

Homologous allergens: A regulatory and clinical perspective

The last decade has ushered new data on the allergenic molecules. Allergens from identical protein families are now known to be present in different allergen sources and are labeled as homologous allergens. An important fact for such allergens is that they may be present among different sources, and their presence is not conditional to taxonomical relationship. These allergenic molecules express sequence identity and clinical cross-reactivity. This principle of homologous allergens was brought forward by Lorenz *et al.*^[1] They also suggested that “classification of allergen sources in one homologous group on the basis of homology and cross-reactivity of allergens is more specific and satisfactory than mere taxonomic relationship.”^[1]

The criteria to classify allergens as “Homologous allergens” is as follows:^[1]

1. “The allergen sources have comparable physicochemical and biological properties, i.e., they derive from comparable tissues and therefore are alike in the overall composition of proteins, carbohydrates, lipids, enzymes, and water content”
2. Demonstration of “cross-reactivity between the allergen sources shown by cross-reactivity of single allergens or the whole extracts”

The first criteria helps in differentiating separate allergens from the same source (e.g., wheat pollen allergens are different from wheat grain allergens; however, wheat pollen is homologous to many grass pollen). The second criteria of cross-reactivity is linked with homology of allergens belonging to identical protein families with a high degree of sequence identities at protein or cDNA level.^[1] The proposed list of homologous allergens is captured in Table 1.^[1,2] The allergens which have been categorized in Table 1 are well studied in different geographies and are well characterized.

From the regulatory perspective for marketing authorization applications, “homologous allergens” fulfill the following criteria:^[1]

1. Comparable physicochemical and biological properties of the source materials
2. Cross-reactivity/structural homology of allergens
3. Identical formulation of the final products and
4. Identical production process of the allergen extracts.

For India, allergens such as the house dust mites (*Dermatophagoides* sp.), Pooideae grass pollen, and

for mountainous regions, the birch group allergens are important. In recent years, several government schemes are promoting plantation of olive trees in the state of Rajasthan. Clinicians and researchers should evaluate the allergenic impact of olive in Indian context.

It should also be noted that data on homology of some Indian-specific allergens such as *Holoptelea integrifolia*, *Prosopis juliflora*, and others are missing.

Regulatory Perspective

It is recognized that determination of all relevant parameters for the allergens within a given extract or a defined allergen extract mixture is impossible. Therefore, the concept of homologous allergens has been introduced and recognized.^[2]

Within the homologous group, one member is selected as the representative species. Data (limited) from the representative allergen can be extrapolated to other members from the same groups. The extrapolated data can include data on quality, safety, and efficacy.^[2]

Importantly, as noted above, some allergens are not included in the homologous allergens. For these, the data for quality, safety, and efficacy have to be provided for each individual product.^[2]

Clinical Perspective

For a clinician, the knowledge of homologous allergens can be utilized for formulating and prescribing allergen immunotherapy.

If a patient is allergic to allergens within a homologous group (such as *Dermatophagoides* species or Pooideae pollens), the use of a single course of AIT with a mixture of allergens that mimics natural exposure is recommended. Examples of such situations are:

- Patient allergic to house dust mites of *Dermatophagoides* species:
 - › A mixture of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* can be used.
- Patient allergic to Pooideae (grass) pollen, such as *Lolium perenne*, *Poa pratensis*, and *Phleum pratense*:
 - › A mixture of the homologous grass allergens can be used.

Table 1: List of homologous allergens

Tree pollen		
The “birch group” or “fagales group”	The group of <i>Oleaceae</i>	The group of <i>Cupressaceae</i>
<i>Betula verrucosa</i> = <i>B. pendula</i> = <i>B. alba</i> (European white birch)	<i>Olea europaea</i> (Olive)	<i>Juniperus</i> sp. (Cedar)
<i>Alnus glutinosa</i> (Alder)	<i>Fraxinus excelsior</i> (Ash)	<i>Cupressus</i> sp. (Cypress)
<i>Carpinus betulus</i> (Hornbeam)	<i>Ligustrum vulgare</i> (Privet)	
<i>Corylus avellana</i> (Hazel)	<i>Syringa vulgaris</i> (Lilac)	
<i>Quercus alba</i> (Oak)		
<i>Castanea sativa</i>		
<i>Fagus sylvatica</i>		
Grass pollen		
The group of sweet grasses of the <i>Poaceae</i> (<i>Gramineae</i>) family, subfamily of <i>Pooideae</i>	Additional grass species belonging to the homologous group of <i>Pooideae</i> with reservations	
<i>Anthoxanthum odoratum</i> (Sweet vernal)	<i>Agropyron</i> sp. (Couch grass)	
<i>Avena sativa</i> (Oat)	<i>Agrostis</i> sp. (Bent grass)	
<i>Dactylis glomerata</i> (Orchard grass)	<i>Alopecurus pratensis</i> (Meadow foxtail)	
<i>Festuca</i> sp. (Meadow fescue)	<i>Arrhenatherum elatius</i> (False oat)	
<i>Holcus lanatus</i> (Velvet grass/Yorkshire fog)	<i>Bromus</i> sp. (Brome grass)	
<i>Hordeum vulgare</i> (Barley)		
<i>Lolium perenne</i> (Perennial ryegrass)		
<i>Phleum pratense</i> (Timothy grass)		
<i>Poa pratensis</i> (Kentucky bluegrass)		
<i>Secale cereale</i> (Cultivated rye)		
<i>Triticum aestivum</i> (Cultivated wheat)		
Weed pollen		
<i>Ambrosia artemisiifolia</i> , <i>Ambrosia trifida</i> (Ragweed)		
<i>Artemisia vulgaris</i> (Mugwort)		
<i>Parietaria judaica</i> , <i>Parietaria officinalis</i> (Pellitory)		
Mites		
The group of house dust mites of the <i>Dermatophagoides</i> genus		
<i>Dermatophagoides pteronyssinus</i>		
<i>Dermatophagoides farinae</i>		
Please note		
Allergens not mentioned in the table but belonging to the different groups captured above are labeled as “nongrouped species” and justification for their inclusion is required. For example, <i>Cynodon dactylon</i> , a grass-pollen, is not included in the homologous allergens for grass pollen		
No homologous groups have been defined for molds, vertebrates, and insect venom		

If the patients are exposed and sensitized to allergen isoforms originating from two or more species in the group, they will develop antibody and T cell responses to both cross-reactive and noncross-reactive epitopes. Therefore, a mixture of the species will provide a broad spectrum of allergens identified by the patient and will lead to therapeutic responses.^[3]

If patients recognize and react to nonhomologous allergens, the allergens should be given as individual allergens as there are no large evidences supporting the use of allergen mixtures. If mixtures are utilized, the following points can be kept in mind:^[2,3]

- Do not use allergens with proteolytic activities in mixtures
- Perennial and seasonal allergens should not be mixed
- Hymenoptera venoms should not be mixed with any other allergens
- Venoms from different genera should not be mixed

- Possible antigenic competition.

Conclusion

Emerging evidences have let the scientific committees to focus on the concept of homologous groups. This concept is important for both regulators and clinicians who can utilize this information in decision-making algorithms.

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References

1. Lorenz AR, Lüttkopf D, May S, Scheurer S, Vieths S. The principle of homologous groups in regulatory affairs of allergen

- products – A proposal. *Int Arch Allergy Immunol* 2009;148:1-7.
2. Committee for Medicinal Products for Human Use. Guideline on Allergen Products: Production and Quality Issues. EMEA/CHMP/BWP/304831/2007; 2008.
3. Demoly P, Passalacqua G, Pfaar O, Sastre J, Wahn U. Management of the polyallergic patient with allergy immunotherapy: A practice-based approach. *Allergy Asthma Clin Immunol* 2016;12:2.

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