Identification of functional peptides with tolerogenic potential in a partially hydrolysed infant formula

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Introduction
Oral tolerance is the default response of the immune system to innocuous food proteins and is characterized by regulation of local and systemic immune responses to these proteins [1]. Failure to induce oral tolerance to food proteins results in food allergy. International prevention guidelines recommend the use of partial hydrolysed cow’s milk-based infant formula in infants with increased risk of developing allergic diseases, when breastfeeding is limited or absent [2, 3]. The aim of this study was to investigate whether a specific partial hydrolysed whey-based infant formula contains unique peptides that might act as functional human T-cell epitopes to support the development of oral tolerance to whey.

Methods
First, a novel liquid chromatography-mass spectrometry (LC-MS) method was developed to characterise beta-lactoglobulin (BLG)-derived peptides present in a whey-based hydrolysed formula with a particular focus on AA13-48 of the mature BLG protein, a region which has previously been described to contain T-cell epitopes with tolerogenic potential [4]. Second, the same formula was subjected to the ProImmune ProPresent® antigen presentation assay to identify HLA-DRB1-restricted, BLG-derived T-cell epitopes. Third, synthetic peptides identical to the BLG-derived peptides identified by LC-MS were tested on human cow’s milk-specific T-cell lines to determine T-cell recognition.

Results
Thirteen BLG-derived peptides of minimal 9AAs long that overlap with the region of AA13-48 of mature BLG were identified. Six of them were found across all batches analysed. It was further confirmed that these peptides were internalized, processed and presented by human dendritic cells. The identified HLA-DRB1-restricted T-cell epitopes were correlated to AA11-30 and AA23-39 of mature BLG. Importantly, the T-cell proliferation assay showed that the synthetic peptides were recognized by cow’s milk-specific T-cell lines and induced T-cell proliferation.

Conclusion
This study demonstrates that the tested partially hydrolysed whey-based infant formula contains functional HLA-DRB1-restricted T-cell epitopes. These functional peptides in turn can potentially support the development of oral tolerance to whey.

References