood sugar monitoring and oral glucose tolerance test showed slightly but significantly elevated values due to fructose feeding, indicating the development of the prediabetic condition. The isolated working heart perfusion revealed diastolic dysfunction in the fructose-fed group. We detected decreased cardiolipin levels with mass-spectrometry due to the increased fructose intake compared to the control group ($28,1 \pm 2,1$ vs. $37,8 \pm 2,1$). Furthermore, we detected significant cardiolipin remodeling in the fructose-fed group. Cardiolipin is essential in mitochondrial and myocardial function, so the defect of this