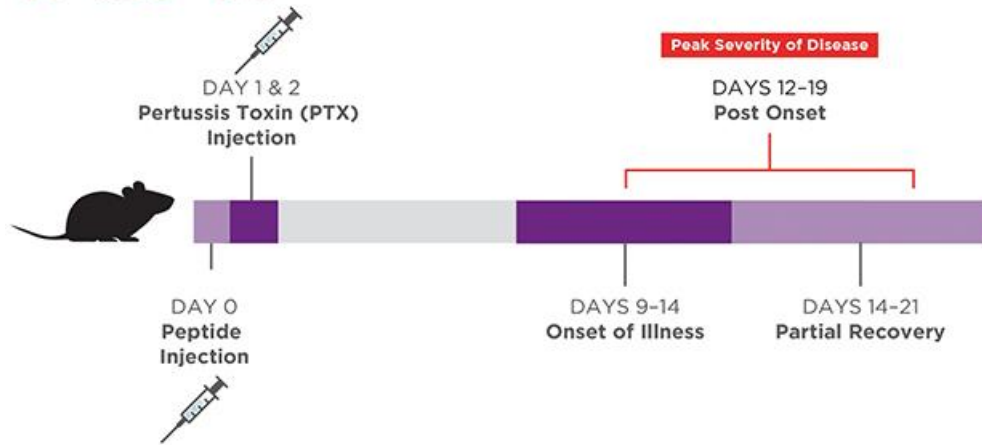
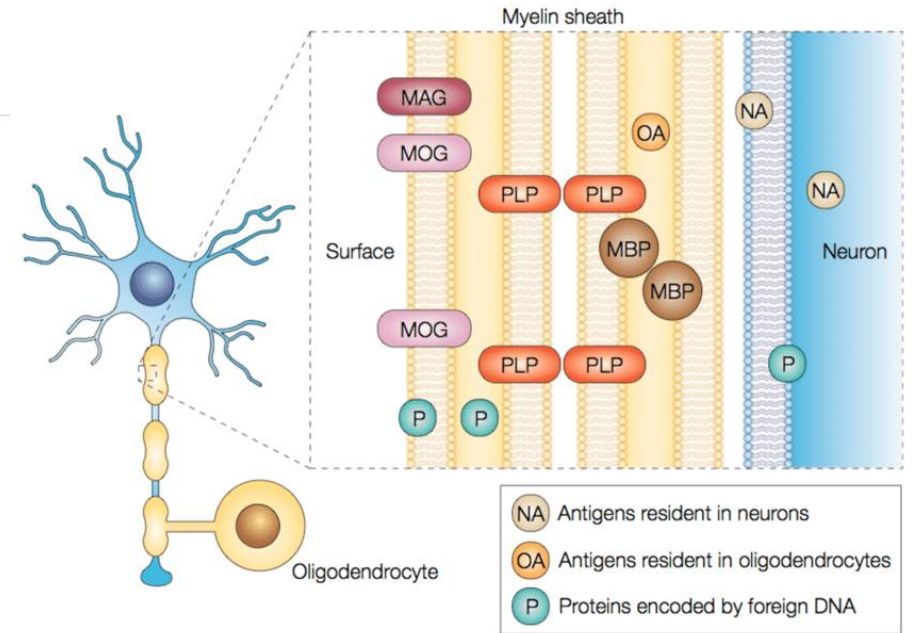


# Treatment with mRNA and EAF

## B6 + MOG + CFA

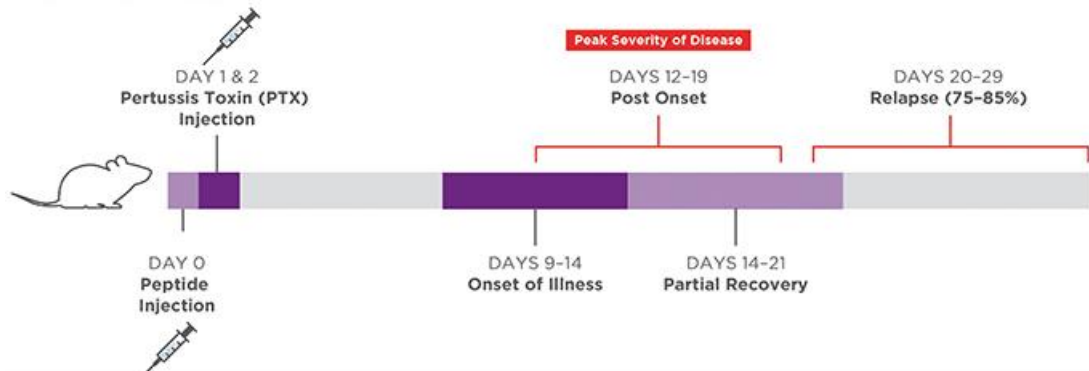


Only 20-30% of B6 will typically show relapsing and remitting disease, SJL mice are more appropriate for relapsing/remitting studies whereas B6 mice make a better chronic model.



## Relapsing/Remitting Model

### SJL + PLP + CFA



75-85% of SJL mice will show the relapsing/remitting phenotype.



MOG/CFA s.c.  
+  
pertussis toxin i.p.

9-16 days later

### TREATMENT:

**Prophylactic**  
From day of immunization

**Semi-therapeutic**  
From time 10-20% of mice are sick

**Therapeutic**  
From first sign of EAE in each mouse

## Paralysis

Clinical scores:

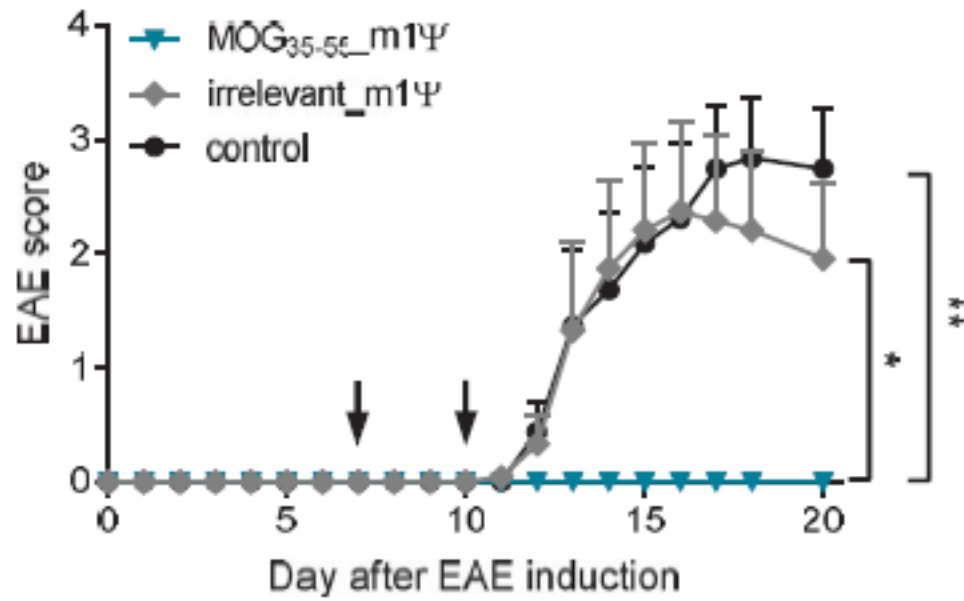
- 1 - limp tail
- 2 - partial hind leg paralysis
- 3 - complete hind leg paralysis
- 4 - complete hind and partial front leg paralysis
- 5 - moribund

# Prevention and therapeutic impact

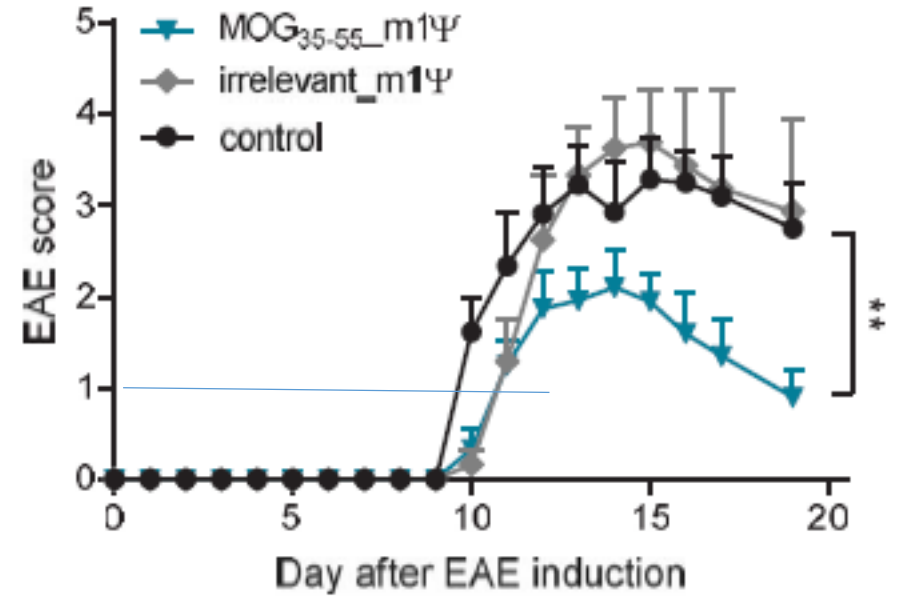
D7 and D10 after induction

Disease progression  
Paralysis of the tail or hind limbs

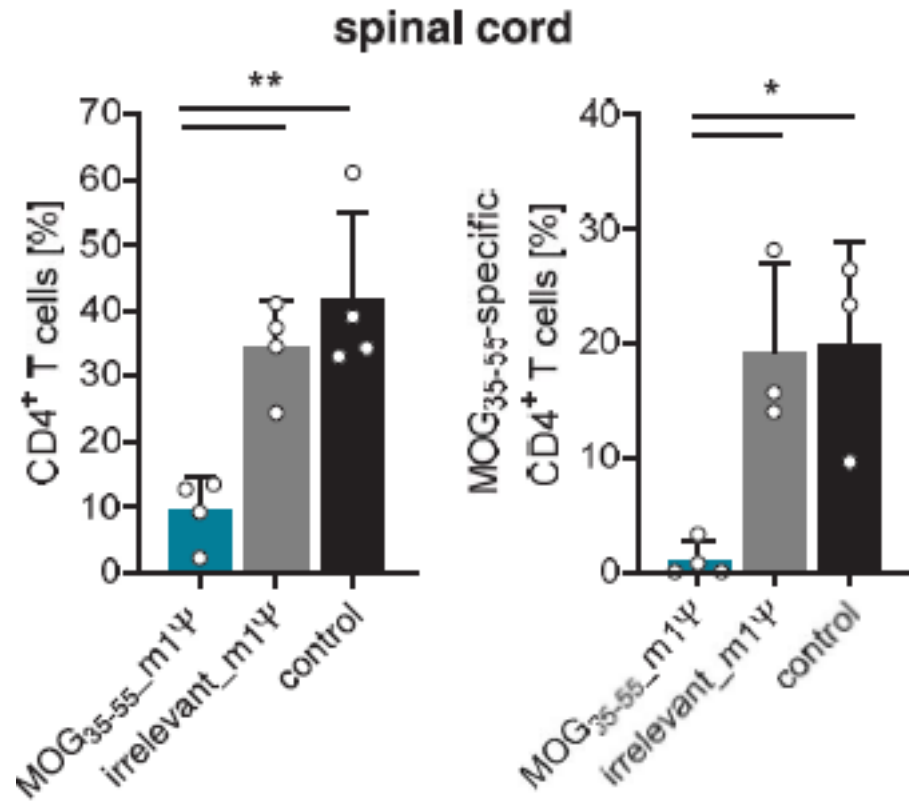
**A**



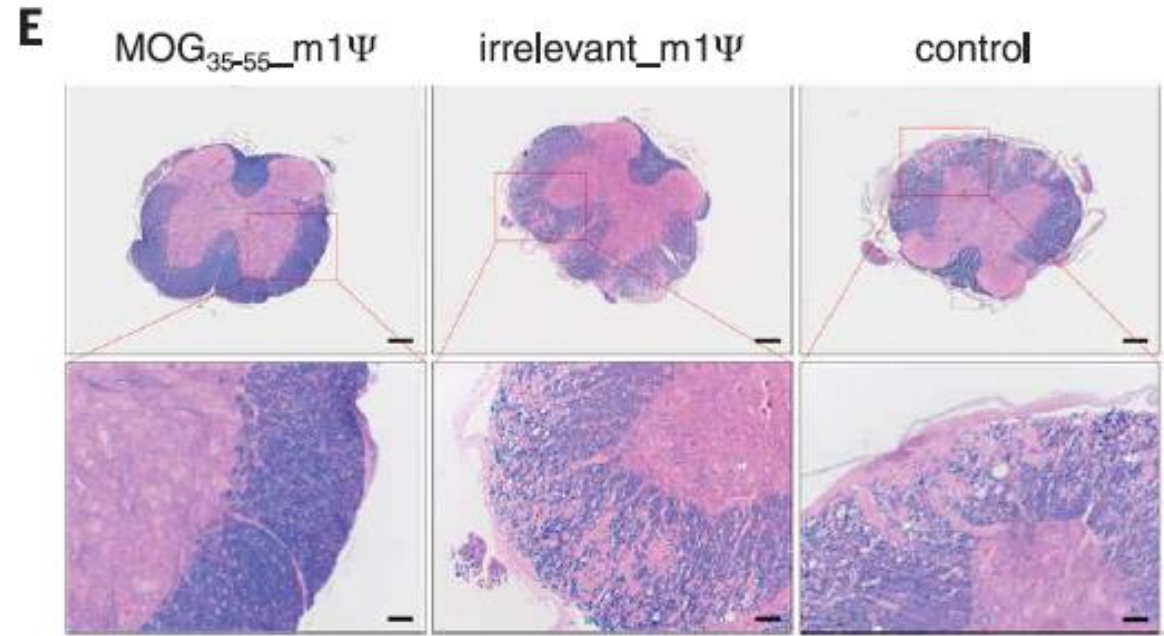
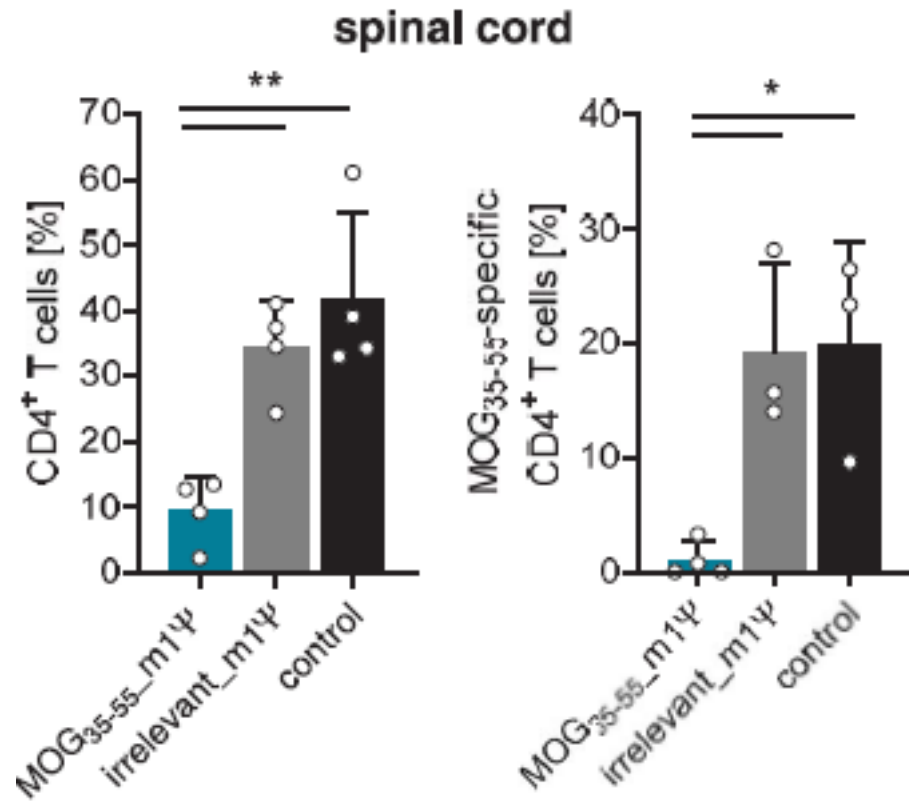
**B**



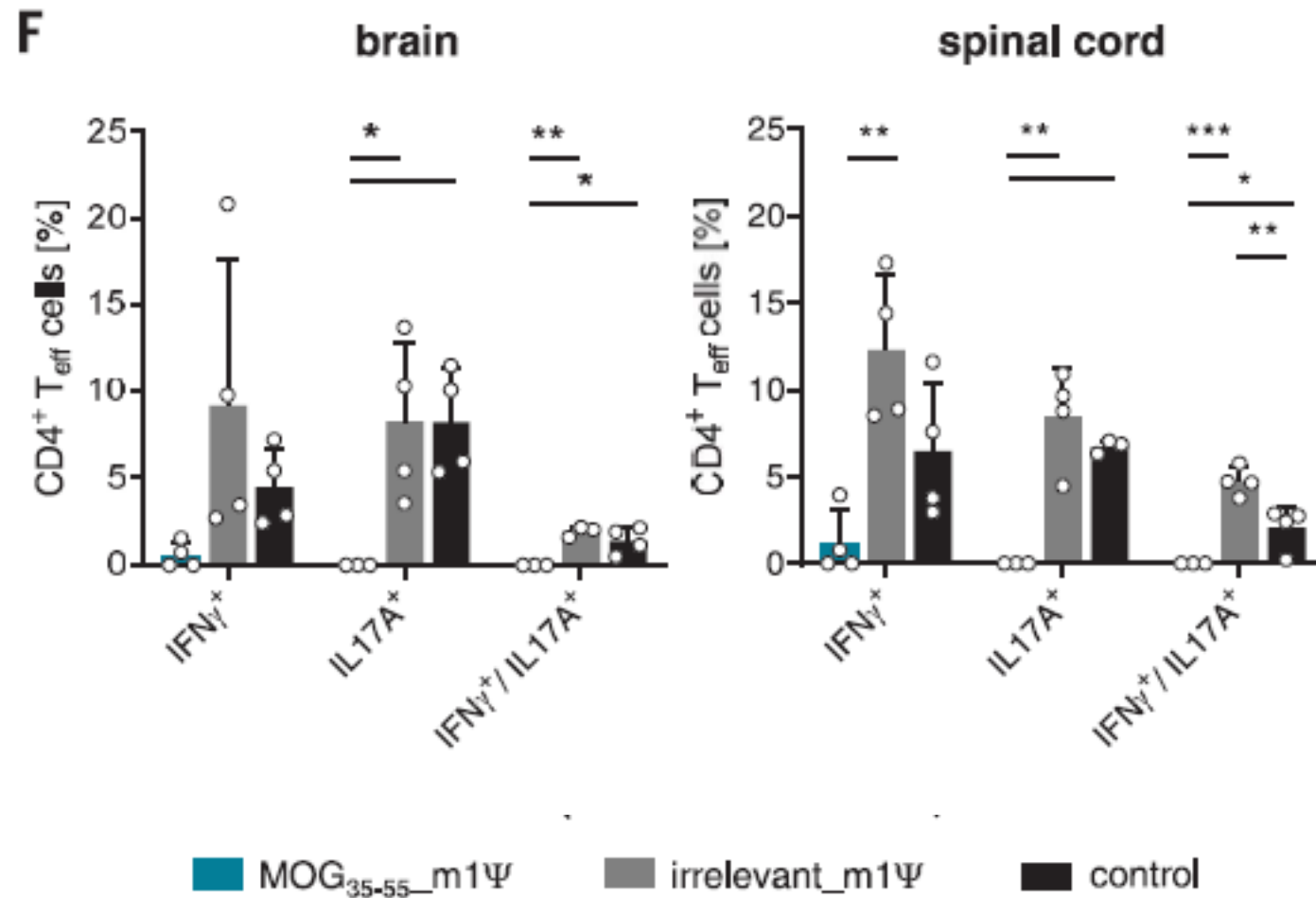
# Impact on CNC infiltration



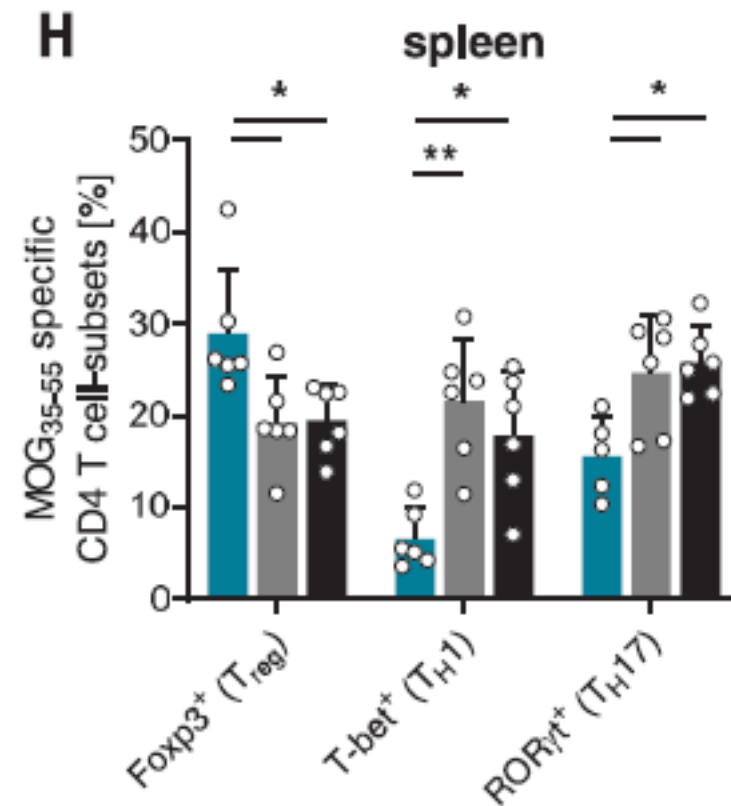
# Impact on CNC infiltration



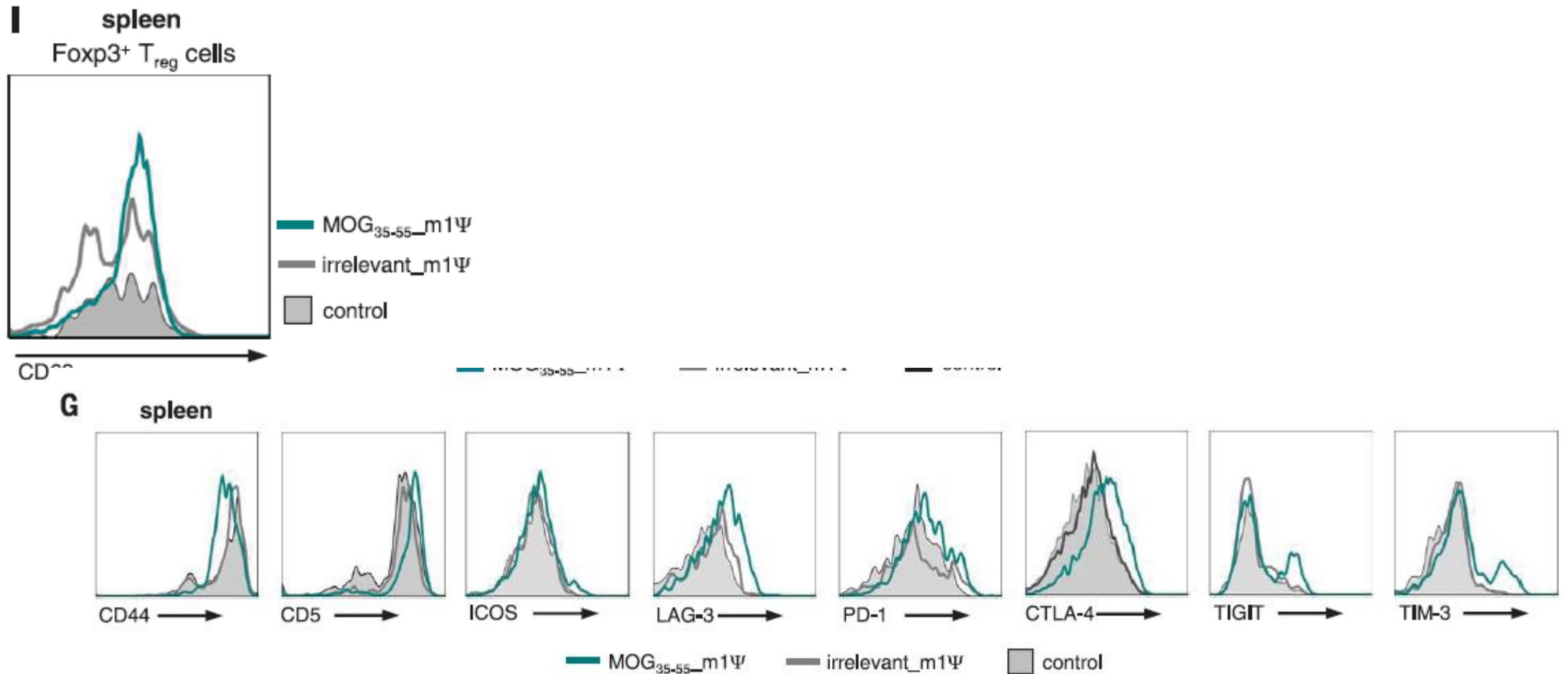
# Impact on CNC infiltration



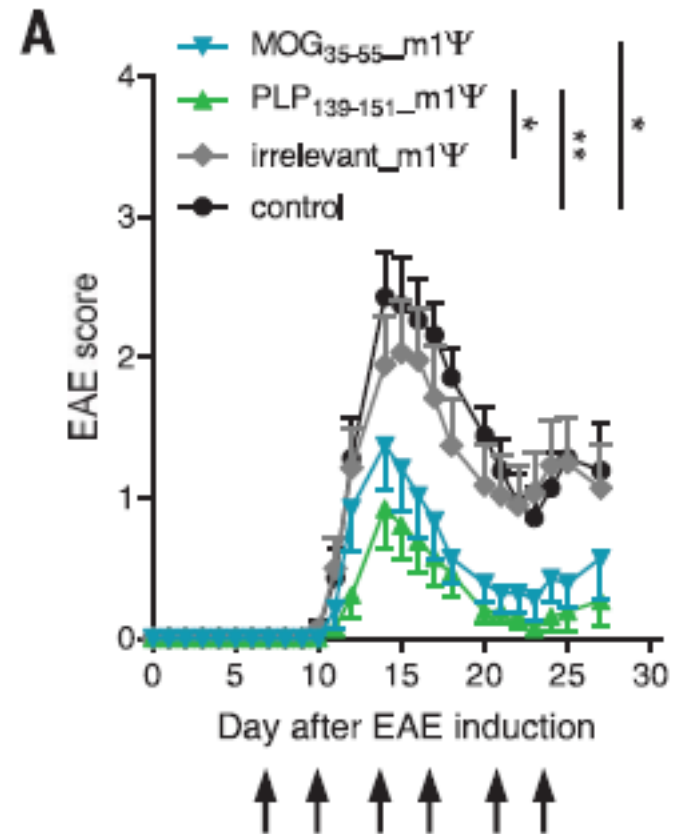
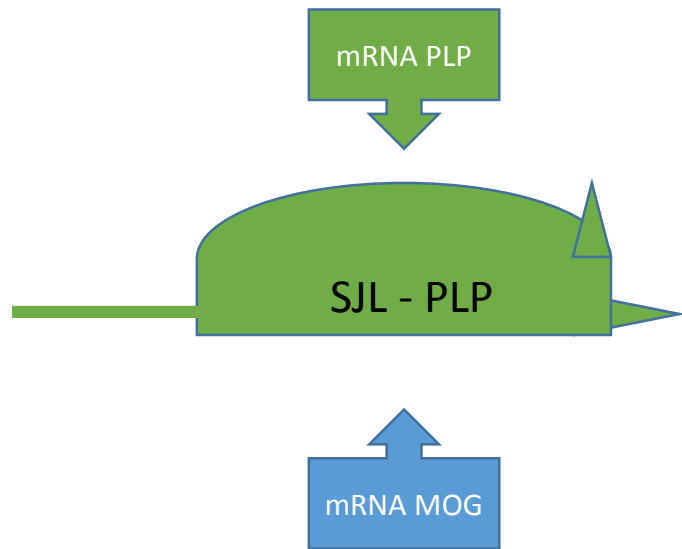
# Characterization of T cells induced by mRNA Prevention – D16



# Characterization of T cells induced by mRNA Prevention – D16

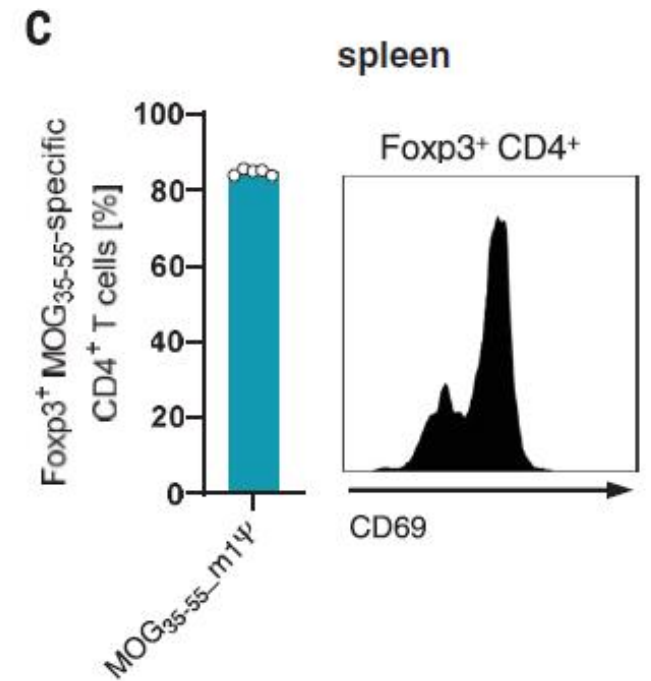
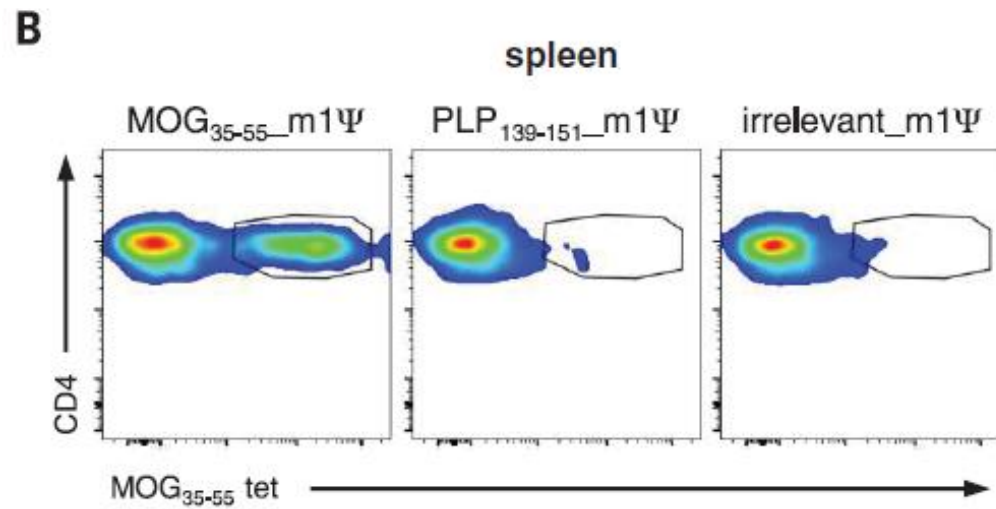
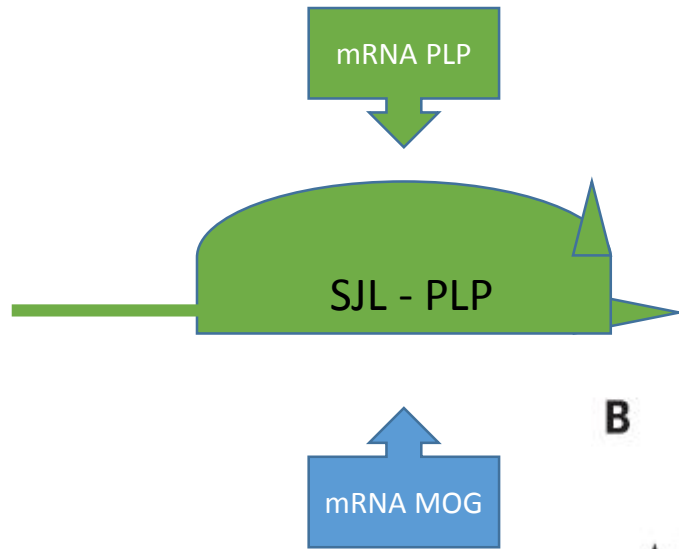


# Induction of bystander tolerance

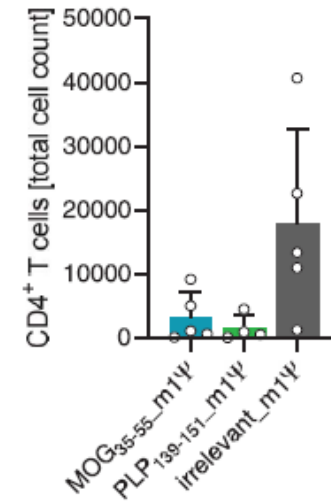
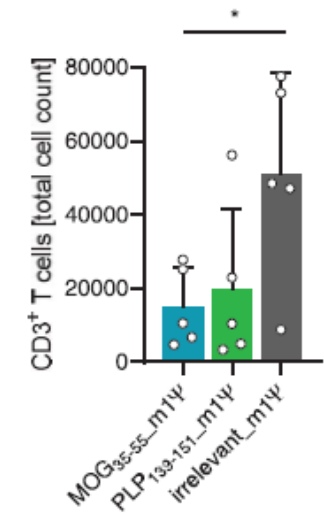
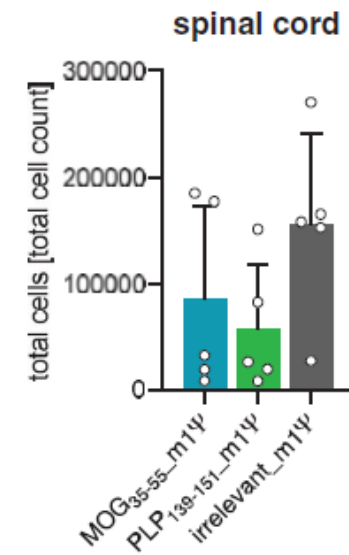
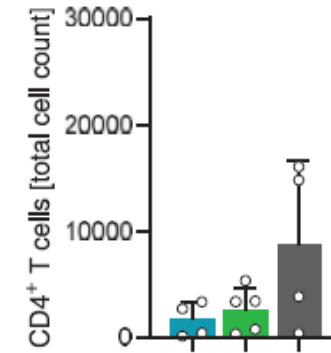
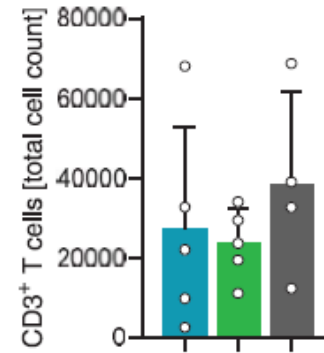
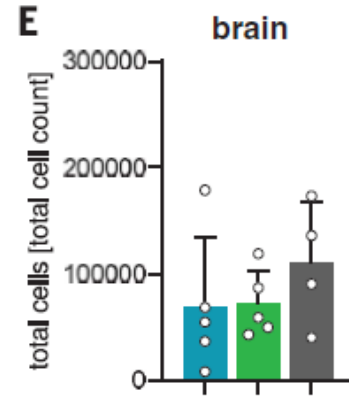
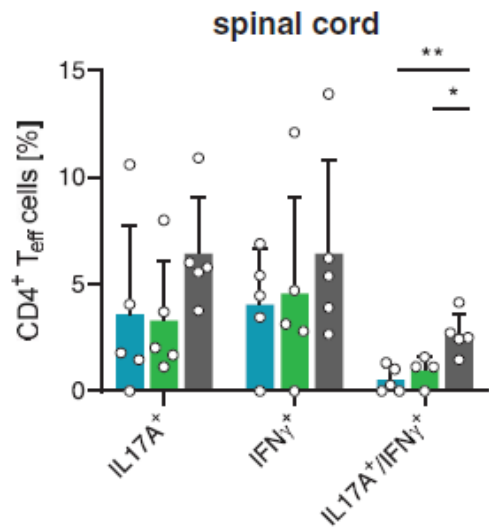
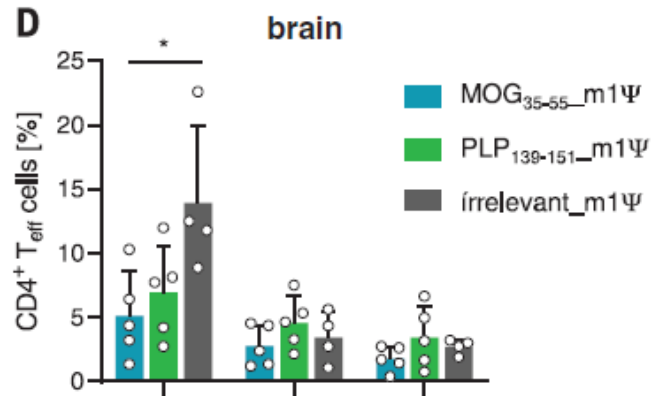
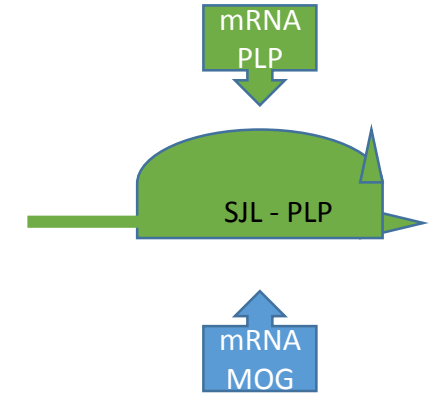




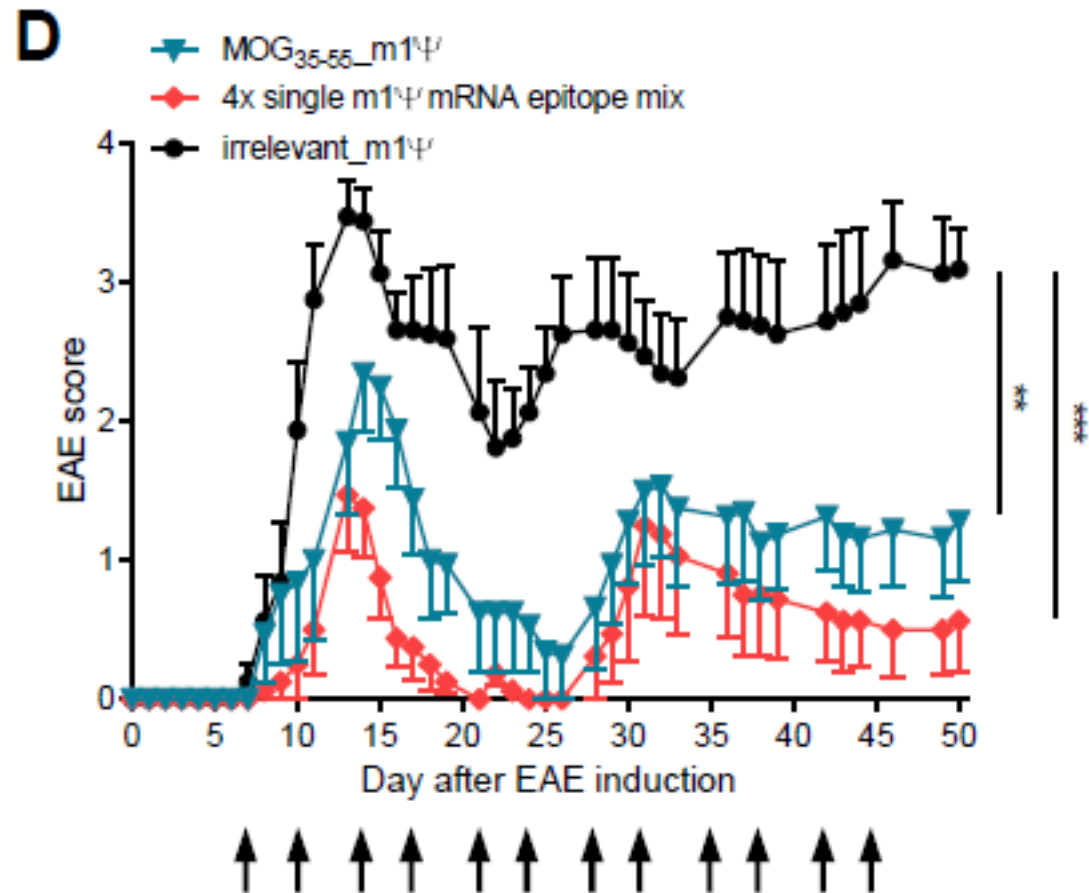
# Induction of bystander tolerance



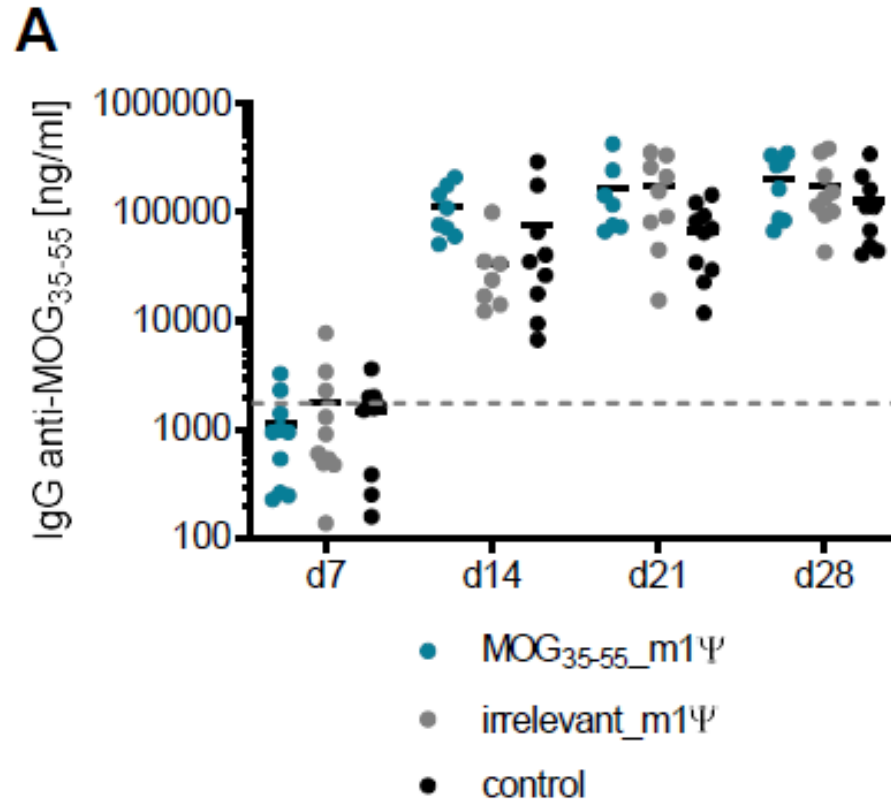
# Induction of bystander tolerance



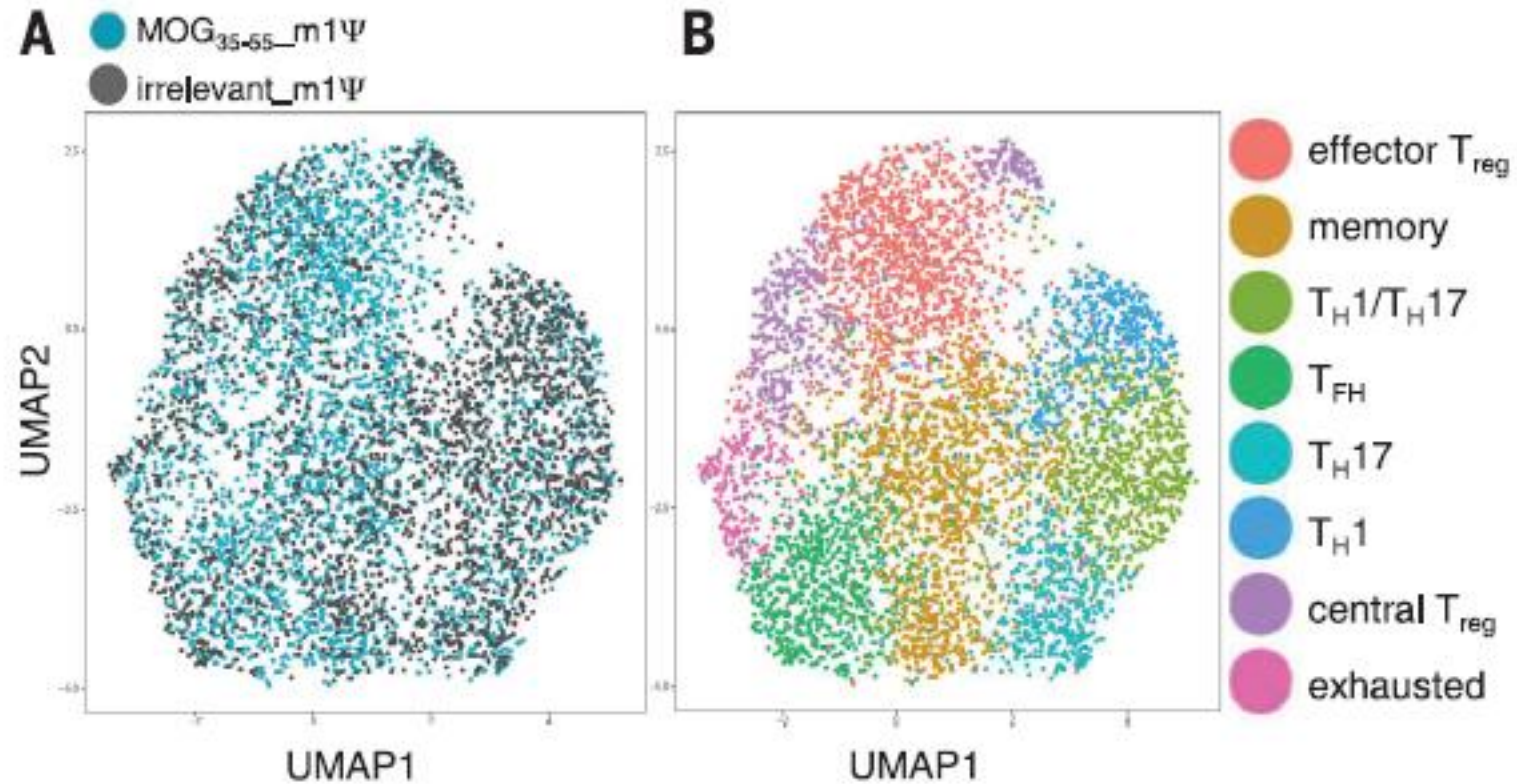
# Impact on polyclonal autoimmune disease driven



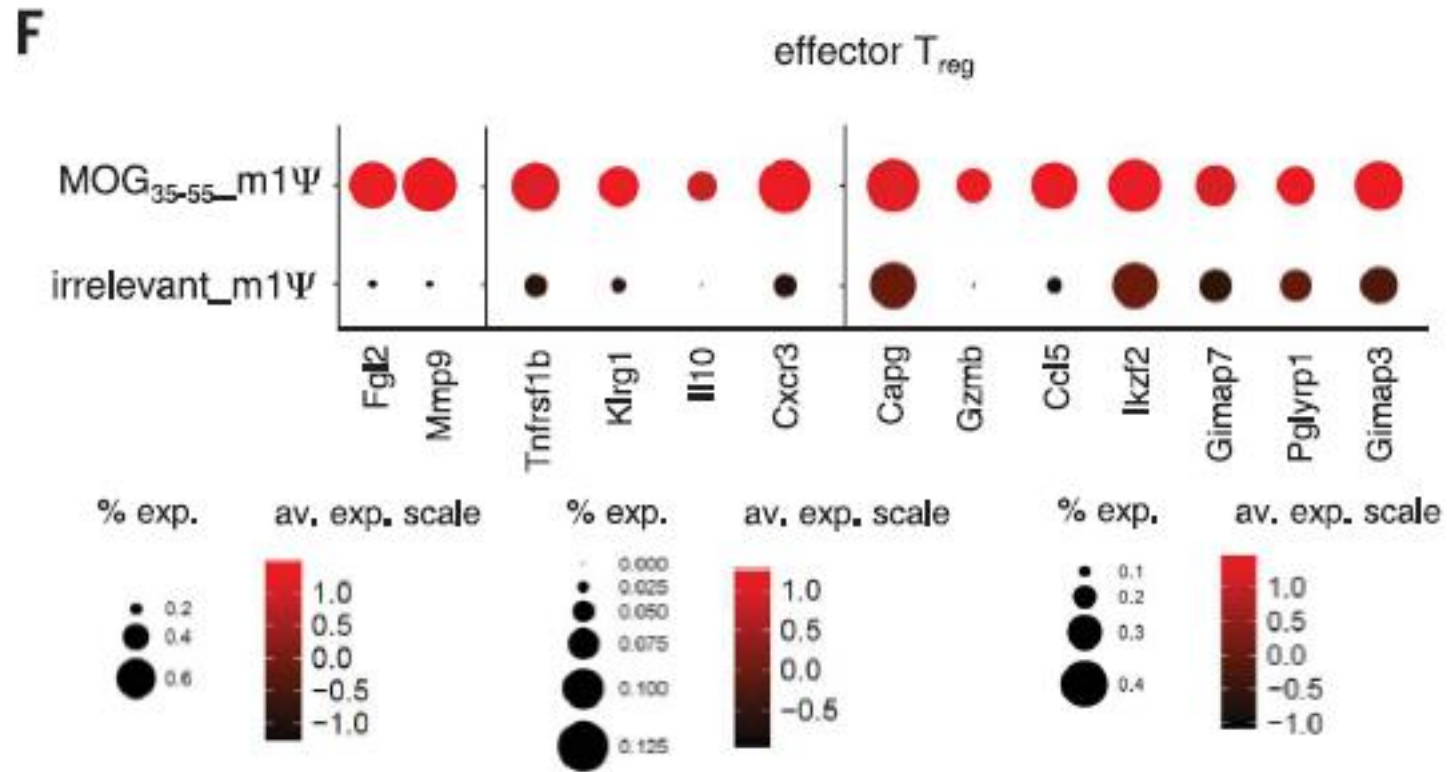
# Absence of autoAg-specific Ab response



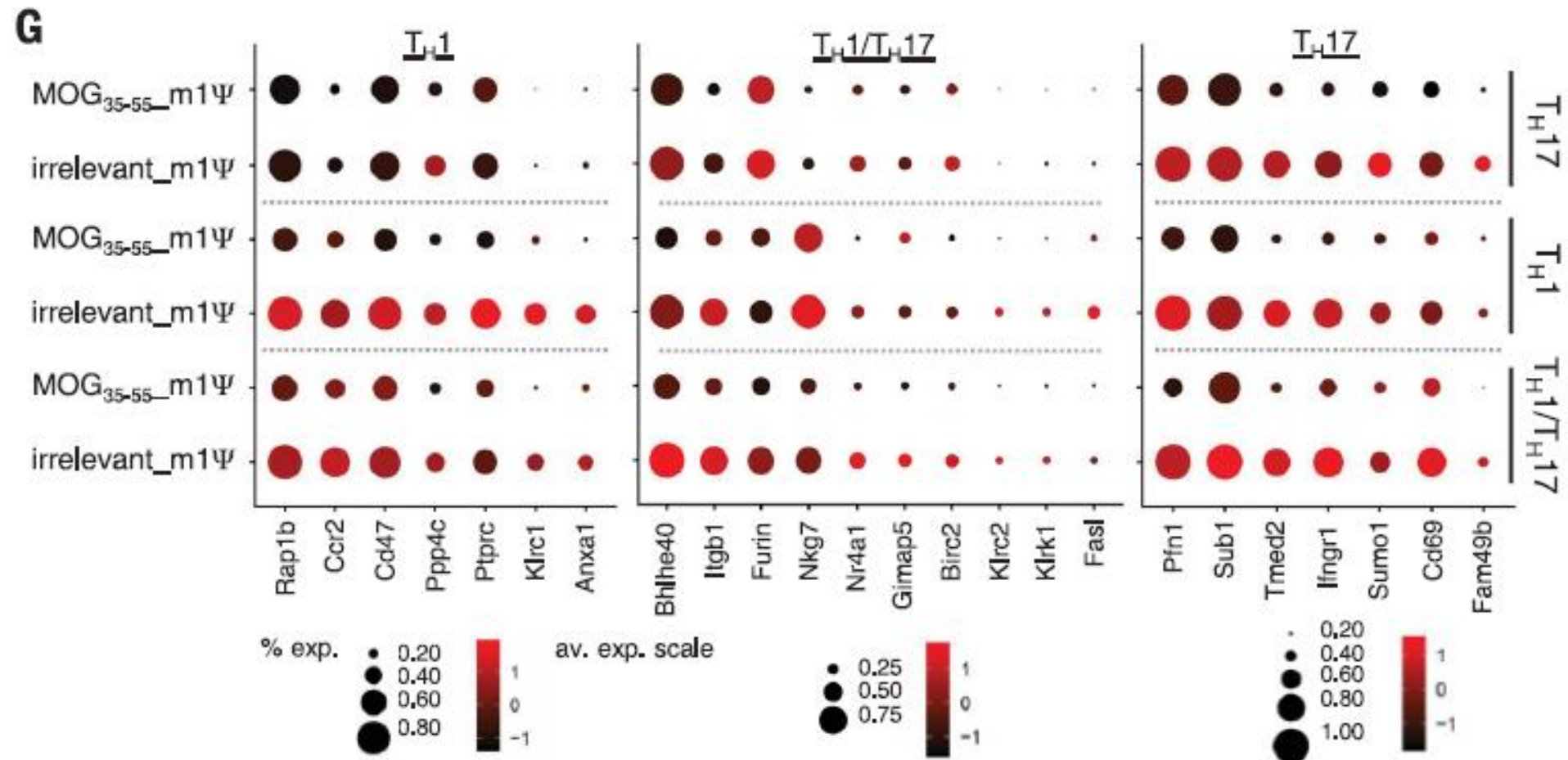
# Phenotypic characterization – single cell RNAseq



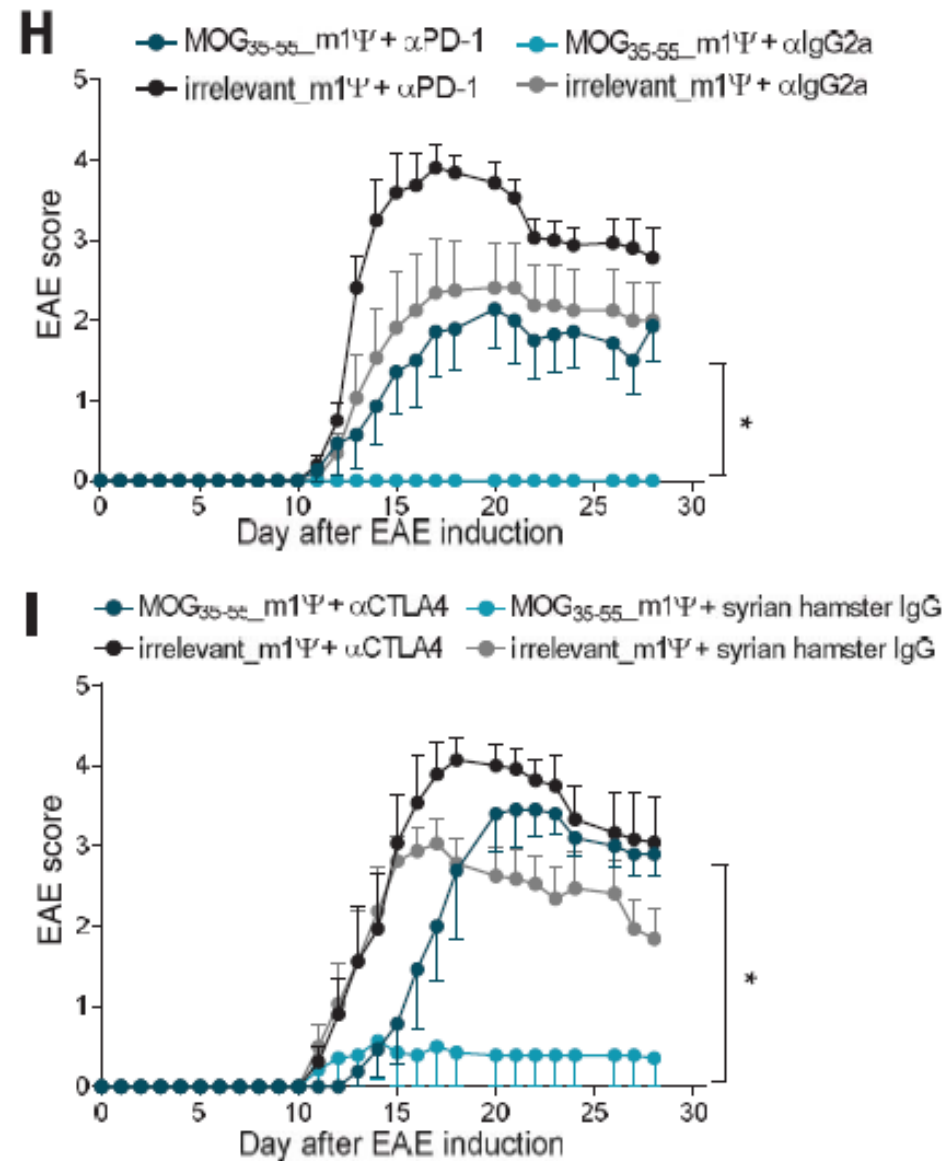
Up-regulation of genes involved in suppressive functions of Treg:  
 TNFR2, KLRG1, IL10, GrB...



Down-regulation of genes involved in migration (ccr2, Pap1b), cytokine prod (Bhlhe40) functions (Cd69) of Teff



# Role of CTLA4 and PD1 axis





# Sum-up: mRNA vaccine in AID!

- What is new?
  - mRNA vaccine in AID
  - m1Ψ and abrogation of TLR7 stimulation
  - Bystander tolerance
  - Treg induction
- Applications?
  - Identification of Auto-Ag
  - Long term efficacy?