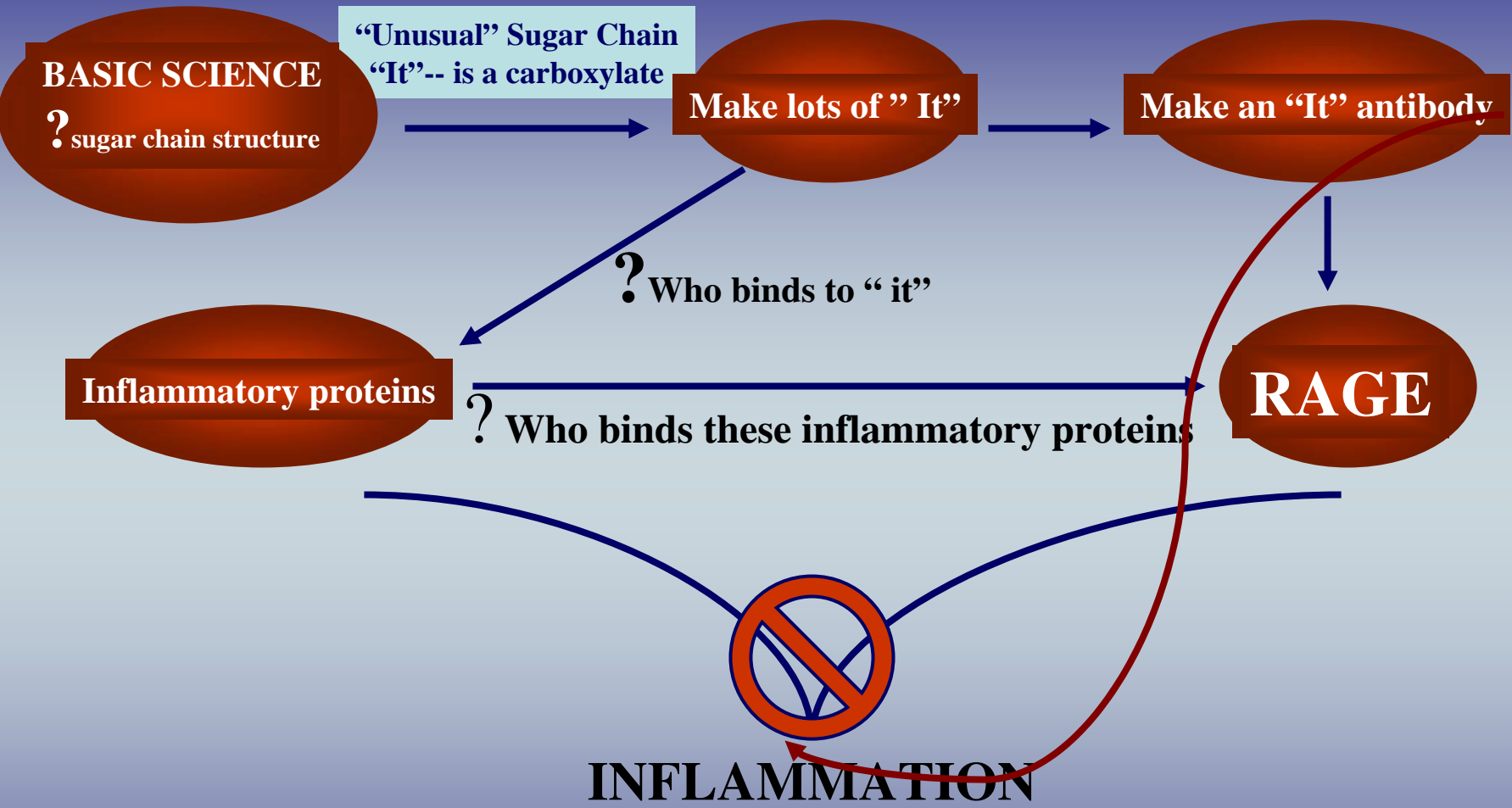
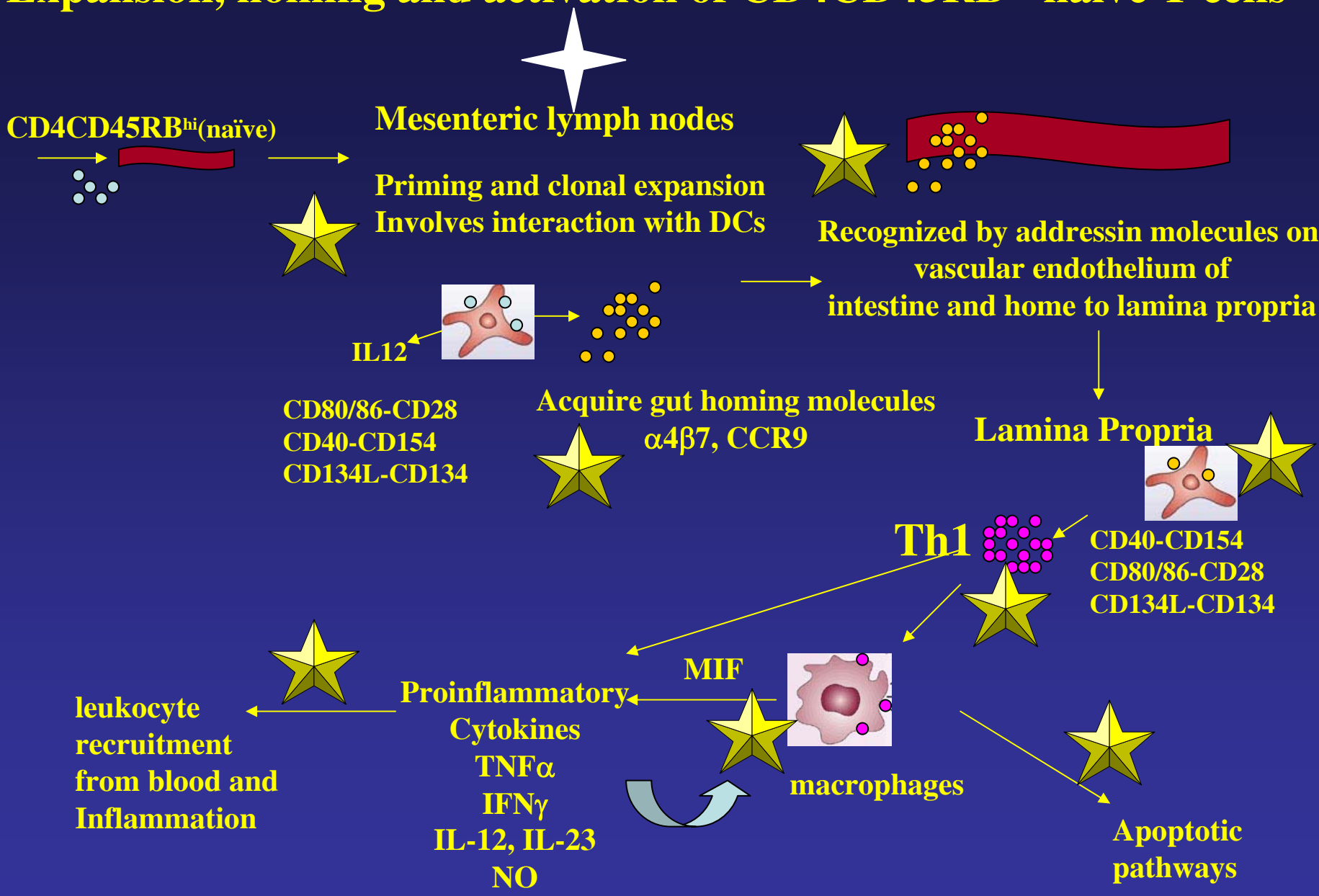
# SUGAR-FREE GLYCOBIOLOGY



# Expansion, homing and activation of CD4CD45RB$^{hi}$ naive T cells



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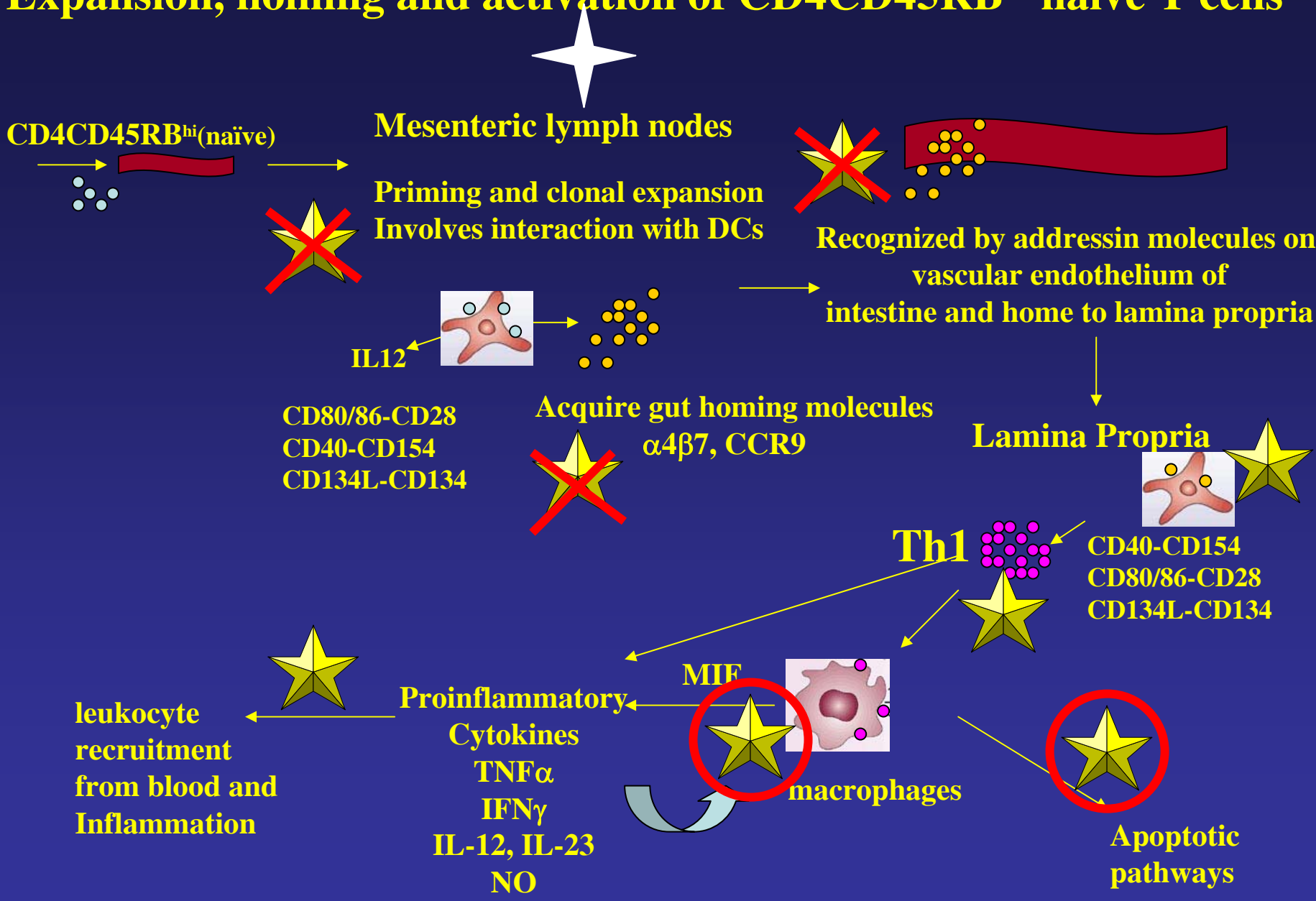
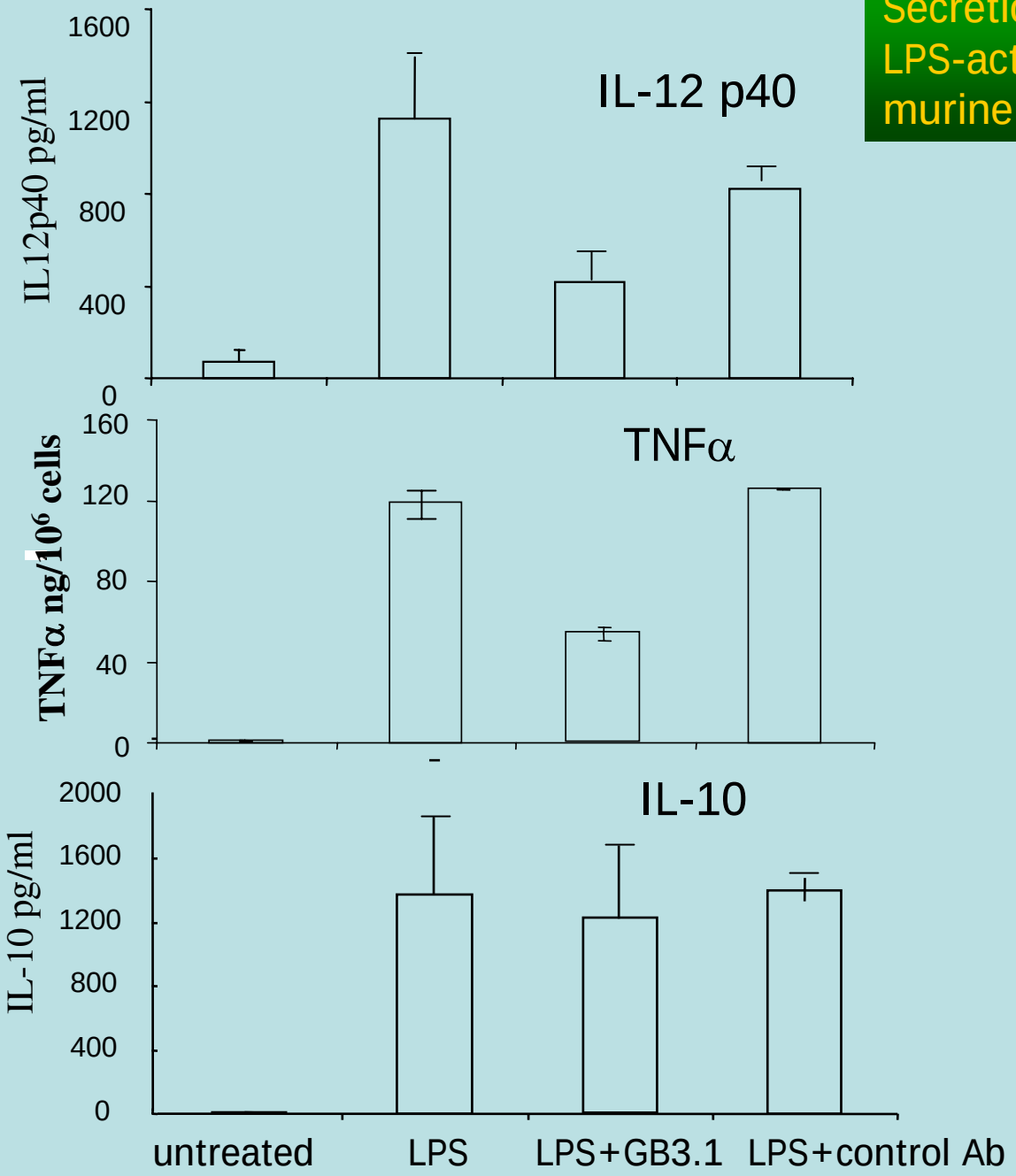
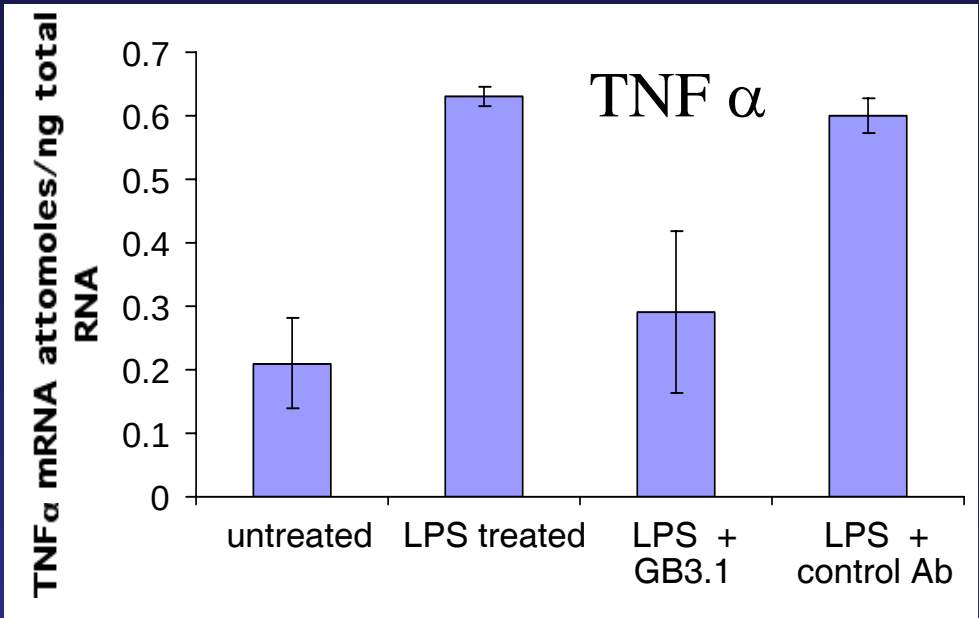
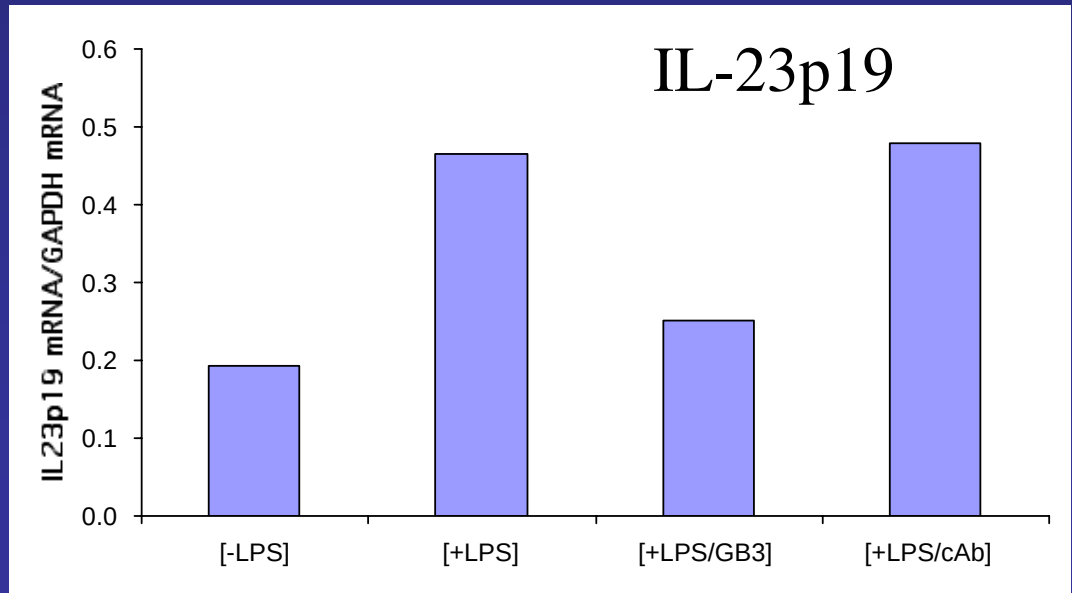


Secretion of cytokines from LPS-activated RAW264.7 murine macrophages

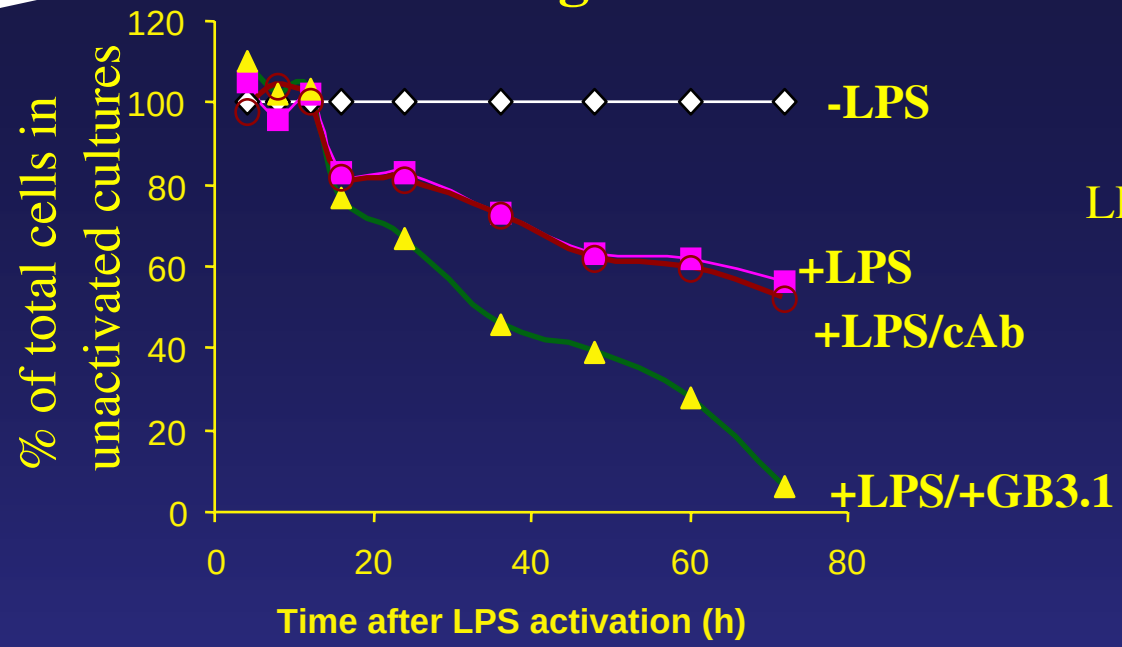


# mAbGB3.1 inhibits LPS-induced TNFα and IL23p19 gene expression in murine macrophages

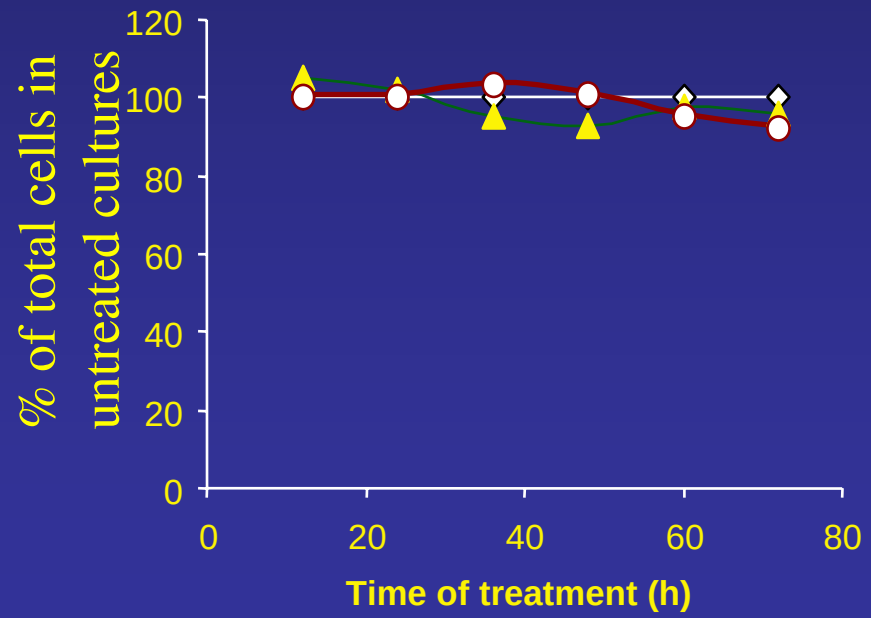


# GB3.1 augments cell death of activated macrophages



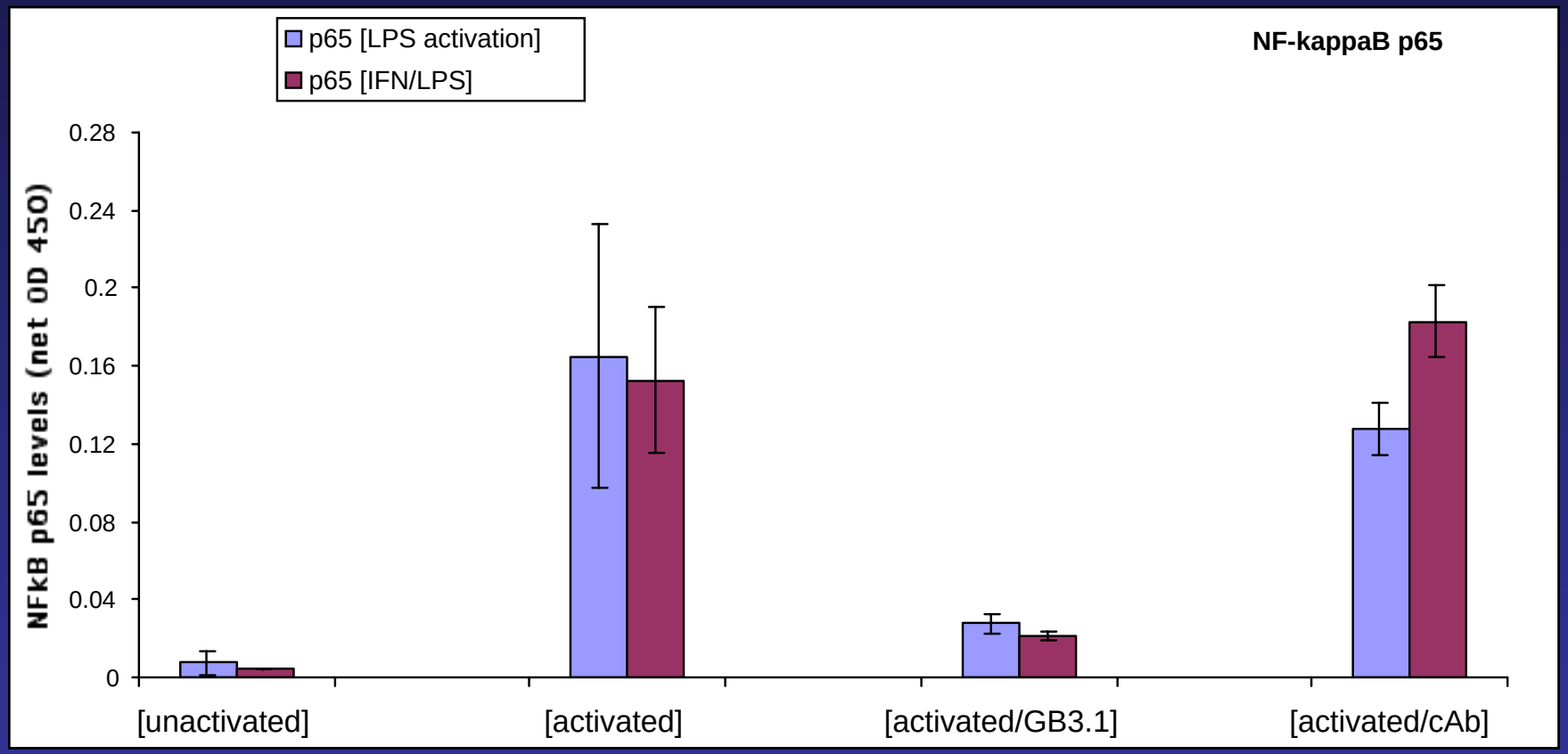

LPS Activated macrophages




Unactivated macrophages

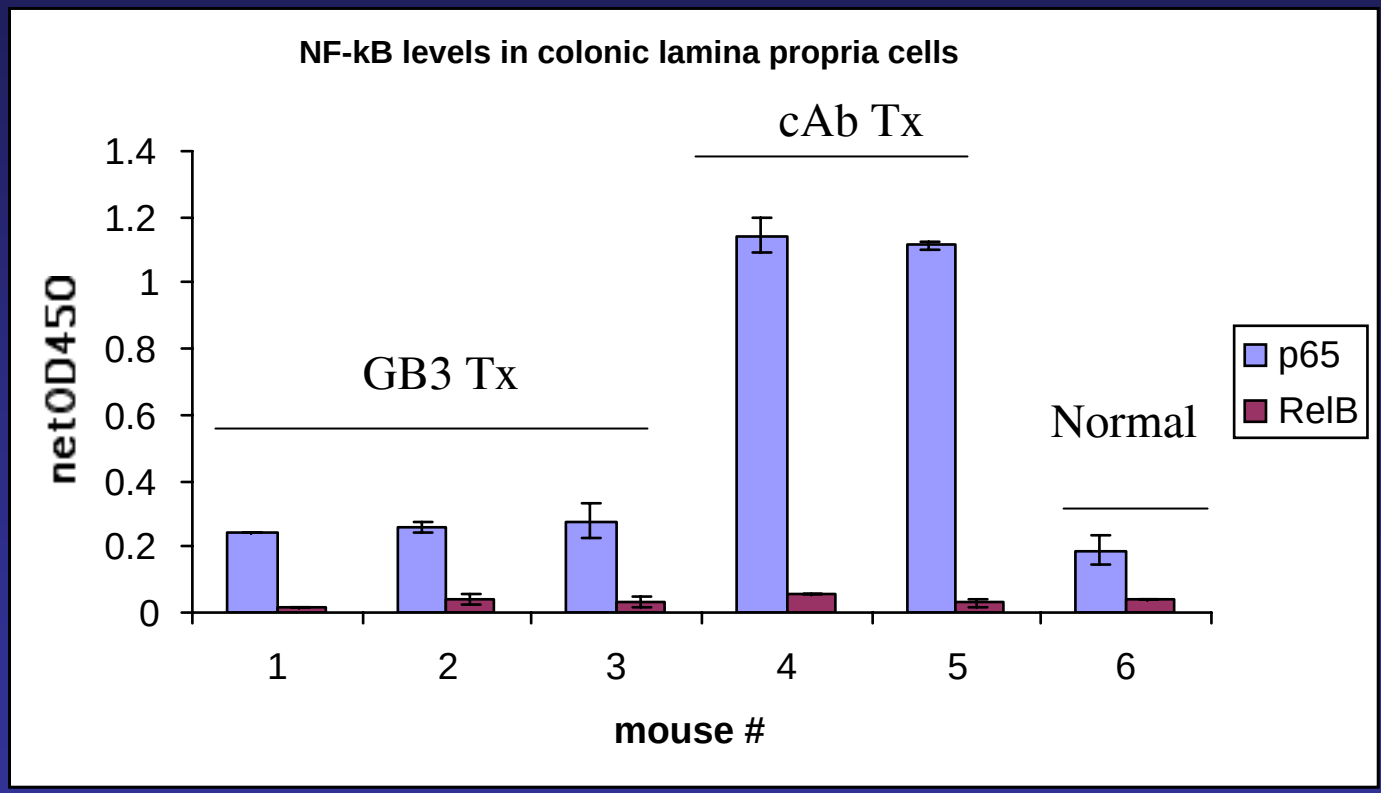
# mAbGB3.1 inhibits onset of colitis

- GB3.1 reduces CD4+ T cell accumulation specifically in colon tissues
- GB3.1 does not induce significant apoptosis of unactivated or activated T-cells
- GB3.1 inhibited recruitment of monocytes into inflammed areas or caused apoptosis of recruited macrophages
- No upregulation of MAdCAM expression
- Proinflammatory cytokine production is reduced
- Signaling pathways involved?

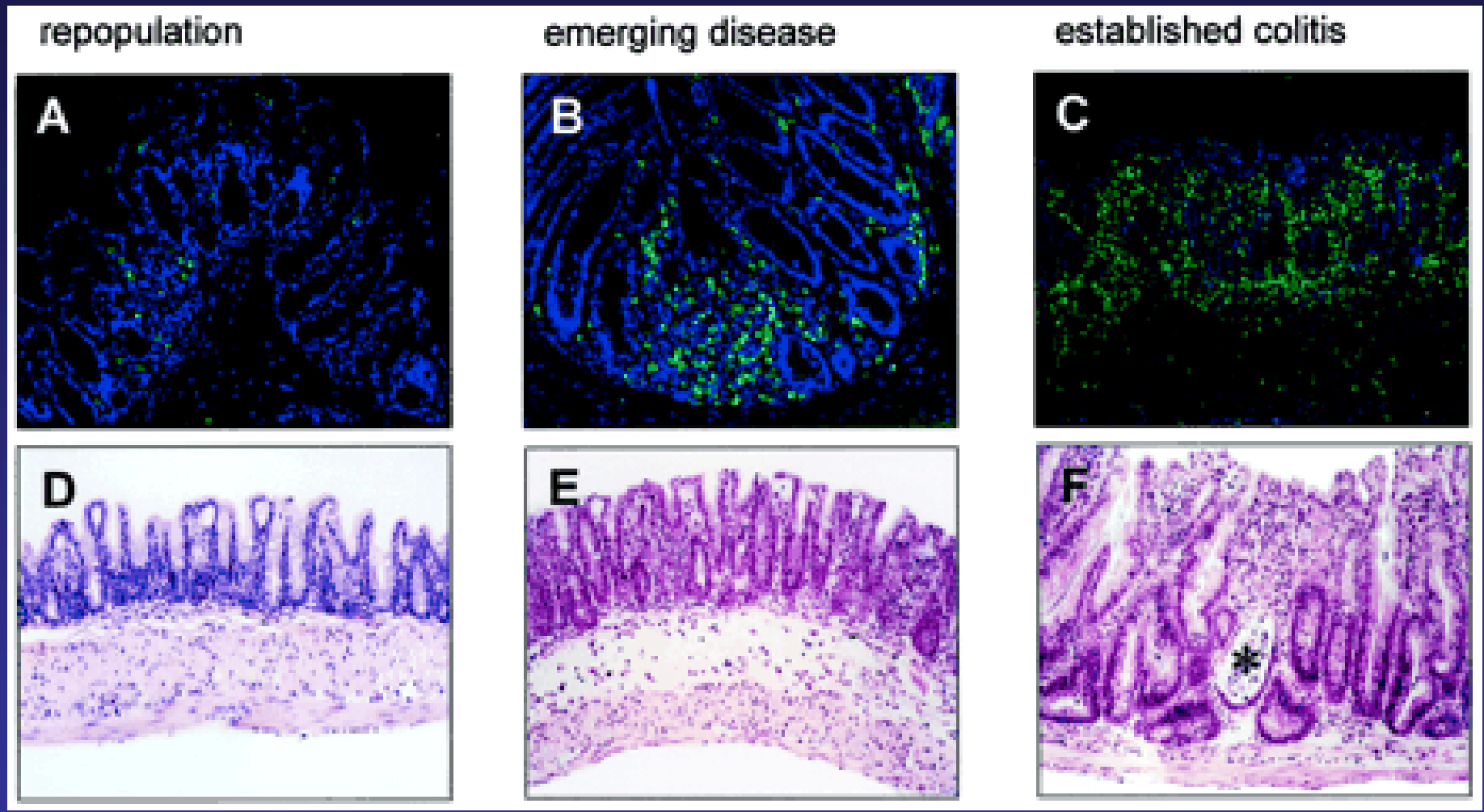

p65 [LPS activation]
p65 [IFN/LPS]
NF-kappaB p65
NFkB p65 levels (net OD 450)
0.28
0.24
0.2
0.16
0.12
0.08
0.04
0
[unactivated]
[activated]
[activated/GB3.1]
[activated/cAb]

# NF-kappaB p65 is enhanced in colon of Crohn's patients

## Did GB3.1 block NF-κB in treated mice cells?



# WILL GB3.1 REVERSE COLITIS?




early

Day 9

Day21

Leithhauser et al
Lab Invest 81, 1339, 2001

## Clinical Symptoms

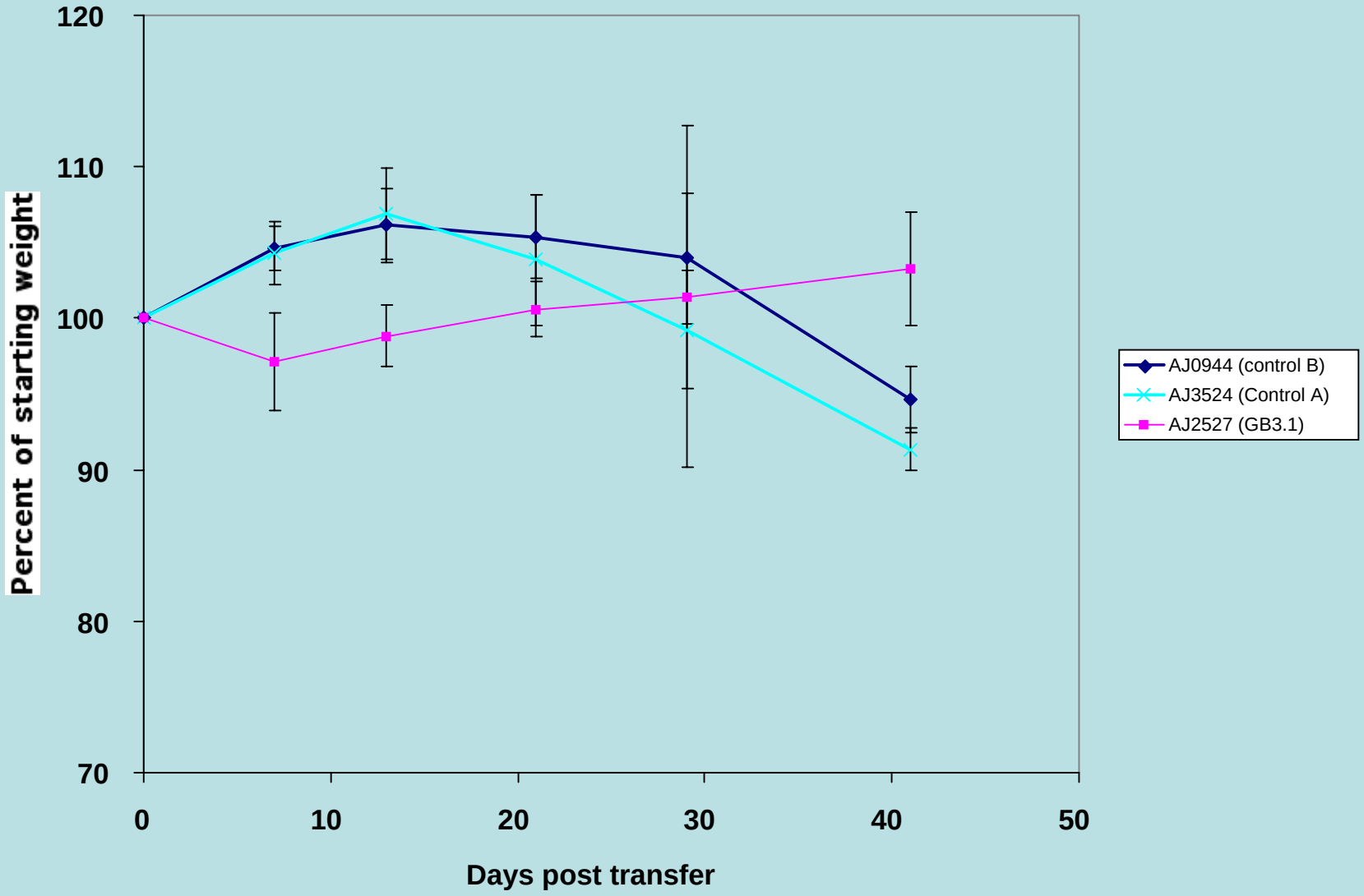
**Reconstituted, Untreated/cAb treated**

**Loss of weight, loss of hair, soft stools, ill**

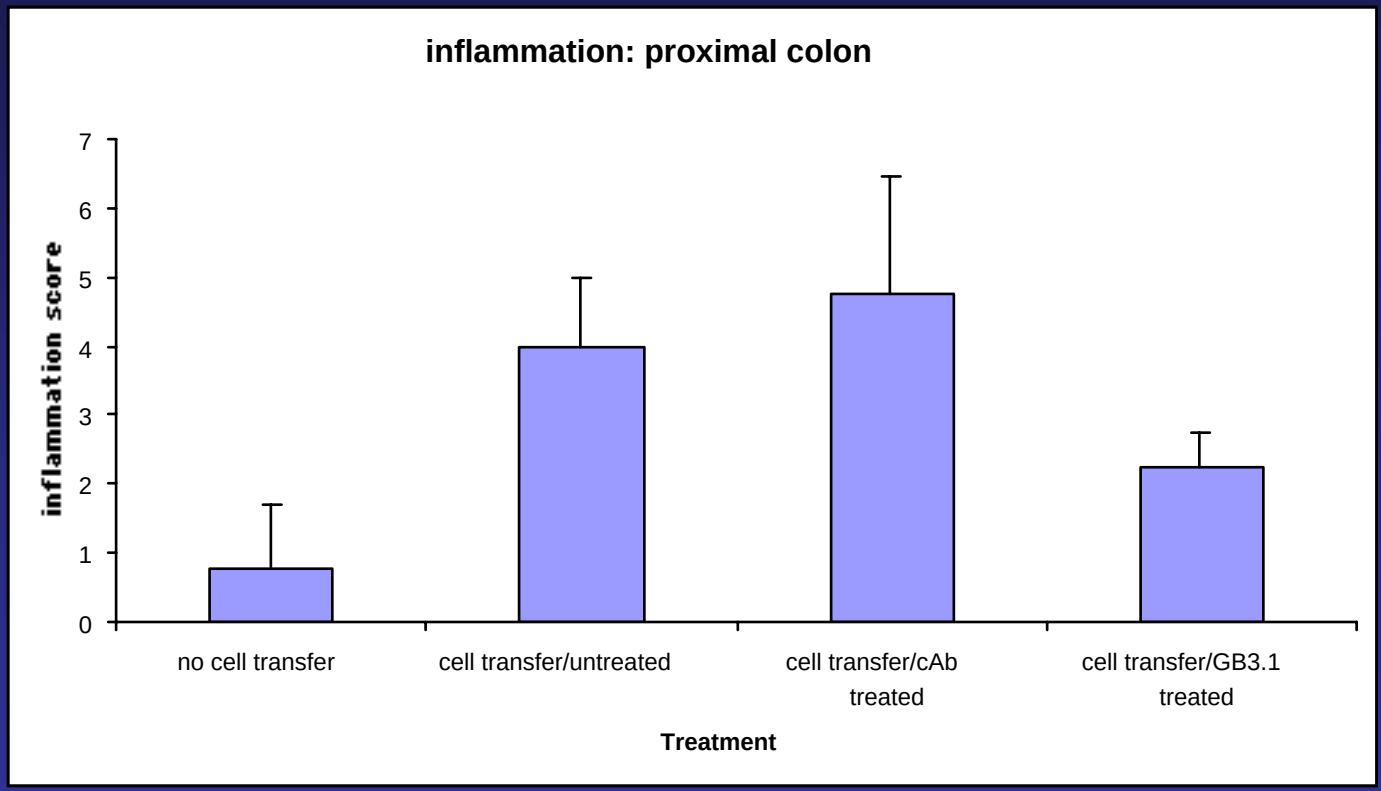
**Reconstituted, GB3.1 treated**

**Minimal weight loss, no hair loss, normal stools, healthy**

# Weight loss curves



# mAbGB3.1 treatment reverses colitis in the emerging phase of disease



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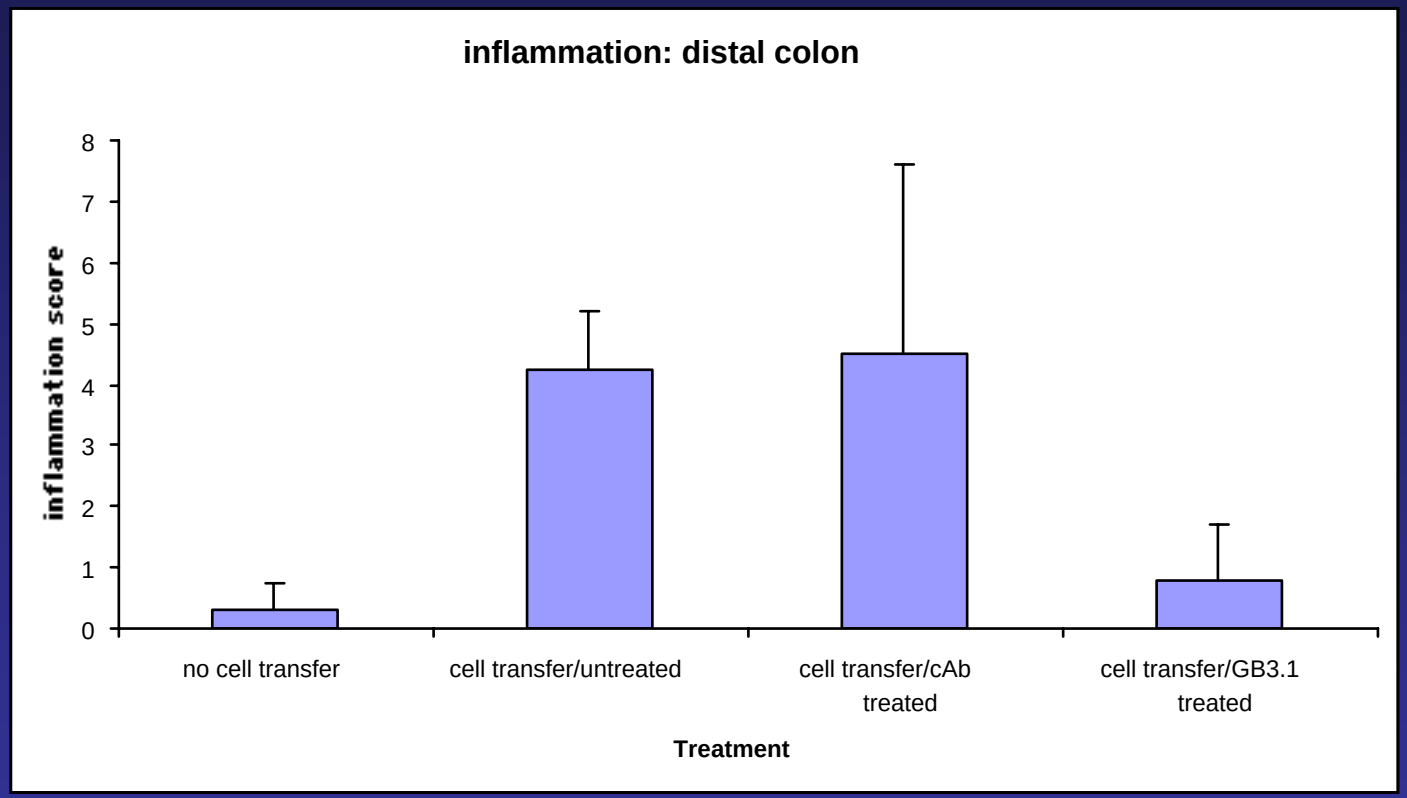
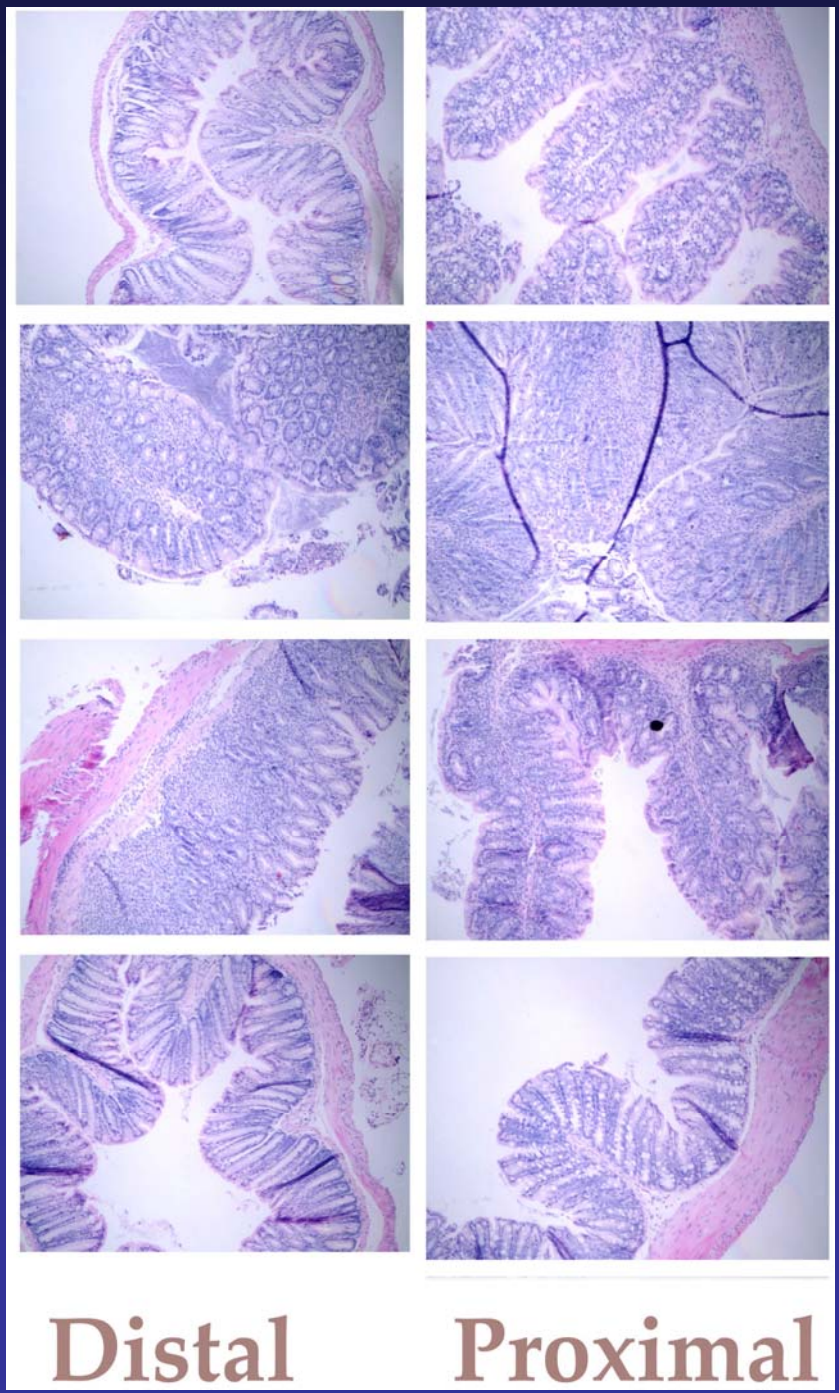


**mAbGB3.1 treatment reverses colitis in the emerging phase of disease**




**No cell transfer**

**Reconstituted/ untreated**

**Reconstituted/ cAb Treated**

**Reconstituted/ mAbGB3.1 treated**

# CONCLUSIONS

ANTICARBOXYLATE ANTIBODY GB3.1 BLOCKS THE ONSET OF COLITIS

THE ANTIBODY ALSO SEEMS TO REVERSES ESTABLISHED COLITIS

EFFECTS ARE PROBABLY MEDIATED BY APOPTOSIS OF ACTIVATED MACROPHAGE

GB3.1 MAY BE A POTENTIAL TREATMENT FOR IBD

**In this collaboration between the Freeze and Kronenberg labs Geetha Srikrishna pioneered these studies and contributed most of the data**