Format for ANSWERING REVIEWERS

February 16, 2015

Dear Editor,

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

Title: Component-Resolved Allergen Testing: The New Frontier

Author: Matthew T Tallar, Mitchell H Grayson

Name of Journal: *World Journal of Translational Medicine*

ESPS Manuscript NO: 16735

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

1. Title changed to reflect that paper discusses allergic component diagnosis and not genetic or other disorders such as Kounis Syndrome.

2. Revision has been made according to the suggestions of the reviewer

(1) Title has been changed to include Allergen.

(2) Allergy components no longer italicized conforming to IUIS Allergen Nomenclature.

(3) Removed redundant "revolutionized/revolutionizing"

(4) Changed statement in abstract using the word unclear in relation to the use of Aeroallergen components in immunotherapy.

(5) In section, **Single Component Versus Microarray Testing,** we did not include multiparameter immunoblot testing or multiplex flow cytometry allergenic molecule-based micro-bead array system. In this editorial we chose to focus on immunocap and immulite systems based on wide availability for both researchers and primary care physicians. We do acknowledge the utility of other methods in research.

(6) Created a table to show advantages and disadvantages of single allergen versus multiplex testing.

(7) In section, **Anaphylaxis**, added comment regarding use of ISAC in diagnosis of idiopathic anaphylaxis and fixed error describing cat albumin glycosylation with alpha-gal. Did not include a section for all high risk important allergens. As an editorial we chose to focus on the 3 most common food allergens and felt that a complete description of all allergens was beyond the scope of this editorial. We did add a comment regarding cited review articles containing these data.

(8) In section, **Allergen Immunotherapy,** added position statement from WAO consensus document. We did not elaborate on all environmental aeroallergens for similar reasons as mentioned regarding high risk food allergens. We chose to focus on grass pollen given commercial SLIT preparations, and birch allergy because of the oral allergy syndrome and cross reactivity to other pollen aeroallergens.

(9) In section, **Hymenoptera Venom Immunotherapy,** abbreviated allergens now include "r" signifying recombinant. Added comment at the end of the section discussing sensitization in those without history of sting. With regards to double sensitization to honeybee and vespid venoms we feel the following statements address this issue: "Cross-reactive carbohydrate determinants (CCD) and homologous protein allergens (e.g. hyaluronidase) are believed to be the causes of this phenomenon[40]. As a result, a patient's true sensitization profile to venom may be inaccurate, leading to unnecessary allergens being added to their immunotherapy prescription…Of patients with positive sIgE testing to both species, only 47% were found to be sensitized to both honey bee and yellow jacket venom

components. Therefore, in over half of these patients, their initial skin testing or serum sIgE testing was clouded by cross-reactivity, which could be sorted out using CRD."

3. Table created to better elucidate differences between single components and ISAC assay.

Thank you again for considering our manuscript in the *World Journal of Translational Medicine*. We look forward to your positive re-review.

Sincerely yours,

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