

TITLE – From allergy risk assessment across Europe towards guiding immunotherapy in clinical practice – computational analysis of allergy-related antibody signatures.

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Background

Allergies are a major public-health burden with a prevalence up to 40%. The underlying immune mechanism, based on a hypersensitivity reaction to normally harmless molecules of our environment, includes the production of allergen specific IgE-antibodies. We aimed to develop a new computational workflow to analyze complex allergy-related antibody signatures, for use in both epidemiology and clinical practice.

Methods

We analyzed deep serum IgE signatures in dogs living in 30 different European countries. Unsupervised clustering was applied to identify IgE patterns for correlations to local pollen exposure (Copernicus database). This computational pipeline was then applied to human IgE and IgG4 signatures, which were measured during oral immunotherapy, for correlation with treatment outcome.

Results

Using a total of N=5,585 samples (1.3 Mio data points), we identified 11 clusters of sensitization across Europe that were found to be dependent on the regional origin of the sera ($P < 0.0001$). Amongst the significant allergens, >90% were found to be relevant for human allergies, e.g. pollen allergens. Pollen allergen clusters correlated with regional pollen exposure, reiterating their interpretability and relevance in the human context. We then succeeded to apply the data clustering tool on a cohort of food-allergic children undergoing oral immunotherapy (12,600 data points). We revealed that patients with successful therapy outcome had significantly stronger IgG4 signatures, reflecting immune adaptability and plasticity, developing during the therapy and after successful desensitization ($P < 0.05$).

Conclusion

Overall we successfully established a data analysis workflow for complex antibody profiles in the allergy context with relevant information for clinical practice.

BIOSKETCH

(Maximum one page)

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