



FACULDADE DE  
**MEDICINA**  
LISBOA

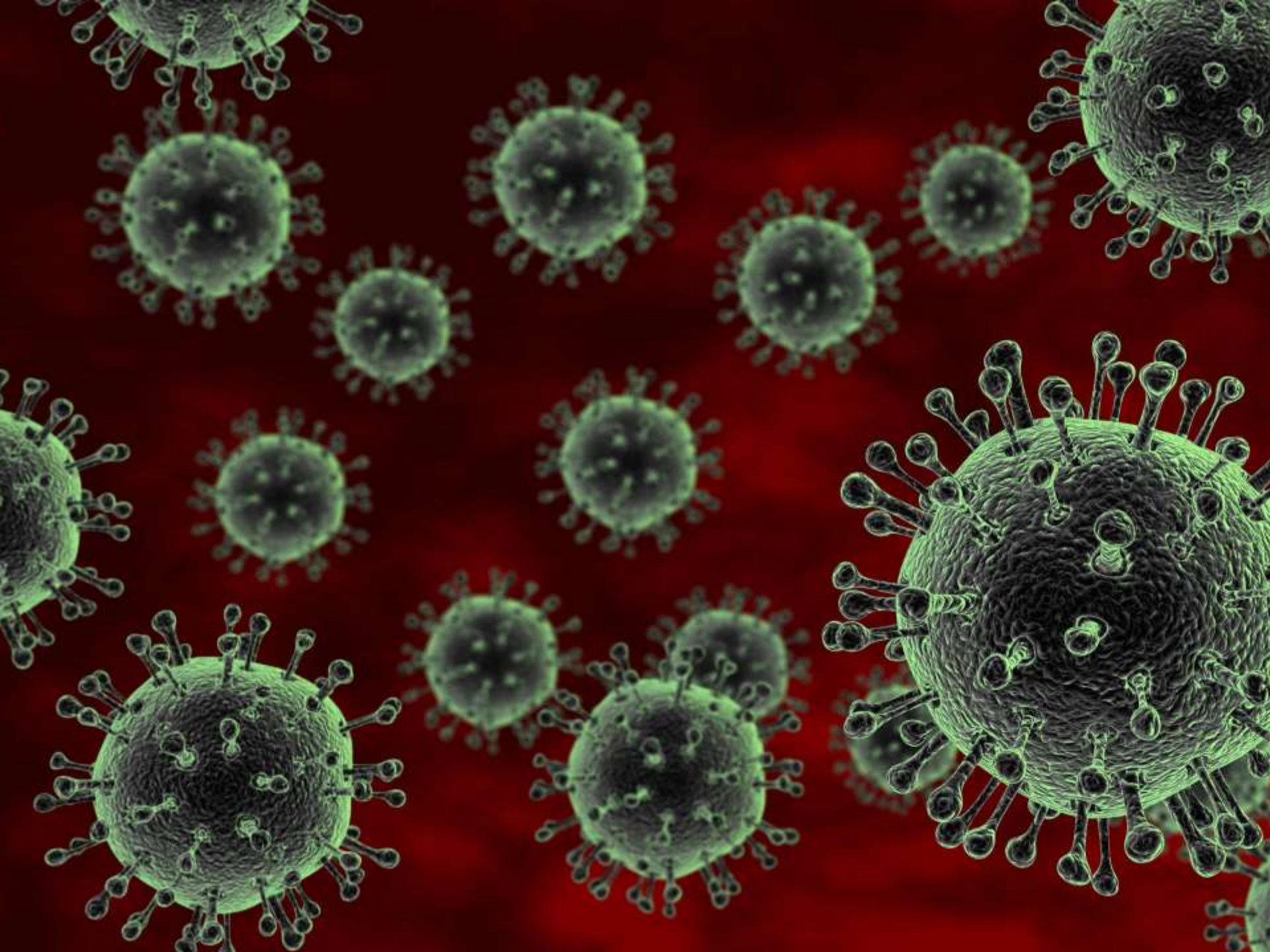


Instituto  
de Medicina  
Molecular

# The regulation of immune responses in health and disease

Luis Graca

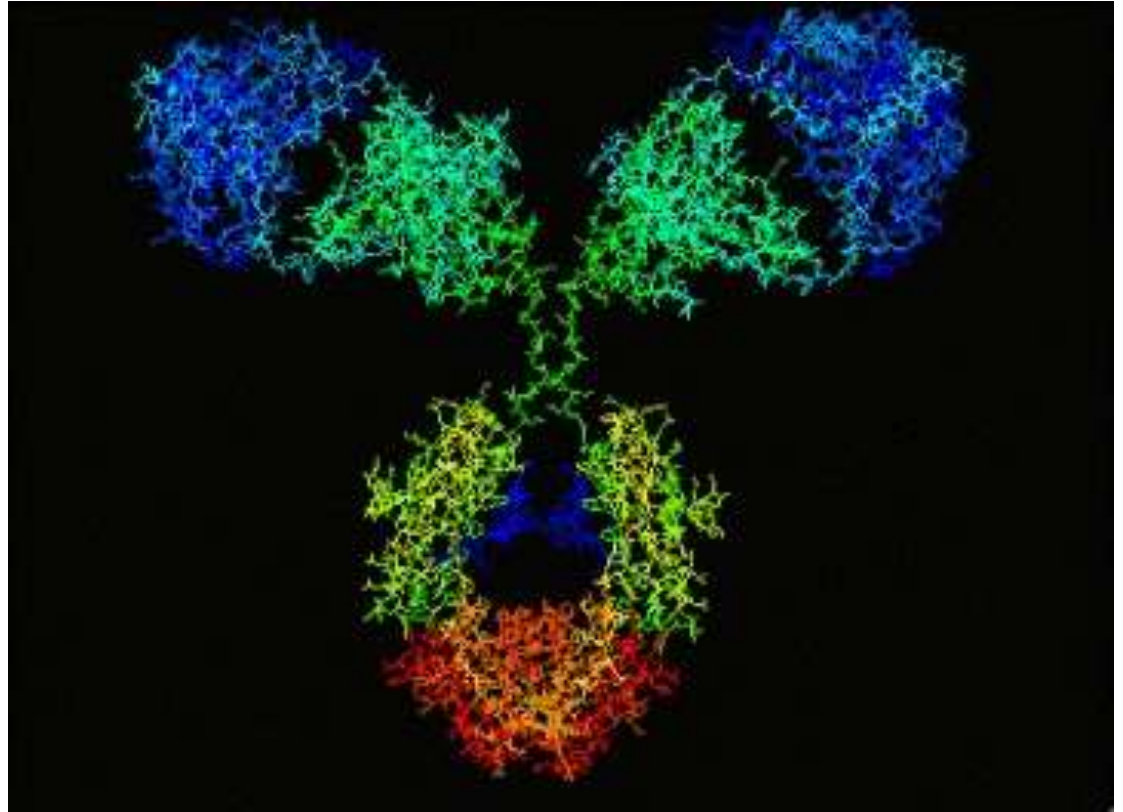
**Instituto de Medicina Molecular,**  
Faculdade de Medicina da Universidade de Lisboa



The immune system can identify any shape that exists, or that does not exist

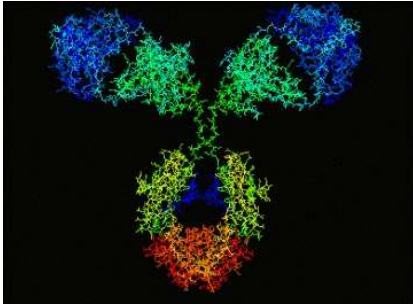


**Karl Landsteiner (1868-1943)**





# Not all our cells have identical genes

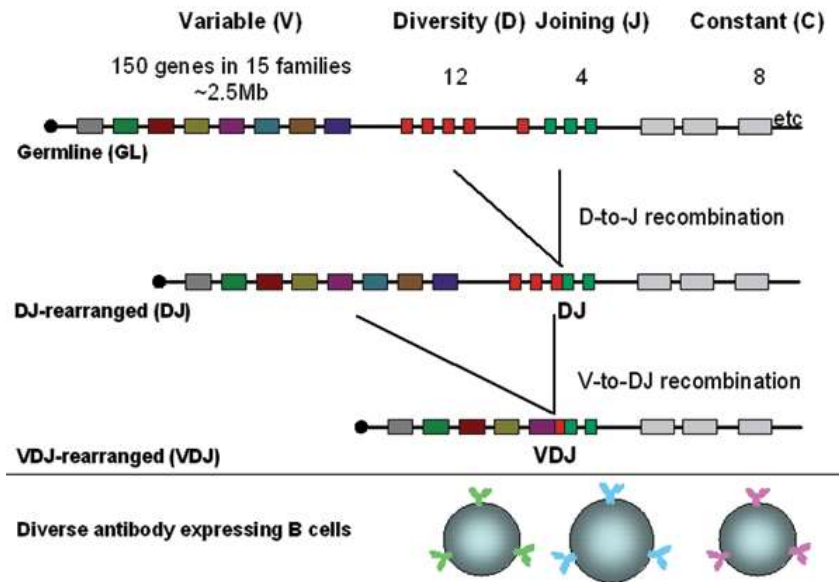


<40,000 genes

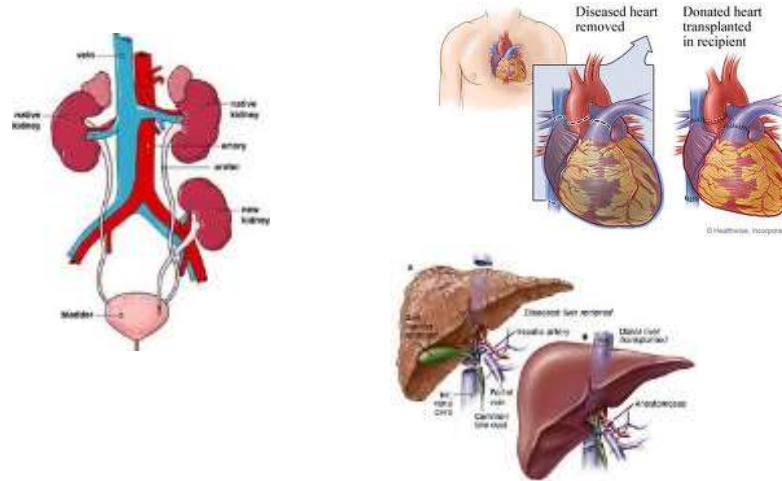
1,000,000,000,000 different proteins



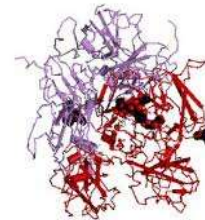
Susumo Tonegawa (1939- )



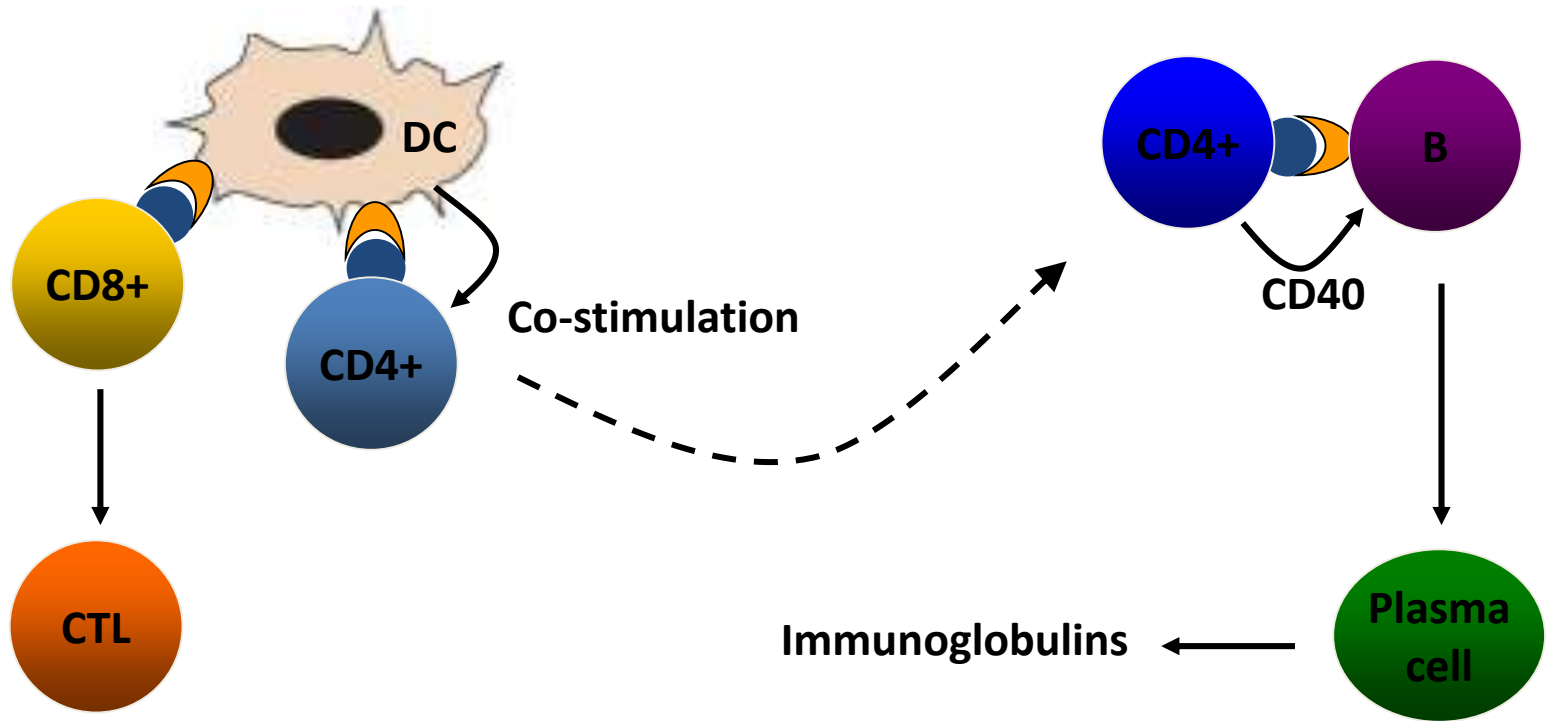
# Protective immunity and immune tolerance

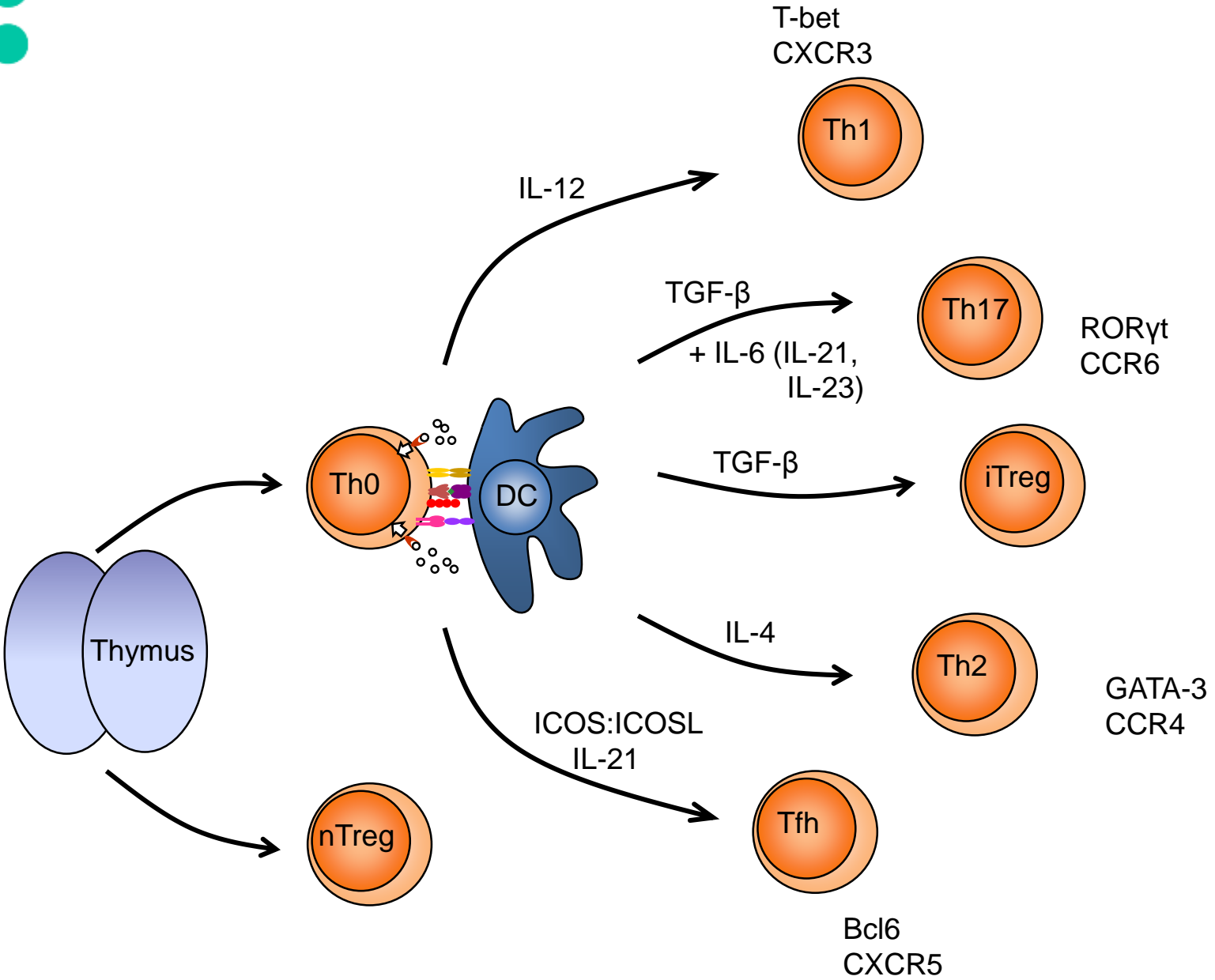


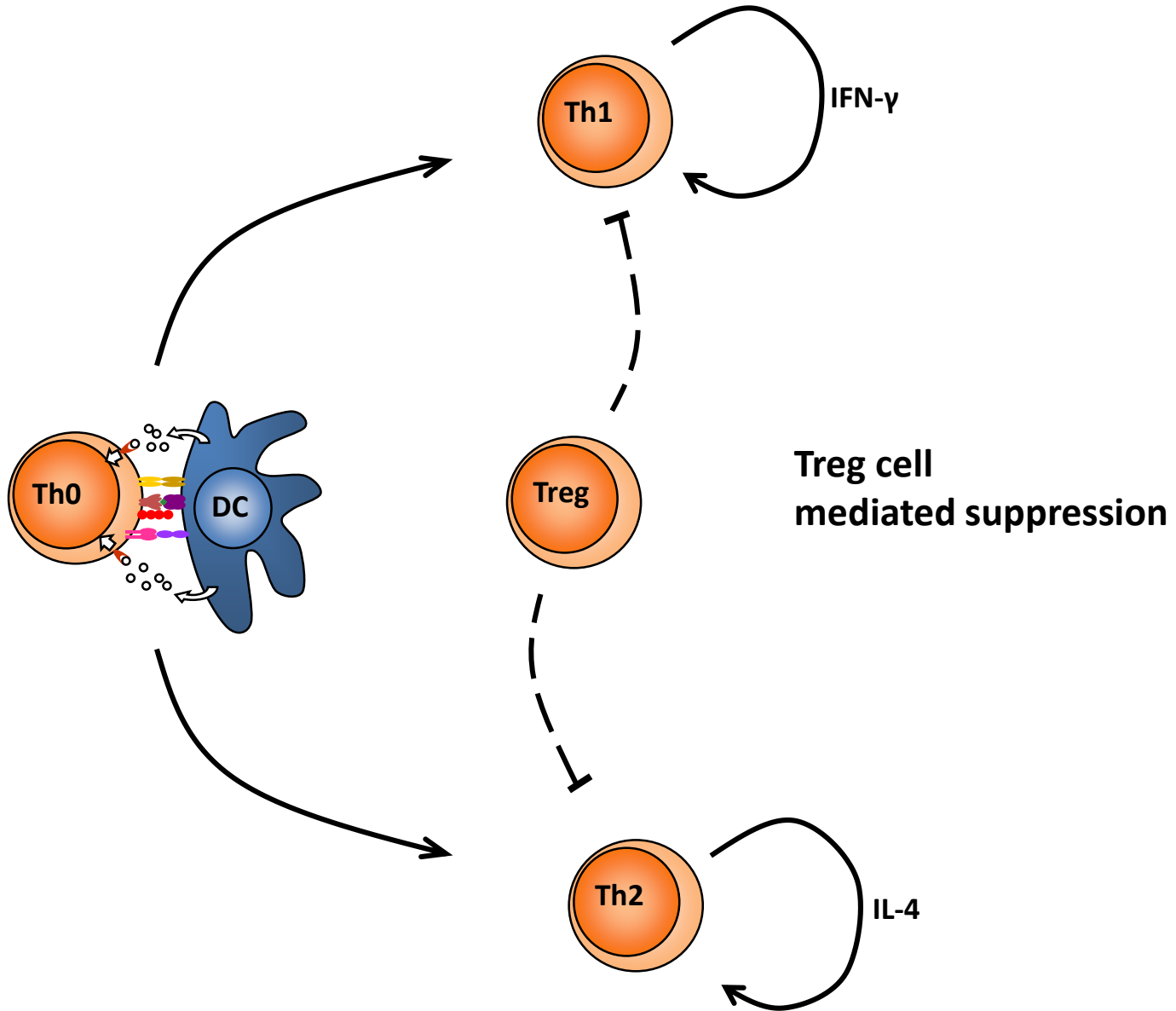
gene therapy  
protein/enzyme replacement therapy



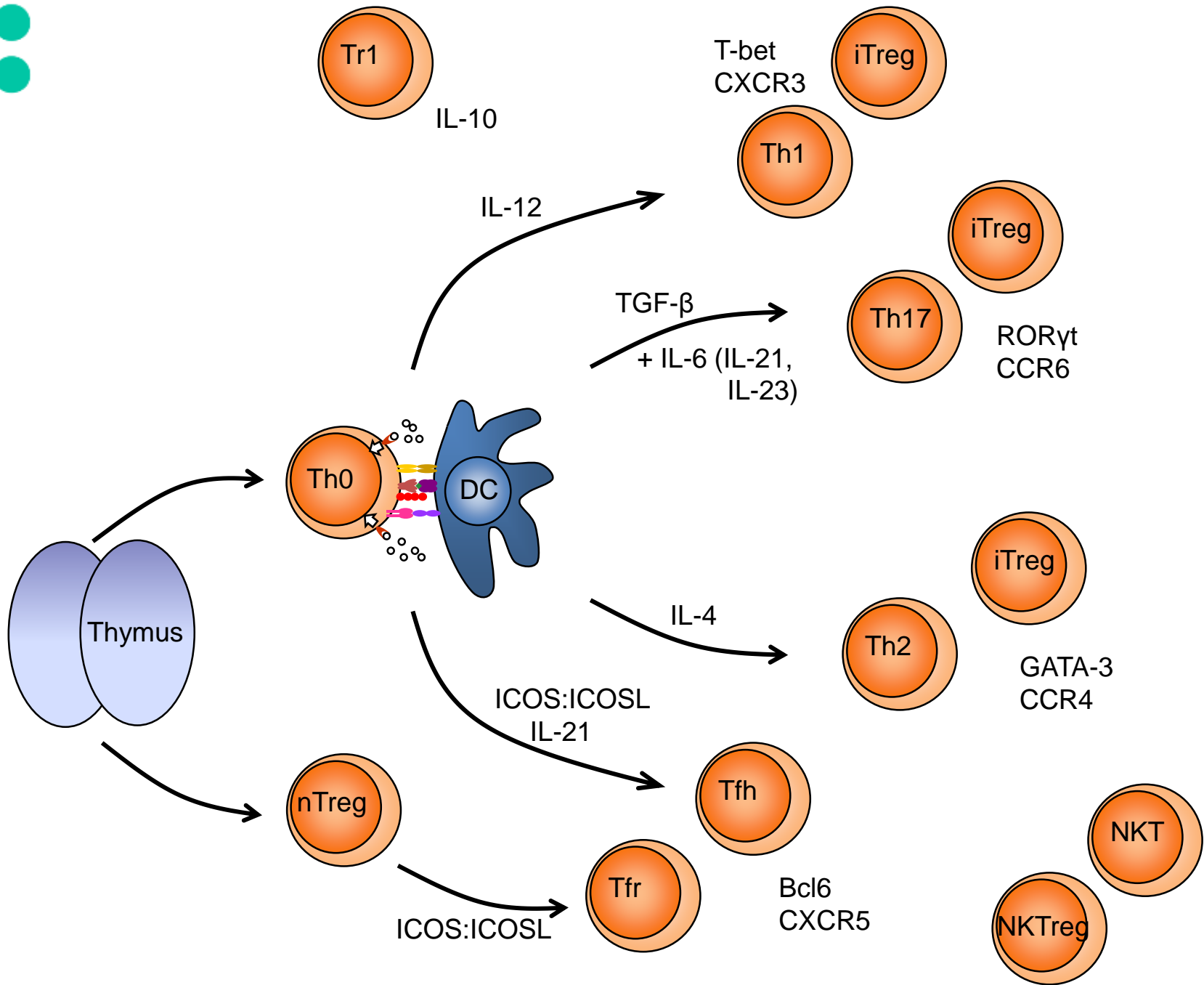
# CD4 T cells are essential for the control of an immune response













# Major achievements

Strategies to induce immune tolerance in several experimental settings (transplantation, autoimmunity, allergy, hemophilia)

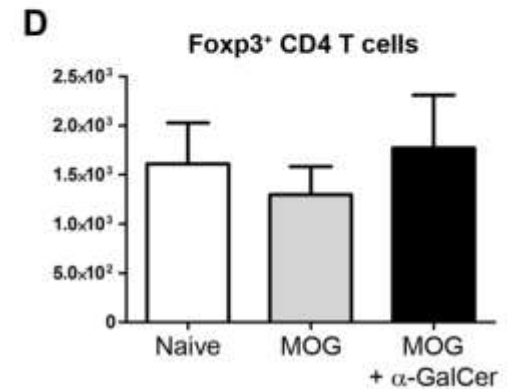
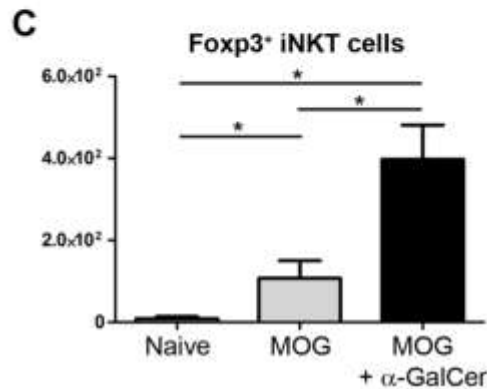
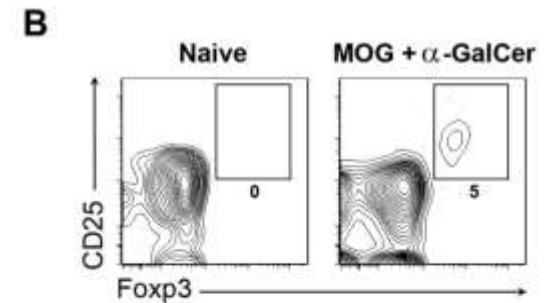
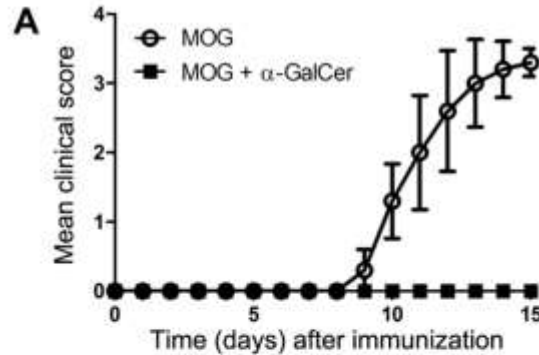
Identification of non-conventional regulatory T cell subsets

**Organ-specific regulatory T cells** (NKTreg cells)

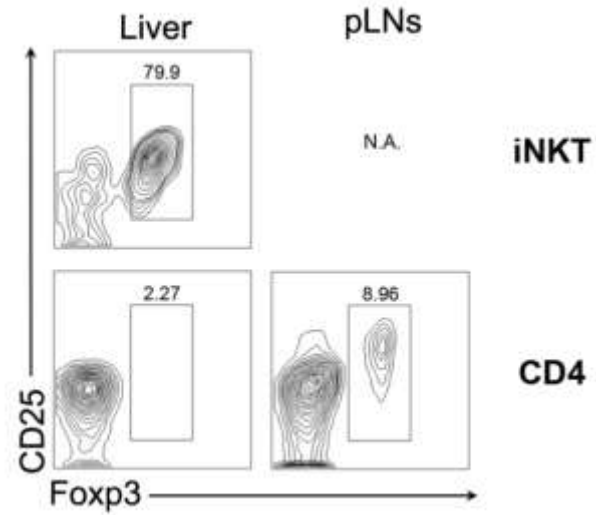
Regulation of germinal center formation and antibody production (Tfr cells)

# Foxp3<sup>+</sup> iNKT cells in cervical lymph nodes of mice protected from EAE

C57Bl/6 – MOG-CFA

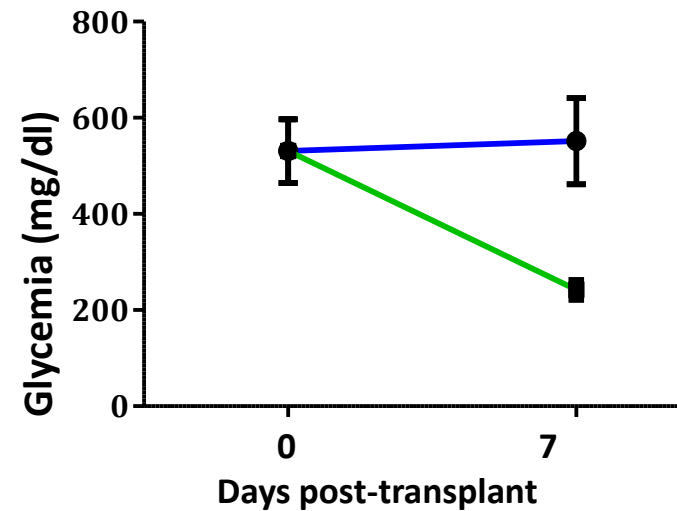
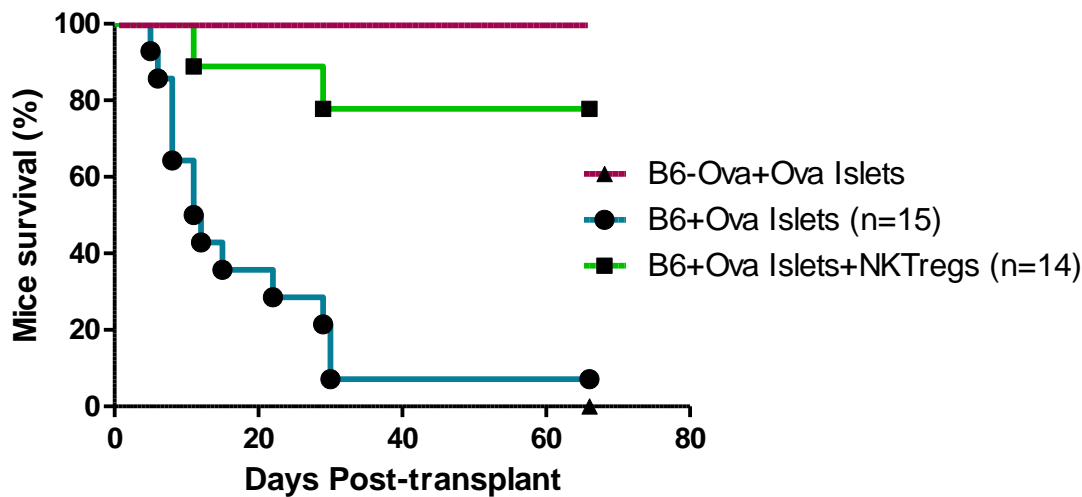


# Adoptive transfer of Foxp3<sup>+</sup> iNKT cells leads to liver accumulation



Liver-specific immune suppression?

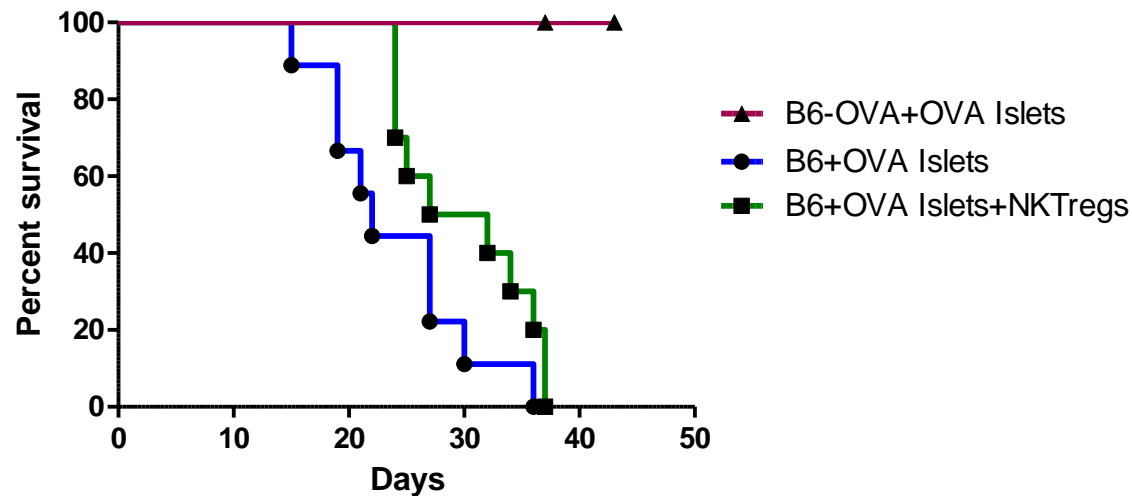
# Foxp3<sup>+</sup> iNKT cells lead to prolonged survival of intra-portal-delivered islet allografts in mice



OVA-expressing islets transplanted into diabetic (STZ-treated) B6 mice  
3 independent experiments, n= 15

*Silvia Almeida, unpublished*

# Foxp3<sup>+</sup> iNKT cells **do not** prolong survival of islet allografts transplanted under the kidney capsule

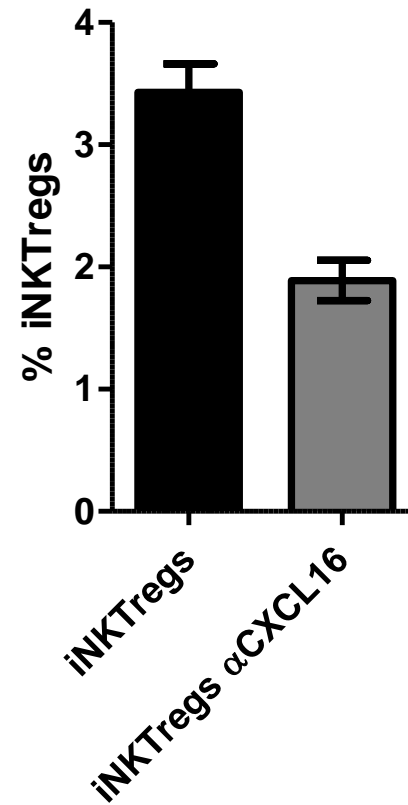
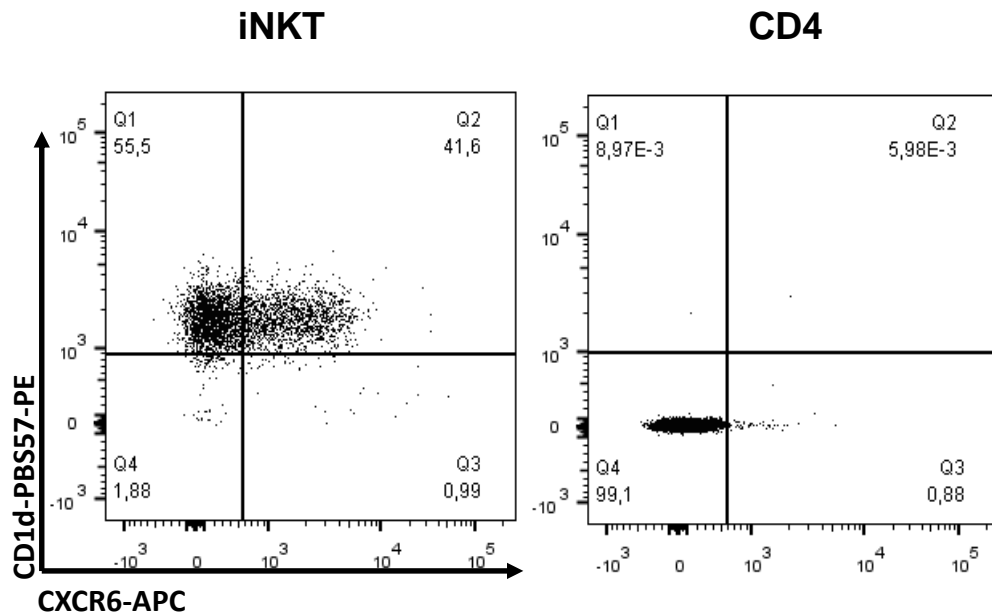


OVA-expressing islets transplanted into diabetic (STZ-treated) B6 mice  
3 independent experiments, n= 15, *P* = non-significant

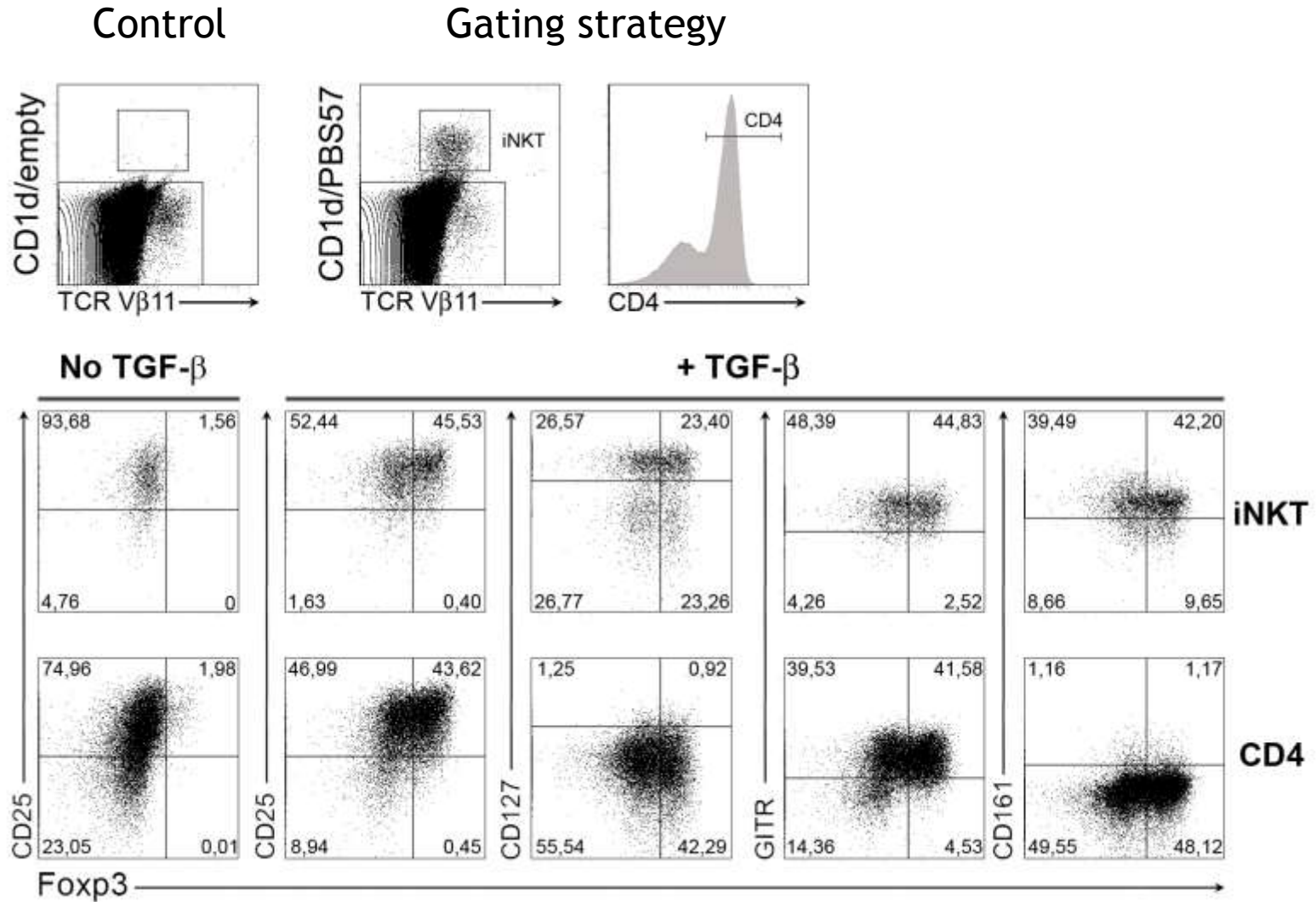
*Silvia Almeida, unpublished*



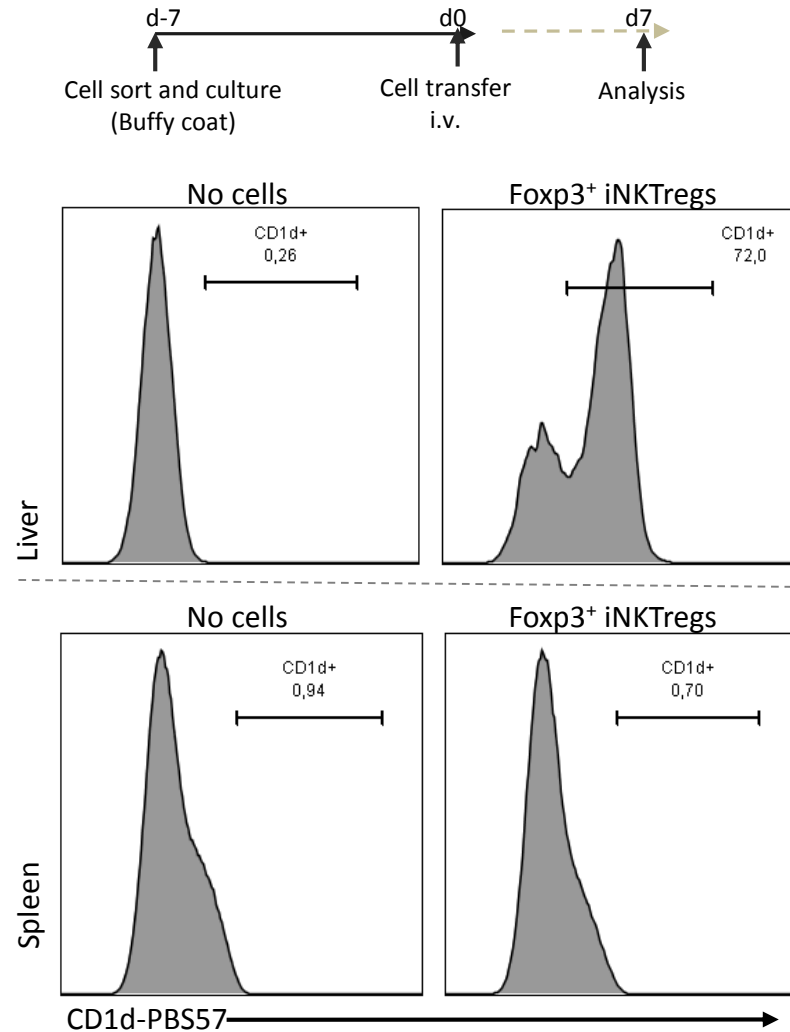
# Migration of Foxp3<sup>+</sup> iNKT cells into the liver is CXCR6-dependent



# Foxp3 can be induced in human iNKT cells



# Human $\text{Foxp3}^+$ iNKT cells migrate to the liver





# Conclusions

Regulatory T cell subset with ability to home to a specific anatomic location

Immunesuppressive effects restricted to an anatomic site

Systemic immune responses remain unaffected



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Molecular

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- Herman Waldmann, Oxford
- Jocelyne Demengeot, IGC, Oeiras
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