April 2022

Food Safety

Risk Assessment

Latent Variables Capture Pathway-Level Points of Departure in High-Throughput Toxicogenomic Data

Danilo Basili, Joe Reynolds, Jade Houghton, Sophie Malcomber, Bryant Chambers, Mark Liddell, Iris Muller, et. al. *Chem Res Toxicol.* 2022 Apr 18;35(4):670-683. doi:10.1021/acs.chemrestox.1c0044. **Article link**

Significance: Study finds that using a new extraction tool captures concentration-response scenarios when investigating biochemical pathway activity. The PLIER tool is not fully constrained by the knowledge base and eases biological interpretation.

Estimation of points of departure (PoDs) from high-throughput transcriptomic data (HTTr) represents a key step in the development of next-generation risk assessment (NGRA). Current approaches mainly rely on single key gene targets, which are constrained by the information currently available in the knowledge base and make interpretation challenging as scientists need to interpret PoDs for thousands of genes or hundreds of pathways. In this work, we aimed to address these issues by developing a computational workflow to investigate the pathway concentration-response relationships in a way that is not fully constrained by known biology and also facilitates interpretation. We employed the Pathway-Level Information ExtractoR (PLIER) to identify latent variables (LVs) describing biological activity and then investigated in vitro LVs' concentration-response relationships using the ToxCast pipeline. We applied this methodology to a published transcriptomic concentration-response data set for 44 chemicals in MCF-7 cells and showed that our workflow can capture known biological activity and discriminate between estrogenic and antiestrogenic compounds as well as activity not aligning with the existing knowledge base, which may be relevant in a risk assessment scenario. Moreover, we were able to identify the known estrogen activity in compounds that are not well-established ER agonists/antagonists supporting the use of the workflow in read-across. Next, we transferred its application to chemical compounds tested in HepG2, HepaRG, and MCF-7 cells and showed that PoD estimates are in strong agreement with those estimated using a recently developed Bayesian approach (cor = 0.89) and in weak agreement with those estimated using a well-established approach such as BMDExpress2 (cor = 0.57). These results demonstrate the effectiveness of using PLIER in a concentration-response scenario to investigate pathway activity in a way that is not fully constrained by the knowledge base and to ease the biological interpretation and support the development of an NGRA framework with the ability to improve current risk assessment strategies for chemicals using new approach methodologies.

Foodborne Pathogens

Controlling *Listeria monocytogenes* Growth and Biofilm Formation Using Flavonoids

Christopher T Gemmell, Valeria R Parreira, Jeffrey M Farber. *J Food Prot*. 2022 Apr 1;85(4):639-646. doi:10.4315/JFP-21-135. **Article link**

Significance: This study identifies five flavonoid compounds as possessing promising antibiofilm and antimicrobial agents against the foodborne pathogen *L. monocytogenes*.

The aim of this study was to investigate the ability of natural plant-derivate products (flavonoid compounds) to inhibit the growth and biofilm-forming ability of *Listeria monocytogenes*. A collection of 500 synthetic and natural flavonoids were tested individually on strains of L. monocytogenes for their antimicrobial and antibiofilm activity. The flavonoids were tested against a *L. monocytogenes* cocktail of five strains at a concentration of 100 μM to determine their effect on

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planktonic growth. The optical density was measured every hour for 24 h at 37°C, and every hour for 48 h at 22°C. A total of 17 flavonoids were chosen for further study because of their ability to significantly reduce the growth of *L. monocytogenes* up to 97%. An additional two flavonoids that increased planktonic growth were chosen as well to investigate whether they had the same effect on biofilm growth. A lower concentration of flavonoid compounds (50 µM) was selected to investigate the individual effects on *L. monocytogenes* biofilm formation using (i) stainless steel coupons to quantify biomass using crystal violet staining and (ii) glass slides using confocal laser scanning microscopic (CLSM) imaging to observe the biofilm architecture. The 19 flavonoids showed various levels of *L. monocytogenes* biofilm growth inhibition, ranging from 2 to 100% after 48 h of incubation at 22 or 10°C. This includes 18 of the 19 flavonoids significantly ($P \leq 0.05$) inhibiting *L. monocytogenes* biofilm formation on stainless steel coupons under at least one of the testing conditions. However, only one flavonoid compound demonstrated significant biofilm inhibition ($P \leq 0.05$) under all conditions tested. Furthermore, 8 of the selected 19 flavonoid compounds showed visible reductions through CLSM in *L. monocytogenes* biofilm formation. Overall, we identified five flavonoid compounds to be promising antibiofilm and antimicrobial agents against *L. monocytogenes*.

Survival Kinetics, Membrane Integrity and Metabolic Activity of *Salmonella Enterica* in Conventionally and Osmotically Dehydrated Coconut Flakes

Ruthchelly Tavares da Silva, Donald W Schaffner, Geany Targino de Souza Pedrosa, Thatyane Mariano Rodrigues de Albuquerque, Janeeyre Ferreira Maciel, Evandro Leite de Souza, Verônica Ortiz Alvarenga, et. al. *Int J Food Microbiol.* 2022 Epub Apr 2;370:109669. doi: 10.1016/j.ijfoodmicro.2022.109669. **Article link**

Significance: *S. enterica* cocktail was studied on conventionally and osmotically dehydrated coconut flakes under four storage regimes. The research finds that the pathogens decline in part due to membrane integrity loss.

Many outbreaks involving *Salmonella enterica* in dehydrated coconut have been reported. Little is known about the survival of *S. enterica* in dehydrated coconut flakes at common retail or domestic storage conditions. This study evaluated the behavior of a *S. enterica* cocktail (*S. Enteritidis* PT4, *S. Typhimurium* PT4, *S.* Bredeney, *S.* Muenster and *S.* Agona) in conventionally and osmotically dehydrated coconut flakes under four storage regimes: 25 °C for 120 days, 25 °C for 30 days then 7 °C for 90 days, 7 °C for 30 days then 25 °C for 90 days, and 7 °C for 120 days. *S. enterica* membrane integrity (using with propidium iodide and bis-1,3-dibutylbarbutyric acid) and metabolic activity (using 5-cyano-2,3-ditolyl tetrazolium chloride) were assessed by flow cytometry analysis after dehydration and storage at 7 °C or 25 °C for 120 days. Lower *S. enterica* inactivation rates (kmax 0.02 to 0.04 1/days) were observed in conventionally dehydrated coconut flakes compared to osmotically dehydrated coconut flakes (kmax 0.16 to 0.20 1/days). Changes in storage temperature did not affect the behavior of *S. enterica* in conventionally or osmotically dehydrated coconut flakes. Results show that *S. enterica* inactiva-tion in conventionally dehydrated coconut flakes could be described by log-linear with tail models. *S. enterica* inactivation in osmotically dehydrated coconut flakes could be described by log-linear with shoulder and tail models. Subpopulations of *S. enterica* cells with damaged membranes and without metabolic activity were larger in conventionally (32.1% and 90.9%, respectively) than osmotically dehydrated coconut (18.5% and 82.2%, respectively) flakes at the beginning of the storage. Subpopulations of *S. enterica* cells with damaged membrane decreased by 9.4-14.4%, while cells with membrane potential and intact membrane increased by 23.7 and 24.2% in conventionally dehydrated coconut flakes after 120 days of storage at 7 °C or 25 °C, respectively. Subpopulations of *S. enterica* with damaged membranes did not change significantly in osmotically dehydrated coconut flakes. Our findings suggest that *S. enterica* populations decline during storage occurs due in part to membrane integrity losses. These data can contribute to the development of risk management strategies for *S. enterica* in dehydrated coconut flakes.

Foodborne Illness

Comparative Genomic Analysis of *Salmonella enterica* Serovar Typhimurium Isolates from Passerines Reveals Two Lineages Circulating in Europe, New Zealand, and the United States

Yezhi Fu, Nkuchia M M'ikanatha, Edward G Dudley. *Appl Environ Microbiol.* 2022 Apr 18;e0020522. doi:10.1128/aem.00205-22. **Article link**

Significance: This comparative genomic analysis explores the emergence, genetic relationship, and evolution of geographically dispersed passerine isolates that spread specific pathogens.

Salmonella enterica serovar Typhimurium strains from passerines have caused wild bird deaths and human salmonellosis outbreaks in Europe, Oceania, and North America. Here, we performed comparative genomic analysis to explore the emergence, genetic relationship, and evolution of geographically dispersed passerine isolates. We found that passerine isolates from Europe and the United States clustered to form two lineages (EU and US passerine lineages), which were distinct from major *S.* Typhimurium lineages circulating in other diverse hosts (e.g., humans, cattle, pigs,

chickens, and other avian hosts, such as pigeons and ducks). Further, passerine isolates from New Zealand clustered to form a sublineage (NZ passerine lineage) of the US passerine lineage. We inferred that the passerine isolates mutated at a rate of 3.2 × 10-7 substitutions/site/year, and the US, EU, and NZ passerine lineages emerged in approximately 1952, 1970, and 1996, respectively. Isolates from the three lineages presented genetic similarity, such as lack of antimicrobial resistance genes and accumulation of the same virulence pseudogenes. In addition, genetic diversity due to microevolution existed in the three passerine lineages. Specifically, pseudogenization in the type 1 fimbrial gene *fimC* (deletion of G at position 87) was detected only in the US and NZ passerine isolates, while single-base deletions in type 3 secretion system effector genes (i.e., *gogB*, *sseJ*, and *sseK2*) cooccurred solely in the EU passerine isolates. These findings provide insights into the evolution, host adaptation, and epidemiology of *S.* Typhimurium in passerines. IMPORTANCE: Passerine-associated *S.* Typhimurium strains have been linked to human salmonellosis outbreaks in recent years. Here, we investigated the phylogenetic relationship of globally distributed passerine isolates and profiled their genomic similarity and diversity. Our study reveals two passerine-associated *S.* Typhimurium lineages circulating in Europe, Oceania, and North America. Isolates from the two lineages presented phylogenetic and genetic signatures that were distinct from those of isolates from other hosts. The findings shed light on the host adaptation of *S.* Typhimurium in passerines and are important for source attribution of *S.* Typhimurium strains to avian hosts. Further, we found that *S.* Typhimurium definitive phage type 160 (DT160) from passerines, which caused decades-long human salmonellosis outbreaks in New Zealand and Australia, formed a sublineage of the US passerine lineage, suggesting that DT160 might have originated from passerines outside Oceania. Our study demonstrates the importance of whole-genome sequencing and genomic analysis of historical microbial collections to modern epidemiologic surveillance.

Mycotoxins

An Update on Immunotoxicity and Mechanisms of Action of Six Environmental Mycotoxins

Yuhang Sun, Kehe Huang, Miao Long, Shuhua Yang, Ying Zhang. *Food Chem Toxicol.* 2022 May;163:112895. doi:10.1016/j.fct.2022.112895. **Article link**

Significance: This review challenges the view that 'immunotoxicity is equivalent to immunosuppression.' Instead, it outlines a mechanistic pathway and how it contributes to immunosuppression or immunostimulation to provide a resource for future research in the area.

Paradoxically, aflatoxin B1 (AFB1), ochratoxin A (OTA), deoxynivalenol (DON), T-2 toxin (T-2), fumonisin B1 (FB1), and zearalenone (ZEA) have both immunosuppressive and immunostimulatory effects. The immunotoxicity of six mycotoxins exhibits immune suppression or stimulation, which depends on multiple factors. Low doses of mycotoxins can induce an inflammatory response, but elevated levels of ones can induce immunosuppression; long-term instead of short-term mycotoxin exposure is immunosuppressive. These six mycotoxins play anti-inflammatory roles when the immunologic stimulants are present but pro-inflammatory roles when the immunologic stimulants are absent. Pigs are most sensitive animals to mycotoxins, followed by humans and poultry, rodent, and marine organism, and ruminants are the least susceptible. Female animals are more susceptible to mycotoxins than male ones. The immunosuppresion mechanism of mycotoxins are mainly in, oxidative stress, apoptosis and autophagy of immune cells, as well as inhibits the immunity-related signal pathways; and AFB1, OTA, DON, and T-2 induce immunostimulation via directly activating the TLRs/NF-κB pathway and other crossing pathways including cyclooxygenase-2 (COX-2) and mitogen-activated protein kinase (MAPK). This review strongly dispels the viewpoint that "immunotoxicity is equivalent to immunosuppression", clearly demonstrates the mechanistic pathway and how it contributes to immunosuppression or immunostimulation, thereby providing reliable references for future studies.

Heavy Metals

Arsenic and Cadmium Induced Macronutrient Deficiencies Trigger Contrasting Gene Expression Changes in Rice

Rishiraj Raghuvanshi, Vaibhavi V Raut, Manish Pandey, Subbiah Jeyakumar, Satish Verulkar, Penna Suprasanna, Ashish Kumar Srivastava. *Environ Pollut.* 2022 May 1;300:118923. doi:10.1016/j.envpol.2022.118923. **Article link**

Significance: This study pinpoints the relative significance of various macronutrients in regulating As- and Cd-tolerance and will help in the design of reduction strategies for metals in foods.

Arsenic (As) and cadmium (Cd), two major carcinogenic heavy metals, enters into human food chain by the consumption of rice or rice-based food products. Both As and Cd disturb plant-nutrient homeostasis and hence, reduces plant growth and crop productivity. In the present study, As/Cd modulated responses were studied in non-basmati (IR-64) and basmati (PB-1) rice varieties, at physiological, biochemical and transcriptional levels. At the seedling stage, PB-1 was found more sensitive than IR-64, in terms of root biomass; however, their shoot phenotype was comparable under As and Cd stress conditions. The ionomic data revealed significant nutrient deficiencies in As/Cd treated-roots. The principal component analysis identified NH4+ as As-associated key macronutrient; while, NH4+/NO3- and K+ was majorly associated with Cd mediated response, in both IR-64 and PB-1. Using a panel of 21 transporter gene expression, the extent of nutritional deficiency was ranked in the order of PB-1(As)<IR-64(As)<PB-1(Cd)<IR-64(Cd). A feed-forward model is proposed to explain nutrient deficiency induced de-regulation of gene expression, as observed under Cd-treated IR-64 plants, which was also validated at the level of sulphur metabolism related enzymes. Using urea supplementation, as nitrogen-fertilizer, significant mitigation was observed under As stress, as indicated by 1.018- and 0.794-fold increase in shoot biomass in IR-64 and PB-1, respectively compared to that of control. However, no significant amelioration was observed in response to supplementation of urea under Cd or potassium under As/Cd stress conditions. Thus, the study pinpointed the relative significance of various macronutrients in regulating As- and Cd-tolerance and will help in designing suitable strategies for mitigating As and/or Cd stress conditions.

Food Packaging

Assessing Chemical Migration from Plastic Food Packaging into Food Simulant by Gas and Liquid Chromatography with High-Resolution Mass Spectrometry

Raegyn B Taylor, Yelena Sapozhnikova. *J Agric Food Chem.* 2022 Apr 27;70(16):4805-4816. doi: 10.1021/acs.jafc.2c00736. **Article link**

Significance: Plastic migration was investigated across 24 unique plastic food packaging products including plastic wrap, storage bags, vacuum bags, and meat trays. Results found 11 putative migrants with potential concerns associated with them.

Some components of plastic food packaging can migrate into food, and whereas migration studies of known components are required and relatively straightforward, identification of nonintentionally added substances (NIAS; unknowns) is challenging yet imperative to better characterizing food safety. To this aim, migration was investigated across 24 unique plastic food packaging products including plastic wrap, storage bags, vacuum bags, and meat trays. Gas and liquid chromatography separation systems coupled with Orbitrap mass analyzers were used for comprehensive nontargeted screening of migrants. Tentative identifications of features were assigned by searching commercial databases (e.g., NIST, MZCloud, ChemSpider, Extractables and Leachables) and filtering results based on mass accuracy, retention time indices, and mass spectral patterns. Several migrants showed elevated levels in specific food packaging types, particularly meat trays and plastic wrap, and varying degrees of migration over the 10 days. Eleven putative migrants are listed as substances of potential concern or priority hazardous substances. Additionally, migration amounts of an Irgafos 168 degradation product determined by semiquantitation exceeded proposed theoretical maximum migration values.

Chemical Contaminants

Extraction and Matrix Cleanup Method for Analyzing Novel Per- and Polyfluoroalkyl Ether Acids and Other Per- and Polyfluoroalkyl Substances in Fruits and Vegetables

Pingping Meng, Noelle J DeStefano, Detlef R U Knappe. *J Agric Food Chem.* 2022 Apr 27;70(16):4792-4804. doi:10.1021/acs.jafc.1c07665. **Article link**

Significance: A new extraction and matrix cleanup method is capable of sensitively quantifying 45 PFAS compounds in fruits and vegetables.

Per- and polyfluoroalkyl ether acids (PFEAs) are a subclass of per- and polyfluoroalkyl substances (PFAS) that are detected with increasing frequency in environmental matrices. Diet can be an important route of PFEA exposure, but the presence of PFEAs in food is poorly understood. Extraction methods for food samples exist for traditionally studied PFAS, but their suitability for PFEAs and other novel PFAS remains unknown. In this study, an extraction and matrix cleanup method was developed to quantify 45 PFAS, including 13 PFEAs, 3 perfluoroalkane sulfonamides, and 6 fluorotelomer carboxylic acids in 10 types of fruits and vegetables. Homogenized samples were extracted with basic methanol, and resulting extracts were diluted with water and cleaned up using solid-phase extraction with weak anion-exchange cartridges. The method was validated by performing spike-recovery experiments at spike levels of 1 ng/g in all 10 matrices and 0.1 ng/g in 2 matrices. For PFAS without a corresponding isotopically labeled internal standard (IS), adopting an IS with a similar chromatographic retention time generated the most accurate recoveries. Dependent

upon the matrix, recoveries of 38-44 PFAS (including 10-13 PFEAs) fell within 50-150% for samples spiked at 1 ng/g. Recoveries of 40 and 38 PFAS in blueberries and corn, respectively, fell within 50-150% for samples spiked at 0.1 ng/g. Method quantification limits (MQLs) of PFAS in pure solvents were determined as the lowest calibration level with an accuracy between 70 and 130%. To compensate for matrix effects, a matrix factor was applied on the basis of the analyte response in different matrices relative to the pure solvent. The MQLs of 45 PFAS (including 13 PFEAs) in 10 matrices ranged from 0.025 to 0.25 ng/g. Overall, this method is capable of sensitively quantifying 45 PFAS in many fruits and vegetables.

Caffeine

Preconception Caffeine Metabolites, Caffeinated Beverage Intake and Fecundability

Alexandra C Purdue-Smithe, Keewan Kim, Karen C Schliep, Elizabeth A DeVilbiss, Stefanie N Hinkle, Aijun Ye, Neil J Perkins, et. al. *Am J Clin Nutr*. 2022 Apr 1;115(4):1227-1236. doi:10.1093/ajcn/nqab435. **Article link**

Significance: This study finds that caffeine exposure from usual low to moderate caffeinated beverage intake likely does not influence fecundability.

Background: Caffeine is the most frequently used psychoactive substance in the United States and >90% of reproductive-age women report some amount of intake daily. Despite biological plausibility, previous studies on caffeine and fecundability report conflicting results. Importantly, prior studies measured caffeine exposure exclusively by self-report, which is subject to measurement error and does not account for factors that influence caffeine metabolism. **Objectives:** Our objective was to examine associations between preconception serum caffeine metabolites, caffeinated beverage intake, and fecundability. **Methods:** Participants included 1228 women aged 18-40 y with a history of 1-2 pregnancy losses in the EAGeR (Effects of Aspirin in Gestation and Reproduction) trial. We prospectively evaluated associations of preconception caffeine metabolites (i.e., caffeine, paraxanthine, and theobromine) measured from 1191 serum samples untimed to a specific time of day, self-reported usual caffeinated beverage intakes at baseline, and time-varying cycle-average caffeinated beverage intake, with fecundability. Using Cox proportional hazards models, we estimated fecundability odds ratios (FORs) and 95% CIs according to each metabolite. Follow-up was complete for 89% (n = 1088) of participants. **Results:** At baseline, 85%, 73%, and 91% of women had detectable serum caffeine, paraxanthine, and theobromine, respectively. A total of 797 women became pregnant during ≤6 cycles of preconception follow-up. After adjusting for potential confounders, neither serum caffeine [tertile (T)3 compared with T1 FOR: 0.87; 95% CI: 0.71, 1.08], paraxanthine (T3 compared with T1 FOR: 0.92; 95% CI: 0.75, 1.14), nor theobromine (T3 compared with T1 FOR: 1.15; 95% CI: 0.95, 1.40) were associated with fecundability. Baseline intake of total caffeinated beverages was not associated with fecundability (>3 compared with 0 servings/d adjusted FOR: 0.99; 95% CI: 0.74, 1.34), nor was caffeinated coffee (>2 compared with 0 servings/d adjusted FOR: 0.93; 95% CI: 0.45, 1.92) or caffeinated soda (>2 servings/d adjusted FOR: 0.92; 95% CI: 0.71, 1.20). **Conclusions**: Our findings are reassuring that caffeine exposure from usual low to moderate caffeinated beverage intake likely does not influence fecundability.

Food Allergens

Allergen-Specific T cells and Clinical Features of Food Allergy: Lessons from CoFAR Immunotherapy Cohorts

M Cecilia Berin, Charuta Agashe, A Wesley Burks, David Chiang, Wendy F Davidson, Peter Dawson, Alexander Grishin, et. al. *J Allergy Clin Immunol*. 2022 Apr;149(4):1373-1382.e12. doi: 10.1016/j.jaci.2021.09.029. **Article link**

Significance: Tracking food-specific type 2 T cells at the baseline of a study is informative of both threshold of reactivity and response to immunotherapy.

Background: Allergen-specific IL-4+ and IL-13+ CD4+ cells (type 2 cells) are essential for helping B cells to class-switch to IgE and establishing an allergic milieu in the gastrointestinal tract. The role of T cells in established food allergy is less clear. **Objective:** We examined the food allergen-specific T-cell response in participants of 2 food allergen immunotherapy trials to assess the relationship of the T-cell response to clinical phenotypes, including response to immunotherapy**. Methods**: Blood was obtained from 84 participants with peanut allergy and 142 participants with egg allergy who underwent double-blind placebo-controlled food challenges. Peanut- and egg-responsive T cells were identified by CD154 upregulation after stimulation with the respective extract. Intracellular cytokines and chemokine receptors were also detected. The response to peanut epicutaneous immunotherapy (Peanut Epicutaneous Phase II Immunotherapy Clinical Trial [CoFAR6]; 49 participants receiving epicutaneous immunotherapy) and egg oral immunotherapy or a baked egg diet (Baked Egg or Egg Oral Immunotherapy for Children With Egg Allergy [CoFAR7];

92 participants) was monitored over time. Results: Peanut-specific type 2 and CCR6+ T cells were negatively correlated with each other and differently associated with immune parameters, including specific IgE level and basophil activation test result. At baseline, type 2 cells, but not CCR6+ cells, were predictive of clinical parameters, including a successfully consumed dose of peanut and baked egg tolerance. Exposure to peanut or egg immunotherapy was associated with a decrease in type 2 cell frequency. At baseline, high egg-specific type 2 cell frequency was the immune feature most predictive of oral immunotherapy failure. **Conclusion:** Food-specific type 2 T cells at baseline are informative of threshold of reactivity and response to immunotherapy.

Enrichment of Formula in Probiotics or Prebiotics and Risk of Infection and Allergic Diseases up to Age 5.5 Years in the Nationwide Etude Longitudinale Française depuis l'Enfance (ELFE Cohort)

Moufidath Adjibade, Camille Davisse-Paturet, Amandine Divaret-Chauveau, Karine Adel-Patient, Chantal Raherison, Marie-Noëlle Dufourg, Sandrine Lioret, et. al. *J Nutr*. 2022 Apr 1;152(4):1138-1148. doi: 10.1093/jn/nxac013. **Article link**

Significance: Associations between the consumption of probiotic-enriched formula and risk of respiratory symptoms differ according to the strain and consumption interval. The consumption of prebiotic-enriched formula was not significantly associated with infection or allergy risk.

Background: An increasing number of infant and follow-on formulas are enriched with probiotics and/or prebiotics; however, evidence for health effects of such enrichment in early childhood remains inconclusive. **Objectives**: The present study aimed to assess whether the consumption of formula enriched with probiotics or prebiotics was associated with the risk of infection and allergic diseases in early childhood. **Methods:** Analyses involved data for 8389 formula-fed children from the Etude Longitudinale Française depuis l'Enfance (ELFE) cohort. Enrichment of the formula with probiotics or prebiotics that was consumed from the age of 2-10 mo was identified by the formula ingredient list. Lower respiratory tract infection (LRTI), upper respiratory tract infection (URTI), gastrointestinal infection, wheezing, asthma, food allergy, and itchy rash were prospectively reported by parents up to the age of 5.5 y. Adjusted logistic regression models were used to assess associations between the consumption of enriched formula and risk of infection and allergic diseases. **Results**: Aged 2 mo, more than half of formula-fed infants consumed the probiotic-enriched formula and only 1 in 10 consumed the prebiotic-enriched formula. Consumption of the Bifidobacterium lactis-enriched formula at 2 mo was associated with a lower risk of LRTI [OR (95% CI) = 0.84 (0.73-0.96)]. Consumption of the Bifidobacterium breve-enriched formula up to 6 mo was associated with a higher risk of LRTI [OR (95% CI) = 1.75 (1.29-2.38)] and asthma [OR (95% CI) = 1.95 (1.28-2.97)], whereas its consumption from 6 to 10 mo was associated with a lower risk of LRTI [OR (95% CI) = 0.64 (0.48-0.86)] and asthma [OR (95% CI) = 0.59 (0.40-0.88)]. Moreover, the consumption of Streptococcus thermophilus from 6 to 10 mo was associated with a higher risk of asthma [OR (95% CI) = 1.84 (1.29-2.63)]. No significant association was found for gastrointestinal infection, food allergy, and itchy rash. Overall, the consumption of prebiotic-enriched formula was not significantly associated with infection and allergy risk. **Conclusions**: Associations between the consumption of probiotic-enriched formula and risk of respiratory symptoms differ according to the strain considered and consumption period. Further well-designed studies are needed to confirm these results.

Emerging Science Areas

Emerging area: Food Safety

Category: Novel Foods

Safety of Beta-Lactoglobulin as a Novel Food Pursuant to Regulation (EU 2015/2283. EFSA Panel on Nutrition, Novel Foods and Food Allergens

(NDA), Dominique Turck, Torsten Bohn, Jacqueline Castenmiller, Stefaan De Henauw. *EFSA Journal* 2022;20(4):7204, 08 April 2022. doi.org/10.2903/j.efsa.2022.7204 **Article link**

Significance: A novel protein made from bovine whey by crystallization under acidic or neutral conditions was approved by EFSA for use in isotonic sport drinks, whey protein and milk-based drinks, and for medical purposes. The Panel found intake of the novel ingredient posed no nutritional disadvantages, safety concern from genotoxic testing, or adverse effects from a subchronic toxicity study, at the highest intake dose of 1,000 mg product/kg bw/day. The Panel concluded that the ingredient was safe for the general population under the proposed conditions of use.

Following a request from the European Commission, the EFSA Panel on Nutrition, Novel Foods, and Food Allergens (NDA) was asked to deliver an opinion on beta-lactoglobulin (BLG) as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF (≥ 90% w/w dry matter protein) consists of BLG as primary component (≥ 90% of total protein),

which is equivalent to BLG present in bovine milk and whey protein isolate (WPI). The NF is produced from bovine whey by crystallization under acidic or neutral conditions. The NF is proposed to be used as a food ingredient in isotonic and sport drinks, whey powder and milk-based drinks and similar products, and in food for special medical purposes as defined in Regulation (EU) No 609/2013. The target population is the general population. The highest daily intake of the NF was estimated for children of 3 to < 10 years of age as 667 mg/kg body weight (bw) per day. The NF presents proximate composition and content of essential amino acids similar to those in WPI. The Panel notes that the highest mean and highest 95th percentile daily protein intakes from the NF are below the protein population reference intakes for all population groups. Although a tolerable upper intake level has not been derived for protein, the protein intake from the NF may nevertheless further contribute to an already high dietary protein intake in Europe. The exposure to the reported minerals does not raise concerns. The Panel considers that the consumption of the NF is not nutritionally disadvantageous. No genotoxic concerns were identified from the standard in vitro test battery. No adverse effects were observed in the sub chronic toxicity study, up to the highest dose tested, i.e., 1,000 mg NF/kg bw per day. The Panel concludes that the NF is safe under the proposed conditions of use.

Engage with IAFNS

IAFNS and Arkansas Children's Nutrition Center Team Up for 3-Part Webinar Series May 17, 23 and 26th.

- Join childhood nutrition researchers as they share their latest findings in a series of May webinars. Scholars from Arkansas Children's Nutrition Center (ACNC) — a National Human Research Center established as a partnership between Arkansas Children's Research Institute and USDA-ARS — will be sharing their most recent findings during a planned series of webinars slated for May 17, May 23 and May 26, 2022. The webinar series will focus first on the early life determinants of metabolic health to be followed by a second webinar on the gut and developing brain. The final webinar will address maternal and child dietary patterns and physical activity. For more information, click **here**.

7th World Conference on Research Integrity
Cape Town, South Africa
May 29, 2022 - June 1, 2022

- The World Conferences on Research Integrity (WCRI) foster the exchange of information and discussion about responsible conduct of research. At the 7th WCRI, IAFNS will be presenting its updated Guiding Principles for Funding Food Science and Nutrition Research. Ensuring Integrity in Science: Updated Guiding Principles for Funding Food Science and Nutrition Research. For more information, click here. For more information, click **here**.

GS1 Connect 2022. June 7–9, 2022. San Diego, CA.

- IAFNS is representing the Partnership on the USDA Global Branded Food Products Database at GS1 Connect 2022. This event brings trading partners together to learn about standards-based business processes and best practices for optimum efficiencies in managing the supply and demand sides of their value chain. IAFNS' presentation will focus on sharing data within the USDA Branded Food Product Database. For more information, click **here**.

IAFNS Annual Meeting & Science Symposium: Advancing Science for Impact
June 21-23, 2022, at the National Press Club in Washington DC.

- The IAFNS Annual Meeting & Scientific Symposium is a forum for the presentation and discussion of research and ideas—focusing on science with impact. The focus will be on science that supports credible decision making by government regulators, industry professionals and academic researchers. The conference offers an exceptional learning environment and brings together a range of experts, including food and nutrition researchers, healthcare professionals, opinion leaders, industry representatives, government officials, and future leaders. The Keynote address will be delivered by Dr. Susan Mayne, Director of the Center for Food Safety and Applied Nutrition (CFSAN) at the US Food and Drug Administration. To register, click **here**.