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Introduction: Humans are exposed to nanoparticles from a variety of sources through a broad range of exposure ways since nanomaterials are increasingly used in different productive sectors. Titanium dioxide (TiO2) is enclosed in many consumer products including pharmaceuticals, cosmetics, and foods. TiO2 (E171) is daily ingested as mixed nano- and submicron-sized particles since it is approved as a white pigment in Europe in a variety of food products. Noteworthy, the relevant risk assessment has never been satisfactorily concluded and growing alarms for human hazards deriving from TiO2 exposure are incrementally reported.
Objectives: The objective of the present study was to establish conceivable mechanisms by which nano-sized TiO2 particles affect physiological function of the intestinal epithelium layer. The well-established Caco-2 cell line differentiated on permeable supports was used as a predictive model of the intestinal barrier due to its ability to naturally differentiate into polarized cells which resemble the intestinal architecture. The resultant system was adopted to investigate changes triggered by TiO2 nanoparticles in monolayer barrier since intestinal epithelial barrier is crucial for the maintenance of physiological function and the prevention of uncontrolled antigens trafficking.
Results: Exposure to nanoparticles disrupted the tight junctions-permeability barrier with a prompt effect detectable after 4h incubation time and wide effects on barrier integrity at 24h. Transport and ultrastructural localization of TiO2 nanoparticles were determined by ICP-OES, TEM and ESI/EELS analysis, respectively. Nano-sized particles were efficiently internalized and preferentially entrapped by monolayers. Storage of nanoparticles inside the cells affected enterocytes viability and triggered the production of pro-inflammatory cytokines, including TNF-alpha and IL-8.
Conclusion: Taken together these data indicate that nano-sized TiO2 particles exert detrimental effects on the intestinal epithelium layer.

A9
INTERPLAY BETWEEN THE TOXIC ALPHA-GLIADIN PEPTIDE 31-43 AND TYPE 2 TRANSGLUTAMINASE ENZYME IN CELIAC DISEASE

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Introduction: Celiac disease (CD) is a widespread enteropathy triggered by a diet containing cereals with gliadins in genetically predisposed individuals. Alpha-gliadin peptide 31–43 (p31-43) is considered the main responsible of the innate immune response in CD patients and type 2 transglutaminase (TG2) enzyme is involved in CD by enhancing gliadin immunogenicity. Evidence has been reported on a role of TG2 in modulate p31-43 uptake by intestinal cells; indeed, antibodies to TG2 specifically reduced both p31-43 uptake by cells and its biological activity. However, little is known about molecular mechanism underlying p31-43 uptake. We aim to investigate the effect of p31-43 on TG2 expression and activity into a model of skin-derived CD fibroblasts; furthermore we investigate whether cell surfaceTG2 could be directly responsible of p31-43 translocation into intestinal cells.
Methods: We analysed TG2 levels by PCR and western blot analysis and we monitored TG2 activity by a microplate assay using the pentylamin-biotine as substrate in skin-derived CD fibroblasts. To visualize probable complex between cell surface TG2 or membrane proteins and p31-43 we chemical cross-linked of p31-43 on intestinal cell surface proteins and next, pulled-down peptide-proteins complexes using antibodies raised against p31-43.
Results: We found that p31-43 stimulation induced TG2 activity more in skin-derived control fibroblasts than in CD cells. On the contrary, TG2 expression was more markedly induced in celiac cells than in control ones. We also found that that cell surface TG2 was not necessary for p31-43 internalization, even if it had a regulating role in the process.
Conclusions: We demonstrated that p31-43 did not behave as a classical ligand; indeed, membrane composition and organization, instead of a specific receptor protein, may have a major role in p31-43 internalization by cells. The interplay between p31-43 and TG2 has an important role in CD pathogenesis.

A10
CELLULAR AND SYSTEMIC ANALYSIS BASED ON POLYUNSATURATED FATTY ACIDS PROTECTIVE EFFECTS AGAINST INSULIN- RESISTANCE CONDITION

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Introduction: ω3 Poly-unsaturated Fatty Acids (PUFA-ω3) have a protective and therapeutic role to prevent insulin – resistance (IR). In this study, the protective effect was evaluated through: 1) serum parameters related to IR (HOMA index and apelin serum levels); 2) hepatic insulin signaling pathway markers (phosphorylated protein kinase B, p-Ser473-AKT/PKB); 3) endoplasmic reticulum (ER) stress marker (phosphorylated transcription factor p-eIF2α); 4) mitochondrial dynamics marker (Mitofusin 2, Mfn2).
Methods: These parameters were evaluated into 3 Wistar rats groups, so treated for 6 weeks: 1- N rats, treated with a standard diet (10.6% fats J/J); 2- L rats, treated with a high fat diet, rich in lard (40% fats J/J); 3- F rats, treated with a high fat diet rich in fish oil, major PUFA-ω3 source (40% fats J/J). Standard methods were used to analyse glucose and insulin serum levels and to determine HOMA index. ELISA assay was utilized for serum apelin levels. Hepatic p-Ser473-AKT/PKB, p-eIF2α and Mfn 2 levels were determined by western blot.
Results and conclusions: L group exhibited systemic and hepatic IR (as showed by increased HOMA index and p-Ser473-AKT content, respectively) associated with ER stress (as showed by increased p-eIF2α content). At the systemic level, F group showed reduced HOMA index associated with increased apelin serum level compared to L group. Furthermore, we observed increased hepatic insulin sensitivity (as showed by reduced p-Ser473-AKT content) associated to ER stress reduction (reduced p-eIF2α content) in F group compared to L group. A fundamental role seems to be played by Mfn2, that increased in F vs L group, preventing not only mitochondrial integrity, but also eIF2α phosphorylation. In this way, fish oil may have positive effect in the prevention of ER stress and IR onset.

A11
EFFECTS OF SOME NUTRACEUTICALS ON THE TPC1 THYROID CELL LINE

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The majority of thyroid carcinomas come from follicular cells and are defined as differentiated thyroid tumors (DTC) and the two histological subtypes are papillary CT and follicular CT. Curcumin has a wide variety of biological functions, currently, in the literature has considerable attention. The present work defines the role of curcumin on the modulation of gene expression of different cell markers and cell cycle modulation. The study was carried out using CURCUMA NATUREX and adding other nutraceuticals such as piperine and vit. And, in order to define the role of these in the modulation of gene expression of cell and tumor markers.
TPC-1 cells were the cellular model. Initially treated with the different turmeric extracts and examined the expression levels of markers (proliferative, inflammatory, antioxidant, apoptotic). Thereafter TPC-1 cells were treated with MIX of turmeric, piperine and vitamin E to understand its efficacy and biomodulation on thyroid papillary carcinoma. Treatment with the three different curcumin extracts shows

anti-inflammatory, antioxidant and cell cycle influencing properties. The isolated treatment of turmeric and combined with the various nutraceuticals influence the cell cycle regulators (cyclin D1, β-catenin, p21, p53) and apoptosis activators or inhibitors (BAX, pro-caspase3, Bcl-2). The bioavailability of turmeric increases in association with piperine and vitamin E on cell proliferation involving different markers, such as inhibition of: beta-catenin, cyclinD1 and p53. Therefore, a possible candidate for the use of turmeric and its bio-modulators as adjuvant therapy to that currently used in oncology is hypothesised.

A12
POTENTIAL FUNCTIONALITY OF PROTEIN HYDROLYSATES FOR GLYCAEMIA CONTROL

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Introduction: Dietary proteins may contain some bioactive peptides (BAPs) encrypted within their primary structures. BAPs may be delivered in the food during processing and/or in the gastro-intestinal tract during food digestion and can exert some biological effects beyond nutrition such as antimicrobial, anti-thrombotic, antihypertensive, opioid and immunomodulatory effects. BAPs modulating blood glucose response are promising ingredients for functional foods development. They work through inhibition of the enzyme dipeptidyl peptidase IV (DPP-IV) that modulate glucose homeostasis by cleaving GLP-1 and GIP (Lacroix et al.,2016). The aim of this study was to evaluate the potential activity of casein (CH) and soy (SH) protein hydrolysates as well as of CH and SH enriched biscuits (CHB and SHB) on post-prandial glucose response in vitro.
Methods: Control biscuits (ConB) without protein hydrolysates and two types of CH and SH-enriched biscuits providing 4.5% (CHB1 and SHB1) and 13% (CHB2 and SHB2) of each hydrolysate were developed. CH, SH, CHB1, CHB2, SHB1 and SHB2 were subjected to in vitro simulated gastrointestinal digestion and the ability of the digested samples to inhibit DPP-IV activity was assessed. In vitro glycaemic index (GI) of the biscuits was also measured.
Results: Data showed that CH and SH behaved as mixed and competitive inhibitor of DPP-IV with an IC50 of 2.59 mg/ml and 3.56 mg/ml ($p < 0.05$), respectively, when tested alone. No significant difference between digested biscuits for the inhibition of DPP-IV activity was observed. The GI of the biscuits was in the order ConB>CHB1>SHB1>CHB2>SHB2.
Conclusions: This study suggested that CH and SH maybe functional ingredients for glycaemia control through inhibition of DPP-IV activity. A food matrix effect could hide the bioactivity of CH and SH at the doses used in the biscuits during in vitro enzymatic digestion.

A13
PLASMA MICRORNA EXPRESSION PROFILES ARE ASSOCIATED WITH EARLY CHILDHOOD OBESITY: RESULTS OF THE I.FAMILY STUDY

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Introduction: Nearly ten years ago, the WHO reported the increasing prevalence of obesity worldwide as a challenge for public health due the associated adverse consequences. Omic studies demonstrated that microRNA (miRNA) changes in tissues correlate with several diseases, including obesity. Other studies suggested a remarkable stability of miRNA also in blood, emphasing their potential as theranostic agents. This study investigated the profiles of circulating miRNAs in plasma samples of normal weight ($n = 159$) and overweight/obese ($n = 149$) children participating to the I.Family study, an EC funded study finalized to investigate the etiology of overweight, obesity and related disorders in children of eight European countries (www.ifamilystudy.eu). Differences in miRNA expression patterns with respect to anthropometric and biochemical variables were explored.
Results: A high degree of variability in levels of circulating miRNAs was recognised among children from different countries. Several miRNAs differentially expressed in overweight/low grade obesity children were characterized (miR-551a and miR-501-5p up-regulated; miR-10b-5p, miR-191-3p, miR-215-5p and miR-874-3p down-regulated). ROC curves were constructed for confirmed miRNAs. Single miRNAs exhibited low AUC values with the highest values for miR-874-3p and miR-501-5p which in combination provided an interesting value (AUC = 0.755). Pearson's analysis confirmed that miR-10b-5p, miR-215-5p, miR-501-5p, miR-551a, and miR-874-3p correlated with BMI z-score. Molecular interactions of obesity-associated miRNAs were also predicted. Computational analysis indicated that miRNAs act as key regulators of metabolism, playing pivotal roles in early stages of obesity by affecting multiple candidate genes.
Conclusions: Although causal pathways cannot be definitely inferred it is conceivable that circulating miRNAs may be new biomarkers of early childhood obesity.

A14
MEDITERRANEAN, BUT NOT LACTO-OVO-VEGETARIAN, DIET POSITIVELY INFLUENCE CIRCULATING PROGENITOR CELLS FOR CARDIOVASCULAR PREVENTION: THE CARDIVEG STUDY

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Introduction: Recent studies have suggested that diet may modulate the number of progenitor cells. Our aim was to evaluate the possible association between dietary habits and progenitor cells using data obtained from the CARDIVEG study, a randomized crossover trial that compared the effects of a lacto-ovo-vegetarian (VD) and a Mediterranean diet (MD).
Methods: Eighty clinically healthy subjects with a low-to-moderate cardiovascular risk profile (61 F; 19 M; mean age: 50.7 years) were randomly assigned to isocaloric VD and MD diets lasting three months each, and then crossed. Endothelial progenitor cells (EPCs), circulating progenitor cells (CPCs), and circulating endothelial cells (CECs), were obtained from each participant at the beginning and at the end of each intervention phase.
Results: The 2 diets showed no effects on EPCs and CECs but opposite effects on CPCs. In fact, VD determined significant ($p < 0.05$) and negative changes on CPCs, with an average geometric variation of -130 cells/106 events for CD34+, -80 cells/106 events for CD133+, and -84 cells/106 events for CD34+/CD133+ while MD determined significant ($p < 0.05$) and positive changes for CD34+ levels, with a geometric mean increase of +54 cells/106 events. No significant correlations were observed between changes in progenitor cells and changes in inflammatory parameters during the VD phase. On the other hand, during the MD phase negative correlations between changes of CD34+ and interleukin-6 ($R = -0.324$; $p = 0.004$) as well as interleukin-8 ($R = -0.228$; $p = 0.04$) and monocyte chemotactic protein-1 (MCP-1) ($R = -0.277$; $p = 0.01$) were observed. These correlations remained significant after adjustment for confounding factors only for CD34+ and interleukin-6 ($ß = -0.282$; $p = 0.018$) and MCP-1 ($ß = -0.254$; $p = 0.031$).
Conclusions: MD, but not VD, reported a significant and positive effect on CPCs in a group of subjects at low-to-moderate cardiovascular risk, probably acting through the modulation of inflammatory parameters.