March 2021

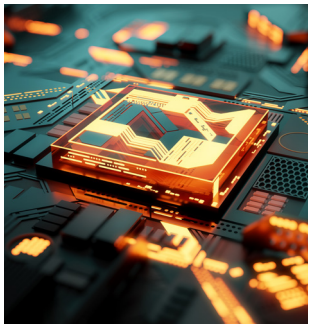
Food Safety Briefs

Machine Learning in Food Safety

Emerging Applications of Machine Learning in Food Safety

Deng X, Cao S, Horn AL. *Annu Rev Food Sci Technol.* 2021 Mar 25;12:513-538. doi: 10.1146/annurev-food-071720-024112. **Article link**

Significance: Machine learning can leverage large data sets in food safety efforts and help the prediction of antibiotic resistance, source attribution of pathogens and foodborne outbreak detection and risk assessment.



Food safety continues to threaten public health. Machine learning holds potential in leveraging large, emerging data sets to improve the safety of the food supply and mitigate the impact of food safety incidents. Foodborne pathogen genomes and novel data streams, including text, transactional, and trade data, have seen emerging applications enabled by a machine learning approach, such as prediction of antibiotic resistance, source attribution of pathogens, and foodborne outbreak detection and risk assessment. In this article, we provide a gentle introduction to machine learning in the context of food safety and an overview of recent developments and applications. With many of these applications still in their nascence, general and domain-specific pitfalls and challenges associated with machine learning have begun to be recognized and addressed, which are critical to prospective use and future deployment of large data sets and their associated machine learning models for food safety applications.

Foodborne Pathogens

Quantification of Survival and Transfer of *Salmonella* on Fresh Cucumbers during Waxing

Jung J, Schaffner DW. *J Food Prot.* 2021 Mar 1;84(3):456-462. doi: 10.4315/JFP-20-375. **Article link**

Significance: *Salmonella* remaining on contaminated cucumbers after waxing could be detected for a week, and it survived better on cucumbers treated with a petroleum-based wax. These findings should be useful in managing *Salmonella* risks.

Cucumbers found in retail markets are often waxed to improve visual appeal and retard moisture loss. This waxing may affect bacterial survival, and the waxing process may facilitate cross-contamination between cucumbers. This study assessed the survival of *Salmonella* on waxed and unwaxed cucumbers and the potential for *Salmonella* cross-contamination during the waxing process. Fresh waxed or unwaxed cucumbers were spot inoculated with a cocktail of *Salmonella* enterica strains. Three different wax coatings (mineral oil, vegetable oil, or petroleum wax) were manually applied to unwaxed cucumbers using polyethylene brushes. *Salmonella* transfer from inoculated cucumbers to the brush or to uninoculated cucumbers was quantified. Higher *Salmonella* concentrations were observed on waxed cucumbers during the first 3 days of storage, but the final concentration on unwaxed cucumbers was higher than on waxed cucumbers at the end of storage, regardless of storage temperature. The wax formulation did affect the survival of *Salmonella* inoculated directly into waxes, with a significant decline in *Salmonella* populations observed in vegetable-based wax coating but with populations unchanged over 7 days at 7 or 21°C in mineral oil-based and petroleum-based waxes. *Salmonella* cells could transfer from inoculated unwaxed cucumbers to brushes used for waxing and then to uninoculated cucumbers during waxing. A significantly higher log percentage of transfer to brushes was observed when cucumbers were waxed with vegetable oil (0.71 log percent, P = 0.00441) than with mineral oil (0.06 log percent) or petroleum (0.05 log percent). Transfer to uninoculated cucumbers via brushes was also quantified (0.18 to 0.35 log percent transfer). *Salmonella* remaining on contaminated cucumbers after waxing could be detected for up to 7 days, and *Salmonella* survived better on cucumbers treated with a petroleum-based wax. These findings should be useful in managing the risk of *Salmonella* contamination in cucumbers during postharvest handling.

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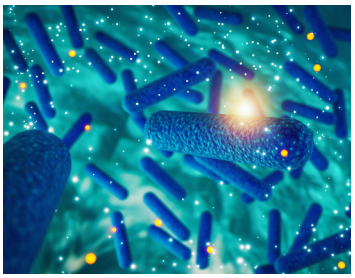
Locus of Heat Resistance (LHR) in Meat-Borne *Escherichia coli*: Screening and Genetic Characterization



Guragain M, Brichta-Harhay DM, Bono JL, Bosilevac JM. *Appl Environ Microbiol.* 2021 Mar 11;87(7):e02343-20. doi: 10.1128/AEM.02343-20. **Article link**

Significance: Sequencing and comparative analysis of select heat-resistant bacteria provides a clearer understanding of stress and heat resistance. Sequencing data may lead to further insights into the genetic background with the optimal bacterial tolerance against heat and other processing treatments.

Microbial resistance to processing treatments poses a food safety concern, as treatment tolerant pathogens can emerge. Occasional foodborne outbreaks caused by pathogenic *Escherichia coli* have led to human and economic losses. Therefore, this study screened for the extreme heat resistance (XHR) phenotype as well as one known genetic marker, the locus of heat resistance (LHR), in 4,123 *E. coli* isolates from diverse meat animals at different processing stages. The prevalences of XHR and LHR among the meat-borne *E. coli* were found to be 10.3% and 11.4%, respectively, with 19% agreement between the two. Finished meat products showed the highest LHR prevalence (24.3%) compared to other processing stages (0 to 0.6%). None of the LHR$^+$ *E. coli* in this study would be considered pathogens based on screening for virulence genes. Four high-quality genomes were generated by whole-genome sequencing of representative LHR$^+$ isolates. Nine horizontally acquired LHRs were identified and characterized, four plasmid-borne and five chromosomal. Nine newly identified LHRs belong to ClpK1 LHR or ClpK2 LHR variants sharing 61 to 68% nucleotide sequence identity, while one LHR appears to be a hybrid. Our observations suggest positive correlation between the number of LHR regions present in isolates and the extent of heat resistance. The isolate exhibiting the highest degree of heat resistance possessed four LHRs belonging to three different variant groups. Maintenance of as many as four LHRs in a single genome emphasizes the benefits of the LHR in bacterial physiology and stress response. **IMPORTANCE:** Currently, a "multiple-hurdle" approach based on a combination of different antimicrobial interventions, including heat, is being utilized during meat processing to control the burden of spoilage and pathogenic bacteria. Our recent study (M. Guragain, G. E. Smith, D. A. King, and J. M. Bosilevac, J Food Prot 83:1438-1443, 2020, https://doi.org/10.4315/JFP-20-103) suggests that U.S. beef cattle harbor *Escherichia coli* that possess the locus of heat resistance (LHR). LHR seemingly contributes to the global stress tolerance in bacteria and hence poses a food safety concern. Therefore, it is important to understand the distribution of the LHRs among meat-borne bacteria identified at different stages of different meat processing systems. Complete genome sequencing and comparative analysis of selected heat-resistant bacteria provide a clearer understanding of stress and heat resistance mechanisms. Further, sequencing data may offer a platform to gain further insights into the genetic background that provides optimal bacterial tolerance against heat and other processing treatments.

Mycotoxins

Thermal Decontamination Technologies for Microorganisms and Mycotoxins in Low-Moisture Foods

Deng LZ, Sutar PP, Mujumdar AS, Tao Y, Pan Z, Liu YH, et al. *Annu Rev Food Sci Technol.* 2021 Mar 25;12:287-305. doi: 10.1146/annurev-food-062220-112934. **Article link**

Significance: This review summarizes the working principles of novel thermal decontamination technologies such as superheated steam, infrared, microwave and radio-frequency heating as well as extrusion cooking. These methods of decontamination can effectively reduce the microbial load on products and moderately destruct the mycotoxins. Meanwhile, several integrated technologies have been developed that synergistically destroy contaminants.

The contamination risks of microorganisms and mycotoxins in low-moisture foods have heightened public concern. Developing novel decontamination technologies to improve the safety of low-moisture foods is of great interest in both economics and public health. This review summarizes the working principles and applications of novel thermal decontamination technologies such as superheated steam, infrared, microwave and radio-frequency heating as well as extrusion cooking. These methods of decontamination can effectively reduce the microbial load on products and moderately destruct the mycotoxins. Meanwhile, several integrated technologies have been developed that take advantage of synergistic effects to achieve the maximum destruction of contaminants and minimize the deterioration of products.

Microbial Detoxification of Mycotoxins in Food and Feed

Xu H, Wang L, Sun J, Wang L, Guo H, Ye Y, et al. *Crit Rev Food Sci Nutr*. 2021 Mar 5:1-19. doi: 10.1080/10408398.2021.1879730. **Article link**

Significance: The need for new microbial detoxification methods to effectively control mycotoxins and treat mycotoxin pollution in food and feed offers the potential for treatment with high efficiency, low toxicity and strong specificity, without damage to nutrients. This article reviews the application of microbial detoxification technology for the removal of common mycotoxins such as Aflatoxin, Ochratoxin, Zearalenone and others.

Mycotoxins are metabolites produced by fungi growing in food or feed, which can produce toxic effects and seriously threaten the health of humans and animals. Mycotoxins are commonly found in food and feed, and are of significant concern due to their hepatotoxicity, nephrotoxicity, carcinogenicity, mutagenicity and ability to damage the immune and reproductive systems. Traditional physical and chemical detoxification methods to treat mycotoxins in food and feed products have limitations, such as loss of nutrients, reagent residues, and secondary pollution to the environment. Thus, there is an urgent need for new detoxification methods to effectively control mycotoxins and treat mycotoxin pollution. In recent years, microbial detoxification technology has been widely used for the degradation of mycotoxins in food and feed because this approach offers the potential for treatment with high efficiency, low toxicity, and strong specificity, without damage to nutrients. This article reviews the application of microbial detoxification technology for removal of common mycotoxins such as Aflatoxin, Ochratoxin, Zearalenone, Deoxynivalenol, and Fumonisins, and discusses the development trend of this important technology.

Food Packaging

Electrospun Nanofibers Food Packaging: Trends and Applications in Food Systems

Sameen DE, Ahmed S, Lu R, Li R, Dai J, Qin W, et al. *Crit Rev Food Sci Nutr*. 2021 Mar 16:1-14. doi: 10.1080/10408398.2021.1899128. **Article link**

Significance: In this study, different parameters, structures of nanofibers, features and fundamental properties of electrospun nanofibers are described, while polymers fabricated through electrospinning with advances in food packaging films are discussed in more detail. The polymers used for the electrospinning of nanofibers as packaging films and their applications for variety of foods are explored.

Food safety is a bottleneck problem. In order to provide information about advanced and unique food packaging technique, this study summarized the advancements of electrospinning technique. Food packaging is a multidisciplinary area involving food science, food engineering, food chemistry, and food microbiology, and the interest in maintaining the freshness and quality of foods has grown considerably. For this purpose, electrospinning technology has gained much attention due to its unique functions and superior processing. Sudden advancements of electrospinning have been rapidly incorporated into research. This review summarized some latest information about food packaging and different materials used for the packaging of various foods such as fruits, vegetables, meat and processed items. Also, the use of electrospinning and materials used for the formation of nanofibers are discussed in detail. However, in food industry, the application of electrospun nanofibers is still in its infancy. In this study, different parameters, structures of nanofibers, features and fundamental properties are described briefly, while polymers fabricated through electrospinning with advances in food packaging films are described in detail. Moreover, this comprehensive review focuses on the polymers used for the electrospinning of nanofibers as packaging films and their applications for variety of foods. This will be a valuable source of information for researchers studying various polymers for electrospinning for application in the food packaging industry.

Chemical Contaminants

Novel Nondestructive Biosensors for the Food Industry

Turasan H, Kokini J. *Annu Rev Food Sci Technol*. 2021 Mar 25;12:539-566. doi: 10.1146/annurev-food-062520-082307. **Article link**

Significance: Biosensors can provide accurate, rapid, selective, qualitative and quantitative detection of analytes for the food industry and their ease of use, low-cost production and portability enables on-site detection.

An increasing number of foodborne outbreaks, growing consumer desire for healthier products, and surging numbers of food allergy cases necessitate strict handling and screening of foods at every step of the food supply chain. Current standard

procedures for detecting food toxins, contaminants, allergens, and pathogens require costly analytical devices, skilled technicians, and long sample preparation times. These challenges can be overcome with the use of biosensors because they provide accurate, rapid, selective, qualitative, and quantitative detection of analytes. Their ease of use, low-cost production, portability, and nondestructive measurement techniques also enable on-site detection of analytes. For this reason, biose nsors find many applications in food safety and quality assessments. The detection mechanisms of biosensors can be varied with the use of different transducers, such as optical, electrochemical, or mechanical. These options provide a more appropriate selection of the biosensors for the intended use. In this review, recent studies focusing on the fabrication of biosensors for food safety or food quality purposes are summarized. To differentiate the detection mechanisms, the review is divided into sections based on the transducer type used.

Adult Female Rats Perinatally Exposed to Perfluorohexane Sulfonate (PFHxS) and a Mixture of Endocrine Disruptors Display Increased Body/Fat Weights Without a Transcriptional Footprint in Fat Cells

Ramskov Tetzlaff CN, Ramhøj L, Lardenois A, Axelstad M, Evrard B, Chalmel F, et al. *Toxicol Lett*. 2021 Mar 15; 339:78-87. doi: 10.1016/j.toxlet.2020.12.018. **Article link**

Significance: Perfluorohexane sulfonate (PFHxS) is suspected to be an obesogenic compound and findings confirm that exposure to female rats, along with other endocrine modulating chemicals, can lead to weight gain without altering gene expression in the fat cells.

Obesity is a complex disease with many causes, including a possible role for environmental chemicals. Perfluorohexane sulfonate (PFHxS) is one of many per- and polyfluoroalkyl substances (PFASs) frequently detected in humans and it is suspected to be an obesogenic compound. We examined the potential long-term effects of PFHxS on metabolic parameters in rats after developmental exposure to 0.05, 5 or 25 mg/kg bw/day, with or without co-exposure to a background mixture of twelve endocrine disrupting chemicals (EDmix). Both male and female offspring showed signs of lower birth weight following intrauterine exposure. Female offspring exposed to both PFHxS and EDmix had increased body weight in adulthood. The retroperitoneal fat pad was larger in the PFHxS-exposed female offspring when compared to those exposed to EDmix alone. An attempt to detect putative molecular markers in the fat tissue by performing whole transcriptome profiling revealed no significant changes between groups and there were no significant effects on plasma leptin levels in exposed females. Our results show that early life exposure to endocrine disrupting chemicals can influence body weight later in life, but the effect is not necessarily reflected in changed gene expression in the fat tissue.

Heavy Metals

Exposure Assessment of Methylmercury in Samples of the BfR MEAL Study

Sarvan I, Kolbaum AE, Pabel U, Buhrke T, Greiner M, Lindtner O. *Food Chem Toxicol*. 2021 Mar;149:112005. doi: 10.1016/j.fct.2021.112005. **Article link**

Significance: Methylmercury exposure in Germany for adult high consumers exceeded the tolerable weekly intake recommended by the European Food Safety Authority in two age groups but no children's exposures exceeded recommend limits. This new database of dietary exposures found that the differences in exposure in four regions of the country were influenced by consumption habits rather than MeHg concentrations in the investigated food.

The BfR MEAL Study is the first German total diet study and will establish a representative and comprehensive database for dietary exposure assessment in Germany. The present study reports first results of the BfR MEAL Study regarding methylmercury in fish, seafood and mushrooms. In total, 34 MEAL foods were purchased nationally or regionally according to a defined sampling plan, prepared in a representative way for German households, pooled into 49 samples, homogenized and subjected to ICP-MS analysis. Dogfish, tuna, ocean perch, halibut and eel were the fish species with highest MeHg concentrations, while levels in mushrooms and mushroom products had markedly lower MeHg levels. Exposure was estimated by matching the present results with consumption data at appropriate levels of food group aggregation. MeHg exposure for adult high consumers (P 95) exceeded the tolerable weekly intake recommended by the European Food Safety Authority in two age groups (14-17 and 18-24 years). In children, no age group exceeded the recommended tolerable weekly intake. Regional samples differed only slightly in MeHg levels. The differences in exposure found in four regions of Germany were influenced by consumption habits rather than MeHg level in the investigated food.

Caffeine

Novel Insights on Caffeine Supplementation, CYP1A2 Genotype, Physiological Responses and Exercise Performance

Barreto G, Grecco B, Merola P, Reis CEG, Gualano B, Saunders B. *Eur J Appl Physiol*. 2021 Mar;121(3):749-769. doi: 10.1007/s00421-020-04571-7. **Article link**

Significance: More mechanistic and applied research is needed to evaluate how the CYP1A2 polymorphism might alter the magnitude of caffeine's ergogenic effect.

Caffeine is a popular ergogenic aid due to its primary physiological effects that occur through antagonism of adenosine receptors in the central nervous system. This leads to a cascade of physiological reactions which increases focus and volition, and reduces perception of effort and pain, contributing to improved exercise performance. Substantial variability in the physiological and performance response to acute caffeine consumption is apparent, and a growing number of studies are implicating a single-nucleotide polymorphism in the CYP1A2 gene, responsible for caffeine metabolism, as a key factor that influences the acute responses to caffeine ingestion. However, existing literature regarding the influence of this polymorphism on the ergogenic effects of caffeine is controversial. Fast caffeine metabolisers (AA homozygotes) appear most likely to benefit from caffeine supplementation, although over half of studies showed no differences in the responses to caffeine between CYP1A2 genotypes, while others even showed either a possible advantage or disadvantage for C-allele carriers. Contrasting data are limited by weak study designs and small samples sizes, which did not allow separation of C-allele carriers into their sub-groups (AC and CC), and insufficient mechanistic evidence to elucidate findings. Mixed results prevent practical recommendations based upon genotype while genetic testing for CYP1A2 is also currently unwarranted. More mechanistic and applied research is required to elucidate how the CYP1A2 polymorphism might alter caffeine's ergogenic effect and the magnitude thereof, and whether CYP1A2 genotyping prior to caffeine supplementation is necessary.

Association Between Maternal Caffeine Consumption and Metabolism and Neonatal Anthropometry: A Secondary Analysis of the NICHD Fetal Growth Studies–Singletons

Gleason JL, Tekola-Ayele F, Sundaram R, Hinkle SN, Vafai Y, Buck Louis GM, et al. *JAMA Netw Open*. 2021 Mar 1;4(3):e213238. doi:10.1001/jamanetworkopen.2021.3238. **Article link**

Significance: This cohort study found small reductions in neonatal anthropometric measurements with increasing maternal caffeine consumption. Findings suggest that caffeine consumption during pregnancy, even below 200 mg/d of caffeine, may be associated with decreased fetal growth.

Question: Is maternal caffeine intake associated with neonatal anthropometry? **Findings:** In this cohort study of 2055 women from 12 clinical sites, measures of caffeine consumption (plasma caffeine and paraxanthine and self-reported consumption) were associated with neonatal size at birth. Increasing caffeine measures were significantly associated with lower birth weight, shorter length, and smaller head, arm, and thigh circumference. **Meaning:** In this study, caffeine consumption during pregnancy, even in amounts less than the recommended 200 mg per day, was associated with smaller neonatal anthropometric measurements. **Importance:** Higher caffeine consumption during pregnancy has been associated with lower birth weight. However, associations of caffeine consumption, based on both plasma concentrations of caffeine and its metabolites, and self-reported caffeinated beverage intake, with multiple measures of neonatal anthropometry, have yet to be examined. **Objective:** To evaluate the association between maternal caffeine intake and neonatal anthropometry, testing effect modification by fast or slow caffeine metabolism genotype. **Design, Setting, and Participants:** A longitudinal cohort study, the National Institute of Child Health and Human Development Fetal Growth Studies–Singletons, enrolled 2055 nonsmoking women at low risk for fetal growth abnormalities with complete information on caffeine consumption from 12 US clinical sites between 2009 and 2013. Secondary analysis was completed in 2020. **Exposures:** Caffeine was evaluated by both plasma concentrations of caffeine and paraxanthine and self-reported caffeinated beverage consumption measured/reported at 10-13 weeks gestation. Caffeine metabolism defined as fast or slow using genotype information from the single nucleotide variant rs762551 (CYP1A2*1F). **Main Outcomes and Measures:** Neonatal anthropometric measures, including birth weight, length, and head, abdominal, arm, and thigh circumferences, skin fold and fat mass measures. The β coefficients represent the change in neonatal anthropometric measure per SD change in exposure. **Results:** A total of 2055 participants had a mean (SD) age of 28.3 (5.5) years, mean (SD) body mass index of 23.6 (3.0), and 580 (28.2%) were Hispanic, 562 (27.4%) were White, 518 (25.2%) were Black, and 395 (19.2%) were Asian/Pacific Islander. Delivery occurred at a mean (SD) of 39.2 (1.7) gestational weeks. Compared with the first quartile of plasma caffeine level (≤28 ng/mL),

neonates of women in the fourth quartile (>659 ng/mL) had lower birth weight (β = −84.3 g; 95% CI, −145.9 to −22.6 g; P = .04 for trend), length (β = −0.44 cm; 95% CI, −0.78 to −0.12 cm; P = .04 for trend), and head (β = −0.28 cm; 95% CI, −0.47 to −0.09 cm; P < .001 for trend), arm (β = −0.25 cm; 95% CI, −0.41 to −0.09 cm: P = .02 for trend), and thigh (β = −0.29 cm; 95% CI, −0.58 to −0.04 cm; P = .07 for trend) circumference. Similar reductions were observed for paraxanthine quartiles, and for continuous measures of caffeine and paraxanthine concentrations. Compared with women who reported drinking no caffeinated beverages, women who consumed approximately 50 mg per day (~ 1/2 cup of coffee) had neonates with lower birth weight (β = −66 g; 95% CI, −121 to −10 g), smaller arm (β = −0.17 cm; 95% CI, −0.31 to −0.02 cm) and thigh (β = −0.32 cm; 95% CI, −0.55 to −0.09 cm) circumference, and smaller anterior flank skin fold (β = −0.24 mm; 95% CI, −0.47 to −0.01 mm). Results did not differ by fast or slow caffeine metabolism genotype. **Conclusions and Relevance:** In this cohort study, small reductions in neonatal anthropometric measurements with increasing caffeine consumption were observed. Findings suggest that caffeine consumption during pregnancy, even at levels much lower than the recommended 200 mg per day of caffeine, are associated with decreased fetal growth.

Allergens

Bayesian Hierarchical Evaluation of Dose-Response for Peanut Allergy in Clinical Trial Screening

Haber LT, Reichard JF, Henning AK, Dawson P, Chinthrajah RS, Sindher SB, et al. *Food Chem Toxicol.* 2021 Mar 12;151:112125. doi: 10.1016/j.fct.2021.112125. **Article link**

Significance: We estimated the dose-response distribution for peanut allergen using data from double-blind placebo-controlled food challenges (DBPCFCs) conducted in the US at multiple sites, testing a population believed to be similar to the general US food allergic population. These findings could aid in establishing improved food labeling guidelines and the management of food allergies.

This research was supported by the IAFNS **Food and Chemical Safety Committee**.

Risk-based labeling based on the minimal eliciting doses (EDs) in sensitized populations is a potential replacement for precautionary allergen labeling of food allergens. We estimated the dose-response distribution for peanut allergen using data from double-blind placebo-controlled food challenges (DBPCFCs) conducted in the US at multiple sites, testing a population believed to be similar to the general U.S. food allergic population. Our final (placebo-adjusted) dataset included 548 challenges of 481 subjects. Bayesian hierarchical analysis facilitated model fitting, and accounted for variability associated with various levels of data organization. The data are best described using a complex hierarchical structure that accounts for inter-individual variability and variability across study locations or substudies. Bayesian model averaging could simultaneously consider the fit of multiple models, but the Weibull model dominated so strongly that model averaging was not needed. The ED01 and ED05 (and 95% credible intervals) are 0.052 (0.021, 0.13) and 0.49 (0.22, 0.97) mg peanut protein, respectively. Accounting for challenges with severe reactions at the LOAEL, by using the dose prior to the LOAEL as the new LOAEL, the ED01 drops to 0.029 (0.014, 0.074) mg peanut protein. Our results could aid in establishing improved food labeling guidelines in the management of food allergies.

The Microbial Origins of Food Allergy

Rachid R, Stephen-Victor E, Chatila TA. *J Allergy Clin Immunol.* 2021 Mar;147(3):808-813. doi: 10.1016/j.jaci.2020.12.624. **Article link**

Significance: Research indicates that microbial colonies may impact the development of food allergy (FA) and these results inform human studies currently in progress that evaluate the role of microbial therapies in FA.

Food allergy (FA) is a significant public health issue, propelled by its rapidly increasing prevalence. Its sharp rise into prominence has focused attention on causative environmental factors and their interplay with the immune system in disease pathogenesis. In that regard, there is now substantial evidence that alterations in the gut microbiome early in life imprint the host gut mucosal immunity and may play a critical role in precipitating FA. These changes may impact key steps in the development of the infant gut microbiome, including its shaping by maternal factors and upon the introduction of solid food (the weaning reaction). These early-life changes may have long-range effects on host immunity that manifest later in time as disease pathology. Experimental studies have shown that resetting the host intestinal immune responses by treatment with either a healthy fecal microbiota transplantation or defined commensal bacterial taxa can prevent or treat FA. The mechanisms by which these interventions suppress FA include restoration of gut immune regulatory checkpoints, notably the retinoic orphan receptor gamma T+ regulatory T cells, the epithelial barrier, and healthy immunoglobulin A responses to the gut commensals. These findings inform human studies currently in progress that evaluate the role of microbial therapies in FA.