March 23, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16640-edited.doc).

Title: Cross-reactivity between aeroallergens and food allergens

Author: Florin-Dan Popescu

Name of Journal: *World Journal of Methodology*

ESPS Manuscript No. 16640

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers

Point-by-point responses are presented below.

Reviewer #1 (02520369) wrote:
the author give an extensive overview for the syndromes and associations related to cross-reactive allergen components, the impact of relevant cross-reactivities between aeroallergens and food allergens, and the molecular-based allergy diagnostic. I do not know any other article summarizing the cross-reactivity between aeroallergens and food allergens. Therefore, I would recommend accepting this article for publication.

Response: I thank the reviewer for the very supportive comments regarding the extensive overview, the originality and uniqueness of the editorial. I also thank the reviewer for considering my manuscript very good, with a grade A (priority publishing) as language evaluation.

Reviewer #2 (02506941) wrote:
very well written paper, a lot of clinically significant facts discussed, over a broad number of interactions. A synthetic table of crossreactive allergens would be of use.

Response: I thank the reviewer for considering my editorial manuscript very well written, with many clinically significant aspects and interactions discussed. As suggested, I created three synthetic tables of cross-reactive allergens. I also thank the reviewer for considering my manuscript very good, with a grade A (priority publishing) as language evaluation.

Reviewer #3 (00053644) wrote:
the manuscript "Cross-reactivity between aeroallergens and food allergen" has an important significance of research, is presented very well and is easily readable. The title reflects the content of the study, but the main and short titles are the same, it would be better to distinguish them. The abstract provides a clear delineation and presents the significant points related to the research background and conclusions. Table 1 is not comprehensive nor exhaustive. It would be preferable to add additional tables or figures that summarize the main data and make reading of the manuscript more fluent.

Response: I thank the reviewer for considering my editorial presentation of significantly important research data from the literature as being very well presented and easily readable. As suggested, I changed the main and short titles in order to better distinguish them, and instead of one table, I created three synthetic tables to summarize the main data presented, and to make the reading more fluent. I also thank the reviewer for considering my manuscript very good, with high priority for publication.

Reviewer #4 (02445848) wrote:
the manuscript is well presented, clearly written and easy to read. I would suggest only minor modifications: 1) Modify the short title 2) I would suggest to have more tables summarizing the presented data, with particular regard to potential clinical applications 3) If possible, more deeply discuss the potential clinical applications (practical advices).

Response: I thank the reviewer for appreciating my editorial presentation as being well presented, clearly written and easy to read. (1) As mentioned, I changed the short titles in order to better distinguish them. (2) As suggested, instead of one table, I created three synthetic tables to summarize the main data presented, and I mention that the syndromes and associations mentioned in the tables are with particular regard and according to the recent expert system for the clinical interpretation of allergen microarray results, recently published in the World Allergy Organization Journal [Melioli G, Spenser C, Reggiardo G, et al. *World Allergy Organ J* 2014; 7(1): 15, DOI: 10.1186/1939-4551-7-15 PMID: 24995073]. (3) In order to more deeply discuss the potential clinical applications, as suggested, I added two paragraphs in the *Conclusions*, with two more references: "Because the era of the characterization of molecular features of food allergens has begun, new data started to bring useful information about cross-reactivity between different sources of food allergens and aeroallergens in order to help the clinicians to provide appropriate prophylaxis approach, and to estimate the types and severity of allergic reactions [Valenta R, Hochwallner H, Linhart B, et al. *Gastroenterology*. 2015 Feb 10. DOI: 10.1053/j.gastro.2015.02.006 PMID: 25680669]. Component-resolved diagnosis is a research method that explains on molecular level allergen cross-reactivity, and allows to distinguish cross-reactions occurring after ingestion of food in patients with IgE sensitization primarily to aeroallergens from the coexistence of inhaled and food allergies. Due to the geographic diversity resulting in different exposure to airborne allergens and dietary factors, studies on allergen components in populations living in different climatic zones give different results. This suggests that the diagnostic and prognostic assessment based on the component-resolved diagnosis results is limited and should always be considered in clinical context [Balińska-Miśkiewicz W. *Postepy Hig Med Dosw*. 2014; 68: 754-67 PMID: 24934534]. I also thank the reviewer for considering my manuscript very good, with priority publishing.

Reviewer #5 (01884933) wrote:
here are my comments and advices on this manuscript: 1. In the introduction, is class 1,2 food allergy related to other contents? If so, please describe further. Otherwise it seems unnecessary. 2. You should make tables and figures with materials having cross-reactivity. 3. Delete one 'mite' from 'mite mite-shrimp' in abstract. 4. Please, change bold lettering in article to normalize type. 5. Unify the font size of all texts in paper. 6. Please clarity the table 1 easy to understand.

Response: I thank the reviewer for the comments and useful advices. Revisions have been made according to the suggestions of the reviewer: (1) In the introduction, regarding the class 1 and 2 food allergy, I rewrote the paragraph according to suggestions, for a better framing in the context: "This editorial underlines the importance of the IgE sensitization *via* the respiratory route to aeroallergens and food allergy due to cross-reactivities between some allergen components. This phenomom should be distinguished from the common food allergy without sensitization to cross-reactive aeroallergens, in which heat- and enzyme-resistant class 1 food allergens induce allergic sensitization *via* the digestive tract, typically being responsible for systemic allergic reactions. Class 2 food allergens are more heat-labile and susceptible to digestion and therefore do not cause gastrointestinal sensitization, but instead provoke allergic reactions in already sensitized patients to cross-reactive aeroallergens through the respiratory route. Typically, pollen-food syndromes are produced by class 2 food allergens. In contrast to class 1 food allergy which mainly affects young children, class 2 food allergy is observed especially in adults as a consequence of sensitization to cross-reactive aeroallergens[8-10]. This traditional classification has a more modern changed approach from a molecular allergy point of view. Important allergen components families involved in cross-reactivity between aeroallergens and food allergens

are presented in Table 1. The clinical expression for IgE sensitization to PR-10 proteins and profilins is mainly oral allergy syndrome." (2) As suggested, I created new tables, one being inserted in the introduction, about important allergen components families involved in cross-reactivity between aeroallergens and food allergens. (3) I corrected the text duplication, as mentioned, deleting one word "mite" from "mite mite-shrimp" in the abstract. (4) As suggested, I changed bold lettering in the manuscript to normalize type. (5) As suggested, I unified the font size of all texts in paper. (6) In order to make the mentioned table more easy to read, I created two synthetic tables summarizing the syndromes and associations according to the recent expert system for the understanding of allergen microarray results, recently published in the World Allergy Organization Journal [Melioli G, Spenser C, Reggiardo G, et al. *World Allergy Organ J* 2014; 7(1): 15, DOI: 10.1186/1939-4551-7-15 PMID: 24995073]. Additional information from case reports defining rare or distinct associations presented in the editorial were only discussed in the text, not put in the tables as general rule for clinical practice, moreover to avoid redundant presentation of data. I also thank the reviewer for considering my manuscript good, with priority publishing.

A careful language revision has been performed throughout the manuscript, accordingly to my abilities on previously published scientific articles and to my formative experience.

I also thank the reviewers for classification of my manuscript **language quality evaluation** as **Grade A** priority publishing: reviewers 02520369 (2015-03-03 15:57), 02506941 (2015-03-02 19:37), 01884933 (2015-02-27 19:32), 02445848 (2015-02-20 22:21), as a guarantee for the language presentation of my manuscript.

3 References and typesetting were corrected

Thank you for considering publishing my manuscript in the prestigious *World Journal of Methodology*.

Sincerely yours,

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