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Molecular interface between food allergy diagnosis and treatment: Value of a multi-omics approach

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Abstract

Due to the ever-increasing prevalence of Food Allergy (FA) in the United States, many studies have been conducted to better understand mechanisms of Food Allergy, diagnosis, and treatment. Traditional diagnosis of FA can be time-consuming, less dependable, and can lead to severe allergic reaction in some patients. In this review, the latest evidence on testing, appropriate biomarkers for diagnosis, and treatment options are presented. The benefits of trained immunity (TRIM), oral immunotherapy (OIT), sublingual immunotherapy (SLIT), and Epicutaneous immunotherapy (EPIT) are discussed in this review as well. Common biomarkers of food allergies are discussed, including 2S albumins, T-cells, and basophil activation markers. The benefits of a multi-omics approach are highlighted by the complex nature of food allergies and the relationship between genes, proteins, metabolites, and the microbiome in response to allergens. Future possibilities of omics studies pertaining to food allergies are also presented to guide future research.

Keywords: Food Allergy; Molecular diagnostic; Mast cell; Th2 response; Innate immunity; Immunotherapy; Risk assessment tools; Multi-omics

1. Introduction

A Food Allergy (FA) is characterized by an immune response triggered by eating a certain food. Immune responses to foods are most commonly produced by immunoglobulin E (IgE) antibodies. Almost 90% of food allergies are in reaction to common foods such as milk, peanuts, wheat, fish, tree nuts, shellfish and shrimp, soy, and eggs.[1] Using an "omics" approach to food allergies is increasingly beneficial because the number of individuals with an FA is rising.[6] Traditional methods of testing for and diagnosing an FA focus on a patient's symptomatic response to an allergen. Using a multi-omics approach is beneficial in for the possibility of early diagnosis and desensitization to an allergen to prevent severe reactions. This paper will review and analyze the current and emerging strategies utilized in diagnosing and treating food allergies.

Approximately 8% of children in the United States (U.S.) suffer from at least one FA, while 5% of adults in the U.S. suffer from at least one FA.[6] The number of children affected by food allergies has increased by almost 18% in the past decade.[8] Phenotypically, the individuals with an FA are highly variable regarding age, sex, and economic status.[3] The burden on public health with food allergies can be vast. Generally, Food Allergy testing is covered by insurance, but uninsured individuals and those without access to allergy testing can go without diagnosis and treatment. These individuals can then at risk for severe disease or death. Epinephrine pens are recommended for all individuals with severe food allergies and provide an extra cost to those individuals. Epinephrine pens typically need to be replaced yearly which also adds to the financial burden. It is estimated that the economic cost of FA reaches $25 billion each year. [10].

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2. Molecular diagnosis to assess risk and safety in food allergies

The most common tests for food allergies consist of skin tests, blood tests, and oral food challenges. Allergen skin prick tests (SPTs) can be done by introducing several allergens onto the skin or injected intradermally. The severity of the reaction is measured by the size of the dermal welt developed after a specified time.[8] The amount of histamine released can also be an indicator of allergy severity. Blood tests can be done to measure the amount of IgE antibodies in the blood. Basophil activation tests (BAT) can also be used to determine an allergen's ability to activate basophils. The biomarkers for this test include CD63 and CD203c, which are basophil activation markers.[8] Mast cell activation (MAT) tests have also been found to diagnose food allergies because it is highly specific but less sensitive than BAT.[7] Oral food challenge (OFC) is one of the most accurate ways to determine FA but comes with risks when facing possible anaphylactic responses.[12] Utilizing other tests with reliable biomarkers is much preferred to mitigate the risks of OFC.

Other biomarkers that can be utilized in diagnosing and monitoring food allergies are 2S albumins and T-cells. Bueno-Díaz et al., (2021) studied the role of 2S albumins which are commonly found in seeds and nuts. Mass spectrometry is used to isolate the proteins. The researchers found that these proteins hold their structure well and do not degrade easily with heat. This suggests that these proteins hold their form even with the heat typically used in food processing.[4] Therefore, 2S albumins are commonly found in the body after consumption of seeds and nuts. Individuals with food allergies typically have T-cells that are skewed to proliferate as Th2, while individuals without food allergies have more Th1. These can be monitored in real time during oral immunotherapy (OIT).[12] Monitoring these values over time can determine when foods may be safe to reintroduce in a person's diet.[7]

Emerging science suggests food allergies may have a genetic component and be caused by gene-environment interactions.[9] This provides an ideal opportunity to explore a multi-omics approach to diagnosis, treating, and preventing food allergies. Genomics, proteomics, and metabolomics are essential to understanding gene-environment interactions and the specific proteins in food that commonly cause allergic reactions. Advances in omics technology has provided a wider variety of testing options and has helped researchers better understand the relationship between genes, proteins, metabolites, and the microbiome in response to allergens. [12]

Though food allergies have a great deal of environmental components, Johansson and Mersha (2021) found that most genetic components relating to food allergies are also closely related to immune responses or skin barrier function.[10] The ability to predict future allergy potential would be invaluable for parents and individuals with food allergies and would allow for early exposure and the possibility of desensitization at an earlier age. The improvement in genomics studies have also provided information on the prevalence of FA in racial and ethnic groups. It has been found that African American children are almost four times as likely to have an FA than European American children.[10]

Since the immune system responds in a comparable way with allergies as it does with autoimmune diseases and autoinflammatory diseases, researchers have investigated the similarities in monocyte activity in individuals with these diseases. Trained Immunity (TRIM) or innate immune memory has traditionally been studied in references to those diseases, but it is now being integrated into FA studies. TRIM refers to the phenotypic changes in monocytes that allows for the innate immune system to remember and specialize reactions to certain infections or environmental exposures.[9] Utilizing this process can be used to alter pathways that influence innate immunity and allergy responses.[9]

Food allergies range from a minor allergic response (oral irritation and itchiness) to severe allergic reactions (hives and anaphylaxis).[15] With current techniques, there are no curative options for food allergies.[8] Symptomatic treatment and avoidance of triggering foods are currently the recommendation for individuals with food allergies. Early detection of food allergies could reduce the likelihood of a severe reaction for an unknown food allergy. This would significantly benefit individuals in rural areas or areas where emergency medical care is not easily accessible. In cases of early detection, desensitization can be used to lower the burden of disease.[8] Reduction of severe disease from food allergies can improve overall health outcomes and quality of life.[3]

A variety of techniques for diagnosing and treating food allergies have been emerging in the past several years due to an integration of multi-omics approaches in research. Several forms of immunotherapy have been shown to increase the threshold of an allergen needed for the body to produce a response. These include oral immunotherapy (OIT), sublingual immunotherapy (SLIT), and epicutaneous immunotherapy (EPIT) (Hardy et al., 2019). OIT, SLIT, and EPIT all involve administering different doses of an antigen. OIT especially has shown to improve short-term desensitization in FA patients.[8] Researchers are hopeful that these therapies can provide long-term desensitization, but further studies are needed to confirm this. Nonspecific allergen therapies, including probiotics and modified proteins, are also being studied as treatment options [14].

Though omics has provided an increased knowledge of FA biomarkers some limitations still apply to these diagnostics. The presence of biomarkers does not necessarily equate an allergic response or nonresponse in a patient. Also, some patients are allergic to multiple foods, so OIT is less helpful because it is food specific. Completing several OITs would be time consuming and less realistic for some patients [12].

3. Relevance and Discussion

Omics studies have allowed researchers to better understand the relationship between plant health and the microbiome of the body. Pesticides and antibiotics in the food chain can lead to a decimation of organisms necessary for healthy gut flora. [2] Utilizing this research could be beneficial in better understanding why FA has been increasing in the U.S. population in the past decade. Research has found that nutrients in foods can modify normal methylation patterns in the body and cause allergic reactions.[5] This could lead to further studies to understand this mechanism and how to prevent possible allergy production. Gene editing techniques will also be an area of research to reduce FA prevalence.[11] Using omics, researchers can identify genes that can lead to the transcription of allergen proteins. Gene editing could provide an option to remove or alter allergen proteins in certain foods. Omics can even further provide a look into nutrition in the U.S. by improving food safety along with gene editing techniques to produce more nutritious crops [13].

4. Conclusion

Food allergies are a rising concern across the United States due to increased prevalence. Advances in omics sciences have led to improvements in testing, diagnosis, and treatment by offering safer and more reliable options. Though oral food challenge (OFC) has traditionally been the most accurate test for FA, it comes with severe risks. Newer tests, through omics studies, provide different biomarkers that can be detected like BAT tests, MAT tests, and 2S albumin levels. Techniques like TRIM, OIT, SLIT, and EPIT are useful in immunotherapy treatments for patients as well. These techniques can be implemented along with monitoring of T-cells to provide a patient-specific treatment plan. Omics techniques provide a promising opportunity to better improve food safety and food allergies through gene editing. Omics sciences have been extraordinarily beneficial in the study of food allergies and can continue to contribute to the wealth of knowledge in this field.

Compliance with ethical standards

Disclosure of conflict of interest

The Authors declare no conflict of interest.

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