

Mechanisms of extracorporeal photochemotherapy-induced tolerance : Mouse model of CHS



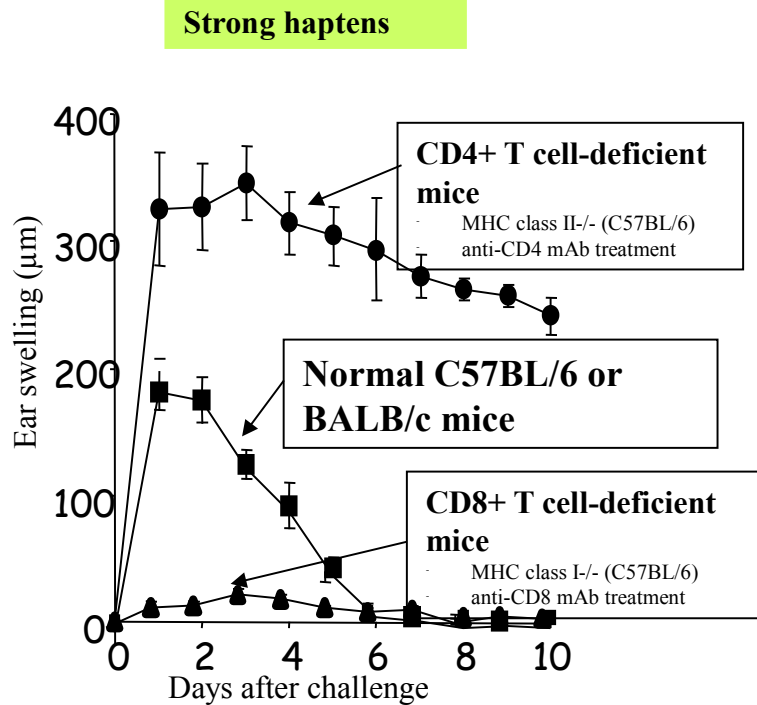
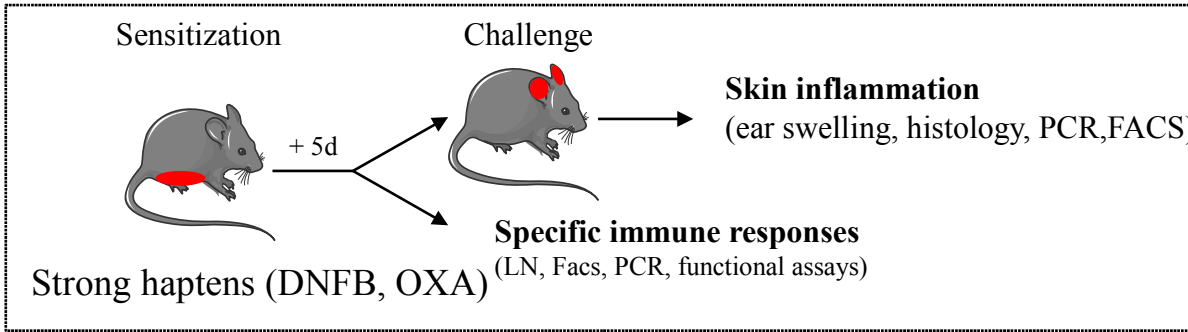
Olivier HEQUET
Marc VOCANSON
Aurélie GUIRONNET PAQUET
Deborah ARNAUD
INSERM U1111 - CIRI
Team leader: **Prof. JF. NICOLAS**

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APHERESIS UNIT
Centre Hospitalier Lyon-Sud
LYON - France

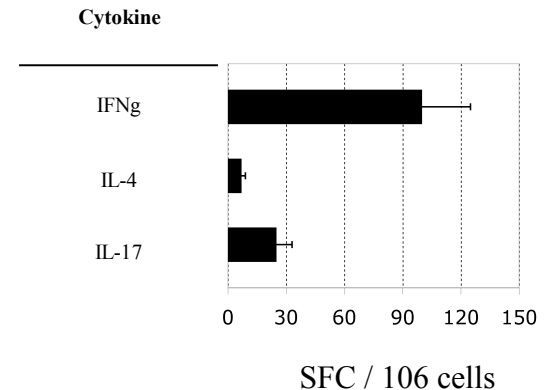
CHS pathophysiology - Mouse Ear Swelling Test (MEST)

CD8+ T cells are mandatory for the development of skin allergy

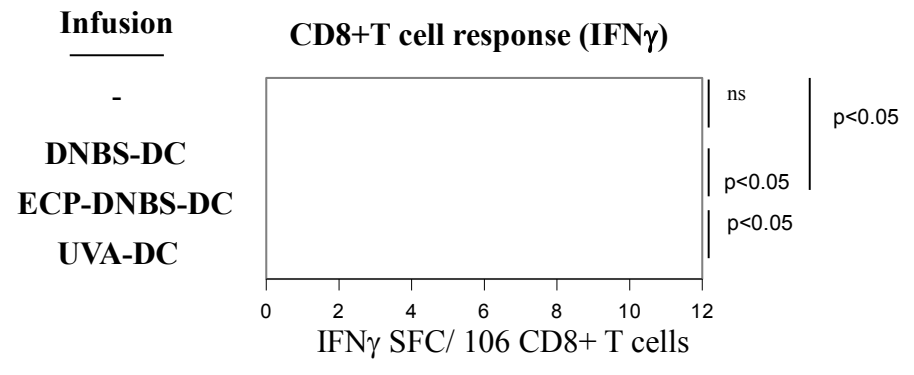
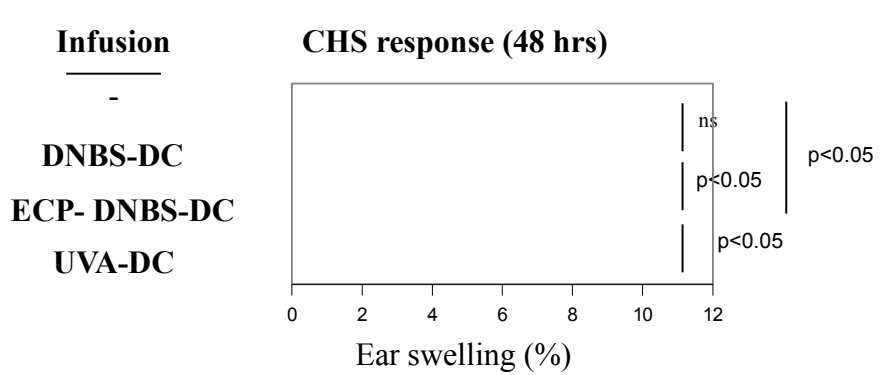
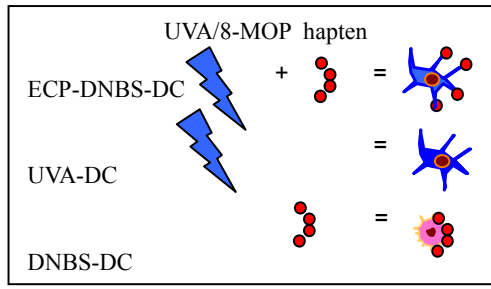
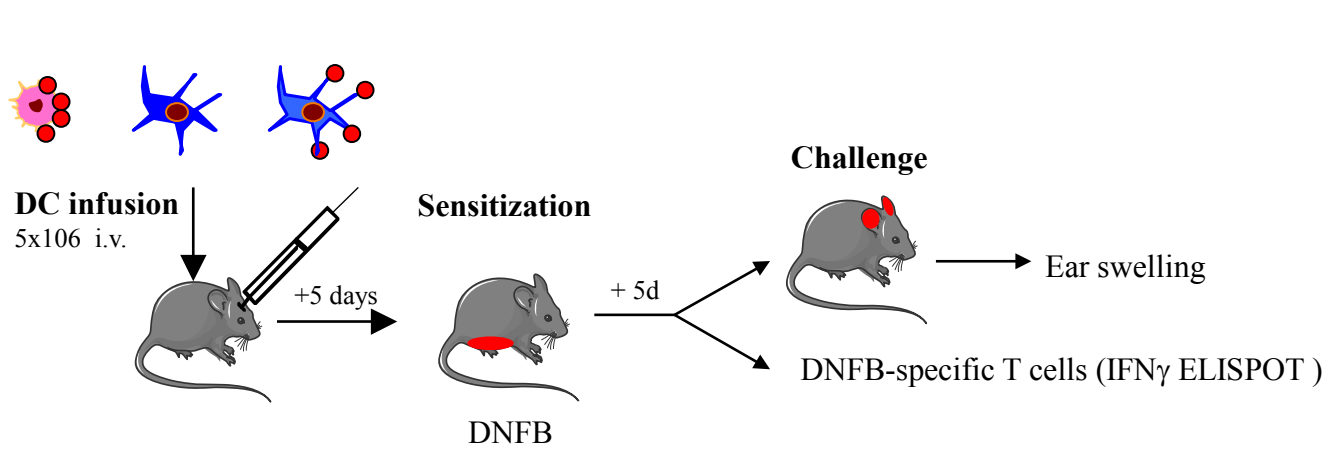


- **CD8+ T cells are effector cells**
- **CD4+ T cells comprise regulatory T cells**

Major production of IFN γ – mainly CD8+ T cells

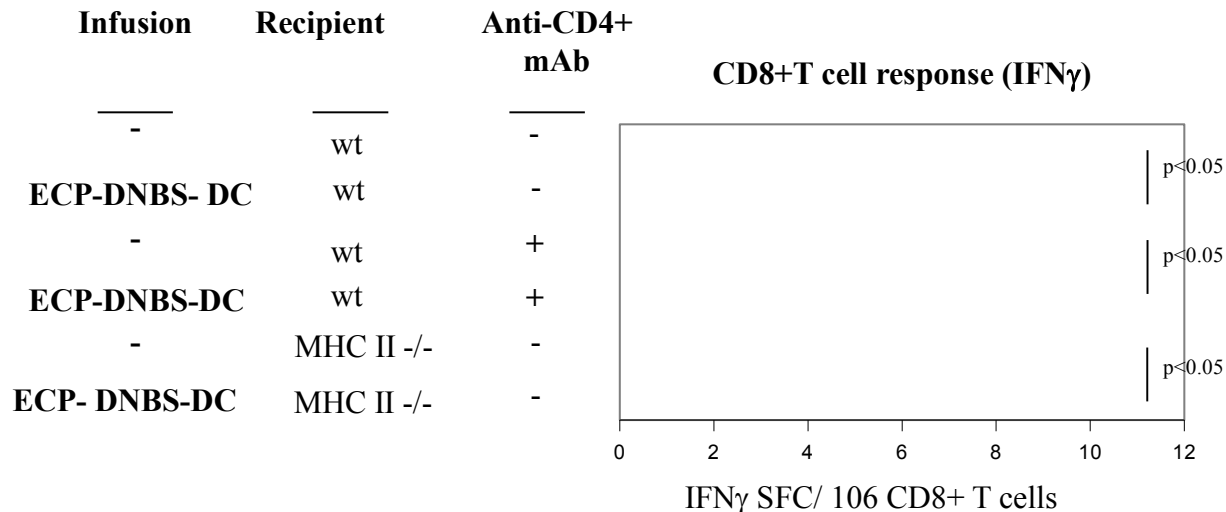
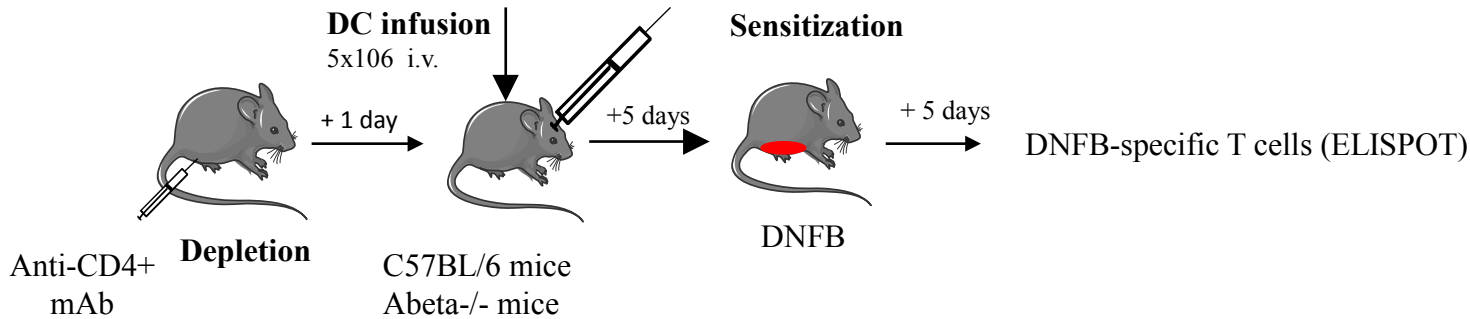
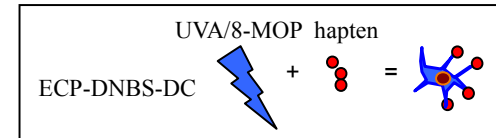


Infusion of ECP-treated DC before DNFB sensitization hampers the priming of CD8+Teff and the development of CHS reaction



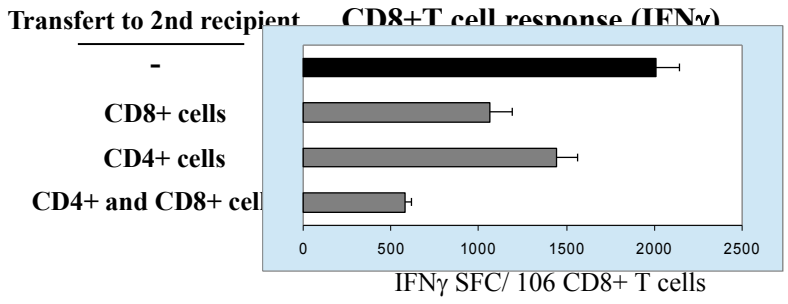
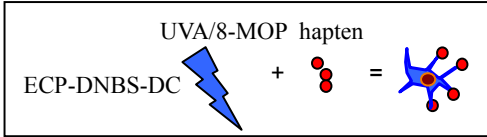
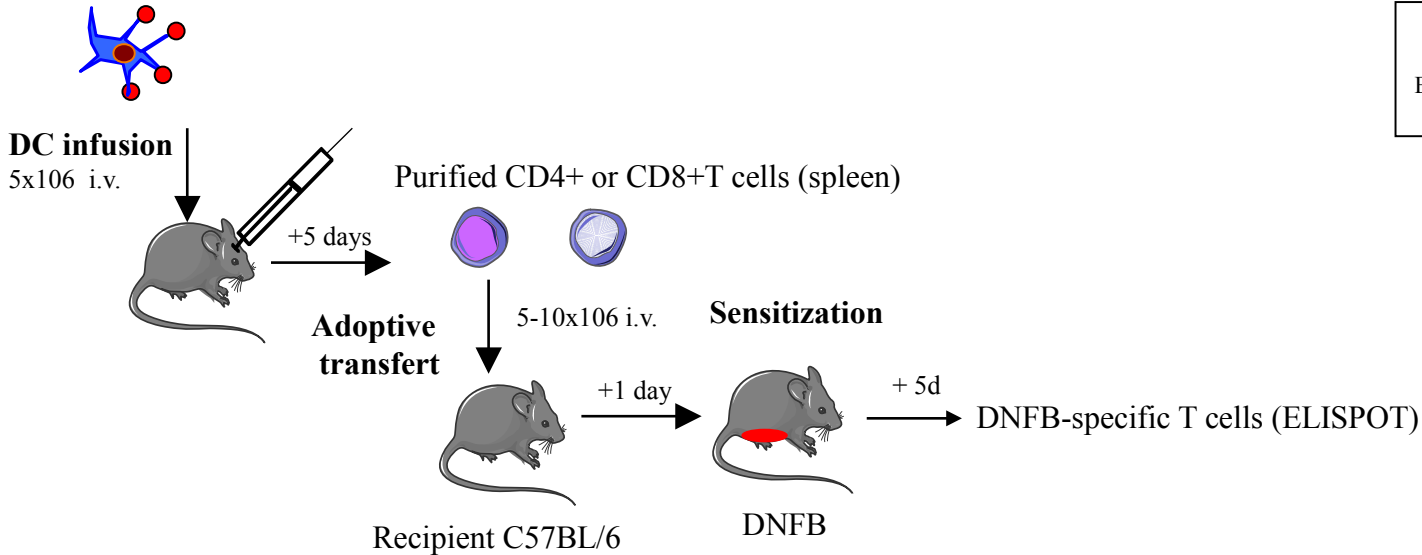
ECP treatment allows for a robust tolerance in the model of CHS to DNFB

Infusion of ECP-treated DC confer tolerance in Treg-deficient mice



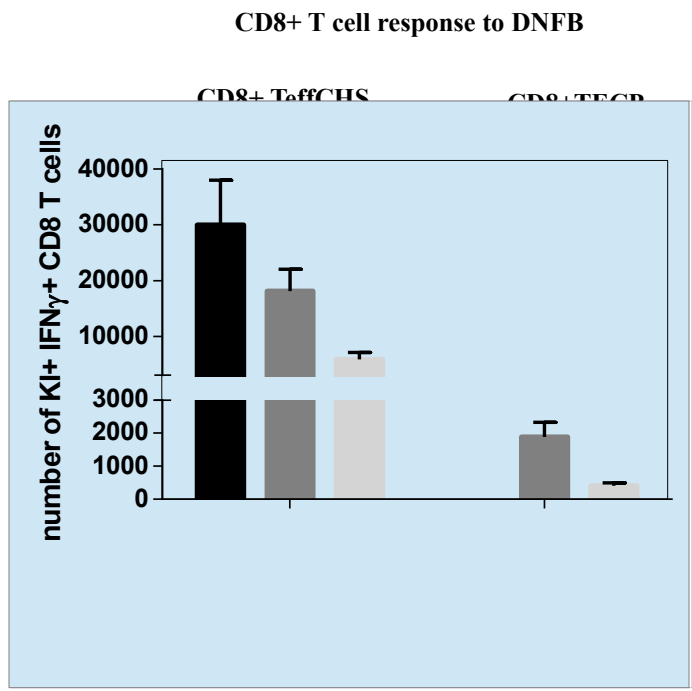
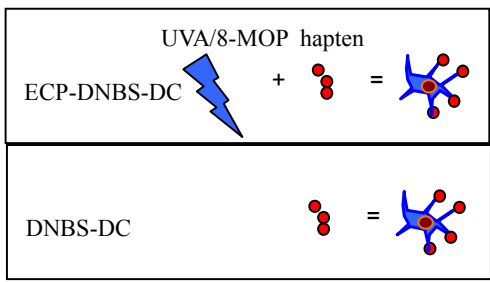
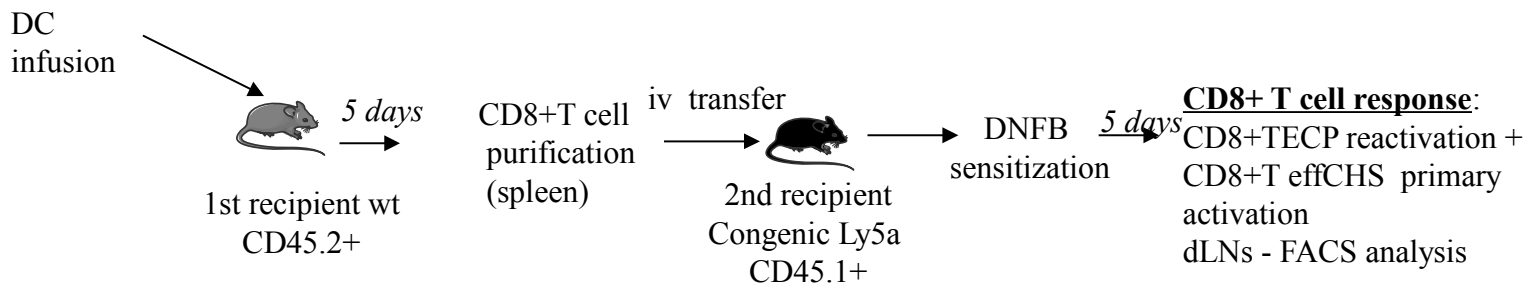
Potent tolerance in mice deficient in CD4+ Tregs

CD8+TECP cells complement CD4+TECP cell subset to confer ECP tolerance

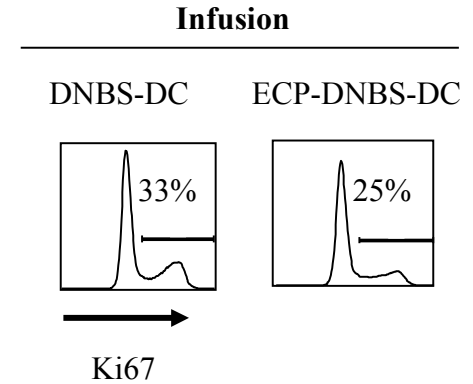
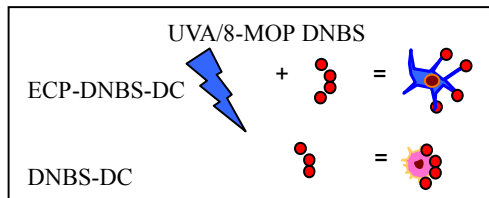
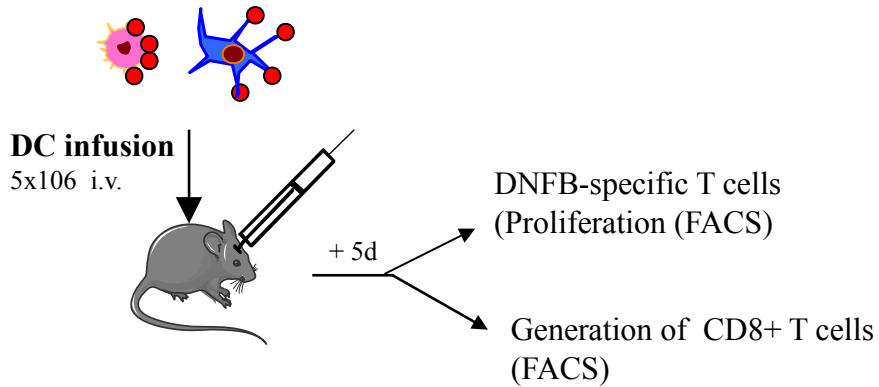


CD8+ T cells collected from the spleen of infused-animals confer Ag-specific tolerance upon adoptive transfer, demonstrating that they are endowed with suppressive activities

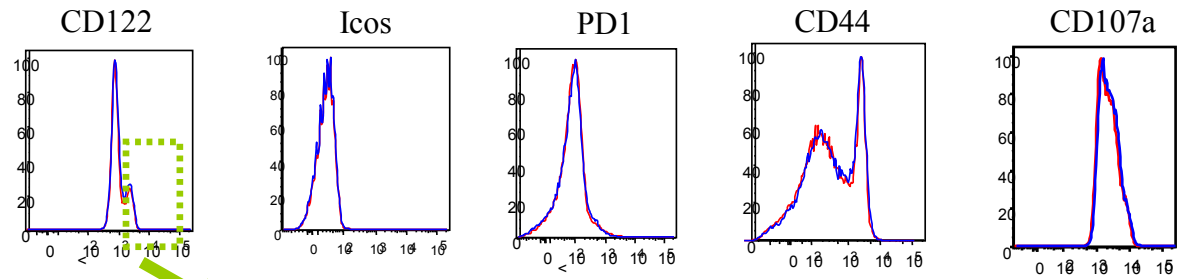
CD8+ECP T cells hampered the priming of CD8CHS effector cells upon adoptive transfer



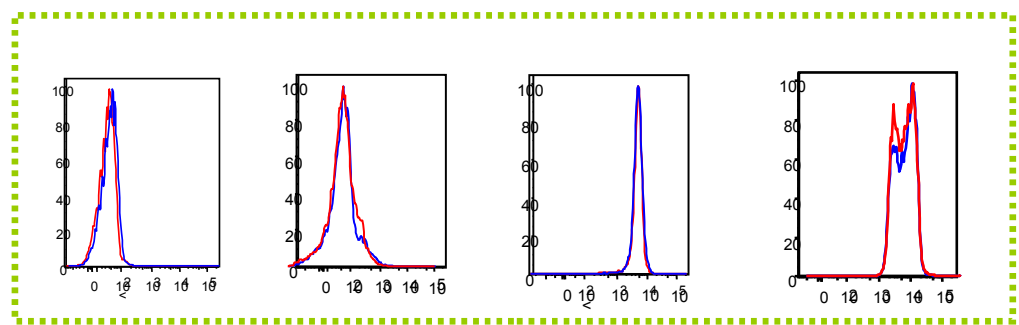
Phenotypic analysis of CD8+ T cell response upon infusion of ECP-treated DC



Activation



■ ECP-DNBS-DC
■ DNBS-DC



Conclusions

- **ECP-treatment hinders T cell priming and promotes CD8+ T ECP cells endowed with appreciable effector properties (cytotoxicity).**
- **CD8+ T ECP cells confer tolerance in CHS model by preventing the priming of new T eff CHS cells and their differentiation in TEM.**
- **CD8+ T ECP persist 1 month after generation and reactivation, suggesting potential maintenance of ECP-induced tolerance.**

Perspectives

Important issues to uncover:

- **Which mechanisms for tolerance?**
 - **No IL-10, negative costimulation (PD-1, RANK...), Qa-1-restricted CD8+Tsupp?, Trail (sepsis model)?, transfer of regulatory miRNA?**
 - **Characterise phenotype and function of ECP- DC**
- 📄 **Mechanisms are common to other strategies of tolerance?**
- **Feasibility of strategies aiming at re-inducing tolerance in patients**