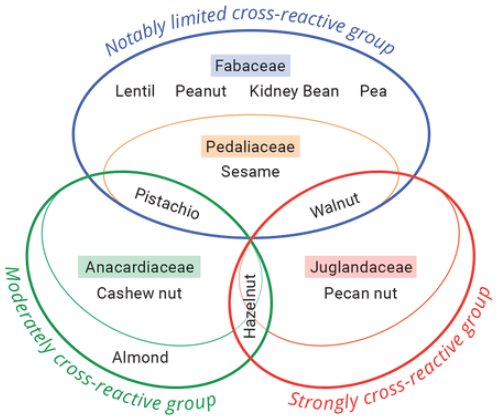
Food Allergy Institute

Why is Biosimilar Protein Matching Important in the Tolerance Induction Program?



We study and leverage taxonomic relationships to identify and predict **biosimilar proteins** to treat a vast array of food allergies. Biosimilar proteins are safe, non-allergenic proteins that mimic the molecular structure of an allergic protein but do not elicit a reaction.

The **Tolerance Induction Program** reconditions the immune system to tolerate allergic proteins by introducing biosimilar foods, leading to a decrease in allergen-specific IgE, an increase in IgG4, and immune modulation (B Cells and T Cells) that reduces allergic reactions.

Another key aspect of **biosimilar components** is their interaction with IgE-binding antibody domains. These domains are categorized into protein "superfamilies" based on their botanical classification. The binding of IgE to these domains is analyzed using **component-resolved diagnostics** (CRD), which provides a detailed assessment of specific allergic responses.

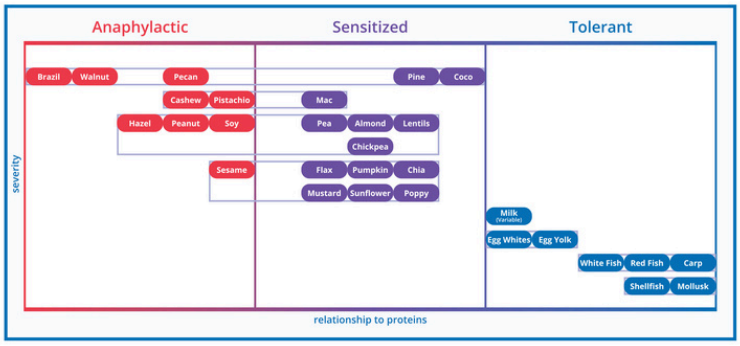
Protein Superfamily	Cupin			Prolamin		
Protein family	Vicilin or 7S globulin	Legumin or 11S globulin		2S albumin		nsLPT
Allergen	Ara h 1	Ara h 3	Ara h 2	Ara h 6	Ara h 7	Ara h 9
Isoallergen (UniProt)	Ara h 1.0101 (P43238)	Ara h 3.0101 (O82580) Ara h 3.0201 (Q9SqH7)	Ara h 2.0101 (Q6PSU2) Ara h 2.0201 (Q6PSU2)	Ara h 6.0101 (Q647G9)	Ara h 7.0101 (Q9SQH1) Ara h 7.0201 (B4XID4)	Ara h 9.0101 (B6CEX8) Ara h 9.0201 (B6CG41)
Molecular mass (kDa) and theoretical pI	monomer 63.5 kDa; pI 4.6 occurs as trimer of 180 kDa	monomer 60.0 kDa; pI 4.6 occurs as hexamer of 360 kDa	16.6 kDa; pI 5.8 18.0 kDa; pI 5.5	15.0 kDa; pI 5.5	16.4 kDa; pI 5.6 17.4 kDa; pI 7.5	9.1 kDa; pI 9.5 9.1 kDa; pI 9.3
Representative protein structure						
	Ara h 1PDB: 3S7E [34]	Ara h 3 PDB: 3C3V [47]	Ara h 6 PDB: 1W2Q [63]			Pru p 3 PDB: 2 ALG [115]
Biological function	provide nourishment for the growth of the seedling		sources of amino acids for growth of seedlings; involved in defense against pathogens			involved in defense against pathogens and in the formation of hydro-phobic layers in plant
Prevalence of IgE binding	30-80% [17, 83]	16-57% [17, 83]	42-100% [116, 83]	86-92% [79, 116]	43% [79]	8-60%, strong association with peach allergy [84, 83]
Cross-reactivity	with other legume and tree nut vicilins and Ara h 2 and Ara h 4 [43, 11]	with other legumes and tree nut legumins and Ara h 1, 2, and 6 [43, 11]	with 2S albumins from almond and Brazil nut, and Ara h 1, 3, and 6 [11, 26]	with Ara h 1, 2, 3 [11]	not known	with peach and hazelnut nsLTPs (Pru p 3 and Cor a 8) [84]

As noted by Bublin et al (https://link.springer.com/article/10.1007/s11882-014-0426-8), the specific protein superfamilies are unique but shared across different allergens such as peanuts, seeds, tree nuts and grains. The IgE binding to some domains is well described and potentially available as a commercial blood test. However, others are available only for research purposes only.

Retraining The Body's Immunoresponse

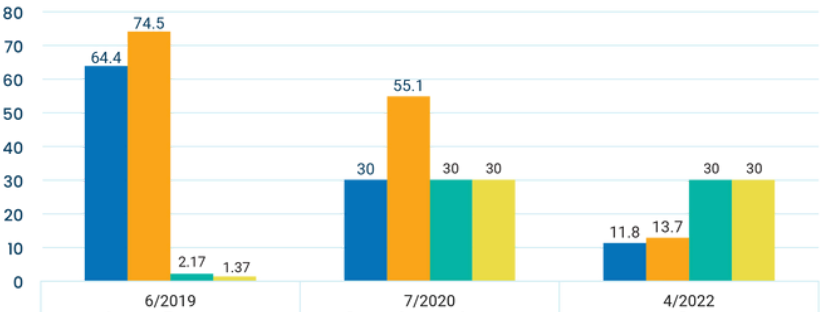
Our proprietary machine-learning systems leverage patient diagnostic data and medical history to generate a highly accurate **Allergy Snapshot**, a visual representation of a patients allergen sensitivities, including specific proteins and severity. This Snapshot serves as the foundation for a **data-driven Food Dosing Strategy**, which precisely calculates the milligrams of food needed to retrain the immune system and achieve food allergy remission. Through extensive diagnostics and lab work trends, including shifts in IgE and IgG4 levels, TIP systematically moves allergens toward the tolerant column, guiding each patient toward sustained unresponsiveness.

Allergy Snapshot



Food Dosing Strategy

Lab Work Trend



	6/2019 Starting Treatment	7/2020 Before Starting Cashew	4/2022 Annual Remission
Pistachio IgE	64.4	30	11.8
Cashew IgE	74.5	55.1	13.7
Pistachio IgG4	2.17	30	30
Cashew IgG4	1.37	30	30