FASI-10: The Food Allergy Research & Innovation Summit

Poster Title & Abstracts

FASI
FOOD ALLERGY SCIENCE INITIATIVE

TRANSFORMING THE SCIENCE OF FOOD ALLERGIES 10 YEARS

POSTER ABSTRACTS

1. BCR Density Limits Survival of IgE Germinal Center B Cells

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Abstract

IgE antibodies are central to allergic disease, yet the B cells that produce them are strongly biased toward producing secreted IgE (sIgE) while expressing only low levels of membrane IgE (mIgE) on the cell surface. This imbalance is influenced by three non-canonical polyadenylation sites downstream of the last IgE membrane exon, which are less efficient than the canonical secreted polyadenylation site (spA) and thereby limit mIgE production. To test the hypothesis that intrinsic regulation at the heavy chain locus influences isotype-specific B cell fate, we generated spA deletion mice by CRISPR-Cas9 gene editing, in which the spA was deleted at the IgE heavy chain locus (IgEspAd). Deletion of spA abolished secreted IgE and increased surface BCR density in IgEspAd B cells. Following intranasal challenge with Alternaria alternata, IgEspAd mice exhibited reduced IgE germinal center (GC) B cells and a reduction in plasmablasts. To isolate the effect of BCR density from secretion, we generated IgEspAd–wild-type mixed bone marrow chimeras, in which secreted IgE was present. In these chimeras, IgEspAd-derived IgE GC B cells showed reduced apoptosis compared to wild-type, demonstrating that increased BCR density directly reduces apoptosis in vivo. Similarly, in Verigem mice, which retain secreted IgE while exhibiting increased BCR density, IgE GC B cells also displayed reduced apoptosis and modestly increased numbers, while plasmablast differentiation remained intact. Notably, IgE GC B cell numbers were not reduced in Verigem mice or in IgEspAd–wild-type chimeras, supporting a role for secreted IgE in IgE GC accumulation. These findings identify BCR density as a key determinant of IgE B cell apoptosis and suggest new ways to manipulate IgE immunity in allergy and immunotherapy.

2. Beyond Intestinal Fluid Secretion: Multi-Organ Responses to Acute Cholera Toxin Exposure

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Abstract

Cholera toxin (CTx), an enterotoxin produced by Vibrio cholerae, is the main virulence factor responsible for the watery diarrhea associated with cholera. Although cholera is traditionally classified as a noninflammatory secretory disease, innate immune responses have been reported in patients during the acute phase of infection. Furthermore, CTx is a potent mucosal adjuvant. While its cellular effects on intestinal epithelial ion transport and its mucosal adjuvant properties are well established, the early tissue-level and systemic responses to CTx remain incompletely understood. We hypothesized that a single exposure to CTx would trigger a systemic defensive response and alter immune cell composition in intestinal tissues. Here, we investigated the acute physiological, metabolic, intestinal, and hepatic consequences of CTx exposure in male C57BL/6 mice. Mice received a single nonlethal intragastric dose of CTx and were monitored for 24 hours. Physiological parameters, including body temperature and the occurrence of diarrhea, were assessed alongside metabolic measurements, intestinal transcriptomics, immunofluorescence, flow cytometry, and targeted hepatic gene-expression analyses. CTx caused pronounced diarrhea and hypothermia, accompanied by a transient reduction in energy expenditure and altered fuel utilization. In the proximal small intestine, CTx induced a robust transcriptional response characterized by the activation of cellular stress, autophagy, NF-κB and MAPK signaling, and oxidative stress pathways, together with the suppression of mitochondrial processes. CTx also altered epithelial transcriptional programs associated with nutrient and ion transport, mucus production, and enteroendocrine signaling. These transcriptional changes were accompanied by alterations in intestinal epithelial cell composition and in the frequencies of multiple immune cell populations within the epithelial and lamina propria compartments. Finally, CTx induced a selective hepatic transcriptional response involving stress mediators, detoxification pathways, fatty acid metabolism, and bile acid synthesis, without evidence of a robust canonical acute-phase response. Together, these findings demonstrate that acute CTx exposure in male C57BL/6 mice elicits a coordinated response involving intestinal epithelial and immune remodeling, systemic metabolic alterations, and hepatic transcriptional adaptation, revealing effects that extend beyond intestinal fluid secretion. Defining these early intestinal and systemic responses may improve our understanding of cholera pathophysiology in patients and reveal mechanisms contributing to the mucosal adjuvant activity of CTx.
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3. An IgG-Macrophage Neuronal Axis Suppresses Allergic Itch

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Abstract

Chronic allergic itch is a debilitating condition that often resists standard therapy. Here we demonstrate that systemic IgGs engage activating Fcγ receptors (FcγRs) on neuron-associated macrophages to inhibit IgE-driven itch through a macrophage-neuron signaling axis.

In a passive cutaneous challenge model, mice sensitized with allergen-specific IgE and then treated with allergen-specific IgG2a showed a marked reduction in scratching behavior upon allergen re-exposure, despite unchanged mast cell degranulation, indicating that IgG2a acts downstream of mast cell activation rather than by blocking IgE-triggered degranulation itself. Enzymatic removal of IgG2a Fc glycans abolished activating FcγR binding, measured by biolayer interferometry, and protection in vivo, establishing a strict requirement for activating FcγR engagement. Depleting macrophages with clodronate liposomes attenuated IgG2a-mediated suppression of itch, confirming that macrophages are necessary for protection. Sensory neuron-associated macrophages, marked by CX3CR1, were found to express CD39/CD73, key ectonucleotidases required to convert pro-inflammatory ATP into immunosuppressive adenosine. Mechanistically, blocking either CD73 or the adenosine A1 receptor abolished IgG2a's anti-pruritic effect. Immunostaining showed sensory nerve fibers expressing the A1 receptor in close proximity to macrophages. Using GCaMP3reporter mice, we found that mice treated with allergen-specific IgG2a had markedly decreased calcium flux within the trigeminal ganglia, indicating locally confined signaling.

This protective mechanism generalized across disease-relevant contexts. In the MC903-induced model of atopic dermatitis, an itch driven by a basophil–leukotriene axis rather than mast cell/histamine signaling, IgG2a co-administration reduced scratching to near baseline, demonstrating efficacy beyond histaminergic itch. In mice actively immunized with house dust mite (HDM), which develop an endogenous polyclonal IgE response and pronounced itch upon cutaneous HDM challenge, a single dose of monoclonal IgG2a against the major allergen DerP1 was sufficient to suppress scratching. Critically, the phenotype extended to human biology. In humanized FcγR mice, antigen-specific human IgG1 recapitulated the anti-pruritic effect observed with mouse IgG2a, underscoring the translational relevance of this pathway.

Together, these data define a unifying neuroimmune axis in which protective IgG antibodies engage activating FcγRs on macrophages to trigger CD73-dependent adenosine release, silencing IgE-driven itch circuits at the level of the sensory neuron. This IgG–FcγR–macrophage–adenosine axis represents a promising therapeutic target for allergic itch. Strategies to boost protective IgG responses, engage activating FcγRs, or exploit adenosine signaling may offer durable relief for patients suffering from chronic pruritic disorders.

4. Xenobiotics Act as Adjuvants and Hijack Poison-Defense Circuitry to Drive Food Allergy

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Abstract

Allergy is a chronic condition in which the immune system mounts a type 2 response against dietary protein, producing a robust expulsion reaction upon re-exposure, including itching, sneezing, vomiting, and diarrhea. In severe cases, the response can be systemic, resulting in anaphylaxis and even death. In the past few decades, the incidence of allergy has dramatically increased worldwide, a trend too rapid to be explained by genetic mutation alone, which implicates environmental triggers. We hypothesized that xenobiotics, a class of chemicals introduced during industrialization, commonly found in food preservatives and over-the-counter medications, are acting as adjuvants that instruct the immune system to form immune memory to otherwise harmless dietary proteins. Taking advantage of the common ovalbumin (OVA) model of sensitization, we screened different classes of chemicals commonly used as food preservatives and non-steroidal anti-inflammatory drugs for their potential adjuvant effect. We observed that coadministration of OVA and certain xenobiotics leads to the production of OVA-specific IgG and IgE and, upon intravenous challenge, to anaphylaxis. We term this xeno-sensitization. Mechanistically, we observed that TRPA1, an ion-gated channel that is activated during poisoning and irritant responses, is necessary for xenobiotic adjuvancy. TRPA1 activation triggered serotonin release, which drove intestinal epithelial cells to produce TSLP, an alarmin central to type 2 immunity. TSLP is necessary and sufficient to induce sensitization to oral antigen and ablating its cognate receptor in DCs or T cells prevents xeno-sensitization. We propose that food allergy can arise from the coincidental co-exposure of a dietary protein with a xenobiotic capable of activating the gut's intrinsic poison-response circuitry via TRPA1–serotonin–TSLP signaling, hijacking the same physiological program that defends the organism against accidental poisoning.

5. CRISPR screening reveals a key role for sensory neuronal PKCβ–RASGRP1 axis in protease allergen-triggered neuroinflammation

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Abstract

Neuroimmune interactions are increasingly recognized as a key regulatory circuit in inflammatory diseases. We previously demonstrated that sensory neurons act as frontline sentinels that detect noxious stimuli, such as protease allergens, and communicate with immune cells through neuropeptide release, thereby orchestrating type 2 inflammation. These findings establish neuron-derived neuropeptides as central regulators of immune initiation. However, the molecular mechanisms governing neuropeptide release remain largely elusive. Because the plasma membrane of peripheral sensory neurons serves as the primary interface for sensing environmental cues and communicating with immune cells, we hypothesize that signaling events at the neuronal membrane are critical for regulating neuroimmune interactions. Furthermore, although extensive studies have examined the functional consequences of inflammatory disease-associated genetic variants within the immune compartment, it remains unclear whether these variants also exert neuron-specific effects that contribute to disease pathogenesis.

To address this, we performed a CRISPR screen using a library of nociceptor-enriched genes associated with inflammatory diseases to identify regulators of neuropeptide release in neuroimmune communication. Using the protease allergen papain to specifically induce Substance P release from mouse dorsal root ganglion (DRG) neurons—a key mediator of inflammatory responses—we identified multiple regulators of Substance P release. Among these, the PKCβ–RASGRP1 signaling axis, which functions as components of the molecular switch at the neuronal membrane, emerged as a critical pathway regulating sensory neuron responses to protease allergens. Depletion of Prkcb or Rasgrp1 in DRG neurons selectively impaired papain-induced Substance P release without affecting pore-forming toxin-induced CGRP release, demonstrating stimulus-specific regulation of neuropeptide release. Consistent with these findings, in vivo CRISPR-mediated targeting of Prkcb or Rasgrp1 in skin-innervating DRG neurons via intrathecal AAV delivery inhibited papain-induced migration of $CD301b^+$ dendritic cells (DCs), a critical step in the initiation of Th2 immune responses. Furthermore, pharmacological inhibition of PKCβ significantly suppressed papain-induced itch behavior in mice, while catechin hydrate, a reported RASGRP1 inhibitor, reduced papain-induced $CD301b^+$ DC migration in vivo. Together, these findings deepen our mechanistic understanding of how peripheral sensory neurons respond to protease allergens during the earliest step of neuroimmune interactions and identify the PKCβ–RASGRP1 signaling axis as a potential therapeutic target for allergic diseases.

6. NSAIDs augment anaphylaxis and increase transit of substances across the intestine

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Abstract

INTRODUCTION: Food-specific IgE is necessary but not sufficient for symptomatic allergy, indicating that other biological factors modify the response to allergen ingestion. We previously showed that intestinal cysteinyl leukotriene levels are one such factor, with higher levels corresponding to more severe allergic response. Non-steroidal anti-inflammatory drugs (NSAIDs) block the synthesis of prostaglandins, which are synthesized from the same precursor as leukotrienes. NSAIDs can act as another factor that can modify the allergic response, reducing the threshold for and severity of allergic reactions. Though this phenomenon has been well described in clinical data, the underlying mechanism is not fully resolved.

METHODS: C57BL/6 MICE were sensitized to peanut and challenged with crude peanut extract via gavage with or without NSAID pretreatment. Transit from the intestine to the serum was measured by gavage of a solution containing FITC-dextran and subsequent detection of fluorescence in serum.

RESULTS: Mice that received NSAID pretreatment exhibited significantly greater hypothermia and clinical scores indicating more severe response following oral allergen challenge. NSAID pretreatment also augmented transit of 40 kDa FITC-dextran from the intestine into systemic circulation. Treatment with exogenous prostaglandin E1 (PGE1) reversed these effects in NSAID-treated mice, reducing both hypothermia and transit across the intestinal barrier.

CONCLUSIONS: Similar to the observed effect in patients, NSAID treatment leads to greater reaction severity following oral allergen challenge in a mouse model of food allergy. These data also suggest that acute disruption of prostaglandin production is sufficient to elevate transit of substances across the intestine. In the context of an ingested allergen in an allergic individual, this NSAID-mediated increase in transit of substances from the intestine to circulation may be responsible for a reduction in reaction threshold and an increase reaction severity.

7. Lipid-induced gut invariant natural killer T cell activation in mice leads to development of food allergy

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Abstract

Food allergy is caused by pathogenic food-specific IgE, yet the environmental triggers that induce these antibodies remain enigmatic. We show that gut viral infections and perturbations to the gut microbiome do not lead to food-specific antibody production in mice. Instead, we find that oral administration of food alongside the glycosphingolipid α-galactosylceramide, which activates CD1d-restricted invariant natural killer T (iNKT) cells, leads to the production of anaphylactic food-specific IgE. This IgE production requires type 2 conventional dendritic cells (cDC2s) to activate iNKT cells that secrete IL-4, which reciprocally activates cDC2s. These activated cDC2s then prime Tfh cells in the mesenteric lymph nodes, leading to IgE responses against food proteins. cDC2s must express CD1d and MHCII, and both antigen presentation molecules must be co-expressed on the same antigen presenting cell to induce food-specific IgE. Thus, a single cDC2 must present both an adjuvant-derived lipid on CD1d to become licensed, and an allergen-derived peptide on MHCII to prime the requisite $CD4^+$ T cell that induces IgE producing B cells. These data define a mechanism whereby lipid-induced activation of gut iNKT cells promotes “collateral priming” of allergen-specific $CD4^+$ T cells, ultimately contributing to the development of food allergy and implicating lipids as a potential culprit of disease pathogenesis.

8. Beyond the Allergen Station: A Staged, Patient-Informed Model for Campus Food Allergy Safety

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Abstract

Background. Food allergy affects approximately one in ten college-age students, and the transition to university compounds risk through loss of pediatric care, unsupervised eating, and documented underreporting of reactions. In December 2022, a 19-year-old student at a Maine college died of anaphylaxis; stock epinephrine was not available. Food allergy science continues to advance diagnostics and therapeutics, but the benefit of that science ultimately depends on whether institutions can deliver safety in the environments where students actually eat. That delivery layer remains uncharacterized. Institutional responses are typically fragmented, addressing menu labeling, staff training, or emergency epinephrine in isolation, and no described model specifies how comprehensive campus infrastructure is built or in what sequence.
Program description. We describe the staged development of food allergy infrastructure across two campuses at the University of New England serving 6,573 students, beginning with a single station excluding the top nine allergens and progressing to an integrated, institution-wide system. Beyond emergency epinephrine, the components that carried the system were preventive rather than reactive. Dual-model training reached 100 percent of full-time dining staff, with new hires trained at onboarding so competency survives turnover. Training content was patient-informed, built from guest-reported experience: the psychology of why students do not ask, how staff hesitation is read as risk, and where cross-contact occurs in service. Ingredient-level menu data with allergen icons, a student intake form with named contacts, guided allergen-focused dining tours, and a public webpage documenting protocols and stated limitations shifted allergen response from reactive to anticipatory and made safe choices legible before a student had to ask. The contracted operator, Parkhurst Dining, and university staff provided operational grounding, with the initiative led by student advocates living with food allergies.
Implementation. The build unfolded over roughly two years, with each stage building on the staff capability established by the last and requiring coordination across five institutional departments. Most stages carried little direct cost, which made coordination rather than funding the rate-limiting constraint. The epinephrine stage took six months to approval and two months to installation; principal barriers were interdepartmental coordination, training sequencing, and institutional buy-in. The emergency epinephrine components were donated, and remaining stages were absorbed into existing dining and on-campus safety and security operations. Student Health holds the standing order and assumes replenishment. A student-led advocacy chapter and recurring allergen-friendly cooking programs sustained engagement throughout. The model is now being applied across additional operator accounts in corporate and higher education settings.
Preliminary findings. External assessment on the FARE college search improved from 10 of 14 accommodations in late 2023 to 13 of 14 in 2024 and 14 of 14 in early 2026, and the institution became the first in Maine to earn FARECheck Silver certification on both campuses. Training reached 100 percent of full-time dining staff. Staff capability and institutional visibility proved mutually reinforcing: external validation drew prospective allergic students, and Admissions reports families citing the program, with allergen safety now incorporated into institutional marketing and admissions tours. No epinephrine administration events have occurred since installation in June 2026. The institution collected no baseline prevalence data before 2026; a structured intake instrument, administered under participant consent, now captures allergy disclosure and epinephrine-carriage data and establishes a framework for prospective measurement. These are primarily process measures at this stage.
Conclusions. This work delivers a staged, patient-informed model for campus food allergy infrastructure, taking a single institution from one allergen station to a fully integrated system independently validated at the highest available benchmark and first in its state. It demonstrates that comprehensive infrastructure can be built without dedicated grant funding, largely through existing operations, and that the binding constraint is organizational coordination rather than capital. It also surfaces a structural gap the field has overlooked: institutions serving large allergic populations collect no baseline data on them, and this work introduces an instrument built to close it. Critically, the model is transferable. It is a sequenced, reproducible pathway that other institutions can adopt directly, translating the advances of food allergy science into the institutional infrastructure required to deliver them. What remains untested is whether integrated, patient-informed infrastructure measurably outperforms the fragmented status quo, and this framework is now positioned to test it.

9. Defining and Leveraging the Biogeography of Food Proteins

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Abstract

Food is fundamental to human health, with what we eat increasingly linked to diverse health outcomes. Proteins are a crucial component of the human diet, acting as our source of essential amino acids required for biosynthesis and energy metabolism. While necessary, proteins have a two-sided relationship with human health: the same protein that nourishes the body can also induce immunological chaos. Although decades of research have elucidated the immune pathways involved in allergic sensitization and tolerance, we lack a mechanistic understanding of how immune responses to food proteins are first generated. At the root of this, there is a fundamental gap in our knowledge of what happens to a food protein after it's ingested. Our current understanding of protein digestion operates under a one-size-fits-all model, assuming all proteins are treated and digested equally following ingestion. This assumption, however, ignores the fact that food proteins are diverse, both structurally and compositionally. By systematically characterizing food protein digestion across the foods in our diet, we identify protein fragments that escape host digestion, providing critical insight into their biogeography and how they are first sensed at the gut-immune interface. Here, we combine in vitro and in vivo digestion models with LC-MS proteomics to identify the resistant food peptides and proteins throughout the gastrointestinal system. Using fluorescently conjugated food proteins, we probe the biogeography and cellular uptake of food proteins in vivo, revealing how uptake varies across diverse food protein sources and changes in host digestibility. Additionally, we ask whether the gut microbiome – recognized for it's role in glycan digestion – plays a role in the digestion of resistant food peptides. We have identified several candidate colonic microbes capable of digesting food proteins in vitro, including those resistant to host digestion. Using these candidates, we aim to leverage the gut microbiome for digestion in vivo, testing whether this alters cellular uptake and shifts downstream immune responses. Ultimately, this work provides critical insight into food protein digestion, transformation, and uptake across diverse sources, establishing a framework for microbial control of protein fate and function for interventions in food allergy.

10. A duodenal atlas reveals persistent alterations of cellular networks in food-allergic individuals

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Abstract

The intestine is formed by a complex cellular network that must balance nutrient absorption, food tolerance and microbial commensalism with immune defenses against enteric pathogens. Food allergies are defined by a breakdown of this tolerance potentially resulting in severe anaphylactic reactions. To define the cellular networks associated with this condition, we profiled 292,171 cells from 24 pediatric subjects, including 15 with clinically confirmed food allergy and 9 controls. Our analyses reveal extensive changes in food-allergic patients, including an expansion of lamina propria T cells and a loss of Brunner's gland epithelium. The epithelium of these subjects was characterized by an increase in proliferative and metabolic programs, potentially driven by stromal ephrin signaling, whereas controls displayed an increase in interferon-responsive gene signatures and antigen presentation. Altogether, this work defines food allergy-associated alterations in the proximal intestine and highlights epithelial-stromal-immune communication as a driver of this process.

11. High-density lipoprotein priming enhances allergen-mediated MC_T activation

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Abstract

Mast cells (MCs) can be categorized into two distinct populations: subepithelial MCs that co-express tryptase and chymase (MC_{TC}) and epithelial MCs that express tryptase alone (MC_T). Due to their in vivo location, MC_T are likely central drivers of allergic responses in the airways and digestive tissues, but little is known about the differential sensitivity of each subset to activation. Historically, in-vitro systems for differentiating primary MCs give rise exclusively to MC_{TC}, restricting the ability to evaluate potential differences and similarities in activation between the two. We recently published a novel culture system allowing selective differentiation of either MC_T or MC_{TC} from adult peripheral blood. To evaluate and compare activation patterns of MC subsets, we sensitized MC_T and MC_{TC} with serum from physician-diagnosed cat allergic patients, stimulated with cat dander extract and measured activation using flow cytometry. We have identified that MC_T sensitized with cat-allergic patient serum are significantly more activated than MC_{TC} assessed in parallel. However, sensitizing MC subsets with monoclonal IgE and stimulating with corresponding antigen resulted in the complete opposite phenotype, with MC_{TC} exhibiting enhanced activation compared with MC_T. Adding non-allergic serum during sensitization with monoclonal IgE restored enhanced activation in MC_T compared with MC_{TC}, suggesting a serum dependent factor responsible for enhanced MC_T activation. Our current work suggests that a component of the high-density lipoprotein (HDL) subfraction found in serum drives enhanced MC_T activation. Future studies will seek to define the mechanism utilized by HDL to drive enhanced MC_T activation.

12. $PRDM16^+$ tolerizing dendritic cells instruct food antigen-specific Treg cell differentiation and oral tolerance

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Abstract

Failure to establish oral tolerance to dietary antigens can lead to pathogenic type 2 responses and food allergy. We recently identified $PRDM16^+$ tolerizing dendritic cells (tolDCs) as a distinct antigen-presenting cell population required for the differentiation of food- and microbiota-specific peripherally induced regulatory T (pTreg) cells. Using multiple genetic models, we found that disruption of tolDCs through deletion of Prdm16, Rorc(t), or the Rorc(t)+7 kb cis-regulatory element abolished food antigen-specific pTreg cell differentiation and instead increased antigen-specific Th2 cells. To examine the consequences in a model that more closely reflects gastrointestinal manifestations of food allergy, we generated tolDC-deficient Rorc(t)+7 kb knockout mice on the BALB/c background. Following oral tolerization and intragastric antigen challenge, control littermates were protected from diarrhea, whereas tolDC-deficient mice were not. We also investigated the developmental origin and persistence of this population. $PRDM16^+$ tolDCs were labeled by both IL-7R- and CSF1R-based fate-mapping approaches, and disruption of either pathway alone was insufficient to eliminate tolDC development. Notably, tolDC development and function were independent of common γ chain signaling. Moreover, inducible depletion of tolDCs in adult mice abrogated the generation of food antigen-specific pTreg cells. The tolDC population recovered over time, together with its capacity to induce food antigen-specific pTreg cell differentiation. Together, these findings establish $PRDM16^+$ tolDCs as a central regulator of food antigen tolerance and provide new insights into their development and maintenance.

13. Harnessing Artificial Intelligence and Natural Language Processing to Enhance the Diagnosis and Management of Pediatric Anaphylaxis

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Abstract

Anaphylaxis is a life-threatening systemic hypersensitivity reaction with a highly variable clinical presentation, particularly in children, contributing to frequent underdiagnosis and delayed treatment. Despite established diagnostic criteria, early recognition remains challenging due to symptom heterogeneity, overlap with other conditions, and limited utility of laboratory testing in acute care settings. Delayed or missed diagnosis can lead to significant morbidity and mortality, while timely administration of epinephrine remains the only definitive treatment.

In this study, we developed and evaluated an artificial intelligence (AI)-driven clinical decision support approach to improve the diagnosis and management of pediatric anaphylaxis. Using real-world clinical data, we constructed a natural language processing (NLP)-based algorithm incorporating semantic embedding techniques to distinguish anaphylaxis from other allergic reactions and mimicking conditions. The model demonstrated improved diagnostic accuracy compared to standard clinical assessment by effectively identifying nuanced patterns in patient presentations.

We further analyzed current management practices for cases identified as allergic reactions or anaphylaxis by examining clinical documentation, diagnoses, and treatment decisions relative to established guidelines. This analysis revealed variability in care and highlighted gaps in adherence to recommended practices, particularly in the timely administration of epinephrine.

Overall, our findings demonstrate that AI-driven NLP models can enhance diagnostic precision and provide valuable insights into real-world management patterns. Integration of such tools into clinical workflows has the potential to improve early recognition, support timely intervention, and ultimately reduce morbidity associated with pediatric anaphylaxis.

14. Bidirectional crosstalk between sensory neurons and γδ T cells regulates allergic responses

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Abstract

Sensory neurons densely innervate the skin where they directly detect allergens, leading to itching sensations and the release of neuropeptides that regulate the downstream allergic immune response. We recently identified a poorly characterized subset of epidermal γδ T cells, termed GD3 cells, whose production of IL-3 fine-tunes the responsiveness of sensory neurons to allergens upon first exposure, governing both allergic itch and allergen sensitization. However, the upstream factors that regulate GD3 cells, thereby underlying allergen sensitivity, are obscure. Here, we found an unexpected role of sensory neurons in the homeostatic maintenance of GD3 cells in the skin. Confocal microscopy revealed that GD3 cells are closely associated with sensory neurons, forming direct contacts with free nerve endings in the epidermis. Furthermore, inducible deletion of sensory neurons in vivo led to a significant reduction in GD3 cells, but not other skin γδ T cell subsets. To further investigate the interaction between sensory neurons and GD3 cells, we performed in vitro co-cultures and found that sensory neurons directly promoted GD3 cell survival, proliferation, and cytokine production. Mechanistically, sensory neurons supported GD3 cells in a manner partially dependent on the γδ TCR. These findings suggest that GD3 cells and sensory neurons engage in dynamic bidirectional crosstalk and that alterations in this neuroimmune axis may underly individual differences in allergic susceptibility.

15. Mechanisms of IgE Trafficking from Origin to Effector Tissues

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Abstract

Food allergy is an IgE-mediated immune response that can progress to life-threatening anaphylaxis. However, the mechanisms governing IgE production and its distribution from the site of origin to effector tissues remain poorly understood. Here, we investigated antibody-dependent vascular permeability using an active anaphylaxis mouse model evaluated via Evans blue dye extravasation. Mice were sensitized subcutaneously in the right hock with ovalbumin and alum, followed by intravenous antigen challenge at defined time points to assess vascular leakage and systemic anaphylaxis. To delineate the relative contributions of IgE- and IgG-dependent pathways, we utilized multiple knock-out mouse strains (including AID-KO and IgE-deficient mice) alongside FcγRII/III blocking (clone 2.4G2). Following antigen challenge, day 7 responses showed localized, asymmetrical leakage at the immunization site accompanied by a mild transient drop in body temperature. By day 10, vascular leakage became systemic and was accompanied by sustained hypothermia. Experiments in AID-KO mice confirmed that vascular permeability requires class-switched antibodies. In IgE-deficient mice, both local and systemic leakage were driven by IgG1. Conversely, FcγR-blocked wild-type mice exhibited IgE-driven local leakage on day 10 and systemic leakage by day 14. Together, these findings demonstrate that vascular leakage evolves temporally from a localized to a systemic response, driven sequentially by IgG1 and IgE. This highlights the dynamic trafficking of antibodies during anaphylaxis and defines key regulatory mechanisms governing IgE distribution in effector tissues.

16. Defining the Plant Small Molecule-Microbiome axis in Type 2 immunity

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Abstract

Plant small molecules (PSMs) comprise an extremely diverse range of chemicals encompassing over 200,000 distinct substances, including polyphenols, terpenoids, anthraquinones, and flavonoids. Different modifications applied via the host, microbiome, and plant drastically expands the structural diversity and chemical complexity of these dietary small molecules. However, how and which of this vast chemical diversity acts across the host-microbiome interface and regulate Type 2 (T2) immune response, mucosal alarmin signals, and food allergy (FA) pathogenesis remain incompletely understood. To address this gap, we constructed a standardized screening pipeline leveraging immortalized bone marrow derived macrophages (iBMDMs) and dendritic cell T cell (DC-T) co-cultures to map the immunomodulatory activity of 53 structurally diverse PSM aglycones across seven major chemical classes (including flavonoids, stilbenes, coumarins, and chalcones). Multiple flavonoid, stilbene, and coumarin aglycones suppressed IL-6 secretion with potency exceeding the nonsteroidal anti-inflammatory drug indomethacin. Furthermore, several compounds displayed divergent cytokine regulation, selectively inhibiting IL-6. In vitro macrophage activation assays revealed that PSMs across multiple chemical classes act as potent inducers of Growth Differentiation Factor 15 (GDF-15), which functions to suppress type 1, but enhance type 2 immunity as a potent tissue tolerance inducer. In DC-T cell co-culture assays, flavonoids selectively rewritten T cell helper profiles. To illustrate, baicalein and chrysin significantly enhanced IL-4 production, and kaempferol and isorhamnetin upregulated both IL-4 and IL-13 alongside T17 (IL-17A) responses, uniquely modulating T2 responses. To determine whether these in vitro immunological programs are reflected in vivo, oral delivery of dietary flavonoid aglycones to mice models were conducted, which rapidly modulated distal gut mucosal immunity. Consistent with our DC-T co-culture findings, non-toxic T2-modulating flavonoids like kaempferol and isorhamnetin specifically triggered the expression and secretion of key epithelial alarmins and T2 cytokines in the ileum and colon.Our data suggests that dietary plant small molecules directly shape host immune modules, driving acute T2 alarmin release, cytokine expression, and DC-T cell polarizations. These insights establish a foundation for developing targeted dietary and microbiome-based interventions to modulate Type 2 immunity and prevent food allergy.

17. A Brain-Heart-Immune Program of Postpartum Adaptation Driven by Maternal-Offspring Interaction

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Abstract
Organisms have evolved strategies to tolerate, resist, and ultimately adapt to external challenges that cannot be avoided, thereby preserving fitness and ensuring species survival. We propose the mammalian postpartum period as a unique example of extreme physiological adaptation driven by the extraordinary demands of motherhood. Following birth, nursing mothers must simultaneously sustain lactation, remodel multiple tissues, care for their offspring, and maintain a new homeostasis while responding to environmental challenges such as infection and food availability. Although postpartum women experience well-documented changes in immune tolerance and susceptibility to certain diseases, the mechanisms developed to maintain maternal homeostasis during this period remain largely unknown.
We hypothesize that the sensory cues generated through maternal-offspring interaction are integrated within the maternal brain to coordinate immune and tissue adaptation, thereby preserving homeostasis and promoting tolerance and resistance during the postpartum period. To investigate this we examined how the postpartum period and maternal care influence the dam's response to diverse inflammatory challenges. We found that nursing dams exhibit remarkable resilience to anaphylactic shock, endotoxemia and listeriosis, despite mounting robust inflammatory responses. This phenotype is independent of lactation but requires continuous maternal-offspring interaction. Disruption of these interactions rapidly abolishes resilience, resulting in cardiac edema and dysfunction. Selective chemogenetic recall of the neuronal network associated to maternal separation is sufficient to recapitulate both the adaptive and maladaptive phenotypes driven by interaction and separation, respectively. Together, these findings support the existence of a unique postpartum brain-heart-immune program that is actively maintained by maternal-offspring interactions and promotes tolerance to inflammatory stress without compromising host defense. We aim to define the maternaloffspring signals that sustain this adaptive state and to identify the neural, cardiovascular and immune mechanisms through which postpartum homeostasis is maintained.

18. Extraction Efficiency Studies and Quantification of Major Peanut Allergens in Peanut Challenge Meals and Peanut Flour

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Abstract
Background
Extraction efficiency of Ara h 1, Ara h 2, Ara h 3 and Ara h 6 from different matrices will have a direct effect on the measured allergen content. This study looks to identify the optimum extraction buffer and procedure for component peanut allergens Ara h 1, Ara h 2, Ara h 3 and Ara h 6 from 3 different matrices: 2 peanut challenge meal (PCM) formulations (each at 3 different strengths) and peanut flour.
Method
Three extraction buffer compositions were studied per peanut component allergen in peanut flour and PCM 6months+/4years+ (low and high strength) and 2 for the 0% w/w PCM formulations. Allergen levels were quantified, using allergen-specific ELISA. For the PCMs, matrix-recovery of component allergens was calculated using average specific allergen content determined in peanut flour, adjusted to %w/w peanut flour.
Results
PCM matrix-recovery of Ara h 2, Ara h 3 and Ara h 6 from PCM 4y+ (low and high strength) were within 82% to 101%. Ara h 1 recovery was lower at 1% to 32%. For PCM 6m+ (low and high strength) recoveries were within 91% to 138%. Allergen was below method limit of detection in the 0% w/w PCM samples. Extraction replicates had highly agreeable allergen content, with an average %CV of 5-13%.
Conclusion
Extraction buffers have been identified for Ara h 1, Ara h 2, Ara h 3 and Ara h 6 across multiple matrices. The data suggests the extraction and analytical methodology are robust and repeatable and the challenge meals are uniform in allergen content. This is important for quality, safety and efficacy controls in standardising materials for allergy diagnosis.

19. Characterization of Humoral Immune Responses via High-Throughput Profiling of Fc-dependent Antibody Effector Functions

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Abstract
Food allergy is characterized by complex and incompletely understood humoral immune responses to allergens. SeromYx has developed a high-throughput 'Systems Serology' platform that enables comprehensive, multiplexed characterization of antigen-specific humoral immune responses. Our approach integrates biophysical interaction assays, including Fc receptor and FcRn binding, with cell-based functional assays to comprehensively characterize Fc-mediated antibody activity and relate Fc effector functions to clinical outcomes. The platform is designed to generate multidimensional immune profiles from limited volumes of clinical samples. Integrated computational and machine-learning approaches can be used to identify patterns within multidimensional antibody responses and relate immune signatures to clinical phenotypes or other study endpoints. Common applications include infectious disease, autoimmunity, cancer, translational research, and clinical development. Application of this Systems Serology approach to food allergy studies has the potential to provide a comprehensive framework for investigating the humoral immune response to food allergens. By integrating quantitative antibody profiling with functional Fc characterization and computational analysis, the approach may provide new insights into the biology of food allergy and identify immune signatures that complement existing diagnostic and clinical measures.

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