

The human body has an immune system that naturally combats dangers to good health such as infection and allergy. According to Food Allergy Information, 1 to 5% of the global population has exhibited allergy to food.¹ About 90% of allergic reactions are caused by eight types of food: eggs, milk, peanuts, tree nuts, fish, shellfish, wheat, and soy. These foods may cause mild to severe reactions such as rashes, stomach upset, breathing and swallowing problems, and dizziness. The whole body can be at risk especially during anaphylaxis the most severe allergic reaction.² Allergy is a serious condition, and thus introduction of novel food products such as GM food are carefully studied.

How are GM crops tested for allergens

The World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO) established the Codex Alimentarius, a “Food Code” on international food standards, guidelines, as well as codes of practice for the safety, quality, and fairness of international food trade.³ FAO and WHO states in a report on evaluation of GM food allergenicity that:

“...the characteristics of the novel gene products (proteins) must be evaluated in light of their similarities to known food and environmental allergens. In addition, if an examination of the genetically modified food in comparison to its conventional counterpart reveals the presence of any unintended, new proteins resulting from the transformation events, these unintended, new proteins should also be assessed for their possible allergenicity using a similar approach.”⁴

Testing for allergens is therefore conducted at the start of GM crop development and all throughout the research phase. Scientists test if the proteins in the GM crop match a known allergen. If a match is found, additional studies are conducted. If the tests conclude that the GM crop has allergenic potential, then the development of that particular GM crop is stopped completely. On the other hand, if there is no matching protein and known allergen, the research continues but the new trait is continuously monitored for allergenic potential.⁵

The only documented case where allergenicity testing resulted to positive in an experiment was during the development of GM soybean with improved nutritional quality using a Brazil nut protein. The protein was identified as an allergen in the GM soybean variety, which led the scientists to stop the experiment, thus that particular variety of GM soybean did not reach the market.⁶

No commercially available GM crops contain allergens.^{6,7,8} The AllergenOnline database, which is managed by a group of allergy experts from all over the world, lists all known proteins that have been proven or may potentially cause allergic reaction. The database does not show any allergen coming from GM crops.^{8,9}

With the rigorous testing and regulation implemented, consumers are ensured that all GM crops available in the market do not pose allergy risk unless the conventional

counterpart naturally contains allergens.⁸ For instance, if a person is allergic to soybean, he may have allergic reaction to GM soybean because it is compositionally equivalent with conventional soybeans.

Removing allergens through biotechnology

Genetic engineering has been used by scientists to decrease or get rid of plant-derived allergens in food crops through downregulation of deleterious genes or overexpression of preferable genes.¹⁰

An international team of researchers are developing a new variety of wheat with less gluten. They suppressed the enzyme needed in making gluten in wheat, leading to GM wheat plants with 76.4% less gluten in its seeds.¹¹ The study demonstrates that celiac patients may soon get a taste of wheat products like bread without getting sick.

Scientists are also seeking to alleviate peanut allergy using genetic engineering. Ara h 2 protein, the allergen present in peanuts, was successfully eliminated in transgenic peanut seeds using RNA interference or gene silencing. The allergenicity of the transgenic peanut seeds was evaluated using sera from individuals with peanut allergy. Results showed significant reduction in the antibody binding capacity of transgenic seeds compared to wild type.¹²

Expression of tomato allergen Lyc e was downregulated in transgenic tomato plants. The researchers suppressed the accumulation of Lyc e 3 through double-stranded RNAi inhibition leading to reduction of the allergen below detection limit (less than 0.5% of the wild-type protein). The allergenic potential of the transgenic tomato fruits was assessed by measuring the histamine release from sensitized human basophils exposed to transgenic and parental tomato extracts. Results showed significant decrease (10 to 100-fold) in histamine release of human basophils exposed to transgenic tomato extracts as compared with the control.¹³

RNAi technology was also used by scientists in University of Copenhagen to produce hypo-allergenic Elstar apples. Expression of allergen, Mal d 1, was reduced by up to 10,000 fold. The transgenic apple plantlets were grafted to promote development of fruit-producing trees but suppression of the allergen remained the same.¹⁴

In 2007, anti-allergy rice, which has been proven to be effective in treating Japanese cedar pollinosis, was commercialized in Japan. The transgenic rice was developed by scientists from the National Institute of Agrobiological Sciences, Japan. The transgenic rice seeds express *7crp* gene modified cedar pollen allergens (Cry j 1 and 2) which give low antibody reaction but contain seven major human T-cell epitopes. These trigger mucosal immune tolerance to cedar pollen allergens. The anti-allergt GM rice is also considered as an edible vaccine against cedar pollen allergy.^{15, 16, 17}

One of the common fears about biotechnology is that it may cause introduction of new allergens in food. However, no GM crops have been reported and documented to actually cause allergic reactions because of the rigorous monitoring conducted in all phases of GM crop development. Instead of causing harm, biotechnology actually provides solution to allergy problems by enabling development of allergen-free or hypoallergenic food crops. These crops, when commercialized, will bring allergy-

relief in the future and at the same time address malnutrition especially in developing countries.

References

1. Food Allergy Information. n.d. How Many People are Affected by Food Allergy? http://www.foodallergens.info/Facts/How_Many.html.
2. American College of Allergy, Asthma, and Immunology. 2014. Types of Allergies: Food Allergy. <http://acaai.org/allergies/types/food-allergy>.
3. FAO. 2016. About CODEX. <http://www.fao.org/fao-who-codexalimentarius/about-codex/en/>.
4. FAO and WHO. 2001. Evaluation of Allergenicity of Genetically Modified Foods. <http://www.fao.org/docrep/007/y0820e/y0820e04.htm>.
5. GMO Answers. 2016. How are GMOS Tested for Allergies? <https://gmoanswers.com/studies/infographic-how-are-gmos-tested-allergies>.
6. GMO Answers. 2014. Are GMOs are Causing an Increase in Allergies? <https://gmoanswers.com/ask/are-gmos-are-causing-increase-allergies-submitted-part-gmo-answers-top-consumer-questions-survey>.
7. Food Allergy Information. n.d. GMO and Food Allergy. <http://www.foodallergens.info/Facts/GMO.html>.
8. Genetic Literacy Project. 2014. Are GMOs Causing an Increase in Allergies? <https://www.geneticliteracyproject.org/2014/04/16/are-gmos-causing-an-increase-in-allergies/>.
9. University of Nebraska-Lincoln. 2016. AllergenOnline. <http://www.allergenonline.org/>.
10. Gallo M. and Sayre R. 2009. Removing Allergens and Reducing Toxins from Food Crops. *Current Opinion in Biotechnology* 20(2): 191-96. <http://www.sciencedirect.com/science/article/pii/S0958166909000330>.
11. Wen, S., N Wen, J Pang, G Langen, RA Brew-Appiah, JH Mejias, C Osorio, M Yang, R Gemini, CP Moehs, RS Zemetra, KH Kogel, B Liu, X Wang, D von Wettstein, and S Rustgi. 2012. Structural Genes of Wheat and Barley 5-Methylcytosine DNA Glycosylases and their Potential Applications for Human Health. *PNAS* 109(50): 20543-8. <https://www.ncbi.nlm.nih.gov/pubmed/23184965>.
12. Hortense D., K Konan, F Chen, M Egnin, and O Viquez. 2007. Alleviating Peanut Allergy Using Genetic Engineering: The Silencing of the Immunodominant Allergen Ara h 2 Leads to Its Significant Reduction and a Decrease in Peanut Allergenicity. *Plant Biotechnology Journal* 6(2): 135-145. <http://onlinelibrary.wiley.com/doi/10.1111/j.1467-7652.2007.00292.x/abstract>.
13. Lien QL, Y Lorenz, S Scheurer, K Fötisch, E Enrique, J Bartra, S Biemelt, S Vieths, and U Sonnewald. 2006. *Plant Biotechnology Journal* 4(2): 231-242. <http://onlinelibrary.wiley.com/doi/10.1111/j.1467-7652.2005.00175.x/full>.
14. Krath, BN, FD Eriksen, BH Pedersen, LJWJ Gilissen, WE Van De Weg, and LO Dragsted. 2009. Development of Hypo-allergenic Apples: Silencing of the Major Allergen *Mal d 1* Gene in 'Elstar' Apple and the Effect of Grafting. *The Journal of Horticultural Science and Biotechnology* 84(6): 52-57. <http://www.tandfonline.com/doi/abs/10.1080/14620316.2009.11512595>.
15. ISAAA's GM Approval Database. 2012. Event 7Crp#10. <http://www.isaaa.org/gmapprovaldatabase/event/default.asp?EventID=223&Event={recEvents.EventName}>.

16. Takagi, H, T Hiroi, L Yang, Y Tada, Y Yuki, K Takamura, R Ishimitsu, H Kawauchi, H Kiyono, and F Takaiwa. 2005. A Rice-based Edible Vaccine Expressing Multiple T Cell Epitopes Induces Oral Tolerance for Inhibition of Th2-mediated IgE Response. PNAS 102(48): 17525-17530.
<https://www.ncbi.nlm.nih.gov/pubmed/17276883>.
17. Wakasa, Y, H Takagi, S Hirose, L Yang, M Saeki, T Nishimura, O Kaminuma, T Hiroi, and F Takaiwa. 2013. Oral Immunotherapy with Transgenic Rice Seed Containing Destructed Japanese Cedar Pollen Allergens, Cry j 1 and Cry j 2, against Japanese Cedar Pollinosis. Plant Biotechnology Journal 11(1): 66-76.
<https://www.ncbi.nlm.nih.gov/pubmed/17714439>.

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