Clustering of Tree Allergen Components and Phylogenetic Analysis of Patient Profiles Reveal Key Combinations for Allergen Immunotherapy

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BACKGROUND AND AIMS

Polysensitisation to tree pollen allergens is a central challenge in the diagnosis and management of respiratory allergy, particularly in regions spanning multiple bioclimatic zones. Identifying the molecular architecture of sensitisation profiles rather than relying solely on whole-allergen extracts is increasingly recognised as essential for effective allergen immunotherapy (AIT). This study applied component-resolved diagnostics and bioinformatic clustering to characterise real-world sensitisation patterns across Ukraine.[1]

MATERIALS AND METHODS

Data were drawn from 7,518 individuals from 17 Ukrainian regions who were sensitised to tree pollen components and tested between 2020–2022, using the ALEX multiplex microarray platform (Macro Array Diagnostics, Vienna, Austria; 295 allergen components). Agglomerative clustering with Ward's method was applied to all 295 molecular components to identify co-sensitisation patterns. The most frequent allergen combinations (pairs, triplets, and four- or five-molecule sets) within patient profiles were enumerated computationally. Phylogenetic analysis of allergen amino acid sequences, using the Multiple Alignment using Fast Fourier Transform (MAFFT), Multiple Sequence Comparison by Log-Expectation (MUSCLE), and ClustalW alignment algorithms with the Iterative Quick Tree (IQ-TREE) maximum-likelihood framework, was performed to compare biologically driven groupings against clinical clustering.

RESULTS

Clustering analysis revealed that most allergen groupings aligned with established biochemical classes: pathogenesis-related protein 10 (PR-10) proteins (Bet v 1, Aln g 1, Cor a 1.0103, Fag s 1, Mal d 1), non-specific lipid transfer proteins (Pla a 3, Cor a 8, Mal d 3), profilins (Bet v 2, Hev b 8), and pectate lyases (Cry j 1, Amb a 1), each formed coherent, phylogenetically supported clusters. The most frequent binary sensitisation combination was co-reactivity to the pectate lyases Amb a 1 (ragweed) and Cry j 1 (Japanese cedar/Cupressaceae), reflecting cross-reactivity to ragweed with ornamental conifers widely planted in Ukrainian cities. Co-sensitisation to Bet v 1 and the food homologue Mal d 1 (apple) was found in 23.1% of tested individuals, a prevalence equal to that of the Bet v 1 – Amb a 1 combination and a clinically recognised predictor of pollen-food allergy syndrome. The major cat allergen Fel d 1, despite lacking structural homology to any tree allergen, recurred prominently in triplet and higher-order profiles alongside pollen molecules; a pattern attributed

to its adjuvant-like ubiquity in indoor environments rather than cross-reactivity. Grass components (Phl p 1, Lol p 1, and notably the subtropical Cyn d 1) appeared in approximately one-fifth of complex profiles, suggesting climate-driven northward migration of southern species and an extension of the effective allergy season.

CONCLUSION

The integration of clinical clustering with phylogenetic analysis demonstrates that co-sensitisation in this population is driven by a combination of protein homology, regional ecology, and indoor allergen exposure rather than by random accumulation. The dominant molecular nodes identified (PR-10 proteins and pectate lyases, each affecting over 40% of sensitised individuals) provide a rational basis for designing precision allergen immunotherapy formulations. The authors propose that Cry j 1 positivity in cedar-free zones should be interpreted as a marker for local Cupressaceae cross-reactivity, that early detection of Bet v 1 and Phl p 1 sensitisation in children should prompt prophylactic intervention, and that urban landscaping policy should consider the allergenic burden of ornamental tree selection. Further investigation into cross-kingdom sensitisation pathways and the immunological basis of phylogenetically non-obvious allergen clusters is warranted.

Reference

1. Yasniuk M et al. Clustering of tree allergen components and phylogenetic analysis of patient profiles reveal key combinations for allergen immunotherapy. Abstract 001848. EAACI Congress, 12-15 June, 2026.