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ABSTRACT BOOK

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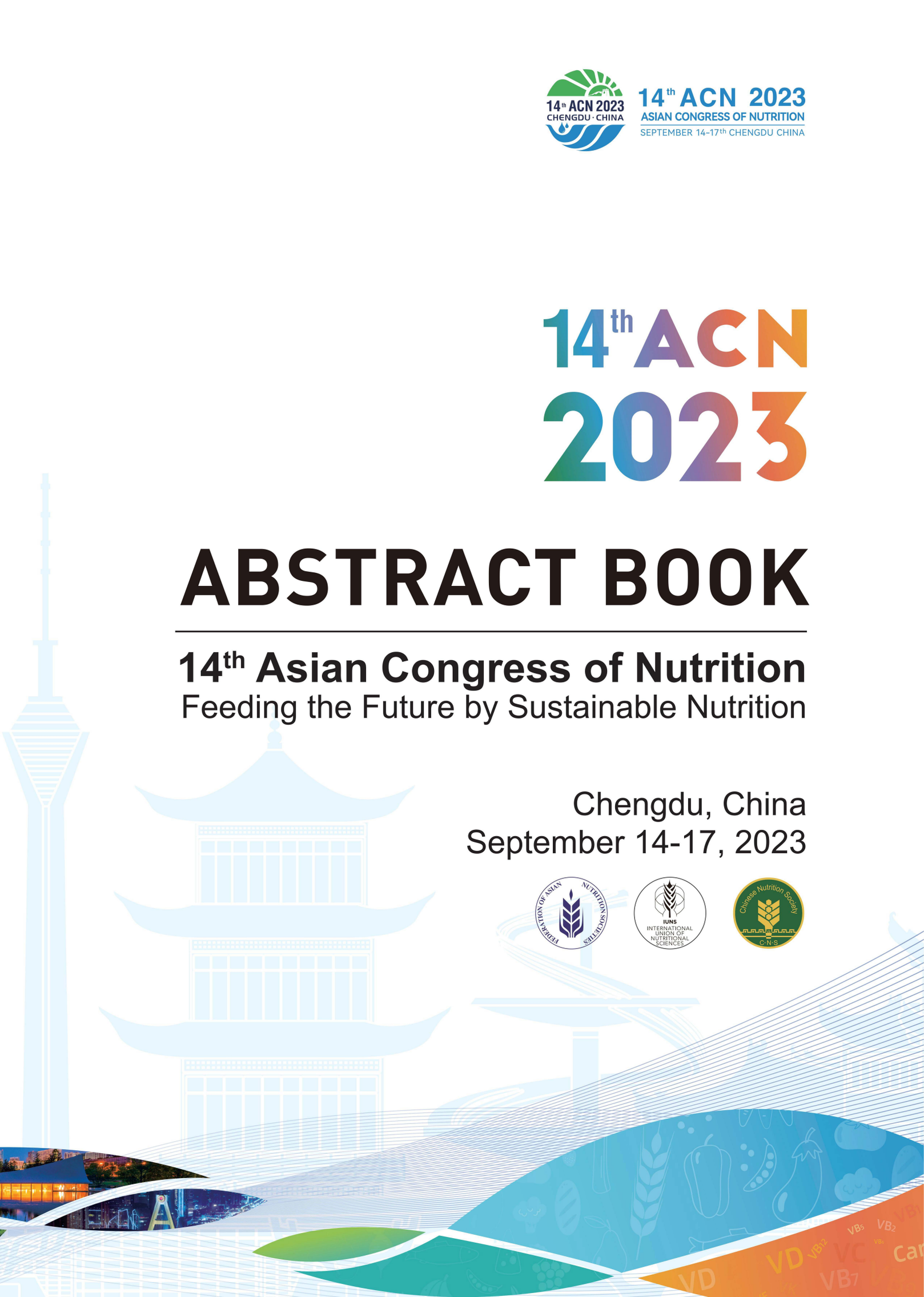

Category: Basic Nutrition& Research

High-sucrose aggravates arthritis via TLR4 pathway in surgically induced osteoarthritis model

Hyun-Jin Jang,Fang Feng,Thi My Tien Truong,Inhae Kang*
Jeju National University

Background and objectives: Toll-like receptor 4 (TLR4) plays a crucial role in initiating inflammation in response to pathogens or endogenous molecules through the activation of nuclear factor-κB (NF-κB). In previous study, we have demonstrated that excessive sucrose consumption contributed to osteoarthritis (OA) pathogenesis with hepatic inflammation. However, little is known regarding the role of high sucrose (HS)-mediated inflammatory responses on OA pathogenesis. Thus, we investigated effect of HS using destabilized medial meniscus (DMM) mice model according to TLR4 expression.

Methods: Eight-week-old male C57BL/6J mice either wild-type (WT) or TLR4 knock-out (TLR4 KO), were subjected to two dietary conditions: standard chow or HS diets, containing 66% sucrose for an eight weeks. The pathogenesis of knee OA, metabolic parameters, inflammation levels in the liver and intestine morphology were investigated.

Results: HS diet resulted in slightly increased the severity of OA, as indicated by the Osteoarthritis Research Society International (OARSI) score and synovitis following DMM surgery, but no differences found in body or metabolic organ weight. Interestingly, TLR4 KO markedly reduced synovitis in HS-fed group. HS supplementation significantly induced hepatic lipid accumulation with pro-inflammatory gene expressions such as Tumor necrosis factor-α and Interleukin-1β, whereas these changes were restored in HS fed TLR4 KO mice. Moreover, HS-mediated increased villus length of small intestine and crypts depth of large intestine significantly shorten the crypts depth of both small and large intestine.

Conclusions: These findings suggested that excessive sucrose intake deteriorates OA, hepatic stress and intestine morphological changes via TLR4-mediated immunomodulation.

Key words Osteoarthritis, High sucrose, TLR4, Hepatic Inflammation, Intestine morphology

Category: Basic Nutrition& Research

p-Coumaric acid-enriched peanut sprout extract suppresses liver inflammation and fibrosis in high fat/high sucrose diet-fed aging mice

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Background and objectives: Aging is a ubiquitous biological process that induces diseases and mortality in response to various stressors. It has been reported high fat/high sucrose (HFHS) diet contributes to metabolic inflammation in the liver during aging. Previously we demonstrated the beneficial effect of *p*-Coumaric acid (PCA) enriched in peanut sprouts extract (PSE) in attenuating hepatic fibrosis and inflammation in HFHS-fed young C57BL/6 mice. However, the impact of PCA and/or PSE on aging and senescence-associated liver pathophysiology have not been well established. Therefore, we aimed to investigate whether PSE and PCA could reduce the susceptibility of hepatic inflammation and fibrosis response to HFHS in aging mice.

Methods: C57BL/6 male old (15 months) mice were fed with low-fat diets (11% calories fat, LF) or high-fat diets (60% calories fat, 0.2% cholesterol) with 20% sucrose drink (HFHS). A subgroup of HFHS-old mice received PSE (10 mg/kg BW, HFHS+PSE) or PCA (10 mg/kg BW, HFHS+PCA) by oral gavage for 11 weeks. C57BL/6 male young (5 weeks) mice were used as a negative control.

Results: While consuming an HFHS increased body weight gain, adipose tissue mass, hyperglycemia, hyperinsulinemia, and hypercholesterolemia compared to the LF diet, these effects were mitigated by PSE and PCA treatment. Additionally, PSE and PCA improved the hepatic triglyceride, total cholesterol, lipid peroxidation, and hepatic lipogenesis against HFHS challenged. Histological analysis revealed reductions in collagen accumulation induced by HFHS with the treatment of both PSE and PCA, indicating their potential to decrease fibrosis. Moreover, PSE and PCA significantly diminished gene expression signatures of inflammation and fibrosis, suggesting their beneficial effects on mitigating these processes caused by HFHS consumption.

Conclusions: Our study suggested the potential role of PSE and PCA in improving HFHS-mediated hepatic inflammation and fibrosis response in aging mice.

Key words Liver inflammation and fibrosis, Peanut sprouts, p-Coumaric acid, High fat and high sucrose, Aging

Category: Basic Nutrition& Research

Evaluation of various cooking methods on the Glycemic Response of Jasmine White Rice

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Background and objectives: Jasmine White Rice is a commonly consumed rice in Asia. The GI for white rice is always at the medium to high range by cooking in the conventional way which is using a rice cooker. There has been no research done to assess and compare the effects of cooking rice in other methods to reduce the glycemic response. In this study, we aimed to evaluate the effect of various cooking methods compared to the conventional way of cooking rice on the glycemic response. **Methods:** Ten healthy participants participated in the study. They were served 60g of raw Jasmine White Rice prepared by six different cooking methods. The participants were reminded via text message to consume food that were high in carbohydrates and to fast overnight for 10-14 hours on the evening prior to the test sessions. **Results:** There were no significant differences between the five cooking methods and the conventional method. However, there was significant reduction in glycemic response between overnight rice and porridge. There was also significant difference between rice cooked and drained in 1:7 water and porridge, and between retorted rice and porridge. **Conclusions:** Compared to porridge, storing the cooked rice in a chiller and reheating, cooking and draining in 1:7 water, and retort cooking the rice can improve glycemic response. Other methods can result in different glycemic responses but are found to not be statistically significant.

Key words Glycemic response, white rice

Category: Basic Nutrition& Research

Peyssonnelia caulifera Okamura extract improves the high fat diet-induced intestinal barrier dysfunction and gut microbiota imbalance

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Background and objectives: A high-fat diet can increase the permeability of the gastrointestinal tract, which is known as leaky gut. Recent studies have shown that defects in the gut barrier are associated with a variety of diseases, including metabolic disorders such as obesity, diabetes, and arthritis. *Peyssonnelia caulifera Okamura* (PC), a red seaweed native to Jeju Island in South Korea, which has been subject to limited research regarding its effects on obesity and/or barrier dysfunction. Thus, the aim of our study is to identify the impact of PC extract (PCE) on obesity-mediated impermeable gut barrier.

Methods: 6-weeks C57BL/6 male mice were randomly divided into three groups: (1) low-fat diet (LF) with 11% of calories from fat; (2) high-fat diet (HF) with 60% of calories from fat; (3) HF+PCE. HF+PCE group were orally administered 10mg/kg BW of PCE via gavage for 8 weeks *ad libitum*.

Results: Compared to HF-fed group, PCE for 8 weeks significantly reduced inflammatory gene expressions such as monocyte chemoattractant protein-1 (Mcp1) and tumor necrosis factor α (Tnfα), in adipose and liver tissue without affecting body weight and fat/liver mass. In addition, PCE treatment restored the expression of tight junction protein, such as occluden, claudin-1 and claudin-4 in the colon. Interestingly, mice fed with PCE showed an increase in autochthonous protective bacteria, including *Lachnospiraceae* and *Ruminococcaceae*. Additionally, the PCE group of mice exhibited an improved Firmicutes/Bacteroidetes ratio, which contributed to maintaining normal intestinal homeostasis.

Conclusions: Our result showed that PCE administration restored expressions of inflammatory gene and tight junction protein with prevent gut microbiota imbalance, against long-term consumption of HF diet.

Key words Peyssonnelia caulifera Okamura extract; leaky gut, intestinal permeability, Tight junction; High fat diet.

Category: Basic Nutrition& Research

Peanut sprout extracts mitigate dexamethasone-induced skeletal muscle atrophy in mice on a high-fat/high-sucrose diet

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Background and objectives: Sarcopenia and muscle atrophy, prevalent conditions associated with aging and various factors, result in the decline of skeletal muscle mass and function, posing significant health risks and impairing cellular energy production. While our previous studies have shown that peanut sprout extract (PSE) effectively reduced lipid accumulation, and mitigated high-fat diet-induced obesity, its effects on myosteatosis and sarcopenia have not yet been investigated.

Methods: To investigate the effect of PSE on muscle atrophy and myosteatosis, C57BL/6 male mice were divided into four groups: (i) Control, (ii) dexamethasone (Dex), (iii) Dex+high fat/high sucrose (HFHS), and (iv) Dex+HFHS+PSE. The mice were orally administered PSE (10 mg/kg BW) along with either low-fat diet (LF, 11 % kcal fat) or HFHS (60 % kcal fat with 20 % sucrose in D3) for a duration of 10 weeks. In the last 6 days, dexamethasone (Dex, 10 mg/kg BW) was treated to exacerbate the muscle atrophy.

Results: The results showed that PSE treatment reduced triglyceride levels of skeletal muscle, preserved muscle fiber size compared with Dex+HFHS. Interestingly, Dex and HFHS mediated impaired grip strength and muscular strength, biomarkers for functional muscle atrophy, were significantly ameliorated by PSE administration. Additionally, PSE treatment decreased the expression of muscle atrophy markers and improved the protein expression level of mitochondrial transcription factor A (TFAM) and oxidative phosphorylation (OXPHOS) in skeletal muscles. The aggravated proinflammatory responses such as tumor necrosis factor-α (TNFα) gene expression and nuclear factor-κB (NFκB) protein expression were inhibited by PSE in skeletal muscles. We also confirmed the protective effect of PSE against muscular atrophy *in vitro* using C2C12 cells treated with Dex.

Conclusions: These findings indicated that PSE effectively mitigated skeletal muscle atrophy induced by Dex and HFHS *in vivo* and *in vitro* inhibition of proinflammatory responses and amelioration of mitochondrial function.

Key words Skeletal muscle atrophy, Sarcopenia, Peanut sprout, High fat and high sucrose, Dexamethasone

Category: Basic Nutrition& Research

HUMAN MILK OLIGOSACCHARIDE SUPPLEMENTATION DURING AND AFTER ANTIBIOTIC TREATMENT AFFECTS THE MICROBIOME AND THE INFLAMMATORY ENVIRONMENT OF THE GUT

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Background and objectives:

The objective of this study was to investigate the effect of human milk oligosaccharide (HMO) supplementation during and after antibiotic treatment on the microbiome, short chain fatty acid (SCFA) concentrations and the cytokine profile in the gut.

Methods:

Thirty-two BALB/C mice were divided into four groups receiving either no treatment, ampicillin, or ampicillin+HMO1 or HMO2 for seven days. During the subsequent two weeks of recovery the mice either received no supplement or continued to receive HMOs. Fecal samples were collected for 16S sequencing at baseline, on day 7, 14 and 21 (upon euthanasia). Ileum tissue and cecum content were collected for cytokine and (SCFA) concentrations, respectively.

Results:

16S sequencing of fecal samples revealed an almost complete elimination of the microbiota after seven days of ampicillin treatment with a gradual recovery of bacteria over the next two weeks. Bray-Curtis dissimilarity test showed a continued distinction between the HMO supplemented groups and both the control and ampicillin treated groups on day 14 and 21.

Analysis of cecum content showed an increase in the concentration of acetate when animals where supplemented with ampicillin+HMO1 compared to ampicillin alone. Cytokine measurements on ileum homogenates showed a decrease in pro-inflammatory cytokines (e.g. IFNγ, IL-17 and MCP1) when animals received HMOs during and after antibiotic treatment compared to control and ampicillin alone.

Although the overall results were similar between the two HMO supplemented groups, there were distinct differences in both the microbiome composition and cytokine profile of the gut following the supplementation.

Conclusion:

HMO supplementation during and after ampicillin treatment affects the microbiome composition, and the pro- and anti-inflammatory cytokine environment in the gut. The changes were similar between the two HMO groups, but with slight differences indicating different mechanism of action for the HMOs.

Key words Human milk oligosaccharides, antibiotic recovery, microbiome, cytokines

Category: Basic Nutrition& Research

Diets enriched in sugar, refined or whole grain differentially influence plasma and liver cholesterol and triglyceride concentrations with concurrent changes in gut microbiota composition in ApoE-/- mice

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Aims: We aimed to compare the effects of diets enriched in sugar, refined grain (RG) or whole grain (WG) on plasma and liver total cholesterol (TC) and triglyceride (TG) concentrations, liver biomarkers of oxidative stress, and gut microbiota composition in $ApoE^{-/-}$ mice.

Methods: Forty-four male $ApoE^{-/-}$ mice aged 8wk old were randomly fed an isocaloric WG, RG or sugar-enriched diet for 12wk. Diets were matched for similar macronutrient composition but differed in types of carbohydrates. Fecal samples were collected from week 8 to 12 and liver tissues were collected following euthanization at week 12. Concentrations of plasma and liver TC and TG, liver oxidative stress biomarkers, including superoxide dismutase (SOD) and malondialdehyde (MDA), and gut microbiota composition were measured using standard methods.

Results: Sugar-enriched diet resulted in higher plasma and liver TC concentrations than WG-enriched diet and higher plasma TG concentrations compared to both RG- and WG-enriched diets (all $P<0.05$). Liver TG and MDA concentrations and SOD activity were not significantly different among diet groups. In comparison to WG-enriched diet, sugar-enriched diet resulted in lower relative abundance of Alistipes and Bacteroides, which was inversely associated with plasma or liver TC concentrations, and higher relative abundance of Lactobacillus, which was positively associated with plasma and liver TC concentrations and inversely associated with the liver SOD activity (all $P<0.05$). The relative abundance of Colidextribacter and Lachnoclostridium were lower in WG- than RG-enriched diet, and they were inversely associated with liver SOD activity and MDA content (all $P<0.05$).

Conclusions: Sugar-enriched diet had unfavorable effects on concentrations of plasma and liver TC and liver TG compared to WG-enriched diet, with concurrent changes in the relative abundance of gut microbiota. These results suggested that changes in gut microbiota composition could partially contribute to alterations in TC and TG profiles induced by different types of carbohydrates.

Key words sugar; refined grain; whole grain; total cholesterol; triglyceride; oxidative stress; gut microbiota

Category: Basic Nutrition& Research

Establishment of Asian Food Composition Database - Philippines

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The importance of food composition tables and databases is essential in understanding human nutrition and recommending appropriate dietary interventions, analyzing nutrient intakes, formulating dietary guidelines for a specific population, and crafting nutrition, food security, health, and agricultural policies.

This three-year project is an initiative to preserve the Asian food culture and biodiversity and improve the Asian Food and Agriculture Cooperation Initiative (AFACI) member countries' capacity to set up a Food Composition Database (FCDB). The project also aims to develop an FCDB of the Philippines' primary production and export of food items which will be linked and integrated with the databases created by AFACI member countries to build the Asian Food Composition Database. To establish this FCDB, a steering committee was established to recommend food items and review the project's accomplishments. The project team collected samples from 10 different commercial and distribution sources in other regions and submitted them for analysis to selected ISO-Certified Laboratories.

The project team members' capacity development highlights the project's first year. This was accomplished by selecting the 100 food items, which will be part of the database, procurements, and documentation of the food sources and analyzing the mandatory nutrients of the project's 20 out of 100 food item requirements. This project is expected to improve the capacity of AFACI member countries in setting up an FCDB by providing the essential infrastructure for food and nutrition research and dietary practice and promoting regional advocacy and international cooperation.

Key words food composition database, AFACI, Philippines

Category: Basic Nutrition& Research

Effects of eel essence on fat oxidation and anti-fatigue property in diet-induced obesity mice model

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Eel meat contains high-quality protein and various essential amino acids, fatty acids (EPA/DHA), special nutrients and other chemical components. The more of amino acid composed content are glutamine, branched-chain amino acids, alanine, lysine and arginine. The purpose of this experiment is to evaluated the Nutraceutical functions of eel essence. In this experiment, 4 groups of C57BL/6J mice were respectively fed diets containing either normal fat (16 kcal%, AC), high fat (54 kcal%, HC), AC group or HC group were fed by oral gavage the eel essence (767 mg/kg body weight, AEE and HEE), for 8 weeks, based on a 2 × 2 factorial design, to test the significance of the effect of fat quantity, the effect of eel l essence and their interaction.

Compared to the AC group, the HC group and the HEE group had significantly more body weight, more fat composition percentage, higher feed efficiency and higher energy efficiency. The HC group was a diet-induced obesity animal model. Improvement of some Metabolic syndrome risk factors could be observed in the groups fed eel essence, including higher serum HDL concentration and lower serum LDL concentration. But abdominal fat accumulation was not improved in HEE group. The higher strength of Whole-limbs grip measurement and longer time of exhaustion of swimming was observed in eel essence groups.

The gene expression of hepatic acyl-CoA thioesterase 1 (ACOT1) was significantly decreased in the HEE group. ACOT1 regulates fasting hepatic fatty acid metabolism by balancing oxidative flux and capacity. It is speculated that the excessive fatty acids oxidation was reduced by the eel essence. Hence, it was concluded that eel essence has the potential to regulate fat oxidation and anti-fatigue.

Key words Eel, Diet-induced-obesity, LDL, Anti-fatigue, Acyl-CoA thioesterase 1

Category: Basic Nutrition& Research

A formulated beverage containing Mulberry Leaf extract and Tryptophan taken with evening-meal results in improved sleep and next-day cognitive function in adults: a double-blind placebo-controlled cross-over RCT

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Background and objectives: Poor sleep is associated with cognitive impairment across the lifespan. Diet and nocturnal metabolism are modifiable factors that could potentially improve sleep quality. This study evaluated the effectiveness of a formulated beverage containing Mulberry Leaf extract (750mg) and Tryptophan (120mg) taken with evening-meal to improve sleep and next-day mood and cognitive performance in healthy adult poor-sleepers.

Methods: A double-blind, 2-arm, cross-over RCT was conducted (ClinicalTrials.gov: NCT05372900). Adults (age 25-50) self-identifying as poor sleepers were recruited. Poor sleep was confirmed at screening by the Pittsburg Sleep Quality Index (score >5) and actigraphy (<85% mean sleep efficiency) over 14-days. All participants received standardized evening meals (glycemic load of 55 ±10%) and test beverages to be consumed concurrently ~4-hours before bed. Intervention phases lasted 14-days punctuated with a 28-42day washout period. Primary outcomes were: Sleep Efficiency (SE) and Sleep Onset Latency (SOL) measured by actigraphy. Secondary outcomes included: mood, sleep quality and cognitive performance measures at breakfast, lunch and dinner time (~1-1.5hours, 6 and 12-hours post-morning waking).

Results: Intention-to-treat analysis were performed using linear mixed model adjusting for baseline and treatment order. Consumption of the treatment compared to control resulted in significant improvement of SOL (actigraphy=-3.48 mins, p=.026; self- report=-16.7mins, p=.031), albeit no significant effect on SE (p=.230). The following morning participants reported feeling significantly less sleepy (p=.041) and more aroused (p=.026). Cognitive performance was improved on several tests at breakfast, lunch and dinner timepoints: For psychomotor vigilance, reaction time (p=.598, p=.051, p= .024) and lapses (p=.027, p=.005, p=.004) were significantly reduced. Participants also produced fewer false alarms on the 2-Back task (p=.014, p=.045, p=.030). Additionally, participants reported improved perceived performance over the day (p=.014, p=.063, p=.010).

Conclusions: These findings may represent a new simple strategy to support sleep, mood and cognitive benefits in the general adult population.

Key words mulberry leaf extract, tryptophan, sleep, cognition

Category: Basic Nutrition& Research

印度农村少女血清铁调素水平与贫血的关系

Association of serum hepcidin levels with anemia among rural adolescent girls in India

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Introduction: In India, anemia affects around 40% adolescent girls (CNNS, 2018) and is associated with adverse functional consequences on physical and cognitive health. Hepcidin is the iron-regulatory hormone and an early marker of iron deficiency anaemia. The present study was undertaken to assess the association of serum hepcidin with anaemia and other factors among rural adolescent girls in India.

Methodology: A cluster randomized control trial study was conducted in Ballabgarh block of Faridabad District, Haryana, India. Baseline data of a total of 198 non-anaemic and 202 anaemic adolescent girls (12–19 years) was analysed for haemoglobin and serum level of hepcidin, ferritin, folate acid, soluble transferrin receptor, vitamin B 12 and CRP. Iron deficiency was characterized as ferritin deficiency plus sufficient folate amongst participants with CRP ≤ 5 mg/l in addition to individuals with elevated sTfR and sTfR–ferritin index in participants with CRP >5 mg/l. Folate deficiency was characterised as sufficient ferritin along withdeficiency of folate, irrespective of CRP concentrations.

Results: Serum hepcidin was found to negatively correlated with hemoglobin (r= -0.128, p=0.026), folate (r= -0.207, p<0.001), vitamin B 12 (r=-0.1151, p=0.049) and positively correlated with Soluble transferrin receptor (mg/L) (r=0.167, p=0.010). Anaemic participants had significantly higher hepcidin levels (β, 31.16; p= 0.047). Hepcidin levels were significantly higher in girls with folate deficiency (β, 0.0003; p= 0.009) and lower in girls with inflammation (β, -0.0002; p= 0.043).

Conclusion: Serum hepcidin is significantly associated with anemia, folic acid deficiency and inflammation but not with iron deficiency. The utility of serum hepcidin as a marker for diagnosis of anemia and iron deficiency needs further research.

Key words Hepcidin, Anaemia, Iron, Folate

Category: Basic Nutrition& Research

Effect of canola oil or soybean oil on the pathological conditions of spontaneously hypertensive rats stroke-prone (SHRSP)

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Background and Objections

Canola oil (Can) and several edible oils reduce the lifespan in stroke-prone spontaneously hypertensive rats (SHRSP) compared to soybean oil (Soy). However, the cause or mechanism of this abnormal action of Can is unknown. In the present study, biological and physiological parameters were measured in SHRSP fed a Can or Soy diet to determine the mechanism of Can-induced reduction in survival.

Methods

Male or female SHRSP rats were fed a test diet from 4 or 5 weeks of age. The test diets consisted of a conventional diet or AIN-93G mixed 9:1 with Can or Soy, without Soy mixed with 7% oil. After a fixed period of consumption of the test diets, blood and tissue samples were harvested, and biological parameters were measured using GC, LC/MS/MS, ELIZA, RT-PCR, and histological analysis.

Results

During the feeding period, body weight, and food intake did not differ between the two dietary groups. In male SHRSP, systolic blood pressure was higher on the Can diet than on the Soy diet. Life expectancy on the Can diet was shorter than on the Soy diet for both sexes. Serum and liver lipid levels reflected those of the test diet, but phytosterol levels were significantly higher in the Can group. The Can diet also influenced serum steroid hormone levels, decreasing testosterone, increasing aldosterone, and altering the genes involved. Histological analysis revealed that the Can diet promotes the pathogenesis of renal dysfunction in SHRSP.

Conclusion

Feeding SHRSP on a Can diet causes an increase in systemic blood pressure, phytosterol accumulation in tissues, and changes in steroid hormone levels. These biological changes are thought to promote renal dysfunction, increased blood pressure, and fatal strokes associated with a shortened life span.

Key words canola oil, soybean oil, SHRSP, lifespan, steroid

Category: Basic Nutrition& Research

Molecular mechanism of intestinal alpha-glycerophosphocholine metabolism and TMAO production

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Backgrounds and objectives: Choline is an important nutrient for phospholipids and acetylcholine synthesis. Alpha-glycerophosphocholine (GPC) has been expected for the prevention of brain disorders such as Alzheimer's disease. However, recent studies showed that high intake of choline-containing compounds can be metabolized to trimethylamine (TMA) by intestinal microflora and subsequently converted to trimethylamine N-oxide (TMAO) in the liver, which is tightly associated with atherosclerosis progression. In this study, we examined the TMAO production by GPC supplementation and explored the mechanism of the absorption and metabolism of GPC in the digestive tract in vivo.

Methods: Male 7 weeks old ICR mice were orally administered choline (500mg/kg) and an equimolar dose of GPC to examine blood TMAO level. Next, this study used human intestinal epithelial cell (Caco-2) model with transwell system Caco-2 cells to examine GPC permeability and metabolism in the digestive tract. We focused on an enzyme GDE5 which can convert GPC to choline and created intestinal epithelial cell-specific GDE5 knockout mice (GDE5KO mice). GDE5KO mice were subjected to oral administration of GPC to clarify the key roles of GDE5 in GPC absorption and metabolism.

Results: GPC supplementation showed higher blood TMAO levels than free choline. Exogenously added GPC was hydrolyzed to choline in the apical medium from Caco-2 cells. GDE5 deletion in the intestinal epithelial cells alleviates GPC-induced TMAO boost in blood in vivo.

Conclusion: GPC is possibly converted to choline in the absence of gut microbiota. Intestine-specific GDE5 KO mice decrease TMAO production, suggesting the involvement of the intracellular enzyme GDE5 in GPC degradation and choline/TMA synthesis in the digestive tract. New food pairing to inhibit intestinal GPC degradation would be a promising strategy not only to enhance GPC absorption which is key for the prevention of brain diseases but also to decrease a risk related to TMAO production.

Key words GPC, Glycerophosphocholine, TMAO, choline, GDE5

Category: Basic Nutrition& Research

Energy cost of selected physical activities among community-dwelling older Filipinos in Taguig City, Philippines

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Background and objectives: Aside from a healthy diet, regular physical activity is essential for healthy aging. However, more older adults tend to be physically inactive. Current measures of energy cost of physical activity are based on the adult populations. Considering the different physiologic changes on older adults, this study aimed to measure and determine the energy cost of selected physical activities to have a better understanding of their health as well as their capabilities to perform physical activities.

Methods: This is a cross-sectional study among 16 Filipinos, 60-79 years old, residing in Taguig City. The study used the Global Physical activity Questionnaire (GPAQ) to determine the level of physical activity among the participants. A Dual X-Ray Absorptiometry (DXA) machine was used to measure the body composition while the indirect calorimeter (COSMED Fitmate) was utilized in measuring the resting metabolic rate (RMR) of the participants. The energy cost of the three exercise routines including treadmill walking, self-paced walking, and exercise routine based on DOST-FNRI developed manual were measured using a portable indirect calorimeter (COSMED K5). Results were presented as percentage and average.

Results: Results revealed that 29.4% of the participants are not meeting the recommended physical activity level based on the GPAQ score. Meanwhile, 21.0% have low muscle mass based on body composition. The average RMR of the participants was 1228 + 268.7. The average METs for walking on treadmill at different speeds ranges from 2.3-2.5; 2.1-3.9 METs for self-faced walking and 1.5-2.2 METs for the exercise routine based on DOST-FNRI developed manual.

Conclusion: The measured METs of the different activities performed using an indirect calorimeter were presented in this study. The results may serve as basis in the development of a more appropriate guideline and interventions for physical activity of Older Filipinos.

Key words energy costs, older adults, indirect calorimetry, Filipinos

Category: Basic Nutrition& Research

Evaluation of Prebiotic Activity Score of Tapioca Resistant Maltodextrin

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Background and Objectives: Tapioca resistant maltodextrin (TRM) is a novel non-viscous, soluble resistant starch with potential health benefits. This study seeks to evaluate the TRM's prebiotic activity score (PAS) in comparison to commercial prebiotics including inulin, fructooligosaccharides (FOS), and konjac glucomannan hydrolysate (KGMH).

Methods: The PAS measures prebiotic efficacy based on the ability to promote probiotic growth and inhibit pathogen growth. Probiotic strains (*Lactobacillus salivarius* B37, *L. acidophilus* LA5, *L. paracasei* L45, *L. rhamnosus* L34, and *L. paracasei* TISIR 2593) and the pathogen *Escherichia coli* ATCC 25922 were inoculated at 1% (v/v) into their respective culture media: Tryptic Soy Broth (TSB) for probiotics and de Man, Rogosa and Sharpe (MRS) broth for enteric culture. Media were supplemented with 1% (w/v) of either inulin, FOS, KGMH, TRM, or glucose. Cultures were incubated at 37 °C for 24 hours. Bacterial cell counts were determined pre- and post-incubation using the pour plate method and PAS calculations.

Results: Among tested strains, *L. salivarius* B37 exhibited the highest PAS with KGMH (0.226), followed by TRM (0.005), while inulin and FOS displayed negative results. In the growth of *L. acidophilus* LA5, *L. paracasei* L45, and *L. rhamnosus* L34, TRM (with PAS values of 0.435, 0.224, and 0.238, respectively) and KGMH (with PAS values of 0.323, 0.656, and 0.121, respectively) demonstrated superior PAS compared to inulin. For *L. paracasei* TISIR 2593, TRM (0.376) and inulin (0.216) presented positive PAS values, whereas FOS and KGMH presented negative PAS values. Notably, FOS displayed negative PAS values for all probiotic strains, while TRM showed positive results across all probiotics.

Conclusions: The findings indicated that TRM exhibits the highest PAS for *L. acidophilus* LA5, *L. paracasei* TISIR 2593, and *L. rhamnosus* L34 without negative effects on any probiotics. These results highlight the potential health benefit of TRM.

Key words Tapioca resistant maltodextrin, Prebiotic activity score, Probiotic, Dietary fiber

Category: Basic Nutrition& Research

Supplementation with N3 milk shows bifidogenic effect and improves health-linked microbial-metabolites in plasma: A randomized, double-blind, controlled trial

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Background and objectives

Supplementation with galacto-oligosaccharides (GOS) has been previously linked to several health benefits, predominantly via gut microbiome modulation. N3 milk is transformed from standard milk by one-step in situ trans-galactosylation, where 90% of lactose is converted to a GOS blend and small amounts of glucose and galactose. In a clinical study, we investigated the hypothesis that N3 milk modulates gut microbiome and a range of health-linked biomarkers.

Methods

A randomized, double blinded, controlled clinical trial in n=26 healthy volunteers using crossover design (2 weeks intervention periods and 2 weeks washout period). Participants consumed once daily 33 g of N3 milk powder dissolved in approximately 200 ml of liquid during the intervention period and the same amount of lactose-free skimmed milk during the control period. Stool and overnight fasting blood samples were collected at the start and the end of both intervention periods. Gut microbiome was assessed using shotgun metagenomics. Plasma metabolites were analyzed with both targeted and untargeted metabolomics methods.

Results

Two weeks of supplementation with N3 milk led to highly significant increase in proportion of gut bifidobacteria, compared to lactose-free milk ($p<0.0001$). Plasma acetate ($p<0.025$), caprylic acid ($p<0.05$), ketone bodies ($p<0.04$), beta alanine ($p<0.01$) and vitamin B3 ($p<0.025$) also increased. Untargeted plasma metabolomics revealed a shift in amino acid metabolism with N3 milk, manifesting as an increase in 3-indole propionate ($p=0.01$), accompanied by a decrease in two uremic toxins, p-cresol sulphate ($p=0.02$), and indoxyl-sulphate ($p=0.04$).

Conclusions

N3 milk increased the relative amount of bifidobacteria present in the gut, along with microbiome-mediated plasma metabolites linked to immune and metabolic health benefits.

Key words Bifidobacteria, milk, galacto-oligosaccharides, acetate, 3-indole propionate

Category: Basic Nutrition& Research

Dietary calcium intake controls intestinal development via 1,25(OH)2D3-VDR signaling

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Background and objectives

Active vitamin D [$1,25(OH)_2D_3$]-vitamin D receptor (VDR) signaling is responsible for the mechanism on the intestinal active calcium absorption. Since the expression of $1,25(OH)_2D_3$-VDR responding calcium transporters were decreased by dietary calcium supplementation, changes in luminal calcium concentrations also affect vitamin D action. In this study, we evaluated the effect of calcium intake on $1,25(OH)_2D_3$ action with both intestinal epithelial cells and tissues derived from mice, and investigated the importance of $1,25(OH)_2D_3$-VDR signaling during intestinal tissue formation.

Methods and Results

Firstly, we evaluated the cellular response to $1,25(OH)_2D_3$ treatment in intestinal epithelial cells from p53-null mice when calcium concentration in the culture medium was changed. The expression levels of targets responding $1,25(OH)_2D_3$-VDR signaling, such as *cyp24a1* and *trpv6*, increased by $1,25(OH)_2D_3$ treatment in dose-dependent manner when calcium concentration was 1mM, but this change disappeared when concentration was increased to 5mM. In the next step, to investigate whether the dietary calcium intake altered the responsiveness of $1,25(OH)_2D_3$-VDR signaling in the intestinal epithelium, mice lacking VDR activity in the intestine were demonstrated and the changes in expression of vitamin D responsive molecules were assessed in mice receiving 0.5% and 1.0% calcium diets. The signals of epithelial localization of vitamin D-responsive cell adhesion factor (claudin2) were enhanced by an increase in dietary calcium intake, indicating the importance of appropriate amounts of calcium intake. Further, intestinal epithelial organoids were developed with the intestinal crypts derived from mice lacking genetic VDR activity (VDR-), and the importance of $1,25(OH)_2D_3$-VDR signaling during intestinal tissue formation was evaluated. As a result, the efficiency of organoid formation was markedly reduced in VDR- compared to those from wild type mice.

Conclusions

These results suggest that calcium in the intestinal lumen is a determinant of $1,25(OH)_2D_3$-VDR signaling in the intestine, and considered to be the facilitative factor for normal development of intestinal tissues.

Key words vitamin D, vitamin D receptor, calcium, intestinal epithelium, intestinal organoid

Category: Basic Nutrition& Research

The role of cross-talk axis between vitamin D and phosphorus metabolism in mice

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Background and objectives: Vitamin D endocrine system regulates phosphorus transport broadly. In phosphorus homeostasis, extracellular ATP is one of a capable supplier for inorganic phosphorus and those system is partly promoted by ENPP1 action. Our previous study demonstrated the vitamin D-dependent transcriptional control of ENPP1. In this study, to examine the interaction of vitamin D and ENPP1-mediate phosphorus metabolism, the effect of dietary phosphorus on the regulation of phosphorus homeostasis was demonstrated in mice.

Methods and Results: Firstly, to examine phosphorus homeostasis, a normal diet (0.5% phosphorus) and a low phosphorus diet (0.25%) were administrated to ENPP1 lowering-of-function mutant mice (ENPP1asj). ENPP1asj fed a normal diet had lower serum phosphorus concentrations than wild-type mice. Compared to mice with normal diet, low-phosphorus diet did not further reduce serum phosphorus concentrations. In addition, osteoclast bone resorption activity observed by histological analysis was increased by low phosphorus diet in ENPP1asj mice. These results suggested that phosphorus homeostasis was maintained by osteoclast bone resorption. Secondly, to examine the interaction between vitamin D and ENPP1 in phosphorus metabolism, we generated vitamin D receptor-deficient mice lacking vitamin D function (VDRKO). Whereafter, VDRKO was crossed with ENPP1asj to generate double mutant mice (VDRKO-ENPP1asj). Serum phosphorus levels were reduced in VDRKO and ENPP1asj compared to wild-type mice. A greater reduction in serum phosphorus concentrations were observed in VDRKO-ENPP1asj. The impaired bone resorption in VDRKO was improved in VDRKO-ENPP1asj. These results indicated that phosphorus mobilized by bone-resorption was not sufficient to maintain homeostasis in mice lacking both vitamin D and ENPP1 action.

Conclusions: In conclusion, dietary phosphorus restriction did not disturb phosphorus homeostasis in the presence of vitamin D-VDR signaling regardless of ENPP1 action. Furthermore, ENPP1 was suggested to maintain phosphorus homeostasis through a mechanism independent of vitamin D function with respect to phosphorus metabolism.

Key words phosphorus metabolism, phosphorus, vitamin D, enpp1, calcium

Category: Basic Nutrition& Research

The Effect of Breed and Lactation Period on Sheep Milk Oligosaccharides

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Background and objectives: Milk oligosaccharides are abundant in human milk and have numerous biological functions for newborns, and milk oligosaccharides found in domestic animals also have similar physiological functions to human milk oligosaccharides. Sheep milk is currently growing in China and is mainly used for home consumption and production of infant formulas. However, there are few studies on sheep milk oligosaccharides. Thus, this study was conducted to provide an analysis of sheep milk oligosaccharides among different breeds and lactation periods. Methods: The sheep milk oligosaccharides in different breeds (Hu sheep, East Friesen sheep, East Friesen-Hu crossbred sheep) at different lactation periods (colostrum, mature milk) were extracted using ethanol and purified by graphitized carbon SPE columns. Qualitative and quantitative analyses of sheep milk oligosaccharides were performed using ultrahigh-performance liquid chromatography-electrospray ionization-tandem mass spectrometry. Results: Among 19 milk oligosaccharides identified in sheep milk, 9 were neutral and 7 were sialylated. There were 19 and 16 types of oligosaccharides in colostrum and mature milk from Hu sheep, 18 and 15 types from East Friesen sheep, and 15 and 14 types from East Friesen-Hu crossbred sheep, respectively. Moreover, Hu sheep colostrum had the highest abundance of milk oligosaccharides among six sheep milks, followed by East Friesen sheep colostrum, while East Friesen-Hu crossbred sheep mature milk had the lowest abundance of milk oligosaccharides. Conclusions: The abundance of sheep milk oligosaccharides was significantly influenced by the breeds and lactation period ($P < 0.05$) while the type of sheep milk oligosaccharides was not greatly affected. These findings provide evidence for the potential value of sheep milk for the commercial applications of milk oligosaccharides in functional foods.

Key words oligosaccharides, sheep milk, Hu sheep, East Friesen sheep, East Friesen-Hu crossbred sheep

Category: Basic Nutrition& Research

Altered Intestinal Phenotype and Microbiota in Osteogenesis Imperfecta Mouse Models

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Osteogenesis imperfecta (OI) is an inheritable bone fragility disorder characterized by age-dependent hypermetabolism. OI is mainly caused by genetic mutations in collagen-I, a dominant intestinal component sustaining intestinal structure and function. With rising attention on the gut-bone axis, it remains unclear whether OI-related collagen-I defects affect the intestinal structure and microbiota.

This project randomly assigned OI mice (Col1a1$^{Jrt/+}$, Oim$^{-/-}$) and their wild-type counterparts to three age groups (4-, 8-, and 12 weeks). Body weight and intestinal length were determined during dissection. The intestinal structure was evaluated via histomorphometry. Cecal microbial fatty acids profiling was conducted using gas chromatography. Real-time polymerase chain reaction analyzed total RNA expression in duodenal samples.

Results showed that male and female OI mice had less weight gain over 4 to 12 weeks of age. Further, Col1a1$^{Jrt/+}$ and Oim$^{-/-}$ mice had longer relative intestinal lengths. Healthier villus-crypt units were also observed in Col1a1$^{Jrt/+}$ mice at all ages. Genetically, collagen-I and III, critical for intestinal structure, were less expressed in male Col1a1$^{Jrt/+}$ and Oim$^{-/-}$ mice, while tight junction proteins' expression significantly decreased in female Oim$^{-/-}$ mice. Noticeably, expression of CYP24A1 was significantly lower in all OI mice at 4 weeks old, suggesting better calcitriol-mediated calcium uptake in the duodenum. Lastly, cecal fatty acids profiling addressed decreased saccharolytic and proteolytic activities in 4-week female Col1a1$^{Jrt/+}$ mice.

This study demonstrates that collagen-I mutation results in a unique intestinal phenotype in OI. Longer intestines with healthier villi and decreased CYP24A1 expression suggest potential compensating mechanisms in OI mice. Additionally, decreased microbial activities in female OI mice imply potential microbial composition alterations. In summary, this study provides valuable insights into intestinal phenotype contribution and potential microbial involvement in OI pathophysiology, which may ultimately lead to the development of novel strategies addressing the nutritional and metabolic needs of OI patients.

Key words Microbiota, intestinal phenotype, gut barrier, osteogenesis imperfecta, gut-bone health

Category: Basic Nutrition& Research

The bone-derived components from adult chickens provide a protective action against impaired bone metabolism in VDRKO mice

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Background and objectives

Post-laying hens called adult chickens are characterized by the presence of medullary bone forming a reticular structure in the endocortical domain, which is resorbed during the formation of the eggshell to supply calcium. Remarkable bone metabolism occur in the hen's body, and medullary bone is considered to contribute to calcium homeostasis. In this study, we tested whether the oral administration of bone-derived components from adult chickens to animals could improve bone metabolism.

Methods

The effects of bone-derived components from adult chickens were investigated in systemic vitamin D (VD) receptor knockout mice (VDRKO), in which VD-dependent calcium homeostasis are disrupted. Meat samples were prepared from adult chickens or young chickens with no egg-laying experience by pressing meat parts including bones, heat-sterilizing, and freeze-drying. The test diets (adult chicken bone-containing diet and young chicken bone-containing diet) were prepared by replacing 25% of the diet weight with each meat sample. The control diet didn’t contain meat sample. Wild-type mice (WT) and VDRKO were fed one of each diet for 4 weeks from 5 weeks of age.

Results

Hypocalcemia and decreased bone strength, characteristic of VDRKO, was observed only in the young chicken bone-containing group and the control diet group and improved to the same level as WT in the adult chicken bone-containing diet group (adult chicken group). Micro-CT analysis of the femurs showed a significant increase in cortical bone and cancellous bone mineral density in VDRKO adult chicken group compared to the control diet group. The impaired apparent calcium absorption in VDRKO was partly recovered by the dietary treatment, the adult chicken group significantly increased only in female mice.

Conclusions

These results suggest that bone-derived components from adult chickens contain VD-independent factors that contribute to bone health, one that improves calcium absorption in the intestinal tract and one that has a direct improving effect on bone.

Key words bone metabolism, adult chicken, calcium absorption efficiency, bone strength, bone mineral density

Category: Basic Nutrition& Research

Randomized control trial on Weekly Iron and Folic Acid Supplementation (WIFAS) in Malaysia

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Background and objectives: Weekly iron and folic acid supplementation (WIFAS) providing 60 mg of iron and 2.8 mg of folic acid is recommended by WHO to prevent iron-deficiency anemia. However, given the lack of high-level evidence, it has not been recommended to reduce the risk of neural tube defects (NTDs). The aim of this study was to investigate the effect of two doses of folic acid, compared with placebo, on red blood cell (RBC) folate, a biomarker of NTD risk.

Methods: This study was conducted in Malaysia using a three-arm double-blind efficacy trial. Non-pregnant women (n=331) were randomized to receive 60 mg iron and either 0, 0.4, or 2.8 mg folic acid once weekly for 16 weeks.

Results: At 16 weeks, women receiving 0.4 mg and 2.8 mg folic acid per week had a higher mean RBC folate than those receiving 0 mg (mean difference (95% CI) 84 (54 to 113) and 355 (316 to 394) nmol/L, respectively). Women receiving 2.8 mg folic acid had a 271 (234 to 309) nmol/L greater mean RBC folate than those receiving 0.4 mg. Moreover, women in the 2.8 mg group were seven times more likely to achieve an RBC folate >748 nmol/L, a concentration associated with a low risk of NTD, compared with the 0.4 mg group. Other factors such as folate intake and selected snp were looked into as well.

Conclusion: Weekly IFA supplements containing 2.8 mg folic acid increases RBC folate more than those containing 0.4 mg. This shows the potential for RBC folate to increase to concentrations associated with a reduced risk of NTDs. Thus, a guideline revision and inclusion of WIFAS in the WHO Essential Medicine List (EML) would be warranted to accelerate the reduction of NTDs and anemia worldwide.

Key words Weekly Iron Folic Acid Supplementation (WIFAS), neural tube defects, Essential Medicines List

Category: Basic Nutrition& Research

ANTI-OBESITY ACTIVITY OF Momordica cochinchinensis L. SPRENG FRUIT ARIL EXTRACTS ON SPRAGUE DAWLEY RATS FED WITH HIGH FAT DIET AND GENES EXPRESSION (PPARγ, C/EBP AND UCP1)

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Momordica cochinchinensis L. Spreng or gac fruit has a high concentration of carotenoids. There is no study on the gac carotenoids as anti-obesity. The study aimed to investigate the effects of gac aril carotenoid rich-extract (GACRE) against rats fed with a high-fat diet (HFD), through biochemical parameters, adipose tissue mass, adipocyte number and size, liver- and kidney histology, and PPARγ, C/EBP and UCP1 gene expression. The Sprague Dawley rats (n=32); were grouped into G1: regular diet (ND), G2: HFD and G3 and G4: HFD with eight-week GACRE supplementation using oral gavage at 50 mg/kg (GACRE-50) and 200 mg/kg (GACRE-200), respectively. As a result, rats fed with HFD and supplemented with GACRE-50 and GACRE-200 did not significantly decrease in body weight. Rats given GACRE-200 had significantly lower aspartate transaminase levels, but no differences in the level of alanine transaminase, direct-, or total bilirubin. Both groups of rats supplemented with GACRE-50 and GACRE-200 showed a significant decrease of about 50% in the creatine level, but no significant difference in amylase and lipase. In the cardiac function and blood glucose test, obese rats fed GACRE-200 showed a significant decrease in triglyceride, creatine kinase and blood glucose at 32.17%, 22.16%, and 31.30%, respectively. Besides, the administration of GACRE did not significantly decline white- (WAT) and brown adipose tissue (BAT) mass, adipocyte number, and size. The liver histology of HFD rats supplemented with GACRE-200 developed microvesicular steatosis, hepatic sinusoidal congestion, and widening sinusoidal space. PPARγ and UCP1 gene expression was higher in BAT compared to WAT, that linearly proportionate

to BAT numbers that are significantly higher than WAT. Higher BAT numbers increased activation of UCP1 and thermogenesis, leading to the effectiveness of GACRE has anti-obesity effects. The results indicate that GACRE exhibited minimal anti-obesity effects at a dosage of 200 mg/kg.

Key words Momordica cochinchinensis, Gac aril carotenoids rich extract, liver histology, anti-obesity, PPARγ, C/EBP and UCP1 gene expression

Category: Basic Nutrition& Research

无麸质饮食的演变及其在炎症性疾病治疗中的关系

Evolution of the gluten free diet and their relation in treatment for inflammatory diseases

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BACKGROUND AND OBJECTIVES: According to OMS, a diet is considered healthy when it's main goal is to protect humans, their organism from denutrition in all ways. There are some diseases and intolerance to food that need special diets to keep people healthy, this is the case of the gluten free diet which is a special diet that has to be followed for healthy reasons in cases such as arthritis, irritable bowel syndrome or celiac disease. The main goal of this research is to determine the effect of a dietary plan with a gluten free diet, also to observe the role of the diet in a gut microbiota level and how it interferes with the absorption of some nutrients.

METHODS: this investigation is a review. The pages for investigation used were proquest, pubmed and scielo. The criterias used were types of inflammatory diseases and their treatment, also gut microbiota and its correlation with nutrients.

RESULTS: in all studies they had a result that gluten free diet is a good option of treatment for inflammatory diseases, however in the absorption level and microbiota, there was evidence of some nutrients that weren't absorbed completely such as some vitamins and minerals. It is recommendable to take probiotics to keep the gut microbiota diversity.

CONCLUSIONS: In the last 20 years there has been an incidence of inflammatory diseases worldwide. People decided to adopt certain lifestyles considering nutrition as their main goal to control inflammation. It is important to have a diet with fiber and vitamins

Key words arthritis, celiac disease, gluten free diet, gut microbiota, inflammatory disease.

Category: Basic Nutrition& Research

儿童和青少年血清锌水平与呼吸系统疾病发病风险的队列研究

A cohort study of plasma zinc levels with risks of incident respiratory diseases in children and adolescents

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Respiratory diseases (RDs) remains a major health risk in children and adolescents. However, whether a higher level of plasma zinc reduced the risk of RDs in children and adolescents is still unknown. We aimed to examine the association of plasma zinc levels with RDs incidence based on a Chinese multi-communities' prospective cohort.

Methods:

We registered the 3753 participants aged 6 to 17 years, who were free of prevalent RDs at baseline, from 14 districts or counties across Sichuan Province, China between September 9, 2016 to Jun 30, 2017. The incident RDs for the participants were followed through the provincial level hospital admission database until December 31, 2020. We estimated the hazard ratios of plasma zinc levels with the risk of incident RDs using cox proportional hazards regression models. The effect modifications by father's education, ethnicity, child's BMI, and child's sex were evaluated through stratified analyses.

Results:

The participants whose fathers were retired or farmer or Han ethnicity, as well as the participants with a higher BMI, or were males, or aged younger than 12 years were at higher risks of incident RDs. The adjusted HRs were 0.67(95% CI: 0.46-0.97), 0.67(95% CI: 0.45-0.99), 0.60(95% CI: 0.40-0.90), and 0.66(95% CI: 0.45-0.98) for the participants in the 2nd, 3rd, 4th, and 5th quintiles of plasma zinc levels, compared with those from the lowest quintile level, respectively. The participants who had higher BMI levels were particularly at higher risks. The study associations remained largely unchanged after excluding parental asthma prevalence cases, or additionally adjusting for the dietary factors.

Conclusion:

Higher levels of plasma zinc were associated with a lower risk of incident RDs in children and adolescents. Developing plasma zinc levels could benefit respiratory health in children and adolescents.

Key words plasma zinc, respiratory diseases, children and adolescents, prospective cohort

Category: Basic Nutrition& Research

长期高脂饮食通过肠道菌群及其代谢物对肥胖性肌肉衰减症的影响及机制研究

Long-term high-fat diet induces sarcopenic obesity in natural aging rats by modulating the gut microbiota and metabolites

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Background: The lack of suitable animal models for sarcopenic obesity (SO) limits in-depth research on the mechanism, prevention and treatment of the disease, and the role of gut microbiota and its metabolites in SO is still unclear. Thus, we aimed to investigate whether long-term high fat-diet (HFD) can cause SO in natural aging animal models, and the effects of gut microbiota and its metabolites on the development of SO.

Results: After feeding for 80 weeks, HFD resulted in obesity-related metabolic disorders, including body weight gain, dyslipidemia, impaired glucose tolerance, insulin resistance, and systemic inflammation in natural aging rats. HFD also promoted a decrease in muscle mass, strength, function, and fiber cross-sectional area and an increase in muscle fatty infiltration in natural aging rats. 16S rRNA, non-targeted and targeted metabolomics analysis revealed thatHFD contributed to the dysbiosis of gut microbiota and its related metabolites in natural aging rats, mainly characterized by an increase in pathogenic bacteria and metabolites including g__Eubacterium_hallii_group, g__Coprococcus, g__Collinsella, g__unclassified_f__Eggerthellaceae and trimethylamine N-oxide (TMAO), as well as a decrease in probiotics and metabolites, including g__Butyricimonas, g__Akkermansia, g__Flavonifractor, g__Intestinimonas and short-chain fatty acids (SCFAs). HFD also destroyed the gut barrier function in natural aging rats, as evaluated by reducing levels of colonic mucin-2, tight junction proteins, goblet cells and elevating serum level of FITC-dextran 4. Correlation analysis revealed that the positive association between pathogenic bacteria, TMAO and SO-related phenotypes, and the negative association between probiotics, SCFAs, and SO-related phenotypes. Moreover, removing gut microbiota with antibiotics treatment partially ameliorated HFD-induced SO and decreased the levels of SCFAs and TMAO in natural aging rats. In addition, TMAO treatment could cause systemic inflammation and sarcopenia in HFD-fed, aged rats.

Conclusions: Long-term HFD leads to SO in natural aging rats, partially through the gut－microbiota－metabolites－muscle axis.

Key words High fat-diet; Natural aging; Sarcopenic obesity; Gut microbiota; Metabolites; Trimethylamine N-oxide

Category: Basic Nutrition& Research

遵守2018年WCRF/AICR饮食建议与肠道微生物群和炎症水平的关系

Associations of adherence to the 2018 WCRF/AICR dietary recommendations with gut microbiota and inflammation levels

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Background: Whether adherence to the World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) dietary recommendations has an effect on gut microbiota and inflammatory status in people at high risk for CRC remains unclear.

Objectives: We aimed to assess the association of adherence to the WCRF/AICR diet with gut microbiota and inflammation in a cross-sectional setting.

Methods: The WCRF/AICR diet adherence scores were calculated for 151 participants from 7-day dietary records. The gut microbiota was analyzed by 16S rRNA gene sequencing. Inflammatory marker levels (FCP, IL6, IL8, IgA, IgM, and IgG) were assessed in 97 adenoma patients. In multivariate-adjusted linear regression analyses, we investigated the association of individual and total dietary adherence scores with gut microbiota and inflammatory marker levels, with a gender-stratified analysis for inflammation.

Results: Participants with higher total adherence score had lower relative abundance of *Proteobacteria* (β -0.041, 95%*CI* -0.073; -0.009), *Enterobacteriaceae* (β -0.035, 95%*CI* -0.067; -0.003), and an unidentified *Enterobacteriaceae* (β -0.029, 95%*CI* -0.055; -0.003) at the genus level compared with those reporting low adherence scores. Intake of plant-based food was associated with increased abundance of *Phascolarctobacterium* (β 0.013, 95%*CI* 0.001; 0.026); Limiting fast food was associated with increased abundance of *Bacteroidaceae* (β 0.149, 95%*CI* 0.040; 0.257) and *Bacteroides* (β 0.149, 95%*CI* 0.040; 0.257). Limiting sugary drinks was associated with lower abundance of *Lachnospiraceae* (β -0.155, 95%*CI* -0.292;-0.018). In terms of inflammation, plant-based food intake (β -0.251, 95%*CI* -0.450; -0.052) and 'fast food' restriction (β -0.226, 95%*CI* -0.443; -0.008) were associated with lower IGG levels in men; Alcohol restriction was associated with lower IL6 (β -7.095, 95%*CI* -11.286; -2.903) and IL8 (β -7.965, 95%*CI* -14.700; -1.230) in women, but with higher IL6 (β 0.918, 95%*CI* 0.161; 1.675) in men.

Conclusion: Our findings support the association of adherence to the WCRF/AICR diet with gut microbiota and inflammation.

Key words Diet; WCRF/AICR; Colorectal cancer; Gut microbiota; Inflammation;

Category: Basic Nutrition& Research

日粮烟酰胺核酸对骨骼肌和下丘脑功能调控的量效机制研究

Dietary nicotinamide riboside affects motor function and hypothalamic gene expression in a dose-dependent manner

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Nicotinamide ribose (NR) is a dietary vitamin B3 that is a precursor for the essential metabolic cofactor nicotinamide adenine dinucleotide (NAD+). We previously established that among a range of concentrations, 30 mg NR per kg diet best supported metabolic health in mice. High, as well as low levels of NR had negative health effects through distinct mechanisms. Since motor performance and hypothalamic responses are important physiological read-outs for metabolic health, we now investigated this in detail. Male C57Bl/6JRccHsd mice were fed a semi-purified obesogenic diet (40% fat) containing 0.14% L-tryptophan and either 5, 30, or 900 mg NR per kg diet for 15 weeks. Compared to 30NR- fed mice, feeding a 5NR and 900NR diet lowered grip strength in mice, which was dependent on intervention time. The 900NR diet negatively affected motor coordination. Anti-oxidant defense genes *Prdx3* and *Sod1* were decreased by 900NR in the skeletal muscle. In the hypothalamus, gene expression of *Tdo2*, the first rate limiting enzyme in the de novo NAD+ synthesis, was upregulated by 900NR feeding, whereas *Qdpr* was unaffected. The 5NR group displayed an upregulation of hypothalamic *Mapk1* (Erk2), a gene associated with neuronal plasticity, as well as of *Mthfs*, a key enzyme in folate metabolism. In conclusion, high dose NR reduces motor performance, which was associated with a reduction of the anti-oxidant defense in skeletal muscle. Low intake of NR implicates an interaction in the hypothalamus between the two B-vitamins folate and vitamin B3, with unknown functional consequences. Our results strengthen our previous observations that 30NR is the optimal dose to support metabolic health.

Key words Nicotinamide riboside; motor function; transcriptional signature; dose-dependent response

Category: Basic Nutrition& Research

一株四川泡菜源乳酸菌对单核细胞增生李斯特氏菌的抑制作用

Inhibition of Listeria monocytogenes by a lactic acid bacterium isolated from Sichuan pickles

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Objective: To screen a strain of lactic acid bacteria (LAB) from traditional Sichuan pickles with the best antibacterial activity against *Listeria monocytogenes*, and to investigate its antibacterial substances. **Methods**: The Oxford cup and drilling method were used to screen a strain of LAB9 with the best inhibitory effect on *Listeria monocytogenes*. Bacterial identification was done through 16S rDNA gene sequencing. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined using the dilution ratio method. Preliminary analysis of antibacterial substances was performed through organic acid exclusion assay, protease, acid-base and heat sensitivity tests. To investigate bacteriocin encoding gene, polymerase chain reaction (PCR) was performed by specific primers. Then, its drug resistance and safety were evaluated. **Results**: LAB9 was identified as *Lactobacillus plantarum*. The diameter of antibacterial circles of LAB9 against *L. monocytogenes* were measured to be 19.85 ± 0.14 mm and 11.84 ± 0.16 mm by two inhibition assays. The MIC and MBC of LAB9 were 4 mg/ml and 32 mg/ml, respectively. According to preliminary investigations, antibacterial substances were mainly bacteriocins, although the effect of organic acids cannot be excluded. The PCR detection of several bacteriocin coding genes revealed that LAB9 was harboured six bacteriocin gene among the tested genes, including PLNJK, plnW, plnEF, plnA, plnQ, nis, and plnXY. Among the seven commonly tested antibiotics, only gentamicin and vancomycin showed tolerable effects on the strain. In addition, LAB9 did not exhibit hemolytic activity. **Conclusion**: This study screened a strain of *Lactobacillus plantarum* LAB9 that produces bacteriocins but does not exclude organic acids, and exhibits strong inhibitory effects on *Listeria monocytogenes*. These findings provide a valuable foundation for the control of *Listeria monocytogenes* at low temperatures and the development of novel antimicrobial drugs suitable for application in the food industry.

Key words Listeria monocytogenes, lactic acid bacteria, Lactobacillus plantarum, antibacterial substances

Category: Basic Nutrition& Research

一株泡菜源乳酸菌对副溶血性弧菌的抗菌物质分析与生物膜抑制作用研究

Analysis of antibacterial substances and biofilm inhibition of Vibrio parahaemolyticus by a pickle-derived lactic acid bacteria strain

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Objective: To screen a strain of lactic acid bacteria (LAB) from traditional Sichuan pickles that exhibits antibacterial activity against *Vibrio parahaemolyticus* and inhibiting biofilm formation. **Methods**: A strain of LAB29 with the best inhibitory effect on *V. parahaemolyticus* was screened using the Oxford cup and double agar diffusion method. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined using the dilution ratio method. Bacterial identification was done through 16S rDNA gene sequencing. Preliminary analysis of antibacterial substances was performed through organic acid exclusion assay, protease, acid-base and heat sensitivity tests. To investigate bacteriocin encoding gene, polymerase chain reaction (PCR) was performed by specific primers. Biofilm biomass was assessed by crystal violet staining. **Results**: Strain LAB29 was identified as *Lactobacillus plantarum*. The inhibition circles of LAB29 against *V. parahaemolyticus* were measured to be 17.41 ± 0.06 mm and 26.36 ± 0.21 mm by two inhibition assays. The MIC and MBC of LAB29 were 8 mg/ml and 16 mg/ml. According to preliminary investigation, the antibacterial substances were bacteriocins, which were sensitive to temperature changes and acidic conditions. These bacteriocin-encoding genes in LAB29 were identified using PCR amplification, including *nis*, *plnQ*, *plnEF*, *plnW*, and *plnA*. Moreover, LAB29 significantly inhibited *V. parahaemolyticus* biofilm formation and showed potential for effective removal of mature biofilm. Treatment with strain product at concentrations of 64 and 128 mg/mL for 12 h resulted in 63.70% and 29.90% inhibition rates of biofilm. Even after 96 h, the inhibition rates remained at 49.10% and 1.23%. **Conclusion**: This study successfully screened a bacteriocin-producing strain, *Lactobacillus plantarum* LAB29. It can exhibit potential as a novel LAB biological agent for preventing and controlling the growth and biofilm formation of *Vibrio parahaemolyticus*. This research contributes to the development of new antibacterial agents and the elimination of pathogenic bacteria biofilm contamination.

Key words Vibrio parahaemolyticus, lactic acid bacteria, Lactobacillus plantarum , antibacterial substances, biofilm inhibition

Category: Basic Nutrition& Research

维生素 D3 通过靶向调控 NLRP3 炎性小体活化改善 SARS-CoV-2 核衣壳蛋白引起的过度炎症

Targeting NLRP3 inflammasome by vitamin D3 attenuates SARS-CoV-2 nucleocapsid protein-caused hyperinflammation in vitro and in vivo

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Background: SARS-CoV-2 infection-caused coronavirus disease 2019 (COVID-19), a global crisis, is characterized by severe inflammatory responses with no satisfactory therapies. Vitamin D3 (VD3) with excellent anti-inflammatory properties is considered as a potential candidate for COVID-19 treatment; however, little information is available regarding the exact effects of VD3 on SARS-CoV-2 infection as well as the underlying mechanism. Our study aimed to delineate the effect of VD3 on SARS-CoV-2 infection-caused hyperinflammation and the potential involvement of the NOD-like receptor family pyrin domain containing 3 (NLRP3) inflammasome.

Methods and Study Design: A stable expression SARS-CoV-2 N protein human bronchial epithelial cell line (HBE-N) was established by lentiviral vector transfection. C57BL/6J mice were injected with AAV-Lung-EGFP-N (AAV-N) to induce lung injury, followed by treatment with or without VD3. Western blotting, immunofluorescence analysis, ELISA kits, and enzymatic activity assay kits were used to detect protein levels and activities. Specific inhibitors, agonists or siRNAs transfection, and immunoprecipitation were used to explore the underlying mechanism.

Results: VD3 significantly reduced N protein-caused hyperinflammation in HBE cells. Meanwhile, VD3 decreased NLRP3 expression, caspase-1 activity, and interleukin-1β (IL-1β) release in HBE-N cells. Notably, zYVAD-fmk, MCC950, NLRP3 or caspase-1 siRNA enhanced VD3-induced NLRP3 inflammasome inactivation, with subsequent suppression of IL6 and IL1β release in HBE-N cells, which were abolished by nigercin. Moreover, VD3 increased NLRP3 ubiquitination (Ub-NLRP3) expression and the binding of the vitamin D receptor (VDR) with NLRP3, with decreased BRCC3 expression and NLRP3-BRCC3 association. VD3-induced Ub-NLRP3 expression, NLRP3 inflammasome inactivation and hyperinflammation were improved by G5 or BRCC3 siRNA, which were attenuated by TEI-9647 or VDR siRNA in HBE-N cells. Finally, the results of the in vivo study in AAV-N-infected lungs were consistent with the findings of the in vitro experiment.
Conclusions: VD3 attenuated SARS-CoV-2 N protein-caused hyperinflammation by inactivating the NLRP3 inflammasome partially through the VDR-BRCC3 signaling pathway.

Key words Vitamin D3; COVID-19; NLRP3 inflammasome; VDR; BRCC3

Category: Basic Nutrition& Research

四川泡菜源乳酸菌的耐药性分析及安全性评价

Drug resistance analysis and safety evaluation of lactic acid bacteria from Sichuan pickles

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Objective: To analysis the drug resistance and evaluate the safety of 34 strains of lactic acid bacteria (LAB) isolated from traditional pickles in Sichuan. **Methods**: The K-B paper diffusion technique and the antibiotic resistance gene test were used to analyze the drug resistance of the 34 LAB strains. Safety evaluation was evaluated by the hemolysis test, toxicity-related enzyme test, and biogenic amine characterization test. **Results**: The results showed that all 34 strains of LAB exhibited varying degrees of resistance to 12 commonly used antibiotics, and indicating full multi-drug resistance. Vancomycin and streptomycin had the highest rates of antibiotic resistance (100.00%), followed by gentamicin (97.06%), levofloxacin (94.12%), sulfisoxazole (91.18%), tetracycline (64.71%), and clindamycin (58.82%). Conversely, five other antibiotics showed relatively low resistance rates, or even zero resistance to chloramphenicol. Vancomycin resistance gene (*van*X) and rifampicin resistance gene (*rpo*B) were found in 79.41% and 11.76% of LAB strains, respectively. Furthermore, all the tested LAB strains were considered safe as they did not showed either gelatinase, tryptophanase, lecithinase, DNAse or hemolytic activity, and produce biogenic amines. **Conclusion**: This study aimed to evaluate the drug resistance and safety of the 34 isolated LAB strains in order to prevent the selection of drug-resistant or unsafe strains. The findings provide a foundation for the production and application of novel lactic acid bacteria.

Key words Lactic acid bacteria, drug resistance, safety evaluation, antibiotic resistance genes

Category: Basic Nutrition& Research

后生元：定义、制备、健康益处、应用现状及未来展望

Postbiotics: Current Status and Future Perspectives on Definition, Production, Health Benefits, and Applications

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Postbiotics are defined as a "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host". As a new class of functional food ingredients, postbiotics have gained increasing attention in recent years due to their potential health-promoting effects and their safety profile compared to probiotics. However, the regulatory framework for postbiotics is still lacking in many countries, which poses a challenge for their development and commercialization. The health benefits of postbiotics have been demonstrated in numerous studies, including improving gut health, modulating the immune system, and preventing and treating various diseases. Various methods have been developed for the preparation and identification of postbiotics, such as cell-free supernatant, exopolysaccharides, and peptidoglycans. In terms of industrial applications, postbiotics have been used in the food, feed, cosmetics and pharmaceutical industries, showing great potential for improving human and animal health. However, further research is needed to fully understand the mechanisms underlying the health benefits of postbiotics and to optimize their production and formulation. This review summarizes the current understanding of postbiotics, including their definition, regulatory status, health benefits, preparation and identification methods, industrial applications, and future prospects. It is expected to provide a reference for establishing regulatory guidelines, optimizing production processes, and exploring new application areas of postbiotics.

Key words Postbiotics, Definition, Health benefits, Regulatory, Application

Category: Basic Nutrition& Research

转录组学探究不同减重方式对肥胖小鼠多器官功能的影响

Distinct effects of weight loss paradigms on multiple organs transcriptome of diet-induced obese mice

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Sh

Obesity and its related metabolic diseases bring great challenges to public health. In-depth understanding on effects of weight loss interventions is critical for weight management. We used high-fat-high-fructose (HFHF) diet induced obese mice model to investigate how exercise, intermittent fasting, or the change of daily diet from HFHF to normal chow could affect multiple organs (i.e., quadriceps femoris muscles, liver, subcutaneous fat and scapular brown fat) in high-fat-high-fructose diet induced obese mice at the genetic level through high-throughput transcriptomics. The 3 types of weight loss paradigms led to a significant weight loss of obese mice, and no significant difference in weight was found between the mice underwent interventions and normal controls (i.e. mice fed on normal chow) ($p>0.05$). Results from comprehensive analyses on the transcriptome of multiple organs followed by the RT-QPCR verifications indicate tissue-specific effects of 3 paradigms: exercise and intermittent fasting significantly reduced inflammation in mice, and improved the metabolism of glucose and lipid in liver, inhibiting insulin resistance in muscle tissue, amino acid metabolism and thermogenesis in adipose tissue. Exercise in particular enhanced brown fat thermogenesis. Intermittent fasting effectively improved the amino acid metabolism function of the liver and adipose tissue. The change of daily diet however failed to improve metabolic status and biological dysfunctions induced by HFHF in mice, although it caused significant weight loss. Notably, we identified gene contributors that were significantly associated with weight loss induced changes in physiological indicators in obese mice, such as BCAT2, Ubb, Mlycd and Il4i1. Interestingly, those genes could greatly predict the degree of weight gain for those mice after weight loss that retuned to be fed with HFHF. Collectively, our study provides novel insights on the underlying mechanisms of weight loss effects of popular paradigms.

Key words Weight loss, multiple organs, transcriptome , obesity

Category: Basic Nutrition& Research

母乳脂质替代品对初断乳大鼠脂质代谢的影响

The Effects of Human Milk Fat Substitutes on Lipid Metabolism in First-Weaned Rats

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Objective: To investigate the impact of human milk fat substitutes (HMFS) on lipid metabolism and body fat content of first-weaned rats.

Methods: Thirty male Sprague Dawley rats were randomly divided into three groups and fed with blend vegetable oil (BVO) (Control), BVO + OPO (1,3-dioleic acid-2-palmitoyl triglyceride) (OPO), or HMFS for six weeks. Body weight, body fat, serum and liver lipid profile, fecal short-chain fatty acids (SCFAs), gut microbiota, liver lipidomics, and gene and protein expression related to lipid metabolism were measured.

Results: HMFS did not affect the growth performance of rats (body weight: Control: 298.38 ± 26.73 g, OPO: 287.82 ± 19.85 g and HMFS: 302.31 ± 19.21 g) but significantly decreased body fat content (Control: 28.70 ± 1.17 cm3, OPO: 22.51 ± 1.10 cm3 and HMFS: 14.90 ± 0.95 cm3) ($p<0.05$) and serum and liver lipid levels compared to BVO ($p<0.05$). HMFS also increased the abundance of *Bacteroidetes* and SCFAs in the gut and altered the liver lipid metabolism profile, mainly by increasing glycerophospholipids and decreasing glycerides. HMFS upregulated the expression of genes and proteins involved in lipid oxidation and downregulated those involved in lipid synthesis in the liver.

Conclusion: HMFS can reduce body fat content in rats by modulating the "*Bacteroidetes*-SCFAs-glycerophospholipid metabolic pathway" through the "microbiota-gut-liver axis". HMFS may have nutritional benefits for infants and provide a theoretical basis for its application in infant formula.

Key words human milk fat substitutes; lipid metabolism; body fat; intestinal microbiota; SCFAs

Category: Basic Nutrition& Research

成人血清25-羟维生素D水平与高脂血症发病风险的队列研究
A cohort study of serum 25-hydroxyvitamin D levels and the risk of hyperlipidemia in adults

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Abstract: [Objective]: To investigate the association between serum 25(OH)D levels and the risk of hyperlipidemia development in an adult population by a three-year follow-up survey using a prospective cohort study design. [Methods] Cox risk regression models were constructed to explore the relationship between serum 25(OH)D levels and the incidence of hyperlipidemia based on the data; the relationship between serum 25(OH)D levels and the risk of developing hyperlipidemia was obtained by stratified analysis of traditional risk factors for hyperlipidemia at baseline, providing a reliable basis for vitamin D prevention of hyperlipidemia. [Results] The overall 25(OH)D level in the study population was 25.89(21.50,29.82) ng/ml, the vitamin D deficiency rate was significantly higher in women than in men (22.06% vs. 10.94%); Using vitamin D-sufficient respondents as a reference, vitamin D deficient hyperlipidemia prevalence was 1.612 times higher than the prevalence of hyperlipidemia in those with adequate vitamin D (95% CI: 1.228-2.116; P=0.001); Further stratified analysis found that vitamin D deficiency increased the risk of developing hyperlipidemia in those with a positive family history of diabetes, low education, BMI <24, not exercising, smoking, alcohol consumption and residence in an urban area were characteristics of the subgroup of respondents in which vitamin D insufficiency increased the risk of developing hyperlipidemia. For the critical value of 25(OH)D level that predicts the occurrence of hyperlipidemia, a subject operating characteristic curve (ROC) was constructed, from which an AUC value of 0.664 (95% CI: 0.631-0.697), and, a 25(OH)D critical value of 31.65 ng/ml can be derived.[Conclusion] The findings suggest that low levels of 25(OH)D population has a higher incidence of hyperlipidemia . Vitamin D insufficiency increases the risk of hyperlipidemia. It is recommended that vitamin D supplementation be given in people with vitamin D insufficiency to reduce the occurrence of hyperlipidemia.

Key words Vitamin D; Hyperlipidemia; Cohort study

Category: Basic Nutrition& Research

飞燕草素通过降低 PD-L1 表达阻断 TNBC 免疫逃逸

Delphinidin blocks TNBC immune escape by Reducing PD-L1 expression

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Abstract Objective To investigate the potential mechanism of Delphinidin in inhibiting suppresses PD-L1 expression pathway on the cell membrane of Triple negative breast cancer and the underlying immune escape, and to provide a new measure for Delphinidin to improve TNBC treatment with immune checkpoint blockades. Methods MDA-MB-231 were treated with different concentrations of Delphinidin (0, 20, 40, 80μM), the ability to detect cell proliferations and drug sensitivity by CCK-8, and the biological characteristics of Delphinidin on MDA-MB-231 cells were detected by Wester-blot. Ficoll density gradient centrifugation separated lymphocytes in peripheral blood, and NK and CD8+ T cells were sorted by immunomagnetic beads to construct a co-culture system with MDA-MB-231 cells to simulate the immune microenvironment. Settings: Blank control control group; Co-culture group of NK, CD8+T and TNBC; Co-culture of the dosing Co-culture + Delphinidin group, a total of 3 groups. The apoptosis status of MDA-MB-231 cells was detected by flow cytometry Annexin-V-FITC/PI double staining and immunofluorescence multicolor staining experiments, the killing activity of T cells and NK cells was verified, and the effect of Delphinidin on the ratio of PD-L1 and CD8+T/NK cells in each group and the mechanism of PD-L1 protein expression on the cell surface were analyzed. Results Compared with the control group, Delphinidin effectively inhibited the proliferation of MDA-MB-231 cells and induced apoptosis. Compared with the Control group and Co-culture group, the proportion of PD-L1 and CD8+ T/NK cells in the Co-culture + Delphinidin group decreased, the tumor killing activity of CD8+ T and NK cells was enhanced, and the expression level of PD-L1 protein in the experimental group was significantly reduced . Conclusion Delphinidin can effectively inhibit the proliferation of MDA-MB-231 cells, increase the killing activity of immune cells and block immune escape by reducing the expression level of PD-L1 on the surface of TNBC cells.

Key words Triple-negative breast cancer; Delphinidin; PD-L1; Immune evasion; In vitro co-culture

Category: Basic Nutrition& Research

肠道Reg4缺乏通过增加小鼠肠道脂肪吸收而导致高脂肪饮食诱导的肝脏脂肪变性

Intestinal Reg4 deficiency confers susceptibility to high-fat diet-induced liver steatosis by increasing intestinal fat absorption in mice

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Background & Aims: Regenerating gene family member 4 (REG4) is a novel marker for enteroendocrine cells and is selectively expressed in specialised enteroendocrine cells of the small intestine. However, the exact roles of REG4 are largely unknown. In this study we investigate the effects of REG4 on the development of dietary fat-dependent liver steatosis and the mechanisms involved.

Methods: Mice with intestinal-specific Reg4 deficiency (Reg4DIEC) and Reg4-floxed alleles (Reg4fl/fl) were generated to investigate the effects of Reg4 on diet-induced obesity and liver steatosis. Serum levels of REG4 were also measured in children with obesity using ELISA.

Results: Reg4DIEC mice fed a high-fat diet demonstrated significantly increased intestinal fat absorption and were prone to obesity and hepatic steatosis. Importantly, Reg4DIEC mice exhibit enhanced activation of adenosine monophosphate-activated protein kinase (AMPK) signalling and increased protein abundance of the intestinal fat transporters, as well as enzymes involved in triglyceride synthesis and packaging at the proximal small intestine. Moreover, REG4 administration reduced fat absorption, and decreased the expression of intestinal fat absorption-related proteins in cultured intestinal cells possibly via the CaMKK2-AMPK pathway. Serum REG4 levels were markedly lower in children with obesity with advanced liver steatosis ($p < 0.05$). Serum REG4 levels were inversely correlated with levels of liver enzymes, homeostasis model assessment of insulin resistance, low-density lipoprotein cholesterol, and triglycerides.

Conclusions: Our findings directly link Reg4 deficiency with increased fat absorption and obesity-related liver steatosis, and suggest that REG4 may provide a potential target for prevention and treatment of liver steatosis in children.

Key words Liver steatosis; Fat absorption; Reg4; AMPK; Childhood obesity.

Category: Basic Nutrition& Research

菊花挥发油的化学成分、抑菌和抗肿瘤活性

Chemical composition, antibacterial and Antitumor activity of the essential oils of Chrysanthemum morifolium Ramat

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The essential oils of Chrysanthemum morifolium Ramat were extracted by steam distillation and analyzed by Gas chromatography-mass spectrometry (GC－MS). The volatile oil was evaluated for antibacterial activity against five Gram-positive bacteria (Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, V. Streptococci, S. pneumoniae), three Gram-negative bacteria (Escherichia coli, Pseudomonas aeruginosa, Shigella flexneri) and two molds (Candida albicans, Cryptococcus neoforman). In vitro, cell proliferation inhibition action on human liver cancer HepG-2 was examined by 3-(4,5-dimethyl)-2,5-diphenyl-2H(MTT) method and cell apoptosis was observed using flow cytometry. In vivo, S-180 tumor-bearing mice were used to research antitumor effect. A total of 59 compounds were identified and caryophyllene oxide was the most abundant volatile component (7.39%). The volatile oil showed promising antibacterial activity against 5 Gram-positive bacteria (S. aureus, S. epidermidis, B. subtilis, V. Streptococci, S. pneumoniae) and 2 molds (Candida albicans, Cryptococcus neoforman). The oils showed significant antitumor activity towards HepG-2 cells with IC50 valued 1.42 μL/mL and increased the apoptotic rates in a dose dependent manner. In addition, the oils inhibited tumor growth of S-180 tumor-bearing mice and the tumor suppressor rate of high dose reached 54.94%. Giving the oils improved the thymus/weight index of tumor-bearing mice which means it increased immune function. All these findings suggest that the essential oil has antibacterial and antitumor activity. It is a candidate for exploring new health foods, the food additive and drugs.

Key words Chemical composition; Antibacterial activity; Antitumor activity; Chrysanthemum morifolium Ramat; Essential oil

Category: Basic Nutrition& Research

学龄儿童患甲状腺结节者甲状腺激素与血清微量元素关系：病例对照研究

Association between thyroid hormone status and trace elements in serum of school-aged children with Nodular Goiter: A case-control study

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Objective: The importance of the thyroid gland in maintaining human health is well recognized. Certain microelements, except for iodine, have been involved in thyroid hormone metabolism in the last decades. However, few studies evaluated the individual iodine status.

Method: The present study was conducted based on a cross-sectional survey of dietary reference intake of iodine in children with different iodine intake areas in Shandong, China. In this comparative study, 182 children without goiter (control group) and 91 adults with diagnosed thyroid nodules (TN) were examined. The 24-h urine iodine excretion assessed iodine status. Serum samples were collected to determine thyroid stimulating hormone (TSH), free thyroxine (FT4), free-iodothyronine (T3), and trace elements. Inductively coupled plasma mass spectrometry (ICP-MS) was used for the measurements of 17 trace elements in the serum of patients with NG and the control group. The subjects of the case-control study were matched by propensity score matching.

Results: Patients with nodular goiter had lower serum values of Zn and higher serum values of I, Ni and Cd than those in the control group. The result revealed a significant positive trend among the odds of TN and I, Ni and Cd [the OR was 4.21 (95% CI: 1.50, 11.84), 4.00 (95% CI: 1.33, 12.03) and 3.33 (95% CI: 1.11, 10.01) for the high concentration, respectively, Ptrend<0.05]. The risk of TN was significantly increased with insufficient Zn [relative to Q2, OR=2.51 (95% CI: 1.08, 5.83) for Q1, Ptrend<0.05]. The ROC showed that the addition of multiple elements of I, Zn, Ni and Cd significantly improved the prediction of TN in children than serum iodine and urine iodine excretion.

Conclusion: This study proved that a combination of high concentrations of I, Ni and Cd and low concentration of Zn in blood serum resulted in the highest risk of thyroid nodules.

Key words Nodular goiter Serum microelements School-aged Children Case-control study

Category: Basic Nutrition& Research

丝氨酸缺乏对母体及其子代健康和硒蛋白表达的影响

Effects of insufficient serine on health and selenoprotein expression in rats and their offspring

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Objective: To observe the impact of insufficient exogenous and/or endogenous serine on selenoprotein expression and health of pregnant rats and their offspring. Method: Experiment 1 was conducted in male rats, in which the dose-dependent effects of serine on selenoprotein expression and thyroid hormones (T3, T4 and TSH) were investigated by feeding either a serine adequate diet (20C), serine-deprived diet (20CSD) or 20CSD with different serine levels (0.5, 1.0, and 2.0 times the amount of serine in 20C). In experiment 2, a PHGDH inhibitor was administrated to pregnant rats fed either 20C or 20CSD. Blood and organ tissues of pregnant rats and offspring were subjected to the analyses of thyroid hormone, serine and homocysteine and GPx3 and SELENOP in plasma and expression of GPx1 and DIO1, 2 in tissues respectively. Result: In experiment 1, plasma SELENOP and GPx3 levels in adult male rats increased with the increasing dose of serine. Immunohistochemical results showed that GPx1 expression in liver and kidney of male rats also increased with increasing serine supplementation. Amongst all diet groups, only male rats fed 20CSD had significantly lower plasma TSH and T4 levels ($P<0.05$). In experiment 2, GPx1 and DIO2 expression in the liver and kidney were suppressed in pregnant rats administered with a PHGDH compared to those who were not ($P<0.05$). Also, offspring born to pregnant rats administered with a PHGDH inhibitor exhibited slower growth rates and hyperhomocysteinemia compared to offspring from mothers not administered with the inhibitor ($P<0.05$).Conclusions: Insufficient exogenous serine through the diet decreased selenoprotein synthesis in adult male rats. However, this was not observed in pregnant rats, whereby exogenous or endogenous serine deficiency had no effect on the selenoprotein levels. A possible explanation is that dams may have an adaptive mechanism to limit maternal serine utilization and ensure adequate supply to the fetus.

Key words Serine, PHGDH inhibitor, GPx, SELENOP, DIO2

Category: Basic Nutrition& Research

短双歧杆菌 207-1 对生命早期抗生素暴露小鼠肠道菌群构建、肠道发育以及远期炎症性肠病的影响

Effects of Bifidobacterium breve 207-1 on gut microbiota composition, gut development and long-term inflammatory bowel disease in antibiotic-exposed mice in early life

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SICHUAN University

Objective: To explore the possible mechanism of Bifidobacterium breve207-1 (B.breve207-1) on the changes of intestinal microbiota, mucosal barrier and immune response in antibiota-exposed mice in early life, and the effect of B.breve207-1 on long-term inflammatory bowel disease (IBD) in antibiota-exposed mice in early life.

Methods: Neonatal mice were randomly divided into five groups and received interventions from birth to 7 weeks of age: NS-Water, NS-DSS, Ceftri-DSS, Ceftri+207-1-DSS, Ceftri+207-1-207-1+DSS.

Results: Compared with the blank control group, the colitis model group had a significant increase in the pathological score (P< 0.05).Compared with the colitis model group, the pathological scores of the 207-1 short-term group were significantly decreased (P< 0.05).At the age of 7 weeks, the Chao1 index and ACE index of Ceftri+207-1-DSS group were higher than those of NS-Water, NS-DSS, CEFtri-DSS and Ceftri+207-1-207-1+DSS groups.According to the analysis of intestinal microbiota, the relative abundance of Firmicutes in Ceftri+207-1-DSS group was significantly higher than that in other groups.Compared with NS-Water and Ceftri-DSS, the early treatment of Ceftri+207-1-DSS promoted the higher expression of MUC2, Clauding-1, ZO-1, Occludin and secretory immunoglobulin A (sIgA). In terms of immune level, the levels of serum immune factors IL-6, IL-17A and TNF-α in Ceftri+207-1-DSS group were significantly lower than those in CEFTri +207-1-DSS group (P< 0.05).

Conclusions: Antibiotic exposure in early life significantly changes the composition of gut microbiota in neonatal mice, reducing the species richness and evenness of gut microbiota to varying degrees. These changes will affect adulthood and participate in the development of long-term inflammatory bowel disease. Short-term use of B.breve 207-1 can regulate intestinal flora, reduce the damage of intestinal flora caused by antibiotics, and have a profound regulatory effect on the composition of intestinal microbiota, the immune system and the development of intestinal mucosal barrier in early life.

Key words Bifidobacterium breve 207-1; Intestinal mucosal barrier; Gut microbiota; Colitis; Antibiotics

Category: Basic Nutrition& Research

脂肪组织Fas信号影响肠道微生物群稳态及促进非酒精性脂肪肝的发展

Adipose tissue Fas signaling affects gut microbiota homeostasis and promotes the development of non-alcoholic fatty liver

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Background and Objectives

Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases, and obesity has been recognised as a risk factor for NAFLD. However, the underlying mechanisms of obesity-associated NAFLD pathogenesis remain largely unknown. Fas (CD95) is a member of the tumour necrosis factor (TNF) receptor superfamily and is upregulated in adipose tissue of obese individuals. Adipose tissue-activated Fas signaling does not cause adipocyte apoptosis, but affects adipocytes in a non-apoptotic manner. The development of NAFLD is associated with adipose tissue inflammation and intestinal dysfunction. Here, we aimed to investigate the effect of adipose tissue-specific Fas overexpression on high-fat diet (HFD)-induced NAFLD in mice.

Methods and Study Design

Adipose tissue-specific overexpressing Fas mice (Adi-Fas) mice and littermates ($Fas^{CKI/CKI}$) were fed with normal chow or HFD for 10weeks to induce obesity and non-alcoholic fatty liver disease. Body weight gain was checked weekly. Hepatic steatosis was monitored by histological analysis. Gut microbial composition was analyzed by 16S rRNA gene sequencing.

Results

We demonstrated that adipose tissue Fas signaling is enhanced in obesity. After HFD/ND feeding, hepatic steatosis was more severe in Adi-Fas mice compared to $Fas^{CKI/CKI}$ mice .16S rRNA gene sequencing revealed that the beta diversity of the microbiome was significantly different between Adi-Fas and $Fas^{CKI/CKI}$ mice. At the genus level, there were four significantly different genera between the two groups: *Akkermansia, Lactobacillus, Odoribacter, Anaeroplasma. Akkermansia muciniphila* (Akk), a member of the *Akkermansia* genus, is a well-known beneficial bacterium in the gut microbiota. It can regulate immunological and metabolic functions. We found that the abundance of Akk was significantly decreased in Adi-Fas mice.

Conclusions

Our study has shown that Fas overexpression in the adipose tissue may promote the progression of NAFLD through changes in the abundance and species of the gut microbiota.

Key words NAFLD; obesity; adipose tissue; Fas signaling; gut microbiota

Category: Basic Nutrition& Research

生命早期补充短双歧杆菌 207-1 可缓解小鼠肠道菌群失调并具有长期代谢益处

Supplementation of Bifidobacterium breve 207-1 in early life alleviates intestinal microbiota dysbiosis and has lasting metabolic benefits in mice

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Intestinal microbiota alterations in early life are reported to have lasting metabolic consequences in adulthood, providing potential approaches for the prevention of metabolic diseases. This study investigated whether the short-term use of a potential probiotic strain *Bifidobacterium breve* 207-1 (207-1) could alleviate intestinal microbiota dysbiosis in mice following antibiotic exposure in early life and thus improve long-term metabolism on a high-fat diet (HFD). Exposure to ceftriaxone in the first 2 weeks of life significantly impaired glucose metabolism and intestinal microbiota construction of mice at weaning (4 weeks). Oral administration of 207-1 at 2 to 4 weeks effectively protected mice from damage due to antibiotic exposure, including reducing fasting blood glucose level, improving glucose tolerance, increasing intestinal microbiota diversity, and increasing fecal short-chain fatty acids level. The HFD starting from week 4 to 9 led to significant metabolic disorders in mice such as increased visceral and subcutaneous fat levels, increased liver fat accumulation, impaired glucose tolerance, insulin resistance, and leptin resistance. However, mice exposed to ceftriaxone in early life did not develop more severe disruptions in lipid and glucose metabolism after feeding HFD. Of note, short-term use of 207-1 in the early stage of life improved lipid metabolism after feeding HFD in adulthood, including reduced visceral fat, lower serum cholesterol levels, lower liver triglyceride levels, and increased serum glucagon-like peptide-1 levels; the relative abundance of beneficial intestinal bacteria such as *Ligilactobacillus* and *Dubosiella* was significantly increased in these mice. Collectively, short-term supplementation of 207-1 in early life can alleviate intestinal microbiota dysbiosis and improve glucose metabolism caused by antibiotic exposure, and has a long-lasting metabolic protection effect in mice.

Key words early life; intestinal microbiota; Bifidobacterium; metabolism; high-fat diet

Category: Basic Nutrition& Research

副干酪乳杆菌 207-27 对生命早期抗生素暴露的小鼠远期结肠炎保护作用与机制

The protective effect and mechanism of Lacticaseibacillus paracasei 207-27 on chronic colitis in antibiotic-exposed mice in early life

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Evidence shows that antibiotic exposure in early life increases the risk of IBD by causing intestinal flora dysbiosis and affecting the development of the intestinal immune system. This study aimed to investigate the possible protective effect and mechanism of short- and long-term application of Lactobacillus paracasei 207-27 to ameliorate intestinal flora disorders caused by early-life antibiotic exposure in mice with DSS-induced colitis. In this study, we intervened neonatal mice with Ceftriaxone, and L.paracasei 207-27 was administered two hours after antibiotics. L.paracasei 207-27 were used for continuous gavage for three weeks and six weeks. The first batch of mice was executed on day 21, and the second batch of mice was executed on day 46, after a four-day intervention with 3% DSS to induce colitis.The results showed that on day 21, the alpha diversity of intestinal flora, short-chain fatty acids levels, and splenic immune factor levels were higher in the Ceftri+207-27 group compared to the Ceftri group, with significantly lower serum IL-6 and TNF-α levels. On day 46, in splenic and serum IL-6 and TNF-α levels, the 207-27 short-term group was similarly lower than the Ceftri-DSS group. In colonic IL-17, TNF-α, and INF-γ levels, there was a decreasing trend in the 207-27 short- and long-term groups compared to the Ceftri-DSS group, and the 207-27 long-term group has significantly higher levels of Claudin and sIgA. In conclusion, short-term administration of L.paracasei 207-27 improves intestinal flora composition and effectively alleviates colitis symptoms, and long-term use of L.paracasei 207-27 has a protective effect on the intestinal barrier.

Key words Lacticaseibacillus paracasei 207-27; chronic colitis; antibiotic; early life;

Category: Basic Nutrition& Research

人参对脑卒中后血脑屏障的保护作用

Protective effect of ginseng on the blood-brain barrier after stroke

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Stroke is the leading cause of disability globally and the second leading cause of death in China, with ischemic stroke accounting for 86% of all strokes. Its high incidence imposes a serious burden on society. Chinese medicine ginseng is the root of the plant ginseng of the five-plus family, which has the effect of tonifying vitality, tonifying the spleen and benefiting the lungs, and calming the spirit. Here, we investigate the role of ginseng in mouse ischemic stroke models as well as the mechanism of action. Ginseng extract gavage was performed 24h after mouse MCAO(I/R)(Middle Cerebral Artery Occlusion and Reperfusion) modeling, and administered continuously for 3 days. After 3 days, the area of cerebral infarction decreased, the permeability of the blood-brain barrier decreased, and the tight junction protein Claudin-5(closed protein-5), Occludin, and ZO-1(closed small cyclin 1) decreased. At the same time, the expression of pro-inflammatory factors IL-1β, TNF-α and IL-6 decreased. Therefore, we conclude that ginseng may increase the structure and function of the blood-brain barrier after acute stroke by reducing the inflammatory response.

Key words ginseng, stroke, blood-brain barrier, MCAO(I/R), tight junction protein

Category: Basic Nutrition& Research

超重和肥胖患者血液和血液外泌体中的 miR-3064-5p 与代谢性炎症有平行关系

The miR-3064-5p in Blood and Blood Exosomes Has a Parallel Relationship with Metabolic Inflammation in Overweight and Obese Patients

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Objective: Metabolic inflammation promotes the development of chronic metabolic diseases such as obesity, type 2 diabetes, etc. This study aimed to explore whether miR-3064-5p in blood and blood exosomes has parallel relationship with inflammation in overweight and obese people and to analyze its potential as a marker for metabolic inflammation.

Method: A case-control design was used to recruit volunteers into the case group (BMI≥24, n=73) and the control group (18.5<BMI<24, n=73). The body composition and retrospective dietary questionnaire were determined. The level of miR-3064-5p in blood and blood exosomes and inflammatory cytokines (IL-6/Hs-CRP) in serum were analyzed. The t-test or Mann-Whitney U test was used to compare the differences between the two groups. Spearman rank correlation and multiple regression analysis were used for correlation analysis.

Result: As compared to the control group, overweight and obese volunteers in the case group have significantly higher ($p<0.05$) waist-to-hip ratio (WHR), body fat mass, visceral fat index (VFI), basal metabolism, and skeletal muscle mass, and significantly increased ($p<0.05$) daily intake of energy, fat, carbohydrates, saturated fatty acids, unsaturated fatty acids, n-6 and linolenic acid. Furthermore, volunteers in the case group have significantly elevated ($p<0.05$) levels of miR-3064-5p in blood and blood exosomes, which was positively correlated with BMI, WHR, body fat mass and VFI. The miR-3064-5p level was also significantly associated with obesity (odds ratio of 6.96, 95% CI 3.37-14.37) and overweight (odds ratio of 2.26, 95% CI 1.65-3.10). Meanwhile, volunteers in the case group have significantly higher ($p<0.05$) levels of IL-6 and Hs-CRP which were correlated positively with the miR-3064-5p level in blood and blood exosomes.

Conclusion: The miR-3064-5p in blood and blood exosomes has a parallel relationship with metabolic inflammation in overweight and obese patients, suggesting that it has potentials as a new marker for predicting the development of metabolic inflammation.

Key words Metabolic inflammation; miR-3064-5p; Obesity; Overweight; Cytokines

Category: Basic Nutrition& Research

多组学揭示肥胖易感和肥胖抵抗小鼠肠道菌群和代谢功能图谱

Exploring Gut Microbiota and Metabolomics in Obesity-Prone and Obesity-Resistant Mice: A Multi-Omics Study

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Background and Objectives

The same high-calorie diet does not cause obesity or metabolic disorders in some people (called "obesity-resistant (OR)). Another group of people experience substantial weight gain and metabolic disorders (called "obesity-prone (OP)). In this study, we analyzed the gut microbiota and metabolomics in OP and OR mice to provide a theoretical basis for obesity phenotype differences.

Methods and Study Design

The methods included constructing an OP and OR model by inducing mice with a long-term high-fat diet, and integrating microbial genomics (16S rDNA), metabolomics (serum samples and fecal samples) and pathology methods.

Results

We successfully constructed an OP and OR mice model. We identified the respective dominant bacteria of OP and OR mice, and found that Clostridium sensu stricto, Blautia, Helicobacter, Dubosiella, Phocea, Harryflintia, Roseimarinus, etc. were significantly increased in OP mice; on the contrary, Intestimonas, Duncaniella, etc. were significantly increased in OR mice. In addition, we found that there were differential metabolites in the systemic and gut microbiome-related metabolism of OP and OR mice. These differential metabolites were involved in various metabolic pathways such as amino acid metabolism, energy metabolism, and nervous system. By studying the relationship between the differential intestinal bacteria and metabolites of OP and OR mice, we obtained the relationship pairs that may contribute to the differences in OP and OR phenotypes.

Conclusions

We identified and analyzed the dominant intestinal bacteria, metabolic characteristics and functional spectrum of OP and OR mice, respectively. Furthermore, we elucidated the potential roles of key gut bacteria and metabolites in mice with differential OP and OR phenotypes.

Key words obesity susceptibility, obesity resistance, microbial genomics, metabolomics, gut microbiota

Category: Basic Nutrition& Research

补充维生素D3通过调节肠道菌群的组成改善高脂饮食诱导的小鼠肥胖

Vitamin D3 supplementation improves obesity induced by high-fat diet in mice by regulating the composition of gut microbiota

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Purpose: Individuals with vitamin D (VD) insufficiency have a greater tendency to develop obesity and increase systemic inflammation. Gut microbiota is involved in the regulation of host inflammation and energy metabolism, which plays a role in the pathogenesis of obesity. The present study aimed to evaluate the effects of different doses of VD_3 on body weight, serum lipids, inflammatory factors and intestinal barrier function, and the regulatory effect on gut microbiota in obese mice.

Methods: Male C57BL/6J mice received a normal chow diet (NCD, 10% fat) or high-fat diet (HFD, 60% fat) to induce obesity within 10 weeks. Then, obese mice were supplemented with 5,650, 8,475, or 11,300 IU VD_3/kg diet for 8 weeks. Finally, body weight, average food intake and VD_3 intake, serum and epididymis adipose tissue $25(OH)D_3$, TG, TC, LDL-C, HDL-C, glucose, TNF-α, IL-1β, MCP-1, lipopolysaccharide, zonula occludens-1 and occludin were analyzed. And 16s rRNA analysis was performed to analyze gut microbiota composition in caecum contents.

Results: VD_3 supplementation reduced body weight and the levels of $25(OH)D_3$, TG, TC, HDL-C, TNF-α, IL-1β and lipopolysaccharide, and increased the mRNA relative expression of zonula occludens-1 of caecum in HFD-fed mice. Moreover, VD_3 increased α-diversity, reduced *Firmicutes/Bacteroidetes* ratio and altered microbiota composition by increasing relative abundance of *Bacteroidetes, Proteobacteria, Desulfovibrio, Dehalobacterium, Odoribacter,* and *Parabacteroides,* and reducing relative abundance of *Firmicutes* and *Ruminococcus.* There were significant differences between HFD and NCD groups in several metabolic pathways, including endotoxin biosynthesis, tricarboxylic acid cycle, lipid synthesis and metabolism, and glycolysis.

Conclusions: VD_3 inhibited weight gain, reduced levels of blood lipids and inflammatory factors, improved endotoxemia, gut barrier function and regulated gut microbiota dysregulation in obese mice, with the low and middle internal exposure doses showing better effects than high internal exposure dose in improving gut microbiota dysregulation.

Key words vitamin D; obesity; gut microbiota; inflammation; gut barrier

Category: Basic Nutrition& Research

人参皂苷 Rg2 通过 Akt/FoxO1 途径调节 HepG2 细胞的糖代谢和糖原代谢进而缓解胰岛素抵抗

Ginsenoside Rg2 alleviates insulin resistance by regulating gluconeogenesis and glycogen metabolism via Akt/FoxO1 pathway in HepG2 cells

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Jilin Agricultural University

Background: Ginsenoside Rg2 is a key bioactive compound from Panax ginseng Meyer and shows anti-cancer, antidiabetic, anti-amnestic, and neuroprotective effects. However, the impact of Rg2 on hepatic glucose production via the Akt pathway is not addressed.

Purpose: To investigate the protective effect of Rg2 against insulin resistance via the Akt pathway.

Methods: HepG2 cells were stimulated with 1 μM insulin for 36 h to establish a reliable insulin resistance cell model. Then, Metformin HCL, Rg2, and Akt inhibitor were added to treat the obtained cells. The glucose consumption and glycogen synthase were determined so as to evaluate hepatic glucose production. Moreover, the genes involved in gluconeogenesis, glycogenolysis and glycogenesis were explored with RT-q-PCR and western blot. At last, the critical role of Rg2 in the Akt/FoxO1 pathway was further identified with Akt inhibitor, triciribine.

Results: Our findings suggested that Rg2 decreased hepatic glucose production by activating Akt at Ser473 in HepG2 cells. Akt inactivated FoxO1 by promoting nuclear export and reducing the levels of phosphoenolpyruvate carboxykinase and glucose 6-phosphatase. Moreover, Rg2 enhanced GSK3β phosphorylation and weakened GS phosphorylation via Akt/FoxO1 pathway, thus increasing glycogen synthase.

Conclusion: Rg2 alleviated insulin resistance by inhibiting gluconeogenesis and glycogenolysis and induced glycogenesis via the Akt/FoxO1 pathway in HepG2 cells. Our results highlighted that Rg2 might be utilized to develop healthy foods and prevent diabetes.

Key words ginsenoside Rg2, insulin resistance, gluconeogenesis, glycogenesis, glycogenolysis

Category: Basic Nutrition& Research

生命早期母乳菌群与婴儿肠道菌群构建的关系

The relationship between breast milk microbiota and the construction of infant intestinal microbiota

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Objective:

To examine the relationship between breast milk microbiota and the construction of infant intestinal microbiota.

Methods:

A mother-infant cohort study was conducted from November 2020 to July 2021 in West China Second Hospital, Chengdu, China. 21 mother-infant pairs who were vaginally delivered and exclusive breast fed were included in this study. Infants' stools and breast milk were collected at 0 day, 7 day and 30 day after birth. The 16S rRNA sequencing and bioinformatic analysis was used for identifying the diversity and composition of microbiota, and source tracking analysiswas performed to determine the contribution of breast milk microbiota to infant gut microbiota.

Results:

The alpha diversity indices of microbiota in breast milk were significantly higher than that in infant intestine (adjusted $P<0.01$, respectively), bacterial communities were more closely related between infants' gut and breast milk at day 0, then developed into different communities. At the phylum level, Firmicutes, Actinobacteriota and Proteobacteriashowed similar trend in both infant gut and breast milk within 1 month. At the genus level, the most predominant taxa in infant intestine shipped from Escherichia-Shigella to Bifidobacterium, while Streptococcus in breast milk was stably predominant taxa within first month; and Bifidobacterium showed a similar trend in infant gut and breast milk. Microbial source tracking revealed that, breast milk contributed 40.4% to 50.94% microbes to infant intestine, breast milk and infant gut shared proportion of 60.64% to 67.89% of Bifidobacterium within 1 month.

Conclusion:

These findings suggest that microbiota composition of breast milk and infant intestine differed from each other and both in highly dynamic variation during first month after birth. Breast milk microbiota, particularly Bifidobacterium, influence the breast-fed infants' intestinal microbiota establishment and development, and provide more convincing evidence for microbial contribution of breast feeding.

Key words early life; breast feeding; infant gut microbiota; breast milk microbiota; Bifidobacterium

Category: Basic Nutrition& Research

硒与食管癌：一项基于生信分析的病例对照研究

Selenium and Esophageal Cancer: A Case - control Study Based on Bioinformation Analysis

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Southeast University

Objective

This paper attempts to investigate the relationship between selenium and esophageal cancer (EC) and the role of glutathione peroxidase 3 (GPx3) in it based on the bioinformatic analysis. A case - control study was conducted to verify the relationship between selenium and precancerous esophageal lesions (EPLs).

Methods

Using databases such as GEPIA and TCGA, we clarified the differential expression of GPx3 in EC tissues and normal tissues, screened differentially expressed genes (DEGs), and performed visualization analysis of GO and KEGG pathway enrichment and protein interaction network (PPI). One hundred pairs of dietary and plasma samples from EPLs cases and health controls from Huai'an, Jiangsu were screened, and the level of dietary selenium, and the concentration of plasma selenium and related enzymes in the two groups were analyzed using inductively coupled plasma mass spectrometry (ICP-MS) and enzyme-linked immunosorbent assay (ELISA) kits.

Results

Data from 182 tumor tissues and 286 normal tissues were obtained from the database, and the expression of GPx3 in tumor tissues was found to be significantly lower than that in normal tissues. Further analysis revealed that in EC tissues with high expression of GPx3, DEGs were mainly involved in fat digestion and absorption pathways, and the core protein fatty acid binding protein 1 (FABP1) was significantly downregulated. Our case-control study found that dietary selenium levels and plasma selenium concentration were not associated with the EPLs risk. However, both the decrease concentration in GPx3 and the increase in FABP1 were positively correlated with the EPLs risk in a significant manner.

Conclusion

The validation of bioinformatic analysis by our case - control study suggests the potential of selenium to play a role in EC prevention and control at the stage of EPLs. In addition, whether GPx3 can affect EC through the expression of FABP1 needs to be further studied.

Key words esophagus cancer; esophageal precancerous lesions; selenium; GPx3; FABP1

Category: Basic Nutrition& Research

肠道菌群特征及小肠 RNA 甲基化水平下降与高脂饮食压力下 GLP1 分泌紊乱之间的关联研究

An associations between the disordered gut microbiota , decreased small intestinal RNA methylation level and disturbed GLP1 secretion under high-fat diet stress

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High-fat diet disturbs the microbiota, causing metabolic disorders and promoting the occurrence and development of obesity through direct and/or indirect interactions between the microbiota, the metabolites and local or remote tissues. Reduced glucagon-like peptide-1 (GLP1) level is often observed in obese mice, which is proposed to be associated with microbiota and their metabolites. Numerous studies have revealed the critical role of epigenetic modifications in gene expression and metabolism, with m6A methylation on RNAs as the most abundant modification across their metabolism. In the present study, we found that the expression of small intestinal gcg and pc3, two key genes for GLP1 expression, were significantly downregulated in obese mice, which should be directly responsible for the reduced GLP1 level. Immunohistochemistry analysis indicated that high-fat diet slightly increased the density of enteroendocrine L cells in the small intestine, implying that the decreased GLP1 levels was not caused by changes in the number of L cells. Instead, the small intestine m6A level as well as the expression of known “writers”, mettl3/14 and wtap, were found to be positively correlated with the expression of gcg and pc3. Fecal microbiota transplantation with feces from normal and obese mice daily to the pseudo-sterile mice reveled that high-fat diet aggravated microbial dysbiosis, contributing to the reduced epigenetic modification. However, as the most direct and universal methyl donor, production of fecal S-adenosylmethionine was neither affected by the different dietary patterns nor their shaped microbiota, while S-adenosylmethionine levels in intestinal tissues are associated with different dietary patterns. These results suggested that the decreased GLP1 level in obese mice may be mediated by the microbiota-regulating epitranscriptome, and highlighted the epitranscriptomic modifications as an additional level of interaction between diet and the individual health.

Key words gut hormones; Western diet; m5C; m6A; obesity

Category: Basic Nutrition& Research

限制时间饮食对阿尔兹海默症认知功能障碍的改善作用及肠脑轴机制研究进展

Time-Restricted Feeding Alleviates Cognitive Impairment in Alzheimer's Disease: Exploring the Role of Gut-Brain Axis Mechanism

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Abstract

Background and Objectives: In recent years, research on improving brain cognitive function through non-pharmacological interventions such as time-restricted feeding (TRF) has become a hot topic in the field of nutrition. The gut and brain interact through the nervous and circulatory systems. Our previous studies have shown that intermittent fasting can regulate the gut microbiota, increase short-chain fatty acids, tauroursodeoxycholic acid, and indole-3-propionic acid, and ameliorate insulin resistance-induced neuronal energy metabolism dysfunction. However, it is still unclear whether TRF can regulate cognitive dysfunction related to Alzheimer's disease (AD) via regulating the gut-brain axis.

Methods and Study Design: Based on AD transgenic animal models, we conducted a 3-month TRF intervention, utilizing behavioral tests, multi-omics analysis, microbiota removal, PET/CT, and inhibitors/lentiviral intervention to analyze the improvement of cognitive dysfunction in AD and the gut-brain axis mechanism.

Results: The current study found that TRF improved cognitive function in AD mice and reduced the excessive deposition of Aβ. TRF intervention reshaped the gut microbiota of AD mice and increased propionic acid levels in feces. Further validation revealed that propionic acid and *Bifidobacterium pseudolongum* (a propionic acid-producing bacterium) supplementation yielded similar results to TRF in improving AD cognitive function. TRF intervention restored brain propionic acid metabolism and inhibited neuroinflammation. Concurrently, our additional research also demonstrates the critical mediating role of the tryptophan metabolite indole-3-propionic acid in the improvement of AD cognitive function through intermittent fasting.

Conclusion: Our research revealed that time-restricted feeding effectively improves AD-related cognitive dysfunction, partly through regulating the expression of neuroprotective gut microbial metabolites. This study provides new theoretical foundations for brain health nutrition intervention strategies through regulating dietary rhythms or intervening in gut microbiota homeostasis.

Key words AD; Gut-Brain Axis; Intermittent Fasting; Propionic Acid; Indole-3-Propionic Acid

Category: Basic Nutrition& Research

中国健康儿童肠道菌群年龄相关的变化

Age-related changes in gut microbiota from healthy Chinese children

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Introduction The composition and function of human gut microbiota is influenced by genetics and lifestyles from birth to the childhood. The age-related alterations in microbiomes vary across populations, our current understanding of the composition and stability of the human gut microbiota is based largely on studies of infants and adults living in developed countries. In contrast, information regarding the gut microbiota in Chinese healthy children is limited.

Objectives In this study, we aim to investigate the age-related changes in gut microbiota in the healthy children living in the northwest region in China.

Methods We conducted shotgun metagenomic sequencing of fecal samples, as well as fecal and blood metabolomics to characterize the gut microbial communities of 100 healthy Chinese children aged 0-12 living in the northwest region in China.

Results We identified a significantly change in the gut microbiota in the children with the age. At the phylum level, the abundances of Actinobacteria were significantly reduced with age increased in children (p value <0.05); at the genus level, the abundances of Eggerthella, Erysipelatoclostridium, Tyzzerella, Flavonifractor, and Bididobacterium were significantly reduced with the age increased (p value <0.05), while Coprobacer, Lactobacillus, Oscillibacter, Odoribacter and Christensenella were significantly increased with the age increased (p value <0.05). Importantly by combining the fecal and blood metabolism, we found caffeine metabolism and steroid hormone biosynthesis were both significantly correlated with age. Moreover, 32 metabolic pathways presented significantly different during aging were observed.

Conclusion Collectively, our study demonstrated age-related changes in children’s gut microbiota using the multiomics analysis, as well as the connections between metabolites and host-microbe interactions, which giving a better understanding of alterations in the human microbiome in a Chinese population.

Key words age; gut microbiota; metabolomics; multiomics analysis; children

Category: Basic Nutrition& Research

三种海藻岩藻聚糖的化学成分及抗氧化能力的测定与比较

Determination and Comparison of Chemical Composition and Antioxidant Capacity of Fucoidan Extracted from Three Species of Seaweed

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Objective: The main aim of this study was to focus on the fucoidan extracted sample (S-5) from New Zealand sporophyll Undaria pinnatifida, and to determine and compare its chemical composition and biological activities with other commercial fucoidan samples of different origin and species. Methods: The methods of quality control were compared to testing standard methods for fucoidan SC/T 3404-2012, published by the People's Republic of China Aquatic Products Industry.

Results: The fucose content from the fucoidan sample S-5 was 44.6 %, and its percentage content was the highest value in all the monosaccharide contents. For the content of sulphate, fucoidan sample S-5 contains the highest percentage of sulphate contents (32.0 %) as compared to the other fucoidan commercial products. Collectively, the aforementioned results may indicate that the three factors which relate to differences between the composition of fucoidan include the extraction method, the seaweed species and its origin. According to the metal analysis results, toxic metal element content, including Pb, As, Hg, Cd and Cr, of fucoidan sample S-5 was significantly and statistically lower than the other fucoidan samples. Pertaining to antioxidant activity, all fucoidan samples generated antioxidant effects in the dose-dependent manner for the anti-oxidant assays. Notably, because fucoidan sample S-5 had the highest sulphate content, it also generated the highest antioxidant effects in comparison to all other fucoidan samples. This was especially true in the treatment concentration range of 0 to 62.5 μg/mL, suggesting that this concentration range is the most effective at producing antioxidant effects from S-5.

Conclusion: The unique environmental conditions made the fucoidan sample extracted by New Zealand sporophyll Undaria pinnatidifa different in its chemical composition, with higher antioxidant activity and less presence of toxic metal elements. Therefore, the sporophyll Undaria pinnatifida from New Zealand is presented as the better source to develop fucoidan-based nutraceutical products.

Key words Fucoidan, Undaria pinnatifida, Seaweed

Category: Basic Nutrition& Research

酿酒酵母和甘露寡糖对生命早期抗生素暴露小鼠远期结肠炎的缓解作用

Saccharomyces cerevisiae and mannan oligosaccharides alleviate long-term DSS-induced colitis in early-life antibiotic-exposed mice

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Aims: To investigate the possible protective effects and mechanisms of *Saccharomyces cerevisiae* and mannan oligosaccharides against long-term colitis in antibiotic-exposed mice in early life.

Methods: Newborn Balb/c mice in the NS-water, NS-DSS, Ceftri-DSS, Ceftri+SC(s)-DSS, Ceftri+SC(l)-DSS and Ceftri+SC+MOS(l)-DSS groups received the corresponding interventions from birth. After 3 weeks of age, mice in the Ceftri+SC(l)-DSS and Ceftri+SC+MOS(l) groups continued to receive SC or SC+MOS intervention, while mice in the rest of the groups stopped the intervention. In 6 weeks-6 weeks+4 days, except for the NS-water group, the drinking water in all other groups was replaced with 3% DSS to induce colitis. HE pathological staining of colonic tissues after DSS treatment was obtained and scored for inflammation. The expression of anti-inflammatory cytokines (IL-5, IL-10, IL-13, TGF-β) and pro-inflammatory cytokines (IL-6, IL-12 (p40), IL-17a, TNF-α, IFN-γ) in colon and spleen tissues was measured. Meanwhile, the levels of cytokines (IL-5, IL-6, IL-10, IL-13, IL-17a, TNF-α, TGF-β) in serum were measured. Using 16s RNA sequencing technology to analyze the change of intestinal microbiota.

Results: Inflammation scores raised significantly in all DSS-induced groups, and the Ceftri+SC(s)-DSS, Ceftri+SC(l)-DSS, and Ceftri+SC+MOS(l)-DSS groups all had lower inflammation scores than the Ceftri-DSS group. *S. cerevisiae* and MOS increased the expression and content of IL-10, IL-13 and TGF-β and decreased the expression and content of IL-17a, TNF-α and IFN-γ). Long-term use of *S. cerevisiae* increased the relative abundance of beneficial intestinal bacteria *Akkermansia* and *Blautia*.

Conclusions: *S. cerevisiae* and MOS alleviate long-term DSS-induced ulcerative colitis in early-life antibiotic-exposed mice. The alleviating effect was mainly through modulating immunity.

Key words early life; antibiotic-exposed; colitis; Saccharomyces cerevisiae; Mannan oligosaccharides; immune response; gut microbiota

Category: Basic Nutrition& Research

中国成年女性膳食硒水平及其与2型糖尿病的关系研究
The dietary Se status and its relationship with T2DM in Chinese Female Adult

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Background: Selenium (Se) plays a crucial role in human health. Determining the plasma/dietary Se levels and describing the distribution of dietary Se intake in Chinese female adults by using the nationally representative data has not been reported. Moreover, the association between dietary Se intake and type 2 diabetes mellitus (T2DM) is controversial. Thus, the present study aimed to describe the distribution of dietary Se intake, analyze the possible factors related to dietary Se levels, and observe the association between dietary Se intake and T2DM in Chinese female adults. Method: Using the multistage stratified random sampling method, a total of 3015 female adults from the China Nutrition and Health Surveillance in 2015 (CNHS 2015) were included. The plasma Se concentrations were detected by inductively coupled plasma mass spectrometry. Daily Se intake was calculated from plasma Se concentrations using the formula lg(Y) = 1.624 lg(X) + 3.389. Results: The P50 (P25-P75) of dietary Se level was 55.19 (40.51-70.25) μg/d. Dietary Se intake varied among subgroups, including nationality, location, latitude, residence region, and education level. The multivariate-adjusted OR of T2DM was 2.025 (95% CI: 1.158-3.541, P＜0.01) for the highest quartile of dietary Se intake in comparison with the lowest quartile. Conclusion: The median dietary Se intake in Chinese female adults was lower than Chinese recommended nutrient intake (RNI, 60μg/d). There were 41.09% of the population having Se dietary levels lower than the Chinese estimated average Requirement (EAR, 50μg/d) and 58.41% lower than the RNI. Nobody exceeded the tolerable upper intake levels (400μg/d, tolerable upper intake level) in our population. Besides, the study supports that a higher dietary Se intake may increase the risk of T2DM in Chinese female adults.

Key words Dietary Se; Chinese Female Adult; Type 2 Diabetes Mellitus

Category: Basic Nutrition& Research

硒缺乏通过 GPx1/H2O2/NF-κB 途径增加肾脏 AT1 受体功能导致高血压的作用及机制

Selenium deficiency causes hypertension by increasing renal AT1 receptor expression via GPx1/H2O2/NF-κB pathway

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Background and objectives: Epidemiological studies show an association between low body selenium and the risk of hypertension. However, whether selenium deficiency causes hypertension remains unknown. Our present study determined the role and mechanism of selenium deficiency in the pathogenesis of hypertension.

Methods and results:

16 weeks of selenium-deficient diet in Sprague-Dawley rats developed hypertension, accompanied with decreased sodium excretion. The hypertension of selenium-deficient rats was associated with increased renal angiotensin II type 1 receptor (AT1R) expression and function that was reflected by the increase in sodium excretion after the intrarenal infusion of the AT1R antagonist candesartan. Selenium-deficient rats had increased systemic and renal oxidative stress; treatment with the antioxidant tempol for 4 weeks decreased the elevated blood pressure, increased sodium excretion, and normalized renal AT1R expression. Among the altered selenoproteins in selenium-deficient rats, the decrease in renal glutathione peroxidase 1 (GPx1) expression was most prominent. GPx1, via regulation of NF-κB p65 expression and activity, was involved in the regulation of renal AT1R expression because treatment with dithiocarbamate (PDTC), an NF-κB inhibitor, reversed the up-regulation of AT1R expression in selenium-deficient renal proximal tubule (RPT) cells. The up-regulation of AT1R expression with GPx1 silencing was restored by PDTC. Moreover, treatment with ebselen, a GPX1 mimic, reduced the increased renal AT1R expression, Na+-K+-ATPase activity, hydrogen peroxide (H_2O_2) generation, and the nuclear translocation of NF-κB p65 protein in selenium-deficient RPT cells.

Conclusions: Our results demonstrated that long-term selenium deficiency causes hypertension, which is due, at least in part, to decreased urine sodium excretion. Selenium deficiency increases H_2O_2 production by reducing GPx1 expression, which enhances NF-κB activity, increases renal AT1R expression, causes sodium retention and consequently increases blood pressure.

Key words Angiotensin II type 1 receptor, Hypertension; Kidney; Oxidative stress; Selenium deficiency

Category: Basic Nutrition& Research

天津某区50-60岁中老年人能量需要量研究

The study of energy metabolism of 50-60y people in one district of Tianjin

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[Abstract] Objective: To measure the basal metabolism and resting metabolism energy consumption, as well as daily exercise energy consumption of the 50-60 years old people, and to accumulate basic data for revising Chinese DRIs. Objects: 20 rural middle-aged and elderly people aged 50-60 year in a certain district of Tianjin, with half male and half female. Male age: 55.6±2.5 years old,

height: 168.6±5.1 centimeters,weight:64.1±5.6kilograms;female age: 55.2±3.2 years old, height: 155.9±2.4 centimeters, weight: 55.5±3.3 kilograms. Methods: Measurement of basal metabolism energy consumption: Every morning before the start of the measurement, warm up the cardiopulmonary function meter for 30 minutes. After each study subject breathes steadily, continue to measure for 15-20 minutes. Measurement of resting metabolic energy consumption: the resting metabolic energy consumption of each subject was measured 2 hours after breakfast every morning. 30 minutes before the measurement, the subjects lay flat and did not perform any activities. Then the resting metabolic energy consumption of each subject was measured by measuring basal metabolism energy consumption. The average value of each subject was taken for 2 consecutive days, and the data of basal metabolism energy consumption and resting metabolism energy consumption were finally obtained. Measurement of exercise energy consumption: During the experiment, each study subject wore an accelerometer at 8 am in the morning. After continuously wearing it for 4 days, the accelerometer was removed to obtain the daily exercise energy consumption of each study subject. The average of the 4-day energy consumption results was calculated to obtain the daily exercise energy consumption of each study subject. Results: basal metabolism: 1619.80± 277.28 kcal for male and 1018.16 ± 195.60 kcal for female; Resting metabolic male: 1867.83 ± 220.36 kcal; Female: 1178.95 ± 203.83 kcal; Daily exercise energy consumption for males: 447.89 ± 250.38 kcal; Female: 356.24 ± 172.52 kcal.

Key words basal metabolism resting metabolism exercise energy consumption

Category: Basic Nutrition& Research

探究肠道微生物及代谢产物与认知功能之间的关系：一项孟德尔随机化研究

Investigating causal associations among gut microbiota, metabolites and cognitive impairment: A Mendelian Randomization Study

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Background: Recent studies have indicated that the gut microbiota was associated with cognitive impairment through the gut-brain axis, among which metabolic pathways played an important role. However, the underlying causality remained unclear.

Objectives: Our study aimed to evaluate potential causal relationships among gut microbiota, metabolites, and cognitive impairment through a Mendelian randomization approach.

Methods: We selected genetic variants associated with gut microbiota traits (N=18340) and gut microbiota-derived metabolites (N=7824) from genome-wide association studies, and cognitive performance data were obtained from a recent study including 373617 participants. Five recognized Mendelian randomization methods were applied to assess causal estimates, with the inverse-variance weighted regression as the primary method. Moreover, we performed sensitivity analyses to test the robustness of causal estimates.

Results: In this study, the significant associations of greater abundance of *Actinobacteria* (OR, 0.955; 95%CI, 0.930-0.982), *RuminococcaceaeUCG005* (OR, 0.968; 95%CI, 0.943-0.993), *Roseburia* (OR, 0.964; 95%CI, 0.934-0.995), and *Collinsella* (OR, 0.966; 95%CI, 0.934-0.998) with lower risk of cognitive impairment were found. While higher levels of *Rikenellaceae* (OR, 1.039; 95%CI, 1.010-1.069), *LachnospiraceaeUCG001* (OR, 1.031; 95%CI, 1.007-1.054), *Dialister* (OR, 1.040; 95%CI, 1.006-1.075), *Rhodospirillaceae* (OR, 1.029; 95%CI, 1.004-1.056), *Faecalibacterium* (OR, 1.029; 95%CI, 1.003-1.057), *Barnesiella* (OR, 1.030; 95%CI, 1.003-1.053), *Bacteroidaceae* (OR, 1.037; 95%CI, 1.001-1.076), and *Bacteroides* (OR, 1.037; 95%CI, 1.001-1.076) were associated with higher risk of cognitive impairment. Meanwhile, we also identified suggestive associations between 2 gut microbiome-dependent metabolites (acetylcarnitine and allantoin) and cognitive impairment.

Conclusion: The present study highlights a landscape of causal relationships among gut microbiota, gut metabolites, and cognitive impairment by a two-sample Mendelian randomization approach. These findings might provide new targets for treatments and offer valuable insights for further studies on the underlying mechanisms.

Key words gut microbiota; metabolites; cognitive impairment; Mendelian randomization

Category: Basic Nutrition& Research

成人血清25-羟基维生素D缺乏与高脂血症相关性研究

Study on the correlation between serum 25-hydroxyvitamin D deficiency and hyperlipidemia in adults

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Objective To explore the relationship between serum vitamin D deficiency and the risk of hyperlipidemia in adults. Methods A total of 2072 eligible subjects over 18 years of age were included in the multi-stage sampling method. Serum 25(OH)D levels and lipid metabolism indexes were detected, and relevant demographic and physical indicators were collected. Serum 25(OH)D levels were divided into adequate, insufficient, and deficient groups. The correlation between serum 25(OH)D level and hyperlipidemia was analyzed statistically. Result The rate of hyperlipidemia was 42.18%, while the rate of vitamin D deficiency was 19.88%, and the rate of vitamin D deficiency was 23.68% in patients with hyperlipidemia. The incidence of hyperlipidemia was significantly higher in subjects with vitamin D deficiency than in patients with vitamin D sufficiency (23.68% vs 17.11%, P = 0.001). After adjusting for age, region, exercise, BMI, fasting blood glucose, and blood pressure, lowering serum 25(OH)D concentration significantly increased the risk of hyperlipidemia (P = 0.0481), and the risk of dyslipidemia increased by 0.842 times for every 10 ng/mL decrease in serum 25(OH)D level (95%CI: 0.728,0.974). After further stratification of hyperlipidemia, compared with the vitamin D adequate group, the risk of total cholesterol abnormality and triglyceride abnormality were 1.459 and 1.578 times of the vitamin D deficiency group after multivariate adjustment. For every 10 ng/mL decrease in serum vitamin D level, the risk of total cholesterol abnormality and triglyceride abnormality were 1.459 and 1.578 times of the vitamin D deficiency group. Abnormal total cholesterol and triglyceride increased the risk by 0.817 times and 0.793 times; There was no significant difference between vitamin D adequate and vitamin D deficient groups in the stratification of LDL and HDL abnormalities. Conclusion Serum vitamin D deficiency may be an independent risk factor for the high incidence of hyperlipidemia in adults.

Key words Vitamin D; hyperlipidemia; Total cholesterol; triglycerid

Category: Basic Nutrition& Research

运动对 TAMO 诱导的 APP/PS1 小鼠高血压的保护作用

Trimethylamine N-oxide induced hypertension in APP/PS1 mice and protective role of voluntary exercise

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Background and Objectives: The effects and potential mechanisms of trimethylamine N-oxide (TMAO) intervention on blood pressure require full exploration. This study aimed to investigate whether TMAO could induce hypertension via the renin-angiotensin system (RAS) in APP/PS1 mice, and whether exercise can reverse TMAO-induced hypertension.

Methods and Study Design: APP/PS1 Mice were randomly assigned into three experimental groups, i.e. control (CON), trimethylamine N-oxide (TMAO) and voluntary exercise (EX) with a total of 12 weeks intervention. A tail-cuff Method , Visitech system Corporation was used to measure systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP and pulse in the conscious mice. Bile acid concentrations in feces were determined via UPLC-MS. Key markers associated with hypertension in kidney were measured via Western blot.

Results: We observed that TMAO induced increased systolic blood pressure in mice, accompanied by insulin resistance and basal metabolic disorders. In the kidney, the expression of angiotensinogen and ACE1 protein was significantly up-regulated, SOD activity was decreased, MDA content was significantly increased, and renal tissue fibrosis was observed. Meanwhile, the expression of FXR and TGR5 protein in colon decreased significantly, and the metabolism of fecal bile acids was abnormal. Exercise treatment was found to reduce systolic blood pressure, increase SOD activity, decrease MDA content and improve kidney injury. An upregulated colonic FXR and TGR5 protein level after exercise treatment resulted in the suppressed bile acid (BA) synthesis. Moreover, Exercise treatment decreased total fecal BA contents, especially fecal secondary BA levels, mainly including muro-cholic acid, hyodeoxycholic acid, 6-Keto-lithocholic acid and 7-Keto-lithocholic acid, and elevated dehydro-lithocholic acid.

Conclusions: TMAO induced hypertension by activating the RAS. Voluntary exercise could reverse the ACE-AngⅡ-AT1R axis, renal injury and BA metabolism induced by TMAO, proposing a novel mechanism for hypertension prevention.

Key words trimethylamine N-oxide, hypertension, voluntary exercise, renin-angiotensin system, bile acid metabolism

Category: Basic Nutrition& Research

人参皂苷提取物通过改善线粒体功能和激活 AMPK 信号通路缓解游离脂肪酸诱导的 HepG2 细胞非酒精性脂肪肝病

Ginsenoside extract alleviates nonalcoholic fatty liver disease by promoting mitochondrial function and activating the AMPK pathway in free fatty acid-induced HepG2 cells

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Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease and is closely associated with the development of various metabolic diseases such as obesity. Hepatic steatosis, oxidative stress, and mitochondrial dysfunction are the main manifestations, and alleviating lipid disorders by inhibiting fatty acid synthesis (FASN) and reducing fatty acid oxidation are effective ways to hinder the process of NAFLD. Ginseng is a valuable medicinal herb rich in many bioactive components such as ginsenosides. It has been reported that ginsenosides Rg1 and CK can reduce lipid accumulation. The moderate cost of ginsenoside extract (GE) makes it more suitable for application than monomer. However, the effect and mechanism of GE on NAFLD are less concerned. In this study, free fatty acid (FFA) induced HepG2 cells were used as the model for NAFLD to investigate the effects and mechanisms of GE. The results suggest that GE exerts antioxidant in FFA induced HepG2 model. Moreover, GE treatment can significantly inhibit hepatic lipid accumulation, reduce reactive oxygen species (ROS) generation, and improve mitochondrial function. Furthermore, GE promotes AMPK phosphorylation, downregulates the expression of sterol regulatory element binding protein-1c (SREBP-1c), FASN, and dperoxisome proliferator activated receptor gamma (PPARγ). The changes contribute to inhibiting fatty acid synthesis and promote fatty acid catabolism. Our findings suggest that GE has the potential for the treatment of NAFLD.

Key words ginsenoside extract; Non-alcoholic fatty liver disease; HepG2; AMPK pathway; mitochondrial function

Category: Basic Nutrition& Research

植物性饮食可以降低胃癌前病变的风险：基于饮食模式评分和粪便代谢组学的新证据

Plant-Based Diet can reduce the risk of Gastric Precancerous Lesions: A New Evidence from Case-control study based on Dietary Pattern Scoring and Fecal Metabolic Profiling

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Background: The relationship between plant-based diet indices and gastric precancerous lesions risk remains unclear. Metabolomics can identify biomarkers of PDIs and GPL and strengthen understanding of the potential mechanisms.

Objectives: The present study aimed to explore the relationship between three indices, including overall plant-based diet, healthy plant-based diet, unhealthy plant-based diet, and GPL.

Methods: In this case-control study, 1,130 subjects were included using 1:1 propensity score matching for age and sex. PDIs were calculated from FFQs. Odds ratios and 95% confidence intervals was calculated using logistic regression. Fecal metabolites of 58 participants were profiled using untargeted metabolomics. With VIP value > 1, log2Fold change > 1 or < -1, t-test ($p < 0.05$) as the standard, the differences in metabolites between the PDIs and case-control groups were screened. Pathway analysis relies on the KEGG database. Pearson's correlation analysis was used to evaluate correlations.

Result: The highest hPDI had lower odds of GPL after controlling for potential confounders (OR, 0.227; 95% CI, 0.112 - 0.457). In contrast, higher the uPDI, higher was the risk of GPL (OR, 2.964; 95% CI, 1.649 - 5.328). Metabolomic analysis identified six different substances between the patients and control group, and KEGG enrichment analysis revealed D-arginine and D-ornithine metabolism ($p = 0.0067$), linoleic acid metabolism ($p = 0.017$), biosynthesis of unsaturated fatty acids ($p = 0.042$), and arginine and proline metabolism ($p = 0.047$) have changed. The correlation analysis results showed that luteolin 7-sulfate may be used as a biomarker for the association between PDIs and GPL, and stable differences in N-acyl amides with PDIs has not been reported before.

Conclusions: Our found a negative correlation between PDIs and GPL risk, and considered luteolin 7-sulfate as a marker between a plant-based diet and GPL. The results support the benefits of a plant-based diet in preventing GPL.

Key words Gastric Precancerous Lesions; Plant-based diet; Metabolomics; Dietary pattern; Case-control study

Category: Basic Nutrition& Research

生命早期补充婴儿双歧杆菌与 2'-岩藻糖基乳糖对小鼠肠道菌群、肠道发育及免疫功能具有潜在的长期益处

Bifidobacterium infantis and 2'-Fucosyllactose supplementation in early life may have potential long-term benefits on gut microbiota, intestinal development, and immune function in mice

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Background: The health benefits of nutritional interventions targeting the gut microbiota in early life are transient, such as probiotics, prebiotics, and synbiotics.

Objective: This study sought to determine whether supplementation with B. infantis 79 (B79), 2'-fucosyllactose (2'-FL), or both would lead to persistent health benefits in neonatal BALB/c mice.

Methods: Neonatal mice were gaveged from birth to postnatal day (PND) 21, and received four times of intraperitoneal injections of Ovalbumin (OVA) from PND 22 to 49, and sacrificed at PND 21 or 56. The neonatal mice were divided into control group, B79 group, 2'-FL group and B79 + 2'-FL group, which were treated with normal saline, B79 bacterial suspension, 2'-FL solution or mixed solution of B79 and 2'-FL respectively. The intestinal development, immune function and gut microbiota of mice were measured.

Results: We found that at postnatal day (PND) 21, Ki67 and MUC2 expression increased while total serum IgE content decreased in the B79, 2'-FL, and B79+2'-FL groups. The gut microbiota's structure and composition altered as well. The levels of propionic acid, sIgA, and IL-10 increased in the 2'-FL group. Moreover, butyric acid content increased while IL-6, IL-12p40 and TNF-a decreased in the B79+2'-FL group. At PND 56, Ki67 and MUC2 expression increased while the gut microbiota remained altered in all three groups. The serum total IgG level increased only in the B79+2'-FL group.

Conclusion: Early life supplementation with B79, 2'-FL, or their combination persistently alters the gut microbiome and promotes intestinal development in mice. The immunomodulatory capacity of B79 and 2'-FL occurs during weaning, and their combination may persist into adulthood.

Key words Bifidobacterium infantis; Human milk oligosaccharides; intestinal development; gut microbiota; immune function

Category: Basic Nutrition& Research

一种植物源性配方对胃癌前病变大鼠肠道微生物组的影响

Effects of Plant-Based Medicinal Food on gut microbiome in rats of Precancerous Lesions of Gastric Cancer model

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Background：The Plant-Based Medicinal Food (PBMF) tested in this study is a novel product formulated by 12g Coix seed, 12g Lentinula edodes, 12g Asparagus officinalis L., 12g Houttuynia cordata, 12g Dandelion, and 9g Grifola frondosa. Although the protective effects of natural plants or edible foods on gastric carcinoma were proved, and dysbiosis of the gut microbiota is also reported in gastric carcinogenesis, little is known about whether gut microbiota is a regulatory target for natural plants in blocking carcinogenesis. Therefore, the study aims to explore the modulation of PBMF on gut microbiota in Precancerous Lesions of Gastric Cancer (PLGC) rats.

Methods: A model of PLGC was established in Wistar rats using a combination of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) in drinking water and 8% NaCl diet for 20 weeks. The establishment of PLGC model was evaluated by histopathological evaluation of gastric tissue. Surviving PLGC rats were randomly divided into model control group, PBMF low-dose, medium-dose, and high-dose groups, and all rats were fed normal drinking water ad libitum, which lasted 14 weeks. Histopathological changes of gastric tissues were evaluated by HE staining. The gut microbiome was evaluated by 16S rDNA gene sequencing of feces samples.

Results: The PLGC rat model was successfully established. Following PBMF administration, inflammation and defects of the mucosa were reduced, the degree of atrophy and atypical hyperplasia of gastric tissues were relieved, pseudo-pyloric metaplasia and dysplasia were rare. PBMF significantly increased the abundance of Ruminococcus and Turicibacter, while decreasing Bacteroides and Escherichia-shigella.

Conclusions: PBMF alleviates the pathologic lesion of PLGC. The mechanism of action is partially regulated by the gut microbiome, manifested as increasing abundance of probiotics such as Ruminococcus and Turicibacter, as well as the decreasing abundance of conditional pathogens such as Bacteroides and Escherichia Shigella.

Key words Plant-Based Medicinal Food, Precancerous Lesions of Gastric Cancer, Histopathological examination of the gastric tissue, 16S rDNA gene sequencing, Gut microbiota.

Category: Basic Nutrition& Research

结直肠癌患者脂代谢相关差异表达的 LncRNAs 筛选和分析

Comprehensive Analysis of Differentially Expressed LncRNAs associated with Lipid Metabolism in Patients with Colorectal Cancer

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Abstract:Colorectal cancer (CRC) is one of the most common cancers worldwide and is related to diet and obesity.Currently, crosstalk between lipid metabolism and CRC has been reported; however, the specific mechanism is not yet understood. In this study, we screened differentially expressed long non-coding RNAs (lncRNAs) and mRNAs from primary cancer, paracancer, and white adipose tissue of CRC patients. We screened and analyzed the genes differentially expressed between primary and paracancer tissue and between paracancer and white adipose tissue but not between primary and white adipose tissue. We identified a lncRNA (MIR503HG) that may be involved in the crosstalk between CRC and lipid metabolism through exosome delivery. Despite the limited sample size in this study, the findings raise the possibility of crosstalk between lipid metabolism and CRC through the exosomal delivery of lncRNAs.

Key words colorectal cancer; lncRNA; white adipose tissue; high-throughput sequencing; bioinformatics

Category: Basic Nutrition& Research

基于脂质组学对不同泌乳期绵羊乳中特征脂质的定性和定量比较

Lipidomics-based study of the differences in lipid composition between ewe colostrum and mature milk and screening for its biomarkers

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Background and Objectives Ewe milk, a gradually valued source of special quality small variety milk, has incrementally attracted the attention of researchers because of its nutritional abundance and distinct characteristics. In recent years, with the trend of consumer upgrading in the mother and baby industry, the infant formula market is also heating up rapidly. However, there are few international studies on non-ruminant small species milk sources, and few studies have been reported on the nutritional composition of Chinese ewe milk and its mechanisms of change and nutrition in relation to lactation. Methods and Study Design In this study, a lipidomic technique based on ultra-high performance liquid chromatography coupled with a triple quadrupole mass spectrometry was used to analyze the lipid composition in ewe milk at different lactation periods. Results Herein, 877 lipids assigned to 26 subclasses were identified in ewe colostrum and mature milk. A total of 606 peaks in positive ion mode and 271 peaks in negative ion mode were detected, 108 significantly different lipids were investigated (variable importance in projection > 1.0, fold change ≥ 2 or ≤ 0.5, and P < 0.05). Absolute quantitative analysis of differential lipids showed that lipid subclasses such as PC, PE, LPE, HexCer and TG were significantly increased in ewe mature milk. Four potential lipid biomarkers, namely, LPE(0:0/16:0), LPE(16:0/0:0), Carnitine(C14:1), and Carnitine(C18:1), were selected from the 108 significantly different lipids based on fold change values. Conclusions Analysis of the related metabolic pathways of the significantly different lipids revealed that they mainly affect vitamin digestion and absorption, fat digestion and absorption, and cholesterol metabolic pathways. Our results improve the understanding of the differences between ewe colostrum and mature milk and provide effective precision nutrition information for functional studies of ewe milk and related product development.

Key words Lipidomics; ewe colostrum; ewe mature milk; differential lipids; precision nutrition

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丁酸盐通过调控肠道黏膜屏障和神经炎症改善 LDLR-/- 小鼠认知功能的机制研究

Ameliorative effects of butyrate on cognitive impairment via regulation of gut mucosal barrier function and neuroinflammation in LDLR-/- mice

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Short-chain fatty acids, the main metabolites produced by bacterial fermentation of dietary fiber, possess neuroactive properties. The present study aimed to investigate if and how intestinal mucosal barrier function, neuroinflammatory signaling and tryptophan metabolism mediate butyrate's effect on the brain's cognitive function in a mouse model. Sixteen LDLR knockout mice were fed with an atherosclerotic diet and concomitantly treated by intragastric administration with either normal saline as model group or 400mg/kg/day sodium butyrate for 8 weeks. In the intestinal tissue, butyrate ameliorated mucosal barrier function, increased expression of tight junction protein, and inhibited inflammatory pathways by targeting the toll-like receptor 4 signaling and the nod-like receptors domain containing 3 inflammasome. Consequently, butyrate reduced not only the serum level of lipopolysaccharide but also its capability to cross the blood-brain barrier, leading to the suppression of both tau phosphorylation and neuroinflammation in the cortex and hippocampus. Subsequently, butyrate delayed cognitive impairment via decreasing latency to the platform and lengthening swimming distance in the target quadrant. Nevertheless, butyrate showed no effect on serotonin, indoleacetic acid, L-kynurenine, niacinamide, and their metabolites, indicating that the observed effects on cognitive function are unrelated to the tryptophan pathway. In summary, the present study provided the novel experimental evidence that butyrate played a neuroprotective role by improving intestinal mucosal barrier function and reducing the penetration of intestinal endotoxin from the gut to the central nervous system, and then alleviating neuroinflammatory response.

Key words Butyrate, Cognition, Neuroinflammation, Gut mucosal barrier, Tryptophan metabolism

Category: Basic Nutrition& Research

富含皂苷、黄酮和生物碱的物质治疗自身免疫性疾病的效果：一项基于动物实验的系统评价和 Meta 分析

Efficacy of substances containing 3 types of active ingredients-saponins, flavones, and alkaloids in regulation of cytokines in autoimmune diseases: a systematic review and Meta-analysis

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Background and Objectives: Autoimmune diseases bring a heavy economic and medical burden. To systematically evaluate the effects of treatment with substances containing saponins, flavones, and alkaloids in animals with autoimmune diseases (AIDs).

Methods and Study Design: The protocol for this systematic review and meta-analysis was prospectively registered with PROSPERO (CRD42023395741). Searches were conducted in the China National Knowledge Infrastructure, Wanfang, Chinese Science and Technology Journals, China Biomedical, PubMed, Cochrane Library, and Embase databases to screen for animal studies investigating the therapeutic effects of saponins, flavones, or alkaloids on autoimmune diseases; consequently, corresponding data extraction tables were prepared. Systematic Review Centre for Laboratory Animal Experimentation was used to assess the risk of methodological bias in the included literature. RevMan 5.4 was used for the meta-analysis on the 8 serum cytokines.

Results: A total of 31 studies were included, all of which were randomized controlled studies. Meta-analysis indicated that substances rich in saponins, flavones, and alkaloids reduced serum levels of interleukin-1β (SMD = -1.94, 95% CI [-2.99, -0.90], P = 0.0003), interleukin-6 (SMD = -1.65, 95% CI [-2.33, -0.97], P < 0.00001), interleukin-17 (SMD =-2.41, 95% CI [-3.61,-1.20], P < 0.0001), tumor necrosis factor α (SMD =-1.84, 95% CI [-2.61,-1.06], P < 0.0001), and interferon γ (SMD =-1.54, 95% CI [-2.43, -0.65], P = 0.0007), but increased serum levels of interleukin-4 (SMD = 1.30, 95% CI [0.15, 2.44], P = 0.03) and interleukin-10 (SMD = 2.05, 95% CI [1.39, 2.70], P < 0.00001) in animal models. However, no significant regulatory effect of these three active components was observed on serum levels of interleukin-2 (SMD = -0.63, 95% CI [-1.82, 0.57], P = 0.30).

Conclusions: Substances containing saponins, flavones, and alkaloids regulated the changes of immune-related cytokines, it may be a novel dietary substance to relieve and control autoimmune diseases in the future.

Key words autoimmune disease, saponin, flavone, alkaloid, system evaluation, meta-analysis

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吡喃花色苷Vitisin A对脂质代谢紊乱的调控作用

Regulatory effect of pyranocyanoside Vitisin A on lipid metabolism disorder

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Red wine is a popular alcoholic beverage that has been consumed worldwide for hundreds of years. The color of red wine has always been considered to be one of its major sensorial attributes which is first perceived by the consumer. This characteristic was originally associated with the presence of anthocyanins, an important group of water-soluble phenolic pigments. Pyranoanthocyanins, a group of anthocyanin-derived pigments, are produced in red wines during the fermentation and aging processes, which formed a new pyran ring from C4 and C5 hydroxyl condensation, These compounds are responsible for a gradual change of the red-purple color towards orange hues, which are particularly important for imparting the color to aged red wines. In recent years, pyranoanthocyanins have attracted attention primarily because of their better chemical stability, higher color intensity, and higher antioxidant potential compared to their anthocyanin counterparts in vitro, but few in vivo studies on bioactivities of pyranoanthocyanins . Vitisin A is the main pyranoanthocyanin detected in aged wines, which forms upon the reaction between pyruvate with anthocyanins. In our previous study, we found that vitisin A exhibited a better hypocholesterolemic activity than its counterpart Cyanidin-3-O-glucoside (C3G) in HepG2 cells. However, the plasma lipid-lowering effect of Vitisin A in vivo is still unclear. The present study was carried out to compare the plasma lipid-lowering activities of Vitisin A with its anthocyanin counterpart C3G in ApoE-/- mice fed a high-fat diet, and to explore the underlying mechanism related to lipid metabolism.

Key words Red wine, Vitisin A, C3G, HepG2 cells, ApoE-/- mice, lipid metabolism.

Category: Basic Nutrition& Research

RGS12 在人类肿瘤中的作用：一项泛癌分析

Roles of RGS12 in Human Cancers: a Pan-Cancer Analysis

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Background: RGS12, a member of the Regulator of G-protein signaling (RGS) protein family, enhance the deactivation of G proteins to turn off GPCR signaling and is increasingly thought to play significant roles in human tumors. This study aims to explore the potential role of RGS12 with a view to providing insights on pathologic mechanisms implicated here.

Methods: The potential roles of RGS12 in 33 different tumors were investigated based on The Cancer Genome Atlas (TCGA), Genotype-tissue expression (GTEx), Cancer Cell Line Encyclopedia (CCLE), Tumor Immune Estimation Resource (TIMER), and Clinical Proteomic Tumor Analysis Consortium (CPTAC) datasets and various other bioinformatic tools. The expression difference, protein mutation and phosphorylation status, survival, pathological stage, DNA methylation, protein–protein interaction, and immune cell infiltration related to RGS12 were analyzed. Then lentivirus was transfected to knockdown the expression of RGS12 in NSCLC cells and the migration was analyzed using single-cell motility assay and wound healing assay.

Results: Differential expression levels of RGS12 were observed in most cancer types. RGS12 expression in tumor samples correlates with poor overall survival in several cancers. Enhanced phosphorylation levels of S172, S174, S711, and S849 were observed in several tumors, including breast cancer. RGS12 correlated with tumor immunity and associated with different immune cells and genes in different cancer types. DNA methylation correlated with RGS12 dysregulation in cancers. RGS12 was notably associated with most immune cells in most cancers. RGS12 in cancer correlates with tumor progression and the immune response, although these data require further confirmation. Furthermore, knockdown of RGS12 inhibit the migration of NSCLC cells.

Conclusion: Our study offers a comprehensive understanding of the oncogenic roles of RGS12 across different tumors. RGS12 may correlate with tumor immunity.

Key words pan-cancer; RGS12; prognostic biomarkers; immunotherapy; cell migration

Category: Basic Nutrition& Research

营养、肠道菌群和疾病：相互作用和影响

Nutrition,Gut Microbiota and Disease: Interaction and Influence

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The relationship between different dietary methods, nutrients, gut microbiota and diseases has become the focus of recent research.

The composition of the gut microbiota is influenced by dietary habits and food intake components. Research showed that various dietary choices, including Mediterranean diet, intermittent fasting and low-fat vegan diet, can alter changes in the gut microbiota, contribute to reduce cardiovascular risk factors, loss weight and improve mood. Nutrients also have a certain impact on gut microbiota. Natural foods such as vegetables, nuts, Konjaku flour, cocoa powder and some probiotics foods effectively increase the diversity of gut microbiota, change the composition and function of gut microbiota. Poor dietary habits such as high-fat diet and long-term use of protein supplements may have a negative impact on the gut microbiota. Previous studies revealed that besides metabolic diseases such as type 2 diabetes, chronic kidney disease and obesity, as well as cardiovascular diseases such as hypertension and coronary heart disease, cancers such as breast cancer and colorectal cancer also have a certain relationship with gut microbiota.

Research on brain disorders such as Parkinson's disease, Alzheimer disease and depression have revealed that bidirectional communication between the brain and the intestine is influenced by gut microbiota and related metabolites, and interacts with the host through biochemical and functional inputs, thereby affecting the host's homeostasis and health. Nutrients can influence physiological and psychological responses through microbiome－gut－brain axis, subtly intervening in brain activity and the function of known regions that regulate emotions and stress responses.

The gut microbiota not only affects the host's metabolism, but also has a certain relationship with the host's physical and mental health, and related diseases. The pathogenesis of gut microbiota related diseases and how to improve gut microbiota to enhance quality of life are issues worth paying attention to in the future.

Key words nutrition;gut microbiota; interaction;influence;disease

Category: Basic Nutrition& Research

中国上海地区母血、脐带血和母乳中的类胡萝卜素含量及其与母亲饮食摄入的关系

Carotenoid profile in maternal/cord blood, breast milk, and its associations with maternal dietary intake: a longitudinal study in Shanghai, China

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Carotenoids are important bioactive substances in breast milk that promote vision, cognition and respiratory health in infants. This study aims to explore the carotenoid profile in breast milk and maternal/cord plasma of healthy mothers in Shanghai, China and its correlation with dietary intake. Maternal blood, umbilical cord blood, and breast milk samples from five lactation stages (colostrum, transitional milk, and early-, mid-, and late-term mature milk) were collected. Concentrations of carotenoids were analyzed by high-performance liquid chromatography. The maternal carotenoid dietary intake was evaluated through the 24-hour dietary review questionnaire and the food frequency questionnaire. The results show that the concentrations of carotenoids in breast milk changed over the progress of lactation. β-Carotene was the primary carotenoid in colostrum. Lutein accounts for approximately 50% of the total carotenoids in transition milk, mature milk and cord blood. A high correlation between carotenoids in umbilical cord blood, breast milk and maternal blood was observed. Dietary carotenoid intakes of lactating mothers also differed significantly across lactation stages, although no correlation with breast milk was found. These findings may shed light on the transport mechanism of carotenoids between mothers and infants and help guide the development of formulas for Chinese infants as well as the nutritional diets of Chinese lactating mothers.

Key words breast milk; carotenoids; lactation stage; maternal/cord blood; maternal diet; China

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支链氨基酸代谢紊乱介导高脂喂养 APP/PS1 小鼠的阿尔兹海默症病理的恶化

Aberrant branched-chain amino acids metabolism mediates high fat diet-induced aggravation of Alzheimer's disease-related pathology in APP/PS1 mice

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Background and Objectives

Type 2 diabetes has been recognized as a risk factor for developing Alzheimer's disease (AD), and studies indicate that insulin resistance plays an important role in AD-related pathology. However, mechanisms underlying the effects of insulin resistance on AD remains largely unclear. Some studies presented a correlation between insulin resistance and impaired branched-chain amino acids (BCAAs) metabolism in epidemiology and experiment . Moreover, increases in blood BCAAs levels are reported to associate with the risk for AD. Nevertheless, it needs to be further confirmed whether aberrant BCAAs metabolism participates in insulin resistance-related development of AD. Thus, this study is aimed to investigate the role of BCAAs metabolism disorders in high fat diet (HFD)-induced exacerbation of AD-related pathology.

Methods and Study Design

Three-month old male APP/PS1 mice were fed HFD, HFD with high BCAAs (+100%), HFD with low BCAAs (-50%) or control diet, respectively. After nine-month treatment, oral glucose tolerance test and Morris water maze were performed. Serum BCAAs and branched-chain α-keto acids (BCKAs) levels, BCAAs metabolism-related protein levels in liver, Aβ deposition and microglia activation in brain were determined.

Results

Compared to control diet feeding, mice in HFD group displayed impaired glucose tolerance and hepatic BCAAs degradation, followed by increases in serum BCAAs and BCKAs levels. Cognitive impairment, larger cerebric Aβ deposition, and over-activated cerebric microglia were observed in HFD fed mice. Meanwhile, HFD with low BCAAs feeding decreased serum BCAAs and BCKAs levels, and alleviated AD-related pathology in mice compared to HFD group. Conversely, HFD with high BCAAs feeding further worsened above pathologies.

Conclusions

HFD feeding leads to insulin resistance, suppressed hepatic BCAAs metabolism, aggravated AD-related pathology in APP/PS1 mice. Results of BCAAs adjustment in HFD farther reveals that aberrant BCAAs metabolism contributes to insulin resistance-induced acceleration of AD progression. Targeting BCAAs metabolism may become a potential therapeutic intervention for AD.

Key words Insulin resistance; Alzheimer's disease; branched-chain amino acids; APP/PS1; High fat-diet

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短链脂肪酸和微生物组对中国农村人口 2 型糖尿病的影响： 来自河南农村队列的证据

The effect of short-chain fatty acids and the microbiome on type 2 diabetes in a Chinese rural population: Evidence from the Henan Rural Cohort

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Objectives We aim to evaluate the dose-response relationship between faecal short-chain fatty acids (SCFAs) and T2DM risk and explored the contribution of the intestinal microbiome in a population-based cohort.

Methods This study recruited 100 subjects from the Henan rural cohort and performed an integrated analysis of the microbiome and targeted metabolomics. Logistic regression and restricted cubic spline assessed the associations between SCFA concentrations and T2DM risk. Generalized linear models identified the gut microbial traits related to SCFAs and T2DM.

Results Comparing with the lowest triple of total SCFA, acetate and butyrate, the risk of T2DM was respectively 0.291 (95%CI: 0.085-0.991), 0.160 (95%CI: 0.044-0.574) and 0.171 (95%CI: 0.047-0.620), with S-shaped dose-response relationships ($P < 0.05$). Both valerate and caproate levels performed significant differences on the alpha-diversity indices and overall microbiota composition. The ACE index interacted with high valerate on GLU level and the Shannon index interacted with medium butyrate on INS level (all $P < 0.05$). Three specific microbiota taxa with regard to valerate or caproate, including genus Prevotella_9, Odoribocter and Blautia, were also found to correlate with T2DM risk.

Conclusion T2DM were negatively linked to faecal SCFA levels in a non-linear manner, and gut microbial traits about SCFA also influenced T2DM in the rural Chinese population. Significantly, increasing microbial diversity attenuated the association between SCFAs and T2DM risk factors.

Key words T2DM; SCFAs concentrations; intestinal microbiome; dose-response relationships; interaction

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短链脂肪酸水平和膳食质量与2型糖尿病的关系：基于河南农村队列的巢式病例对照研究

Association between fecal short-chain fatty acid levels, dietary quality and type 2 diabetes: a nested case-control study based on Henan Rural Cohort

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Background and Objectives: There is limited evidence on the relationship between short-chain fatty acid levels (SCFAs), diet quality and type 2 diabetes (T2D) in rural Chinese populations. We aimed to investigate the characteristics of SCFAs in rural population and to examine the relationship between SCFAs levels, dietary quality and T2D.

Methods and Study Design: A total of 97 adults were recruited to the nested case-control study. Dietary quality was assessed by the Alternate Healthy Eating Index 2010 (AHEI-2010) and SCFAs levels were analyzed using the GC-MS system. Generalized linear regression and restricted cubic splines analysis were conducted to calculate the odds ratio for T2D relative to SCFAs level and investigate the dose-response relationship. Finally, generalized linear regression models were used to study the combined effect of SCFAs levels and AHEI-2010 scores on T2D and to calculate their additive and multiplicative scales.

Results: T2D participants had lower levels of acetic acid and butyric acid, with higher fecal acetic acid levels associated with an 85.7% reduction in risk of T2D and butyric acid levels were 80.3% lower at the extreme third after adjusting for confounding factors. We also observed a significantly lower risk of T2D with acetic acid levels >1338.588 mg/g or butyric acid levels >588.122 mg/g. In addition, the risk of higher acetic acid levels of T2D was 0.002 (95% CI:0.000, 0.114) compared to participants with lower AHEI-2010 scores (All P<0.05).

Conclusions: In this study, participants have low adherence to the dietary guidelines for Chinese residents, and those with T2D have lower fecal levels of acetic and butyric acid. Higher levels of acetic and butyric acid are negatively associated with risk of T2D, with a non-linear dose-response relationship. Higher AHEI-2010 scores and fecal levels of acetic acid may have a positive joint effect on the reduced risk of T2D.

Key words Short-chain fatty acids; Dietary quality; T2D; Nested case-control study, Henan Rural Cohort

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GPR116过表达在胃癌预后评估中的意义

Significance of Overexpression of GPR116 in the Evaluation of Prognosis of Gastric Cancer

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Objective: This study aims to investigate the expression of G protein-coupled receptor 116 (GPR116) in gastric cancer (GC) and the significance of clinical prognosis.

Methods: The expression level of GPR116 mRNA in GC was analyzed using Gene Expression Omnibus and Ualcan database. The expression of GPR116 in GC tissue was detected by immunohistochemistry. The correlation between the GPR116 protein and clinicopathological parameters was analyzed. The relationship between the expression of GPR116 and the prognosis of GC patients was analyzed and further validated by Kaplan-Meier plotter database. The correlation between the GPR116 and any identified differentially expressed genes was analyzed by linkedOmics database. The gene enrichment analysis of GPR116-related genes was carried out using Web-based gene set analysis tool.

Results: The expression of GPR116 was significantly up-regulated in the GC tissue. Its expression level was significantly correlated with TNM staging and depth of invasion. Prognostic analysis suggested that the high GPR116 expression was significantly correlated with poor overall survival in GC patients. Multivariate COX analysis showed that the GPR116 overexpression was an independent prognostic indicator in GC patients (HR=1.855; 95% IC 1.021-3.370; P=0.043). The results of enrichment analysis showed that the GPR116 and related genes were mainly involved in extracellular matrix-receptor interaction pathway, focal adhesion pathway, cell adhesion molecule pathway, PI3K-Akt signal pathway, DNA replication, cell cycle and so on tumor-related pathways.

Conclusion: GPR116 is highly expressed in the GC tissue and is correlated with the poor prognosis of GC patients. It is expected to be a potential new target for GC treatment.

Key words GPR116, gastric cancer, bioinformatics analysis, immunohistochemistry, prognosis, signal pathway

Category: Basic Nutrition& Research

不同妊娠期母体叶酸浓度与新生儿出生体重之间的关系：系统综述

Associations between maternal folate concentrations at different trimesters and neonatal birth weight: a systematic review

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OBEJCTIVE: A systematic review using PRISMA guidelines was conducted to evaluate an association between maternal serum/plasma or red blood cell (RBC) folate concentrations at different trimesters and neonatal birthweight.

METHODS: PubMed, Scopus, Embase, Web of Science and Cochrane Library databases were searched up to April 19th 2022. Eligible studies included an exposure of maternal serum/plasma, or RBC folate and birthweight or low birthweight outcomes: small-for-gestational-age (SGA), fetal growth restriction (FGR), and low birth weight (LBW). All studies were summarized in detail but only the studies reporting OR or β coefficients were included in the discussion.

RESULTS: Thirteen studies were identified, of which, 6 studies and 4 studies reported β or ORs coefficients for an association with birthweight and low birthweight outcomes, respectively, one study reported both of the two indicators. Studies examining birthweight as an outcome reported statistically significant positive associations with serum/plasma, or RBC folate in early (n=3) and late pregnancy (n=3), but not in mid-pregnancy (n=5). Statistically significant inverse or no associations were reported between maternal folate concentration and odds of low birthweight (LBW, SGA, FGR) in early (n=2), mid- (n=1), and late (n=3) pregnancy. Increased odds of low birthweight outcomes were only observed in the lowest categories of exposure indicating folate deficiency and in socio-economically disadvantaged populations.

CONCLUSIONS: Maternal folate concentration may be positively associated with birthweight in early and late pregnancy. Maternal folate concentrations in each trimester might have inverse association with SGA, LBW and FGR in pregnant women at risk of nutritional deficiencies. More well-designed studies considering major potential confounders including BMI, education, and socio-economic status are warranted to further clarify the roles of maternal serum/ plasma and RBC folate concentrations at different trimesters in neonatal birth weight.

Key words folate concentration; trimesters; birthweight; small-for-gestational-age; fetal growth restriction; low birth weight

Category: Basic Nutrition& Research

肠道微生物对氧化偶氮甲烷诱导的小鼠结直肠癌癌前病变发展的影响及其可能的潜在机制

Effect of intestinal microbes on the development of azomethane-induced colorectal precancerous lesions in mice and its possible underlying mechanism

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BACKGROUND:
Gut microbiota contributes to the carcinogenesis of colorectal cancer (CRC). In this study, the effects of gut microbiota alteration caused by broad-spectrum antibiotics on azoxymethane (AOM)-induced CRC and the underlying mechanisms were investigated in vivo.
METHODS:
Eighty 3- to 4-week-old male ICR mice were randomly divided into Control group, AOM intervention group (AOM group), antibiotic intervention group (Abx group), and antibiotic+AOM intervention group (AbxAOM group). The AbxAOM group and Abx group were gavaged with antibiotics solution, Control group and AOM group were gavaged with an equal volume of pure water twice a day for 14 days. Then AOM group and AbxAOM group were intraperitoneally injected with AOM solution (10 mg/kg.bw), Control group and Abx group were injected with the corresponding volume of sterile 0.9% NaCl solution once a week for 4 weeks. On the 28th week of the experiment, the intestinal tissues were collected for histology, real-time quantitative polymerase chain reaction and immunohistochemistry. Feces from mice were detected by 16S ribosomal RNA gene sequencing.
RESULTS:
AOM treatment could lead to colon pathological damage, aberrant crypt foci(ACF) formation and adenocarcinoma development. Compared with AOM group, Abx treatment efficiently mitigated the degree of weight loss and suppressed the formation of ACF. The mRNA expression levels of Vascular cell adhesion molecule-1, Intercellular cell adhesion molecule-1, Ki-67, Interleukin-1β(IL-1β), IL-6, Tumor necrosis factor-α, Vascular endothelial growth factor A, Toll-like receptors 4, Nuclear factor kappa B p65(NF-κB p65) and Cyclooxygenase-2 were substantially downregulated in the mice of AbxAOM group compared with AOM group. Moreover, Abx treatment remarkably decreased the protein expression level of NF-κB p65 and the abundance of bacteria Akkermansia and Streptococcus.
CONCLUSIONS:
These findings suggest that intestinal microbiota alteration caused by antibiotics could prevent AOM-induced intestinal carcinogenesis via reducing the formation of ACF and inhibiting the inflammatory reaction. The underlying molecular mechanisms likely rely on suppressing the TLR4/NF-κB/COX-2 signaling pathway.

Key words Colorectal cancer; Antibiotics; Azoxymethane; Gut microbiota; Carcinogenesis

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肠道菌群和 COVID-19 的因果关系研究-两样本孟德尔随机化
Causal Association between Gut Microbiome and COVID-19 - A two-sample Mendelian Randomization Study

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Aims:

Although COVID-19 is primarily a respiratory disease, it causes a full spectrum of harm, with substantial evidence that it affects gastrointestinal function. This study was performed to investigate the causal association between covid-19 and gut microbiota using Mendelian randomization (MR).

Methods:

The GWAS statistics with COVID-19 were obtained from the results of the seventh round of the COVID-19 Host Genetics Initiative study. GWAS statistics for gut microbiota were derived from the largest available meta-analysis of genome-wide association studies conducted by the MiBioGen consortium (n = 13,266).

Results:

Reverse variance-weighted estimates demonstrated that Peptococcus was protective against COVID-19 (OR = 0.96, 95% CI: 0.94-0.99, P = 0.027) and that Dorea and Rikenellaceae (RC9gut group) increased the risk of COVID-19 (OR = 1.07, 95% CI. 1.01-1.13, P = 0.014; OR = 1.03, 95% CI: 1.00-1.06, P = 0.024, respectively). Reverse MR analysis showed that COVID-19 was positively associated with LachnospiraceaeNK4A136group and Oscillospira (OR = 1.19, 95% CI. 1.02-1.39, P = 0.024; OR = 1.25, 95% CI: 1.00-1.55, P = 0.046, respectively), but negatively associated with Paraprevotella and Subdoligranulum (OR = 0.74, 95% CI. 0.59-0.97, P = 0.040; OR = 0.86, 95% CI: 0.74-1.00, P = 0.048, respectively).

Conclusion:

We confirmed the causal relationship between gut microbiome and COVID-19, providing an innovative perspective for COVID-19 research: prevention and treatment of COVID-19 is facilitated by specific regulation of gut microbiome.

Key words COVID-19; gut microbiome; Mendelian randomization

Category: Basic Nutrition& Research

染料木黄酮通过雄激素受体途径抑制去势抵抗前列腺癌
Genistein inhibits castration-resistant prostate cancer via the androgen receptor pathway

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Background: Prostate cancer is one of the most frequent malignant tumours. The patients' survival time is significantly shorter after prostate cancer develops into castration-resistant prostate cancer (CRPC). Genistein has different biological activities, including the prevention and treatment of PCA disease.

Objectives: This study aimed to investigate the antitumor effect of Genistein in the de novo pathway and AR signalling pathway in CRPC and potential mechanisms of action.

Methods: The expression of key enzymes in the de novo pathway was detected by Western blot. DHT and T levels were measured by ELISA kits. AR distribution was assessed by laser confocal.

Study Design: A xenograft tumor mouse model established with 22R V1 cells was divided into the experimental group and the control group, and the former was given 100 mg/kg.bw/day of Genistein. Divide Genistein into different concentrations (0, 12.5, 25, 50, 100 μM) to treat 22RV1 and VCaP cells for 48 h.

Results: Genistein inhibits CRPC cell proliferation and in vivo tumorigenesis. Genistein blocks de novo androgen synthesis by downregulating the expression of AKR1C3, SRD5A2, CYP11A1, and 3βHSD in the de novo synthesis pathway in CRPC cells. Moreover, Genistein can inhibit the activation and nuclear translocation of the AR signalling path.

Conclusions: Genistein inhibits the progression of CRPC via the androgen receptor pathway.

Key words Genistein; castration against prostate cancer; de novo pathway.; androgen receptor; nuclear translocation

Category: Basic Nutrition& Research

白介素33通过诱导肝窦内皮细胞功能障碍促进糖尿病小鼠肝纤维化

Interleukin 33 promotes hepatic fibrosis by stimulating liver sinusoidal endothelial cell dysfunction in diabetic mice

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Objective: We intended to investigate the role of IL-33 in diabetes-associated hepatic fibrosis and the underlying mechanisms.

Methods: Eight-week-old C57BL/6J mice and IL-33-/- mice were established to type 2 diabetes as shown in Figure 1A. Wild-type diabetic mice were given an intraperitoneal injection of anti-IL-33 neutralizing antibody (αIL-33, 37 μg/kg·BW), recombinant mouse IL-33 (rIL-33, 12.5 μg/kg·BW) for the last 12 weeks, or rapamycin (1 mg/kg·BW) twice a week for last 8 weeks. Serum, liver, and other biological samples were collected for serological and histopathological examination.

Scanning electron microscopy was applied to measure hepatic sinusoidal cell capillarization. The expression levels of autophagy-related proteins LC3II/I and p62 were detected by Western Blot. The human liver endothelial cell line SK-Hep1 and human hepatic stellate cell line LX-2 were cultured to identify the role of IL-33 in endothelial dysfunction and the following hepatic stellate cell activation in vitro.

Results: Compared with non-diabetic mice, the diabetic mice exhibited increased hepatic collagen deposition. IL-33 knockout or αIL-33 administration alleviated diabetes-associated liver fibrosis as shown by Sirius Red staining and hepatic hydroxyproline content. Furthermore, exogenous IL-33 blocked blunted liver sinusoidal endothelial cell dysfunction and endothelial inflammation during diabetic liver fibrosis progression. In vitro, rIL-33 aggravated autophagy disruption in the presence of palm acid and high glucose in SK-Hep1 cells, which was blunted by autophagy agonist rapamycin treatment. LX-2 co-cultured with rIL-33-pretreated SK-Hep1 displayed augmented activation as demonstrated by immunoblot staining of αSMA.

Conclusion: We underscore the importance of IL-33 signaling in the development of diabetic liver fibrosis. During the progression of diabetes-associated liver disorder, IL-33 promotes liver fibrosis by driving LSEC dysfunction through autophagy inhibition. Our findings demonstrate that IL-33 is an attractive therapeutic target for diabetic liver fibrosis.

Key words IL-33, liver fibrosis, liver sinusoidal endothelial cell, autophagy, hepatic stellate cell

Category: Basic Nutrition& Research

不同阶段轻度认知障碍者氧化固醇、肠道微生物群和脑葡萄糖摄取的关联性:一项巢式病例对照研究

Association of oxysterols, gut microbiota and brain glucose uptake in different stages of mild cognitive impairment: A nested case-control study

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Background and Objectives

Studies have proven that cholesterol and its metabolite oxysterols, the gut microbiota, and brain glucose uptake are regulatory factors for mild cognitive impairment (MCI), but their association remains unclarified. This study was conducted to explore the relevance of these factors above in early MCI (EMCI) and late MCI (LMCI) patients.

Methods and Study Design

369 middle-aged and elderly Chinese participants [123 EMCI subjects, 123 LMCI subjects, and 123 matched controls (CON)] were recruited from a prospective cohort based on their cognitive functions. Dietary cholesterol was assessed by food-frequency questionnaires. Serum cholesterol, oxysterols, gut microbiota along with glucose uptake factors were detected. Spearman correlation and regression model were used to identify their correlations and distinguish MCI patients from healthy controls.

Results

Compared to CON group, higher serum Triglyceride and 27-hydroxycholesterol (27-OHC, an abundant oxysterol in the periphery) in the LMCI group, and higher 7α-hydroxycholesterol/7β-hydroxycholesterol (7α-OHC/7β-OHC) in the EMCI group were observed. A lower abundance of *Firmicutes* and *Clostridiales*, but a higher abundance of *Bacteroidetes*, *Prevotellaceae*, *Proteobacteria*, and *Enterobacteriaceae* were found in the LMCI group. Increased levels of fasting blood glucose and hemoglobin A1c (HbA1c), while decreased serum concentration of glucose transporter 1 (GLUT1) and glucose transporter 4 (GLUT4) were found in the EMCI and LMCI groups compared to CON group. Additionally, 7α-OHC/7β-OHC was positively correlated with HbA1c (r=0.158, P=0.002) but inversely associated with *f_Lachnospiraceae* (P<0.05). Besides, there was a positive association between 3β-hydroxy-5- cholestenoic acid (27-CA)/27-OHC with GLUT1 (r=0.210, P=0.034) and *g_Rodentibacter* (P<0.05). Further, the combination of oxysterol, gut microbiota, and glucose uptake-related factors could effectively predict the onset of MCI (AUC= 0.950).

Conclusion

Cholesterol/oxysterols, gut microbiota, and glucose uptake were remarkably changed with a significant correlation in different MCI stages, whose combination showed a prominent predictive value for MCI. Potential mechanism deserves further exploration subsequently.

Key words cholesterol, oxysterol, gut microbiota, brain glucose uptake, mild cognitive impairment

Category: Basic Nutrition& Research

维生素 D3 联合叶酸调节 27-羟基胆固醇代谢和认知功能：一项随机对照试验

Vitamin D3 combined with folic acid supplementation regulates 27-hydroxycholesterol metabolism and cognitive function: a randomized controlled trial

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Background and Objectives

The deficiency of vitamin D (VD) and folic acid (FA) are risk factors for mild cognitive impairment, which might be associated with 27-hydroxycholesterol (27-OHC) metabolism and its synthetase CPY27A1. However, the role of VD and FA supplementation on cognition is still controversial. This study aimed to investigate the effects and mechanisms of different doses of VD combined with FA on the global or domain-specific cognitive functions of VD deficiency patients.

Methods and Study Design

516 participants with VD deficiency were randomly divided into 4 groups, placebo, 400 μg FA (FA), 800 IU VD with 400 μg FA (LVD+FA) or 1600 IU VD with 400 μg FA (HVD+FA) daily respectively for 6 months. Global and domain-specific cognitive tests were conducted, and blood concentrations of 25-hydroxyvitamin D [25(OH)D], FA, homocysteine (Hcy), 17 kinds of oxysterols, and the activities of 27-OHC metabolic enzymes were assessed. A generalized linear mixed model and Bayesian structural equation were applied to analyze the relationships between the indicators above.

Results

Serum 25(OH)D was positively associated with Montreal Cognitive Assessment and domain-specific cognition, while Hcy showed reverse effects ($P<0.05$), despite no difference in global or domain-specific cognitive functions.

There was higher serum 25(OH)D in LVD+FA and HVD+FA groups, but lower in FA group ($P<0.05$). Meanwhile, serum FA was increased in groups intervened with FA ($P<0.001$), while serum Hcy was decreased in FA and LVD+FA groups ($P<0.05$). The serum 25(OH)D level was stimulated by 27-OHC, Hcy and interventions, investigated by Bayesian.

Besides, serum 3β-hydroxy-5-cholestenoic acid, the metabolite of 27-OHC, was increased in HVD+FA group. 7-keto-27-hydroxycholesterol and 7α/β-hydroxycholesterol were decreased in LVD+FA and HVD+FA groups. Moreover, CYP27A1 and CYP27B1 in FA and HVD+FA groups were significantly lower than placebo group ($P<0.05$).

Conclusions

The supplementation of VD combined with FA improves global and domain-specific cognitive functions by regulating serum 25(OH)D, FA, Hcy and 27-OHC metabolism.

Key words Vitamin D, Folic acid, 27-hydroxycholesterol, Cognitive function, Randomized controlled trial

Category: Basic Nutrition& Research

蜜橘黄素通过自噬- hippo 通路减轻肝纤维化中肝细胞的上皮间质转化

Nobiletin alleviated epithelial-mesenchymal transition of hepatocyte in liver fibrosis based on autophagy-Hippo pathway

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Objective: Nobiletin is a polymethoxy flavone with diverse bioactivities, yet information regarding its impact on liver fibrosis remains limit. The objective of this study was to investigate the effects of nobiletin on liver fibrosis and elucidate its underlying mechanisms. Methods: The present study employed a carbon tetrachloride (CCl4)-induced liver fibrosis mouse model and administered nobiletin via gavage for three weeks. In vitro experiments were conducted using LO2 cells stimulated with transforming growth factor β1 (TGF-β1) to induce epithelial-mesenchymal transition. Chloroquine, 3-methyladenine, and siYAP were utilized to investigate the involvement of the autophagy-Hippo/YAP pathway in nobiletin-treated liver fibrosis. Results: Nobiletin effectively inhibited liver fibrosis in CCl4-induced mice by reducing inflammation and fiber deposition in the liver. Furthermore, it attenuated epithelial-mesenchymal transition in hepatocytes, thereby alleviating inflammation and reactive oxygen species generation. The comprehensive investigation unveiled that the hepatoprotective effect of nobiletin against liver fibrosis was attributed to the activation of autophagy, as evidenced by a significant increase in LC3 II expression and concomitant degradation of p62 upon nobiletin treatment. Moreover, nobiletin was found to activate the Hippo/YAP pathway by downregulating YAP expression and its downstream effectors in liver fibrosis. The results of experiments with chloroquine, 3-methyladenine, and siYAP suggested that autophagy mediated the inhibitory effects on YAP. Conclusion: Nobiletin exhibited a protective effect against liver fibrosis, and the underlying mechanism may be attributed to autophagy-Hippo/YAP pathway activation.

Key words Nobiletin; liver fibrosis; autophagy; Hippo; epithelial-mesenchymal transition

Category: Basic Nutrition& Research

27-羟基胆固醇通过调节 Th17/Treg 平衡及其相关的免疫反应引起学习和记忆功能下降

27-hydroxycholesterol impairs learning and memory via regulating Th17/Treg balance and the related immune responses in vivo

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Background and Objectives Oxysterols, especially 27-hydroxycholesterol (27-OHC), have received extensive attention in the pathogenesis of cognitive decline. Oxysterols are reported to be the agonist of retinoic acid-related orphan receptor-γt (RORγt), which is specifically involved in the differentiation and functionality of Th17 cells. However, whether 27-OHC impairs the learning and memory ability by regulating RORγt expression and the related immune responses is still unclear.

Methods and Study Design In this study, 40 male C57BL/6J mice (10 mice/group) were treated with 27-OHC (5.5mg/kg) combined with SR1001(RORγt inhibitor, 25mg/kg) for 21 days. The neurobehavioral tests were conducted to assess the learning and memory ability of mice. The proportion of Th17 and Treg cells was determined by flow cytometry (peripheral blood mononuclear cell (PBMC), hippocampus). The mRNA and protein expression level of T-cell-specific transcription factors and the immunomodulatory factors were detected by qRT-PCR, western blot and ELISA (serum, cerebral cortex).

Results We found that there were higher proportion of Th17 cells but lower Treg cells in PBMC and hippocampus of 27-OHC treated mice. Using of SR1001 significantly inhibited the expression of RORγt mRNA and protein in cerebral cortex. Compared with the 27-OHC group, the Th17 cells proportion in hippocampus, as well as the serum level of IL-17A and IL-17A/IL-10 ratio were remarkably decreased in 27-OHC+SR1001 group; while the Treg cells proportion was increased and the expression level of transforming growth factor-β (TGF-β) and interferon-λ2 (IFN-λ2) was also upregulated. In addition, reduced amyloid-beta (Aβ) plaque area and downregulated expression of amyloid precursor protein (APP) were observed in cerebral cortex of 27-OHC+SR1001 mice, and their performance in Morris water maze test was significantly improved.

Conclusions Our study indicates that 27-OHC induces learning and memory impairment by upregulating the expression of RORγt and disturbing the Th17/Treg balance and the related immune responses.

Key words 27-hydroxycholesterol; RORγt; Th17/Treg; learning and memory; C57BL/6J mice

Category: Basic Nutrition& Research

维生素D联合叶酸和维生素B12通过CYP27A1 SUMO化修饰调节学习记忆能力

Vitamin D combined with folic acid and vitamin B12 regulate learning and memory ability through CYP27A1 SUMOylation

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Aims

The aim of this study is to explore the intervention and mechanisms of vitamin D combined with folic acid and vitamin B12 through CYP27A1 SUMOylation on learning and memory ability, and to provide new ideas for potential pathways and targets from the perspective of dietary nutrition in cognitive dysfunction related diseases.

Methods

The C57BL/6J wild-type mice were used to establish vitamin D-deficient and CYP27A1 knockdown (Cyp27a1-/-) mouse model, randomly divided into 5 groups according to body weight, included control group, vitamin D deficiency and 27-OHC treatment group, vitamin D and folic acid/vitamin B12 treatment group, 2-D08 (SUMOylation inhibitor) treatment group and Cyp27a1-/- knockdown group, respectively. The learning and memory ability of the mice were evaluated by Morris water maze and Novel object recognition test; blood and brain level of 27-OHC was detected by HPLC-MS; SUMOylation of CYP27A1 and its related factor were determined by qRT-PCR, Western Blot and immunoprecipitation; brain Aβ deposition was observed by immunohistochemistry.

Results

Vitamin D deficiency can work together with 27-OHC load, increase brain Aβ deposition, further impair learning and memory ability. CYP27A1 protein can occur SUMOylation modification, vitamin D deficiency and 27-OHC load can increase SUMOylation modification level, inhibiting CYP27A1 expression can reduce the level of SUMOylation modification. Vitamin D combined with folic acid and vitamin B12 supplementation can moderate CYP27A1 SUMOylation level, down-regulate CYP27A1 expression, decrease peripherals and brain 27-OHC load, reduce Aβ deposition and improve the learning and memory ability.

Conclusion

From the perspective that CYP27A1 participate in both 27-OHC and vitamin D metabolism, the study indicated that vitamin D combined with folic acid and vitamin B12 can moderate CYP27A1 SUMOylation and CYP27A1 expression, reduce blood and brain 27-OHC load, then decrease brain Aβ deposition, improve the learning and memory ability. CYP27A1 SUMOylation modification is an important target for cognitive dysfunction early identification and intervention.

Key words 27-hydroxycholesterol; vitamin D; CYP27A1; SUMOylation; learning and memory ability

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透明质酸作为天然味觉增强剂的应用和机理初探

Hyaluronic Acid Applied as a Natural Flavor Enhancer

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Creating natural flavor enhancers presents a promising approach to reducing excessive seasoning consumption. This study aimed to determine whether food-grade hyaluronic acid (HA) could serve as a viable option to decrease salt content in low-sodium foods without sacrificing saltiness. Using both an artificial tongue and Quartz crystal microbalance with dissipation (QCM-D), we examined the effects of different molecular weights (100 kDa, 400 kDa) and concentrations (0.2% w/v, 0.4% w/v) of HA on the saltiness perception of NaCl solutions. HA has been confirmed with a taste-enhancing effect. Furthermore, when added to the pre-made dishes such as Sichuan fish and black pepper steak, HA was found to reduce salt content by 10 % while maintaining both saltiness and consumer preference. Simulation with a hydrogel artificial tongue revealed that Na+ adhesion correlated with increasing molecular weight and concentration of HA. The QCM-D results supported this finding, showing that 100 kDa HA enabled greater permeation of Na^+ into the oral mucosal layer and thus showed stronger perception of saltiness in comparison to 400 kDa HA. Overall, the mucoadhesion and mucopenetration of HA make it a promising alternative to traditional seasonings and could facilitate the pursuit of healthier dietary habits.

Key words hyaluronic acid; taste perception; molecular weight; mucoadhesion; mucopenetration

Category: Basic Nutrition& Research

烟酰胺单核苷酸通过提高抗氧化能力和减少ECM产生缓解呼吸性粉尘诱导的肺损伤

Nicotinamide mononucleotide alleviates respiratory dust-induced lung injury by enhancing antioxidant capacity and reducing ECM production

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Objective: Pulmonary diseases caused by respirable dust still threaten tens of millions of people's health, such as pneumoconiosis and chronic obstructive pulmonary disease. Nicotinamide mononucleotide (NMN) is a B vitamin derivative with anti-inflammatory and antioxidant effects. The purpose of this study aimed to investigate the beneficial role of NMN in respiratory dust-caused pulmonary injury and its mechanism.

Methods: The lung injury mouse model was established using silica by intratracheally administration, and NMN (500/1000 mg/kg.bw) was given via intragastric administration. Histopathological staining was used to evaluate the effect of NMN on silica-induced lung injury, and transcriptome sequencing was used to further analyze the underlying mechanism. Then, the involved key molecules were verified by q-PCR and Western blot.

Results: NMN alleviates silica-induced lung injury, characterized by reducing inflammatory infiltration and inhibiting cell proliferation. Compared with the control group, 1962 genes were significantly up-regulated (595 genes were down-regulated by NMN treatment), and 1518 genes were significantly down-regulated (275 genes were up-regulated by NMN treatment) after silica exposure. KEGG enrichment analysis showed that the down-regulated genes after NMN treatment were mainly enriched in ECM receptor binding ($P<0.0001$) and cytokine-cytokine binding pathway ($P<0.0001$), while the up-regulated genes were mainly enriched in metabolism of xenobiotics by cytochrome P450 ($P<0.0001$), retinol metabolism ($P<0.001$) and glutathione metabolism pathway ($P<0.01$), suggesting that NMN treatment alleviates silica-induced oxidative injury and inhibits ECM production. Furthermore, q-PCR results showed that the mRNA expressions of MMP-9, Col1a1, and Fn1 were significantly decreased, while Cyp2f2 was increased, and NMN inhibited the expression of extracellular matrix protein.

Conclusion: NMN alleviates silica-induced lung injury by improving antioxidant capacity and reducing ECM production in the lung microenvironment, suggesting that NMN has the potential to mitigate respiratory dust-induced lung injury.

Key words Nicotinamide mononucleotide; Lung injury; respiratory dust; antioxidant; ECM production

Category: Basic Nutrition& Research

血浆镁与中国45岁以上成年人代谢综合征的关系研究

Association of plasma Magnesium with metabolic syndrome in Chinese adults over 45 years old

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Magnesium (Mg) is an essential nutrient for the maintenance of vital physiological functions. Mg deficiency is frequent in obese patients, subjects with type-2 diabetes (T2DM), and metabolic syndrome (MetS). This study aimed to evaluate the relationship between plasma magnesium levels and metabolic syndrome (MetS) in people over 45 years of age in China. A total of 2101 subjects were randomly selected from the China Nutrition and Health Surveillance (CNHS) (2015-2017). According to the criterion of the International Diabetes Federation (IDF) in 2009 to define participants with MetS. The plasma Mg was tested by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). The plasma Mg was categorized into quintiles. Multivariate logistic regression analysis showed that plasma Mg was inversely associated with MetS, IFG, Hypertension, and increased TG, but not with decreased HDL-C and central obesity. This association was not altered by further adjustment for potential confounding variables including age, gender, education, nationality, area, residence, BMI, and heart rate. Restricted Cubic Splines (RCS) analysis showed that the curve leveled off when plasma Mg was below 0.85 mmol/L, and then tended to decrease as plasma Mg increased. Our results suggest that plasma Mg is inversely associated with MetS and the odds risk of MetS was reduced with increasing plasma Mg and the threshold value was 0.85 mmol/L in people over 45 years of age in China.

Key words magnesium; metabolic syndrome； CNHS； RCS

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大豆卵磷脂可减轻SAMP8小鼠的记忆缺陷和肌肉衰减

Soy lecithin alleviates memory deficits and muscle attenuation in SAMP8 mice

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Background and Objective: Soy lecithin (SL) have beneficial effects on many chronic diseases including age-associated neurodegenerative disease and sarcopenia. However, the specific mechanisms and regulation targets are unclear. In this study, we investigated the effects of SL on learning and memory impairment and muscle attenuation in SAMP8 mice. Meanwhile, we explored the regulatory mechanism of FNDC5/irisin in muscle-brain crosstalk.

Methods: SAMP8 mice were randomly divided into 3 groups: model (M) group, 200 mg/kg·d soy lecithin (200-SL) group, 100 mg/kg·d soy lecithin (100-SL) group. SAMR1 were as the control group. The mice in M and control groups were treated with 0.5% CMC-Na, and other groups were provided SL by daily intragastric administration for 8 weeks. Morris water maze test was used to evaluate the cognitive decline. Grip strength and rotarod tests were used to evaluate the attenuation of muscle. The activity of superoxide dismutase (SOD) and malondialdehyde (MDA) content in brain were measured to assess the physiological changes. Moreover, mRNA and/or protein expressions of FNDC5/irisin was gauged.

Results: In behavior test, compare with M group, the latency of Morris water maze test of 200-SL group and 100-SL group were significantly reduced, while number of crossing the platform and time in target quadrant were increased. Mice in 200-SL and 100-SL group had greater grip strength and the latency for the mice to fall from the rod were increased. Meanwhile, the improvement of 200-SL group was better than that of 100-SL group ($P < 0.05$). Similar trend was observed in physiological changes. The MDA level was effectively decreased and the SOD activity increased in hippocampus of SL groups ($P < 0.05$). Besides we got the phenomenon that soy lecithin could up-regulate the mRNA and protein expressions of FNDC5/irisin in brain.

Conclusion: Soy lecithin could alleviate the impairment in learning and memory and motor coordination in SAMP8 through regulating FNDC5/irisin pathway.

Key words soy lecithin; cognition; memory; sarcopenia; muscle attenuation; FNDC5; SAMP8; irisin

Category: Basic Nutrition& Research

长链非编码 RNA TCONS_00077866 通过靶向抑制 miR-1231 进而上调 IGF1R 的表达参与调节高硬脂酸诱导的 β 细胞衰老

LncRNA TCONS_00077866 silencing alleviates stearic acid-evoked β-cell senescence via relieving its suppression of miR-1231 and then upregulating IGF1R expression.

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Objective: Chronic exposure to high concentration of stearic acid leads to β-cell senescence, leading to the development of type 2 diabetes. However, the underlying molecular mechanisms remain largely unclear. Here, we aimed to investigate the role of lncRNA TCONS_00077866 (lnc866) in stearic acid-induced β-cell senescence.

Methods: Expressions of senescence related genes and senescence-associated β-galactosidase activity were used to measure β-cell senescence. Co-expression network of lncRNA-miRNAs-mRNA was constructed to predict the potential downstream target of lnc866. Gain and loss of function approaches were applied to identify the role of lnc866 and miR-1231 in stearic acid-induced β-cell senescence and dysfunction. Smart Silencer and Adeno-associated Virus were used to knockdown lnc866 expression in vitro and in vivo, respectively. Luciferase reporter activity assay was used to verify the binding sites between lnc866 and miR-1231, as well as miR-1231 and Igf1r.

Results: Stearic acid significantly increased lnc866 and decreased miR-1231 expressions. Inhibition of lnc866 effectively ameliorated high stearic acid diet-induced upregulation of Cat, Ldha, Igf1r, Bambi, Cdkn2a, Trp53bp1, Cd99, Ccl2, Il1a, Il6, Tnfα and downregulation of Ins1, Mafa, as well as the increase in senescence-associated β-galactosidase activity both in mice and β-TC6 cells. Meanwhile, overexpression of miR-1231 also alleviated stearic acid-induced β-cell senescence and impaired glucose-stimulated insulin secretion in β-TC6 cells. Silencing lnc866 and overexpression of miR-1231 significantly suppressed stearic acid-increased IGF1R level. Transfection of miR-1231 mimic showed inhibitory effect on luciferase activity in human embryonic kidney 293 cells transfected with plasmid carrying lnc866 or 3′ UTR of the Igf1r gene.

Conclusions: Silencing lnc866 ameliorates stearic acid-induced β-cell senescence by alleviating its suppression of miR-1231 on IGF1R. These findings not only enrich our understating of the molecular mechanisms of stearic acid-induced β-cell dysfunction but also provide potential targets for preventing high fat diet-induced type 2 diabetes.

Key words stearic acid, lncRNA, miRNA, β cell senescence, Igf1r

Category: Basic Nutrition& Research

轻度认知功能障碍与肌肉衰减症之间的相关性：脂质在此关系中的前瞻性作用

Correlation between Mild Cognitive Impairment and Sarcopenia: The prospective role of Lipids in the link

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There is evidence of correlation between mild cognitive impairment (MCI) and sarcopenia (SA). However, the influencing factors and the mechanism such as age-related lipid redistribution remain unknown. This study aimed to clarify the role of dietary fats and erythrocyte lipids profile in the link of MCI and SA. 1050 participants aged 65 to 85 were divided into control, MCI, SA, and MCI&SA groups. Bioelectrical impedance analysis was used to evaluate appendicular lean mass. Cognition and dietary nutrition were detected by neuropsychological tests and food frequency questionnaire. UHPLC-QExactive-MS/MS and UHPLC-Qtrap-MS/MS were used to conduct the lipidomics analysis. Lower dietary intake of different phospholipids, unsaturated fatty acids and kinds of choline were significantly associated with MCI&SA. Least absolute shrinkage and selection operator, multivariate logistic regression, receiver operating characteristic curve and validation tests gave the evidence that specific phospholipids and unsaturated fatty acids might be the critical factors in the processing of MCI and SA as well as in their link. The lipidomic analysis observed a clear discrimination of the lipid profiles in the individuals who are in MCI, SA or MCI&SA compared with control. Lower expressions in certain phospholipid species such as sphingomyelin and phosphatidylethanola-mines, decreased phosphatidylcholine with more unsaturated double bonds, lower level of lipids with C20:5 and C20:4, higher level of lipids with C18:2 and lipids with remodeling length of acyl chain might be closely related to the link of MCI and SA. Inadequate dietary intake and lower concentration of erythrocyte lipid profile of phospholipids and unsaturated of fatty acids might be the key points in the progress of MCI and SA as well as in their link. They could be used as the prospective biomarkers for the higher-risk of cognitive decline and/or SA in elderly population.

Key words Mild cognitive impairment; Sarcopenia; Dietary fats; Lipid profile; Lipidomics

Category: Basic Nutrition& Research

Akkermansia muciniphila 通过调节 db/db 小鼠肠道微生物组成和代谢改善 2 型糖尿病相关认知功能障碍

Akkermansia muciniphila reverse type 2 diabetes-associated cognitive dysfunction by regulating gut microbial composition and metabolism in db/db mice

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Objective: Type 2 diabetes-associated cognitive dysfunction (TDACD) is one of the central nervous system complications of type 2 diabetes mellitus (T2DM). Akkermansia muciniphila was reported beneficial for T2DM, obesity, and Alzheime's disease (AD). However, the effect and underlying mechanisms of A. muciniphila on TDACD remain unknown. Here, we aimed to confirm the effect of A. muciniphila treatment in improving db/db mice and associated mechanisms.

Methods: The db/db mice were treated with alive or pasteurized A. muciniphila for 5 weeks. Morris water maze was performed to measure spatial learning and long-term memory. The impacts of A. muciniphila on neuronal loss, neuroinflammation, intestinal barrier, and hepatic steatosis were determined. The 16S rRNA high-throughput sequencing was employed to analyze gut microbiota composition in mice feces. Using liquid chromatography-mass spectrometry analysis, we performed the integrative untargeted metabolomic analysis of metabolite alterations in the serum and brain tissues.

Results: Alive and pasteurized A. muciniphila treatment effectively improved spatial learning and long-term memory, increased the levels of GFAP, and alleviated the reduction of colonic mucus cells. Alive A. muciniphila inhibited the loss of hippocampal neurons in CA1 and CA3 subsets. Moreover, A. muciniphila modulated gut microbial diversity but did not induce major rearrangements of the fecal microbiota. A. muciniphila treatment altered the levels of various metabolites in serum and brain tissues of db/db mice, which were involved in multiple metabolic pathways and were mainly involved in the glycine, serine and threonine metabolism pathway, glyoxylate and dicarboxylate metabolism pathway, and aminoacyl-tRNA biosynthesis pathway.

Conclusions: These findings revealed that the gut microbiota has a role in the prevention and treatment of TDACD by A. muciniphila, and that the microbiota-gut-brain axis and the regulatory effects of metabolites are significant protective mechanisms of A. muciniphila. It represents a novel probiotic dietary intervention for delaying the progression of TDACD.

Key words Akkermansia muciniphila, type 2 diabetes mellitus, cognitive dysfunction, gut microbiota, metabolomics

Category: Basic Nutrition& Research

妊娠期糖尿病产妇母乳低聚糖的变化及其对婴儿生长发育的影响

Changes of breast milk oligosaccharides in women with gestational diabetes mellitus and their effects on infant growth and development

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Objective: The aim of this study was to investigate the changes and differences between the levels of HMOs in GDM mothers and healthy mothers at different stages of lactation, and to understand the association between HMOs and infant growth and development.

Methods: This study was selected from healthy full-term newborns delivered at Peking University Third Hospital and Beijing Haidian District Maternal and Child Health Hospital from June 2021 to April 2022 (mother-infant pairs), and they were divided into GDM group and healthy control group according to whether the mothers had GDM. The levels of 14 HMOs in colostrum, transition milk and mature milk were measured using ion chromatography analysis, and analyzed according to the type of secretory phenotype.

Results: A total of 53 maternal and infant pairs were obtained, including 28 pairs in the GDM group and 25 pairs in the healthy group. The total levels of the 14 HMOs decreased with lactation time in both groups and were higher in the GDM group than in the healthy group. Most HMOs showed a clear temporal trend, decreasing with increasing lactation time; however, 2'-FL remained unchanged or experienced fluctuations and remained at higher levels. LNnT was significantly higher in the GDM group than in the healthy group at all time points, and its concentration was negatively correlated with the length-for-age Z score of 3-month-old infants in the GDM group; Significant group differences were also found in LNT, 3-FL, LNFP-II, 3'-SL and LST c, but not in all stages of lactation.

Conclusion: We found differential HMOs in mothers with and without GDM of the $Se^{+}Le^{+}$ phenotype, which may be key factors influencing infant growth and development, and are associated with growth-related indicators in infants, but the results are not uniform and all need further study.

Key words Gestational diabetes mellitus, Human milk oligosaccharides, Secretory phenotype, Infant growth and development

Category: Basic Nutrition& Research

基于蛋白质组学探讨 AKK 菌对肥胖大鼠胆固醇代谢的影响与机制

Lable-free Quantitation Proteomics Reveals Akkermansia muciniphila Improve cholesterol metabolism in obese rats

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Abstract: objective to investigate the effect and mechanism of Akkermansia muciniphila on cholesterol metabolism in obese rats.

Methods: SD rats were divided into 3 groups:LF group(fed with normal diet + normal saline), HF group(fed with HFD+ suspension without Akkermansia muciniphila), and AKK group(fed with HFD+ suspension containing Akkermansia muciniphila). Rats in each group were given intragastric administration once a day for 4 weeks. Serum TG, TC, HDL-C and LDL-C were detected. The liver protein were analyzed by Lable-free Quantitation Proteomics analysis.The difference of CYP7A1 protein expression in liver was detected by Western blot.

Results: the body weight, TG, TC and LDL-C levels of rats in the AKK group were significantly lower than those in the HF group. 4220 proteins were identified by proteomics. 44 up-regulated proteins and 28 down-regulated proteins were found in AKK group compared with HF group, 176 up-regulated proteins and 313 down-regulated proteins in HF group compared with LF group. The enrichment analysis of differential protein signaling pathways showed that there were 10 differential protein pathways between AKK group and HF group, and 15 signal pathways between HF group and LF group. Among them, multiple protein expression differences were found in the pathways closely related to cholesterol metabolism, such as primary bile acid synthesis pathway, steroid hormone synthesis pathway and PPAR pathway. The expression of CYP7A1, CYP4A2 and CYP3A9 in AKK group was significantly higher than that in HF group. Western blot results showed that the expression of CYP7A1 protein in AKK group was significantly higher than that in HF group.

Conclusion: Akkermansia muciniphila can significantly reduce the body weight and cholesterol level of obese rats induced by high-fat diet, which may be related to the up-regulation of the expression of CYP7A1, CYP4A2, CYP3A9 and the synthesis of primary bile acid and steroids.

Key words Akkermansia muciniphila; obesity; rats; cholesterol metabolism; proteomics

Category: Basic Nutrition& Research

岩藻多糖免疫调节作用与构效关系研究进展

Research progress on the immune regulatory mechanism and structure-activity relationship of fucoidan

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Objective Fucoidan is a water-soluble polysaccharide composed of L-fucose and organic sulfate groups, mainly exists in the cell wall matrix of brown algae. It has significant immunomodulatory activity and has good development value in food and medicine fields. Here we systematically summarize the immune regulatory mechanism of fucoidan, and the relationship between the chemical structure and immune regulation in this paper, aiming to provide reference basis for deeper study and development of the structure-activity relationship of fucoidan.

Methods: We used the Fucoidan, Chemical modification, Immune regulation, and Biological activity as search terms, conducted literature searches on databases such as PubMed, Web of Science, MEDLINE, China Knowledge Network, Wanfang Database, and Vip Database.The literatures of the past decade were selected and analyzed.

Results: Fucoidan can significantly increase the immune organ index of the spleen and thymus, and enhance the activity of immune organs and promote the proliferation of immune cells and improve the cellular and molecular immune response levels, regulate the cytokine secretion. Moreover, fucoidan stimulates the innate and adaptive immune defense systems of the body by interfering with the process of virus adsorption, transcription, and synthesis, which can be used as an immune adjuvant to increase the production of antigen specific antibodies in the body. It can bind to receptors, then activates the intracellular pathways, activates immune cells, promote the release of cytokine and enhance immune activity. The relative molecular weight, monosaccharide composition, glycosidic bond types, chemical modifications, and advanced conformation of fucoidan can affect its immunomodulatory activity.

Conclusion: This paper has significance for further studying on the range of molecular weight, monosaccharide types, glycosidic bond types, chemical modification methods and advanced conformations of fucoidan, and it is of great significance in revealing its structure-activity relationship and developing more effective analogues or derivatives as novel drugs for disease treatment.

Key words Fucoidan; Immunoregulation; Chemical structure; Advanced conformation

Category: Basic Nutrition& Research

每日运动大鼠的免疫生理变化

Daily Exercises Causes Immune physiological changes in Rats

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Objective To investigate the effect of daily continuous exercise on physiological changes of weight and immune factor levels of rats.

Methods Twelve healthy SD male rats (200±20 g) were randomly divided into one control group and one exercise group. All rats were kept in polypropylene boxes in a controlled animal breeding cabinet, under standard environmental conditions with controlled temperature (20–25 ℃) and relative humidity of 50–60%. Rats were free to water and standard diet. The rats in the exercise group received a fixed 1 h (0.5 h each in the morning and in the afternoon) daily treadmill running in a normal temperature environment. The experiment lasted for 4 weeks. Weight of all rats was measured at the beginning of the experiment and the end of every week. After the experiment, blood samples were collected and serum was separated for biochemical analysis.

Results Compared with the initial level, the weight of rats in both groups significantly increased at day 28 (both $P<0.05$); however, the D-value of weight gain in exercise group was lower than that in control group ($P<0.05$). Compared with control group, the spleen and thymus indexes of rats in exercise group significantly increased, the content of serum hs-CRP significantly decreased, the level of TNF-α and IL-6 significantly increased (all $P<0.05$), and the expression of Nrf2 was up-regulated. There was no difference in IL-2 and liver index between two groups.

Conclusion Our findings suggested that increased immune organ index and anti-inflammatory factors, as well as down-regulation of pro-inflammatory factor might be contributed to continuous running. Exercise daily had an effect on decreased body weight, which was related to promoting energy consumption.

Key words Exercise, Immune, Weight, Rat

Category: Basic Nutrition& Research

甜菜碱通过抑制 NLRP3 炎症小体的激活改善同型半胱氨酸诱导的认知障碍

Betaine ameliorates homocysteine-induced cognitive dysfunction by suppressing NLRP3 inflammasome activation

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Sun Yat-sen University

Background:

Dementia is one of the major public health problems, and homocysteine (Hcy) increases dementia risk. Betaine, as an important methyl donor in the human body, can reduce Hcy, but whether betaine can improve cognition by reducing Hcy is not yet clear. We aimed to investigate the effect and mechanism of betaine on Hcy-induced cognitive impairment in SD rats.

Methods:

Nine-week-old SD rats were administered Hcy (400 μg/kg) via vena caudalis injection for 14 days, along with normal or betaine-supplemented (2.5% w/v) drinking water. The learning and memory behavior of the SD rats was evaluated by the Y-maze and novel object recognition test 24 h after the last administration. Histological damage was observed using HE staining. Immunofluorescence and Western blot assays measured microglial activation and expression of NLRP3 inflammasome-associated molecules in the hippocampus.

Results:

The results of Y-maze and new object recognition experiments showed that the time and distance in the new arm were decreased, the time to explore new objects and the discrimination index were reduced in the Hcy group, and betaine supplementation could improve their learning and memory abilities. In addition, pericellular spaces were enlarged and cell morphology was disturbed in the Hcy group and betaine supplementation could significantly alleviate the pathological damage. Betaine ameliorated Hcy-induced inflammatory response by inhibiting NLRP3/caspase-1/GSDMD pathway.

Conclusions：

We found that betaine could improve cognitive ability in Hcy-induced SD rats, and the possible mechanism was the inhibition of neuroinflammation. Our results provide new ideas for improving cognitive performance and the application of betaine.

Key words betaine，homocysteine，cognitive，inflammation

Category: Basic Nutrition& Research

蓝莓花色苷对老年轻度认知功能障碍患者认知功能及炎性水平的影响

Effect of blueberry anthocyanins on cognitive function and inflammatory level in elderly mild cognitive impairment patients

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Objectives: This study aimed to assess the effect of blueberry extracts supplementation and the underlying mechanism on improving the cognitive function in the elderly patients with mild cognitive impairment (MCI). Methods: 48 subjects aged 60-90 years from all screened subjects participated in the intervention study. The subjects participated in the intervention study were randomly assigned to the intervention group or blank control group. The former received blueberry extracts treatment for 12 weeks, while the latter did not receive any intervention. The neuropsychological test was the Clinical Dementia Rating (CDR), the Mini-Mental State Examination (MMSE) and the basic cognitive aptitude test (BCAT). The inflammation factors measured was Interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α). Results: After 12 weeks of intervention, we observed significant improvement in their total BCAT score, space imagery efficiency, working memory and recognition memory of subjects in patients with blueberry extracts supplementation comparing to those in the control group (P=0.006, 0.023, 0.000, 0.005, respectively). However the levels of inflammatory factors (IL-6 and TNF-α in serum) showed no significant changes after intervention. Conclusion: These results indicate that blueberry has a beneficial effect on cognitive function of the elderly MCI patients, which might provide therapeutic potential for Alzheimer’s disease.

Key words blueberry extracts; mild cognitive impairment; cognitive function; inflammation factors

Category: Basic Nutrition& Research

花色苷调节星形胶质细胞-神经元乳酸穿梭缓解 APP/PS1 小鼠认知障碍的机制研究

Anthocyanin regulates astrocyte-neuron lactate shuttle to alleviate cognitive impairment in APP/PS1 mice

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Background: As most common cause of dementia, Alzheimer's disease (AD) is becoming a dire global health concern among the elderly. Previous studies have found that diet, rich in anthocyanins, is an effective way to delay AD progress, but the mechanism is still unclear.

Objective: To identify the promoted effects for astrocyte-neuron lactate shuttle (ANLS) of Cyanidin-3-O-glucoside (Cy3G), the most common anthocyanin in diet, and find out the related mechanism of mTOR-HIF1α pathway.

Methods: Six-month-old APP/PS1 mice were gavaged with Cy3G (50 mg/kg·bw) and HIF1α inhibitor PX-478 for 2 months, behavioral tests and related proteins were detected to confirm whether Cy3G promotes ANLS through HIF1α pathway. Furthermore, the co-culture model of primary rat astrocytes and neurons was established in vitro. The protection of Cy3G on $A\beta_{25-35}$-induced neuron activity damage and the inhibition of Cy3G on $A\beta_{25-35}$-induced astrocyte activation were detected by CCK-8. In addition, whether Cy3G could promote lactate metabolism through mTOR-HIF1α pathway was evaluated by detecting ANLS-related proteins and glycolysis rate after added HIF1α inhibitor PX-478 or mTOR inhibitor Rapa.

Results: Cy3G effectively alleviated cognitive impairment, inhibited brain damage, decreased proinflammatory cytokines levels and neuronal loss in APP/PS1 mice. Furthermore, Cy3G inhibited activation, changed the metabolic pattern, up-regulated the expression of ANLS-related proteins, and elevated the glycolysis of cultured astrocytes through the mTOR-HIF1α pathway. Strikingly, Cy3G promoted ANLS and protected primary cultured neurons induced by $A\beta_{25-35}$ in astrocyte-neuron co-culture system.

Conclusion: Our study identifies lactate metabolism disorder and ANLS inhibition are important features of AD, and suggests Cy3G promotes ANLS and provides reliable theoretical basis for the formulation of nutritional prevention programs for AD.

Key words Cyanidin-3-O-glucoside; Cognitive impairment; astrocyte-neuron lactate shuttle; Alzheimer's disease; mTOR-HIF1α pathway

Category: Basic Nutrition& Research

蓝莓提取物经 MEK-ERK-BDNF/UCH-L1 信号通路拮抗 Aβ25-35 神经毒性对大鼠和小鼠海马神经保护作用的研究

Blueberry extracts antagonize Aβ25-35 neurotoxicity and exert a neuroprotective effect through MEK-ERK-BDNF/UCH-L1 signaling pathway in rats and mice hippocampal

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Background: Alzheimer's disease (AD) is an age-related neurodegenerative disorder. Previous studies have indicated that the blueberry (BB) extracts have protective effects on brain function. However, its underlying mechanism remains largely unexplored.

Objective: Our research planned to explore the effects and mechanism of BB extracts in improving the learning and memory capacity of AD mice based on the pathway of MEK-ERK.

Methods: 3-month-old APP/PS1 transgenic mice were divided into AD+BB, AD, and control (CT) group. Morris water maze test (MWMT) was applied to evaluate the learning and memory capacity. Moreover, the swimming distance and time in the acquisition trial, as well as swimming distance, swimming time, and crossing times in the target quadrant in the probe trial, were recorded. In vitro, the Aβ25-35-injured rat hippocampal neurons were exposed to BB extracts of different concentrations. In addition, the expressions of MEK-ERK-BDNF/UCH-L1 pathway-related genes at the mRNA and protein levels were assessed.

Results: Our data showed that the AD mice exhibited weak learning and memory capacity in the acquisition trial and probe trial of the MWMT, while the AD+BB group exhibited significantly better performance. In the AD group, the expressions of both MEK2 and ERK1/2 at the mRNA and protein levels were significantly elevated, the expression of UCH-L1 at the mRNA level was decreased and the expression of BDNF was increased significantly. With the treatment of BB extracts, the expressions of MEK2 and ERK1/2 were inhibited, and the expressions of UCH-L1 and BDNF at the mRNA level returned to normal. A similar regulate effect of BB extracts on the expressions of UCH-L1 and BDNF was observed.

Conclusions: BB extracts might be beneficial for AD by improving the learning and memory capacity. Excessively activated MEK-ERK pathway and abnormal expressions of BDNF and UCH-L1 might be risk factors for AD.

Key words Blueberry extracts, Alzheimer's disease, MEK-ERK, BDNF, UCH-L1

Category: Basic Nutrition& Research

不同嘌呤含量食源性低聚肽对大鼠血尿酸的影响

Effects of food-derived oligopeptides with different levels of purine on hyperuricemia rats

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The Airforce Military Medical University

Objective: To determine the purine content of food-derived oligopeptides from different food sources and to study the effects of food-derived oligopeptides with different purine contents on blood uric acid level, renal function and renal structure in hyperuricemia rats. Methods: The purine content of 10 different kinds of food-derived oligopeptides was determined by high performance liquid chromatography. And soybean peptide, mung bean peptide and marine fish protein peptide were selected as high, medium and low purine food-derived oligopeptides as gavage intervention substances in rats. Hyperuricemia rat model was constructed with 10%fructose. Blood samples were collected to detect uric acid, creatinine and urea nitrogen on 7 d,14 d,21 d and 28 d after modeling, and kidney tissues were collected and stained with HE to observe the histological changes of kidneys at 28 d after the experiment. Results: Soybean peptide with high purine content had the effect of reducing blood uric acid at four time points in the experiment($P<0.05$). The renal injury was significantly improved, and the blood creatinine and urea nitrogen were decreased($P<0.05$). However, the effect of low and medium purine food-derived oligopeptides was similar to that of soybean peptides only after 7 days of modeling, and there was no effect of reducing uric acid and improving kidney damage in the late modeling period; The marine fish protein peptide with low purine also had the effect of increasing blood uric acid after 14 days of modeling. Conclusion: The purine content of food-derived oligopeptides is not consistent with the source food. Soybean food-derived oligopeptides can continuously reduce the blood uric acid, alleviate kidney injury and renal dysfunction in model rats.

Key words food-derived oligopeptides; hyperuricemia; serum uric acid; serum creatinine; renal function.

Category: Basic Nutrition& Research

基于代谢组学的高尿酸血症和血脂异常关系分析

Metabolomics-based analysis of the relationship between hyperuricemia and dyslipidemia

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Objectives:Although the strong correlation between dyslipidemia and hyperuricemia has been acknowledged, little is understood regarding the underlying relationship between these two factors. The goal of this work was to determine the differential metabolites produced by human umbilical vein endothelial cells (HUVECs) following treatment with uric acid (UA) and to look into how hyperuricemia and dyslipidemia interact.

Methods: Metabolomic profiling of 16 cell samples, 8 of which were treated with UA (8 mg/dl) for 24 hours and 8 of which were not, was performed via a liquid chromatograph with mass spectrometry (LC -MS). Finding the differential metabolite associated with lipid metabolism through a metabolomic approach, and then adequately validating its protective function on HUVECs using assays such as cellular vitality, reactive oxygen species, migration potential, and gene and protein expression of inflammatory pathway and downstream inflammatory factors.

Results:Taurochenodeoxycholic acid(TCDCA) (the differential metabolite of human umbilical vein endothelial cells, HUVECs) and the TCDCA-involved primary bile acid synthesis pathway were significantly negatively correlated with high uric acid (UA) levels, according to metabolomics analysis. Compare to the outcomes observed in UA-treated HUVECs, TCDCA protects against UA-induced cell damage and oxidative stress, increases proliferation and migration, and decreases apoptosi. Meanwhile, TCDCA may protect HUVECs by inhibiting UA-induced P38MAPK/NF-B p65 pathway gene and protein expression, as well as downstream inflammatory factors.

Conclusions: Our findings suggest that hyperuricemia, which is frequently associated with dyslipidemia, may be related to a decrease in bile acids caused by high levels of UA.

Key words Hyperuricemia, Dyslipidemia, Taurochenodeoxycholic acid, Vascular endothelial injury

Category: Basic Nutrition& Research

生命早期肠道菌群紊乱可性别差异性地影响幼年期大鼠血压调节

Gut Microbiota Perturbation at Early Life could Influence Pediatric Blood Pressure Regulation in a Sex-dependent Manner in Juvenile Rats

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Backgroud and objectives: The present study aimed to investigate whether gut dysbiosis induced by ceftriaxone in early life could influence pediatric blood pressure regulation in childhood with or without exposure to a high-fat diet (HFD).

Methods: Sixty-three newborn pups of Sprague-Dawley rats were administered ceftriaxone sodium or saline solution until weaning at 3 weeks, and the rats were fed a HFD or regular diet from 3 to 6 weeks. Tail-cuff blood pressure; the expression levels of genes of the renin-angiotensin system (RAS); the concentrations of IL-1β, IL-6, and TNF-α in the colon and prefrontal cortex; the composition of fecal microbiota were analyzed.

Results: Ceftriaxone treatment significantly increased the diastolic blood pressure of male rats at 3 weeks. At 6 weeks, systolic blood pressure (SBP) was significantly increased only in ceftriaxone treated male rats fed with HFD. The RAS showed increased activation in the kidney, heart, hypothalamus, and thoracic and abdominal aorta of male rats, but only in the kidney, heart, and hypothalamus of female rats. HFD-fed female rats showed a decreased level of IL-6 in the colon. α diversity of gut microbiota decreased and the Firmicutes to Bacteroidetes ratio increased in both male and female rats at 3 weeks; however, these parameters recovered to various degrees in female rats at 6 weeks.

Conclusions: Early-life gut dysbiosis induced by antibiotics combined with a HFD in childhood could be involved in pediatric blood pressure regulation and increase SBP in juvenile rats, and these effects occurred in a sex-dependent manner.

Key words gut microbiota; blood pressure; ceftriaxone; high-fat diet; pediatric hypertension

Category: Basic Nutrition& Research

中国育龄女性机体铁代谢与2型糖尿病的关系:中国成人慢性病和营养监测(2015)的结果

Association of Body Iron Metabolism with Type 2 Diabetes Mellitus in Chinese Women of Childbearing Age: Results from the China Adult Chronic Disease and Nutrition Surveillance (2015)

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Up to now, evidences for the associations of iron metabolism biomarkers other than ferritin with Type 2 Diabetes Mellitus (T2DM) are sparse and inconsistent, and whether there is a threshold effect remains controversial. In the present study, we aimed to examine the associations between various iron biomarkers, including serum ferritin (SF), transferrin, soluble transferrin receptor (sTfR), transferrin saturation (TSAT), serum iron, total body iron (TBI), and sTfR-to-lgferritin index, and risk of T2DM as well as impaired glucose metabolism in Chinese women of childbearing age. A total of 1145 women were divided into three groups based on the levels of fasting blood glucose and HBA1c [normal blood glucose metabolism group (NGM); impaired glucose metabolism group (IGM); T2DM group]. The levels of SF, sTfR, and TBI in IGM and T2DM groups were higher than those in NGM group ($p < 0.05$). There was no significant difference in transferrin levels among the three groups. After adjusting for age, sociodemographic, life-style, and body mass index, blood pressure, lipids, hypersensitive C-reactive protein, and α-acid glycoprotein, SF and sTfR were positively associated with the risk of IGM [fourth vs first quartile: SF odds ratio (OR) = 1.93 (95% CI 1.17-3.20) and sTfR OR = 3.08 (95% CI 1.84-5.14)] and T2DM [SF OR = 2.39 (95% CI 1.40-4.06) and sTfR OR = 3.84 (95% CI 2.53-5.83)]. Neither transferrin nor TSAT were associated with IGM and T2DM risk. There was a nonlinear relationship between SF and the T2DM risk (p for non-linearity < 0.01). Our findings suggested that the SF and sTfR could be independent predictors for T2DM risk.

Key words iron metabolism biomarkers; type 2 diabetes mellitus; association; women of childbearing age

Category: Basic Nutrition& Research

学龄前儿童尿碘浓度和尿碘/肌酐比值的变化

Variation in Urinary Iodine Concentration and Urinary Iodine/Creatinine Ratio in Preschool Children

Rui Yang*
Tianjin Medical University

Background

Variation in different urinary measurements for evaluation of iodine status is of concern to clinicians and researchers.

Objective

The present study aims to analyze the inter- and intra-individual variations of urinary iodine concentration (UIC), urinary iodine/creatinine ratio (UI/Cr) and evaluate their application in assessing iodine nutrition of preschool children.

Methods

Four repeated spot urine samples were collected from 163 children at different time within one day. Urinary iodine concentration (UIC) and urinary creatinine concentration (UCr) were measured, and UI/Cr was calculated.

Results

The UIC ($p<0.001$) and urinary iodine/creatinine ($p=0.019$) of multiple measurements were significant different. UIC of morning urine was highest (99.83 μg/L) and then gradually decreased with collection time ($P<0.001$). On the contrary, the UI/Cr of morning urine samples increased with time. By computing the mean coefficients of variance (CV) of intra-individual and inter-individual, the intra-individual variation of UI/Cr (68%) was significantly lower than that of UIC (86%), but the inter-individual was lowest in the UIC (78.62%) of morning urine. In addition, UIC and UI/Cr showed moderate correlations ($r=0.52$, $p<0.001$), with kappa values of 0.42 in assessing iodine nutrition.

Conclusions

UIC of morning urine was more stable and reliable in evaluating iodine nutrition of preschool children at the population level. UI/Cr has lower intra-individual variation and may be more suitable for evaluating individual iodine nutrition.

Key words Iodine, urinary iodine concentration, urinary creatinine, urinary iodine/creatinine ratio

Category: Basic Nutrition& Research

住院的学龄前儿童的人体测量参数与其碘营养状态的关系

Association of anthropometric parameters with iodine status in hospitalized preschool children

Rui Yang*
Tianjin Medical University

Abstract:

Background: Iodine is a trace element necessary for the synthesis of thyroid hormones. Especially it is crucial for neurodevelopment and intellectual development of children. Our study aimed to investigate iodine status in hospitlized children, and explore the association between their anthropometric parameters with iodine nutrition.

Methods: A total of 535 hospitalized children aged 3-7 years from Tianjin Children's Hospital were enrolled. Anthropometric data, dietary data, urine samples and blood samples were collected. Urinary iodine concentration (UIC) and creatinine were determined, and the urinary iodine/creatinine ratio (UIC/Cr) was calculated. Usual food intake was determined using a short food frequency questionnaire.

Results: The mean age was 4.6±1.1 years old and the median UIC was 51.7 (18.3, 120.9) μg/L. UIC (40.1μg/L vs. 123.0μg/L) and UIC/Cr (297 μg/g vs. 497μg/g) were significantly lower in in-patient children when compared to out-patient children. Both UIC and UIC/Cr were decreased as height z-score and weight z-score, UICs were significantly lower in children with weight z-score > 1(39.4 μg/L) and height z-score >1 (33.6 μg/L). In addition, UIC was negatively correlated with height (). Adjusted by age, sex and parent education, it was found height-z score >1 was the risk factor for UIC<100μg/L (OR=3.6 (1.2, 10.8), P=0.020). This trend was only found in in-patient children.

Conclusions: The iodine nutriton of hospitalized preschool children was insufficient. Height z-score>1 was probably the risk factor for iodine deficiency in children after hospital admission.

Key words Urinary iodine concentration; anthropometric parameters; Iodine deficiency; Micronutrients; Public health.

Category: Basic Nutrition& Research

精制青稞在改善肥胖和血糖方面表现出与全谷物青稞相似的特性

Refined Highland Barley Display the Similar Properties with Whole Grain Highland Barley in Ameliorating Obesity and Blood Glucose

Zijian Dai*
China Agricultural University

Highland barley has attracted much attention due to its extremely rich nutritional and functional ingredients. Previous studies revealed that whole grain highland barley (WGHB) could help reduce the risk of several chronic and metabolic diseases, including obesity and diabetes. However, whether refined highland barley (RHB) could still play a beneficial role, and the potential mechanisms by which RHB and WGHB improve obesity and glucose tolerance, need further investigation. This study evaluated the anti-obesity and hypoglycemic effects of RHB in high-fat diet (HFD)-fed mice and further compared it with the intervention of WGHB. The results showed that both RHB and WGHB could suppress weight gain and improve glucose tolerance. In addition, they could significantly increase the abundance of genus Lachnospiraceae_NK4A136_group, Akkermansia, Bifidobacterium, Lachnospiraceae_UCG-001, and Alloprevotella in feces, and alter the liver gene transcription profile. Overall, our findings suggested that RHB could ameliorate obesity and glucose tolerance via remodeling gut microbiota, and we also found that it had similar effects to WGHB.

Key words hulless barley; refined grain; inflammation; hypoglycemic effect; gut microbiota

Category: Basic Nutrition& Research

白藜芦醇通过抑制肠道 FXR 和清道夫受体 SR-B1 减少乳糜微粒分泌

Resveratrol intervention attenuates chylomicron secretion via repressing gut Farnesoid X receptor and scavenger receptor SR-B1

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Two common features of dietary polyphenols have hampered our mechanistic understanding of their beneficial effects for decades: targeting multiple organs and extremely low bioavailability. We show here that resveratrol intervention (REV-I) in high fat diet (HFD)-challenged male mice inhibited chylomicron secretion, associated with reduced expression of jejunal but not hepatic scavenger receptor class B type 1 (SR-B1). Intestinal-mucosa-specific SR-B1$^{-/-}$ mice on HFD challenge exhibited improved lipid homeostasis but showed virtually no further response to REV-I. SR-B1 expression in Caco-2 cells cannot be repressed by pure resveratrol while fecal-microbiota transplantation from mice on REV-I suppressed jejunal SR-B1 in recipient mice. REV-I reduced fecal levels of bile acids including chenodeoxycholic acid (CDCA) and activity of fecal bile-salt hydrolase (BSH), while CDCA stimulated FXR and SR-B1 in Caco-2 cells. We conclude that gut microbiome is the primary target of REV-I, and REV-I improves lipid homeostasis at least partially via attenuating CDCA-stimulated gut SR-B1 elevation.

Key words resveratrol; chylomicron; gut microbiota; bile acids; SR-B1

Category: Basic Nutrition& Research

高脂饮食和高糖饮食通过调控不同的肠道微生物源性胆汁酸代谢诱导小鼠葡萄糖稳态失调

High fat diet and high sugar intake divergently induce dysregulation of glucose homeostasis through distinct gut microbiota-derived bile acid metabolism in mice

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igh calorie diet such as excessive fat and sugar intake always accompanied by impaired glucose homeostasis. However, it remains unclear how fat and sugar individually affect host glucose metabolism. In this study, mice were fed with high fat diet (HFD) or 30% sucrose in drinking water (HSD) for 24 weeks, and glucose metabolism, gut microbiota composition, as well as bile acid (BA) profile were investigated. In addition, the functional changes of HFD or HSD-induced gut microbiota were further verified by fecal microbiota transplantation (FMT) and ex vivo culture of gut bacteria with BAs. Our results showed that both HFD and HSD caused dysregulated lipid metabolism, while HFD feeding had a more severe effect on impaired glucose homeostasis, accompanied by reduced hyocholic acid (HCA) levels in all studied tissues. Meanwhile, HFD had a more dramatic influence on composition and function of gut microbiota as well as secondary BA producers than HSD. In addition, the phenotypes of impaired glucose homeostasis and less formation of HCA caused by HFD can be transferred to recipient mice by FMT. Ex vivo culture with gut bacteria and BAs revealed HFD-altered gut bacteria produced less HCA than HSD, which might closely associated with the reduced relative abundance of C7 epimerase-coding bacteria g_norank/unclassified_f_Eggerthellaceae and bile salt hydrolase-producing bacteria Lactobacillus and Bifidobacterium in HFD group. Our findings revealed that the divergent effects of different high-calorie diets on glucose metabolism may be due to the gut microbiota-mediated generation and metabolism of BA, highlighting the importance of dietary management in T2DM.

Key words high-energy diet, bile acid, gut microbiota, glucose homeostasis, Hyocholic acid

Category: Basic Nutrition& Research

基于碘溢出假设对中国青年人碘膳食参考摄入量的研究

Study on dietary reference intake of iodine using iodine overflow hypothesis in Chinese young adults

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Background Thyroid dysfunction is increasingly attributed to excess iodine intake as the enforcement of Universal Salt Iodization (USI) in China. However, the traditional balance study could be no longer applied in the individuals due to iodine over-nutrition.

Objectives Iodine overflow hypothesis is firstly proposed to build the iodine dietary recommended intake (DRIs) in Chinese young adults, including Estimated average requirement (EAR) and Recommended nutrient intake (RNI).

Methods A total of 74 healthy subjects (male 38 and female 36) were recruited in this study. After the 14-days iodine depletion, iodine supplementation was performed for 6 stages and each of 5 days. Designed diets were provided and all foods and excreta (urine, feces) were collected to examine daily intake, excretion and the incremental (Δ) iodine in relation to stage 1. The dose-response associations of Δ iodine intake and Δ iodine excretion, as well as Δ iodine retention, were fitted by the mixed effects models (MEMs).

Results Daily iodine intake of all subjects increased from 14.9 μg/day to 133.5 μg/day, whilst iodine excretion elevated from 51.5 μg/day to 154.1 μg/day. The Δ iodine intake increased from 16.3 μg/day to 119.4 μg/day, while Δ iodine excretion elevated from 21.8 μg/day to 102.5 μg/day. In final, zero balance in vivo was dynamically achieved as iodine intake at 48.0 μg/day for male and 52.2 μg/day for female. The iodine EAR and RNI were further calculated as 48.0 μg/day and 67.2 μg/day for male and 52.2 μg/day and 73.1 μg/day for female. The RNI values could be corresponded to daily iodine intake of 1.04 μg/kg•day for male and 1.40 μg/kg•day for female, respectively.

Conclusion The iodine overflow hypotesies had been validated and the data indicated that one-half of current dietary iodine intakes could be enough in Chinese young adults, which would be beneficial for the making DRIs in future.

Key words Iodine; Dietary recommended intake; Estimated average requirement; Recommended nutrient intak; Chinese young adults;

Category: Basic Nutrition& Research

四川泡菜中抑菌乳酸菌的筛选及其抑菌物质的初步探究

Screening of antibacterial lactic acid bacteria from Sichuan pickles and characterization of their antibacterial substances

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Objective The study aimed to screen lactic acid bacteria (LAB) from Sichuan Pickles with antibacterial properties against foodborne pathogens and to examine their antibacterial substances. **Methods** Bacterial identification was done through 16S rDNA gene sequencing. The bacteriostasis experiment was performed using the Oxford cup method, while a preliminary investigation of the antibacterial substance was done through acid excretion and protease sensitivity testing. **Results** A total of 42 LAB strains with robust growth abilities were identified. 16S rDNA gene sequencing revealed the presence of 9 species belonging to 3 genera, including 23 strains of *Lactobacillus plantarum*, 10 strains of *Lactobacillus casei* and *Lactobacillus paracasei*, 2 strains each of *Lactobacillus harbinensis*, *Pseudomesenteroides leuconostoc*, and *Pediococcus ethanolidurans*, and 1 strain each of *Lactobacillus acidipiscis*, *Lactobacillus buchneri*, and *Lactobacillus xiangfangensis*. Results of the inhibition experiment indicated that the fermentation supernatant of 39 bacteria strains inhibited *Vibrio parahaemolyticus* and 30 of them still maintained their antibacterial activity after the acid elimination experiment. Among all strains, the strongest inhibitory effect on *Vibrio parahaemolyticus* was observed in *Lactobacillus plantarum* LAB13, with an antibacterial circle diameter of 16.21 mm after acid elimination. Treatment with proteinase K, trypsin, and pepsin resulted in the disappearance of the antibacterial activity of *Lactobacillus plantarum* LAB13, leading to the preliminary conclusion that the main antibacterial substances in the fermentation supernatant were protein. *Lactobacillus plantarum* LAB13 also displayed antibacterial activity against *Listeria mononuclearum* and *Salmonella typhimurium*. **Conclusion** A strain of *Lactobacillus plantarum* LAB13 with inhibitory properties against *Vibrio parahaemolyticus* was identified in Sichuan Pickles. The preliminary analysis of its antibacterial substance suggests it is protein-based. This research serves as a reference for future screening of LAB with antibacterial abilities.

Key words Sichuan pickle; lactic acid bacteria; Vibrio parahaemolyticus; Lactobacillus plantarum; antibacterial activity

Category: Basic Nutrition& Research

二氢杨梅素通过 AMPK/SIRT3/STAT3 信号通路促进 ILC3 细胞激活缓解高脂诱导肠屏障破坏的研究

Dihydromyricetin alleviates high-fat diet induced intestinal barrier damage by promoting ILC3s activation through AMPK/SIRT3/STAT3 signaling pathway

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Objective: To investigate the effects and underlying mechanism of DHM on ameliorating HFD-induced intestinal barrier integrity damage via SIRT3-mediated immune function of ILC3 cells. Methods: C57BL/6 male mice were fed with control, high-fat diet (HFD), or HFD+DHM diets for 12 weeks. The intestinal permeability and expression of intestinal tight junction (TJ) protein were detected to evaluate the effects of DHM on intestinal barrier integrity. The IL-22 expression of group 3 innate lymphoid cells (ILC3s) in small intestine lamina propria was tested by flow cytometry to estimate the effects of DHM on ILC3 function. In addition, MNK3 cell line, expresses the same transcription factors and cytokines as ILC3, was used to investigate the molecular mechanism. In vitro experiments, the total and phosphorylation of AMPK, SIRT3, and STAT3 was detected by qRT-PCR or Western blotting to explore the underlying mechanism under DHM-induced IL-22 expression. Results: DHM effectively reversed the increased intestinal permeability and decreased expression levels of TJ molecules induced by HFD, and that it could promote ILC3 activation and IL-22 secretion. Moreover, DHM promoted the expression of AMPK phosphorylation and SIRT3 activation which in turn to increase STAT3-induced IL-22 expression in MNK3 cells. And this effects of DHM on SIRT3 and IL-22 were attenuated by AMPK inhibition. Conclusions: DHM improved IL-22 production of ILC3 cells to alleviate HFD-induced intestinal barrier destruction via AMPK/SIRT3/STAT3 pathway.（This work was supported by grants from National Natural Science Foundation of China: 81973039 and 81872625）

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Key words Dihydromyricetin; intestinal barrier; IL-22; SIRT3.

Category: Basic Nutrition& Research

二氢杨梅素调控肠道 GLP-1 水平改善 II 型糖尿病的作用及机制研究

Dihydromyricetin improves T2DM induced by high-fat diet via affecting GLP-1 secretion by regulation of intestinal L-cell and IELs

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Objective: To investigate the effect of dihydromyricetin (DHM) on the development of type II diabetes (T2DM) induced by high-fat diet (HFD), and to explore the mechanism involved with GLP-1 expression modulated by intestinal L-cell and IELs.

Methods: C57BL/6 male mice aged 6-8 weeks were fed with HFD (45% fat) for 8 weeks to establish T2DM model. DHM (mass ratio of 0.6%) was added to 45% fat to observe the effect of DHM on T2DM development. The body weight and food intake in each group were recorded, and the blood glucose, blood lipid (LDL-C, HDL-C, CHO, TG), serum GLP-1 and insulin were measured. Intestinal pathology and immunofluorescence detection of GLP-1 expression were detected. 16s RNA high-throughput sequencing analysis of gut microbiota changes and LC-MS analysis of intestinal non-targeted metabolites were carried out. The frequency and phenotype of intestinal epithelial lymphocytes (IELs) and the expression level of DPP4/CD26 were analyzed by flow cytometry.

Results: Compared with the control group, HFD resulted in a reduced glucose tolerance, while an increased fasting blood glucose, serum TG, CHO and LDL-C. And the serum insulin, GLP-1 and HDL-C levels were decreased in HFD group. Gut microbiota and metabolites were notably changed in HFD group. DHM evidently alleviated the HFD-induced increased abundance of *Desulfobacterot*, the decreased abundance of *Verrucomicrobiota* and the decreased ratio of *Firmicutes/Bacteroidetes*. Flow cytometry assay showed that the IELs quantity and the proportion of its different phenotype were apparently altered after DHM treated. And the expression of DPP4/CD26 was decreased by DHM treatment.

Conclusions: DHM might ameliorate GLP-1 secretion in intestinal L cells by regulating gut microbiota and its metabolites, and inhibit GLP-1 degradation by regulating the number and phenotype of IELs and its DPP4/CD26 expression, thereby increasing serum GLP-1 level and improving T2DM development.

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Key words Type II Diabetes; Dihydromyricetin; GLP-1; Gut Microbiota; IELs

Category: Basic Nutrition& Research

二氢杨梅素对胆碱缺乏L-氨基酸限定的高脂饮食诱导的小鼠非酒精性脂肪性肝炎的影响

Effect of dihydromyricetin on a choline-deficient and L-amino acid-restricted high-fat diet-induced non-alcoholic steatohepatitis in mice

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Aim: To investigate the ameliorative effects of dihydromyricetin (DHM) on Non-alcoholic steatohepatitis (NASH) in mice induced by a choline-deficient, L-amino acid-restricted, high-fat diet. Methods and study design: C57BL/6J mice were fed with a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) for 4 weeks to establish a NASH mice model. Mice were randomly divided into four groups: CON group (common diet), CDAHFD group (CDAHFD), DHML group (CDAHFD with DHM of 200 mg/kg/d) and DHMH group (CDAHF with DHM of 400 mg/kg/d). After sacrifice, the HE staining and qRT-PCR assays were used to assess liver inflammation and fibrosis. Liver index and serum biochemicals as well as the levels of TG, TNF-α, IL-1β, SOD and GSH-Px in liver were measured to test hepatic lipids accumulation and oxidative stress. Results: DHM significantly improved pathological changes in liver tissue of CDAHFD-induced NASH mice model, as evidenced by increased hepatocyte hypertrophy, vacuolization, inflammatory cell infiltration, hepatic lipid accumulation and liver index. Meanwhile, DHM treatment remarkably ameliorated HFD-induced hepatic inflammatory injuries, as evidenced by reduced expressions of MCP-1, TNF-α, CCL2, CXCL2 and CXCL10 as well as the reduced levels of TNF-α and IL-1β in liver tissue. Moreover, CDAHFD feeding elicited aggravated oxidative stress in hepatocytes as seen by decreased levels of SOD and GSH-Px, which were dominantly inhibited by DHM. Additionally, DHM administration could significantly ameliorate liver fibrosis and suppress the related gene expression such as a-SMA、Co1α1 and TIMP-1 in CDAHFD-induced mice. Conclusion: Our results suggested that DHM improved liver fibrosis by reducing hepatic lipids accumulation, inflammation and oxidative stress in NASH mice model.

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Key words Non-alcoholic steatohepatitis; Dihydromyricetin; Oxidative stress; Inflammation; Hepatic fibrosis

Category: Basic Nutrition& Research

杨梅素可改善非酒精性脂肪性肝炎小鼠的肝脏炎症和纤维化

Myricetin attenuates liver inflammation and fibrosis in mice with nonalcoholic fatty liver disease

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Objective: The objective of this study was to investigate the potential role of myricetin in attenuating liver inflammation and fibrosis in non-alcoholic steatohepatitis (NASH). Methods and study design: C57BL/6J mice were randomly divided into the CON, NASH, and NASH + Myricetin groups. Mice in the NASH and NASH + Myricetin groups were fed with choline-deficient L-amino acid-defined, high-fat diet, while mice in the CON groups were fed with a standard chow diet. We garaged mice of the NASH + Myricetin group with myricetin of 100mg/kg·bw /day for four weeks, and other groups were garaged with saline solution. We detected the body weight, liver index, liver histology (HE staining, OilrRed O staining, Wolf scarlet staining), serum biochemical indices, TG, and TNF-α levels in liver tissue. And qRT-PCR assay was used to assess liver inflammation and fibrosis. Results: There was a significant accumulation of lipid droplets, a large number of fat vacuoles and bubble-like hepatocytes, increased TG accumulation in liver tissue, and a significantly increased serum ALT level in the NASH group. However, myricetin supplementation could effectively attenuate lipid accumulation and liver injury in the NASH + Myricetin group. Moreover, the serum Tch and HDL-C levels of mice in the NASH group were significantly decreased, which was reversed after myricetin intervention. Meanwhile, compared with the CON group, qRT-PCR results showed that the mRNA expression of liver inflammation-related genes MCP-1, CXCL10, and TNF-α) as well as fibrosis-related genes Col3α1 and TIMP- 1 were significantly increased in NASH group, which were notably inhibited by myricetin intervention indicated. Conclusions: Myricetin could significantly attenuate liver inflammation and fibrosis in mice with nonalcoholic steatohepatitis.

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Key words nonalcoholic steatohepatitis; inflammatory response; fibrosis; myricetin

Category: Basic Nutrition& Research

紫檀芪干预后小鼠盲肠内容物的非靶向代谢组学研究

Non-targeted metabolomics study of cecal contents after pterostilbene intervention

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Background and Objectives

The metabolomics of cecal contents after pterostilbene intervention was studied based on reversed-phase high-performance liquid chromatography and UHPLC-Q-Exactive mass spectrometry.

Methods and Study Design

C57BL/6J male mice were gavaged with pterostilbene (100 mg/kg) and sacrificed at 0,5,15, 30, 60, 90, 120, 180, 270, 360, 480, 600, 720, and 1440 min after intervention. We set up an effective high-performance liquid chromatography assay to quantify pterostilbene concentrations. We performed the metabolomic profile of cecal contents at 0 min (CON), 720 min (CE6H), and 1440 min (CE12H) after pterostilbene intervention by UHPLC-Q-Exactive mass spectrometry.

Results

The peak concentration of pterostilbene in serum, small intestine, cecum, and colon contents of mice was 15 min, 30 min, 4.5 h, and 6 h, respectively. Distinct metabolite clustering was apparent among the CON, CE6H, and CE12H groups with the PCA model. There was a clear separation between the CON, CE6H, and CE12H groups by PLS-DA analysis. Compared with the CON group, we screened a total of 482 differential metabolites in the CE6H group and 360 differential metabolites in the CE12H group. Most of the differential metabolites were steroid-related metabolites in the KEGG compound database. Compared with the CON group, the cholesterol sulfate ($P<0.001$) was significantly increased, and 4a-Methylzymosterol($P<0.05$), L-Arginine($P<0.001$), 16b-Hydroxyestrone($P<0.01$), and L-Glutamine($P<0.001$) were significantly decreased in the CE6H group. However, the 4a-Methylzymosterol and 16b-Hydroxyestrone gradually returned to normal in the CE12H group. KEGG pathway enrichment analysis suggested that metabolic differentials were mainly involved in protein digestion and absorption and arginine and proline metabolism. The cecal testosterone concentrations were significantly increased after pterostilbene intervention.

Conclusions

Our results indicated that pterostilbene might increase testosterone concentrations by promoting the metabolism of steroids and inhibiting testosterone reduction in the cecum.

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Key words Pterostilbene; Cecal contents; Non-targeted metabolomics; High-performance liquid chromatography; Testosterone

Category: Basic Nutrition& Research

白藜芦醇通过上调 ATGL/CGI58 和 Rab7/LC3β 提高 NAFLD 小鼠肝脏脂质分解

Resveratrol enhances hepatic lipid hydrolysis in NAFLD mice by upregulating ATGL/CGI58 and Rab7/LC3β

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Objective

In order to clarify the effect of resveratrol on enhancing hepatic lipid hydrolysis in NAFLD mice through SIRT1 and PLIN2.

Methods and Study Design

32 C57BL/6 male mice aged 6-8 weeks were randomly divided into the control (CON), high-fat (HFD), high-fat with low-dose resveratrol (FLR) and high-fat with high-dose resveratrol (FHR) groups. The body weight, liver weight, blood lipids, blood glucose, liver function indicators were detected. Western blot and tissue immunofluorescence staining were used to detect the protein expression levels of hepatic lipid hydrolysis related molecules SIRT1, PKA, p-PKA, PLIN2, ATGL, CGI58, HSL, Rab7, LC3β and co-location situation of lipolysis and lipolysis pathway related genes (ATGL/CGI58, Rab7/LC3β) in mouse liver.

Results

Compared with CON group, body weight, liver weight, blood glucose, blood lipid, liver function and the relative area of lipid droplets in liver tissue of mice in HFD group tended to increase.Resveratrol intervention significantly inhibited the increase of body weight, liver weight and blood TG content in NAFLD mice, and reduced the hepatic lipid droplet area and the lipid accumulation in the liver of NAFLD mice, indicating that high-fat feeding can successfully establish NAFLD mice model. However, RSV intervention notably reduced lipid accumulation in NAFLD mice, characterized by the increased expressions of hepatic lipid hydrolysis-related genes SIRT1, p-PKA, PLIN2, ATGL, CGI58, HSL, Rab7 and LC3β in liver tissue. Moreover, the co-localization degree of ATGL/CGI58 and Rab7/LC3β were improved in the FLR and FHR groups. These results indicated that resveratrol could increase the expression of hepatic lipid hydrolysis-related molecules, and enhance the degree of co-localization of lipolysis related molecules ATGL/CGI58 and lipophagy related molecules Rab7/LC3β.

Conclusion

RSV improves the hepatic lipid accumulation in NAFLD mice by upregulating ATGL/CGI58 and Rab7/LC3β via PLIN2.

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Key words NAFLD;resveratrol; lipolysis; lipophagy

Category: Basic Nutrition& Research

紫檀芪改善短期睡眠限制小鼠肝脏代谢酶乙酰化水平及分子机制研究

The positive effects of pterostilbene on the acetylation of hepatic metabolizing enzymes of mice subjected to sleep restriction

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Objective

Our previous studies have confirmed that Pterostilbene (PTE) is effective in ameliorating disorders of glucose and lipid metabolism in short-term sleep-restricted (SR) mice, the mechanism is unclear. The aim of this study was to investigate the effect of PTE on acetylation modification and explore the molecular mechanism in terms of influence on NAD+-dependent deacetylase SIRT activity, expression and circadian rhythm oscillation.

Methods

C57BL/6J male mice were randomly divided into three groups: control (CON), sleep-restriction (SR) and sleep-restriction + pterostilbene (SR+PTE). Mice were forced to keep awake in the sleep-disrupted cages for 20h per day lasted for 5 days and PTE(100mg/kg) was given once a day. The liver tissues were collected at Zeitgeber time ZT0(8:00), ZT4, ZT8, ZT12, ZT16, ZT20 and ZT24. Global proteome and lysine acetylation analyses of ZT4 and ZT16 livers were used label-free quantitative proteomics technology and liquid chromatography-tandem mass spectrometry (LC-MS/MS). The transcription and protein expression abundance of deacetylases (Sirt1 and Sirt3) and NAD synthase Nampt were further measured, and rhythm oscillations were analyzed by cosiner. Furthermore, NAD+/NADH content and its catabolic enzyme CD38 activity were detected in vitro.

Results

PTE had an ameliorative effect on the acetylation levels of 11 glycolytic enzymes (17 sites), 8 lipid metabolizing enzymes (8 sites) and 12 protein metabolizing enzymes (22 sites) in the liver of SR mice. PTE increased NAD+/NADH content, Nampt, Sirt1, Sirt3 transcription and protein expression abundance while maintaining rhythm oscillations. PTE inhibited CD38 activity.

Conclusions

PTE intervention corrects metabolic disturbances caused by short-term sleep restriction, which is associated with its improvement of acetylation modification levels of liver metabolizing enzymes, improvement of hepatic NAD+/NADH content, maintenance of hepatic deacetylase Sirt1, Sirt3 expression and possible molecular mechanisms of circadian rhythm oscillations.

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Key words Pterostilbene; Sleep restriction; Deacetylase; Proteomics; Acetylation modification

Category: Basic Nutrition& Research

二氢杨梅素抑制NLRP3炎性小体活性减轻ApoE-/-小鼠动脉粥样硬化的作用机制研究

Dihydromyricetin ameliorates atherosclerosis in ApoE-/- mice by inhibiting NLRP3 inflammasome activity

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Objective

To investigate the effect of DHM (dihydromyricetin) on atherosclerosis in ApoE-/- mice induced by high-fat diet (HFD) and to reveal the molecular mechanism involved with NLRP3 inflammasome activity.

Methods

Forty healthy male ApoE-/- mice were randomly divided into 4 groups: control group, HFD group, HFD+low dose (300 mg/(kg.d)) of DHM group and HFD+high dose (500 mg/(kg.d)) of DHM group. Body weight and oral glucose tolerance test of mice was recorded. Serum TCH, TG, LDL-C, HDL-C, AST and ALT were detected to levels of metabolism. Serum TNF-α and IL-1β were detected to levels of inflammation. Oil red O, HE and EVG staining were used to observe the aortic lesions. The mRNA and protein expression levels of NLRP3 inflammasome activation were measured by qRT-PCR, Western blot and immunohistochemical.

Results

DHM significantly improved the body weight of the high-fat diet groupand the glucose tolerance ($P < 0.05$). The serum TCH, TG, LDL-C, AST, ALT, TNF-α and IL-1β levels were significantly decreased ($P < 0.05$). The atherosclerotic plaque and necrosis area of the aortic valve were reduced ($P < 0.05$), and the collagen fiber content was increased ($P < 0.05$).DHM inhibited the mRNA and protein expression of NLRP3, IL-18 and ASC in HFD mice ($P < 0.05$).Immunohistochemical staining showed that the expression of NLRP3 protein in aorta was significantly improved ($P < 0.05$).

Conclusion

DHM can ameliorate the occurrence of atherosclerotic plaque in ApoE-/- mice induced by HFD, and its protective mechanism may be related to the inhibition of the NLRP3 inflammasome activation.

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Key words dihydromyricetin; endothelial cells; atherosclerosis; NLRP3 inflammasome

Category: Basic Nutrition& Research

二氢杨梅素通过肠道菌群及其代谢物调节高脂饮食诱导的MAFLD小鼠肠黏膜屏障功能的作用研究

Dihydromyricetin regulates the intestinal mucosal barrier function of mice with MAFLD through regulating gut microbiota and its metabolites

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Objective To investigate the effects of dihydromyricetin (DHM) on the intestinal mucosal barrier of mice with metabolism-related fatty liver disease (MAFLD) induced by high-fat diets (HFD) and evaluate the mechanism involved with gut microbiota and its metabolites. **Methods** The mice were fed HFD for twelve weeks to establish a mouse MAFLD model. DHM was mixed into the diets to intervene the mice. After eight weeks of intervention, mixed antibiotics were used to eliminate gut microbiota. After the intervention, the intestinal mucosal barrier functions were measured, including intestinal mucosa's permeability, serum LPS, pro-inflammatory cytokines mRNA expressions, intestinal tight-junction protein expression levels, and electron microscopic ultrastructural changes, respectively. Furthermore, high-throughput sequencing of 16sRNA was used to measure gut microbiota species' diversity comparison and changes. GC-MS was used to detect the changes of short-chain fatty acids in cecal contents. **Results** After the intervention of DHM, the intestinal mucosal barrier functions were significantly improved. The intestinal mucosal permeability and the expression level of pro-inflammatory factors including IL-1β, IL-6, and TNF-α in the colon were decreased. The expression level of intestinal tight junction proteins such as ZO-1 and Occludin were increased, and the intestinal microvilli structure was notably improved. DHM administration resulted in an improved gut microbiota diversity induced by HFD, as evidenced by increased abundance ratio of Bacteroides to Firmicutes, particularly increased flora species such as Faecalibaculum, Lachnospiraceae and Clostridium species, etc. The content of butyric acid was increased significantly. After clearance of the gut microbiota, the ameliorative effect of DHM on the intestinal mucosal barrier of MAFLD mice was eliminated. **Conclusions** DHM improves the intestinal mucosal barrier function of mice with MAFLD by regulating the diversity of gut microbiota and its metabolites.

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Key words dihydromyricetin; metabolism-related fatty liver disease; intestinal mucosal barrier; gut microbiota.

Category: Basic Nutrition& Research

内源性 n-3 PUFAs 通过重塑肠道菌群改善阿尔兹海默模型小鼠疾病的发生发展

Endogenous n-3 PUFAs ameliorate the development and progression of AD via gut microbiota remodeling in mice model

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Objective: To explore the role of gut microbiota in the beneficial effects of endogenous n-3 polyunsaturated fatty acids (n-3 PUFAs) on Alzheimer's disease (AD) in mice. **Method:** AD model mice APPPS1 and Fat-1 mice that could synthesize n-3 PUFA were hybridized. The offspring were divided into four groups according to their genotypes: wild type group (WT), endogenous synthetic n-3 PUFA group (Fat-1), AD model group (APPPS1), and Fat-1/APPPS1 double expression gene group (Fat-1/APPPS1). Learning ability and Aβ amyloid deposition were tested to estimate AD symptoms. Intestinal permeability, endotoxin (LPS) level, and central nervous system (CNS) inflammation were measured to assess intestinal barrier function. Variations in gut microbiota were detected by 16S rRNA gene sequencing. **Result:** Increased endogenous n-3 PUFA significantly improved learning ability, and reduced Aβ amyloid deposition in APPPS1 mice. Meanwhile, elevated endogenous n-3 PUFAs also significantly improved intestinal barrier function and reduced LPS influx, which in turn reduced CNS inflammation and microglial polarization. In addition, elevated endogenous n-3 PUFAs improved the dysbiosis of gut microbiota, raised α diversity, increased the abundance of *Bacteroidales S24-7*, and reduced proportions of several harmful bacterial genera, such as *Faecalibaculum* and *Desulfovibrio*. Moreover, the beneficial effects of endogenous n-3 PUFAs were transferable by gut microbiota transplantation. **Conclusion:** The gut microbiota contributed to the beneficial effects of endogenous n-3 PUFAs on improving AD symptoms and CNS inflammation.

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Key words Alzheimer's disease; gut microbiota; gut-brain axis; n-3 polyunsaturated fatty acids

Category: Basic Nutrition& Research

萝卜硫素改善棕榈酸诱导肝细胞损伤的转录组学研究

The transcriptomics for sulforaphane ameliorating the hepatocyte injury induced by palmitic acid

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Objectives To investigate the effect of Sulforaphane (SFN) in attenuating palmitic acid (PA)-induced hepatocytes injury and to reveal the potential mechanism.**Methods and Study Design** HHL5 cells were treated with 200 μmol/L of PA for 24 h to establish the injury model and then the model was treated with 5 μmol/L of SFN, co-cultured with PA for 24 h. The total RNA of the cells was extracted to establish the library and sequenced by the Illumina platform. Gene ontology (GO) and Kyoto encyclopedia of genes and genomes (KEGG) enrichment analysis for differentially expressed genes (DEGs) were implemented by software with a P-value cutoff of 0.05 to judge statistical significance. HHL5 cells were transfected with siRNA to knock down PCSK9 and then the autophagy-related proteins levels were examined by western blot. **Results** Eighty-six DEGs that changed under the PA treatment and returned to normal levels under the SFN treatment were found, among which the foldchange of PCSK9 was relatively high and was abundant in liver tissue, suggesting that the PCSK9 might play an essential role in this model. GO enrichment showed that the DEGs were enriched in inflammation and oxidative stress. The KEGG pathway analysis showed that DEGs were involved in the autophagy pathway, suggesting that autophagy might be the potential mechanism in the effect of SFN on PA-induced hepatocyte injury. Further validation was done by western blot, and we found that both SFN and knocking down of PCSK9 could increase the protein level of P62 induced by PA and upregulate the protein level of LC3II to a higher degree. **Conclusions** SFN can regulate autophagy to achieve the therapeutic effects of fatty acid induced hepatocyte injury, and PCSK9 might play a vital role in the process.

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Key words sulforaphane, hepatocyte, transcriptome, autophagy, palmitic acid

Category: Basic Nutrition& Research

生酮饮食对中风模型的神经保护作用机制研究进展

Progress in the study of neuroprotective mechanism of ketogenic diet on stroke model

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OBJECTIVE: In recent years, there have been many studies on the effects of ketogenic diet on stroke models. This paper aims to explore the neuroprotective mechanism of ketogenic diet on stroke models, and to provide ideas for future research and application of ketogenic diet in stroke. METHODS: The keywords "Ketogenic diet, Stroke, Neuroprotection, Mechanism of action" were searched in "CNKI, Wan fang and PubMed" databases and summarized. RESULTS: The ketogenic diet is a high-fat, low-carbohydrate diet, and studies have shown that pretreatment with the ketogenic diet in stroke models improves early motor behavior outcomes in ischemic stroke and has neuroprotective effects. According to the present findings, the mechanism of neuroprotective effects of ketogenic diet in stroke models may be the following: (1) Neuroprotective effects through inhibition of Drp1 mitochondrial translocation, inhibition of nucleotide-binding domain-like receptor protein 3 inflammasome activation, inhibition of endoplasmic reticulum stress, and protection of mitochondrial integrity, thereby exerting neuroprotective effects; (2) Elevated extracellular adenosine levels after ketogenic diet intervention, increased Akt and ERK1/2 phosphorylation via A1 adenosine receptor activation, and upregulated HIF and HIF regulatory genes; (3) Neuroprotective effects of ketogenic diet through its own morphology on astrocytes and/or microglia. CONCLUSION: The mechanism of neuroprotective effects of ketogenic diet in stroke models may be related to the protection of mitochondrial integrity, increased phosphorylation of Akt and ERK1/2, upregulation of HIF and HIF regulatory genes, and altered morphology of glial cells.

Key words Ketogenic diet; Stroke; Neuroprotection; Mechanism of action

Category: Basic Nutrition& Research

肠道菌群与糖尿病的机制研究进展

Research progress on the mechanism of gut microbiota and diabetes mellitus

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Intestinal flora is involved in host immunity, nutrition, energy metabolism regulation and other processes.The imbalance of intestinal flora is the clinical manifestation of the occurrence and development of metabolic diseases such as diabetes. The mechanisms of improving the progression of diabetes through intestinal flora include promoting the secretion of incretin, producing short-chain fatty acids to reduce chronic low-grade inflammation, and regulating bile acid anabolic metabolism.To treat diabetes mellitus through interventions targeting to correct the imbalance of intestinal flora (such as diet adjustment, supplement of prebiotics and probiotics, Chinese and western medicine treatment, fecal bacteria transplantation, etc.), therefore, the regulation of intestinal flora has become a new direction in the treatment of diabetes.At present, there are few clinical treatments for regulating intestinal flora with limited effects, and those with health-promoting effects need to be further confirmed and evaluated, and the potential mechanisms of these effects should be evaluated in future studies.In addition, there are no clear criteria for evaluating adverse reactions (AEs) of probiotic-containing products in the current study, and prospective studies with larger samples are needed in combination with metagenomics, transcriptomics, proteomics, and metabolomics studies.In the context of precision medicine, personalized and genetically modified intestinal microflora may be used for the prevention and treatment of metabolic diseases in the future. "Microbiotics" and "microbial therapy", which influence microflora through diet, are expected to become the core of new therapeutic methods.In conclusion, the study of intestinal flora will provide new ideas for the early prevention and treatment and prognosis of metabolic diseases such as diabetes.

Key words Intestinal flora, diabetes, short chain fatty acid, bile acid, microecologics, probiotics, prebiotics

Category: Basic Nutrition& Research

Flavonifractor plautii 菌维持血管弹性网络防止动脉硬化
Flavonifractor plautii maintains vascular elastic network and Protects against Arterial Stiffness

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Flavonifractor plautii maintains vascular elastic network and Protects against Arterial Stiffness

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Aim: Dysbiosis of gut microbiota is closely involved in the development of several cardio-metabolic disorders including obesity, hypertension, type 2 diabetes mellitus (T2DM), metabolic syndrome and atherosclerosis which could damage host physiology and homeostasis. The diversity of gut microbiota has been reported to be inversely associated with arterial stiffness in white women and several evidence from murine models demonstrated that aberrant gut microbiota associated with obesity promoted vascular dysfunction, whereas, depletion of gut microbiota with broad-spectrum antibiotics reversed aging-related arterial stiffness. It is well known that arterial stiffness not only precedes systolic hypertension which has a major impact on cardiovascular health, but also contributes to the damage of several target organs. However, the causal role of gut microbiota in the progression of arterial stiffness and the specific species and metabolites responsible for this change remain largely unknown. Therefore, we aim to figure out the molecular mechanisms mediating the role of altered microbiota in the progression of elevated arterial stiffness.

Methods: A total of 44 medication-naïve subjects with elevated arterial stiffness (defined as brachial-ankle pulse wave velocity (baPWV)≥1400 cm/s) and 45 age- and sex-matched normal controls free of established cardiovascular diseases, obesity, diabetes and hypertension, which were previously reported to be associated with perturbation of gut microbiota, were recruited. The composition and metabolic

capacities between these two groups were compared with the integration of metagenomics of fecal samples and plasma metabolomics. Subsequently, angiotensin II (AngII) and humanized model using fecal microbiota transplantation (FMT) in C57BL/6J male mice were employed to evaluate the protective effect of *Flavonifractor plautii* (*F. plautii*) and its metabolite cis-aconitic acid (CAA) on arterial stiffness. The arterial stiffness of mice was assessed by tail-cuff blood pressure, abdominal and carotid artery PWV and circumferential cyclic strain. For further mechanism linking *F. plautii* to protection against arterial stiffness, elastin fiber staining and collagen fiber staining with Picro Sirius red was performed. Immune histochemical analyses of matrix metalloproteinase-2 (MMP2) and monocyte chemoattractant protein-1 (MCP-1) in mouse aortas were performed to find the regulatory factors of elastin network. Statistical analyses were performed using R software and GraphPad Prism 8.0. Comparison of basic characteristics was conducted with independent Student's t-test or ANOVA for normally distributed data and Wilcoxon rank-sum test or Kruskal-Wallis test for non-normally distributed variables. The normal distribution assumption was tested with Shapirrio -Wilk test and Q-Q plots.

Results: Human fecal metagenomic sequencing revealed a significantly high abundance and centrality of *F. plautii* in normal controls, which was absent in the microbial community of subjects with elevated arterial stiffness which suggested that *F. plautii* was a keystone bacterium closely correlated with arterial stiffness. Moreover, glucose metabolism and blood pressure only mediated part of the effect of *F. plautii* on lower arterial stiffness, suggesting that unknown mechanisms other than these known risk factors mediate the protective effect of *F. platii* on lower arterial stiffness. The microbiome of normal controls exhibited an enhanced capacity for glycolysis and polysaccharide degradation, whereas, those of subjects with heightened arterial stiffness were characterized by increased biosynthesis of fatty acids and aromatic amino acids. Integrative analysis with metabolomics profiling further suggested that increased CAA served as the main effector for the protective effect of *F. plautii* against elevated arterial stiffness. Moreover, supplementation of *F. plautii* attenuated blood pressure and arterial stiffness in both AngII-induced and humanized model of arterial stiffness. Furthermore, the beneficial effect of *F. plautii* on lowered pulse wave velocity was mainly mediated by an inhibition of matrix metalloproteinase-2 (MMP2) and nuclear factor kappa-B activation, resulting in a substantial decrease in elastic fiber fragmentation indicating the protective effect of vascular elastic network.

Conclusions: Collectively, our study uncovers a causal link between dysbiosis of gut microbiota and arterial stiffness. The elevated arterial stiffness is caused partially by a reduction of *F. plautii* in gut, resulting in enhanced activation of MMP2, which in turn exacerbates vascular elastic fragmentation stiffness. From a clinical perspective, the findings raise the possibility of maintaining vascular health by targeting gut microbiota and that *F. plautii* has the potential to be a next-generation probiotics for managing vascular health.

Key words Gut microbiota; Flavonifractor plautii; Arterial stiffness; Elastic fiber