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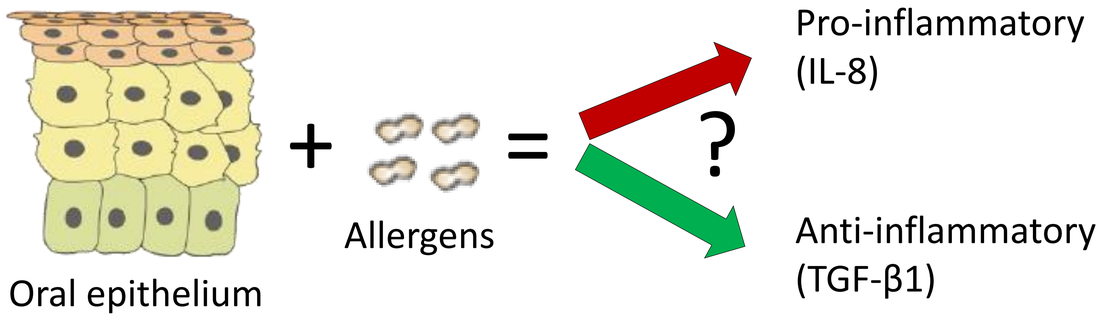
ALLERGEN EXTRACTS AND CALCITRIOL AFFECT IL-8 AND TGF-β1 SECRETION IN A CELL LINE OF CANINE ORAL KERATINOCYTES

Background

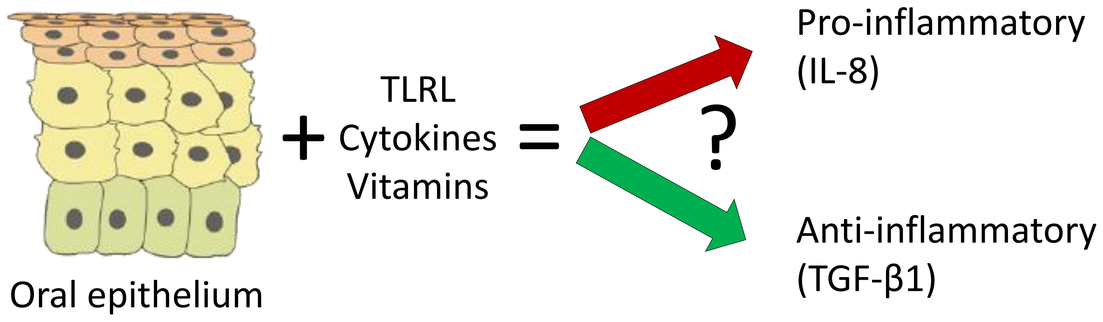
Allergen immunotherapy only has a moderate efficacy, both in humans and animals. During sublingual immunotherapy, the oral mucosa is an easily accessible, immunologically active tissue which could provide the opportunity to modify the local immune response. In humans and mice, oral dendritic cells[1] and the draining lymph nodes of the oral mucosa[2] are known to play an important role in the promotion of tolerance during therapy. Skin and lung epithelial cells can influence the co-stimulatory signal of antigen-presenting cells[3]. Whether oral epithelial cells are capable of immunologically recognizing allergens and could be modulated in playing a tolerance-promoting role has not been specifically investigated.

Objectives of the study

1. To look at the influence of allergens on oral epithelial cells' cytokine secretion



2. To identify substances capable of suppressing the pro-inflammatory immune response in oral epithelial cells

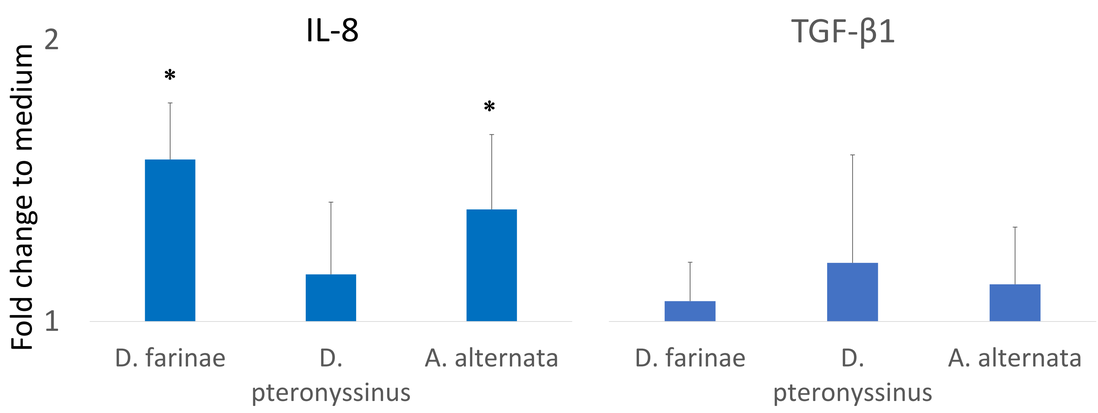


Methods

A cell line of canine oral keratinocytes was incubated with allergen extracts (*Dermatophagoides farinae*, *D. pteronyssinus* and *Alternaria alternata),* different toll-like receptor ligands, canine recombinant cytokines and vitamins (9-cis-retinoic acid and calcitriol). After 24 hours incubation, cytokine production (IL-8 and TGF-β1) was measured with ELISA.

Results

1. Influence of allergens on oral epithelial cells' IL-8 and TGF-β1 cytokine secretion



2. Effect of TLRL, cytokines and vitamins on IL-8 and TGF-β1 cytokine secretion in oral epithelial cells

Substance	IL-8	TGF-β1
TLRL		
Pam3CSK4	**10**	**ns**
FSL-1	**9**	**ns**
ST-FLA	**2.8**	**ns**
Poly I:C	**1.6**	**ns**
HKLM	**1.6**	**ns**
ODN2006	**ns**	**0.7**
Imiquimod	**ns**	**ns**
ssRNA40	**ns**	**ns**
LPS	**ns**	**ns**
LTA	**ns**	**ns**

Substance	IL-8	TGF-β1
Cytokines		
IL-17A	**1.7**	**ns**
IL-4	**1.7**	**ns**
IL-10	**1.5**	**ns**
IFN-γ	**ns**	**ns**
IL-6	**ns**	**ns**
Vitamins		
9-cis-retinoic acid	**ns**	**ns**
Calcitriol	**0.6**	**0.8**

values = fold change to medium
ns = not significant

Conclusion

Just as in skin keratinocytes, house dust mite antigens seem to be capable to induce pro-inflammatory signals in oral epithelial cells. Calcitriol on the other hand seems to downregulate cytokine production in this cell type. The effect of allergens and calcitriol on oral epithelial cytokines that are specifically involved in Th2 immunity should be further investigated. A better understanding of the different substances that can modulate immune responses at the level of the epithelium will allow the selection of specific adjuvants that could enhance the efficacy of local allergen immunotherapy.

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References

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