INSTITUTO DE MEDICINA MOLECULAR

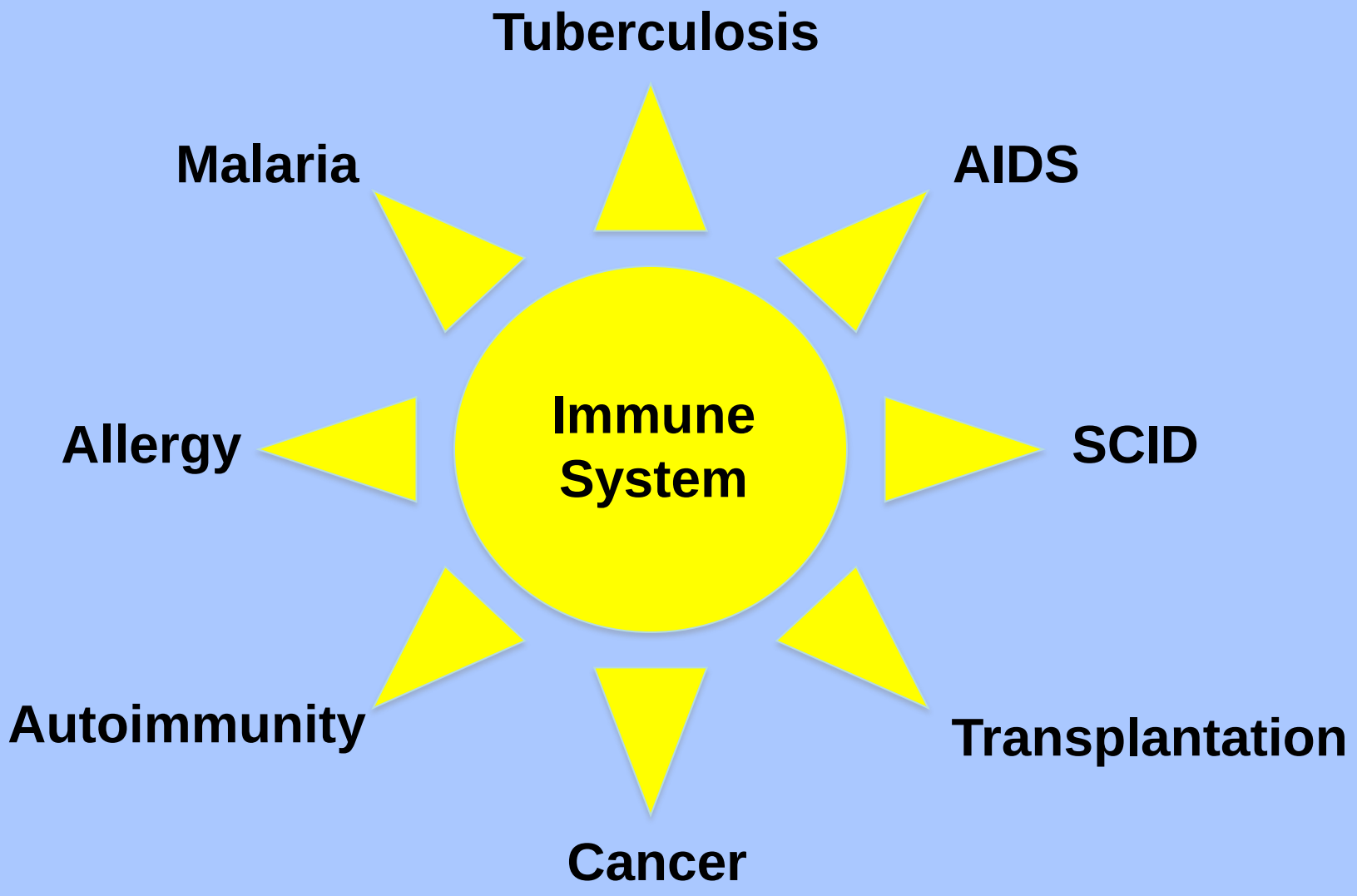
FACULDADE DE MEDICINA DA UNIVERSIDADE DE LISBOA

Molecular control of T cell function in immune responses

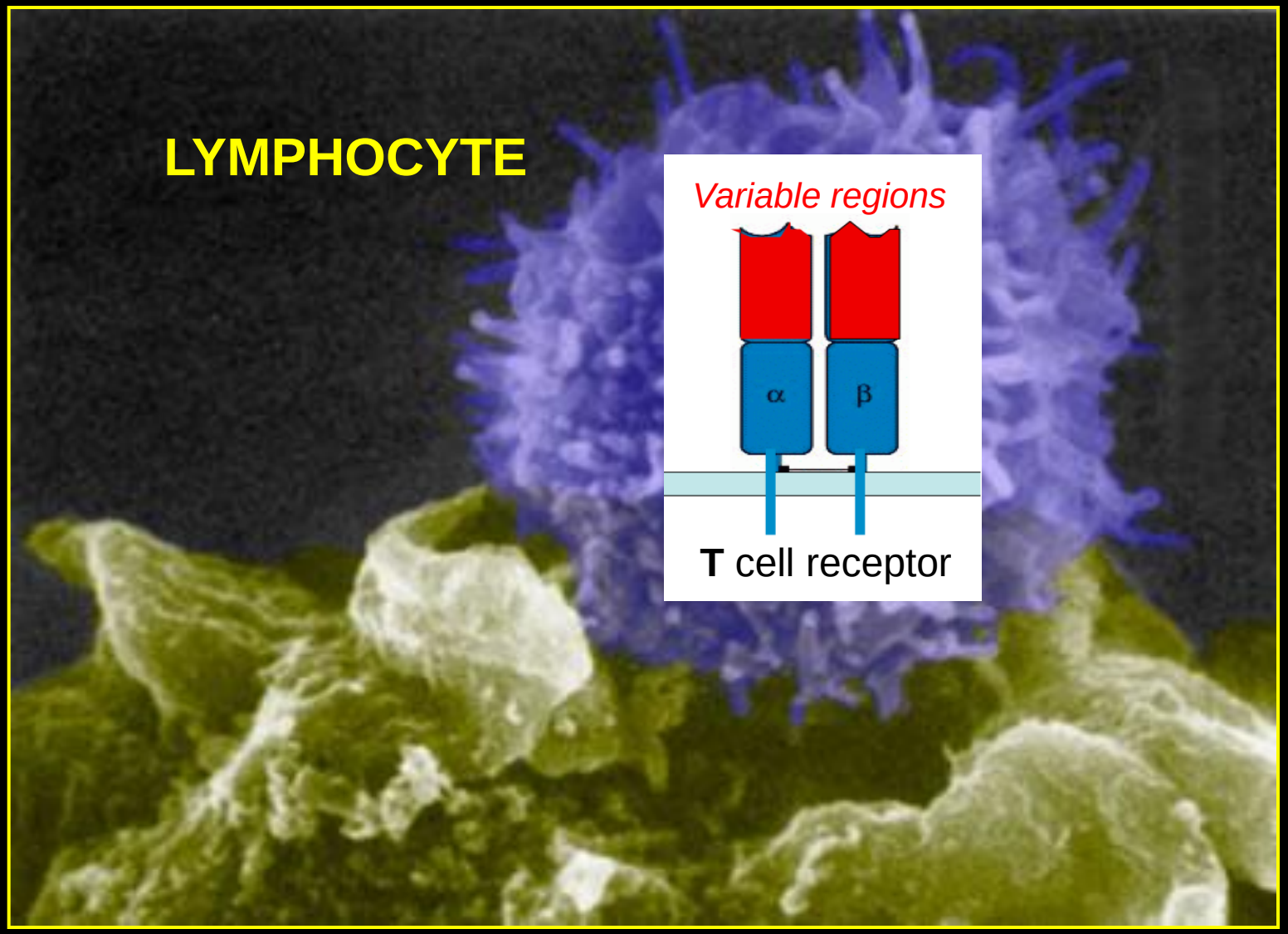
Bruno Silva-Santos

Ciência 2012

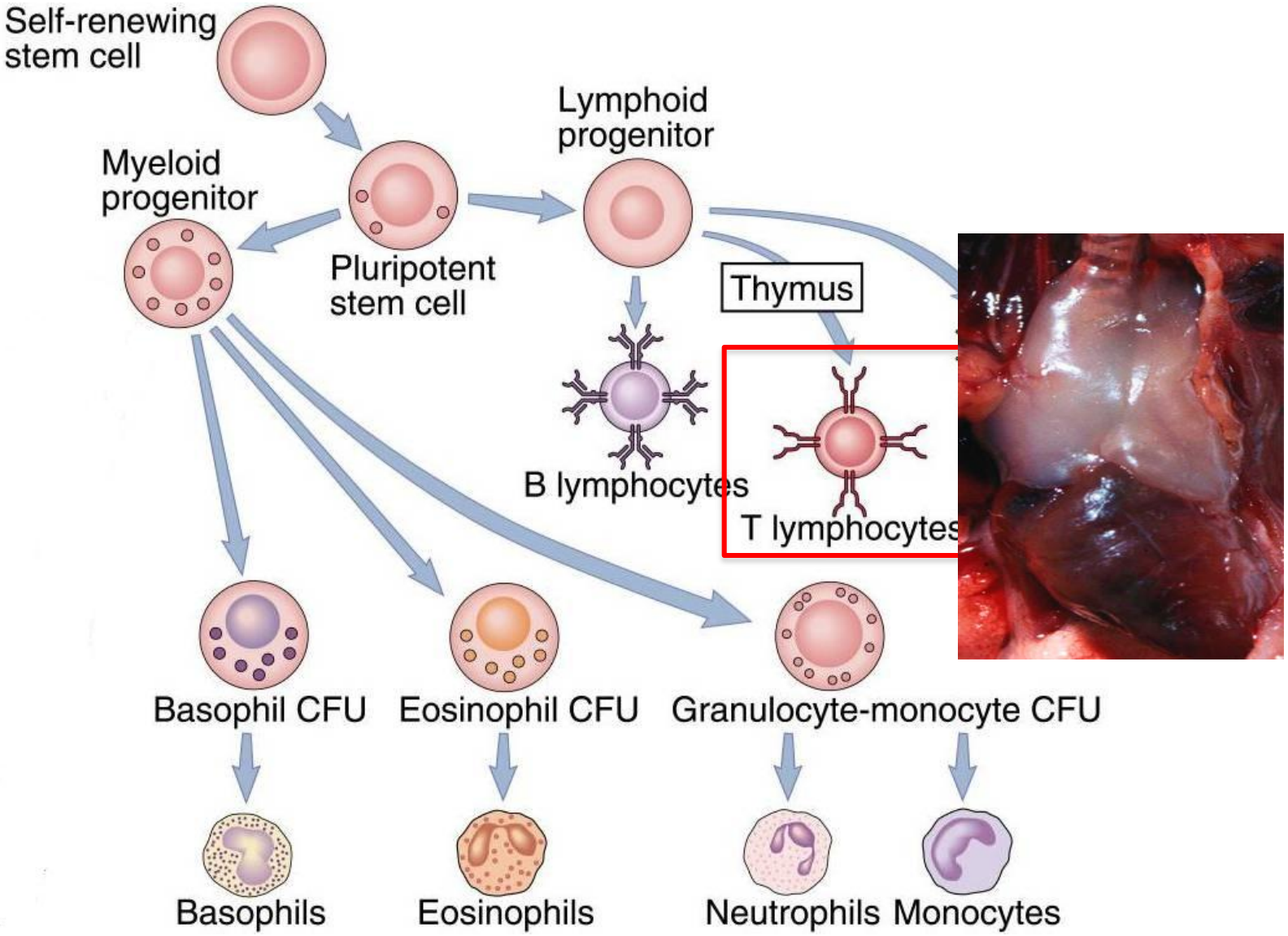
24/4/2012


Tuberculosis
AIDS
SCID
Transplantation
Cancer
Autoimmunity
Allergy
Malaria
Immune System

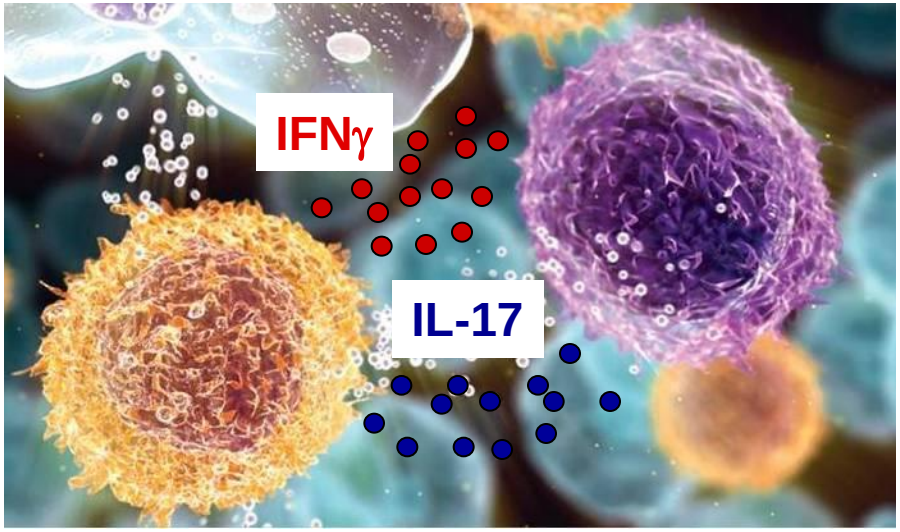
450 M.y. ago - the “Big Bang” of the Immune System

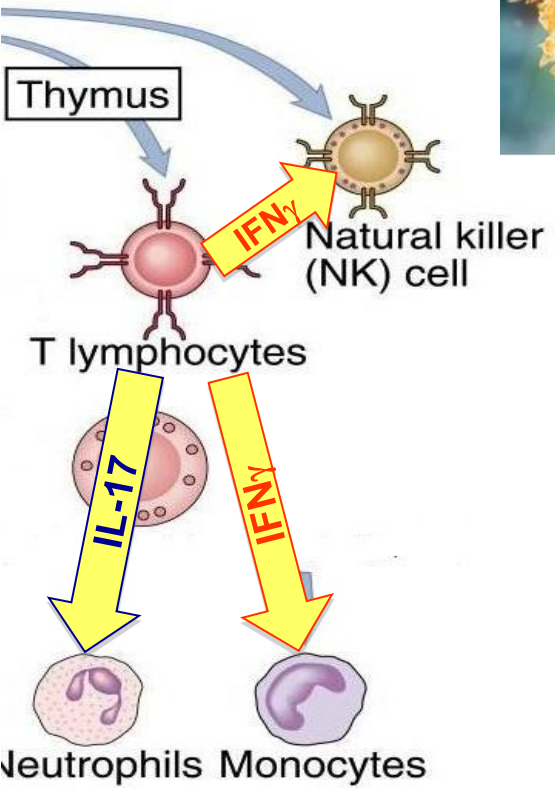


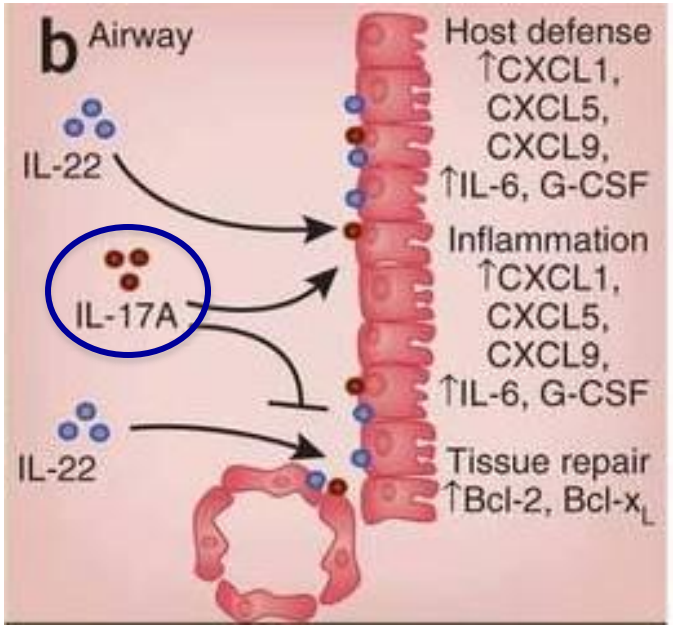
T cells within the immune system



T cells communicate with other cells via cytokines







Viruses

Bacteria (intra)

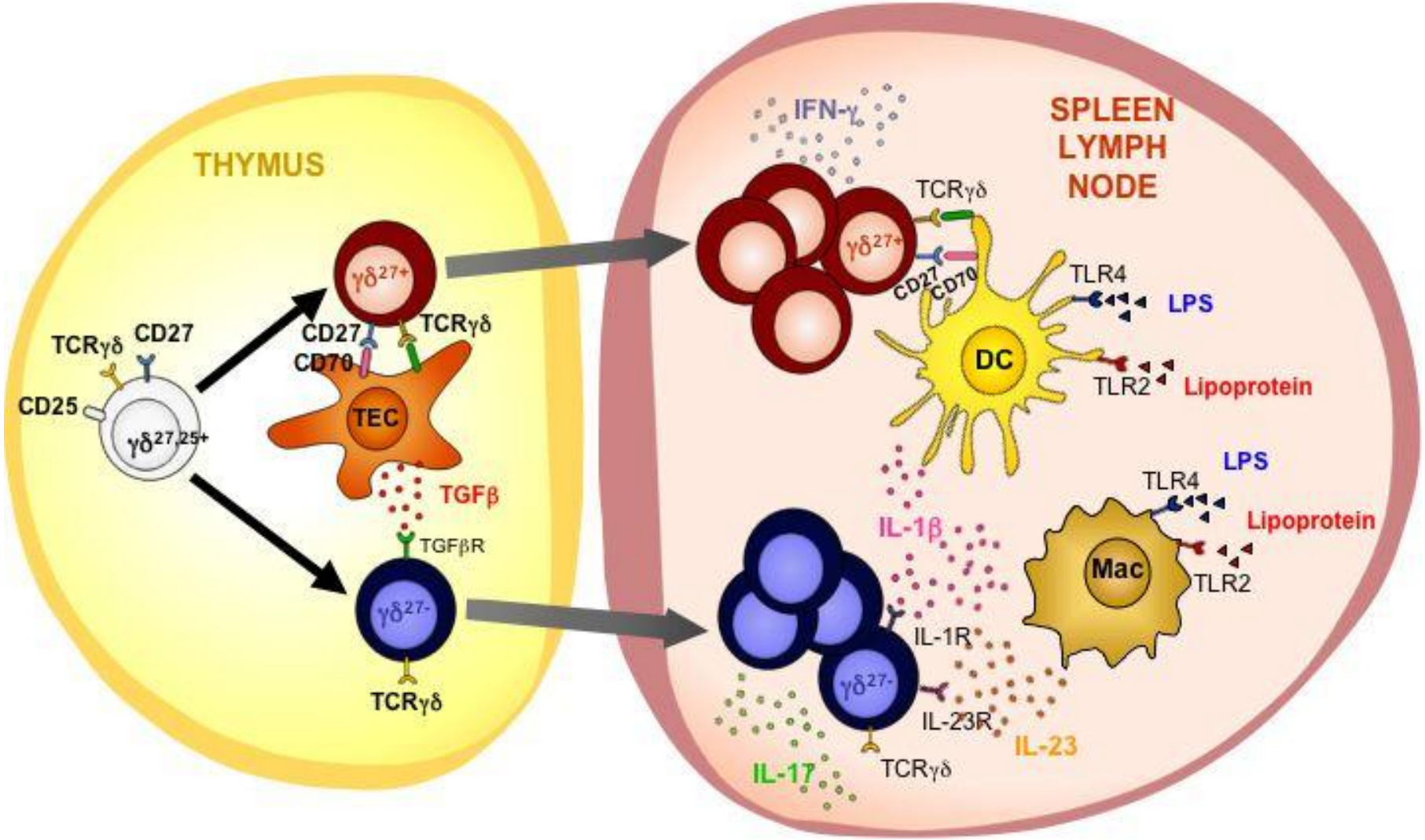
Tumors

Fungi

Bacteria (extra)

Autoimmunity

A new model: two distinct γδ T cell subsets

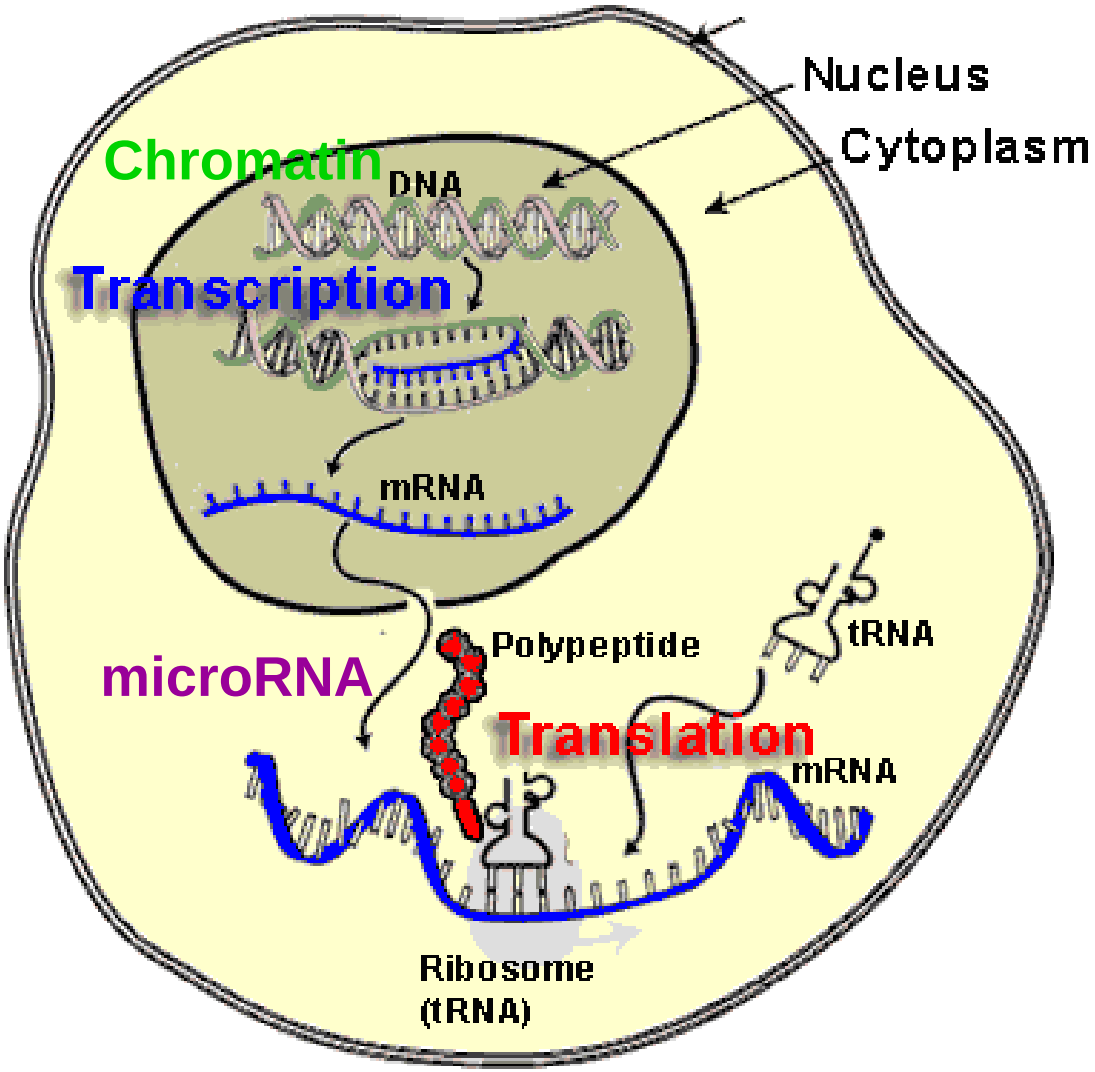


Ribot et al. Nature Immunol 2009

Ribot et al. J Immunol 2010

European Research Council

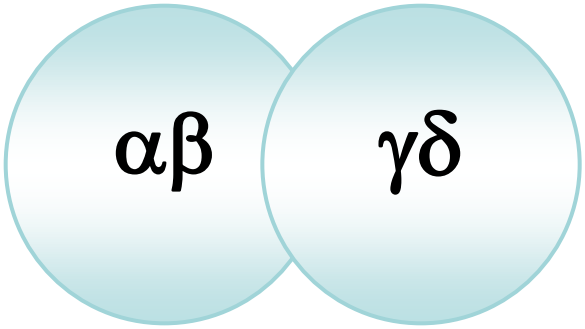
Molecular control of T cell differentiation



European Research Council

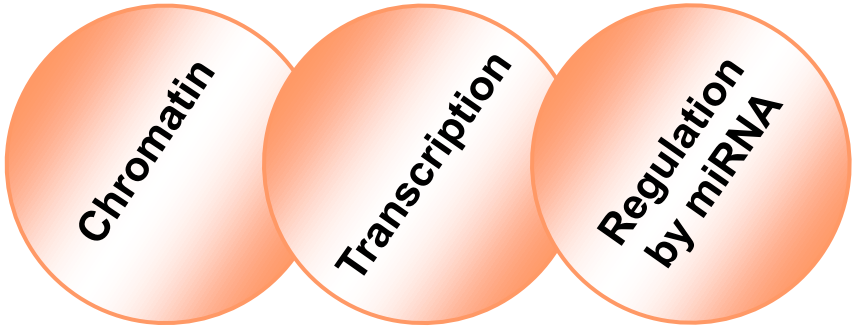
T cell differentiation *in vivo*

The cells



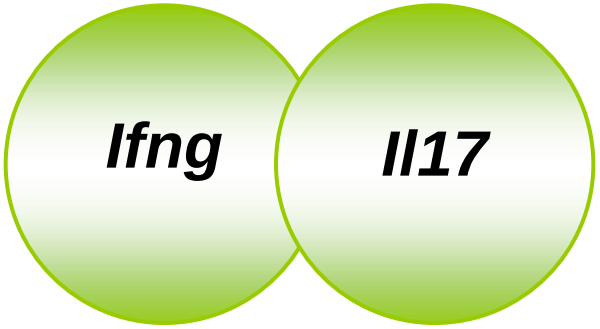
-Thymus
- Periphery
- Naive mice
- Infected mice

The processes



- Histone modif
- DNA methyl
- TF (single cells)
- miRNA

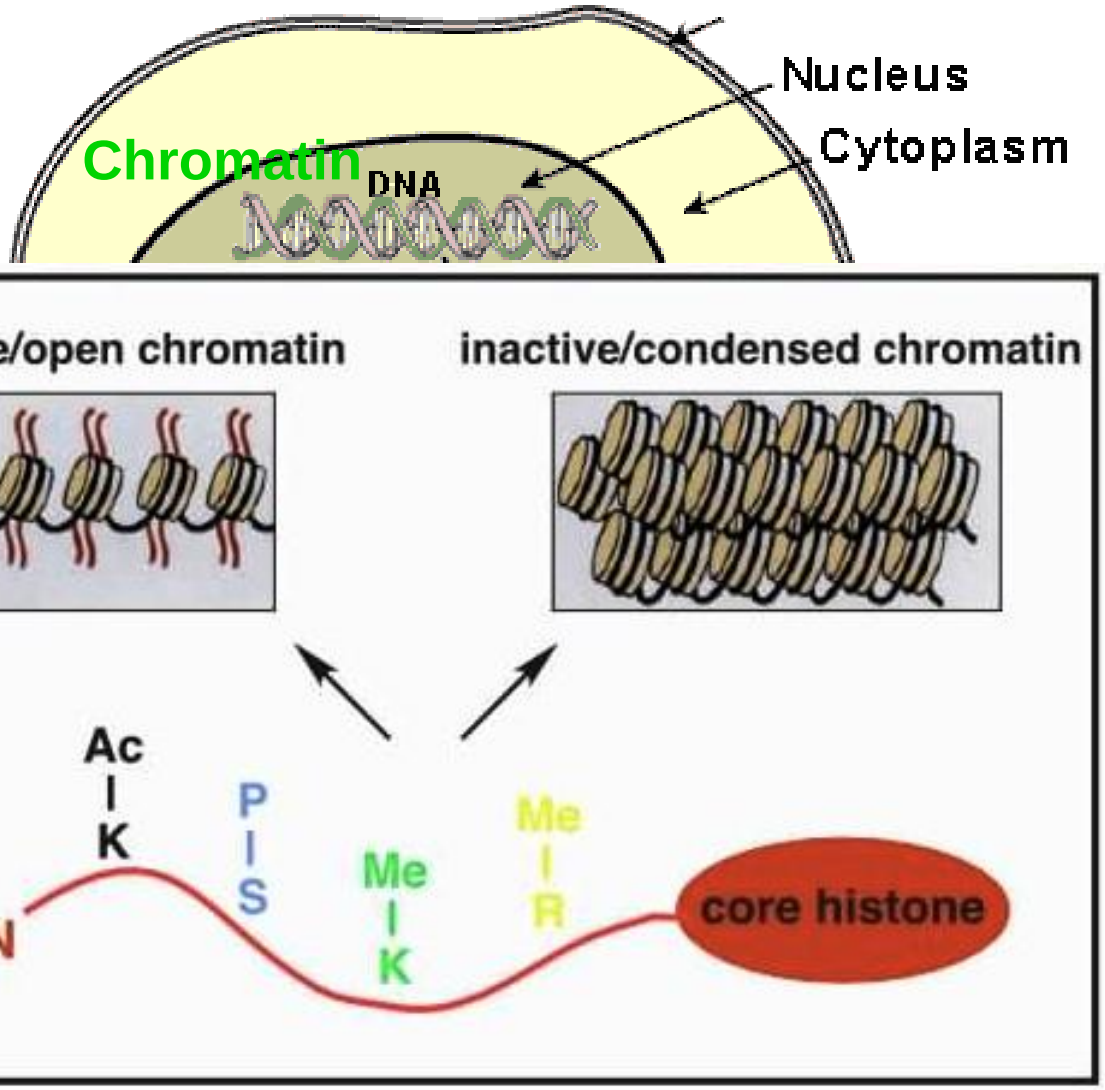
The target genes



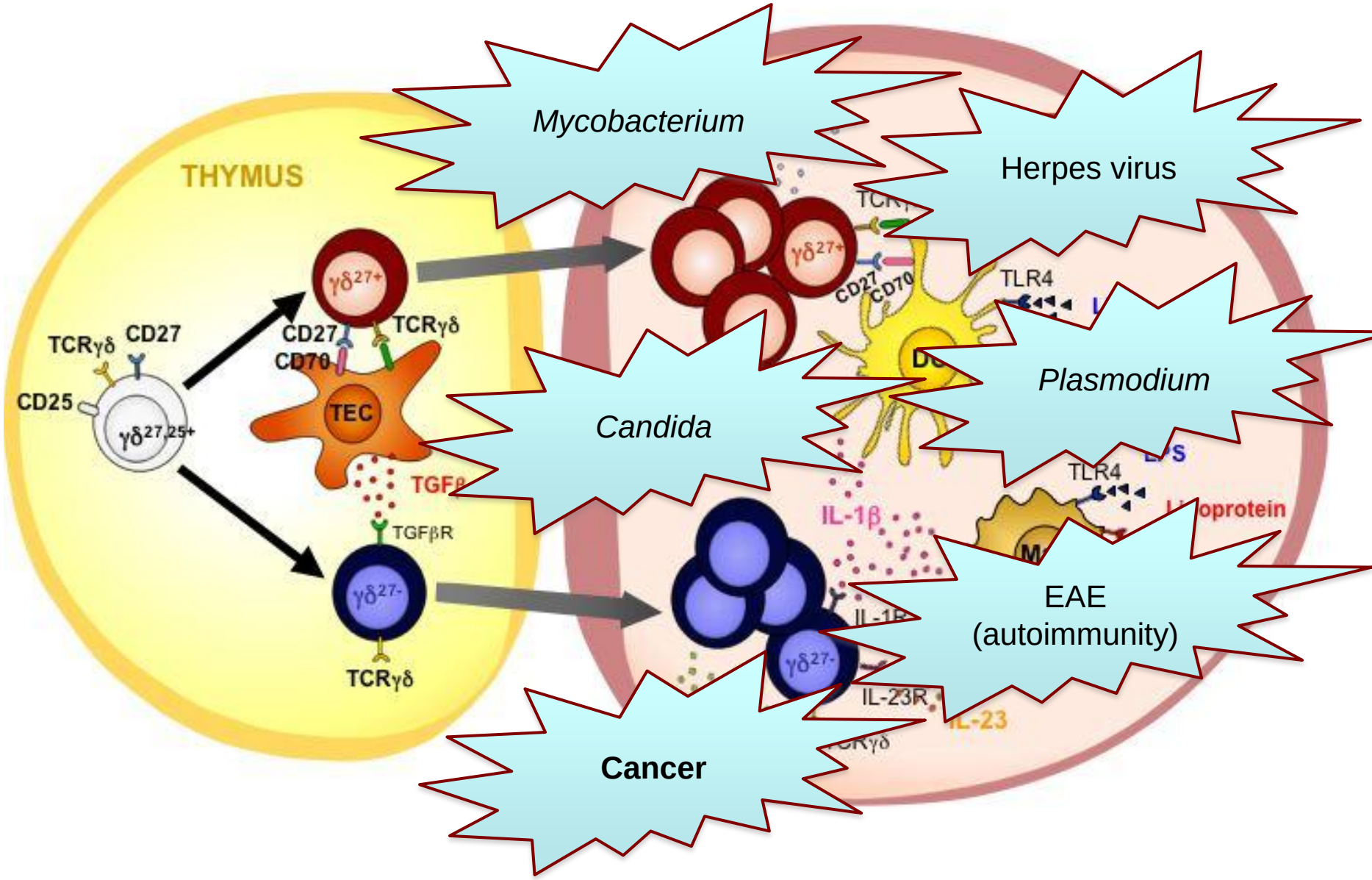
- Reporter mice
- icStaining
- RT-qPCR

European Research Council

Molecular control of T cell differentiation



γδ T cell subsets in immune responses



T cell-based immunotherapy for cancer: ACT

Anti-tumor functions:

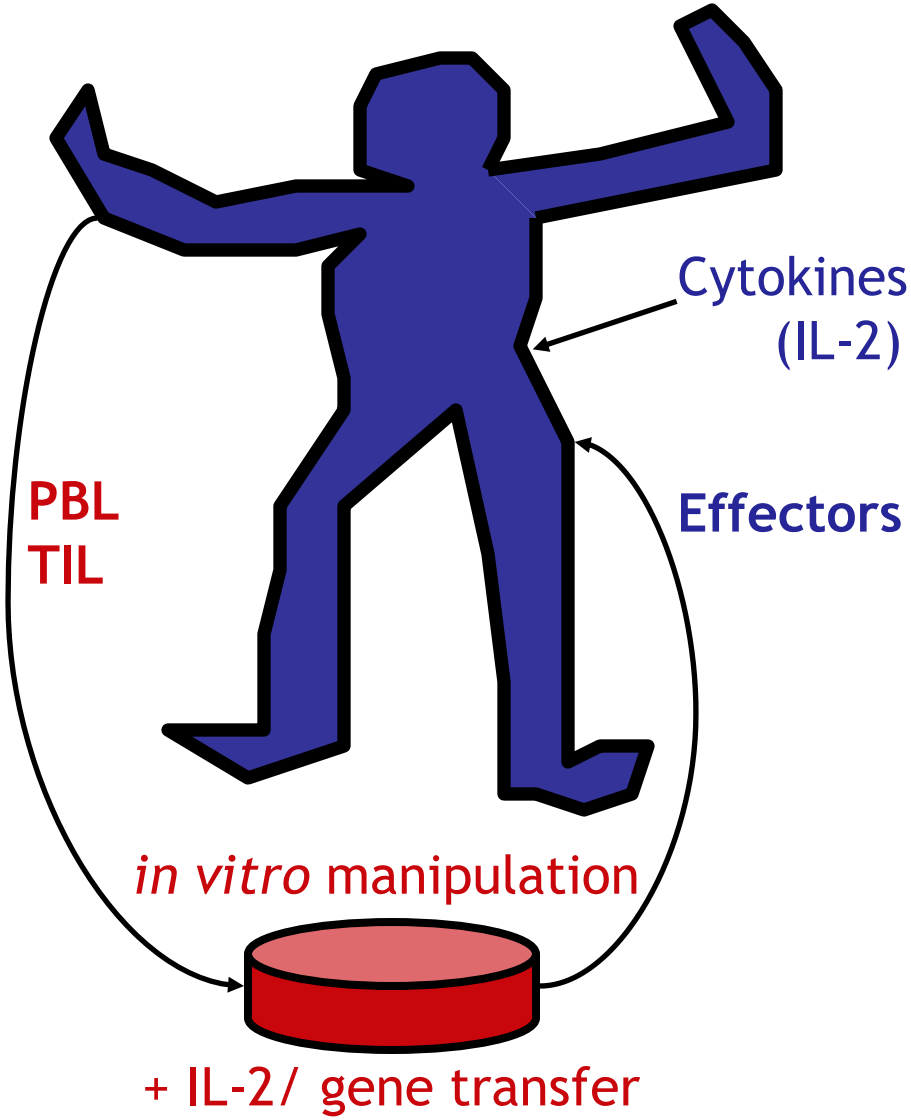
- **Production of IFNγ**
- **Cytotoxicity**

2011: success of clinical trials of

ADOPTIVE CELL TRANSFER

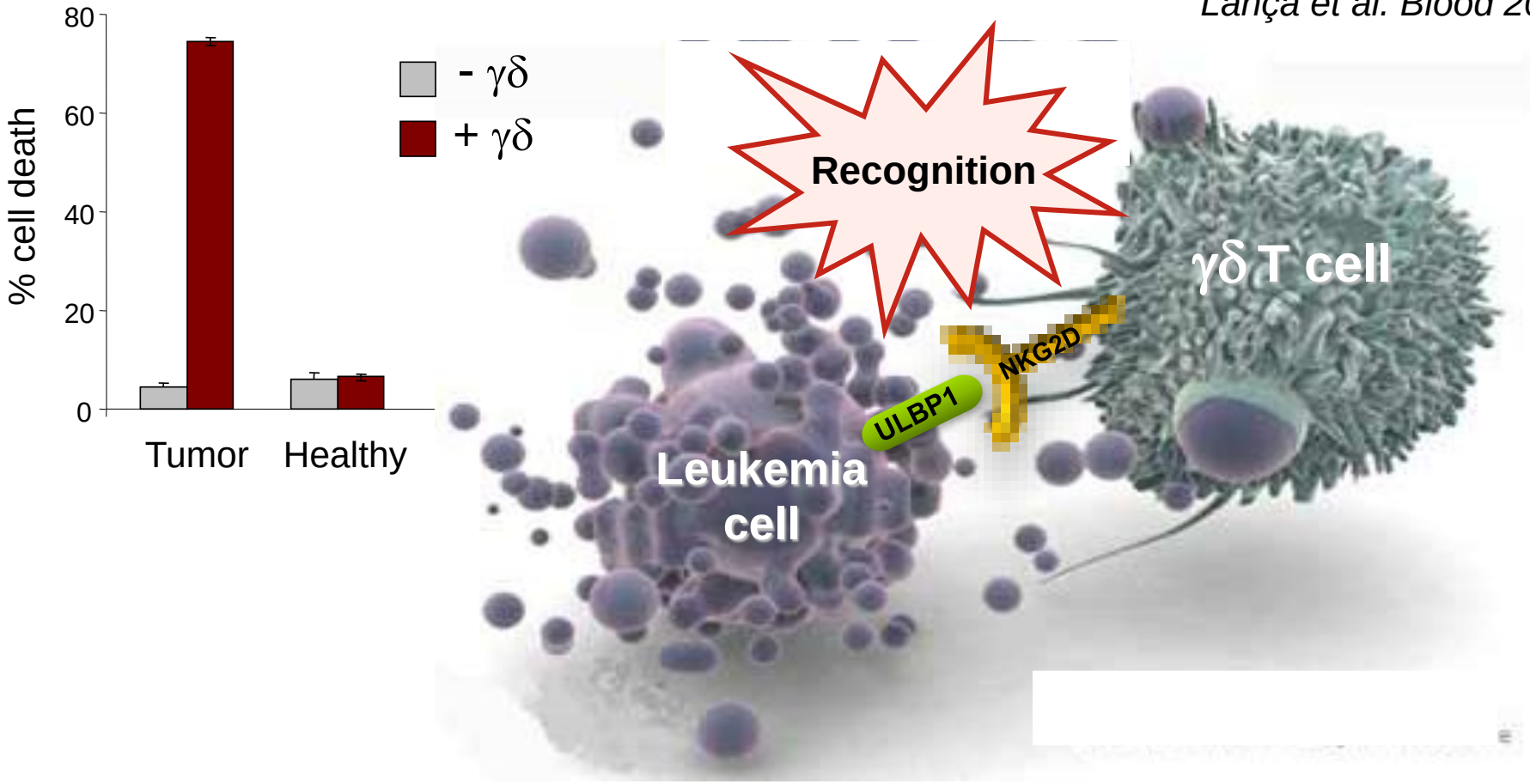
with αCD19 chimeric receptors

in **B-CLL** (Carl June & Steve Rosenberg)



Molecular basis of tumor recognition by γδ T cells

Lança et al. Blood 2010

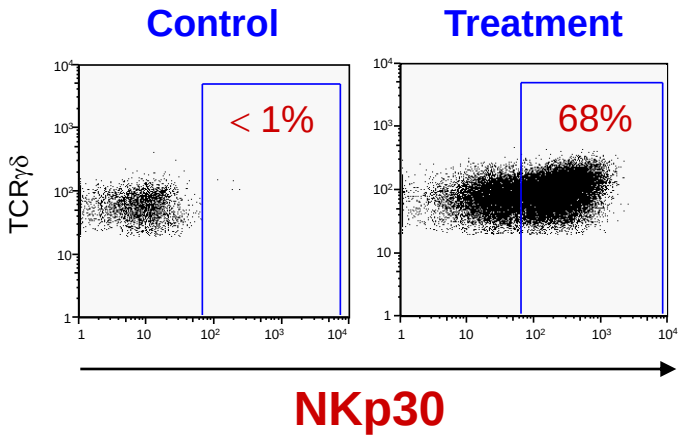


ULBP1 expression in primary samples from **leukemia patients**:

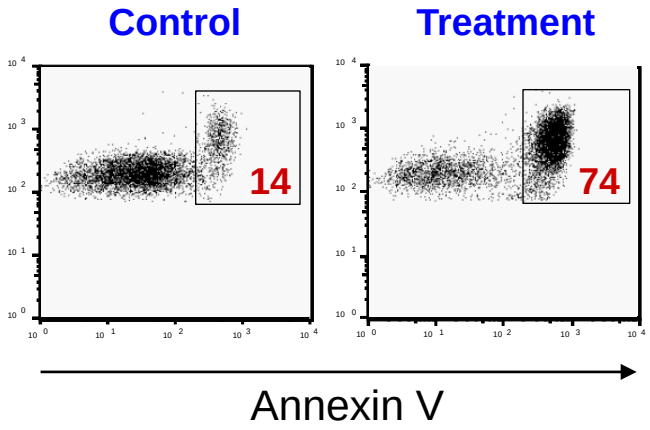
No	No	No	No	Yes	Yes	No	Yes	No	Yes	No	No	Yes	No	No

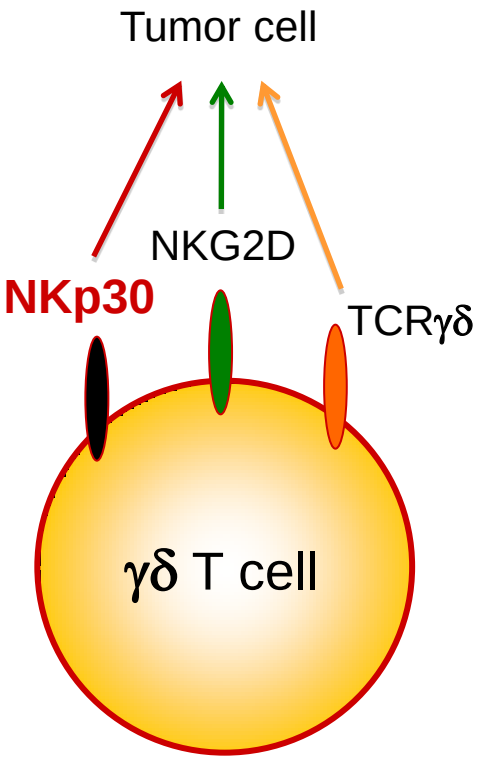
Inducing a new recognition receptor on γδ T cells

Correia et al. Blood 2011



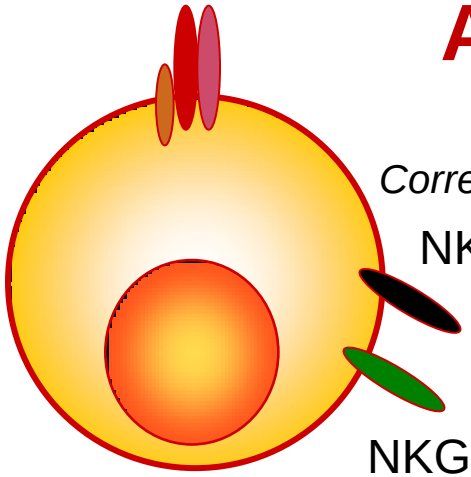
Killing of a highly resistant tumor





Adoptive cell transfer of γδ T cells

(pre-clinical studies)



Correia et al. Blood 2011

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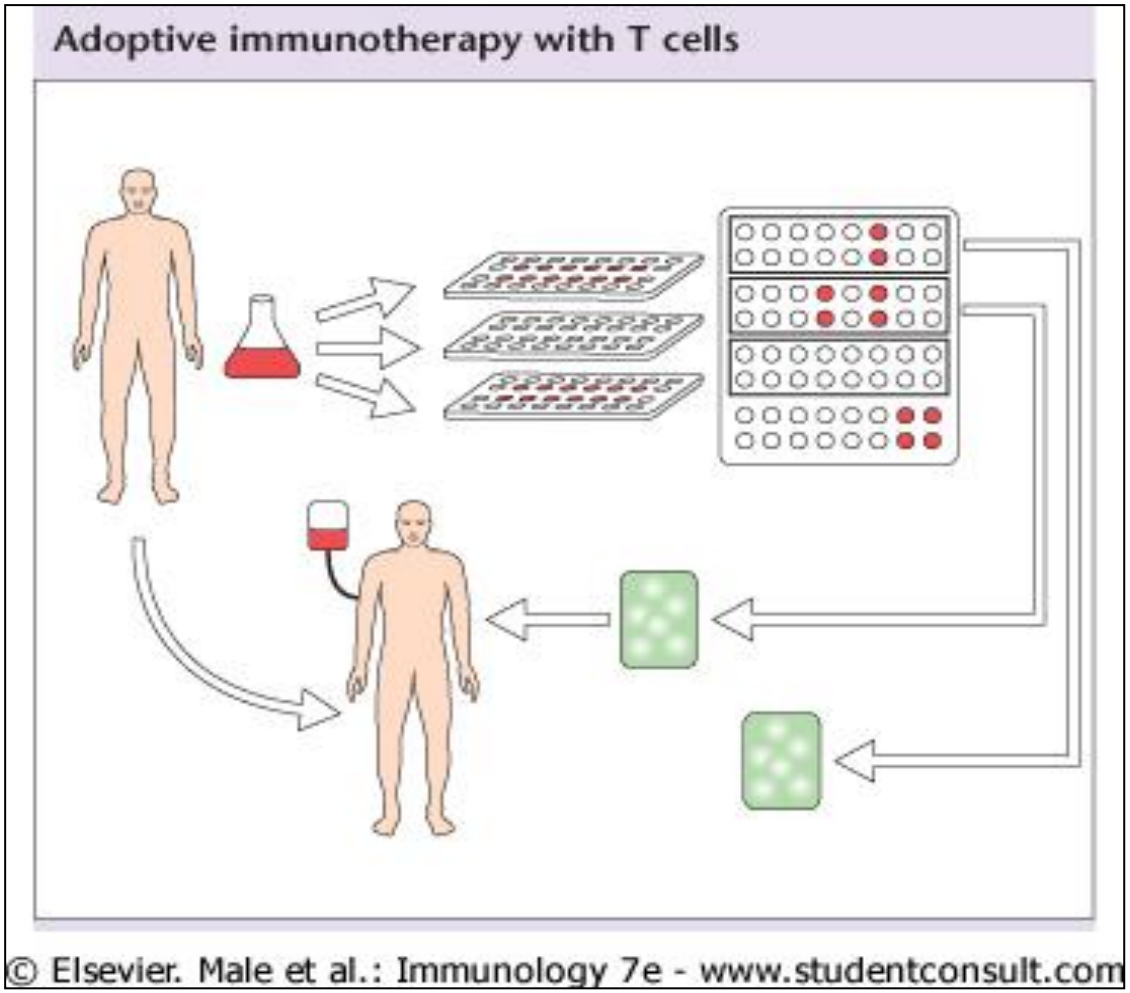

Work funded by:

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