



AMERICAN SOCIETY OF GENE & CELL THERAPY  
13<sup>TH</sup> ANNUAL MEETING | Washington, DC USA May 19-22, 2010

## Presenter Disclosure Michael P. Cancro

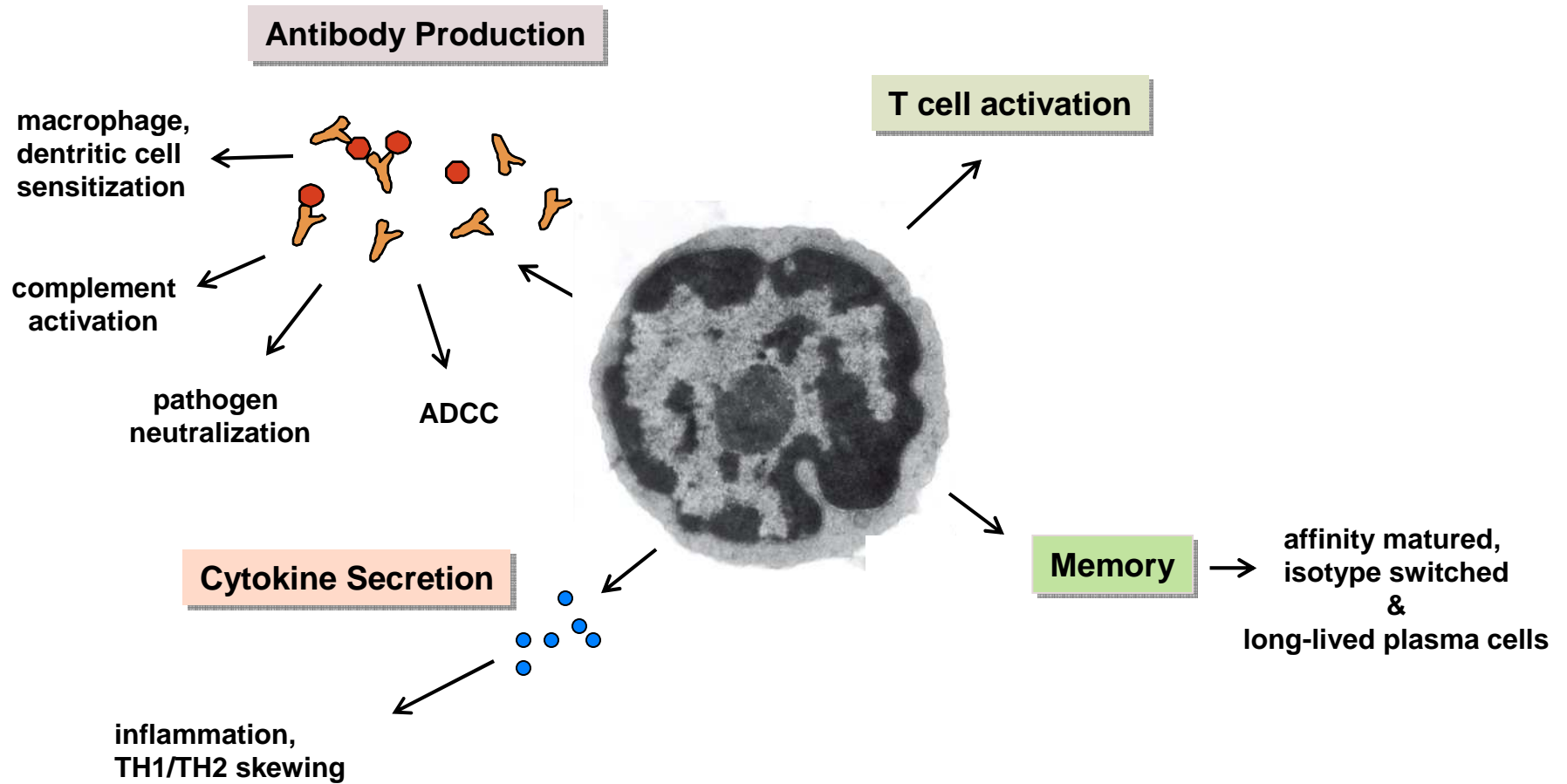
**The following relationships exist related to this presentation:**

**Human Genome Sciences Inc.**

**Sponsored Research Agreement, P.I.**

# Who are the players: B cells and plasma cells

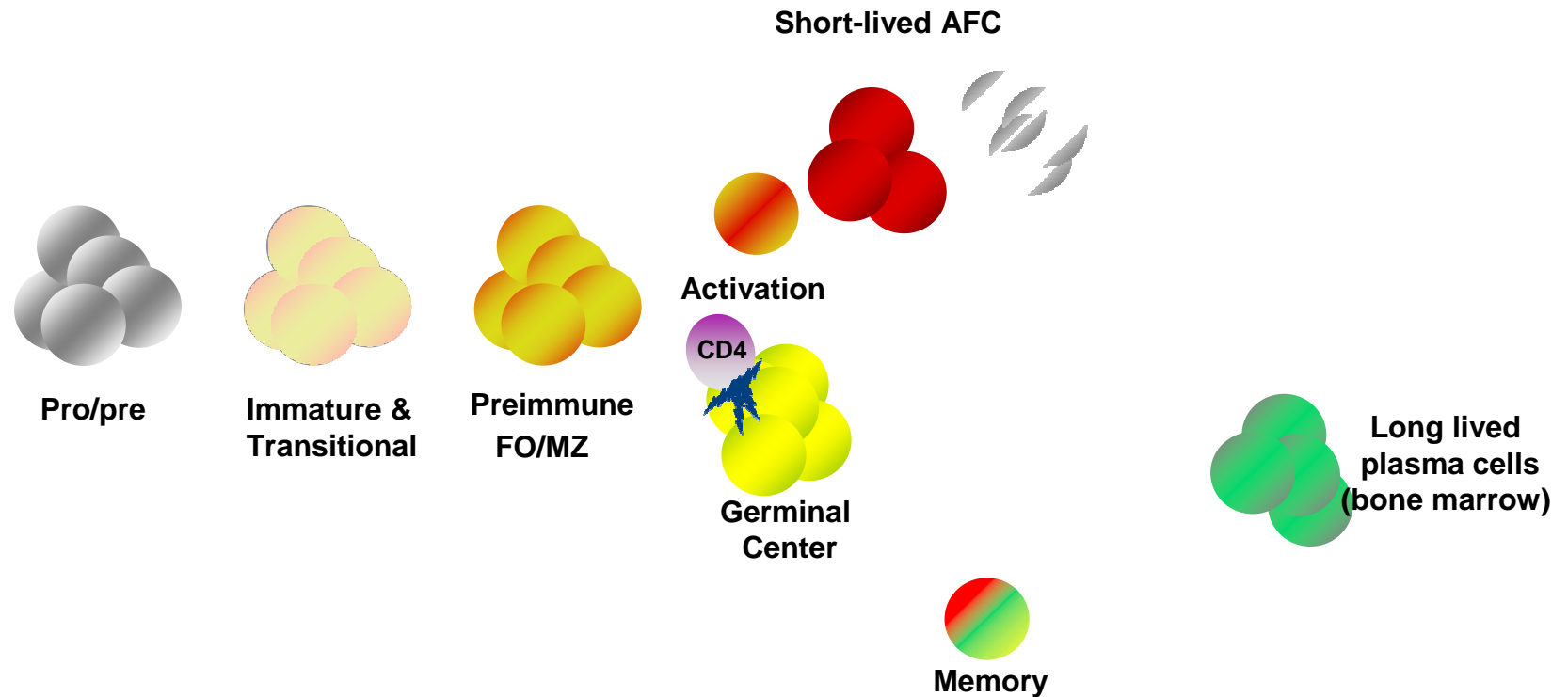
## *Roles for B lineage cells in the immune system*



# What controls entrance and persistence in B cell niches?

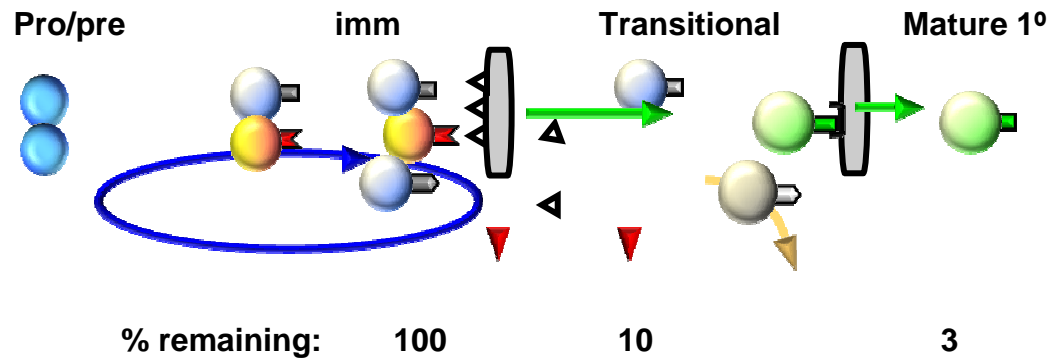
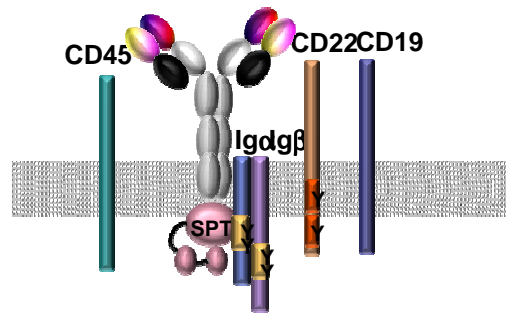
**B cells comprise a series of independently regulated pools**

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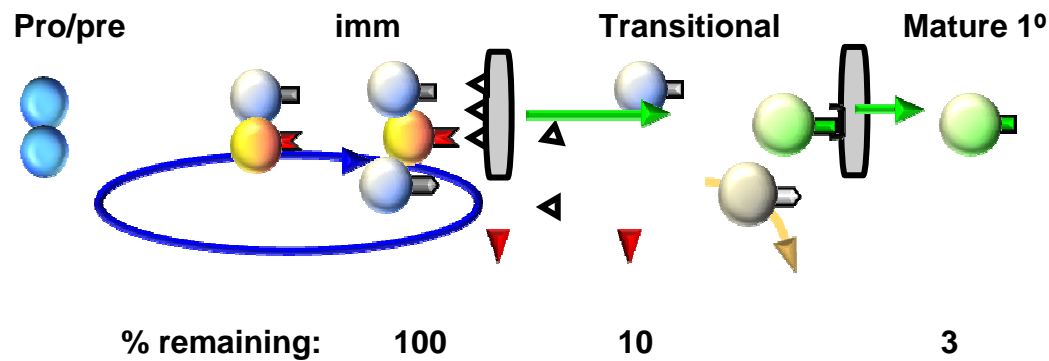
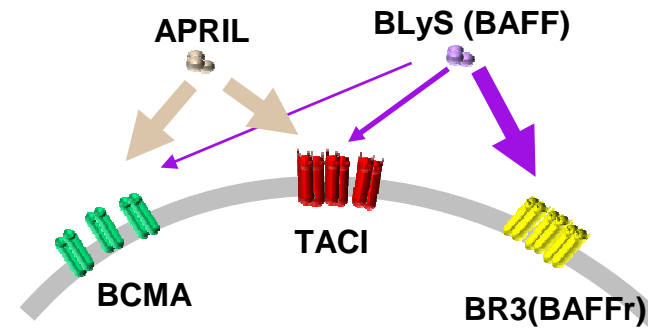
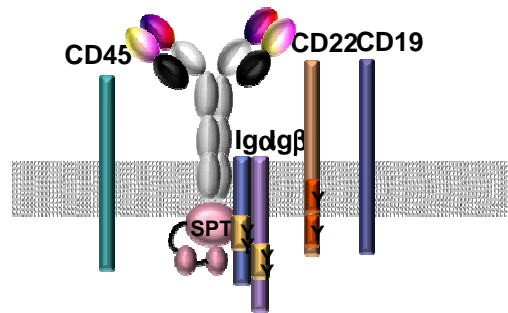
# *BCR specificity determines fitness to enter mature 1<sup>o</sup> pools*

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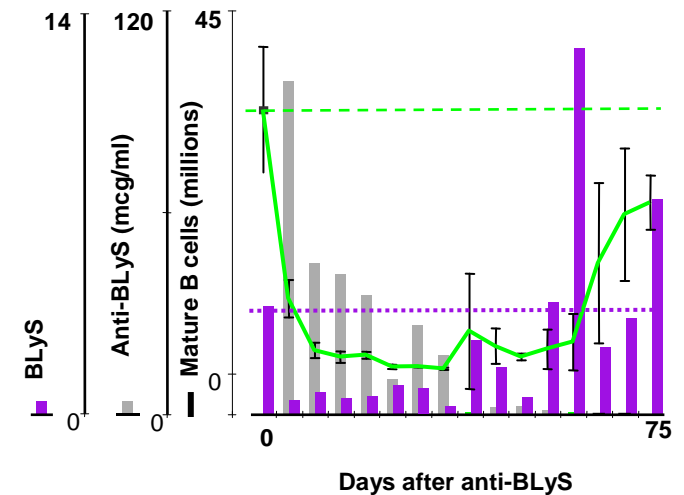
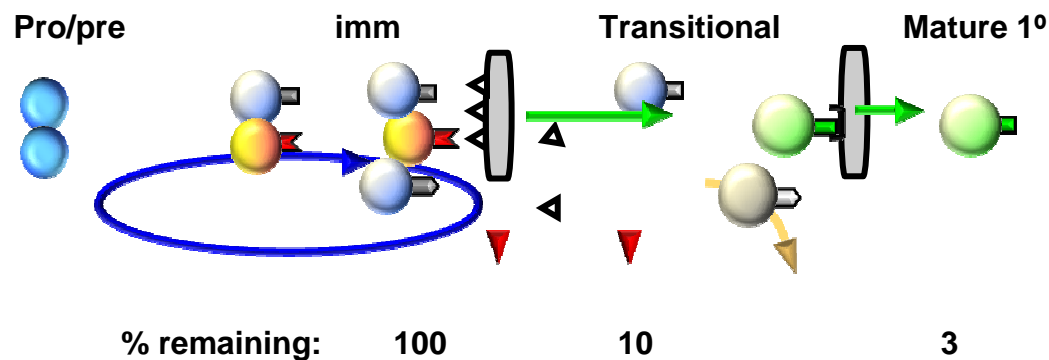
# *BCR specificity determines fitness to enter mature 1° pools*

## *BLyS mediates survival (persistence) in mature 1° pools*

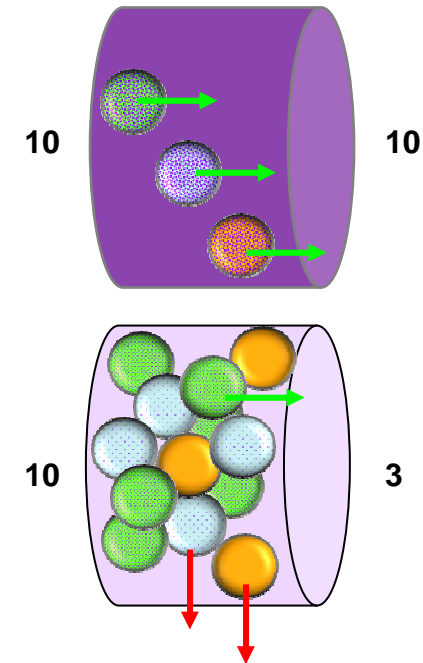
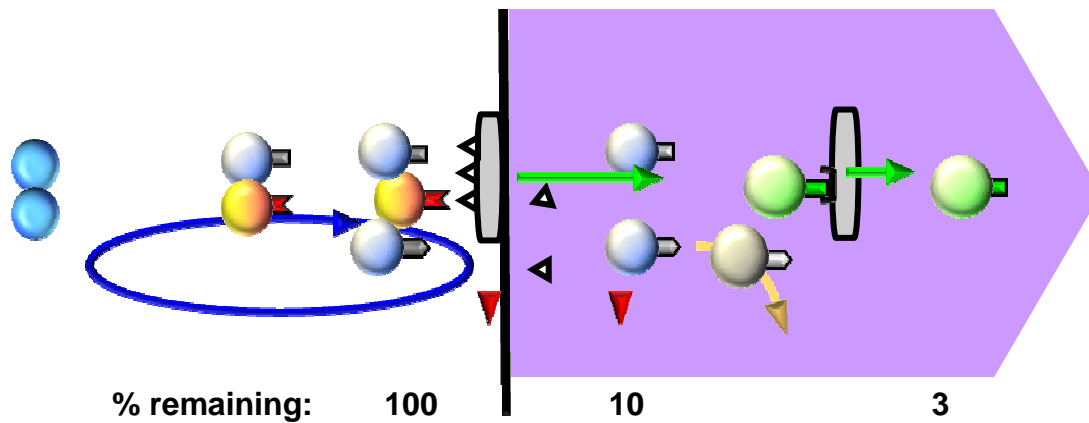
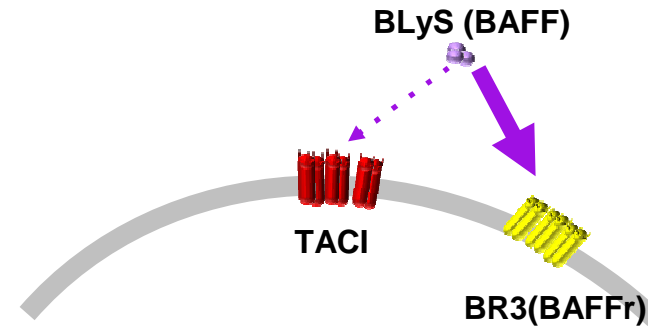
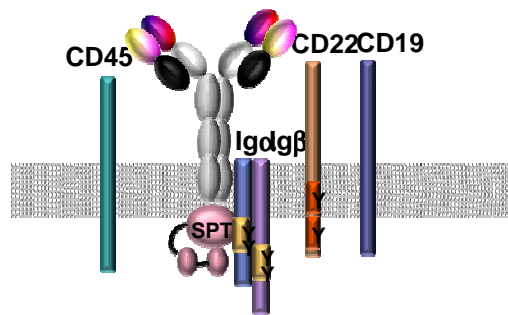


# *BCR specificity determines fitness to enter mature 1° pools*

## *BLyS mediates survival (persistence) in mature 1° pools*

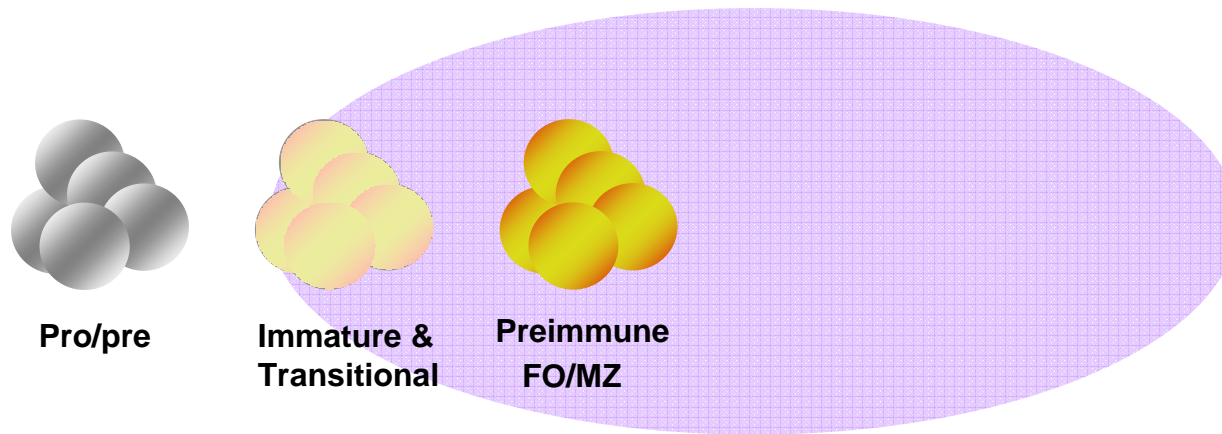


# *BCR and B<sub>L</sub>yS signals modulate each others' effects, yielding plasticity in selection (entrance) and survival (persistence)*



# ***Can the composition of the primary pool be modified or remodeled based on these interactions?***

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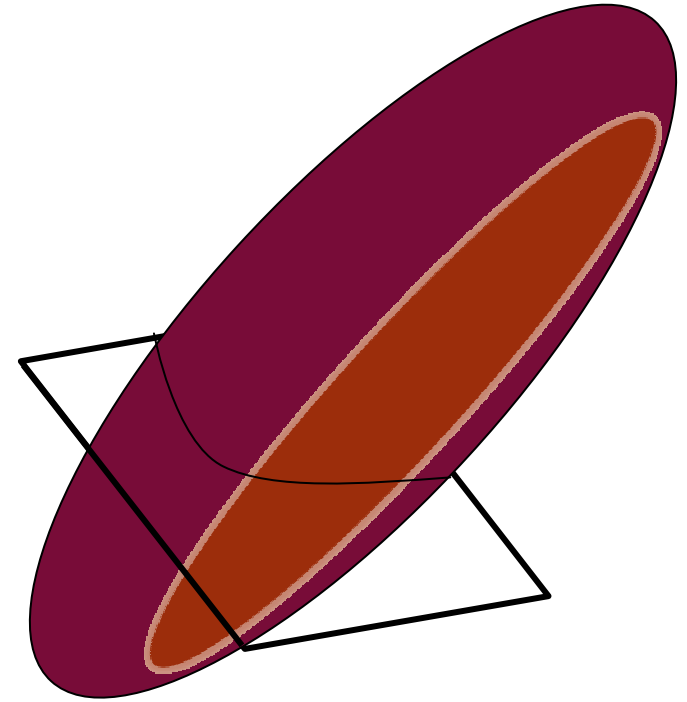
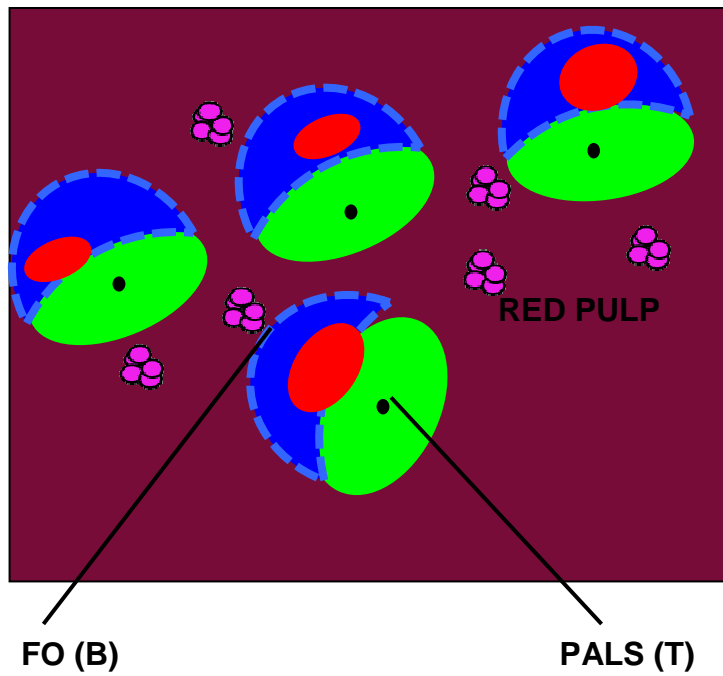


**What about antigen-experienced pools?**

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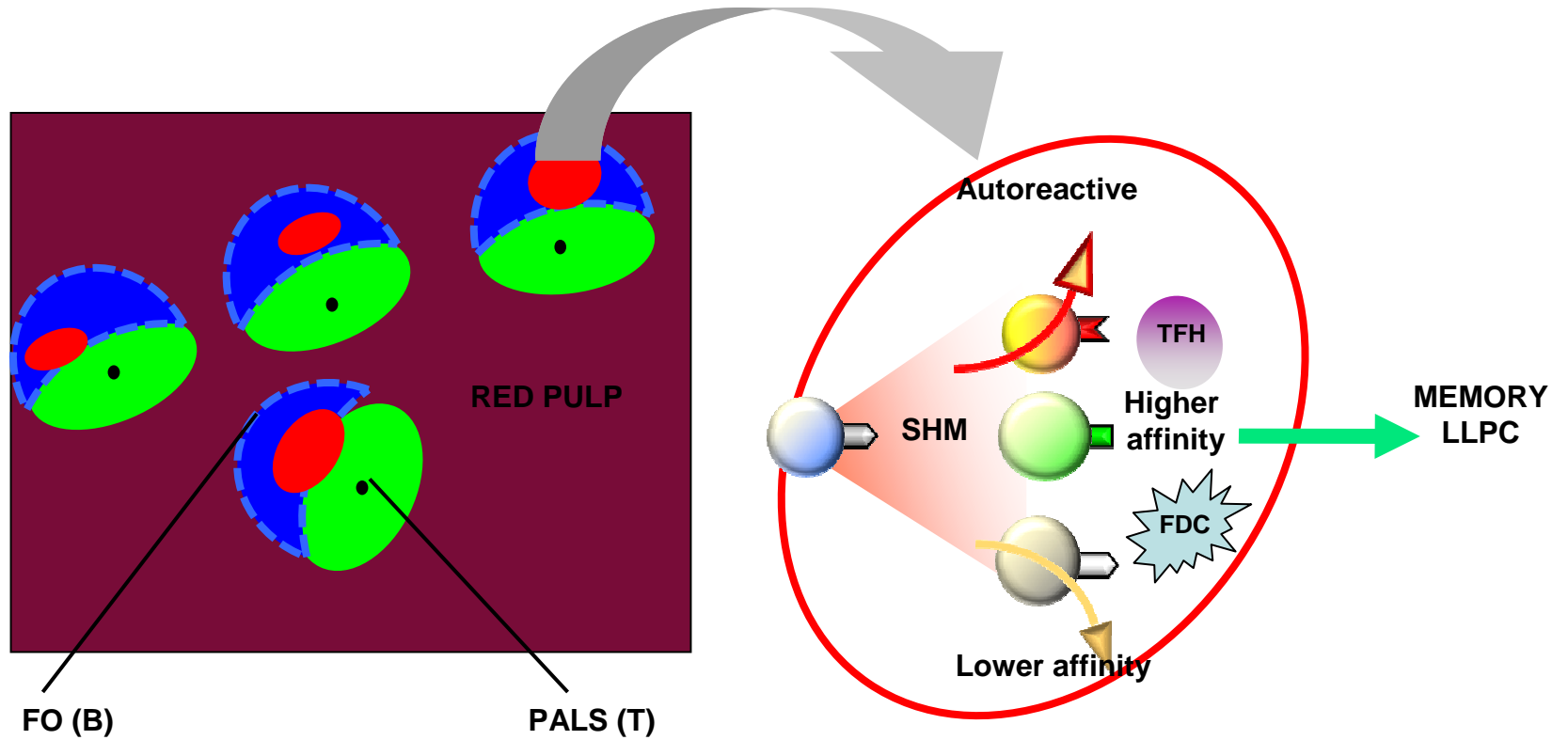
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# What about antigen-experienced pools?

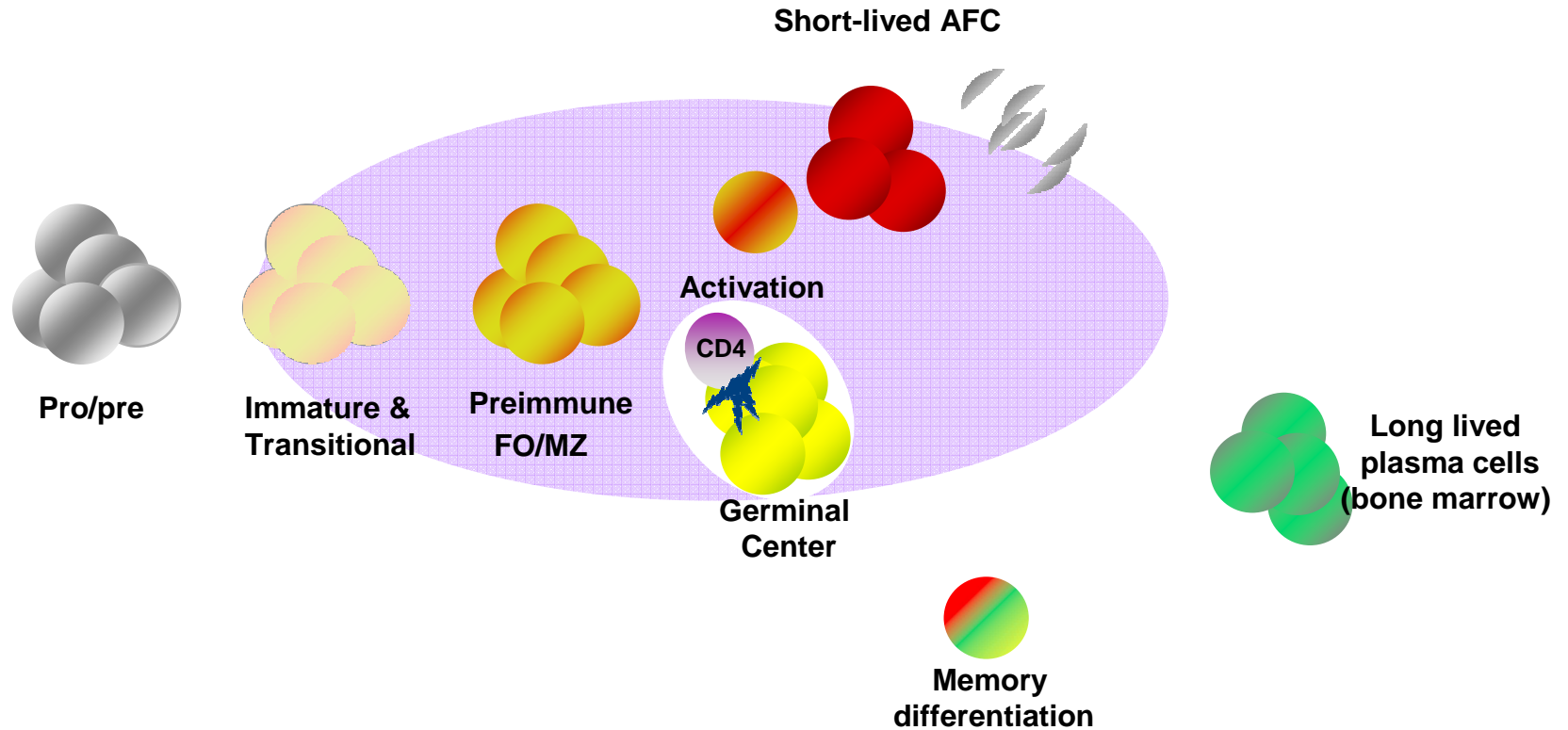
*GC B cells undergo a “second round” of BCR mediated selection*

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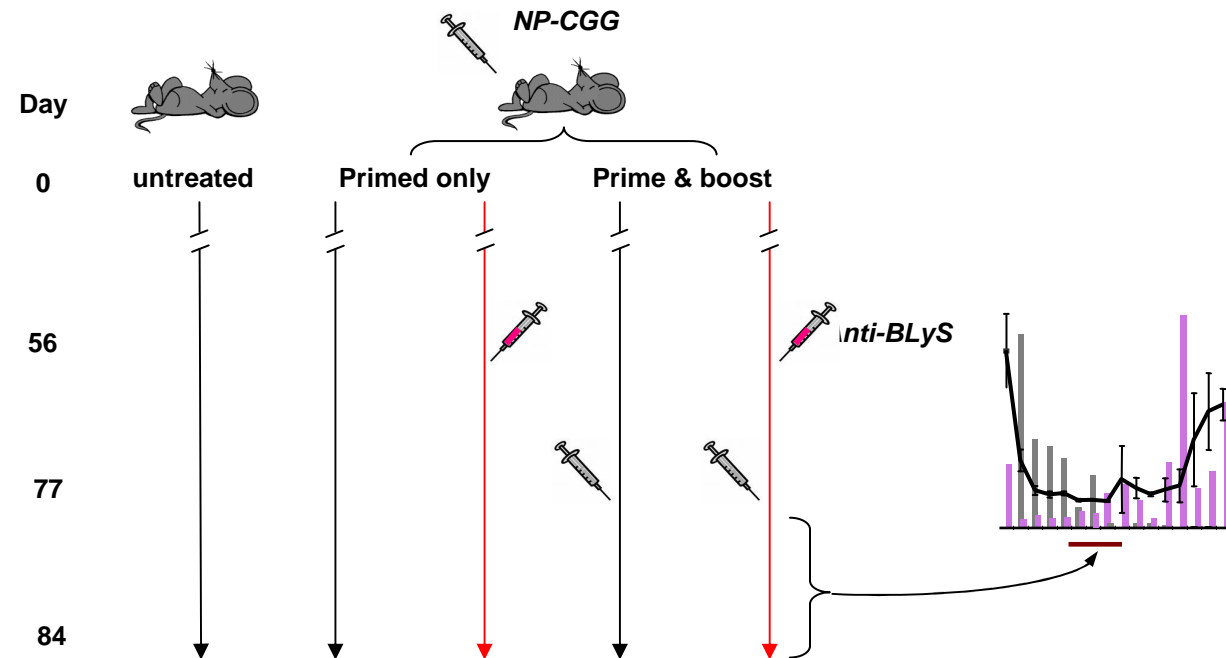
# Are 1° and antigen experienced niches independent?

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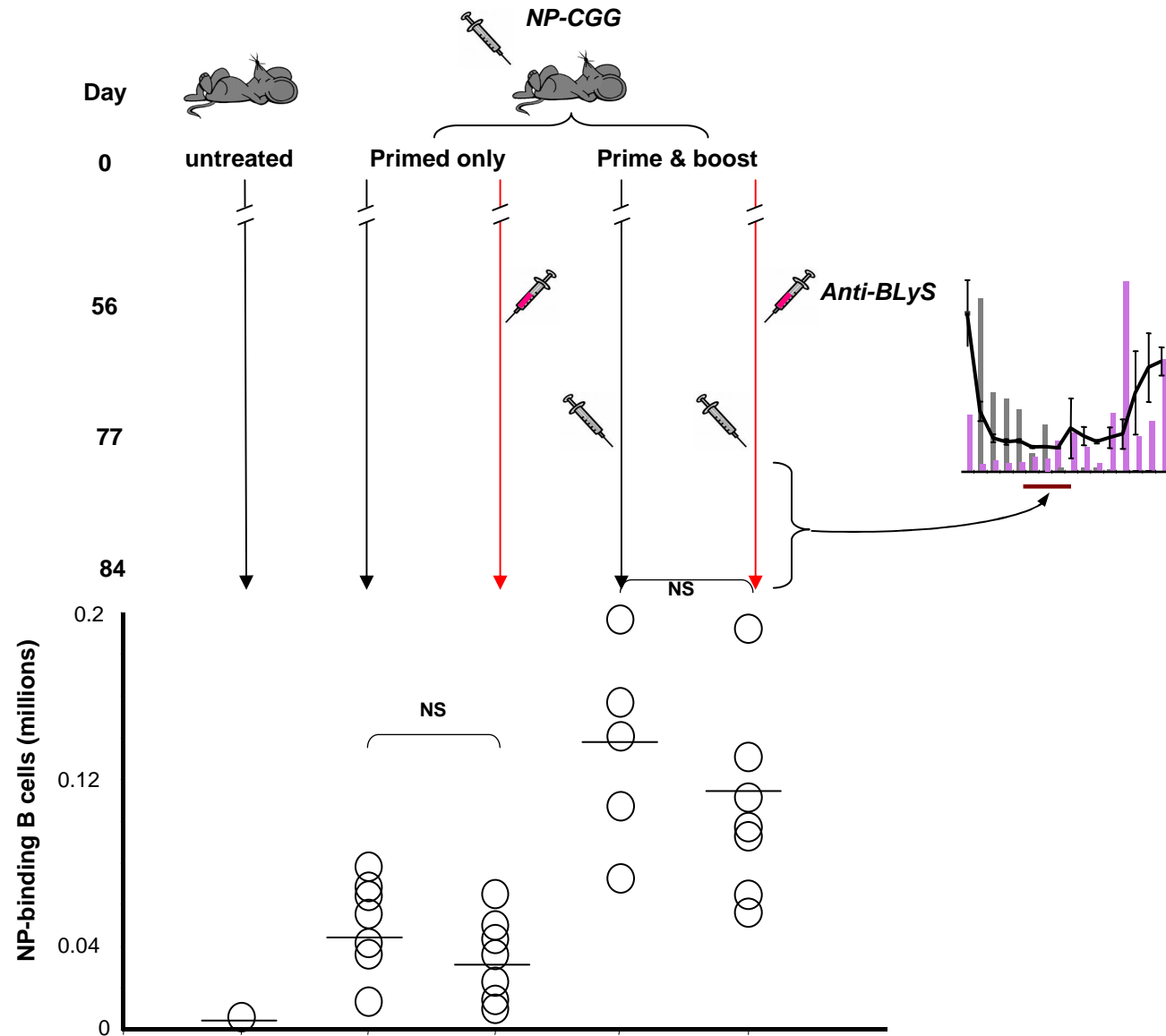
# Separate mechanisms govern persistence in 1<sup>0</sup> vs Ag-experienced pools

## *B cell memory is B<sub>L</sub>ys independent*



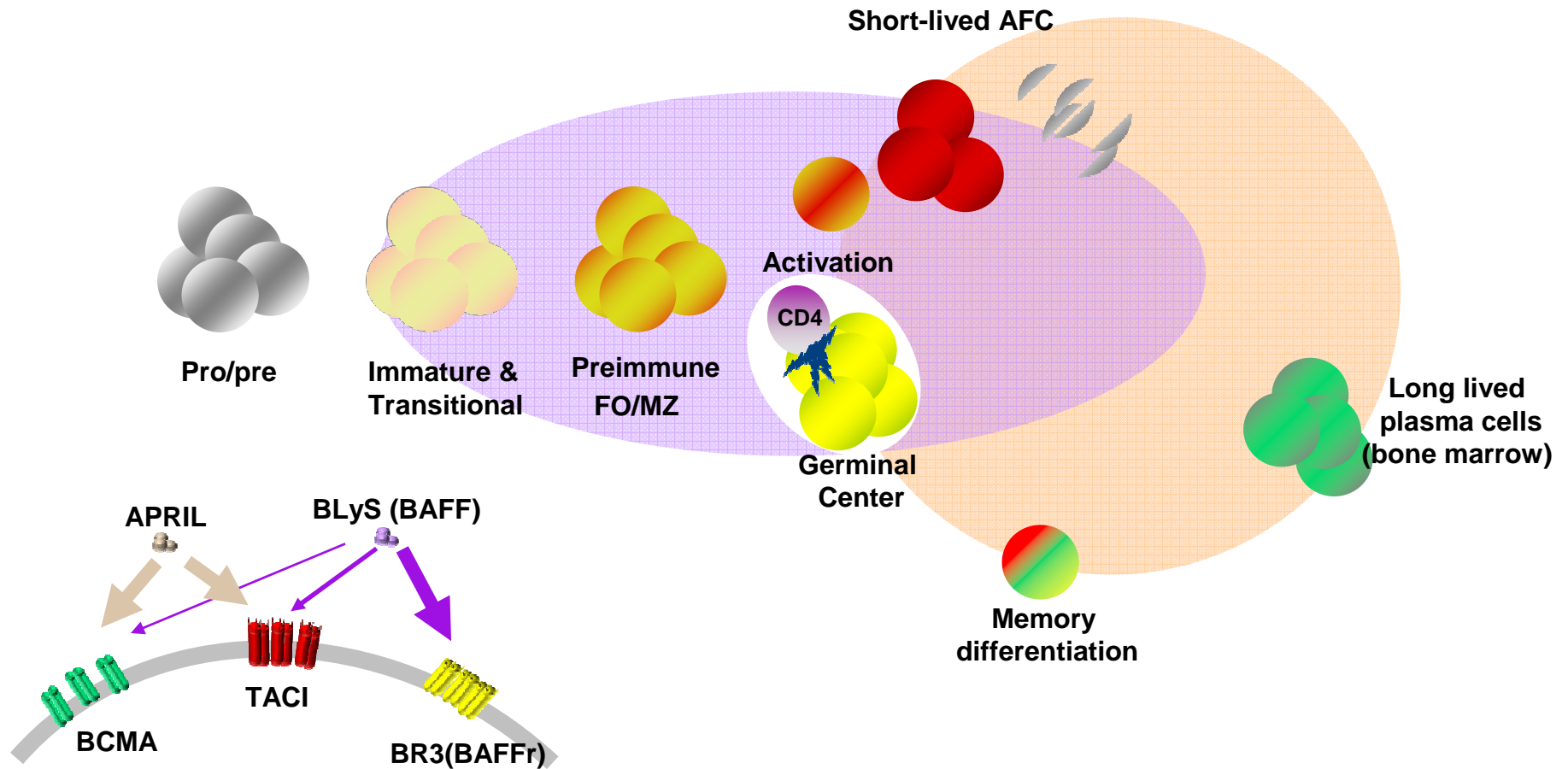
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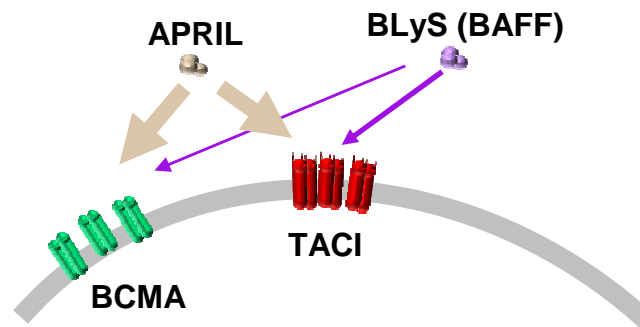
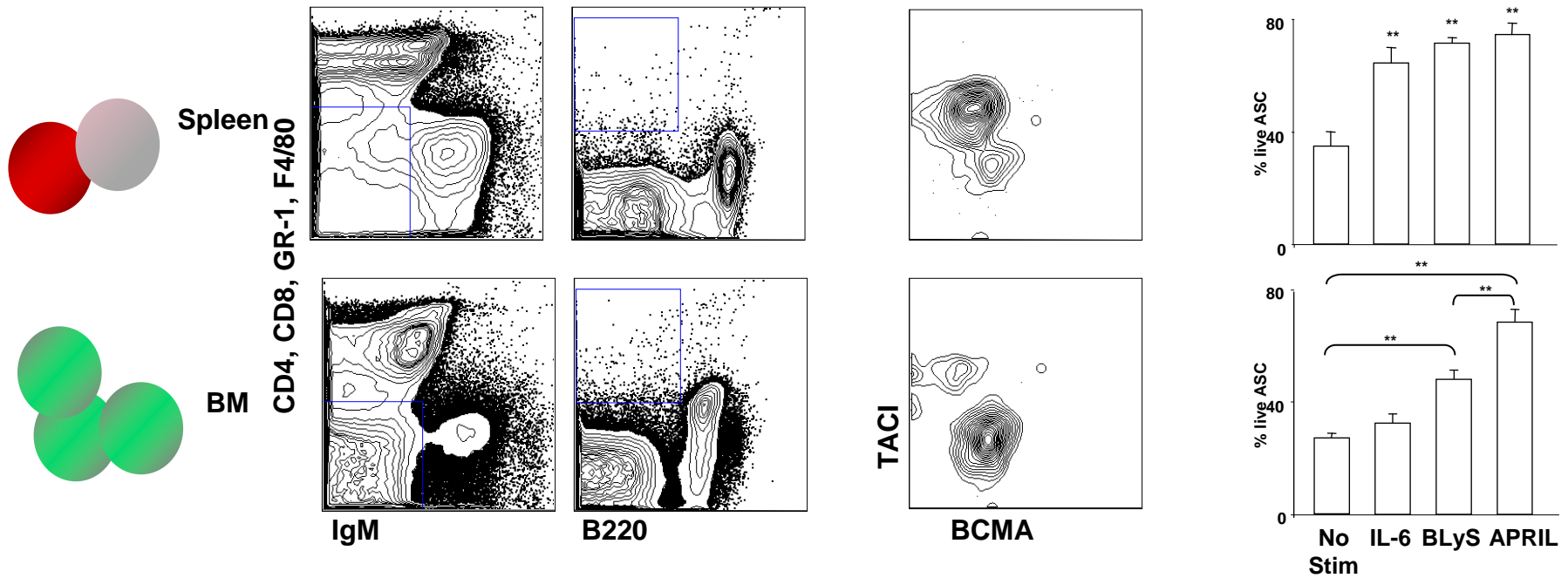
# Separate mechanisms govern persistence in 1<sup>o</sup> vs Ag-experienced pools

*Do Ag-experienced pools possess intrinsic survival-promoting attributes?*

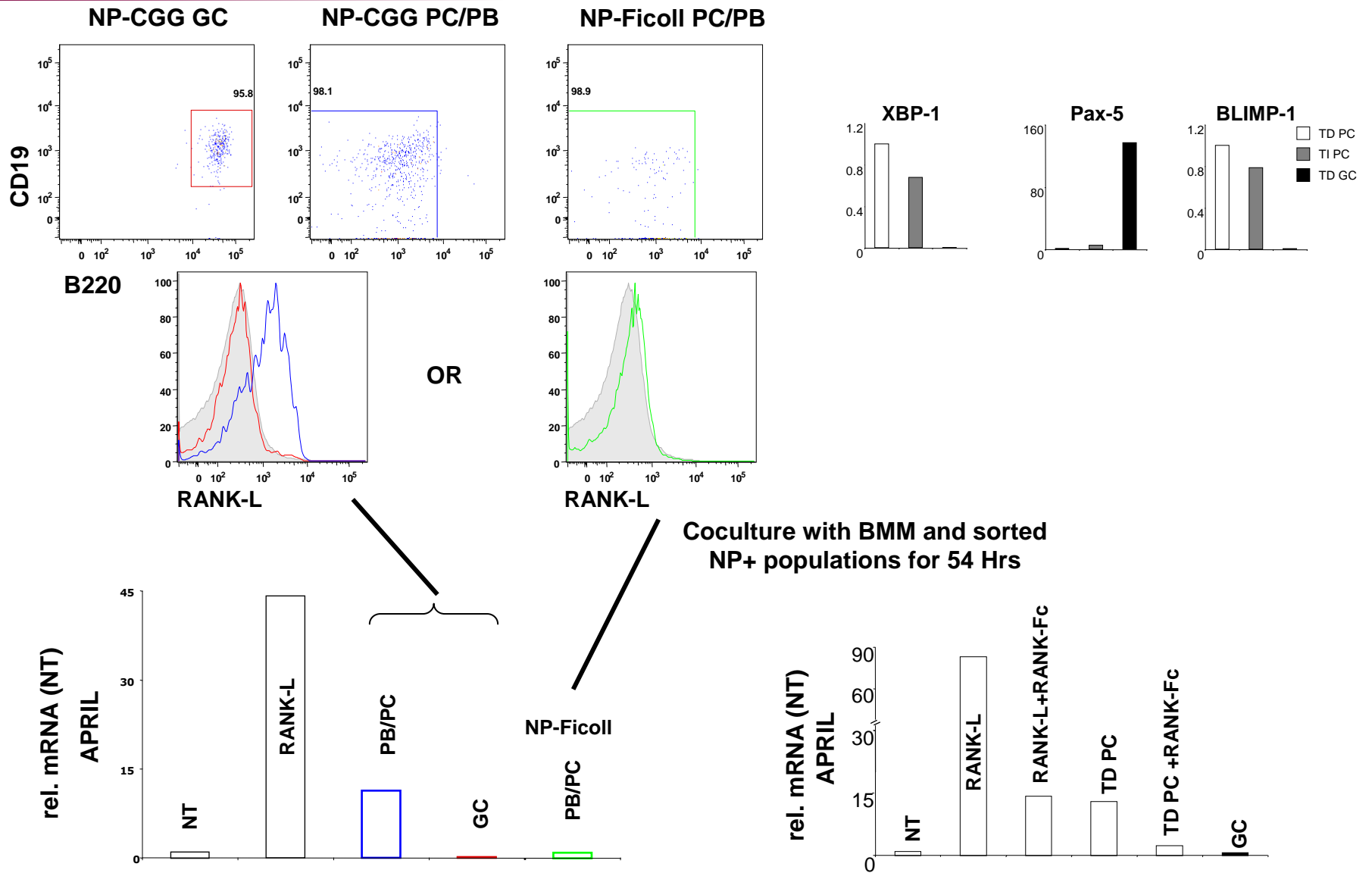


# Does the BLyS family influence antigen-experienced pools?

*Splenic vs BM PCs differ in BLyS receptor profiles and survival requisites*

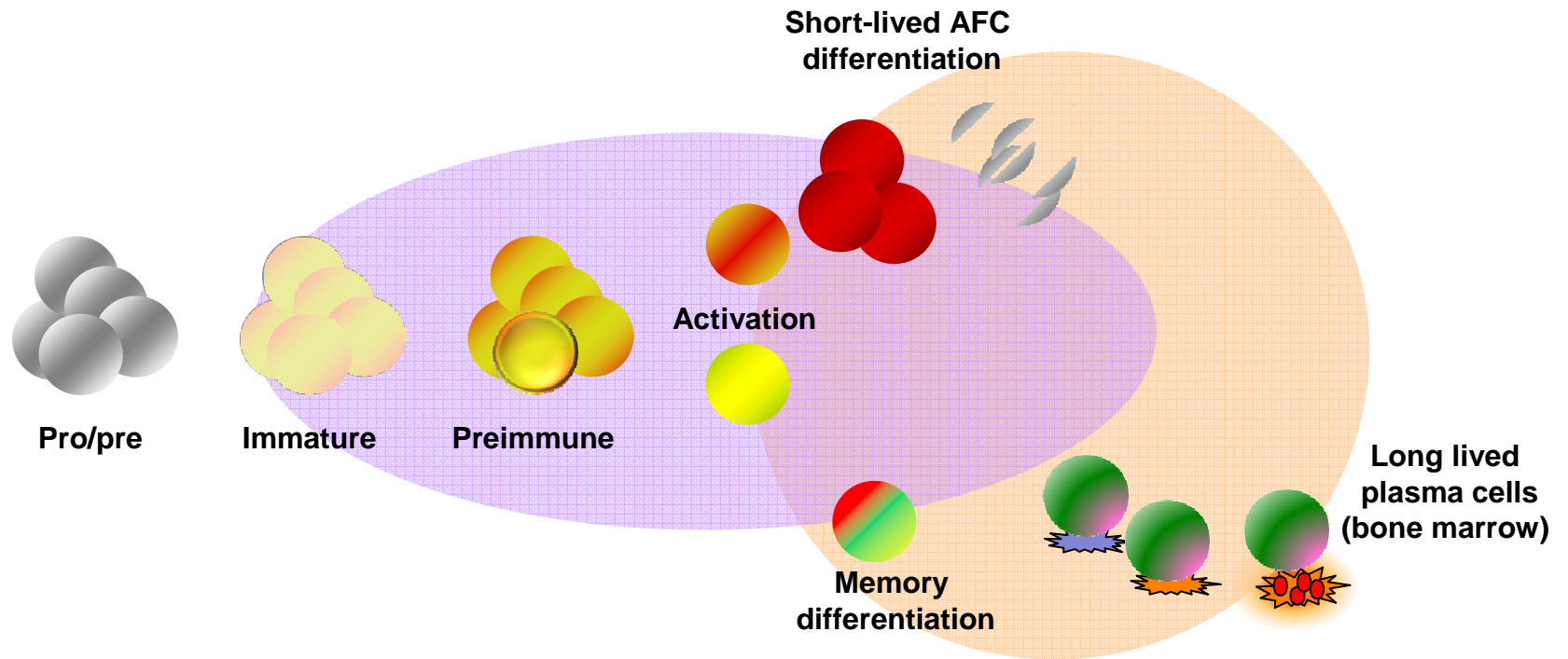


# RANK-L expressing PCs induce APRIL production in BMMs



# Key ideas

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**Pre-immune and antigen-experienced pools occupy separate homeostatic niches**

**Unlike primary pools, which are subject to extrinsically determined constraints for entrance and persistence, some antigen experienced cells (e.g. Long lived plasma cells) can autonomously drive their own niche formation and maintenance**

**Understanding the cellular and molecular mechanisms mediating these processes should yield targets for prospective or retrospective manipulation.**