EFFECTS OF BILIRUBIN ON METABOLIC SYNDROME IN TWO *IN VITRO* MODELS

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Background: Mildly elevated serum bilirubin in Gilbert Syndrome (GS) protects against diabetes, cardiovascular diseases (CVD) and metabolic syndrome (MetS). GS is a benign condition in which unconjugated hyperbilirubinemia occurs in the absence of structural liver disease and without hemolysis. It is caused by a genetic mutation that decreased the hepatic UGT1A1, the enzyme that mediates bilirubin glucuronidation. UGT1A1 variants in GS may confer a strong genetic advantage. Bilirubin, the final endogenous product of oxidative degradation of heme, plays a role in the cellular protection via scavenging peroxyl radicals and it prevents the oxidative modification of lipoproteins and lipids. Strategies to mimic GS may prove to be an attractive intervention in cardiovascular disease and metabolic syndrome.

Aim: The aim is to study the protective role of mild hyperbilirubinemia on oxidative stress, inflammation and ER-stress in two in vitro models of MetS.

Methods: Human kidney tubular epithelial HK-2 and murine heart endothelial H5V cell lines were treated respectively with Advanced Glycated End Products (AGE) and palmitic acid (PA). Cell viability, gene and protein expression, and intracellular ROS were evaluated.

Results: PA treatments on H5V cells cause cell necrosis and mRNA induction of HO-1, IL-6, GRP78, CHOP, E-Selectin, V-CAM, ICAM and iNOS. UCB pre-treatment reverts cell necrosis, reduces CHOP, IL-6 and iNOS mRNA induction and increases HO-1 mRNA expression. CHOP protein induction by PA was also reduced. AGE treatment on HK-2 cells causes significative variation of IL-8, HIF1a, HO-1, GPX and Catalase mRNA expression and increases intracellular ROS. UCB pre-treatment increases the HO-1 and GPX mRNA, and reduces IL-8 and HIF1a mRNA induction and ROS intracellular levels.

Conclusions: UCB plays a role in the modulation of cell viability, intracellular ROS production and mRNA gene expression in the in vitro models of diabetic nephropathy and atherosclerosis studied.

Biography

Annalisa Bianco, after her Bachelor's at Urbino University in Biological Sciences, attended the Master's Degree Course in Functional Genomics at the University of Trieste. She graduated on 20th October 2017 with the final evaluation of 109/110. From 1st November 2017 she enrolls in the PhD School of Molecular Biomedicine at the University of Trieste. She developed her Master's Degree Thesis work at Italian Liver Foundation where she produced the results presented in the present abstract.

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