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Did food allergy develop in the process of animal evolution?

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Abstract
Food allergy is pathophysiologic ally based on stimulation of the immune system at the first exposure, and allergic reactions develop during following exposures. Therefore, memory is the cornerstone of an allergy, as seen in the adaptive immune system. The adaptive immune system was first introduced during evolution in vertebrates, so we can say that invertebrates do not have allergic reactions. We can conclude that food allergy is a complication of animal evolution. Evolution also can cause diseases and complications; therefore, understanding it may help in allergy treatment.
Keywords: Food allergy, Hypersensitivity, Immune system

Dear Editor
Food allergy is a global health problem, and its prevalence is increasing (1). Food allergy is seen in 8% of children and 3%-4% of adults (2). It is responsible for 29%-50% of all anaphylactic reactions (3). Pathophysiology of non-IgE mediated food allergy are cytotoxic reaction, immune complex, or delayed type hypersensitivity reaction (4, 5). Food allergy reactions are regulated by the immune system, in which the adaptive immune system plays a major role. The immune system has improved in the process of evolution, contributing in the formation of allergies. The immune system is responsible for resistance against microorganisms and guarantees existence of creatures. Vertebrates have two immunes systems: innate and adaptive; but invertebrates only have an innate immune system. This system has significantly changed in the process of evolution in order to improve its efficiency. The first adaptive immune system developed 500 million years ago in jawless fish and was based on lymphocytes, which were divided into T- and B-cells in more advanced vertebrae (6). In invertebrate such as starfish, sponge, and tunicate, the immune system is based solely on an innate immune system without lymphocytes (7). The innate immune system is responsible for detecting only a few developed cells, which are mainly microbes. This recognition is based on a pattern recognition receptor (PRR) in which these receptors recognize different parts of microbes, such as gram negative and positive bacteria, viruses, and fungi. The part of the microbe, which is recognized, is called pathogen-associated molecular pattern (PAMP) and is only found in microbes. Another example is the unmethylated CPG DNA sequence, which is seen in microbes and is recognized and deleted by the innate immune system. Bacterial endotoxin, a lipopolysaccharide coating all bacteria, and lipid A, which forms the outer cell membrane, are both part of PAMP. Microbial particles, which are recognized by the innate immune system, are vital parts-microbes cannot exist without them. It is estimated that the innate immune system can recognize 1000 molecular patterns (9). In the innate immune system, PRR works in different ways, e.g., toll-like receptors in the drosophilia fly (8) and interleukin 1 receptors in humans and mammals (11). Invertebrate only have the innate immune system, and, by

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recognizing TRL and/or the C-type lectin receptor by a major signal transduction pathway, it stimulates NF.KB (nuclear factor) and destroys the phagocyted organism (9). The adaptive immune system is seen in vertebrae and has advanced during evolution. Each B- and T-lymphocyte needs to produce a uniquely structured receptor. This process is a somatic recombination, which produces a collection of different and unlimited receptors, each being specific for an antigen. They are able to produce 1015 receptors for immunoglobulin and 1018 for T-cell receptors. Recognition and synthesis of these receptors is based on contact with unknown pathogens. The capability to recognize antigens by somatic recombination is not transmitted to children by genes, whereas, in the innate immune system, the capability of pathogen recognition is transmitted to later generations by natural selection (8, 10).

In vertebrates, not only does the innate immune system react independently, it has a main role in stimulating the adaptive immune system. Dendritic cells are precursors for the innate immune system; therefore, they process antigens by swallowing them and then migrate to draining lymph nodes. During migration they become mature. Dendritic cells secrete chemokines in lymph nodes, which absorb T lymphocytes, leading to transformation of native T-cells into different T-cells such as Th1, Th2, Th17, and regulatory T-cells (8). The innate immune system, the only immune system in invertebrates, does not have a memory, which is also seen in starfish and more developed invertebrates (13). Memory developed in the immune system is 500 million years old, when the first jawed vertebrates were created (stomata and gnash). Most experts consider the immunologic memory as a sign of an adaptive immune system, which is seen in vertebrates (14, 15). The innate immune system has few receptors but recognizes a lot of pathogens, compared with the adaptive immune system, which even recognizes unknown amino acid sequences and saves them in its memory, which can be used rapidly during a second exposure. These amino acids may even be nonmicrobial particles such as food, which can be recognized as a foreign object if the immune system is sensitized, resulting in activation of the adaptive immune system. Food allergy seems to be specifically caused by the adaptive immune system and vertebrates. Even preliminary vertebrates recognize nonpathogenic allergies with difficulty. Food allergies and reaction of the immune system against nonpathogenic antigens will increase with a more potent somatic recombination and a higher recognition ability. The immune system has developed with animal evolution, and it has become an adaptive immune system capable of retrieving 1018 epitopes from an innate immune system with a 1000 epitope recognition capability. This evolution faced complications, such as considering food as a pathogen (called food allergy). Food allergy was not seen in invertebrates. Further research may reveal other diseases caused by evolution, such as autoimmune and rheumatologic diseases, showing hope to discover new treatment modalities.

Conflict of Interest:
There is no conflict of interest to be declared.

Authors' contributions:
All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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