Research Letter

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Examination of Homologies between COVID-19 Vaccines and Common Allergens: The Potential for T Cell-mediated Responses for Allergic Rhinitis and Asthma

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Abstract

As the SARS-CoV-2 virus shares relatively large protein sequences homologous to grass pollens, dust mites, and molds, our objective was to assess the potential overlap between the COVID-19 mRNA vaccines from Pfizer-BioNtech and Moderna and known allergens. We found 7 common allergens with potential for cross-reactivity with the Pfizer vaccine and 19 with the Moderna vaccine, including common grasses, molds, and dust mites. T-cell mediated antigen cross-reactivity between viruses and allergens is a relatively new area of study in clinical immunology; a discipline that may be particularly useful regarding the SARS-CoV-2 virus and the allergic response in humans. These results suggest that vaccination with the Pfizer-BioNtech and Moderna COVID-19 vaccines may contribute to T-cell cross-reactivity with allergens that impact allergic asthma and allergic rhinitis. Further research should assess the clinical implications of COVID-19 vaccination on the severity and symptomatology of the allergic disease, in addition to natural viral infection.

Keywords: Rhinitis, allergic; Allergy; COVID-19; Cross-reactivity; mRNA; Vaccines

Amid the COVID-19 pandemic, it is prudent to determine the potential connection between COVID-19 vaccines and the severity of allergic rhinitis and allergic asthma. Skevaki et al. established that infection from influenza A strain H1N1 in mice served as a mediating factor of severe complications of allergic disease, presenting virus-mediated T-cell cross-reactive responses as a potential protective mechanism in asthma.[1] In the aforementioned study, when presented with an allergen challenge designed to induce allergic airway inflammation, previous influenza infection in mice proved to mitigate future allergic airway reactions. Specifically, according to this study, mice previously infected with influenza experienced decreased mucus production, decreased production of inflammatory Th2 cytokines and thereby eosinophils, and an overall improvement in airway inflammation when presented with an aerosol challenge that historically provokes physiologic effects of asthma. Virus-specific memory T-cell cross-reactivity has previously been shown in other studies regarding pathogens[2,3] and allergens,[4] linking autoimmune responses to certain protein sequences via molecular mimicry.[5]

Further, Balz et al. showed that the SARS-CoV-2 virus shares relatively large protein sequences homologous to grass pollens, dust mites, and molds,[6] thus post-infection, SARS-CoV-2 oriented T-cells may provide a mediated immune response to these allergens. In the context of allergic rhinitis and allergic asthma, an increasing pool of cross-reactive memory T-cells may play an important role in protection against T-cell-mediated chronic inflammation; however, induced immunopathology must also be considered.

Given the protective factor of COVID-19 vaccines against the virus and their mass distribution, our objective was to explore the potential overlap between the COVID-19 mRNA vaccines from Pfizer-BioNtech and Moderna and known allergens indexed through the University of Nebraska's Food Allergy Research and Resource Program (FARRP) Allergen Protein Database (allergenonline.org) and the FASTA tool, using the BLOSUM50 scoring matrix as previously published.[7] Given the Codex Alimentarius Commission recommendation likelihood of cross-reactivity criteria, we reported allergens with 35% (or greater) similarity over segments of 80 amino acids (Criteria A) and those with short (8 or more amino acids) identical matches (Criteria B).

For the Pfizer vaccine, we identified one allergen meeting Criteria A, from pine nuts, and six that met Criterion B from Tufted Grass and Alternaria alternata, the most common fungal allergen associated with asthma [Table 1].[8] For the Moderna vaccine, we found 7 allergens meeting Criteria A and 12 that met Criteria B. Allergens meeting Criteria A included spreading pellitory (grass), lipocalin from guinea pigs, ragweed, wheat endosperm, sesame, and dust mites. Allergens that met Criteria B were Kentucky blue, cat, and Timothy grasses, and *Penicillium crustosum* (mold) [Table 2].

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Table 1: Allergens with 35% (or greater) similarity over segments of 80 amino acids (Criteria A)

Allergen (species)	Common name	IUIS[a] allergen	NCBI reference no.[b]	Highest % seq. ID	Percent similarity (%)
Moderna					
Parietaria judaica	Spreading pellitory	Par j 2.0102	1532056	32.40	85.30
Cavia porcellus	Guinea pig	Cav p 1.0102	1604536257	23.20	75.40
Ambrosia artemisiifolia	Short ragweed	Unassigned	291482308	50.00	74.10
Ambrosia artemisiifolia	Ragweed	Unassigned	291482310	44.40	62.50
Triticum aestivum	Wheat	Unassigned	21743	12.90	62.30
Sesamum indicum	Sesame	Ses i 3.0101	13183177	14.40	59.40
Dermatophagoides farinae	Dust mites	Der f 15.0101	5815436	17.20	57.10
Pfizer					
Pinus koraiensis	Pine nuts	Pin k 2.0101	567773309	18.30	63.30

[a]Column presents the systematic allergen nomenclature recognized by the International Union of Immunological Societies (IUIS; https://iuis.org/) and World Health Organization.

[b]The National Center for Biotechnology Information (NCBI) reference no. is searchable within the United States National Library of Medicine's protein database (https://www.ncbi.nlm.nih.gov/protein/).

Both vaccines showed matching sequences (Criteria B) with perennial ryegrass.

T-cell mediated antigen cross-reactivity between viruses and allergens is a relatively new area of study in clinical immunology; a discipline that may be particularly useful regarding the SARS-CoV-2 virus and the allergic response in humans. Considering our findings of homologous overlap between known allergens and the Pfizer and Moderna vaccines, an altered T-cell mediated immune response may be observed in persons with allergic asthma and allergic rhinitis after vaccination, with Pfizer or Moderna mRNA vaccines, against SARS-CoV-2.

Our findings also contribute to the growing literature regarding the "old friends" hypothesis—persons exposed to infectious agents throughout childhood are less likely to experience histamine-mediated reactions to allergens.[9] While the previously mentioned correlations between influenza infections in mice models and allergic responses[1] support the heterologous immune reactivity theory, this study assessed the potential cross-reactivity among COVID-19 vaccines and common allergens. These results suggest that vaccination with the Pfizer-BioNtech and Moderna COVID-19 vaccines may contribute to T-cell cross-reactivity with allergens that impact allergic asthma and allergic rhinitis. Further research should assess the clinical implications of COVID-19 vaccination on the severity and symptomatology of the allergic disease, in addition to natural viral infection.

Limitations of the study were that only sequenced allergens within the FARRP database were analyzed, which may exclude other potential cross-reactive proteins. Further, these overlaps do not establish cross-reactivity—simply that it may exist. Additionally, the protein composition ratio and amino acid structural style may also play a role in this function. Further research is needed to establish evidence of allergen mediation, histamine activation, or reduction of asthma symptomatology after vaccination.

Table 2: Allergens with ≥ 8 sequential amino acids match (Criteria B)

Allergen	Common name	IUIS[a] allergen	NCBI reference no. GI Classification[b]
Moderna			
Penicillium crustosum	Fungus	Pen cr 26.0101	371537645
Corylus avellana	Hazelnut	Cor a 13.0101	29170509
Lolium perenne	Perennial ryegrass	Unassigned	4416516
Lolium perenne	Perennial ryegrass	Unassigned	6634467
Phleum pratense	Timothy grass	Unassigned	345108717
Poa pratensis	Kentucky bluegrass	Unassigned	113560
Poa pratensis	Kentucky bluegrass	Unassigned	113562
Poa pratensis	Kentucky bluegrass	Unassigned	539056
Poa pratensis	Kentucky bluegrass	Unassigned	113561
Dactylis glomerata	Orchard	Unassigned	14423124
Dactylis glomerata	Orchard	Unassigned	18093971
Holcus lanatus	Velvet grass	Hol l 5.0101	2266625
Pfizer			
Lolium perenne	Perennial ryegrass	Unassigned	4416516
Holcus lanatus	Velvet grass	Hol l 5.0101	2266625
Alternaria alternata	Fungus	Alt a 5.0101	1850540
Alternaria alternata	Fungus	Unassigned	1173071
Davidiella tassiana	Fungus	Cla h 5.0101	5777795
Fusarium culmorum	Fungus	Fus c 1.0101	19879657

[a]Column presents the systematic allergen nomenclature recognized by the International Union of Immunological Societies (IUIS; https://iuis.org/) and World Health Organization.

[b]The National Center for Biotechnology Information (NCBI) reference no. is searchable within the United States National Library of Medicine's protein database (https://www.ncbi.nlm.nih.gov/protein/).

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Conflicts of Interest

None.

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