



Asia Pacific Nutrigenomics Nutrigenetics Organisation  
2020 Virtual Conference  
1,2 December

**ABSTRACTS**  
**&**  
**PROGRAM**



# CONTENTS

<b>Day 1 (December 1) Program</b>	<b>Page 3-4</b>
<b>Abstracts of Day 1 Oral Presentations</b>	<b>Page 5-22</b>
<b>Day 2 (December 2) Program</b>	<b>Page 23</b>
<b>Abstracts of Day 2 Oral Presentations</b>	<b>Page 24-36</b>
<b>Abstracts of other papers</b>	<b>Page 37-59</b>



CHINA TIME	Day 1 (1 <sup>st</sup> December 2020)	
08.50 – 09.00	<b>Opening Remarks:</b> <b>Michael Fenech</b> (Founding President) and <b>Duo Li</b> (President-Elect)	
	<b>NUTRIOMICS</b>	
09.00 – 09.20	<b>Hisanori Kato</b> (Japan)	Genome-Wide Association Study of Food Preference
09.20 – 09.40	<b>Safarina Malik</b> (Indonesia)	Mitochondrial Genetics, Gut Microbiome and Methylation Pattern of the Punans of North Kalimantan
09.40 – 10.00	<b>Keith West</b> (USA)	The Plasma Awesome: Proteomics Applications in Public Health Nutrition
10.00 – 10.20	<b>Rod Dashwood</b> (USA)	Dietary sulforaphane and its structural analog 6-SFN synergize with JQ1 to downregulate ERCC2 during colorectal cancer interception
10.20 – 10.40	QUESTION TIME	
10.40 – 11.00	RECREATION BREAK	
	<b>NUTRIOMICS IN METABOLIC AND CARDIOVASCULAR DISEASE</b>	
11.00 – 11.20	<b>Jun Nishihira</b> (Japan)	Comprehensive understanding of health and nutrition based on the dataset of diet, blood biochemistry, genetics, and gut microbiota in the Japanese population
11.20 – 11.40	<b>Zelei Miao, Yu-ming Chen, Ju-Sheng Zheng</b> (China)	Interaction between marine n-3 fatty acids and CD36 gene on blood lipids: role of gut microbiome
11.40 – 12.00	<b>Wenhua Ling</b> (China)	Nutritional diet and management of cardiovascular metabolic diseases
12.00 – 12.20	<b>Tao Huang</b> (China)	Genetic risk, Lifestyle and Heart Failure
12.20 – 12.40	QUESTION TIME	
12.40 – 13.00	RECREATION BREAK	
	<b>PROFFERED PAPERS</b>	
13.00 – 13.10	<b>Shixiu Zhang</b> , Xin Guo, Ying Yang, Yu Li, Lei Wang, Xueqin Li, Xiaohan Yang, Yanjing Zhang, Mingfei Yan (China)	More than 2 Egg Yolk Per Day Make More Adverse Effects in Healthy Young Adults of SREBF1 Minor Allele Carriers
13.10 – 13.20	<b>Jing Cong</b> , Huaqun Yin (China)	Short chain fatty acids-intestinal microbiota-human health and disease
13.20 – 13.30	<b>Nan Yao</b> , Shoumeng Yan, Yinpei Guo, Han Wang, Xiaotong Li, Ling Wang, Wenyu Hu <sup>1</sup> , Bo Li and <b>Weiwei Cui</b> (China)	The association between carotenoids and subjects with overweight or obesity: a systematic review and meta-analysis
13.30 – 13.40	<b>Dong Chen</b> , Li Dandan, Zhang Zhiyong (China)	Microbial diversity induced by delayed responses in oral cavity based on system dynamics modeling and simulation
13.40 – 13.50	<b>Yik Fah Chee</b> , Satvinder Kaur, Yap Wai Sum, <b>Roseline Wai Kuan Yap</b> (Malaysia)	Association and interaction effect of VEGFR-2 gene polymorphism with dietary patterns on metabolic risk factors of cardiovascular disease in Malaysian Punjabi adults
13.50 – 14.10	QUESTION TIME	
14.10 – 14.20	<b>Kelei Li</b> , Xiaotong Kuang, Yan Shi, Xianfeng Shao, Huiying Li, Duo Li (China)	Gene-diet interaction in response to defatted flaxseed flour supplementation on cardiometabolic health in overweight/obese subjects: a randomized controlled trial



# APNNO 2020 ABSTRACTS

14.20 – 14.30	Min Wu, Xiao-Hui Li, Hong Jiang, Ni Yan, Jia-Qi Wang, <b>Le Ma</b> (China)	Potassium and risk of type 2 diabetes, cardiovascular disease, stroke, and mortality: a dose-response of meta-analysis
14.30 – 14.40	Na Wang, Lv Shijian, Gao Guangyun, <b>Yan Ding</b> (China)	The association of iron status in early pregnancy and glucose metabolism among pregnant Chinese women: a longitudinal cohort study
	<b>NUTRIOMICS (CONTINUED)</b>	
14.40 – 15.00	<b>Elisabetta Damiani</b> (Italy)	Targeting Epigenetic 'Readers' with Natural Compounds for Cancer Interception
15.00 – 15.10	<b>Harry Freitag Luglio Muhammad</b> , Marleen van Baak, Edwin Mariman, Sukma Oktavianthi, Safarina G. Malik (Indonesia)	The Effect of a Low Calorie Low Inflammatory Diet on Inflammation, Telomere Length and Mitochondrial DNA among Obese Adults
15.10 – 15.30	QUESTION TIME	
15.30 – 16.00	RECREATION BREAK	
16.00 – 17.00	<b>APNNO SECRETARIAT &amp; COUNTRY DELEGATES MEETING</b>	



## Genome-Wide Association Study of Food Preference

Hisanori Kato

*Department of Applied Biological Chemistry, Graduate School of Agricultural and Life Sciences, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113-8657, Japan*

**Corresponding author:** Hisanori Kato, Email: [akatoq@g.ecc.u-tokyo.ac.jp](mailto:akatoq@g.ecc.u-tokyo.ac.jp) Phone: +81-3-5841-1607

**Abstract:** Many studies have revealed some genetic variations which are associated with dietary habits and food preference. In collaboration with a personal genome service company, Genequest Inc., we have been investigating such associations using ~300,000 SNPs data and internet questionnaire obtained from over 10,000 Japanese population. We identified and reported loci and SNPs associated with preference to sweet taste<sup>1)</sup>, frequencies of the intakes of coffee<sup>2)</sup>, black tea<sup>3)</sup>, and fish<sup>4)</sup> in Japanese, which were mostly unique to Asian populations. Today's presentation will focus mainly on the 12q24 locus which was found to be associated with the intakes of many foods. Our studies indicate that internet cohort can be used is a very effective approach to identify SNPs associated to dietary habits.

1) Kawafune, K. *et al.*, *J. Human, Genet.* **65**, 939–947 (2020)

2) Jia, H. *et al.*, *BMC Genet.*, 20, **61** (2019)

3) Furukawa, K. *et al.*, *Nutrients*, **12**, 3182 (2020)

4) Igarashi, M. *et al*, *Genes Nutr.* **14**, 21 (2019)

**Keywords:** GWAS, food preference, fish consumption, internet cohort study, Japanese



## Mitochondrial Genetics, Gut Microbiome and Methylation Pattern of the Punans of North Kalimantan

Safarina G. Malik,<sup>1</sup> Lidwina Priliani,<sup>1</sup> Clarissa A. Febinia,<sup>1</sup> Sukma Oktavianthi,<sup>1</sup> Pradiptajati Kusuma,<sup>1</sup> Patricio Kresnatama,<sup>2</sup> Margaret.<sup>3</sup>

<sup>1</sup>*Eijkman Institute for Molecular Biology. Jalan Diponegoro 69, Jakarta 10430, Indonesia*

<sup>2</sup>*Atma Jaya Catholic University of Indonesia. Jl. Raya Cisauk Lapan, Sampora, Kec. Cisauk, Tangerang, Banten 15345, Indonesia*

<sup>3</sup>*Indonesia International Institute for Life Sciences. Jl. Pulomas Barat No.Kav. 88, RT.4/RW.9, Kayu Putih, Kec. Pulo Gadung, Kota Jakarta Timur, Daerah Khusus Ibukota Jakarta 13210, Indonesia*

**Corresponding author:** Safarina G. Malik. Email: [ina@eijkman.go.id](mailto:ina@eijkman.go.id). Phone: +62-21-3148695

**Abstract:** Mitochondria play a crucial role in the development of any disorders, as mitochondria is the center of all metabolic processes and homeostasis, but also very susceptible to changes. The interactions between environmental factors, including nutrition and lifestyle, and mitochondria have been implicated in the pathogenesis of many diseases. Mitochondria contain their own circular DNA genome present in multiple copies within a cell. Loss of mitochondrial DNA copy number (mtDNA-CN) has consistently been associated with obesity and its comorbidities. Accumulating evidence has shown that the impact of diet and lifestyle alteration on individual health is linked to the gut microbiome. The human host rely on these organisms for a variety of functions related to nutrition, immune system training, and prevention of severe infections, as the gut microbiota is involved in functions essential for maintaining human health. Different environmental exposure is reflected in the methylation patterns, as methylation captures both population history and current lifestyle practices. Our recent differential methylation analyses showed enrichment in pathways involved in immunity, emphasizing Indonesia's tropical role as a source of infectious disease diversity. In this study, mitochondrial genetics, gut microbiome and methylation patterns were analysed in several Punan ethnic groups of North Kalimantan, some of which still conduct their life as hunter gatherers. Our results showed that the Punans are diverse and had undergone different selective pressure, which reflect the general condition in the Indonesian archipelago. Understanding how genetics, including mitochondrial genetics, gut microbiome and methylation pattern drive disease risk across diverse populations in Indonesia is important to ensure equality and equity.

**Keywords:** mitochondrial genetics, gut microbiome, methylation, Punans, North Kalimantan.



## The Plasma Awesome: A Proteomics Approach for Revealing Hidden Hunger

Keith P. West, Jr., DrPH<sup>1</sup>, Sun-Eun Lee, PhD<sup>2</sup>, Hyunju Kim<sup>3</sup>, Casey Rebholz<sup>3</sup>, Kerry Schulze, PhD<sup>1</sup>

<sup>1</sup>Center for Human Nutrition, Department of International Health, <sup>2</sup>Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, 21205 USA and <sup>3</sup>The Bill & Melinda Gates Foundation, Seattle, WA, USA

**Corresponding author:** Keith P. West, Jr, [kwest1@jhu.edu](mailto:kwest1@jhu.edu), 1-443-509-2486

### Abstract:

Micronutrient deficiencies from a chronically inadequate diet threaten the health of ~2 billion infants and children in impoverished societies. This estimate, first derived by the WHO in 1992, was based on deficiencies of 3 of ~20 essential micronutrients, and has remained unchanged for three decades. While the global community laments a lack of data to guide prevention, few advances have occurred to reveal Hidden Hunger. State-of-art biochemical analytical methods are costly, logistically and technically demanding and slow, leading to few nutrients typically being assessed in surveys. Results can take a few years to report at a cost of hundreds of thousands of dollars. Needed is a single, inexpensive, technically simple, rapid assay for assessing multiple micronutrient deficiencies. We have pursued a discovery-driven proteomics strategy to address this issue, first in a cohort of 500 Nepalese children, revealing 3 to 242 plasma proteins from among nearly 1000 quantified by tandem mass spectrometry to be non-specifically associated with each of a dozen nutrients at a FDR <0.10. From nutriproteomes, predictors have been modeled to estimate in-population prevalence of deficiencies for some nutrients. Additional protein clusters have been linked to inflammation, circulating lipids, growth and intelligence scores, suggesting a broad public health application for plasma proteomics. Given proof-of-concept, we are seeking to confirm and expand nutriproteomic biomarkers and nutrient predictors in plasma from 450 pregnant women who participated in a multiple micronutrient supplementation trial in NW rural Bangladesh (West et al JAMA 2014), employing protein-capture aptamer technology (SomaLogic, Boulder CO, USA), capable of quantifying 4-5,000 plasma proteins. We anticipate up to 40 proteins may be needed to model distributions and assess deficiencies for ~12 micronutrients with acceptable precision. Plans call for developing a prototype assay to fulfill an essential goal of use in low resource settings to assess nutritional burdens and monitor interventions.

**Keywords:** Proteomics, micronutrient deficiencies, aptamers, Nepal, Bangladesh



## Dietary sulforaphane and its structural analog 6-SFN synergize with JQ1 to downregulate ERCC2 during colorectal cancer interception

Sabeeta Kapoor<sup>1</sup>, Trace Gustafson<sup>1</sup>, Mutian Zhang<sup>1</sup>, Nhung Nguyen<sup>1</sup>, Wan Mohaiza Dashwood<sup>1</sup>, Praveen Rajendran<sup>1</sup> and Roderick Dashwood<sup>1,2</sup>

<sup>1</sup>Center for Epigenetics & Disease Prevention, Texas A&M Health Science Center, and <sup>2</sup>Dept. Translational Medical Sciences, Texas A&M College of Medicine, Houston, TX 77030, USA.

**Corresponding author:** R.H. Dashwood, [rdashwood@tamu.edu](mailto:rdashwood@tamu.edu); +1 (713) 677-7806

**Abstract:** Nucleotide excision repair (NER) plays a critical role in maintaining genome integrity, and aberrant expression of NER proteins such as ERCC2 can affect anticancer treatment outcomes<sup>1</sup>. The current investigation examined ERCC2 changes following epigenetic combination treatment in human colorectal cancer (CRC) cells and in preclinical models. Attention was drawn to ERCC2 based on three observations. First, from online databases, ERCC2 overexpression in colon cancers coincided with poor prognosis in CRC patients. Second, ERCC2 was the most highly downregulated gene when the dietary histone deacetylase 3 (HDAC3) inhibitor sulforaphane (SFN) was combined with JQ1, an inhibitor of the bromodomain and extraterminal domain (BET) family, in human colon cancer cells and in colon polyps from the polyposis in rat colon (Pirc) model<sup>2</sup>. Third, RNA-seq analyses of Pirc colon polyps from rats treated with JQ1 plus the wasabi-derived SFN analog 6-methylsulfinylhexyl isothiocyanate (6-SFN)<sup>3</sup> also identified *Ercc2* as the most highly downregulated gene. Transcriptomic data were corroborated by RT-qPCR and immunoblot experiments, which implicated apoptotic mechanisms that were independent of p53 and p21<sup>Waf1</sup>. This investigation added to the growing body of research supporting HDAC+BET epigenetic combination approaches to cancer interception.

Supported by NIH grants CA122959 and CA090890, by the John S. Dunn Foundation, and by a Chancellor's Research Initiative. No conflicts to report.

**Keywords:** Bromodomain, colorectal cancer, epigenetics, HDAC, sulforaphane.

1. Marteijn JA, Lans H, Vermeulen W, Hoeijmakers HJ. Understanding nucleotide excision repair and its roles in cancer and ageing. *Nat Rev Mol Cell Biol* 2014;15:465-81.
2. Rajendran P, Johnson GS, Li L, Chen YS, Dashwood WM, Nguyen N, Ulasan A, Ertem FU, Zhang M, Li J, Sun D, Huang Y, Wang S, Leung HCE, Lieberman D, Beaver LM, Ho E, Bedford MT, Chang KS, Vilar E, Dashwood RH. Acetylation of CCAR2 establishes a BET/BRD9 acetyl switch in response to combined deacetylase and bromodomain inhibition. *Cancer Res* 2019;79:918–27.
3. Rajendran P, Kidane AI, Wu T-W, Dashwood WM, Bisson WH, Löhr CV, Ho E, Williams DE, Dashwood RH. HDAC turnover, CtIP acetylation and dysregulated DNA damage signaling in colon cancer cell treated with sulforaphane and related dietary isothiocyanates. *Epigenetics* 2013;8:612-23.





## **Comprehensive understanding of health and nutrition based on the dataset of diet, blood biochemistry, genetics, and gut microbiota in the Japanese population**

Jun Nishihira<sup>1</sup> and Mari-Maeda Yamamoto<sup>2</sup>

<sup>1</sup>*Hokkaido Information University, Medical Management and Informatics, 59-2, Ebetsu, 069-8585 Hokkaido, Japan*

<sup>2</sup>*Healthcare Innovation Research, National Agriculture and Food Research, Organization (NARO), 2-1-12 Kannonndai, Tuskuba, 305-8642 Ibaraki, Japan*

**Corresponding author:** Jun Nishihira, [nishihira@do-johodai.ac.jp](mailto:nishihira@do-johodai.ac.jp), +81-90-7511-6960

Background: Unbalanced dietary habits can cause health problems. The normalization of an unbalanced diet lowers the risk of lifestyle-related diseases, such as obesity. On the other hand, we sometimes encounter health-related minor complaints, e.g. irritability, stress and lethargy, possibly caused by unbalanced diet. In this regard, research for foods that appropriately meet individual needs to reduce minor complains is of importance. To solve this issue, we started the Cross-ministerial Strategic Innovation Promotion Program (SIP). The primary goal of this study is to provide adequate diets/foods to ameliorate the complains with respect to individual health status. Methods: We obtained a series of health data from 1000 healthy volunteers, ages from 20 to 80, consisting of nutrition, sleep, stress, blood, genes, and gut microbiota. These data were collected twice a year, in summer and winter. Results: Statistical analysis showed differences in blood biochemistry and body composition between the two seasons. In winter, women had increased body fat and high-density lipoprotein cholesterol, while men had increased blood pressure and blood urea nitrogen. We also found that some of genetic polymorphisms contributed to elevated blood uric acid. Furthermore, we successfully categorized variety of symptoms, including dysphoria, insomnia, and constipation into minor complaints through an exploratory factor analysis. The complains were associated with some unique gut microbiota, suggesting that balanced eating habits potentially reduce minor complaints. Discussion: The current comprehensive dataset established by this SIP program would provide valuable information to design specific foods beneficial for health promotion, e.g., reduction of minor complaints. Taken together, the overall outcome of this program promotes personalized nutrition, which brings huge benefits for community health and food business arena.

This work was supported by Cabinet Office, Government of Japan, Cross-ministerial Strategic Innovation Promotion Program (SIP), “Technologies for Smart Bio-industry and Agriculture” (funding agency: Bio-oriented Technology Research Advancement Institution, NARO).

**Keywords:** microbiota, personalized nutrition, polymorphism, sleep, stress



## Interaction between marine n-3 fatty acids and CD36 gene on blood lipids: role of gut microbiome

Zelei Miao<sup>1</sup>, Yu-ming Chen<sup>2</sup>, Ju-Sheng Zheng<sup>1</sup>

<sup>1</sup> Zhejiang Provincial Laboratory of Life Sciences and Biomedicine, Key Laboratory of Growth Regulation and Translational Research of Zhejiang Province, School of Life Sciences, Westlake University, Hangzhou 310024, China.

<sup>2</sup> Guangdong Provincial Key Laboratory of Food, Nutrition and Health; Department of Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China.

**Corresponding Author:** Ju-Sheng Zheng, PhD

Tel: +86 (0)57186915303. Email: zhengjusheng@westlake.edu.cn

### Abstract

**Background:** Previous small studies suggest that not all individuals respond to the marine n-3 polyunsaturated fatty acids (PUFA) equally. Participants carrying CD36-G allele (rs1527483) tended to respond better to the marine n-3 PUFA supplement in improving blood lipid profiles. However, successful replication and the mechanism investigation for this gene-diet interaction have been lacking. In the present study, we examined the interaction of marine n-3 PUFA biomarker with CD36 gene on blood lipids in a large prospective cohort study, followed by a further investigation into the role of gut microbiome in the above gene-diet interaction.

**Methods:** We evaluated CD36-marine n-3 PUFA interaction on blood lipids in the Guangzhou Nutrition and Health Study (n=2,072). The associations between marine-3 PUFA and microbial features (bacterial alpha diversity, genera, short-chain fatty acids) were further analyzed in 1,286 participants according to the CD36 SNP rs1527483 genotypes.

**Results:** We successfully replicated the findings from previous trials that CD36 rs1527483-G allele carriers responded better to high marine n-3 PUFA exposure with improved blood HDL-C during follow-up. Among the CD36-G allele carriers, but not the other genotype group, high marine n-3 PUFA exposure was associated with increased bacterial alpha-diversity, the relative abundance of *Dorea*, *Catabacter*, *Coriobacteriales Incertae Sedis* spp, and microbial propanoic acid. The microbial features found to be associated with DHA among the rs1527483-G allele carriers were significantly linked to blood lipids and the bile acids and phenylalanine metabolism-related serum metabolites.

**Conclusions:** Our findings identified novel bacterial genera and metabolites that associated with marine n-3 PUFA only among CD36 rs1527483-G allele carriers and revealed functional links between the gut microbiome and host metabolism. These findings pave the way for further understanding the mechanisms of gene-diet interaction and provide insight into the interplay between diet, host genetics and gut microbiome to modulate cardiometabolic health.

**Key words:** CD36; marine n-3 PUFA; interaction; blood lipids; microbiota



## Nutritional diet and management of cardiovascular metabolic diseases

Wenhua Ling, Prof.

*Department of Nutrition, School of Public Health, Sun Yat-sen University, Guangzhou, China, 510080*

**Corresponding Author:** Wenhua Ling; [Lingwh@mail.sysu.edu.cn](mailto:Lingwh@mail.sysu.edu.cn), 86-13802980289

Cardiovascular metabolic diseases including cardiovascular disease, stroke and diabetes are major health problem for population worldwide. The primary cause of the diseases is unhealthy nutrition and diet which contributed to 30% of total death among Chinese population. It is essential approach to establish health dietary measures for reducing the mortality of cardiovascular metabolic disease. The conclusion on impact of single nutrient on the diseases is inconsistent. In term of various of foods, a large number of studies demonstrate that consumption of some foods such as vegetables, legumes, nuts/seeds, fish coffee and tea possess health benefits. Oppositely, consumption of unprocessed red meat and processed meat, SSBs-sugar-sweetened beverages, alcohol and trans fatty acids exert cause the harmful effects. More recently, the dietary pattern such DASH diet and Mediterranean dietary pattern are recommended for promoting health.

Compared with animal food, plant foods have been attracted in the aspect of healthy promotion. A various of phytochemicals derived from plant foods such as resveratrol, anthocyanin, tea polyphenol has been reported to play active functions against cardiovascular metabolic disease. These compounds exert a series of functions including anti-oxidation, anti-inflammation, anti-aging and improving dyslipidemia, diabetes, cardiovascular disease and cancer. Among the chemicals, anthocyanin has been extensively studied in our research group. The red/purple/black foods contain high amount anthocyanin as compared to other general foods. Anthocyanin improves insulin resistance, dyslipidemia, NAFLD and atherosclerosis through antioxidation, anti-inflammation, promoting endothelial function as well as facilitating reverse cholesterol efflux. Recently, we demonstrated that supplementation of anthocyanin (80mg/D-320mg/D) improve inflammation and oxidative stress in dose-dependent pattern in dyslipidemia. The findings may be useful to guide population to consume higher anthocyanin-containing foods to reduce the risk of cardiovascular disease.



## Genetic risk, Lifestyle and Heart Failure

Ruotong Yang, MD<sup>1</sup>, Tao Huang, PhD<sup>1,2,3#</sup>

<sup>1</sup>Department of Epidemiology & Biostatistics, School of Public Health, Peking University, 100191 China.

<sup>2</sup>Department of Global Health, School of Public Health, Peking University, 100191 China.

<sup>3</sup>Key Laboratory of Molecular Cardiovascular Sciences (Peking University), Ministry of Education, 100191 China.

**Corresponding author:** Tao Huang, PhD, Department of Epidemiology & Biostatistics, School of Public Health, Peking University, China. 38 Xueyuan Road, Beijing, 100191 China. Phone: (86) 010-82801528. Email: [huangtaotao@pku.edu.cn](mailto:huangtaotao@pku.edu.cn)

**Background:** Genetic, lifestyle factors and cardiovascular health metrics contribute to the risk of developing heart failure, but whether combined lifestyle factors and cardiovascular health metrics are associated with similar risk among individuals with different genetic risk remains unclear.

**Methods:** A healthy lifestyle score (HLS) based on smoking, drinking, physical activity, diets, body mass index, and waist circumference, an ideal cardiovascular health metrics (ICVHMs) based on the American Heart Association Recommendations, and genetic risk scores (GRS) for heart failure were constructed in the China Kadoorie Biobank (CKB) of 96 014 participants and UK Biobank (UKB) of 335 782 participants which were free from heart failure and severe chronic diseases at baseline.

**Results:** During the median follow-up of 11.38 and 8.73 years, 1 451 and 3 169 incident heart failure events were documented in CKB and UKB participants with genetic data respectively. In both cohorts, cumulative incidence of heart failure can be well stratified by HLS and ICVHMs categories ( $P < 0.05$  for all log-rank tests). Heart failure risk increased monotonically across GRS (CKB: HR, 1.19; 95% CI, 1.07, 1.32; UKB: HR, 1.07; 95% CI, 1.03, 1.11;  $P$  for trend test  $< 0.001$ ). Participants with high genetic risk had higher risk of incident heart failure than those with low genetic risk (CKB: HR, 1.15; 95% CI, 1.02, 1.29; UKB: HR, 1.16; 95% CI, 1.06, 1.27). Compared with participants with favorable HLS, the adjusted HRs (95% CIs) of those with unfavorable HLS were 1.47 (1.17, 1.84) in the CKB, and 3.12 (2.73, 3.57) in the UKB. Compared with participants with favorable ICVHMs, the adjusted HRs (95% CIs) of those with unfavorable ICVHMs were 1.82 (1.36, 2.46) in the CKB, and 2.94 (2.54, 3.40) in the UKB. Compared with low genetic risk and favorable HLS or ICVHMs, participants with high genetic risk and unfavorable HLS (CKB: HR, 1.94; 95% CI, 1.37, 2.73; UKB: HR, 3.98; 95% CI, 3.17, 5.01) or ICVHMs (CKB: HR, 2.25; 95% CI, 1.43, 3.54; UKB: HR, 3.52; 95% CI, 2.73, 4.54) had highest risk of heart failure. Neither significant interaction between GRS and HLS nor GRS and ICVHMs was observed. Among participants with high genetic risk, participants with a favorable HLS (CKB: HR, 1.47; 95% CI, 1.02, 2.12; UKB: HR, 3.26; 95% CI, 2.59, 4.12) or ICVHMs (CKB: HR, 2.10; 95% CI, 1.30, 3.39; UKB: HR, 2.74; 95% CI, 2.12, 3.53) developed heart failure risk compared with an unfavorable groups.

**Conclusions:** In the China Kadoorie Biobank and the UK biobank, unfavorable behavioral lifestyle and cardiovascular health metrics were strong incremental risk factors and predictors of incident heart failure. There were no interactions between genetic risk and poor lifestyle or cardiovascular risk metrics. Favorable lifestyle and cardiovascular health were associated with a lower heart failure risk among participants with a high genetic risk.

**Keywords:** Heart failure, Lifestyle, Genetic Risk



## More than 2 Egg Yolk Per Day Make More Adverse Effects in Healthy Young Adults of SREBF1 Minor Allele Carriers

ZHANG Shixiu<sup>1</sup>, GUO Xin<sup>1</sup>, YANG Ying<sup>2</sup>, LI Yu<sup>3</sup>, Wang Lei<sup>3</sup>, LI Xueqin<sup>3</sup>, YANG Xiaohan<sup>1</sup>, ZHANG Yanjing<sup>1</sup>, YAN Mingfei<sup>1</sup>

<sup>1</sup>Department of Nutrition and Food Hygiene, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, 250012, China

<sup>2</sup>Shandong Institute for Food and Drug Control, Jinan, Shandong, 250101, China

<sup>3</sup>Campus Hospital, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, 250012, China

### Corresponding authors:

ZHANG Shixiu, [amyzhangsx@sdu.edu.cn](mailto:amyzhangsx@sdu.edu.cn), 18678785565

Guo Xin, [xguo@sdu.edu.cn](mailto:xguo@sdu.edu.cn), 15688400953

Our previous correlation analysis showed SREBF1 rs2236513/rs2297508/rs4925119 polymorphism modulated the relation between dietary cholesterol and serum LDL-C/Total Cholesterol. But little is known about how cholesterol from eggs affect lipid profile in healthy people with different gene background. The aim of this study was to characterize the effects of egg yolks compared with egg whites on lipid profiles in healthy young adults with different SREBF1 gene background. The study was a deformed 16-wk, single-blind, randomized crossover dietary trial with two 4-wk intervention periods in 32 rs2236513/rs2297508/rs4925119 minor allele carriers and 32 rs2236513/rs2297508/rs4925119 major homozygotes. The crossover treatments were cooked boiled egg yolks compared with olive oil-fried egg whites of the same amount of protein and energy, separated by a 4-wk washout. Two egg yolks with cholesterol at 347.1±10.7mg/d were given during the first intervention period, and egg yolks with cholesterol at 506.5±67.4mg/d were given during the second intervention period. Besides egg yolks, subjects consumed low cholesterol, low saturated fat and trans-fat diets all through the study. Raised lipids in egg yolk arm were attributed to egg yolk given at higher amount. Comparing with the intervention with egg white, cholesterol from egg yolk at 347.1±10.7mg/d did not change lipid profiles in either genotypes; cholesterol from egg yolk at 506.5±67.4mg/d increased serum Total Cholesterol (P=0.008) and LDL-C (P=0.005) in minor allele carriers, while serum Total Cholesterol (P=0.004) was significantly increased and LDL-C (P=0.061) was marginally increased in major homozygotes. Furthermore, cholesterol from egg yolk at 506.5±67.4mg/d did not raise HDL-C in minor allele carriers (P=0.826) as it was in major homozygotes (P=0.010). For LDL-C/HDL-C, more increment of LDL-C/HDL-C was tested in minor allele carriers (P=0.047) than in major homozygotes. This study showed SREBF1's role in modulating the effect of egg yolk on lipids. SREBF1 minor allele carriers need more dietary restriction on egg takes.

**Keywords:** Dietary cholesterol; SREBF1; LDL-C; HDL-C; LDL-C/HDL-C



## **Short chain fatty acids-intestinal microbiota-human health and disease**

Jing Cong<sup>1\*</sup>, Huaqun Yin<sup>2</sup>

<sup>1</sup>*College of Marine Science and biological engineering, Qingdao University of Science and Technology, Qingdao, 266042, PR China*

<sup>2</sup>*School of Minerals Processing and Bioengineering, Central South University, Changsha, 410083, PR China*

**Corresponding author:** Jing Cong; E-mail: yqdh77@163.com; TEL: +86 18661800251

The occurrence and development of human diseases is a complicated process involved in multiple pathogenic factors. There are now increasing evidences to short chain fatty acids (SCFAs) play key roles in the health maintenance and disease development. The SCFAs are mostly produced by intestinal microbiota during the fermentation of partially and non-digestible polysaccharides. Previous researches mainly focused on their roles on the energy metabolism. In this review, we will provide a comprehensive insight into short chain fatty acids about their production, absorption, transport receptors, relationships with intestinal microbiota, and importantly diverse effects on regulation in kinds of diseases. They probably act as a complex role in the management of host health. Given their levels are regulated by diet and intestinal microbiota, we suppose that the interaction of intestinal microbiota and dietary nutrition should be paid more attentions in modulating the SCFAs to provide the therapy for solving human diseases.

**Keywords:** short chain fatty acids; intestinal microbiota; dietary nutrition; inflammation; health and disease



## **The association between carotenoids and subjects with overweight or obesity: a systematic review and meta-analysis**

Nan Yao<sup>1</sup>, Shoumeng Yan<sup>1</sup>, Yinpei Guo<sup>1</sup>, Han Wang<sup>1</sup>, Xiaotong Li<sup>1</sup>, Ling Wang<sup>1</sup>, Wenyu Hu<sup>1</sup>, Bo Li<sup>1\*</sup> and Weiwei Cui<sup>2\*</sup>

<sup>1</sup>*Department of Epidemiology and Biostatistics, School of Public Health, Jilin University, Changchun, 130021, P. R. China.*

<sup>2</sup>*Department of Nutrition and Food Hygiene, School of Public Health, Jilin University, Changchun, 130021, P. R. China.*

### **\*Corresponding authors:**

**Bo Li:** Department of Epidemiology and Biostatistics, School of Public Health, Jilin University, 1163 Xinmin Avenue, Changchun, 130021, P. R. China. Tel: +86 43185619451 E-mail: li\_bo@jlu.edu.cn

**Weiwei Cui:** Department of Nutrition and Food Hygiene, School of Public Health, Jilin University, 1163 Xinmin Avenue, Changchun, 130021, P. R. China. Tel: +86 431 85619455 E-mail: cuiweiwei@jlu.edu.cn

Excess bodyweight, including overweight and obesity, is one of the significant risk factors contributing to the overall burden of disease worldwide. Carotenoids are the main source of vitamin A in the human body and considered to have potential effects on many diseases. However, the influence of carotenoids on people with excess bodyweight is unclear. A meta-analysis was conducted to evaluate the effect of carotenoids on overweight or obesity subjects. We searched the PubMed, Medline, Cochrane library, Web of science and EMBASE databases from the inception dates to September 2020. Random effects models were conducted to calculate standard mean difference and odd ratios (ORs) with their 95% confidence intervals. Fourteen studies met the inclusion criteria, including seven randomized controlled trials and seven cross-sectional studies, which contained a total of 26648 subjects. Our study found that insufficient of serum carotenoid is a risk factor for overweight and obesity (odd ratio =1.731, confidence interval [1.565,1.913],  $P < 0.001$ ). Moreover, carotenoid supplementation was associated with the significant reduction of body weight (standardized mean difference = -2.34kg, confidence interval [-3.80, -0.87]kg,  $P < 0.001$ ), body mass index (BMI, standardized mean difference = -0.95, confidence interval [-1.88, -0.01],  $P < 0.001$ ) and waist circumference (WC, standardized mean difference = -1.84cm, confidence interval [-3.14, -0.54]cm,  $P < 0.001$ ). In summary, the carotenoid play a promising role in subjects with overweight or obesity. Additional data from large clinical trials are needed.

**Keywords:** Carotenoids; Overweight; Obesity; Meta-analysis; Systematic review





## **Microbial diversity induced by delayed responses in oral cavity based on system dynamics modeling and simulation**

DONG Chen<sup>1</sup>, LI Dandan<sup>1</sup>, ZHANG Zhiyong<sup>1</sup>

<sup>1</sup>*Laboratory of Sport Nutrition and Intelligent Cooking, Shandong Sport University, Jinan 250102, China*

**Corresponding author:** DONG Chen, dongchen@sdpei.edu.cn, 16653159939

**Background:** Previous studies have shown that there is often high microbial diversity in healthy oral cavities, while relatively low in unhealthy oral cavities, however the mechanisms of forming and maintenance of microbial diversity is currently unclear.

**Methods:** In the research, a 100 mixed-gender undergraduates were randomly selected and divided into two groups, 50 testers with chronic periodontitis and 50 testers with health oral cavity, and the abundances of five microbial flora *Granulicatella*, *Porphyromonas*, *Corynebacterium*, *Leptotrichia*, *Tannerella* were sampled and measured periodically, which illustrated that dynamic responses of microbial populations in periodontitis oral cavities are fundamentally stationary stochastic processes, while they significantly appear to be asynchronous fluctuations in healthy oral cavities.

**Results:** Then two basic response delays, i.e. reproductive delay and reaction delay were identified through experimental data and delay Monod equation, which accompanied interspecific delay and substrate decomposing delay. Finally, the highly valid kinetic models of microbial flora succession in both periodontitis and health oral cavities were developed based on proposed hypothesis, observed phenomena and experimental data, and the hypothesis was eventually proved based on a large number of simulation experiments. Namely these four delay responses can cause asynchronous fluctuations of microbial populations in healthy cavity, giving rise to significant reduction of interspecific competition to form and sustain a microbial diversity in health oral cavity.

**Conclusion:** The results of this study can lay the theoretical foundation to understand the forming and maintenance mechanism of microbial diversity in health oral cavity and providing an effective guidance of prevention and treatment oral cavity disease.

**Keywords:** Nutrition; Oral microbial diversity; Delay responses; System dynamic model; Digital simulation;





## Association and interaction effect of *VEGFR-2* gene polymorphism with dietary patterns on metabolic risk factors of cardiovascular disease in Malaysian Punjabi adults

Yik Fah Chee<sup>1</sup>, Satvinder Kaur<sup>2</sup>, Yap Wai Sum<sup>2</sup>, Roseline Wai Kuan Yap<sup>1</sup>

<sup>1</sup> School of Biosciences, Faculty of Health and Medical Sciences, Taylor's University, 1, Jalan Taylors, 47500 Subang Jaya, Selangor, Malaysia.

<sup>2</sup> Faculty of Applied Sciences, UCSI University, No. 1, Jalan Menara Gading, UCSI Heights, 56000 Cheras, Kuala Lumpur, Malaysia.

**Corresponding author:** Roseline Wai Kuan Yap, PhD; roselineyap@yahoo.com; 012-2157256

**Background:** Globally, the prevalence of cardiovascular diseases (CVDs) is high in Punjabi population. This could be due to genetic predisposition and diets high in dietary fats and refined grains. However, gene-diet interaction studies involving Malaysian population including Punjabis are scarce. Vascular endothelial growth factor receptor 2 (*VEGFR-2*) was selected based on the significant findings on metabolic risk factors (MRFs) of CVDs involving Malaysians. Hence, this study aims to determine the association and interaction effect of *VEGFR-2* (rs2071559) gene polymorphism with dietary patterns on MRFs of CVDs in Malaysian Punjabi adults.

**Methods:** Dietary intake information of 164 (35% males; 65% females) Punjabis were obtained from food frequency questionnaire for the development of major dietary patterns using principal component analysis. Anthropometric measurements: weight and height for body mass index calculation, body fat percentage, waist circumference, systolic and diastolic blood pressure; and biomarkers: blood lipid profiles, blood glucose (BG), and glycated haemoglobin A1c were obtained. Genotyping of *VEGFR-2* (rs2071559) was performed by real-time PCR using TaqMan probes.

**Results:** 'Whole grains, condiments and beverages Diet' (WCBD) and 'protein diet' (PD) were derived from all subjects. Significant associations were obtained for WCBD with TC ( $p=0.010$ ), LDL-C ( $p=0.015$ ) and apolipoprotein B100 ( $p=0.038$ ). The allele frequencies were T:0.59; C: 0.41 for rs2071559. No significant genetic associations were obtained on all MRFs of CVDs for rs2071559. The significant gene-diet interactions adjusted for potential confounders were rs2071559xWCBD on BG ( $p=0.004$ ; power=86.7%) and rs2071559xPD on BG ( $p=0.014$ ; power=74.9%), total cholesterol (TC) ( $p=0.001$ ; power=93.0%), low-density lipoprotein cholesterol (LDL-C) ( $p=0.039$ ; power=62.3%) and apolipoprotein B100 ( $p=0.033$ ; power=64.4%).

**Conclusion:** The significant associations and gene-diet interaction effects between *VEGFR-2* (rs2071559) and WCBD; and *VEGFR-2* (rs2071559) and PD on BG, TC, LDL-C and apolipoprotein B100 may provide insights on the risk of MRFs of CVDs in Malaysian Punjabis, particularly in high blood glucose and hyperlipidemia.

**Keywords:** gene-diet interaction, cardiovascular disease, Malaysian Punjabis, *VEGFR-2* gene polymorphism, dietary pattern.



## Gene-diet interaction in response to defatted flaxseed flour supplementation on cardiometabolic health in overweight/obese subjects: a randomized controlled trial

Kelei Li<sup>1</sup>, Xiaotong Kuang<sup>1</sup>, Yan Shi<sup>1</sup>, Xianfeng Shao<sup>1</sup>, Huiying Li<sup>1</sup>, Duo Li<sup>1\*</sup>

<sup>1</sup> *Institute of Nutrition and Health, Qingdao University, Qingdao China*

**Corresponding Author:** Professor Duo Li

Institute of Nutrition and Health, Qingdao University, 38 Dengzhou Road, Qingdao 266071, China

Tel: +86 532 82991018

Fax: +86 532 82991018

E-mail: [duoli@qdu.edu.cn](mailto:duoli@qdu.edu.cn)

The beneficial effect of defatted flaxseed flour supplementation on cardiometabolic health has been demonstrated in our previous randomized controlled trial. The aim of the present study was to evaluate whether gene variants on FTO and NPY genes could modulate the effect of flaxseed flour on cardiometabolic health in overweight/obese subjects. Fifty-one overweight/obese adults were randomly allocated to two groups to consume control biscuits (n=24) or biscuits containing defatted flaxseed flour (n=27) at breakfast for 60 days. Two SNPs were genotyped, including rs11076023 on FTO gene and rs16147 on NPY gene. A general linear regression model was used to evaluate the gene-diet interaction, and age, sex and baseline level were adjusted as confounding factors. Compared with control biscuits, flaxseed flour biscuits significantly decreased body weight in A allele carriers (AA+AT) of rs11076023 on FTO gene (mean difference of change (MD), -2.48 kg; 95% CI, -3.93 to -1.04 kg; p=0.001) but not in non-carriers (TT) (p for interaction = 0.005). Compared with control biscuits, flaxseed flour biscuits significantly decreased low density lipoprotein cholesterol in subjects with TT genotypes of rs11076023 (MD, -0.30; 95% CI, -0.56 to -0.03; p=0.032), but not in A allele carriers (p for interaction=0.06). Compared with control biscuits, flaxseed flour biscuits significantly decreased fasting glucose in subjects with CC genotype of rs16147 on NPY gene (MD, -0.35 mmol/L; 95% CI, -0.64 to -0.07 mmol/L; p=0.019) but increased fasting glucose in T allele carriers (TT+TC) (MD, 0.26 mmol/L; 95% CI, 0.04 to 0.48 mmol/L; p=0.021) (p for interaction=0.002). In conclusion, gene variants on FTO and NPY genes could modulate the effect of flaxseed flour on cardiometabolic health.

**Keywords:** gene-diet interaction; overweight; flaxseed flour; cardiometabolic health; randomized controlled trial.



## **Potassium and risk of type 2 diabetes, cardiovascular disease, stroke, and mortality: a dose-response of meta-analysis**

Min Wu, Xiao-Hui Li, Hong Jiang, Ni Yan, Jia-Qi Wang

<sup>1</sup>*Xi'an 710061, Shan Xi, China*

**Corresponding author:** Le Ma, male@mail.xjtu.edu.cn, 18202906588

**Background:** Abnormal circulating potassium and experimental restriction of dietary potassium increase arrhythmias. However, whether or not circulating, dietary, or urinary potassium at usual concentrations, intakes or excretions alters the risk of metabolic diseases and mortality in general population is unclear.

**Objective:** To summarize evidence from cohort studies regarding associations between potassium and risk of developing type 2 diabetes (T2D), cardiovascular disease (CVD), coronary heart disease (CHD), stroke, and all-cause mortality.

**Methods:** PubMed, Web of Science, and EMBASE databases were searched for cohorts with data on potassium and outcomes of interest until April 31, 2020. Inclusion decisions and data extraction were performed in duplicate. Multivariate-adjusted relative risks (RRs) and 95% confidence intervals (CIs) were extracted using a random or fixed-effect model. Dose-response analyses were conducted whenever feasible.

**Results:** 49 studies were identified, totaling more than 1 million participants (follow-up 2.6 to 29.3 years), 5,664 cases of T2D, 20,454 cases of CVD, 9,429 cases of CHD, 23,655 cases of stroke, and 50,759 deaths. Higher potassium intake was associated with 13%, 11%, 16%, and 20% reduction, respectively, in the risk of CVD, CHD, stroke, and overall mortality. Furthermore, high-normal circulating potassium was associated with a 12% higher risk of CVD and a 25% higher risk of all-cause mortality. Dose-response analysis revealed a U-shaped relationship between circulating potassium and death, with the lowest risk at 4.2–4.7 mmol/L. No significant association was evidenced between urine potassium and the outcome of interest.

**Conclusions:** Increasing habitual potassium intake is associated with a reduced risk of CVD, CHD, stroke, and all-cause mortality, but not T2D. High-normal circulating potassium increased the risk of CVD and all-cause mortality. These findings support the notion that higher consumption of potassium-rich foods might provide health benefits.

**Keywords:** potassium, type 2 diabetes, cardiovascular disease, mortality, meta-analysis



## **The association of iron status in early pregnancy and glucose metabolism among pregnant Chinese women: a longitudinal cohort study**

Na Wang, Lv Shijian, Gao Guangyun, Yan Ding

*Obstetrical Department, Obstetrics and Gynecology Hospital of Fudan University, No. 128, Shenyang Road, Yangpu District, Shanghai 200090, China*

**Corresponding author:** Yan Ding, Email: jonish@vip.sina.com, Telephone number: +86 13795357887

**Background:** Previous prospective studies about the association of iron status and the risk of GDM in pregnancy did not examine the correlation of iron status with insulin resistance, an essential role in the pathogenesis of GDM. The aim of this study was to investigate maternal iron status and insulin resistance in early pregnancy and the subsequent risk of gestational diabetes mellitus (GDM) using a comprehensive panel of iron biomarkers.

**Methods:** A prospective cohort study of 891 pregnant women was conducted in a tertiary obstetrics and gynecology hospital. The participants were followed up during their initial prenatal visit to 24-28 weeks of gestation after completing an oral glucose tolerance test (OGTT). The relationships between iron status and insulin resistance during early pregnancy were analyzed by multivariate linear regressions. The contribution of iron status during early pregnancy, iron intake from food, and iron supplement to GDM risk were analyzed using multivariate logistic regression models.

**Results:** In Quartile1, serum ferritin correlated positively with other iron indicators including transferrin saturation, serum iron, and hemoglobin and inversely correlated with glycosylated hemoglobin and OGTT-1h. In Quartile 4, serum ferritin concentrations correlated positively with fasting plasma glucose, fasting insulin, and homeostasis model assessment of insulin resistance (HOMA-IR) during early pregnancy. In the multivariate linear regression models, serum ferritin and hemoglobin significantly correlated with HOMA-IR ( $\beta=0.002$ , 95% confidence interval (CI): 0.001-0.003;  $\beta=0.014$ , 95% CI: 0.009-0.019), while transferrin saturation inversely correlated with HOMA-IR ( $\beta=-1.635$ , 95% CI:-2.083- -1.187). Neither iron status in early trimester nor iron intakes were associated with the risk of GDM.

**Conclusions:** Elevated iron stores are associated with increased insulin resistance in early gestation. Our results suggested that neither high nor low concentrations of serum ferritin were optimal for pregnant women.

**Key words:** ferritin; hemoglobin; insulin resistance; diabetes, gestational



## Targeting Epigenetic ‘Readers’ with Natural Compounds for Cancer Interception

Elisabetta Damiani<sup>1</sup>, Munevver N. Duran<sup>2</sup>, Nivedhitha Mohan<sup>2</sup>, Jason Schultz<sup>2</sup>, Dharmanand Ravirajan<sup>3</sup>, Wan-Mohaiza Dashwood<sup>2</sup>, Magnus Hook<sup>3</sup>, Praveen Rajendran<sup>2</sup>, Roderick H. Dashwood<sup>2,4</sup>

<sup>1</sup>*Department of Life and Environmental Sciences, Polytechnic University of the Marche, Ancona, Italy;*

<sup>2</sup>*Center for Epigenetics & Disease Prevention, <sup>3</sup>Center for Infectious & Inflammatory Diseases, Institute of Biosciences & Technology, Texas A&M Health Science Center, Texas A&M University, Houston, Texas;*

<sup>4</sup>*Department of Translational Medical Sciences, Texas A&M College of Medicine, Houston, Texas, USA.*

**Corresponding author:** Elisabetta Damiani; [e.damiani@univpm.it](mailto:e.damiani@univpm.it); +390712204135

Natural compounds from diverse sources, including botanicals and commonly consumed foods and beverages, exert beneficial health effects *via* mechanisms that impact the epigenome and gene expression during disease pathogenesis. By targeting the so-called epigenetic ‘readers’, ‘writers’ and ‘erasers’, dietary phytochemicals can reverse abnormal epigenome signatures in cancer and preneoplastic lesions. Thus, such agents provide avenues for cancer interception *via* prevention and/or treatment strategies. To date, much of the focus on dietary agents has been directed towards writers (e.g., histone acetyltransferases, HATs) and erasers (e.g., histone deacetylases, HDACs), with less attention given to epigenetic readers (e.g., bromodomain proteins). Bromodomain (BRD)-containing proteins act as epigenetic readers by recognizing lysine acetylation on histone and non-histone proteins and regulating various transcriptional processes. The drug JQ1 was developed as a prototype epigenetic reader inhibitor, selectively targeting members of the bromodomain and extra-terminal domain (BET) family, such as BRD4. Clinical trials with JQ1 as a single agent, or in combination with standard of care therapy, revealed antitumor efficacy but not without toxicity or resistance. In pursuit of second-generation epigenetic reader inhibitors, attention has shifted to natural sources, including dietary agents that might be repurposed as ‘JQ1-like’ bioactives. This presentation will summarize the current status of nascent research activity focused on natural compounds as inhibitors of BET and other epigenetic ‘reader’ proteins such as BRD9, and identifies dietary polyphenols as potential epigenetic reader inhibitors *via* interaction with BRDs, providing new insights in the field of nutrigenomics and precision medicine.

**Keywords:** epigenetic readers; natural compounds; flavonoids; bromodomain proteins; cancer prevention and therapy



## The Effect of a Low Calorie Low Inflammatory Diet on Inflammation, Telomere Length and Mitochondrial DNA among Obese Adults

Harry Freitag Luglio Muhammad<sup>1</sup>; Marleen van Baak<sup>2</sup>; Edwin Mariman<sup>2</sup>; Sukma Oktavianthi<sup>3</sup>; Safarina G. Malik<sup>3</sup>

<sup>1</sup>*Department of Nutrition and Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada*

<sup>2</sup>*NUTRIM, School of Nutrition and Translational Research in Metabolism, Maastricht University*

<sup>3</sup>*Eijkman Institute for Molecular Biology*

**Corresponding author:** Harry Freitag Luglio Muhammad; Department of Nutrition and Health, Universitas Gadjah Mada, Jalan Farmako, Sekip Utara, Yogyakarta.

E-mail: [harryfreitag@ugm.ac.id](mailto:harryfreitag@ugm.ac.id)

**Background:** The objective of this study was to investigate the effect of a low calorie low inflammatory diet (LCID) on inflammation markers, body weight, metabolic syndrome parameters, mitochondrial DNA copy number (mtDNA-CN) and relative telomere length (RTL) in obese adults.

**Methods:** This is a randomized controlled trial among Indonesian adults with obesity. Participants (n=61) were divided into 2 groups: low-calorie diet (LCD) (n=30) and low calorie low inflammatory diet (LCID) (n=31). The LCID was an adaptation of the Mediterranean diet principle to a low-calorie diet regime. The length of the weight loss program was 8 weeks, and participants were followed for 8 weeks of the weight maintenance period.

**Results:** Subjects in the LCID group had a lower hs-CRP ( $p=0.03$ ) compared to those in the LCD group, but no difference was seen in plasma levels of TNF- $\alpha$  ( $p=0.32$ ) and IL-6 ( $p=0.63$ ). Subjects in both groups had a significant reduction in body weight, body fat, lipid profile and blood pressure (all  $p<0.05$ ) with no differences between groups (all  $p>0.05$ ). The mtDNA-CN was unchanged ( $p=0.96$ ) after weight loss while RTL was shown to be increased ( $p=0.002$ ). Changes in RTL were higher in LCID than those in the LCD group ( $p=0.036$ ), while mtDNA-CN showed no difference. Weight changes after weight loss and maintenance period were not associated with inflammation markers, mtDNA-CN or RTL (all  $p>0.05$ ).

**Conclusion:** This study showed that the LCID had a beneficial effect on hs-CRP during a weight loss intervention compared to the LCD, but not on TNF- $\alpha$  and IL-6. The weight loss program was associated with the elongation of telomere length and those in LCID responded with significantly longer telomeres as compared to LCD despite a similar degree of weight loss.

**Keywords:** obesity, weight loss, inflammation, telomere length, mitochondrial DNA



<b>CHINA TIME</b>	<b>Day 2 (2<sup>nd</sup> December 2020)</b>	
	<b>NUTRIOMICS &amp; CANCER PREVENTION</b>	
09.00 – 09.20	<b>Young-Joon Surh</b> (Korea)	Nutritional chemoprevention of cancer
09.20-09.40	<b>Hye-Kyung Na</b> (Korea)	Salsolinol, an Endogenous Catechol Isoquinoline, Induces Heme Oxygenase-1 through Nrf2 Activation in the SK-Hep1 Hepatoma Cells
	<b>NUTRIOMICS &amp; INFLAMMATION</b>	
09.40 – 10.00	<b>Chin Kun Wang</b> (Taiwan)	Dietary intake and inflammation
10.00 – 10.20	<b>Michael Fenech</b> (Australia)	Breaking the vicious cycle of DNA damage and inflammation nutritionally
10.20-10.40	<b>QUESTION TIME</b>	
10.40-11.00	<b>RECREATION BREAK</b>	
	<b>PRESIDENT'S LECTURE</b>	
11.00 – 11.20	<b>Duo Li</b> (China)	Sustainable and Optimal Vegetarian/vegan diets
	<b>PROFFERED PAPERS</b>	
11.20 – 11.30	<b>Lynette R Ferguson</b> (New Zealand)	Nutrigenomics and nutrigenetics research in New Zealand
11.30 – 11.40	<b>Jacus Nacis</b> (Philippines)	Priming the advent of genotype-based nutrition and lifestyle recommendation in the Philippines: The InGeSt Project
11.40 – 11.50	Meilan Xue, Nan Zhang, Yushan Jiang, Zhongqian Pei, Kunpeng Qin, Ying Liu, <b>Hui Liang</b> (China)	Protective effects of fucoidan on intestinal mucosal barrier function and behavior in alcohol-exposed mice
11.50 - 12.00	Yaqi Xue, Mengxuan Ye, Fei Jiang, Ping Wang, Hailong Pei, Wentao Hu, Guangming Zhou, <b>Zengli Zhang, Bingyan Li</b> (China)	Expression profile of lncRNAs identifies the potential lncRNAs associated with both EMT and Vitamin D signaling
12.00 - 12.20	<b>QUESTION TIME</b>	
12.20 – 12.30	<b>Huifeng Zhang</b> (United Kingdom)	Meat consumption is cross-sectionally associated with higher dementia risk among APOE ε4 carriers
12.30 – 12.40	<b>Xiaotong Kuang</b> , Xianfeng Shao, Yan Shi, Huiying Li, Kelei Li, Duo Li	PCSK1, SCARB1 and BDNF gene variants modulate the effect of defatted flaxseed flour intake on weight loss in overweight/obese subject: a randomized control trial
12.40 – 12.50	<b>Zhenhuang Zhuang</b> , Meng Gao, Ruotong Yang, Wenxiu Wang, Xueer Zhang, <b>Tao Huang</b> (China)	Causal relationships between rheumatoid arthritis and gut microbiota: A bi-directional Mendelian randomization study
12.50 – 13.00	Bei-lei Zhu, .....Man-man Zhang, <b>Bo Yang</b> (China)	Controlling Nutritional Status (CONUT) Score is a Prognostic Indicator for Patients with Hemorrhagic Stroke: Results from a 3-month Follow-up Study
13.00 – 13.20	<b>QUESTION TIME</b>	
13.20 – 13.30	<b>Closing Remarks: Duo Li</b> (President-Elect)	





## **Nutritional chemoprevention for cancer**

**Young-Joon Surh**

*Tumor Microenvironment Global Core Research Center, College of Pharmacy, Seoul National University, Seoul 08826, South Korea*

Recently, much attention has been focused on the nutritional prevention of cancer. Numerous biologically active substances derived from fruits, vegetables, nuts, herbs and spices, collectively termed ‘phytochemicals’, have been reported to possess the cancer preventive potential. These include those present in cruciferous vegetables (e.g., cabbage and broccoli), Allium vegetables (e.g., garlic and onion), green tea, Citrus fruits, soybeans, tomatoes, berries, turmeric, and ginger, as well as in medicinal plants. Several lead compounds, such as genistein (from soybeans), lycopene (from tomatoes), sulforaphane (from broccoli), indole-3-carbinol (from cabbage), and resveratrol (from grapes and peanuts) have been in preclinical or clinical trials for evaluating cancer chemopreventive potential. Some marine products also contain distinct bioactive substances (e.g., DHA and EPA) that exert cancer preventive as well as other health beneficial effects. Dietary products have great potential in cancer prevention because of their safety, low cost, and oral bioavailability. This presentation will highlight selective edible natural products with chemopreventive effects on multi-stage carcinogenesis and their mechanisms of action.

**Keywords:** Cancer, Cancer prevention, Chemoprevention, Nutrition, Phytochemicals





## **Salsolinol, an Endogenous Catechol Isoquinoline, Induces Heme Oxygenase-1 through Nrf2 Activation in the SK-Hep1 Hepatoma Cells**

Hongkyung Yang<sup>1</sup>, Jeong-Eun Lee<sup>2</sup>, Young-Joon Surh<sup>3</sup>, Hye-Kyung Na<sup>1,2</sup>

<sup>1</sup>*Department of Future Applied Sciences, College of Natural Sciences, Sungshin Women's University;*

<sup>2</sup>*Department of Food Science and Biotechnology, College of Knowledge-Based Services Engineering, Sungshin Women's University, Seoul 01133, Republic of Korea. <sup>3</sup>Tumor Microenvironment Global Core Research Center, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea*

**Corresponding author:** Hye-Kyung Na, [nhkdec28@gmail.com](mailto:nhkdec28@gmail.com), 82-2-920-7688

**Background:** Salsolinol (SAL) is an endogenous catechol isoquinoline which is generated by condensation of dopamine with acetaldehyde formed as a consequence of alcohol metabolism. Nrf2 and its target protein, heme oxygenase-1 (HO-1) have been overactivated/overexpressed in many different types of human malignancies, which facilitates the remodeling of tumor microenvironment in a way advantageous for cancer cells. In this study, we have investigated the effect of SAL on Nrf2/HO-1 signaling in the human liver cancer SK-Hep1 cells.

**Methods:** The effect of SAL on expression of antioxidant enzymes was analyzed by Western blot and quantitative polymerase chain reaction (qPCR) analyses. The nuclear localization of Nrf2 was determined by immunofluorescent staining and Western blot analyses in liver cancer SK-Hep1 cells. To investigate whether Nrf2 plays an important role in induction of HO-1, the cells were transiently transfected by Nrf2 siRNA. Generation of reactive oxygen species (ROS) in cells treated with SAL was determined by DCF-DA staining.

**Results:** SAL induced the expression of HO-1 and the nuclear translocation of Nrf2 in SK-Hep1 cells. SAL-induced HO-1 expression was attenuated in the cells harboring Nrf2 siRNA. SAL induced the phosphorylation of Akt. SAL generates ROS and the general antioxidant N-acetylcysteine suppressed phosphorylation of Akt, nuclear translocation of Nrf2, and expression of HO-1 induced by SAL in SK-Hep1 cells. SAL treatment suppressed clonogenicity of SK-Hep1 cells, which was attenuated in the presence of N-acetylcysteine.

**Conclusion:** SAL induced Nrf2-mediated expression of HO-1 through generation of ROS. Nrf2-mediated expression of HO-1 by SAL may contribute to the growth suppression of SK-Hep1 cells.

**Keywords:** Salsolinol, ROS, HO-1, Liver Cancer Cells, Anticancer



## **Dietary intake and inflammation**

Chin-Kun Wang

*Chung Shan Medical University, 110, Sec.1, Jianguo North Rd., Taichung, 402, Taiwan*

**Corresponding Author:** Chin-Kun Wang, wck@csmu.edu.tw, +886936642829

Inflammation is very critical for many diseases. Natural food resources and dietary intake can greatly improve the inflammation and terminate the advanced disease development. Phytochemicals from daily vegetables, fruits and foods are found to suppress the inflammation by specific pathway. Propolis is obtained from bees' nest and contains thousands of pytochemicals. Propolis extracts were used to evaluate the bioactivities by using cell model, animal model and human clinical trial and confirm its real application. Results clearly show that, propolis extracts greatly inhibit the inflammation through NF  $\kappa$  -B in cell and animal models. Intervention in oral submucous fibrosis, leukoplakia and oral carcinoma patients strongly showed propolis extract improve the inflammation, syndrome and reduce tumor size. Caffeic acid phenethyl ester (CAPE) was the major contributor for antiinflammation. CAPE dose-dependently inhibited IFN-  $\gamma$  -induced Try701 and Ser 727 phosphorylation in STAT1. It was also observed that CAPE inhibited promoter activity of IP-10 gene and the secretion of IP-10 protein. CAPE has very poor bioavailability and stability, its modified similar compound K36 were also found positive effect on neurodegeneration.

**Keywords:** Propolis, NF  $\kappa$  -B, CAPE, STAT1, K36



## **Breaking the vicious cycle of DNA damage and inflammation nutritionally**

Michael Fenech<sup>1,2</sup>

<sup>1</sup>*Clinical and Health Sciences, University of South Australia, Adelaide, SA, 5000, Australia*

<sup>2</sup>*Genome Health Foundation, North Brighton, SA, 5048, South Australia*

**Corresponding author:** Michael Fenech, michael.fenech@unisa.edu.au

Formation of micronuclei due to mitotic malsegregation of whole or broken chromosomes, excessive telomere shortening, and loss of mitochondrial DNA integrity increase chronologically and accelerate the ageing process by causing genomic instability and cellular dysfunction. Furthermore, these DNA damage events induce cellular senescence and leakage of DNA into cytoplasm which trigger pro-inflammatory senescence mechanisms such as (i) the Senescence Associated Secretory Phenotype (SASP) and (ii) the cGMP-AMP synthase-stimulator of interferon genes (cGAS-STING) cytosolic DNA sensing pathway, respectively. In this presentation I shall (i) discuss current knowledge on the mechanisms by which nutritional deficiencies and excesses cause DNA damage, (ii) explain why loss of DNA integrity accelerates ageing and induces inflammation, (iii) review emerging evidence that specific nutrient intake may mitigate against inflammation induced by SASP and cGAS-STING either by inhibition of chemokine signaling or elimination of persisting senescent cells.

**Keywords:** Nutrition, DNA damage, inflammation, cGAS-STING, SASP



## PRESIDENT'S LECTURE

### Sustainable and optimal vegetarian/vegan diets

Duo Li

*Institute of Nutrition & Health, Qingdao University, Qingdao, China*

*Department of Food Science & Nutrition, Zhejiang University, Hangzhou, China*

*Department of Nutrition, Dietetics and Food, Monash University, Melbourne, Australia*

Email: [duoli@qdu.edu.cn](mailto:duoli@qdu.edu.cn) Telephone number: +86 13819484621

Vegetarians state that their diet must exclude all animal flesh. There are different varieties of vegetarianism, which exclude or include various foods. Raw veganism includes only fresh and uncooked fruit, nuts, seeds, and vegetables. Fruitarianism permits only fruit, nuts, seeds, and other plant matter that can be gathered without harming the plant. Su vegetarianism (such as Buddhism in China) excludes all animal products as well as vegetables in the Allium family such as onion, spring onion, garlic, scallions and leeks. In general, compared with an omnivorous diet, vegetarian diets are rich in fiber, magnesium,  $\text{Fe}^{3+}$ , folic acid, vitamins C and E, n-6 polyunsaturated fatty acid (PUFA), phytochemicals, and antioxidants but low in total fat, saturated fatty acid (SFA), cholesterol, sodium, zinc,  $\text{Fe}^{2+}$ , vitamins A,  $\text{B}_{12}$ , and D, and especially n-3 PUFA. Low intake of total fat, SFA, and sodium and increased intake of fiber, phytochemicals, and antioxidants in vegetarians is associated with decreased blood pressure and BMI. These factors are known to reduce the risk of CVD. However, there is concern over whether vegetarians, and particularly vegans, have an adequate intake of several important nutrients, particularly Fe, Zn, vitamin  $\text{B}_{12}$ , and n-3 PUFA. Regular intake of appropriate amount of fermented soybean products can meet the intake of vitamin  $\text{B}_{12}$  in vegetarians. In order to meet the intake of n-3 PUFA, Vegetarians are suggested to use canola or soybean oils for cooking, and flaxseed, perilla or chia seed oils for salads and cold dishes. A well-designed vegetarian diet with variety of plant-based food can satisfy all nutrients intake.

**Keywords:** Vegetarian, vegan, vitamins, minerals, nutrients intake



## Nutrigenomics and nutrigenetics research in New Zealand

Lynnette R. Ferguson<sup>1</sup> and Matthew P.G. Barnett<sup>2, 3, 4</sup>

<sup>1</sup>*Discipline of Nutrition and Dietetics, Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92019, Auckland, New Zealand,*

<sup>2</sup>*The Riddet Institute, Palmerston North, New Zealand.*

<sup>3</sup>*Food Nutrition & Health Team, AgResearch Limited, Palmerston North, New Zealand.*

<sup>4</sup>*The High-Value Nutrition National Science Challenge, Auckland, New Zealand.*

**Corresponding author:** Lynnette R. Ferguson, [l.ferguson@auckland.ac.nz](mailto:l.ferguson@auckland.ac.nz), 027 817 6878

Nutrigenomics New Zealand was a collaborative research programme built among three organisations – The University of Auckland, AgResearch Limited and Plant and Food Research. The programme ran for ten years, between 2004 and 2014, and was tasked with developing the then emerging field of nutrigenomics, investigating its applications to New Zealand, and potential benefits to the plant food and agricultural sectors. In this country, nutrigenomics has been divided into two fields – nutrigenetics and nutrigenomics, the first of which is now more commonly called personalised nutrition. Personalised nutrition has recently been recognised and severely criticised by the elements of the dietetics and management sector in New Zealand, who currently do not appear to recognise the evolving nature of the field, and the differing validity of various companies offering the tests that form the basis of this personalisation. Various science laboratories are utilising “omics sciences”, including transcriptomics, metabolomics, proteomics and comprehensive analysis of microbial communities such as the gut microbiota, in order to understand mechanisms by which certain food products and/or diets, relevant to New Zealand, confer a health benefit, and the nature of potential health claims that may be made on the basis of this information.

**Keywords:** Nutrigenomics, nutrigenetics, transcriptomics, proteomics, microbiome



## **Priming the advent of genotype-based nutrition and lifestyle recommendation in the Philippines: The InGeSt Project**

Jacus S. Nacis<sup>1</sup>, Diana Glades A. Domalanta<sup>1</sup>, Marietta P. Rodriguez<sup>1</sup>, Jason Paolo H. Labrador<sup>1</sup>

<sup>1</sup>*Department of Science and Technology-Food and Nutrition Research Institute, General Santos Avenue, Bicutan, Taguig City 1631 Metro Manila, Philippines*

**Corresponding author:** Jacus S. Nacis, [jsn@fnri.dost.gov.ph](mailto:jsn@fnri.dost.gov.ph); jacusnacis@gmail.com; +632 8 837 2071 ext. 2299

Nutritional genomics and its promise to offer personalized and precise nutrition have been heralded as one of the most important breakthroughs in nutrition to date. However, to optimize its intended benefits, it is but important to highlight and understand contextual factors of nutritional genomics while gradually integrating it into nutrition practice.

The Interventions using Genomics-based Strategies (InGeSt) is a multiphase and interdisciplinary research program that aims to integrate nutritional genomics in nutrition practice by developing evidence-informed genome-based nutrition and lifestyle recommendations. It adheres to the overarching goal of nutritional genomics of providing tailored nutrition advice, meant to highlight the importance of preventive approach towards optimum health. The project has three main work packages: (1) an exploratory phase that covers formative research and a systematic review of the available evidence, specifying the effectiveness of genome-based nutrition and lifestyle interventions in the real-world setting; (2) the development phase that tackles the creation of a genome-based recommendation for a given set of modifiers or nutrition outcomes. This recommendation will serve as the intervention agent that will be used in the integration phase, the third important segment of the research program. The third phase will commence with a proof-of-concept randomized controlled trial to generate preliminary empirical evidence prior to the application of such recommendation in the broader, real-life context.

The InGeSt Project aims to contribute greatly to the understanding of the role of nutritional genomics in fostering health and wellness. Furthermore, beyond the integration of genomics in nutrition practice, this project aspires to offer novel perspectives in the advent of genome-based personalized nutrition in the Philippine context, and beyond.

**Keywords:** Personalized nutrition, proof-of-concept, genome-based nutrition advice



## Protective effects of fucoidan on intestinal mucosal barrier function and behavior in alcohol-exposed mice

Meilan Xue<sup>1</sup>, Nan Zhang<sup>1</sup>, Yushan Jiang<sup>2</sup>, Zhongqian Pei<sup>1</sup>, Kunpeng Qin<sup>1</sup>, Ying Liu<sup>1</sup>, Hui Liang<sup>2\*</sup>

<sup>1</sup>*Department of Biochemistry and Molecular Biology, Basic Medical College, Qingdao University of Medicine, 308 Ningxia Road, Qingdao 266021, PR China;*

<sup>2</sup>*Department of Human Nutrition, College of Public Health, Qingdao University of Medicine, Qingdao 266021, PR China.*

**Corresponding author:** Hui Liang, E-mail address: qdlianghui@qdu.edu.cn or lianghuiyxb@163.com; Tel./fax: +86 532 83812434.

**Background:** This study was to investigate the effects of fucoidan on intestinal mucosal barrier function and behaviors in alcohol-exposed mice.

**Methods:** Twenty-four male C57BL/6J mice were randomly divided into three groups (8 /group) : (1) control group; (2) model group; (3) fucoidan treatment group (300 mg/kg). The animals in the model group and fucoidan group received fresh tap water freely from 8:00 a.m. to 4:00 p.m., and then 15 % alcohol solution (v/v) until 8:00 a.m. the next day. The mice in the control group received tap water freely from Monday to Friday. The experiment lasted for 10 weeks. The behavioral and cognitive functions of mice were determined by sucrose preference test (SPT), tail suspension test (TST), forced swimming test (FST), elevated plus maze (EPM) and Y maze free alternate experiment. The levels of 5-hydroxytryptamine (5-HT) and brain-derived neurotrophic factor (BDNF) and inflammatory factors were detected in cerebral cortex. The levels of serum endotoxin, D-lactic acid (D-LA) and fatty acid-binding protein 2 (FABP2) were measured by ELISA. The permeability of ileum tissues was observed using tracer test. The expression of tight junction proteins in the ileum was measured by western blotting and immunofluorescence.

**Results:** Fucoidan treatment significantly improved cognitive dysfunction and depression-like behavior in mice exposed to alcohol. Fucoidan treatment increased preference for sweet solution and time in open arm in EPM, and reduced immobilization time in TST. The levels of brain BDNF and 5-HT in the fucoidan group were both higher than those in the model group ( $P<0.05$ ). Fucoidan treatment decreased the levels of brain interleukin-1 $\beta$ , tumor necrosis factor- $\alpha$  levels and monocyte chemokine protein-1 compared to model mice. Immunofluorescence data showed reduced expressions of CD68 and GFP, markers of activated microglia and astrocytes respectively in the fucoidan group. Moreover, after fucoidan treatment, serum endotoxin, FABP2 and D-LA levels were decreased, the cell junction and permeability were improved, and the expression levels of ZO-1 and Claudin-2 were higher than those in model mice.

**Conclusion:** Oral supplement of fucoidan could effectively alleviate cognitive dysfunction and depression-like behavior in mice exposed to alcohol, and its mechanism may be related to the protective effect of fucoidan on intestinal mucosal barrier in mice.

**Keywords:** Alcohol; Fucoidan; Cognitive dysfunction; Depression-like behavior; Intestinal mucosal barrier



## Expression profile of lncRNAs identifies the potential lncRNAs associated with both EMT and Vitamin D signaling

Yaqi Xue<sup>1†</sup>, Mengxuan Ye<sup>1†</sup>, Fei Jiang<sup>1†</sup>, Ping Wang<sup>1</sup>, Hailong Pei<sup>2</sup>, Wentao Hu<sup>2</sup>, Guangming Zhou<sup>2</sup>, Zengli Zhang<sup>1\*</sup>, Bingyan Li<sup>1\*</sup>

<sup>1</sup> Department of Nutrition and Food Hygiene, School of Public Health, Soochow University, Suzhou 215123, Jiangsu, China.

<sup>2</sup> State Key Laboratory of Radiation Medicine and Protection, School of Radiation Medicine and Protection, Soochow University, Suzhou 215123, Jiangsu, China.

<sup>†</sup>These two authors contributed equally to this paper.

**Corresponding authors:** Zengli Zhang and Bingyanli, E-mail: zhangzengli@suda.edu.cn and Bingyanli@suda.edu.cn, telephone number 86 512 65882636

The identification of long non-coding RNAs (lncRNAs) genes has progressed rapidly since their recognition. lncRNAs are likely to play an important role in many biological processes and human diseases. The epidemiological, preclinical and clinical studies support that vitamin D compounds may apply as preventative and therapeutic anticancer agents. However, it remains to be clarified that the expression profile of lncRNAs is regulated by 1 $\alpha$ ,25-dihydroxyvitamin D<sub>3</sub> (1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub>) in cancer. Therefore, we aimed to investigate the lncRNAs profiling regulated by 1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub> may be associated with epithelial to mesenchymal transition (EMT); 2) Methods: After human ovarian cancer SKOV-3 cells were treated with 100 nmol/L 1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub> for 48h, total RNA were used to determine differentially expressed lncRNAs using Agilent Human lncRNA V5 microarray; 3) Results: Differentially expression profile showed that 139 lncRNAs and 105 mRNAs were significantly dysregulated by 1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub>. Five lncRNAs including lnc-BCAS1-4\_1, lnc-RWDD4-5\_1, lnc-ZNF599-3\_6, and lnc-MBOAT1-4\_2 and lnc-KRT7-2\_2, were validated by qRT-PCR. Interesting, both lnc-BCAS1-4\_1 and vitamin D metabolic enzyme CYP24A1 were most upregulated by 1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub>. And, the sequence of lnc-BCAS1-4\_1 was shown to be similar to two nucleotide sequence of CYP24A1. In functional analysis, dysregulated lncRNAs can participate in more than one GO/KEGG pathway involved in systemic lupus erythematosus, alcoholism, osteoclast differentiation and cancer pathways, such as Wnt, TNF and TGF- $\beta$  receptor signaling. Both dysregulated lncRNAs and co-expressed mRNA genes may be mainly regulated by three transcription factors, TAF7, POU2F2 and KAT2A. Furthermore, 17 lncRNAs were identified by co-expressed networks of vitamin D receptor, CYP24A1 and epithelial marker E-Cadherin genes, indicating that these lncRNAs act as the connection to associate vitamin D signaling with EMT; and 4) Conclusion: These data constitute the first report of lncRNA expression patterns regulated by 1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub> in human ovarian cancer cells, and will provide new evidence that lncRNAs sever as target for the anti-tumor of 1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub>.

**Keywords:** lncRNAs, 1 $\alpha$ ,25(OH)<sub>2</sub>D<sub>3</sub>, cancer, EMT, vitamin D metabolite.





## **Meat consumption is cross-sectionally associated with higher dementia risk among APOE $\epsilon$ 4 carriers**

Huifeng Zhang<sup>1</sup>, Laura J Hardie<sup>2</sup>, Darren C Greenwood<sup>3</sup>, Janet E Cade<sup>1</sup>

<sup>1</sup>*Nutritional Epidemiology Group, School of Food Science and Nutrition, University of Leeds, Leeds LS2 9JT, UK.*

<sup>2</sup>*Division of Clinical and Population Sciences, Leeds Institute of Cardiovascular and Metabolic Medicine, School of Medicine, University of Leeds, Leeds LS2 9JT, UK.*

<sup>3</sup>*Leeds Institute for Data Analytics, University of Leeds, Leeds LS2 9JT, UK.*

**Corresponding author:** Huifeng Zhang, email: fshz@leeds.ac.uk, Tel: +44 1133439580

Diet as a modifiable lifestyle factor represents prevention targets for the globally increasing dementia whose development is associated with the apolipoprotein E (*APOE*)  $\epsilon$ 4 allele. This study was to examine the relationship between meat consumption and dementia risk under different *APOE*  $\epsilon$ 4 carrying status in UK Biobank. At baseline over half million participants were recruited between 2006-2010, of them 411960 participants mean age 56.5 years (SD: 8.1) with *APOE*  $\epsilon$ 4 genotyping available were included in this study. The intake frequencies per week of total meat comprising red meat, processed meat, and poultry were assessed via a 47-item food frequency questionnaire, and prevalent dementia cases were identified via self-reporting or hospital and mortality registries at recruitment. Odds ratios (OR) for each additional portion of meat/week in relation to dementia risk were estimated in logistic regression models. There were 441 prevalent dementia cases mean age 59.3 years (SD: 7.6). Our results show that increased odds of dementia were observed in consumption of total meat (adjusted OR: 1.06, 95% CI: 1.01 to 1.12,  $P=0.030$ ), processed meat (1.14, 95% CI: 1.06 to 1.23,  $P=0.001$ ), and red meat (1.11, 95% CI: 1.02 to 1.20,  $P=0.010$ ), but not poultry (0.94, 95% CI: 0.85 to 1.04,  $P=0.203$ ). In addition, associations between dementia prevalence and consumption of processed meat or total meat were pronounced in *APOE*  $\epsilon$ 4 carriers (1.33, 95%CI: 1.19 to 1.50,  $P<0.001$  for processed meat; 1.12, 95% CI: 1.03 to 1.22,  $P=0.007$  for total meat), but not in *APOE*  $\epsilon$ 4 non-carriers (1.04, 95% CI: 0.94 to 1.15,  $P=0.486$  for processed meat; 1.02, 95% CI: 0.96 to 1.09,  $P=0.449$  for total meat). Our findings suggest that higher frequency of meat consumption, especially processed meat, is associated with greater dementia prevalence, especially among *APOE*  $\epsilon$ 4 carriers in the UK.

**Key words** Dementia; *APOE*  $\epsilon$ 4; Meat consumption; Processed meat; UK Biobank



**PCSK1, SCARB1 and BDNF gene variants modulate the effect of defatted flaxseed flour intake on weight loss in overweight/obese subject: a randomized control trial**

Xiaotong Kuang<sup>1,2</sup>, Xianfeng Shao<sup>1,2</sup>, Yan Shi<sup>1,2</sup>, Huiying Li<sup>1,2</sup>, Kelei Li<sup>1,2\*</sup>, Duo Li<sup>1,2\*</sup>

<sup>1</sup>*Institute of Nutrition and Health, Qingdao University, Qingdao, China*

<sup>2</sup>*School of Public Health, Qingdao University, Qingdao, China*

**Corresponding authors:**

Duo Li, PhD; Institute of Nutrition and Health, Qingdao University,  
Qingdao 266071, China; Tel: +86 532 82991018; Fax: +86 532 82991018; E-mail: [duoli@qdu.edu.cn](mailto:duoli@qdu.edu.cn)

Kelei Li, PhD; Institute of Nutrition and Health, Qingdao University, Qingdao 266071, China  
E-mail: [likelei@qdu.edu.cn](mailto:likelei@qdu.edu.cn)

**Background:** Our previous clinical trial indicated that defatted flaxseed flour supplementation could improve body weight and BMI in overweight/obese subjects. The aim of the present study was to evaluate whether gene variants of PCSK1, SCARB1 and BDNF could modulate the weight-loss effect of defatted flaxseed flour.

**Methods:** In a double-blind randomized controlled trial, 51 overweight and obese adults (18-36 years of age) were randomized to consume control biscuits (n=24) or biscuits rich in defatted flaxseed flour (n=27) for their breakfast for 60 days (approximately 100 g/day). Three SNPs were genotyped, including rs155971 of PCSK1 gene, rs5888 of SCARB1 gene and rs6265 of BDNF gene. Linear regression model was used to examine the interaction between defatted flaxseed flour intervention and variants of PCSK1, SCARB1 and BDNF genes on weight loss.

**Results:** Significant interaction was observed between defatted flaxseed flour supplementation and the three gene variants on body weight and BMI at endpoint and changes of body weight and BMI from baseline to endpoint (all p values for interaction < 0.05). Stratified analysis showed that compared with control group, flaxseed flour supplementation lead to a significantly lower body weight and BMI at endpoint only in TC/TT genotypes of rs155971, GG genotypes of rs5888 and TC/TT genotypes of rs6265 but not in other genotypes (p value < 0.05).

**Conclusion:** Variants of PCSK1, SCARB1 and BDNF genes could modulate the effect of flaxseed flour supplementation on weight loss in overweight/obese subjects.

**Keywords:** Obese, Genetic variants, Interaction, Flaxseed meal, Weight loss



## Causal relationships between rheumatoid arthritis and gut microbiota: A bi-directional Mendelian randomization study

Zhenhuang Zhuang, MD<sup>1</sup>, Meng Gao, MD<sup>1</sup>, Ruotong Yang, MD<sup>1</sup>, Wenxiu Wang, MD<sup>1</sup>, Xueer Zhang, MD<sup>1</sup>, Tao Huang, PhD<sup>1,2,3,4</sup>

<sup>1</sup>Department of Epidemiology & Biostatistics, School of Public Health, Peking University, 100191 China.

<sup>2</sup>Department of Global Health, School of Public Health, Peking University, 100191 China.

<sup>3</sup>Key Laboratory of Molecular Cardiovascular Sciences (Peking University), Ministry of Education, 100191 China.

<sup>4</sup>Center for Intelligent Public Health, Institute for Artificial Intelligence, Peking University, 100191 China

**Corresponding author:** Dr. Tao Huang, PhD, Department of Epidemiology & Biostatistics, School of Public Health, Peking University, China. 38 Xueyuan Road, Beijing, 100191 China. Phone: (86) 010-82801528. Email: [huangtaotao@pku.edu.cn](mailto:huangtaotao@pku.edu.cn)

Convincing studies have proposed that the pathogenesis of rheumatoid arthritis (RA) is influenced by gene-environment interaction, especially the host gut microbiome. Although the associations of the gut microbiota with various diseases has been observed before, there is little evidence on the causal role of gut microbiota composition in RA. In this study we aimed to investigate the causal relationships between the risk of RA and gut microbiota, including 40 operational taxonomic units (OTUs) and 58 taxa ranging from the genus to the phylum level. We performed a two-sample bi-directional Mendelian randomization analysis by using genetic variants from genome-wide association studies ( $n=1,812-103,638$ ) as instrumental variables for gut microbiota and RA, respectively. We found no significant associations of host-genetic-driven increase in microbiota with the risk of AD. In the other direction, genetically increased RA risk was causally related to higher relative abundance of *OTU5370 Prevotella* (per 1-unit odds ratio:  $\text{Beta} \pm \text{SE}$ ,  $0.598 \pm 0.232$ ;  $P=0.01$ ), *unclassified Erysipelotrichaceae* ( $0.163 \pm 0.080$ ;  $P=0.042$ ), *Actinobacteria class* and *Actinobacteria phyla* ( $0.171 \pm 0.085$ ;  $P=0.044$ ). Our findings for the first time provide evidence of potential causal links between RA and gut microbiota, indicating that RA may alter the gut microbiota composition but not vice versa. Therefore, looking at specific microbiota dysfunction in RA patients could be an intriguing field for better understanding this disease. The underlying mechanisms of associations between gut microbiota and RA need to be further corroborated by new and strong evidence.

**Keywords:** Rheumatoid arthritis, Gut microbiota, Mendelian randomization, Genetic association, Causality



## Controlling Nutritional Status (CONUT) Score is a Prognostic Indicator for Patients with Hemorrhagic Stroke: Results from a 3-month Follow-up Study

Bei-lei Zhu<sup>1\*</sup>, Yan-zhi Wu<sup>2\*</sup>, Zhong-ming Cai<sup>2</sup>, Cheng-wei Liao<sup>2</sup>, Le-qiu Sun<sup>3</sup>, Zhi-peng Li<sup>2</sup>, Hao-man Chen<sup>2</sup>, Xue-rong Huang<sup>4</sup>, Ren-qian Feng<sup>2</sup>, Sheng-lie Ye<sup>2</sup>, qun-Li Line<sup>5</sup>, Xu-dong Zhou<sup>6</sup>, Man-man Zhang<sup>1#</sup>, Bo Yang<sup>7,1</sup>

<sup>1</sup>Department of Neurology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang, China

<sup>2</sup>Department of First Clinical Medical School, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, China

<sup>3</sup>Department of Neurology, Yueqing People's Hospital, Wenzhou 325000, Zhejiang, China

<sup>4</sup>Department of Neurology, Ruian People's Hospital, Wenzhou 325000, Zhejiang, China

<sup>5</sup>Department of Neurology, Yongjia County People's Hospital, Wenzhou 325000, Zhejiang, China

<sup>6</sup>Department of Neurology, The People's hospital of Pingyang, Wenzhou 325000, Zhejiang, China

<sup>7</sup>School of Public Health and Management, Wenzhou Medical University, Wenzhou 325000, Zhejiang, China

\*The two authors contributed this work equally

**Corresponding author:** Professor Bo Yang, M.D., PhD; E-mail: yb@wmu.edu.cn; fax: (86) 577-86687632; Tel: (86) 577-86687632.

**Co-Corresponding author:** Man-man Zhang, M.D., PhD; E-mail: zhangmanman@wmu.edu.cn; fax: (86) 577-55578033; Tel: (86) 577-555780166.

**Background:** Controlling Nutritional Status (CONUT) Score, as calculated from serum albumin, total cholesterol concentration, and total lymphocyte count, was shown to be useful for nutritional screening, which may have predicted functional prognosis in acute ischemic stroke. Nevertheless, clinical use of CONUT score as a prognostic marker is scarce in acute hemorrhagic stroke (AHS). This study aimed to explore whether CONUT score may predict a 3-month functional outcome in AHS patients.

**Methods:** We consecutively recruited 349 patients with incident AHS and their malnutrition risk were evaluated by using the CONUT score. The cohort patients were divided into high-CONUT ( $\geq 2$ ) and low-CONUT ( $< 2$ ) groups, according to the receiver operating characteristic analysis. Poor functional outcomes were evaluated by using a modified Rankin Scale (mRS) score at the end of 3-month follow-up, and defined as the mRS score of  $\geq 3$ . Odds ratios (OR) with 95% confidence intervals (CI) for the associations of CONUT scores with poor functional outcomes were estimated by using multivariate-adjusted logistic analyses.

**Results:** A total of 328 patients (mean age,  $60.4 \pm 12.83$  years; 66.8% male) were included. High-CONUT patients tend to have lower proportions of hyperlipidemia than low-CONUT patients ( $p = 0.067$ ), but no significant difference for age, gender, body mass index and stroke-related clinical measurements was found between the two groups. Patients with the high-CONUT scores had higher hospitalization costs ( $p = 0.021$ ), lower Barthel Index ( $p = 0.001$ ), and more infectious complications ( $p = 0.002$ ) than those with the low-CONUT scores. There was a greater risk for poor functional outcomes after discharge in the high-CONUT compared with the low-CONUT patients at admission (OR: 1.841, 95% CI: 1.019-3.225,  $p = 0.043$ ).

**Conclusion:** High-CONUT scores predict a 3-month poor functional prognosis in AHS, which may be useful to identify the AHS patients who need additional nutritional managements.

**Keywords:** Controlling Nutritional Status Score; Hemorrhagic stroke; Nutrition screening; Prognosis; Modified Rankin Scale



## **Abstracts of other papers**



## Assessment of causal direction between asthma and chronic kidney disease: a bi-directional Mendelian Randomization analysis

Ruotong Yang, MD<sup>1a</sup>, Wang Jiayi, PhD<sup>2a</sup>, Zhenhuang Zhuang, MD<sup>1</sup>, Meng Gao, MD<sup>1</sup>, Wenxiu Wang, MD<sup>1</sup>, Caren E. Smith, DVM<sup>3</sup>, Tao Huang, PhD<sup>1,4,5#</sup>

<sup>1</sup>Department of Epidemiology & Biostatistics, School of Public Health, Peking University, 100191 China.

<sup>2</sup>Department of Pharmacy, Peking University First Hospital, 100191 China.

<sup>3</sup>Nutrition and Genomics Laboratory, Jean Mayer USDA-Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA.

<sup>4</sup>Department of Global Health, School of Public Health, Peking University, 100191 China.

<sup>5</sup>Key Laboratory of Molecular Cardiovascular Sciences (Peking University), Ministry of Education, 100191 China.

**Corresponding author:** Tao Huang, PhD, Department of Epidemiology & Biostatistics, School of Public Health, Peking University, China. 38 Xueyuan Road, Beijing, 100191 China. Phone: (86) 010-82801528. Email: [huangtaotao@pku.edu.cn](mailto:huangtaotao@pku.edu.cn)

**Background:** In observational studies, asthma has been associated with an increased risk of chronic kidney disease (CKD), and vice versa. However, the causal relationship between these associations remains unclear. We aimed to investigate the potential causal association of asthma with renal function estimated by CKD and glomerular filtration rate based on serum creatinine (eGFR<sub>crea</sub>), and further investigate reverse causation between asthma and renal function.

**Methods:** A bi-directional two-sample Mendelian randomization (MR) approach was used to examine causality. A total of 220, 13, and 51 genetic variants were used as instrumental variables (IV) for asthma, CKD, and eGFR<sub>crea</sub>, respectively. Summary-level data was extracted from the Trans-National Asthma Genetic Consortium (TAGC) (23,948 cases, 118,538 controls) for asthma and the CKDGen consortium (n=133,413) for CKD and eGFR<sub>crea</sub>.

**Results:** We found that genetically predicted asthma was causally associated with higher risk of CKD (OR=1.097; 95% CI, 1.070 to 1.125;  $P=8.48 \times 10^{-13}$ ) and lower level of eGFR<sub>crea</sub> ( $\beta=-0.023$ ; 95% CI, -0.028 to -0.019;  $P=1.36 \times 10^{-30}$ ). However, we found no evidence of a causal effect of CKD on asthma (OR=1.000; 95% CI, 0.992 to 1.008;  $P=0.972$ ). A suggestive positive effect of eGFR<sub>crea</sub> on asthma was observed (OR=0.953; 95% CI, 0.912 to 0.995;  $P=0.029$ ).

**Conclusions:** Our MR findings support that asthma increases the risk of CKD and has detrimental effects on glomerular filtration function, whereas the relationship from CKD to asthma is unlikely to be causal.

**Keywords:** Asthma, chronic kidney disease, glomerular filtration rate, Mendelian randomization, causal association.



## Assessment of Causal Relationship between Coagulation Factors and the Risk of Type 2 Diabetes: A mendelian Randomization Study

Xueer Zhang, MD<sup>1</sup>, Tao Huang, PhD<sup>1,2,3,4</sup>

<sup>1</sup>Department of Epidemiology & Biostatistics, School of Public Health, Peking University, 100191 China.

Corresponding author: Full name, email address, telephone number

<sup>2</sup>Department of Global Health, School of Public Health, Peking University, 100191 China.

<sup>3</sup>Center for Intelligent Public Health, Academy for Artificial Intelligence, Peking University, 100191 China.

<sup>4</sup>Key Laboratory of Molecular Cardiovascular Sciences (Peking University), Ministry of Education, 100191 China.

**Corresponding author:** Dr. Tao Huang, PhD. Phone: (86) 010-82801528. Email: [huangtaotao@pku.edu.cn](mailto:huangtaotao@pku.edu.cn)

Coagulation factors have been associated with type 2 diabetes mellitus (T2DM) in observational studies. However, it is unknown whether such associations reflect causality. We aimed to investigate the causal relationship between coagulation factors and T2DM. A Mendelian randomization (MR) analysis was used to test the causal associations using genetic variants associated with coagulation factors and T2DM. Summary data was extracted from a trans-ethnic meta-analysis of T2DM (26,488 cases and 83,964 controls); a multi-ethnic meta-analysis of plasma fibrinogen concentration (n=101,193); a genomic and transcriptomic association study of venous thromboembolism (VTE) plasma levels (n=202,356) and a genome-wide association transethnic meta-analysis of factor VIII (FVIII) and von Willebrand factor (VWF) plasma levels (n= 46,354). Genetically predicted FVIII levels was positively associated with T2MD (per 1-unit higher log odds: odds ratio: 1.37; 95% confidence interval: 1.06-1.77; P=0.015) based on 5 single nucleotide polymorphisms (SNPs), as were VWF levels (1.24; 1.04-1.48; P=0.017) and VTE levels (1.04; 1.00-1.08; P=0.04) based on 8 and 5 SNPs, respectively, after a Bonferroni correction (P<0.05/3). However, the MR analysis did not support a causal relationship of genetically predicted fibrinogen levels on the risk of T2DM (1.14; 0.64-2.06; P=0.64) based on 24 SNPs. These results provide novel evidence of a causal role of coagulation factors on higher risk of T2DM, supporting coagulation factors as a possible target to reduce risk of T2MD.

**Keywords:** Mendelian Randomization, type 2 diabetes mellitus, factor VIII, venous thromboembolism and von Willebrand factor





## Causal relationships between rheumatoid arthritis and gut microbiota: A bi-directional Mendelian randomization study

Zhenhuang Zhuang, MD<sup>1</sup>, Meng Gao, MD<sup>1</sup>, Ruotong Yang, MD<sup>1</sup>, Wenxiu Wang, MD<sup>1</sup>, Xueer Zhang, MD<sup>1</sup>, Tao Huang, PhD<sup>1,2,3,4</sup>

<sup>1</sup>Department of Epidemiology & Biostatistics, School of Public Health, Peking University, 100191 China.

<sup>2</sup>Department of Global Health, School of Public Health, Peking University, 100191 China.

<sup>3</sup>Key Laboratory of Molecular Cardiovascular Sciences (Peking University), Ministry of Education, 100191 China.

<sup>4</sup>Center for Intelligent Public Health, Institute for Artificial Intelligence, Peking University, 100191 China

**Corresponding author:** Dr. Tao Huang, PhD, Department of Epidemiology & Biostatistics, School of Public Health, Peking University, China. 38 Xueyuan Road, Beijing, 100191 China. Phone: (86) 010-82801528. Email: [huangtaotao@pku.edu.cn](mailto:huangtaotao@pku.edu.cn)

Convincing studies have proposed that the pathogenesis of rheumatoid arthritis (RA) is influenced by gene-environment interaction, especially the host gut microbiome. Although the associations of the gut microbiota with various diseases has been observed before, there is little evidence on the causal role of gut microbiota composition in RA. In this study we aimed to investigate the causal relationships between the risk of RA and gut microbiota, including 40 operational taxonomic units (OTUs) and 58 taxa ranging from the genus to the phylum level. We performed a two-sample bi-directional Mendelian randomization analysis by using genetic variants from genome-wide association studies ( $n=1,812-103,638$ ) as instrumental variables for gut microbiota and RA, respectively. We found no significant associations of host-genetic-driven increase in microbiota with the risk of AD. In the other direction, genetically increased RA risk was causally related to higher relative abundance of *OTU5370 Prevotella* (per 1-unit odds ratio:  $\text{Beta} \pm \text{SE}$ ,  $0.598 \pm 0.232$ ;  $P=0.01$ ), *unclassified Erysipelotrichaceae* ( $0.163 \pm 0.080$ ;  $P=0.042$ ), *Actinobacteria class* and *Actinobacteria phyla* ( $0.171 \pm 0.085$ ;  $P=0.044$ ). Our findings for the first time provide evidence of potential causal links between RA and gut microbiota, indicating that RA may alter the gut microbiota composition but not vice versa. Therefore, looking at specific microbiota dysfunction in RA patients could be an intriguing field for better understanding this disease. The underlying mechanisms of associations between gut microbiota and RA need to be further corroborated by new and strong evidence.

**Keywords:** Rheumatoid arthritis, Gut microbiota, Mendelian randomization, Genetic association, Causality





## Depression, Malnutrition and Their Relationship in Older Adults

Mahsa Ghahvechi Chaeipeima<sup>1</sup>, Shaokang Wang<sup>2\*</sup>

<sup>1</sup>Department of Nutrition and Food Hygiene, School of Public Health, Southeast University, Nanjing, China.

<sup>2</sup>Key Laboratory of Environmental Medicine and Engineering of Ministry of Education, and Department of Nutrition and Food Hygiene, School of Public Health, Southeast University, Nanjing, China.

**Corresponding author:** Shaokang Wang, shaokangwang@seu.edu.cn, 8613951087334

**Background:** Aging as a major issue in public health, has its own biological, physiological, psychological and social and economic characteristics. This period in human life has become longer in recent decades and needs more attention. In this paper we aim to review currently available data on depression, malnutrition and their relationship in older age.

**Methods:** In this review studies published since 1985 till 2020 were summarized through PubMed, Google Scholar, Science Direct and Medline by looking up the Depression, Malnutrition, Older People, Elderly as keywords.

**Results:** Results of studies revealed that one of the main symptoms of depression among elderly are significant changes in appetite or weight (Eating more or less than usual). People may be at greater risk of malnutrition in later life. It has been reported that depression may deteriorate the risk of malnutrition in older subject. When the nutrient intake does not meet the nutritional needs, moderate micro nutrient deficiencies may occur, and gradually it may decline into the protein calorie malnutrition. Malnutrition and depression are both complicated and correlated so that depression may lead to appetite loss and under nutrition. On the other hand, malnutrition may deteriorate depression and apathy. Based on the findings the most significant nutrients affecting mental health, with special relevance to depression are mentioned as carbohydrates, proteins, omega-3 fatty acids, vitamin B12, folate, vitamin D and minerals.

**Conclusion:** Aging is associated with a decline in number of physiological functions and increase in depression prevalence among elderly, and this can affect nutritional status. Malnutrition and depression are both correlated. It is important to mention that nutritional interventions should be implemented only as a part of a complete strategy. Paying enough attention to social support, other contributing factors and prevention strategies, are important as well.

**Keywords:** Depression, Malnutrition, Older People, Elderly.



## Health Promotion, Health Education and Their Role in Obesity Prevention Among Students

Mahsa Ghahvechi Chaeipeima<sup>1</sup>, Shaokang Wang<sup>2</sup>

<sup>1</sup>*Department of Nutrition and Food Hygiene, School of Public Health, Southeast University, Nanjing, China.*

<sup>2</sup>*Key Laboratory of Environmental Medicine and Engineering of Ministry of Education, and Department of Nutrition and Food Hygiene, School of Public Health, Southeast University, Nanjing, China.*

**Corresponding author:** Shaokang Wang, shaokangwang@seu.edu.cn, 8613951087334

**Background:** Rates of overweight and obesity have increased dramatically during last decades among children. Childhood obesity strongly ‘tracks’ into adulthood, with implications for morbidity. Considering the serious problems of obesity and difficult treatment of it in adults, this review aims to investigate the role of health education, health promotion and health promoting schools’ framework on prevention of obesity among students.

**Methods:** In this review studies published since 1985 till 2020 were summarized through PubMed, Google Scholar, Science Direct and Medline by looking up the Health Promotion, Health Education, Obesity, overweight and School Students as keywords.

**Results:** Obesity is a complex condition which requires schools’ complex solution and multi-component interventions. WHO’s Health Promoting Schools framework is one of these programs which has three main comprises including health education promoted through the formal school curriculum; changes to the school’s physical and/or social environment; and engagement with families and the wider community. Results of studies showed that interventions which combine curriculum change with environmental change and engagement with parents and community can have small but significant effects on outcomes such as BMI, physical activity and dietary behaviors, this can discuss the fact that why some studies in which parents and community are not included, fail to demonstrate a positive effect on achieving lifestyle changes in children. Report from studies revealed that health education had positive effect on fruit and vegetable consumption, self-reported well-being, significant reductions in overweight and obesity over time and high frequency of consumption of macronutrients and most micronutrients among students.

**Conclusion:** Targeting obesity through health promotion, health education and HPS framework for students, school staffs and parents has been shown to be effective overall in improving physical activity and nutrition, the key determinants of overweight and obesity among students.

**Keywords:** Health Promotion, Health Education, Obesity, overweight and School Students.



## **Docosahexaenoic Acid Attenuated Neurotoxicity Induced by Methamphetamine: a proteomics research**

Fangping Chen<sup>1, 2</sup>, Dan Zheng<sup>3</sup>, Qi Wang<sup>1, 2</sup>, Yi Gong<sup>1, 2</sup>, Chunhua Huang<sup>2</sup>, Shimei Huang<sup>3</sup>, Zhizhong Guan<sup>4</sup>, Bo Yang<sup>6, 2\*</sup>, Didong Lou<sup>2\*</sup>

<sup>1</sup>*Department of Forensic Medicine, Guizhou Medical University, Guizhou, China.*

<sup>2</sup>*School of Basic Medicine Sciences, Guizhou University of Traditional Chinese Medicine, Guizhou, China.*

<sup>3</sup>*Guiyang Maternal and Child Health Care Hospital, Guizhou, China.*

<sup>4</sup>*Key Laboratory of Local Diseases and Minority Diseases, Ministry of Education, Guizhou Medical University, Guizhou, China.*

<sup>5</sup>*Department of forensic clinical medicine, College of forensic medicine, Guizhou Medical University, Guizhou, China.*

<sup>6</sup>*School of Public Health and Management, Wenzhou Medical University, Wenzhou 325000, Zhejiang Province, China*

**Corresponding author:** Prof. Didong Lou; E-mail address: [15761879@qq.com](mailto:15761879@qq.com) ORCID: 0000-0003-0059-1587

**Co-corresponding author:** Prof. Bo Yang; E-mail: [yb@wm.edu.cn](mailto:yb@wm.edu.cn); Tel: +86-577-55579381.

**Background:** Methamphetamine (METH), a sort of highly addictive drugs, extremely burden public health on account of intensive neurotoxicity. It has been proved that Docosahexaenoic Acid (DHA) confers neuroprotection against numerous neurological disorders, while the detailed mechanism behind the neuroprotective efficacy are not fully disclosed. This study aims to investigate the protective effect of DHA on the neurotoxicity induced by METH.

**Method:** 9-plex TMT labeled quantitative proteome was applied to discover the altered proteins in SH-SY5Y cell by the addition of METH with or without DHA. GO analysis and KEGG analysis were performed for the altered proteins by METH. Further, among the altered proteins the reversely regulated proteins by DHA were filtered. The morphology and apoptosis of SH-SY5Y cell in each group was compared to determine the effect of DHA on METH-induced neurotoxicity. Finally, western blot was applied to validate the proteomic data.

**Results:** METH attenuated differentiation and increased apoptosis in human neuroblastoma cell (SH-SY5Y), which could be mitigated by additional DHA. Tandem mass spectrum revealed intensive changes in the protein profile were induced by METH in SH-SY5Y. Caused by METH, the pathways annotating to cellular death and neuroinflammation were significantly increased while cytoskeleton and synaptic function were decreased in expression. Twenty-two filtered proteins were reversely regulated by DHA under the neurotoxic condition of METH, and annotated to cytoskeleton, ribosome and glutathione metabolism, which might be responsible for the neuroprotective effects of DHA.

**Conclusion:** This proteomic research revealed the DHA could attenuate change in the neurotoxicity-related neuronal protein profiles induced by METH, which suggested the benefit of DHA in protecting against METH-induced neuronal damage.

**Keywords:** Methamphetamine; Docosahexaenoic Acid; Proteomics; Cytoskeleton; Neuronal



## Association between obesity and post-stroke anxiety in patients with acute ischemic stroke

Bei-Lei Zhu<sup>1\*</sup>, Ai-Yi Hu<sup>2\*</sup>, Gui-Qian Huang<sup>1\*</sup>, Hui-Hua Qiu<sup>1</sup>, Xian-Chai Hong<sup>1</sup>, Ping-Lang Hu<sup>1</sup>, Cheng-Xiang Yuan<sup>1</sup>, Yi-Ting Ruan<sup>1</sup>, Bo Yang<sup>3#</sup>, Jin-Cai He<sup>1#</sup>

<sup>1</sup>Department of Neurology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang, China

<sup>2</sup>Department of First Clinical Medical School, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang, China

<sup>3</sup>School of Public Health and Management, Wenzhou Medical University, Wenzhou 325000, Zhejiang, China

**Co-first author:** Bei-Lei Zhu, Ai-Yi Hu and Gui-Qian Huang

**Co-Corresponding author:** Bo Yang and Jin-Cai He

Bo Yang, M.D., PhD; E-mail: yb@wmu.edu.cn; fax: (86) 577-86687632; tel: (86) 577-86687632.

Jin-Cai He, M.D.; E-mail: hjc@wmu.edu.cn; fax: (86) 0577 55579363; tel: (86) 0577 55579363.

Post-stroke anxiety (PSA) is a serious psychosomatic comorbidity among stroke patients. Obesity is found to be positively associated with incident anxiety, but whether this association would occur among stroke patients is currently unknown. The purpose of this study was to investigate the potential association between obesity and subsequent anxiety risk in stroke patients. A total of 441 patients with acute ischemic stroke (AIS) onset were consecutively recruited within 7 days, and their PSA status was evaluated by using 17-item Hamilton anxiety Rating Scale at the end of one-month follow-up. Total obesity was defined as body mass index (BMI)  $\geq 28 \text{ kg/m}^2$ , and abdominal obesity was defined as waist circumference (CM)  $\geq 90 \text{ cm}$  for men and  $\geq 85 \text{ cm}$  for women. Relative fat mass (RFM) was calculated by using the formula as previously described. Odds ratio (OR) with 95% confidence interval (CI) was estimated for the risk of PSA by using logistic regression analysis. The incidence of PSA was 25.85% (95% CI: 21.98% to 30.13%) at the end of one-month follow-up, with a significant difference between patients with abdominal obesity and without abdominal obesity (32.3% vs. 19.8%,  $\chi^2 = 5.587$ ,  $p = 0.022$ ). Obesity-related parameters were significantly associated with elevated risk of PSA, and the crude ORs were 1.04 (95%CI: 1.01-1.08;  $P = 0.013$ ) for RFM and 1.93 (95%CI: 1.11-3.34;  $P = 0.019$ ) for abdominal obesity. Even after adjustment for obesity-related risk factors and PSA-related clinical measurements, the association remained to be pronounced with abdominal obesity (OR = 2.154; 95%CI: 1.01-4.46;  $P = 0.047$ ) but not with total obesity (OR = 1.45; 95%CI: 0.74-2.86;  $P = 0.281$ ). Abdominal obesity is independently associated with the PSA, which is likely to predict PSA risk in clinical practice. Further prospective clinical studies with long follow-up duration are warranted to verify this finding.

**Keywords:** Post-stroke anxiety; obesity; abdominal obesity.



## **Maternal iodine status and adherence with recommendation for supplement use in a sample of Chinese pregnant and lactating women: A cross- sectional study**

Shuchang Liu<sup>1,2</sup>, Yang Zhang<sup>1</sup>, Zheng Feei Ma<sup>1</sup>

<sup>1</sup>*Department of Health and Environmental Sciences, Xi'an Jiaotong-Liverpool University, Suzhou 215123, Jiangsu Province, China;*

<sup>2</sup>*Institute of Life Course and Medical Sciences, Faculty of Health and Life Sciences, University of Liverpool, Liverpool L69 3BX, UK*

**Corresponding author:** Dr Zheng Feei Ma, [Zhengfee.Ma@xjtlu.edu.cn](mailto:Zhengfee.Ma@xjtlu.edu.cn), +86 (0) 512 8188 4938

Pregnant women are particularly vulnerable to iodine deficiency because they have increased iodine requirement. Sufficient iodine supply is needed to ensure the production of thyroid hormone in both pregnant and lactating women. Therefore, this study was designed to investigate maternal dietary iodine intake and supplement use in Xi'an, Shaanxi province, China. Participants were asked to complete a socio-demographic questionnaire including iodine-specific food frequency questionnaire and maternal supplement use. Snowball and convenience samplings were used to recruit both pregnant and lactating women. Overall, 151 pregnant and lactating women (mean age 29 years) were included in the final analysis. Majority of participants had a university degree. None reported the use of maternal supplements before pregnancy. Over half of participants used maternal supplements during pregnancy. Moreover, there were more than half of participants who planned not to take maternal supplements while breastfeeding. The median dietary iodine intake plus iodized salt of participants was 256 µg/d, indicating maternal iodine sufficiency. In conclusion, most of women paid more attention on maternal supplement use during pregnancy, while ignored the importance of maternal supplement use on before and after pregnancy. In addition, women with higher level of education were more likely to take maternal supplement use.

**Keywords:** maternal iodine deficiency; maternal supplement use; pregnancy; lactation; China



## Hepatic Lipidomics Reveals the Homeostasis and Profile of Sphingomyelin from Yak Butter in Normal-Fat Diet-Fed Rats

Xin Luo<sup>1</sup>, Wancheng Sun<sup>1</sup>, and Yihao Luo<sup>1</sup>

<sup>1</sup>College of Agriculture and Animal Husbandry, Qinghai University, Ning Da 251, Qinghai Province, Xining 810016, China

**Corresponding author:** Yihao Luo; Email address: [sun0108@163.com](mailto:sun0108@163.com); Telephone number: +86 13519780623

Dietary sphingomyelin was showed to inhibit the uptake of lipids in mice fed with a high-fat diet, however, the effect of sphingomyelin on normal diet was on reported. The current study aims to examine the effects of sphingomyelin extracts from yak butter on hepatic steatosis and inflammation in C57/B6J mice fed with a normal diet. A UHPLC-QTOF-MS based lipidomics method was utilized to screen the liver metabolites and predict the dominant potential metabolic pathways after sphingomyelin feeding. The results showed that sphingomyelin extracts reduced the accumulation of lipid droplets, suppressed the expression of pro-inflammatory factors IFN -  $\gamma$  , IL-6 and TNF -  $\alpha$  , synchronously, promoted the expression of anti-inflammatory factors IL-10, IL-4 and IL-1Ra. In addition, sphingomyelin extracts exhibited the modulation on liver lipid metabolism when supplement sphingomyelin in normal diet for one month and five months. Specifically, 16, 68 different metabolites and 2, 6 metabolic pathways were identified by quantitative lipidomics, respectively. Six CERs including Cer(d18:1/18:0), Cer(d18:1/20:0), Cer(d17:1/22:0), Cer(d17:1/24:1), Cer(d17:1/24:0) and Cer(d17:0/26:1), six SMs including SM(d15:0/24:1), SM(d14:0/26:1), SM(d14:1/24:1), SM(d15:1/22:0), SM(d15:1/24:1) and SM(d19:1/26:1), and PS(18:1/22:6) were identified and can be used as potential biomarkers of steatosis and inflammation. This study highlighted the effects of yak butter sphingomyelin on hepatic steatosis, tissue inflammation and lipid metabolism of mice under a normal diet.

**Keywords:** sphingomyelin, lipidomics, steatosis, inflammation, lipid metabolism



## RNA m<sup>6</sup>A modification and nutrient metabolism

Mayila Maimaiti<sup>1</sup>, Reziya Abulaiti<sup>1</sup>, Lili<sup>1\*</sup>

<sup>1</sup>*Clinical Nutrition Department of the First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, China.*

**Corresponding author:** Lili, xj\_lili@126.com, 13201215011

The term “epitranscriptomics” represents an emerging field of epigenetics, which refers to regulation of RNA fate at post-transcriptional level. Similar to DNA and proteins (e.g., histones), RNA is also modified by covalent chemical groups, and these modifications constitute “epitranscriptomic code” to alter RNA stability as well as function. Among all modifications, N<sup>6</sup>-methyladenosine (m<sup>6</sup>A) is the most abundant and most studied internal modification on messenger RNA (mRNA) that plays crucial roles in regulation of RNA-related bioprocesses. Deposition and function of RNA m<sup>6</sup>A methylation is mainly regulated by RNA methyltransferases (writers), m<sup>6</sup>A binding proteins (readers) and m<sup>6</sup>A demethylases (erasers), making it a dynamic and reversible process. As an emerging component of gene regulatory system, role and function of RNA m<sup>6</sup>A modification in physiological and pathological processes has been increasingly revealed and proven important for maintaining cellular homeostasis. Recently, emerging evidence suggested that RNA m<sup>6</sup>A modification is implicated in nutrients’ metabolism related disease such as obesity and diabetes, while the detailed mechanisms are yet to be elucidated. On the other hand, the nutrients provide essential substrates for m<sup>6</sup>A modification to occur, such as S-adenosylmethionine (SAM), which is synthesized from methionine (Met) by Met adenosyltransferase. Therefore, the regulation between RNA m<sup>6</sup>A modification and nutrient metabolism is mutual and merits further investigation to gain deep insight and cope with nutrient metabolism associated adverse health outcomes.

**Keywords:** epitranscriptomics, N<sup>6</sup>-methyladenosine (m<sup>6</sup>A), nutrients, obesity, diabetes.





## **Metabolome Analysis of the Association of Tea Intake with Frailty and Functional Well-being in the Singapore Longitudinal Ageing Study**

Shivi Takkar<sup>1</sup>, Xinyi Gwee<sup>2</sup>, Denise QL Chua<sup>2</sup>, Vipin Narang<sup>1</sup>, Bernett Lee<sup>1</sup>, Nabil Bosco<sup>3</sup>, Anis Larbi<sup>1</sup>, Ng Tze Pin<sup>2</sup>

<sup>1</sup>*Singapore Immunology Network, #04-01 Immunos, 8A Biomedical Grove, Singapore 138648.*

<sup>2</sup>*Gerontology Research Programme, Department of Psychological Medicine, Yong Loo Lin School of Medicine, National University of Singapore, 119228, Singapore*

<sup>3</sup>*Nestlé Research Singapore Hub, Singapore.*

**Corresponding author:** Tze Pin Ng, [pcmngtp@nus.edu.sg](mailto:pcmngtp@nus.edu.sg), +65-67723478

The health benefits of tea and its constituent polyphenols, flavonoids, amino acids and other molecules are still inadequately studied. We investigated the relationship between tea consumption (0-1 cup/month,  $\leq 2$  cups/day, or  $\geq 3$  cups/day) and frailty in a cohort of 164 elderly ( $\geq 65$  year old) Chinese individuals in Singapore and explored key nutritional and metabolic markers in plasma associated with tea consumption in analyses adjusting for age separately for females ( $n = 107$ ) and males ( $n = 57$ ). Tea drinking was associated with low levels of weakness in both sexes, and in general with a less frailty (adjusted  $p = 0.046$ ). In females, tea consumption was associated with higher levels of the amino acids proline, alanine, serine, eicosenoic and capric fatty acids, and lower inflammation indicated by the levels of interferon gamma. In males, tea consumption was associated with higher levels of several vitamins or vitamers (riboflavin, total B2, all-trans retinol, 4-pyridoxic acid), amino acids (serine, phenylalanine and lysine) and some related metabolites (oxoglutaric acid, 3-methyl-2-oxovaleric acid, alpha-aminobutyric acid, 2-hydroxybutyric acid and creatine) as well as cis-aconitic acid suggesting impact on mitochondrial and liver metabolism and finally, tartaric acid and the bile acid apoCA. At the molecular level, microarray analysis of blood samples indicated differentially expressed genes across the tea consumption groups in both females and males affecting metabolic processes, including glycerol metabolism, phosphatidylcholine synthesis and others, as well as inflammation. In silico network analysis of the statistically associated nutritional and metabolic markers suggest possible mechanism linking tea consumption to functional well-being.

**Keywords:** Tea consumption, Frailty, Cohort study, Metabolome analysis, Aging.





## **Elevated homocystein inhibits cell proliferation through histone homocysteinylation during neural development and subsequent neural tube defects**

Chunlei Wan<sup>1</sup>, Baoling Bai<sup>1</sup>, Haiyan Cao<sup>1</sup>, Dan Li<sup>1</sup>, Ting Zhang<sup>1, \*</sup>, Qin Zhang<sup>1</sup>

<sup>1</sup>*Beijing Municipal Key Laboratory of Child Development and Nutriomics, Capital Institute of Pediatrics, Beijing, 100020, China*

**Corresponding Author:** Dr. Qin Zhang, [maureenq@hotmail.com](mailto:maureenq@hotmail.com), 86-010-85638400. Or to Dr. Ting Zhang, [Zhangtingcv@126.com](mailto:Zhangtingcv@126.com), 86-010-85695585.

**Background:** Maternal nutritional factors hyperhomocysteinemia during pregnancy is associated with increased risk of Neural tube defects (NTDs) in the offspring, while its mechanism remains elusive.

**Methods:** First the nutritional factors homocystein metabolite, homocysteine thiolactone (HTL) was used to induce NTDs model in chicken embryo. The neural groove of incubated white leghorns eggs were injected with 0.5mM HTL to induce NTDs model. Then the cell proliferation level were studied by Immunohistochemistry and immunofluorescence in HTL induced chicken NTDs and HTL treated NE4C cells (Mouse neural stem cells). Further, the cell proliferation pathway related to NTDs were studied by RNA-seq in NE4C cells. At last, whether cell proliferation pathway genes were regulated by histone homocysteinylation were studied by ChIP-seq .

**Results:** We got the HTL-induced chicken NTDs successfully. We found that cell proliferation decreased by PCNA (Proliferating Cell Nuclear Antigen) and SABC (strept avidin-biotin complex) test in HTL-treated chick NTDs. Further, we confirmed that cell proliferation decreased by Edu (5-ethynyl-2'-deoxyuridine) test in HTL treated NE4C cells. Then we found that the protein level of cell proliferation related MAPK pathway genes Fgf13 and Kras decreased in HTL induced chicken NTDs and HTLtreated NE4C cells. At last we found that MAPK pathway genes were regulated by histone homocysteinylation by ChIP-seq and RNA-seq.

**Conclusion:** Our results suggest that nutritional imbalance and metabolic disorder such as higher levels of homocystein contribute to the onset of NTDs through histone homocysteinylation, leading to abnormal expressions of proliferation genes during the early stage of neural development and subsequent neural tube defects.

**Keywords:** neural tube defects, histone homocysteinylation, cell proliferation, homocysteine, chicken NTDs model



## Study on chemical composition antibacterial and antitumor activity of volatile oil from *Chrysanthemum morifolium*

Jihan Sun, Zhaodan Wang<sup>1</sup>, Chen Lin<sup>1</sup>, Zhixiu Song<sup>2</sup>, Feifei Zhang<sup>3</sup>, Guiju Sun<sup>1\*</sup>

<sup>1</sup>Key Laboratory of Environmental Medicine and Engineering of Ministry of Education, and Department of Nutrition and Food Hygiene, School of Public Health, Southeast University, Nanjing 210009, China

<sup>2</sup>Second Clinical Medical College, Nanjing University of Traditional Chinese Medicine, Nanjing 210046, China

<sup>3</sup>Hospital and Institute of Obstetrics and Gynecology, Shanghai Medical College of Fudan University, Shanghai 200011, China

**Corresponding author:** Guiju Sun, gjsun@seu.edu.cn

The essential oils of *Chrysanthemum morifolium* Ramat were extracted 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*, *a-hemolytic streptococcus*, *pneumococci*) and three Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Shigella flexneri*) and two molds (*Candida albican*, *Cryptococcus neoforman*). We used HepG-2 in vitro and S-180 tumor-bearing mice In vivo to research antitumor effect. Total 59 compounds were identified and caryophyllene oxide was the most abundant volatile component (7.389%). The volatile oil showed promising antibacterial activity against 5 Gram-positive bacteria and 2 molds. The oils showed significant antitumor activity towards HepG-2 cells with IC50 valued 1.42 $\mu$ l/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. In conclusion, the essential oil from *Chrysanthemum morifolium* Ramat has antibacterial and antitumor activity. And it's associated with particular chemical compositions.

**Keywords:** Chemical composition; Antibacterial activity, Antitumor activity, *Chrysanthemum morifolium* Ramat, Essential oil



## Low oral bioavailability and partial gut microbiotic and phase II metabolism of Brussels/witloof chicory sesquiterpene lactones in healthy humans

Jiakun Zheng<sup>1</sup>, Hui Weng<sup>1</sup>, Luanying He<sup>1</sup>, Qing Li<sup>1</sup>, Xiuping Liu<sup>1</sup>, Dongliang Wang<sup>1,2,3</sup>

<sup>1</sup>Department of Nutrition, School of Public Health, Sun Yat-sen University (Northern Campus), 510080, Guangzhou, PR China

<sup>2</sup>Guangdong Provincial Key Laboratory of Food, Nutrition and Health, 510080, Guangzhou, PR China

<sup>3</sup>Guangdong Engineering Technology Research Center of Nutrition Translation, 510080, Guangzhou, PR China

**Corresponding Author:** Dongliang Wang, [wqliang@mail.sysu.edu.cn](mailto:wqliang@mail.sysu.edu.cn), 86-20-87332472

Free and glycosylated sesquiterpene lactones (SLs), abundant in leafy vegetables including Brussels/witloof chicory, possess health-promoting effects *in vivo*. However, the pharmacokinetics of dietary source of SLs remains largely unknown. In this open-label and single-dose trial, sixteen healthy volunteers consumed 150 g of Brussels/witloof chicory juice containing 48.77  $\mu\text{mol}$  SLs in 5 min. Blood, urine and fecal samples were collected before and after Brussels/witloof chicory consumption in 24 h. No SLs were detected in serum, urine and fecal samples before Brussels/witloof chicory consumption in all participants. Strikingly, Brussels/witloof chicory consumption increased lactucin, 11 $\beta$ ,13-dihydrolactucin and their glucuronide/sulfate conjugates rather than lactucopicrin and 11 $\beta$ ,13-dihydrolactucopicrin, as well as glycosylated SLs in all biological samples. The peak concentration of total SLs in serum reached 284.46 nmol/L at 1 h, while in urine, this peak was 220.3 nmol between 2 and 6 h. Recovery of total SLs in blood, urine and feces was 7.03%, 1.13% and 43.76% of the ingested dose, respectively. Human fecal suspensions with intestinal microbiota degraded glycosylated SLs in Brussels/witloof chicory, and converted lactucopicrin and 11 $\beta$ ,13-dihydrolactucopicrin to lactucin and 11 $\beta$ ,13-dihydrolactucin, respectively. Collectively, Brussels/witloof chicory SLs are likely to be poorly bioavailable and undergo partial gut microbial and phase II metabolism in humans.

**Keywords:** Brussels/witloof chicory; Gut microbiotic metabolism; Phase II metabolism; Pharmacokinetics; Sesquiterpene lactones



## Correlation analysis between the value of bioelectrical impedance phase angle and prognosis in 248 patients with primary liver cancer

Guang Yang<sup>1</sup>, Jin-Yu Shi<sup>1</sup>, Nan-Ya Wang<sup>1</sup>

*The Cancer Center, Jilin University First Hospital, Jilin, China*

**Corresponding Author:** Prof. Nan-Ya Wang, MD, the Cancer Center, Jilin University First Hospital, No. 71, Xinmin Street, Changchun, Jilin, China; E-mail: [drwangnany@163.com](mailto:drwangnany@163.com); TEL: +86-431-88783984.

**Background:** Phase angle (PA) is an indicator of nutritional status derived from bioelectrical impedance analysis (BIA). Studies have shown that PA is one of the factors affecting the survival of tumor patients. However, the correlation between PA and primary liver cancer prognosis have not been reported. We aim to explore the relationship between PA, nutrition-related indicators and prognosis of patients.

**Methods:** 248 patients who underwent BIA between 2015 to 2019 at the First Hospital of Jilin University were retrospectively analyzed. Patients were divided into two groups according to the median PA, the overall survival (OS) and nutrition-related indicators were compared between the two groups. The correlation between PA, hematological nutrition-related indicators and human composition analysis were identified using Pearson correlation analysis. The independent predictors of the patients' prognosis were identified using univariate and multivariate analyses.

**Results:** The mOS in the high PA group and the low group were 70 months, 54.6 months, respectively ( $p=0.004$ ). Pearson correlation analysis has showed that PA was consistent with hematological nutrition-related indicators and human composition analysis. Multivariable COX regression analysis identified PA as an independent risk factor affecting the prognosis of patients who were BCLC stage A and stage B.

**Conclusion:** PA is a good proxy for human nutritional status. PA is associated with prognosis of primary liver cancer, and low PA indicates poor nutritional status and prognosis.

Key words: phase angle, nutrition, bioelectrical impedance analysis, primary liver cancer, correlation.



## **The natural occurring RRR- $\alpha$ -tocopherol and synthetic $\alpha$ -tocopherol stereoisomers in maternal blood, cord blood and breast milk and associations with maternal diet**

Zeru Lou<sup>1</sup>, Ke Wu<sup>1</sup>, Yingyi Mao<sup>2</sup>, Xiaokun Cai<sup>2</sup>, Yanrong Zhao<sup>2</sup>, Meiqin Cai<sup>1</sup>

<sup>1</sup>*School of Public Health, Shanghai Jiao Tong University, Shanghai 200025, People's Republic of China*

<sup>2</sup>*Abbott Nutrition Research & Development Center, Abbott Ltd, Shanghai 200233, People's Republic of China*

**Corresponding Author:** Meiqin Cai, [caimeiqin@sjtu.edu.cn](mailto:caimeiqin@sjtu.edu.cn), 13601707292

The study aimed to investigate the natural occurring RRR- $\alpha$ -tocopherol and synthetic  $\alpha$ -tocopherol stereoisomers in maternal, cord blood and breast milk in different lactation stages from Chinese mothers, explore the associations with maternal characteristics and diet, providing a reference for further guidance on maternal diet and the addition of vitamin E content and configuration in infant formula. A total of 50 sample sets of longitudinal from maternal blood, cord blood and three stages (colostrum: 1-5 days after delivery; transitional milk 10-15 days; mature milk: 40-45 days) of milk were collected in Shanghai.  $\alpha$ -tocopherol and the stereoisomers were determined by high performance liquid chromatography with a fluorescence detector. The maternal dietary intake was evaluated by 24-h dietary recall and FFQ. The median concentrations of  $\alpha$ -tocopherol in Chinese maternal blood and umbilical cord blood were 14.68 mg/L, 2.31 mg/L and those of RRR were 12.20 mg/L and 1.82 mg/L. As for the breast milk, they were 8.98 mg/L, 8.01 mg/L in colostrum; 4.08 mg/L, 3.49 mg/L in transitional milk; 4.08mg/L, 3.28 mg/L in mature milk. The RRR configuration accounts for more than 80% of  $\alpha$ -tocopherol in all kinds of samples. Overall, there were significant correlations between  $\alpha$ -tocopherol and RRR in maternal blood, cord blood and milk ( $P < 0.001$ ). As well as correlations among  $\alpha$ -tocopherol, RRR in transitional milk and weight-related indicators, including pre-pregnancy weight ( $P < 0.05$ ) and pre-delivery weight ( $P < 0.05$ ). There was no association between dietary intake and  $\alpha$ -tocopherol in all samples. Although there were some differences of  $\alpha$ -tocopherol among different samples, they were both highly enriched in natural forms of RRR- $\alpha$ -tocopherol. This study suggests that RRR- $\alpha$ -tocopherol is the absolute dominant configuration of  $\alpha$ -tocopherol as well as the main active form of VE in the early stage of life, which is of great significance to pregnant women and infants.

**Keywords:** cord blood; human milk;  $\alpha$ -tocopherol; RRR- $\alpha$ -tocopherol; dietary intake



## **Establishment of an evidence-based evaluation index pool based on the effectiveness of nutritional and functional foods for chronic kidney disease**

Ziqi Zhou<sup>1</sup>, Jingsi Song<sup>2</sup>, Jie Gong<sup>1</sup>, Rongzheng Yue<sup>3</sup>, Yi Chen<sup>3</sup>, Wen Hu<sup>1</sup>

<sup>1</sup>*Department of Clinical Nutrition, West China Hospital, Sichuan University, Sichuan Province, Chengdu 610041, Peoples R China*

<sup>2</sup>*Department of Clinical Nutrition, Cheng Du Shang Jin Nan Fu Hospital West China Hospital, Sichuan University, Sichuan Province, Chengdu 610041, Peoples R China*

<sup>3</sup>*Division of Nephrology, Kidney Research Institute, West China Hospital, Sichuan University, Sichuan Province, Chengdu 610041, Peoples R China*

**Corresponding author:** Yuan Liu, liu63415@163.com, +86 18980606459

**Background:** Chronic Kidney Disease (CKD) is one of the five most common causes of reduced human life expectancy. Its prevalence and incidence are increasing each year. Scientific and practical nutritional support is the most basic treatment for CKD. It is an important measure to delay the course of the disease, prolong entry into end-stage renal disease, and reduce the medical burden.

**Methods:** We performed a system search of the global literature on the use of nutritional and functional foods for CKD using the evidence-based method. After screening the extraction indicator, a systematic review was performed to obtain the optimized indicator pool.

**Results:** One hundred and thirty-three outcome indicators were extracted from published studies. All indicators were divided into four indicator domains. These included 79 indicators of clinical efficacy, 13 indicators of safety, 14 indicators of nutritional adequacy, and 27 indicators that could not be assigned to the above three indicator domains.

**Conclusion:** At present, there are different kinds of nutritional and functional foods used for the prevention and treatment of CKD. Since their clinical use is not standardized, their efficacy has not yet been scientifically evaluated, and it is impossible to ensure whether the patients benefit. It is necessary to build further indicators that are uniform, operable, and highly recognized by representatives of multiple interests to help improve product quality and industry development.

**Keywords:** Chronic Kidney Disease ; Nutritional and Functional Foods ; Indicator pool ; Systematic Review ; Evidence Based Medicine ;



## **Effect of mobile WeChat group management on stress adaptation and insulin resistance in GDM women during novel coronavirus pneumonia**

Yan Feng<sup>1</sup>, Qi Feng<sup>2</sup>, Xinna Song<sup>1</sup>, Xiaoyan Li<sup>3</sup>, Yinghong Zhang<sup>3</sup>, Jianwei Hu<sup>4</sup>

*Department of Clinical Nutrition, Yuhuangding Hospital affiliated to Qingdao University, 20# East Yuhuangding Road, Yantai 264000, China.*

**Corresponding Author:** Yan Feng; [fenghanxiao1985@163.com](mailto:fenghanxiao1985@163.com); +86-0535-6691999/+86-15254589366

**Aim:** To evaluate the improvement of glycemic control and stress adaptation in GDM patients by mobile phone WeChat management during novel coronavirus pneumonia.

**Methods:** 75 GDM women were included in this study, 35 women were included in mobile WeChat group management as GDM-M group, and 40 women as GDM group.

**Results:** After mobile WeChat group management, E and NE were lower ( $P<0.05$ ); MDA was lower and SOD was higher ( $P<0.01$ ); HOMA-IR was lower ( $P<0.01$ ). GDM patients who have complete mobile WeChat group management can improve stress adaptation disorder and insulin resistance during novel coronavirus pneumonia.

**Conclusion:** Mobile WeChat management played a positive role in improving insulin resistance of GDM women under special circumstances, especially during the epidemic, which may reduce the risk of complications in maternal and fetal.

**Key words:** Novel coronavirus pneumonia, GDM, Stress adaptation, Insulin resistance, Mobile phone management



## **Anthocyanin Improves Mouse Glucose Intolerance and Insulin Resistance Induced by a High Fat/High Sugar Diet via Regulation of Intestinal Microbiota**

Wenhua Ling

Department of Nutrition, School of Public Health, SunYat-sen University, Guangzhou, China, 510080

**Corresponding Author:** Wenhua Ling; [Lingwh@mail.sysu.edu.cn](mailto:Lingwh@mail.sysu.edu.cn), 86-13802980289

**Background:** Anthocyanin (ACN) is known to improve glucose metabolism with low bioavailability, but the mechanism of action is unclear. This study aimed to investigate whether the anthocyanin induced beneficial effects were mediated through the regulation of gut microbiota.

**Methods:** Male C57BL/6N mice were randomly assigned into 3 groups and fed chow, high fat/high sugar (HFHS) diet, or HFHS diet + 0.4% anthocyanin for 8 weeks. Furthermore, fecal microbial transplantation (FMT) was also explored to assess the effect of anthocyanin on impaired glucose metabolism in HFHS-fed mice. The composition of gut microbiota, systemic inflammation, glucose tolerance, insulin resistance, and intestinal barrier function were determined.

**Results:** The areas under the curve (AUCs) of the oral glucose tolerance test (GTT) and insulin tolerance test (ITT) were 61% and 79% higher in HFHS-fed mice than those in chow-fed mice ( $P < 0.05$ ). Treatment of HFHS-fed mice with ACN improved OGTT ( $P < 0.05$ ) and restored ITT ( $P < 0.05$ ). ACN supplementation also attenuated plasma lipopolysaccharides (LPS) by 65% and FITC by 45% as compared to only HFHS diet ( $P < 0.05$ ). These effects were linked to suppressed LPS and inducible NO-synthase (iNOS) protein production, and upregulation of zonula occludens-1 (ZO-1) and occludin expression in intestine. Moreover, ACN treatment greatly altered gut microbiota composition by increasing the abundance of Bacteroides and reducing Turicibacteraceae. ACN receivers with FMT gained significant improvement in intestinal microbial composition, intestinal barrier function, systemic inflammation, glucose tolerance, and insulin resistance as compared to HFHS or heat-killed (HK)-ACN receivers.

**Conclusions:** The present study demonstrated that anthocyanin improved HFHS-induced glucose intolerance and insulin resistance by regulating the gut microbiota and epithelial barrier.

**Keywords:** Anthocyanin; Intestinal microbiota; Epithelial barrier function





## **A Genetic Approach to Study the Relationship between Maternal Vitamin D Status, Insulin-like Growth Factor 1, and Newborn Anthropometry Measurements: The Vitamin D Pregnant Mother (VDPM) cohort study**

Arif Sabta Aji<sup>1,2\*</sup>, Yusrawati Yusrawati<sup>3</sup>, Safarina G Malik<sup>4</sup>, Julie Anne Lovegrove<sup>5</sup>, Nur Indrawaty Lipoeto<sup>6</sup>, Vimalleswaran Karani Santhanakrishnan<sup>5</sup>

<sup>1</sup> Department of Nutrition, Faculty of Health Sciences, Alma Ata University, Yogyakarta 55183, Indonesia.

<sup>2</sup> Department of Public Health, Alma Ata Graduate School of Public Health, Alma Ata University, Yogyakarta 55183, Indonesia

<sup>3</sup> Department of Obstetrics and Gynaecology, Faculty of Medicine, Andalas University, Padang 25127, Indonesia.

<sup>4</sup> Eijkman Institute for Molecular Biology, Jakarta 10430, Indonesia.

<sup>5</sup> Hugh Sinclair Unit of Human Nutrition, Department of Food and Nutritional Sciences, University of Reading, Reading, UK.

<sup>6</sup> Department of Nutrition, Faculty of Medicine, Andalas University, Padang 25127, Indonesia.

**Corresponding author:** Arif Sabta Aji; Department of Nutrition, Faculty of Health Sciences, Alma Ata University, Yogyakarta 55183, Indonesia; Tel/Fax: +62 857 309 76512. Email: [sabtaaji@almaata.ac.id](mailto:sabtaaji@almaata.ac.id)

**Background:** Vitamin D increases the circulation of IGF-1 concentration by stimulating the expression and activity of the 1 $\alpha$ -hydroxylase enzyme that produces 1,25(OH)<sub>2</sub>D in the kidney, the active of vitamin D form. We investigated the relationship between maternal vitamin D and IGF-1 using a genetic approach and tested the interaction between vitamin D-related genetic variants with 25-hydroxyvitamin D (25(OH)D) and IGF-1 on newborn anthropometry measurements.

**Methods:** A prospective VDPM cohort study was carried out of 366 subjects (183 mothers and 183 infants) in West Sumatra, Indonesia. Vitamin D and IGF-1 were taken during the first and third trimester, respectively and analysed using ELISA. We created a Genetic Risk Scores (GRSs) analysis based on six genes that involved in the synthesis and metabolism of vitamin D. The linear regression model was used to assess the association in this study.

**Results:** The mean of IGF-1 concentration in the third trimester were 26.19 (2.60) ng/mL. There was a significant correlation between 25(OH)D in the first trimester and IGF-1 concentration ( $P = 0.018$ ,  $R = 0.175$ ). The first trimester of maternal vitamin D status was associated with IGF-1 concentration ( $P = 0.021$ ), but not with the third trimester ( $P > 0.05$ ). There was no association between GRSs, IGF-1, and newborn anthropometry status ( $P > 0.05$  for all comparisons). No interaction between GRSs with 25(OH)D and IGF-1 concentration on newborn anthropometry measurements ( $P > 0.05$ ).

**Conclusion:** There was no relationship between vitamin D status and IGF-1 on newborn anthropometry measurements using a genetic approach among pregnant Minangkabau mothers. However, we found a significant association between 25(OH)D and IGF-1 during pregnancy. Improving foetal growth and development through the effect of IGF-1 by considering maternal vitamin D status need to be considered, yet further large studies needed to confirm our findings.

**Keywords:** IGF-1, Vitamin D, Pregnancy, Newborn Anthropometry, West Sumatra



## The Gut Microbiome of the Punans in North Kalimantan

Clarissa A. Febinia<sup>1</sup>, Patricio Kresnatama<sup>2</sup>, Lidwina Priliani<sup>1</sup>, Safarina G. Malik<sup>1</sup>

<sup>1</sup>*Eijkman Institute for Molecular Biology. Jalan Diponegoro 69, Jakarta 10430, Indonesia*

<sup>2</sup>*Atma Jaya Catholic University of Indonesia. Jl. Raya Cisauk Lapan, Sampora, Kec. Cisauk, Tangerang, Banten 15345, Indonesia*

**Corresponding author:** Clarissa A. Febinia. Email: [asha@eijkman.go.id](mailto:asha@eijkman.go.id). Phone: +62-812-8485-5660

The Punan ethnic groups in North Kalimantan are historically hunter gatherers. Currently, their communities are undergoing changes that affect their livelihood and health. In this study, we examined the gut microbiome of 2 Punan populations. P. Aput (n=20) lived in a more remote area and is more dependent on forest produce compared to P. Tubu (n=22). We aimed to identify differences in gut microbiome diversity, taxonomic composition, and functional capabilities between the two Punan groups. We visited Long Sule (P. Aput) and Respen Tubu (P. Tubu) in 2018 and collected fecal samples. Following DNA extraction, we analyzed microbiome composition from all samples (n=42) by sequencing the 16S rRNA gene (V3-V4 region). We also performed Whole Shotgun Sequencing on a subset of samples (n=13) for functional gene analysis. Our preliminary results showed that P. Aput and P. Tubu samples were not significantly different in alpha diversity (Faith, ACE, Shannon). However, both Punan groups had lower alpha diversity compared to others such as Balinese, Americans, Malawian, Guahibo Amerindians. There were subtle but notable differences in taxonomic composition between Punan groups (16 of 178 Genus-level OTUs,  $p < 0.05$ ). Punan microbiome are enriched with *Prevotella*. Notably, we found 4 distinct *Prevotella* OTUs but only one of them is significantly different between P. Aput and P. Tubu. *Bacteroides* is enriched in P. Tubu population, but the difference is not significant. In our functional analysis (using HUMAnN), P. Aput and P. Tubu had similar gene count. However, there was a higher abundance of genes involved in L-isoleucine biosynthesis and reductive TCA cycle in P. Tubu samples. In conclusion, the gut microbiome of P. Aput and P. Tubu are similar in taxonomic composition, but there is an indication of greater functional capabilities in P. Tubu samples. Further analysis is required to confirm these findings.

**Keywords:** microbiome, Punans, lifestyle changes.

**IGF2 and DNMTs gene methylation and elongase6 related fatty acids in metabolic syndrome**

Xiang Li<sup>1,2</sup>, Chen Lyu<sup>3</sup>, Zhong-Cheng Luo<sup>4</sup>, Jing Zhao<sup>1</sup>, Zhongli Wang<sup>5,6</sup>, Chun Yang<sup>7</sup>, Qi Dai<sup>1</sup>, Hui Li<sup>8</sup>, Yunhua Zhou<sup>1</sup>, Zi Li<sup>1</sup>, Fuxue Chen<sup>2</sup>, and Ying Gao<sup>1\*</sup>

1. CAS Key Laboratory of Nutrition, Metabolism and Food Safety, Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences, Shanghai 200031, China

2. School of life sciences, Shanghai University, Nanchen Road 333, Shanghai 200444, China

3. Department of Epidemiology and Biostatistics, School of Public Health-Bloomington, Indiana University, Bloomington 46201, USA

4. Lunenfeld-Tanenbaum Research Institute, Obstetrics and Gynecology, Mount Sinai Hospital, University of Toronto, Toronto M5G1X5, Canada

5. Department of Rehabilitation, Jiaxing Second Hospital, Jiaxing 314000, China

6. Department of Rehabilitation, The First Affiliated Hospital, China Medical University, No.155, North Nanjing Street, Heping District, Shenyang 110000, China

7. School of Public Health, Capital Medical University, Beijing 100069, China

8. Department Of Nutrition and Food Hygiene, School of Public Health, Peking University, Beijing 100871, China

\*Corresponding author:

Ying Gao, CAS Key Laboratory of Nutrition, Metabolism and Food Safety, Shanghai Institute of Nutrition and Health, Chinese Academy of science, 320 Yueyang Rd, Shanghai, 200031, People's Republic of China; Phone, +862154920985, Email: [yinggao@sibs.ac.cn](mailto:yinggao@sibs.ac.cn).

**Abstract**

**Background:** The prevalence of metabolic syndrome is increasing along with rapid socioeconomic development in China in recent decades, aggravating the burden of health care system. Fat metabolic dysfunction has been reported in metabolic syndrome, and the etiology of metabolic syndrome remains unclear. *IGF2*, an imprinting gene, has been reported in association with obesity, diabetes, and metabolic syndrome. DNA methyltransferases (DNMTs) are important in controlling gene methylation.

**Objective:** We aimed to explore the associations of methylation levels in *IGF2*, *H19*, *DNMT1*, *DNMT3a*, and *DNMT3b* genes with metabolic syndrome, and the role of ELOVL fatty acid elongase 6 (ELOVL6) related fatty acids.

**Method:** Fatty acids were measured using Gas Chromatography-Flame Ionization Detector (GC-FID) after organic extraction and gene methylation was quantified by Q-PCR after bisulfite treatment. C18/C16 ratio was used as the indicator of ELOVL6 activity. Odds Ratio (OR) and 95% Confidence Interval (CI) were estimated with logistic regression.

**Results:** We confirmed that ELOVL6 related fatty acids were associated with the metabolic syndrome. In individuals with low C18/C16 ratios ( $\leq$ median), high methylation levels ( $>$ median) in *IGF2a2* (OR=3.1, 95% CI 1.3-7.5) and *DNMT3a* (OR=2.5, 95% CI 1.1-5.8) genes were associated with increased risk of metabolic syndrome, while there were no significant associations in subjects with high C18/C16 ratios ( $>$ median).

**Conclusion:** Methylation levels in *IGF2* and *DNMT3a* genes may affect the risk of metabolic syndrome in an ELOVL6 activity dependent way among Chinese adults. Further studies in other populations are needed to validate this finding.

**Key words:** metabolic syndrome, *IGF2*, methylation, ELOVL6, fatty acids