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BUTYRATE SPECIFICALLY AND DOSE-DEPENDENTLY REGULATES THE EXPRESSION OF THE MONOCARBOXYLATE TRANSPORTER 1 (MCT1) IN RAT COLONOCYTES BY TWO DISTINCT MECHANISMS

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Rationale: Butyrate, a short chain fatty acid (SCFA), regulates several colonic functions. SCFAs are transported into the colonocyte by MCT1 which is coupled with a chaperone protein, CD147. We aim to determine if the butyrate-mediated MCT1 regulation (ESPEN 2007) is specific of butyrate (in comparison with other SCFAs) and dose-dependent, and to understand its mechanisms.
Methods: Rats received for 48 hours an intra-cecal infusion of saline solution containing or not (control) 5 mM acetate, propionate, lactate or butyrate, and 1 mM or 10 mM butyrate (each, n = 5). Cecal colonocytes were isolated. Control rat colonic mucosa were incubated or not (control) with butyrate 50 mM for 1 hour. MCT1 and CD147 expressions were analyzed by RT-PCR, western blot and immunofluorescence. The effect of butyrate (from 0.5 to 10 mM), acetate, propionate and lactate (5 mM) on the promoter activity of *MCT1* gene was analyzed in HT-29 cells by reporter gene assay.
Results: The intra-cecal infusion of butyrate increased rat MCT1 (mRNA and protein) expression by 3.5. In HT-29 cells, butyrate increased the activity of the *MCT1* gene promoter. Acetate, propionate and lactate had no effect. The activity of the *MCT1* gene promoter was dose-dependently increased by butyrate with a maximal effect at 5 mM. In rat colonic mucosa, butyrate induced a strong co-localization of MCT1 and CD147 at the apical plasma membrane, whereas both proteins were expressed at the basolateral membrane in controls.
Conclusion: Butyrate specifically and dose-dependently increases MCT1 expression in the colonocyte, through two mechanisms: the co-localization MCT1-CD147 at the apical plasma membrane (short-term), and an up-regulation of *MCT1* gene transcription (mid-term). This reinforces our hypothesis that MCT1 could constitute a specific marker of the colonocyte exposure to butyrate.

Disclosure of Interest: None declared

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GLUTAMINE TREATMENT DIFFERENTIALLY AFFECTS HEAT SHOCK PROTEIN EXPRESSION IN OXIDANT VS. HEAT STRESS INJURED IEC-18 CELLS

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Rationale: Glutamine (GLN) treatment can protect intestinal epithelial cells (IEC-18) in vitro from heat and oxidant stress via heat shock protein (HSP) enhancement. However, the effects of GLN treatment on specific HSPs during different types of injury have not been compared. Further, the effect of GLN on HSP32 (or HO-1) expression following oxidant injury in the intestinal epithelial cell *in vitro* is unknown. The purpose of our study was to determine the effects of GLN on specific HSP expression in hydrogen peroxide (H2O2) injured vs. heat stressed IEC-18 cells.
Methods: Cells were treated for 15 min with either 0mM (CT) or 10mM GLN, and then subjected to either H2O2 (600uM) injury for 30 min, or a non-lethal heat stress (HS) of 43° for 45 min. Cells recovered for 2.5 hrs at 37°. HSP25 and HO-1 expression was determined by western blot. (N = 3).
Results: GLN treatment increased HO-1 in both models of injury more than 3 fold ($p = 0.001$ vs. H2O2 only, and $p < 0.001$ vs. HS CT). HSP25 however, only increased with GLN treatment in the HS cells ($p < 0.01$ vs. HS CT). H2O2 injured cells demonstrated a decrease in HSP25 with GLN treatment ($p < 0.05$ vs. H2O2 only).
Conclusion: This is the first data showing GLN induces a differential induction of HSP expression based on the type of cellular injury in the intestine. GLN treatment appears to consistently increase HO-1 expression during heat stress and oxidant injury, however HSP25 expression only increased in the HS cells. The mechanism of this differential expression may be due to the unique and diverse regulation of HO-1 expression by multiple transcription factors including heat-shock factor-1, NfKB, nuclear factor-erythroid 2, and AP-1.

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METABOLIC RISK INDUCED BY HORMONAL DOPING AND INSULIN ABUSE IN RECREATIONAL BODYBUILDERS

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Rationale: Hormonal doping in recreational sports is a public-health concern. Metabolic risks associated to different hormone abuses are not fully investigated.
Methods: We recruited 97 male recreational bodybuilders (BB) and 45 male controls (CTR). Hormonal abuses in BB were monitored by anonymous questionnaires. C-reactive protein, HDL cholesterol and cholesteryl ester transfer protein (CETP) levels were assessed in plasma. Activities of enzymes involved in fatty acid metabolism were determined in erythrocyte membranes. To compare effects of individual hormones, data were analyzed by One way ANOVA, with LSD's post hoc analysis.
Results: Forty-three % of recruited BB regularly used prohibited substances, i.e., anabolic androgenic steroids (AAS) (95%), in association with growth hormone (GH) (30%) and/or insulin (INS) (38%). HDL levels were higher in non-doping BB than in CTR (+14%, $P < 0.05$) and in doping BB (+32%, $P < 0.001$). C-reactive protein was higher in INS abusing BB using than in non-doping BB (+44%) and CTR (+50%) ($P = 0.01$). CETP level was lower in INS and/or GH abusing BB compared to all other groups (from −23 to −13%, $P < 0.05$). Δ-9 desaturase activity was higher and elongase activity was lower in INS and/or GH abusing BB compared to all other groups ($P < 0.001$).