PROTEIN MODIFICATIONS AND N-MYE METABOLISM

BACKGROUND: Protein modifications are important post-translational modifications that affect protein function and stability. One of the most studied modifications is N-myristoylation, which involves the covalent addition of myristic acid to a specific glycine residue in the N-terminus of a protein. This modification is crucial for the localization and function of proteins in the cell, including enzymes involved in lipid metabolism.

METHODS: We investigated the role of N-myristoylation in the metabolism of proteins related to lipid metabolism using a combination of proteomics and bioinformatics approaches. The study involved the identification of proteins with N-myristoylation sites and functional enrichment analysis to understand the biological significance of these modifications.

RESULTS: Our findings revealed that proteins involved in lipid biosynthesis and metabolism were predominantly myristoylated. The functional enrichment analysis indicated that N-myristoylation plays a crucial role in regulating the expression and function of enzymes involved in lipid synthesis and degradation. The results also suggested potential therapeutic targets for diseases associated with lipid metabolism disorders.

CONCLUSIONS: This study highlights the importance of N-myristoylation in lipid metabolism and identifies potential therapeutic targets. Further research is needed to understand the biological implications of these modifications in health and disease.
POSTER PRESENTATIONS

findings: cardiac dysfunction – by clinical, echocardiography findings; renal dysfunction – by glomerular filtration rates (GFR), serum creatinine levels and microalbuminuria. Circulating NT-proBNP levels were measured by the immuno-assay method. ALC patients were monitored for 2 years. 12 healthy volunteers (median age: 59.2 yr, 25.08 females) were the control group.

Results: The median NT-proBNP serum levels were significantly increased in patients with decompensated ALC (grade B: 926.5 pg/mL, grade C: 1450.3 pg/mL, versus grade A: 139.4 pg/mL) compared to control group (96.2 pg/mL) (p < 0.001). The NT-proBNP levels correlated with the Child-Pugh score (r = 0.96, p < 0.001), bilirubin levels (r = 0.48, p < 0.01) and albumin levels (r = 0.39, p < 0.01). The high NT-proBNP levels in ALC patients were associated with cardiac dysfunction by reduced left ventricular (LV) ejection fraction and increased LV mass (r = 0.41, p < 0.01; r = 0.51, p < 0.001) and renal dysfunction by decreased GFR and albuminuria (r = 0.45, p < 0.01; r = 0.36, p < 0.03). In following 2 years death occurred in 2 (13.3%) of ALC patients grade B and in 7 (46.7%) of ALC patients grade C of Child-Pugh. NT-proBNP ≥1000 pg/mL was associated with an increased risk of death over 2 years in compensated ALC patients (adjusted HR 2.49 [95% CI 1.25–5.88], p = 0.03).

Conclusions: The high NT-proBNP levels in patients with decompensated ALC may be an independent predictor of cardiac and renal dysfunction as well as severe ALC course and increased risk of death over 2 years.

THU-368
HIGH FREQUENCY OF INFLAMMATORY CD16+ MONOCYTES IN ALCOHOLIC HEPATITIS CAN BE REVERTED WITH PREDNISOLONE
N. Vergi1, W. Khambir1, C. Antoniades1, M. Thurm1 and STOPHAP trial group, Department of Gastroenterology, Imperial College, London, United Kingdom
E-mail: n.vergi@imperial.ac.uk

Background and Aims: Severe alcoholic hepatitis (SAH) is an inflammatory condition associated with the systemic inflammatory response syndrome and high serum levels of inflammatory cytokines. Accordingly, 28-day mortality in this condition can be reduced by treatment with the anti-inflammatory corticosteroid prednisolone. We sought to evaluate the impact of prednisolone versus placebo on the phenotype and function of circulating monocyte subsets in SAH.

Methods: We sampled blood from 23 patients with SAH (DFI > 32) participating in the STOPHAP study. 34 healthy controls (HC) and 9 patients with cirrhosis compensated alcoholic liver disease (CLD). Monoclonal antibody and FACS was used to identify monocyte subsets (classical CD14^CD16^, intermediate CD14^CD16^ and non-classical CD14^CD16^) and surface activation and chemokine receptor markers. Intracellular cytokine staining was used to quantify monocyte subset responses to 100 ng/mL lipopolysaccharide (LPS).

Results: The population of intermediate monocytes was expanded in SAH (11x vs 6x HC, p < 0.001), and the frequency of patrolling non-classical monocytes was conversely diminished (1x vs 5x HC, p < 0.0001). Intermediate monocytes expressed higher levels of the activation marker HLA-DR (vs CLD; p < 0.005). Accordingly, median production of II-10, IL-6 and TNF-α in response to LPS was higher in intermediate compared to classical monocytes, and significantly for TNF-α (p = 0.03). These intermediate monocytes also bore higher expression of the chemokine receptor CCR5 (vs HC, p < 0.01). Strikingly, the frequency of intermediate monocytes was reduced after 7 days treatment with prednisolone (15x reduced to 6x; p = 0.05) vs patients who were treated without prednisolone (11x to 10x; p = 0.9). 7 days treatment with prednisolone also reduced expression of the activation marker HLA-DR on intermediate monocytes.

Conclusions: Th...
THU-301
MCJ/DNAJC15, THE MITOCHONDRIAL FOE IN LIVER INJURY
Lucía Barbier Torres, Paula Irurzunbela, Daniel Tabo, Teresa Cardoso, Nicolás Navas, David Fernández Ramos, Marta Vareis Rey, Virginia Gutiérrez de Juan, Pablo Fernández Tusas, Imanol Zubiaurre Francol, María Isabel Hernández Alvaro, Raúl Andrade, Inmaculada Medina, María Jesús Monte, José Juan García Marin, Javier Crespo, Antonio Zorrano, José María Mato, Juan Anguita, Mercedes Rincon, María Luz Martinez Chantar, Spain

THU-302
PREDICTING MORTALITY IN ALCOHOLIC HEPATITIS USING CLIF-ORGAN FAILURE SCORE
Marco Silva, Patricia Andrade, Susana Rodrigues, Amândo Peixoto, Rui Gaspar, Susana Lopes, Hélder Cardoso, Guilherme Macedo, Portugal

THU-303
THE MECHANISMS UNDERLYING MURINE AND HUMAN IBUPROFEN INTOXICATION
Miguel Eugenio Zolatz, Marina Maximilian Weick, Raúl J. Andrade, M. Isabel Lucena, Christian Trautwein, Francisco Javier Cubero, Germany

THU-304
NOVEL FUNCTION OF MITOCHONDRIAL PROTEASE (LONP) IN A DRUG-INDUCED DUAL MODEL OF ER-STRESS AND MITOCHONDRIAL DYSFUNCTION IN HEPATIC CELLS
Mázlan Polo, Fernando Alegre, Alberto Martí-Rodrigo, Ana Blas-García, Juan V Esplugues, Nádza Apostolova, Spain

THU-305
N. TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE AND PROGNOSIS OF ALCOHOLIC LIVER CIRRHOSIS COURSE
Nataliya Virstyuk, Iryna Kobitovsky, Nataliya Shyka, Oleg Virstyuk, Ukraine

THU-306
HIGH FREQUENCY OF INFLAMMATORY CD16+ MONOCYTES IN ALCOHOLIC HEPATITIS CAN BE REDUCED BY TREATMENT WITH PREDNISOLONE
Nikhil Vergh, Wafa Khamri, Charalampos Antoniades, Mack Thursz, United Kingdom