Reviewer's report

Title: Rhinosinusitis derived Staphylococcal enterotoxin B plays a possible role in the pathogenesis of food allergy

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Reviewer: Harumi Jyonouchi

Reviewer's report:

General
Abstract: Overall better. A little more editorial efforts will be helpful for better understanding the content.

Example: (the following is just an example for better presentation of the study results)
Methods: The study included CRS patients with FA (N=46) or without FA (N=33). Controls included FA patients without CRS (N=26) and healthy volunteers (N=25). In CRS patients, we assessed the parameters associated with FA including prick skin test (PST) reactivity to food allergens, serum levels of allergen-specific IgE and cytokines (IL-4, IL-13, IFN-γ), and the number/rectivity of food-allergen specific Th1/Th2 cells in the peripheral blood before and 2 months after sinus surgery. Changes of these parameters were evaluated in comparison with changes in SEB concentration in the sinus lavage and stool samples and also in vitro reactivity to SEB. In CRS patients with FA, we also assessed changes in reactivity to oral challenge of offending food before and after sinus surgery.

Results: Two months following sinus surgery, we observed statistically significant reduction in PST and oral challenge reactivity in CRS patients with FA in parallel to decrease in serum levels of Th2 cytokines (IL-4 and IL-13) and allergen specific IgE. Improvement of reactivity to food allergens was positively associated with decline in SEB concentrations in the sinus lavage and stool samples. In vitro study results also indicated a role of SEB in aggravation of Th2 skewed responses to food allergens. Such changes were not observed in CRS-non FA patients or control FA patients.

Conclusion:
Last sentence: removal of pathogens Â€” it is better to say Â“removal of SEB-producing pathogensÂ”?

Introduction:
Page 4 Â” last paragraph.
It is better to state clinical observation and rodent study results first, and then state hypothesis

Objectives of the study may be reworded as such:

If our hypothesis is correct, attenuation of FA symptoms is likely to be observed in CRS-FA patients following sinus surgery secondary to reduction of SBE swallowed to the GI tract. We thus examined changes in food allergen reactivity to PST/oral challenge along with other parameters of FA (serum cytokine levels, serum allergen specific IgE, and allergen specific Th2 cells) following sinus surgery in CRS-FA patients in comparison with SEB concentration in the sinus and stool and SEB reactivity.

Results
Serum IFN-g levels: I have never seen the paper with such a high serum level of IFN-g in healthy controls. Although these data are not vital in this study, I cannot comment the results of serum levels of IFN-g.

Skin prick testing:
The first sentence is unnecessary.
No positive PST reactivity was observed in healthy controls or CRS-non FA patients?
Marked Â” markedly.

FESS attenuated reactivity to oral food allergen challenge in CRS-FA patients?

The last sentence: Two months following FESS, CRS-FA patients revealed significant reduction of FA symptoms provoked by oral challenge of offending food allergens. There was no change in reactivity in FA patients in the repeated oral challenge test?
FESS reduced serum levels of Th2 cytokines and allergen specific IgE in CRS-FA patients?

The first sentence is unnecessary. It is still a little difficult to follow. A little better rewording is desirable.

SEB was identified in the sinus lavage and stool samples in CRS-FA patients at high concentration?
Better to delete the first sentence.
Sinus wash fluids À sinus lavage solutions?
Culture and PCR results À can be said as â€œinfectionâ€? More consistent with colonization.

Food allergen-specific Th2 responses are augmented by SEB in vitro in CRS-FA patients but not in FA patients.?

Discussion: Better but still hard to follow. Additional edition is desirable.

The first paragraph:
The 3rd sentence: meaning is unclear. In our experience, the prevalence of CRS is higher in rural area than in cities in China unlike in Western countries where prevalence is higher in industrialized area??

The last sentence: The results of our study revealed evidence of a role of SEB produced as a result of CRS for development and/or aggravation of Th2 responses to food allergens in the gut mucosa.? 

Page 17, the first sentence
The sinus surgery has resulted in an attenuation of Th2 skewed responses to food allergens in CRS-FA patients, most likely secondary to removal the source of SEB.? 

Page 17, the 2nd sentence À better to use the word of colonization?
SEB can induce polyclonal T cell activation, leading to aberrant immune responses?

Page 18 2nd paragraph
The datum indicates that these antigen-specific Th2 cells --- : may be more accurate to say:
The presented data indicate that SEB may further augment responses of food allergen specific Th2 cells directly or by bystander effect?

Page 19 À The last sentence À may be reworded a little more clearly (an example was shown below).
In summary our study revealed significant improvement of reactivity to food allergens by PST and oral challenge in CRS-FA patients after FESS. Improved FA symptoms are paralleled with evidence of attenuated Th2 responses to food allergens and decrease of SEB concentrations in the sinus and the gut. Along with in vitro study results indicating augmenting action of SEB on food allergen specific Th2 responses in CRS-FA patients, the presented data support a role of SEB in development/aggravation of FA in some CRS patients.

Table 1: Demographics of the study subjects?
Table 5: this is not T cell proliferation data À frequency of IL-4+ or IFN-g+ T cells following stimulation with SBE, food allergen, or both.