Reduced polyfunctional T cells and increased cellular activation markers in adult allergy patients reporting adverse reactions to food

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Abstract
Background: The underlying cellular mechanisms causing adverse reactions to food are complex and still not fully understood. Therefore, in this study we aimed to identify functional and/or phenotypical immune cell signatures characteristic for adult patients reporting adverse reactions to food. By mass cytometry, we performed high-dimensional profiling of peripheral blood mononuclear cells (PBMC) from adult patients reporting adverse reactions to food and healthy controls. The patients were grouped according to slgE-positive or slgE-negative serology to common food and inhalant allergens. Two broad antibody panels were used, allowing determination of major immune cell populations in PBMC, as well as activation status, proliferation status, and cytokine expression patterns after PMA/ionomycin-stimulation on a single cell level. Results: By use of data-driven algorithms, several cell populations were identified showing significantly different marker expression between the groups. Most striking was an impaired frequency and function of polyfunctional CD4 + and CD8 + T cells in patients reporting adverse reactions to food compared to the controls. Further, subpopulations of monocytes, T cells, and B cells had increased expression of functional markers such as CD371, CD69, CD25, CD28, and/or HLA-DR as well as decreased expression of CD23 in the patients. Most of the differing cell subpopulations were similarly altered in the two subgroups of patients. Conclusion: Our results suggest common immune cell features for both patient subgroups reporting adverse reactions to food, and provide a basis for further studies on mechanistic and diagnostic biomarker studies in food allergy.

Full-text
Due to technical limitations, full-text HTML conversion of this manuscript could not be completed.
However, the manuscript can be downloaded and accessed as a PDF.

Figures
Figure 1

Individual frequencies of immune cell subpopulations obtained by traditional manual gating of populations according to Table 3 in healthy controls, IgEpos food allergy subjects, and IgEneg food allergy subjects.
CITRUS analyses for the unstimulated cells, clustering on 25 phenotyping markers and comparing median expression of the markers CD371, CD23, CD25, CD28, and HLA-DR between the three groups. A) CITRUS trees in which each node denotes different cell clusters. The red nodes illustrate cell populations were the median marker intensities of the respective functional marker differed statistically significantly between the three groups as determined by SAM analyses, FDR 0.05. The parent clusters (the “highest in the hierarchy” significant node) are named based on marker expression shown in C. B) Median marker intensities for the various functional markers, shown as box plots (expressing interquartile range (IQR) and median values) and values for each individual within the groups of healthy controls, IgEpos, and IgEneg food allergic subjects, for each parent clusters identified in A. Differences between groups are shown as lines, * P ≤ 0.05, ** P ≤ 0.01, *** P ≤ 0.001, and **** P ≤ 0.0001 (Kruskal-Wallis and Dunn’s multiple comparisons test). C) CITRUS histograms for the parent clusters identified in A. For each surface marker, the histogram
shows the 5marker expression on cells in the specific cluster (red) against the marker expression on all other cells (blue).

Figure 3

CITRUS analyses for the stimulated cells, clustering on all 28 surface and intracellular markers and comparing cell abundance in the three groups. A) CITRUS tree in which each node denotes different cell clusters. The red nodes illustrate cell populations were the cell abundance differed statistically significantly between the three groups as determined by SAM analyses, FDR 0.05. B) Cell abundance as proportion of all cells, shown as box plots (expressing IQR and median values) and values for each individual within the groups of healthy controls, IgEpos, and IgEneg food allergic subjects, for the clusters identified in A. Differences between groups are shown as lines, * P ≤ 0.05, ** P ≤ 0.01, *** P ≤ 0.001, and **** P ≤ 0.0001 (Kruskal-Wallis and Dunn’s multiple comparisons test). C) CITRUS histograms for the clusters identified in A. For each surface marker, the histogram shows the marker 594 expression on cells in the specific cluster (red) against the marker expression on all other cells (blue).
CITRUS analyses for the stimulated cells, clustering on all 28 surface and intracellular markers and comparing median expression of the markers TNF-α, IFN-γ, IL-17A, and IL-2 between the three groups. A) viSNE maps of PBMC of one representative subject of the control, IgEpos, and IgEneg allergy group, cells are colored by TNF-α, IFN-γ, IL-17A, and IL-2 expression respectively. B) Median marker intensities for the various functional markers, shown as box plots and values for each individual within the groups of healthy controls, IgEpos, and IgEneg food allergic subjects, for each parent clusters identified in A. Differences between groups are shown as lines, * P ≤ 0.05, ** P ≤ 0.01, *** P ≤ 0.001, and
**** P ≤ 0.0001 609 (Kruskal-Wallis and Dunn's multiple comparisons test). C)CITRUS histograms for the major parent clusters. For each surface marker, the histogram shows the marker expression on cells in the specific cluster (red) against the marker expression on all other cells (blue).

Supplementary Files
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