Depletion of myeloid-derived suppressor cells by gemcitabine does not break immune tolerance and protection against EAE induced by mannan-conjugated myelin autoantigens

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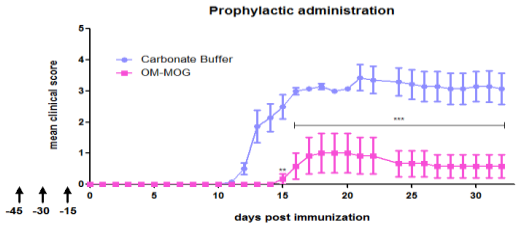
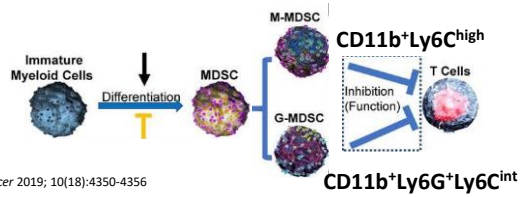
Introduction

- **Mannan-conjugated and mannosylated myelin antigens induce peripheral T cell tolerance and protect mice against EAE in prophylactic and therapeutic protocols.**
- **Tolerance is not associated with known mechanisms (deletion, Th1-Th2 shift, Treg induction) except some features of anergy .**
- **Mannan targets the Mannose receptor that is expressed on cells of myeloid lineage**

  Tseveleki et al 2015, Exp. Neurol. 267:254
  Luca et al, 2005, J.Neuroimm 160:178)

•Administration of OM-conjugated MOG35-55 induces peripheral T cell tolerance and protects mice against MOG-EAE.

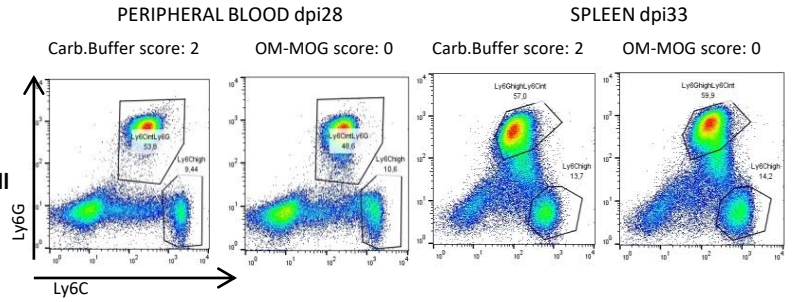




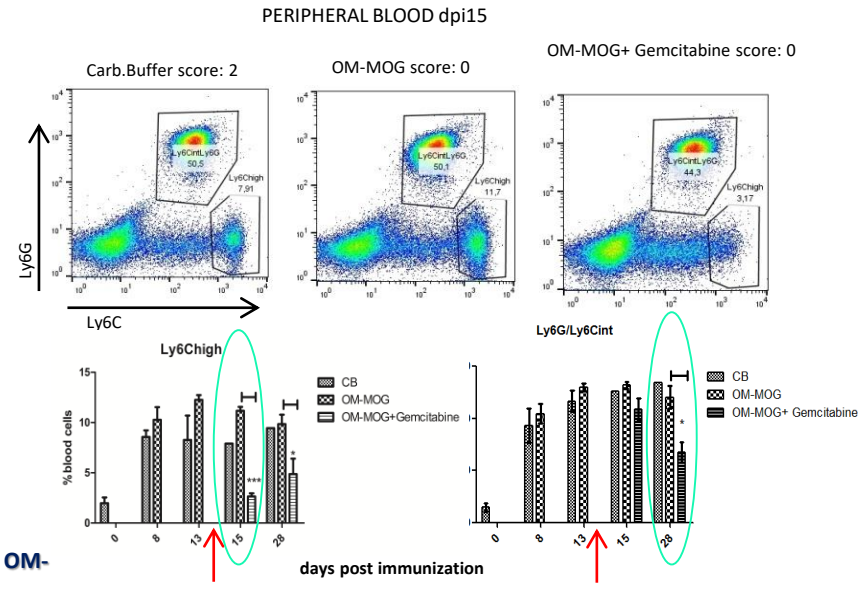
Su Y., et al. J Cancer 2019; 10(18):4350-4356

The purpose of this study is to investigate whether tolerance induced by OM-peptides involves the induction of MDSC.

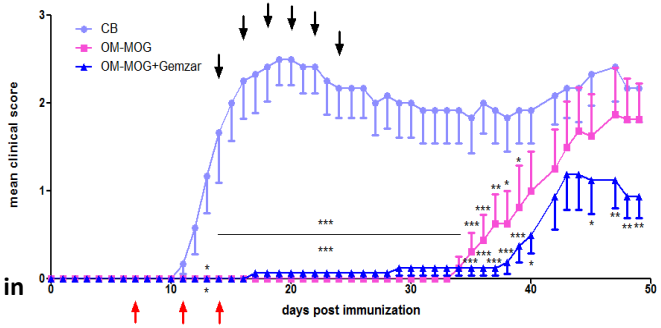
•MDSC expand in peripheral blood and spleens of mice immunized with MOG/CFA/PTx



•Gemcitabine treatment depletes Ly6Chigh and Ly6G/Ly6Cint MDSC in Peripheral Blood of mice immunized with MOG/CFA/PTx



•Depletion of MDSC by gemcitabine does not break OM-MOG induced tolerance and protection against EAE clinical symptoms



Conclusions:

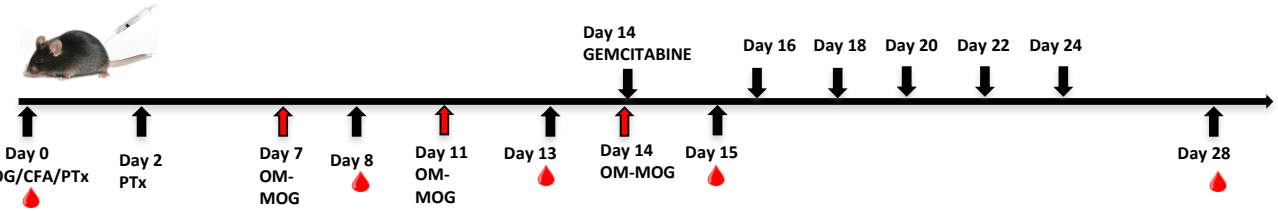
•MDSCs expand in the spleen and peripheral blood of OM-MOG and vehicle-treated mice following immunization with MOG/CFA/PTx for the induction of EAE.

•Gemcitabine efficiently depletes monocytic and granulocytic MDSC in peripheral blood of mice during the development of EAE.

•However, gemcitabine did not break OM-MOG-induced protection of mice against the clinical symptoms of EAE. In contrast, MDSC depletion reduced late-onset clinical symptoms in OM-MOG-tolerized mice.

•These results indicate that gemcitabine-sensitive cells, including MDSC, are not responsible for immune tolerance induced by mannan-conjugated myelin peptides .

Experimental design



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