Risk Assessment

Drivers of and Obstacles to the Adoption of Toxicogenomics for Chemical Risk Assessment: Insights from Social Science Perspectives

Pain G, Hickey G, Mondou M, Crump D, Hecker M, Basu N, et al. Environ Health Perspect. 2020 Oct;128(10):105002. doi: 10.1289/EHP6500. Article link

Significance: This report identifies drivers of and obstacles to adoption of toxicogenomics in chemical risk assessment.

Background: Some 20 y ago, scientific and regulatory communities identified the potential of omics sciences (genomics, transcriptomics, proteomics, metabolomics) to improve chemical risk assessment through development of toxicogenomics. Recognizing that regulators adopt new scientific methods cautiously given accountability to diverse stakeholders, the scope and pace of adoption of toxicogenomics tools and data have nonetheless not met the ambitious, early expectations of omics proponents. Objective: Our objective was, therefore, to inventory, investigate, and derive insights into drivers of and obstacles to adoption of toxicogenomics in chemical risk assessment. By invoking established social science frameworks conceptualizing innovation adoption, we also aimed to develop recommendations for proponents of toxicogenomics and other new approach methodologies (NAMs). Methods: We report findings from an analysis of 56 scientific and regulatory publications from 1998 through 2017 that address the adoption of toxicogenomics for chemical risk assessment. From this purposeful sample of toxicogenomics discourse, we identified major categories of drivers of and obstacles to adoption of toxicogenomics tools and data sets. We then mapped these categories onto social science frameworks for conceptualizing innovation adoption to generate actionable insights for proponents of toxicogenomics. Discussion: We identify the most salient drivers and obstacles. From 1998 through 2017, adoption of toxicogenomics was understood to be helped by drivers such as those we labeled Superior scientific understanding, New applications, and Reduced cost & increased efficiency but hindered by obstacles such as those we labeled Insufficient validation, Complexity of interpretation, and Lack of standardization. Leveraging social science frameworks, we find that arguments for adoption that draw on the most salient drivers, which emphasize superior and novel functionality of omics as rationales, overlook potential adopters’ key concerns: simplicity of use and compatibility with existing practices. We also identify two perspectives-innovation-centric and adopter-centric-on omics adoption and explain how overreliance on the former may be undermining efforts to promote toxicogenomics.

Foodborne Pathogens

Detection and Prevalence of Listeria in U.S. Produce Packinghouses and Fresh-Cut Facilities

Sullivan G, Wiedmann M. J Food Prot. 2020 Oct 1;83(10):1656-1666. doi: 10.4315/JFP-20-094. Article link

Significance: Environmental “routine sampling” plans for LM and other Listeria spp. were developed and implemented in three packinghouses and five fresh-cut facilities in the United States to reveal information on the detection, prevalence and distribution of Listeria in produce operations.

Listeria monocytogenes (LM) contamination of produce can often be traced back to the environment of packinghouses and fresh-cut facilities. Because there is limited information on the detection, prevalence, and distribution of this pathogen in produce operations, environmental “routine sampling” plans for LM and other Listeria spp. were developed and implemented in three packinghouses and five fresh-cut facilities in the United States. For routine sampling, a total of 2,014 sponge samples were collected over six to eight separate samplings per operation, performed over 1 year; vector and preproduction samples (n = 156) were also collected as needed to follow up on positive findings. In addition, a single “validation sampling” visit by an outside
expert was used to evaluate the routine sampling. Among the 2,014 routine sponge samples collected, 35 and 30 were positive for LM and Listeria species other than LM (LS), respectively. LM prevalence varied from 0.8 to 5.8% for packinghouses and <0.4 to 1.6% for fresh-cut facilities. Among the 394 validation sponge samples, 23 and 13 were positive for LM and LS, respectively. Validation sampling found statistically significantly higher LM prevalence compared with routine sampling for three of eight operations. For all samples collected, up to eight isolates per sample were characterized by sequencing of sigB, which allowed for classification into sigB allelic types. Among the 97 samples with more than one Listeria isolate characterized, 28 had more than one sigB allelic type present, including 18 sponges that were positive for LM and another Listeria species and 13 sponges that were positive for more than one LM subtype. This indicates that collection of multiple isolates is necessary to capture Listeria diversity present in produce operations. Additionally, 17 of 77 sponges that were positive for LM were positive at only one enrichment time (i.e., 24 or 48 h), indicating that LM testing after two different enrichment times provides enhanced sensitivity.

**Mycotoxins**

*Bacillus subtilis* Inhibits *Aspergillus carbonarius* by Producing Iturin A, Which Disturbs the Transport, Energy Metabolism, and Osmotic Pressure of Fungal Cells as Revealed by Transcriptomics Analysis

Jiang C, Li Z, Shi Y, Guo D, Pang B, Chen X, et al. *Int J Food Microbiol*. 2020 Oct 2;330:108783. doi: 10.1016/j.ijfoodmicro.2020.108783. [Article link](https://doi.org/10.1016/j.ijfoodmicro.2020.108783)

**Significance:** This study provided new information on the mechanisms for lipopeptides and useful directions to develop more efficient antifungal agents used in agriculture and biomedicine.

The contamination of *Aspergillus carbonarius* causes decreases and great decay of agricultural products and threatens the human and animal health by producing mycotoxins, especially ochratoxin A. *Bacillus subtilis* has been proved to efficiently inhibit the growth of *A. carbonarius*. Revealing the major active compound and the mechanisms for the antifungal of *B. subtilis* are essential to enhance its antifungal activity and control the quality of antifungal products made of it. In this study, we determined that iturin A is the major compound that inhibits *Aspergillus carbonarius*, a widespread fungal pathogen of grape and other fruits. Iturin A significantly inhibited growth and ochratoxin A production of *A. carbonarius* with minimal inhibitory concentrations (MICs) of 10 µg/mL and 0.312 µg/mL, respectively. Morphological observations revealed that iturin A caused swelling of the fungal cells and thinning of the cell wall and membrane at 1/2 MIC, whereas it inhibited fungal spore germination and caused mitochondrial swelling at higher concentrations. A differential transcriptomic analysis indicated that the mechanisms used by iturin A to inhibit *A. carbonarius* were to downregulate the expression of genes related to cell membrane, transport, osmotic pressure, oxidation-reduction processes, and energy metabolism. Among the down-regulated genes, those related to the transport capacity were most significantly influenced, including the increase of energy-related transport pathways and decrease of other pathways. Notably, the genes related to taurine and hypotaurine metabolism were also decreased, indicating iturin A potentially cause the occurrence of osmotic imbalance in *A. carbonarius*, which may be the intrinsic cause for the swelling of fungal cells and mitochondria. Overall, iturin A produced by *B. subtilis* played important roles to inhibit *A. carbonarius* via changing the fungal cell structure and causing perturbations to energy, transport and osmotic pressure metabolisms in fungi. The results indicated a new direction for research on the mechanisms for lipopeptides and provided useful information to develop more efficient antifungal agents, which are important to agriculture and biomedicine.

**Food Packaging**

Smart Traceability for Food Safety

Yu Z, Jung D, Park S, Hu Y, Huang K, Rasco BA, et al. Smart traceability for food safety. *Crit Rev Food Sci Nutr*. 2020 Oct 8:1-12. doi: 10.1080/10408398.2020.1830262. [Article link](https://doi.org/10.1080/10408398.2020.1830262)

**Significance:** This review summarizes various detection strategies for food safety, including portable detection devices, smart indicators and sensors on food packages and data-assisted whole-genome sequencing.

A current food production faces a tremendous challenge due to the growing human population. The global population is estimated to reach 9 billion by 2050 with 70% more food being required. Safe food is an important dimension of food security, and food traceability across the supply chain is a key component of this. However, current food traceability systems are challenged by frequent occurrences of food safety incidents and food recalls that have damaged consumer confidence, caused huge economic loss, and put pressure on food safety agencies. This review focuses on smart food traceability that has the potential to significantly improve food safety in global food supply chains. The basic concepts and critical perspectives for various detection strategies for food safety are summarized, including portable detection devices, smart indicators and sensors integrated on food packages, and data-assisted whole-genome sequencing. In addition, new digital technologies, such as Internet-of-things (IoTs) and cloud computing, are discussed with the aim of providing readers with an overview of the exciting opportunities in smart food traceability systems.
Chemical Contaminants

Transfer of Per- and Polyfluoroalkyl Substances (PFAS) from Feed into the Eggs of Laying Hens. Part 1: Analytical Results Including a Modified Total Oxidizable Precursor Assay

Göckener B, Eichhorn M, Lämmer R, Kotthoff M, Kowalczyk J, Numata J, et al. J Agric Food Chem. 2020 Oct 29. doi: 10.1021/acs.jafc.0c04456. Article link

Significance: The results of this study demonstrate the transfer of PFAAs and their precursors into hens’ eggs and emphasize the contribution of precursors to the overall PFAS burden in edible products.

The group of per- and polyfluoroalkyl substances (PFAS) comprises thousands of chemicals, which are used in various industrial applications and consumer products. In this study, a feeding experiment with laying hens and feed grown on a contamination site was conducted, and PFAS were analyzed in the feed and eggs to assess the transfer of PFAS into eggs. A targeted analysis of perfluoroalkyl acids (PFAAs) and different sulfonamides was performed. Additionally, the total oxidizable precursor (TOP) assay was modified by fully oxidizing small amounts of the samples instead of oxidizing their extracts in order to overcome potential losses during extraction. Targeted analysis showed the presence of known PFAAs and four sulfonamides in the feed and egg yolk samples. In the plant-based feed, short-chain PFAAs, methyl and ethyl perfluorooctane sulfonamidoacetic acid (Me- and EtFOSAA), and perfluorooctane sulfonic acid (PFOS) were the most abundant PFAS. In the eggs, PFOS, FOSAA, and its alkylated homologues showed the highest concentrations. The TOP assay revealed the presence of substantial amounts of precursors with different chain lengths from C4 to C8. The highest relative increase of PFOA after oxidation was observed in egg yolk from the end of the exposure period (828%). The results of this study demonstrate the transfer of PFAAs and their precursors into hens’ eggs and emphasize the contribution of (known and unidentified) precursors to the overall PFAS burden in edible products. The modified TOP assay approach was shown to be a powerful tool to better assess the total burden of samples with PFAS.

Heavy Metals

Mercury, Methylmercury and Long-Chain Polyunsaturated Fatty Acids in Selected Fish Species and Comparison of Approaches to Risk-Benefit Analysis

Cressey P, Miles G, Saunders D, Pearson AJ. Food Chem Toxicol. 2020 Oct 1;146:111788. doi: 10.1016/j.fct.2020.111788. Article link

Significance: The benefits of fish consumption appear to outweigh the risks posed by methylmercury consumption in fish caught in New Zealand waters.

Fish (n = 281) of six species, caught in New Zealand waters, were analysed for total mercury (t-Hg), methylmercury (MeHg) and the long-chain polyunsaturated fatty acids, eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA). Mean t-Hg and MeHg concentrations for the six species were in the range 0.06-0.53 mg/kg and 0.06-0.46 mg/kg, respectively. The mean proportion of t-Hg present as MeHg for the six species considered was in the range 83-93%. Positive associations were observed between t-Hg and MeHg content of fish and measures of fish size (length, weight), although the strength of the associations was species dependent. The mean EPA + DHA content of the six fish species varied in the range 2.0-20.5 mg/g. Two approaches were trialled to compare the risks, due to MeHg, and the benefits, due to EPA and DHA, from consumption of the six fish species. Both approaches identify that for these six fish species the benefits of normal patterns of fish consumption on offspring IQ largely outweigh the risks from MeHg.

Caffeine

The Association Between Coffee Consumption and Metabolic Syndrome in Adults: A Systematic Review and Meta-Analysis

Wong THT, Wong CH, Zhang X, Zhou Y, Xu J, Yuen KC, et al. Adv Nutr. 2020 Oct 28:nmaa132. doi: 10.1093/advances/nmaa132. Article link

Significance: Coffee consumption may not be associated with metabolic syndrome, a finding that is different from previous meta-analyses and could be due to participant variation.
Previous meta-analyses that found an inverse association between coffee consumption and metabolic syndrome pooled data from cross-sectional and longitudinal studies, which could lead to potentially misleading conclusions. Hence, this work aimed to reassess this association by analyzing data from the 2 types of studies separately and including recent studies. Online databases including PubMed, Scopus, Embase, The Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus, and Science Direct were searched for relevant studies published up to July 2020. Both cross-sectional and longitudinal studies were included if published after 1999, reported both effect estimates and CIs, and presented results adjusted for confounding variables. Data of the highest coffee consumption level in each study, as well as those of medium consumption levels in studies with ≥3 consumption categories, were pooled using random-effect models, with sex-stratified and sex-adjusted results being analyzed separately. Results were obtained based on data from 13 cross-sectional studies involving 280,803 participants and 2 longitudinal studies involving 17,014 participants. The overall sex-adjusted association of the highest consumption level was not significant (n = 9 studies; OR: 0.88; 95% CI: 0.70, 1.10; I²: 91.5%) and the 2 longitudinal studies both yielded no association. Subgroup analysis revealed inverse associations in both males and females, as well as in Caucasians with medium coffee consumption (n = 4 studies, OR: 0.88; 95% CI: 0.84, 0.93; I²: 0%). Although residual confounding could affect the results of this meta-analysis, our findings suggested with a low certainty that coffee consumption may not be associated with metabolic syndrome, a finding that is different from those of previous meta-analyses and could be due to variation in characteristics of study participants. More longitudinal studies are also needed to further assess the temporal association between coffee consumption and metabolic syndrome.

Habitual Coffee and Tea Consumption and Cardiometabolic Biomarkers in the UK Biobank: The Role of Beverage Types and Genetic Variation
Cornelis MC, van Dam RM. J Nutr. 2020 Oct 12;150(10):2772-2788. doi: 10.1093/jn/nxaa212. Article link

Significance: In a study of data collected from the UK Biobank, consumption of certain coffee brews such as espresso had unfavorable associations with blood lipids, but consumption of tea had favorable associations.

Background: Mechanisms linking habitual consumption of coffee and tea to the development of type 2 diabetes and cardiovascular diseases remain unclear. Objectives: We leveraged dietary, genetic, and biomarker data collected from the UK Biobank to investigate the role of different varieties of coffee and tea in cardiometabolic health. Methods: We included data from ≤447,794 participants aged 37-73 y in 2006-2010 who provided a blood sample and completed questionnaires regarding sociodemographic factors, medical history, diet, and lifestyle. Multivariable linear regression was used to examine the association between coffee or tea consumption and blood concentrations of glycated hemoglobin, fasting glucose, total cholesterol, HDL cholesterol, LDL cholesterol, fasting triglycerides (TGs), apoA-1, apoB, lipoprotein-a, and C-reactive protein (CRP). Lifestyle and genetic factors affecting caffeine metabolism, responses, or intake were tested for interactions with beverage intake in relation to biomarker concentrations. Results: Compared with coffee nonconsumers, each additional cup of coffee was significantly associated with higher total cholesterol, HDL-cholesterol, and LDL-cholesterol concentrations and lower TG and CRP concentrations in both men and women (P-trend < 0.002). Higher consumption of espresso coffee (≥2 compared with 0 cups/d) was associated with higher LDL cholesterol in men (β: 0.110 mmol/L; 95% CI: 0.058, 0.163 mmol/L) and women (β: 0.161 mmol/L; 95% CI: 0.088, 0.234 mmol/L), whereas no substantial association was observed for instant coffee. Compared with tea nonconsumers, higher tea consumption was associated with lower total and LDL cholesterol and apoB and higher HDL cholesterol (P-trend < 0.002); these associations were similar for black and green tea. Associations were not modified by genetics. Conclusions: In the UK Biobank, consumption of certain coffee brews such as espresso had unfavorable associations with blood lipids, whereas consumption of tea had favorable associations. Findings were not modified by genetic variants affecting caffeine metabolism, suggesting a role of noncaffeine constituents of these beverages in cardiometabolic health.
Food Allergens

Long-term, Open-Label Extension Study of the Efficacy and Safety of Epicutaneous Immunotherapy for Peanut Allergy in Children: PEOPLE 3-Year Results

Fleischer DM, Shreffler WG, Campbell DE, Green TD, Anvari S, Assa’ad A, et al. J Allergy Clin Immunol. 2020 Oct; 146(4):863-874. doi: 10.1016/j.jaci.2020.06.028  Article link

Significance: Daily epicutaneous immunotherapy treatment for peanut allergy beyond one year leads to continued response from a well-tolerated regimen.

Background: The PEPITES (Peanut EPIT Efficacy and Safety) trial, a 12-month randomized controlled study of children with peanut allergy and 4 to 11 years old, previously reported the safety and efficacy of epicutaneous immunotherapy (EPIT) for peanut allergy (250 μg, daily epicutaneous peanut protein; DBV712 250 μg). Objective: We sought to assess interim safety and efficacy of an additional 2 years of EPIT from the ongoing (5-year treatment) PEOPLE (PEPITES Open-Label Extension) study. Methods: Subjects who completed PEPITES were offered enrollment in PEOPLE. Following an additional 2 years of daily DBV712 250 μg, subjects who had received DBV712 250 μg in PEPITES underwent month-36 double-blind, placebo-controlled food challenge with an optional month-38 sustained unresponsiveness assessment. Results: Of 213 eligible subjects who had received DBV712 250 μg in PEPITES, 198 (93%) entered PEOPLE, of whom 141 (71%) had assessable double-blind, placebo-controlled food challenge at month 36. At month 36, 51.8% of subjects (73 of 141) reached an eliciting dose of ≥1000 mg, compared with 40.4% (57 of 141) at month 12; 75.9% (107 of 141) demonstrated increased eliciting dose compared with baseline; and 13.5% (19 of 141) tolerated the full double-blind, placebo-controlled food challenge of 5444 mg. Median cumulative reactive dose increased from 144 to 944 mg. Eighteen subjects underwent an optional sustained unresponsiveness assessment; 14 of those (77.8%) maintained an eliciting dose of ≥1000 mg at month 38. Local patch-site skin reactions were common but decreased over time. There was no treatment-related epinephrine use in years 2 or 3. Compliance was high (96.9%), and withdrawals due to treatment-related adverse events were low (1%). Conclusions: These results demonstrate that daily EPIT treatment for peanut allergy beyond 1 year leads to continued response from a well-tolerated, simple-to-use regimen.