Larger and Stronger Expression of Tregs Gut Homing Receptors with Epicutaneous than with Sublingual or Oral Immunotherapy

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Rationale: Regulatory T cells (Tregs) plays a pivotal role in Epicutaneous Immunotherapy (EPIT) (Dioszeghy, Clin Exp Allergy 2014). Expression of homing molecules by Tregs could potentially modulate their response. The aim of this study was to compare the repertoire of homing receptors of EPIT-induced Tregs to Oral or Sublingual immunotherapy (OIT or SLIT).

Methods: BALB/c mice were sensitized to peanut orally and treated by EPIT, SLIT, or OIT. After 8 weeks of treatment, the proportion of Tregs in spleen, inguinal and mesenteric lymph node (iLN or mLN) and the expression of homing receptors by Tregs were analyzed by flow cytometry.

Results: In spleen, expression of CCR4 increased on Tregs induced by all 3 therapies whereas the expression of CXCR3, CCR6 and CCR8 increased on EPIT-induced Tregs only. Skin homing receptor (CLA) increased on EPIT- but not SLIT- or OIT-induced Tregs. Gut homing receptor CCR9 increased on EPIT- and OIT- but not SLIT-induced Tregs. Interestingly, 81% of the CCR9+ Tregs induced by EPIT expressed CLA whereas only 43% did after OIT. In iLN, Tregs level increased only after EPIT with induction of CLA+CCR9-(22%) and CLA+CCR9+ (12%) Tregs. In mLN, EPIT and OIT significantly induced CCR9+ Tregs, 25% and 18% of them expressing also CLA in EPIT and OIT respectively.

Conclusion: EPIT induced a larger repertoire of homing receptors on Tregs than SLIT or OIT. EPIT was able to induce higher level of gut homing Tregs than OIT, strongly suggesting its relevance in food allergy.

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