Epigenetic changes following epicutaneous immunotherapy in peanut sensitized mice

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**Rationale:** Epicutaneous immunotherapy (EPIT) is a promising route for treating food allergies and animal models show the sustainability of the protection. We investigated in peanut-sensitized mice the implementation of epigenetic mechanisms underlying this long lasting therapeutic effect.

**Methods:** Mice were orally sensitized to peanut and then treated by EPIT or sham. Mice were sacrificed every 2 weeks during EPIT and also 8 weeks after the end of EPIT. DNA methylation was analysed in spleen and blood samplings by restrictive enzyme digestion and quantitative-PCR and also in sorted CD4, CD8 and CD19 cells from spleen and blood by pyrosequencing.

**Results:** In splenocytes, a significant hypermethylation in GATA-3 CpG islands was induced by EPIT versus Sham, starting from the 4\textsuperscript{th} of treatment (p<0.05). This hypermethylation was sustained after the end of EPIT. In circulating blood cells, the hypermethylation in GATA-3 CpG islands was observed only at the 8\textsuperscript{th} week of EPIT (vs Sham, p<0.05). In spleen and blood CD4 cells, a significant hypermethylation for CpG island of GATA-3 was observed from the 4\textsuperscript{th} week of EPIT and persisted following the end of treatment. In parallel, a significant hypomethylation was obtained in Foxp3 CpG islands in spleen and blood CD4 T cells from the 4\textsuperscript{th} week of EPIT compared to Sham, persisting after the end of treatment. No modification was observed for Tbet transcription factor in whole or in sorted T and B cells sorted from spleen and blood.

**Conclusions:** Epigenetic modifications of the DNA expression of Th2 and Treg transcription factor appears a major trait of EPIT induced immunomodulation.

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