Developing an Early Life Mouse Model of Oral Tolerance to Peanut Protein

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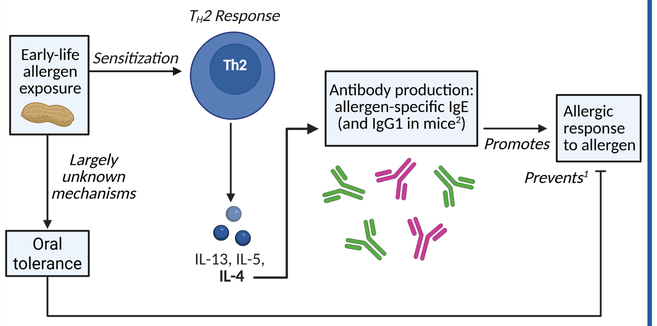
Introduction

- Oral tolerance (OT) is a state of local and systemic immune unresponsiveness towards dietary antigens which is induced by oral consumption.



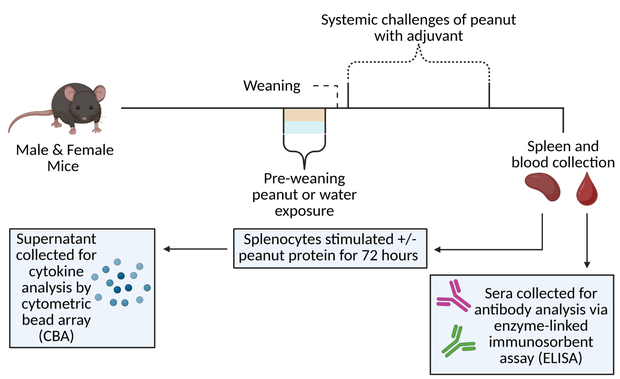
- OT has been primarily studied in adult mouse models. However, these models do not account for the unique immunological and microbiological environment found in early-life[3].
- Most models use the protein ovalbumin from egg white, but mechanisms behind OT development may differ depending on the dietary antigen[1]. Therefore, we decided to focus on another common food allergen, peanut, which has been used more infrequently.

Research Objective

To develop and validate a model of oral tolerance to peanut protein (PE) in mouse pups.

Experimental Design & Methods

Mouse work done by L. Reynolds, R. Mebs, R. FitzPatrick, and S. Knox at UVic with the approval of the University of Victoria Animal Care Committee.



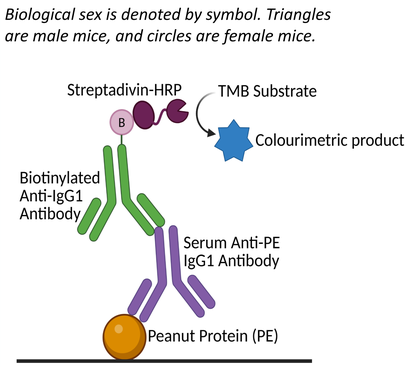
Statistical analysis done using GraphPad Prism 10.6.1. * is $p \leq 0.05$, ** is $p \leq 0.01$, *** is $p \leq 0.001$, **** is $p \leq 0.0001$, and ns is $p > 0.05$. ELISA data are compared using a Kruskal-Wallis or ordinary one-way ANOVA test with a post-hoc Dunn's multiple comparisons test. CBA data are compared using a Wilcoxon matched-pairs signed rank test.

Experiment 1 and Experiment 2 peanut exposures differ based on altered peanut protein extraction.

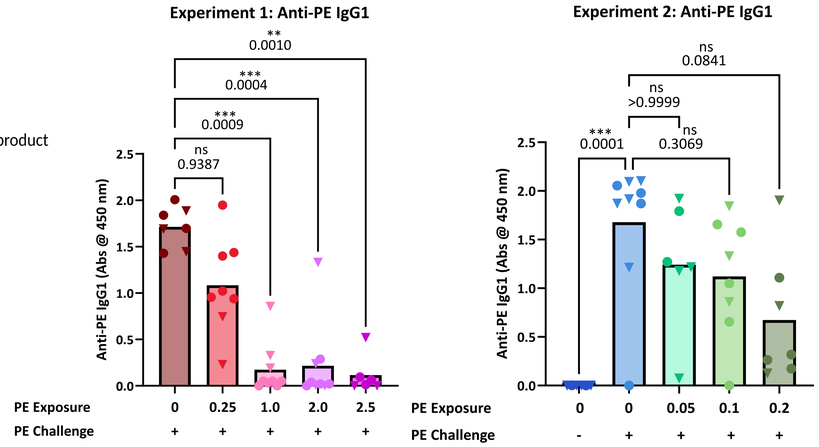
Results

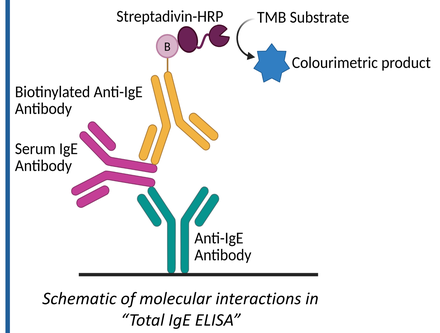
1. Daily exposure of peanut protein (PE) prior to weaning could generate tolerance to later challenge with peanut. However, this effect may be dose dependent.

Biological sex is denoted by symbol. Triangles are male mice, and circles are female mice.

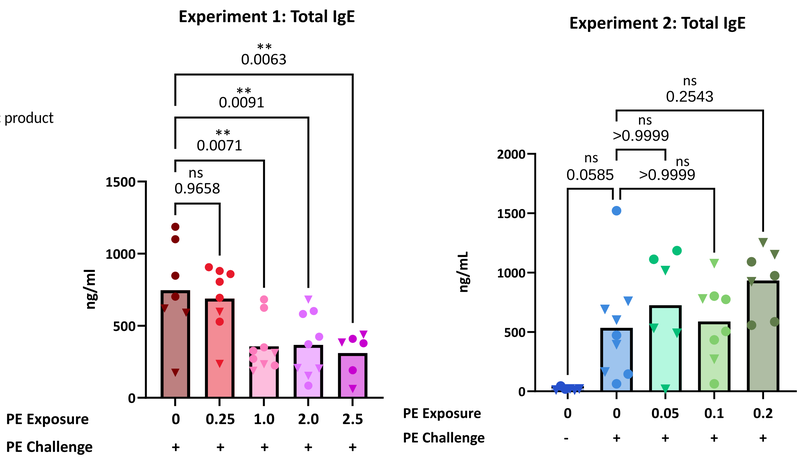


Schematic of molecular interactions in "Anti-PE IgG1 ELISA"



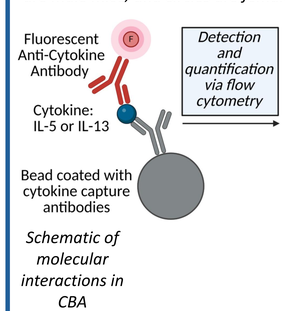


Schematic of molecular interactions in "Total IgE ELISA"

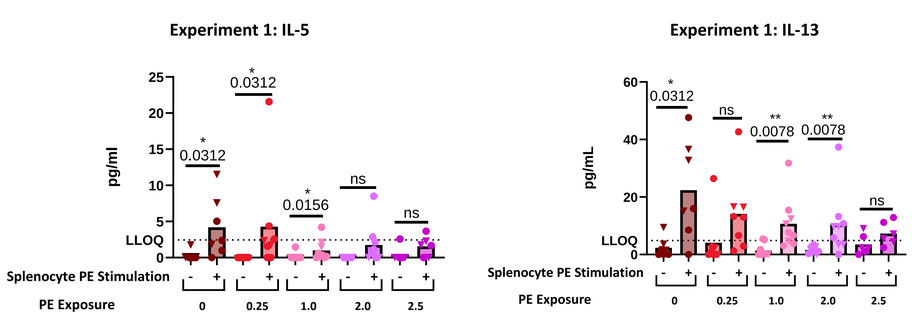


2. There is a trend towards reduced T_H2 cytokine production from splenocytes in mice with higher exposures of PE.

Biological sex is denoted by symbol. Triangles are male mice, and circles are female mice.



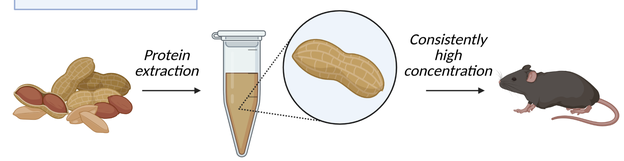
Schematic of molecular interactions in CBA



Conclusions & Future Directions

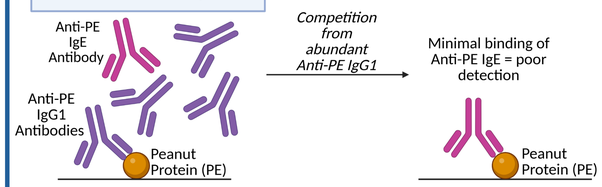
These data suggest that a daily exposure of peanut protein could generate tolerance to a later challenge with peanut. However, this effect may require higher doses. Experimental repeats are needed to confirm the minimum tolerizing dose.

Optimize Protocol



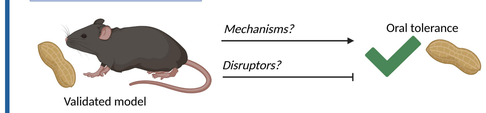
Current experimental readouts provide good indication for whether mice may be tolerized or not. But, the optimal readout to confirm tolerance would be a peanut-specific IgE ELISA. Further work is required to develop a robustly sensitive assay for peanut-specific IgE.

Troubleshoot Anti-PE IgE ELISA



Once the model is validated, mechanistic studies of oral tolerance can begin.

Mechanistic Studies



Acknowledgements

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References

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Supervised by Lisa A. Reynolds