

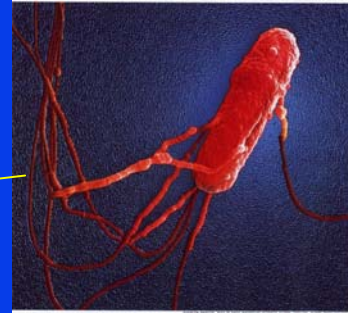
Adaptive Immunity to Flagellin in IBD

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Hypothesis: Potential Roles of Flagellin in IBD

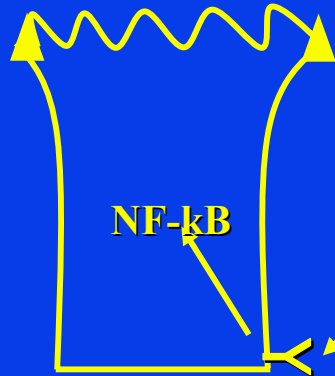


E. Coli

Flagella

Flagellin monomers (About 70,000 per flagella)

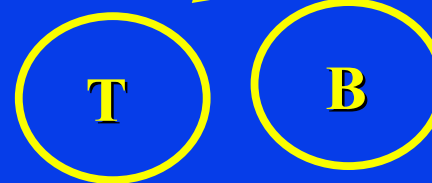
Inestinal epithelial cell



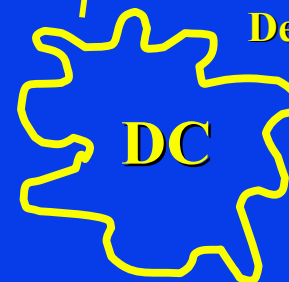
TLR5

1. Drive Innate Immunity
Pro-inflammatory cytokines
PMN recruitment

2. Targeted by Adaptive Immunity
Flagellin specific T-cells, B-cells



3. Promote Adaptive Immunity
Dendritic cell activation



Goal: Define serum anti-flagellin antibody response in mice

- 1. Does generation of flagellin antibodies require T-cells?**
- 2. Is flagellin's activation of innate immunity needed for antibody response? If so, how are these responses linked?**
- 3. How specific are antibody responses to various flagellins?**
- 4. What type of exposure to flagellin is required for generation of flagellin antibodies?**

Methods

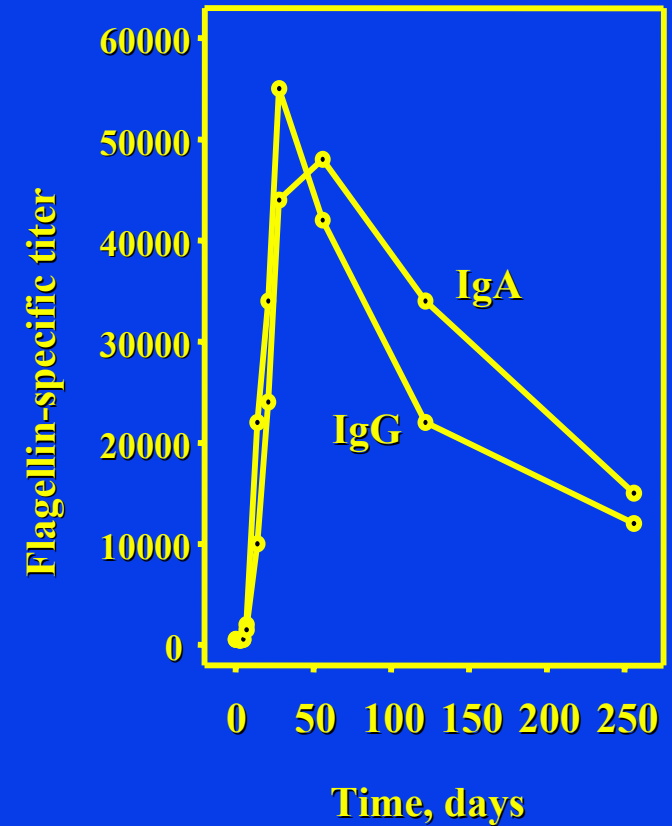
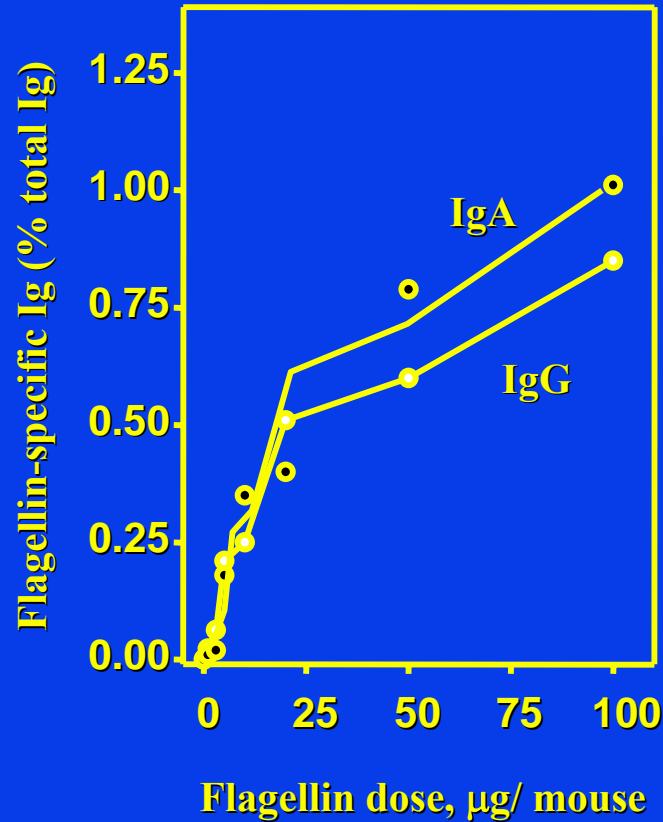
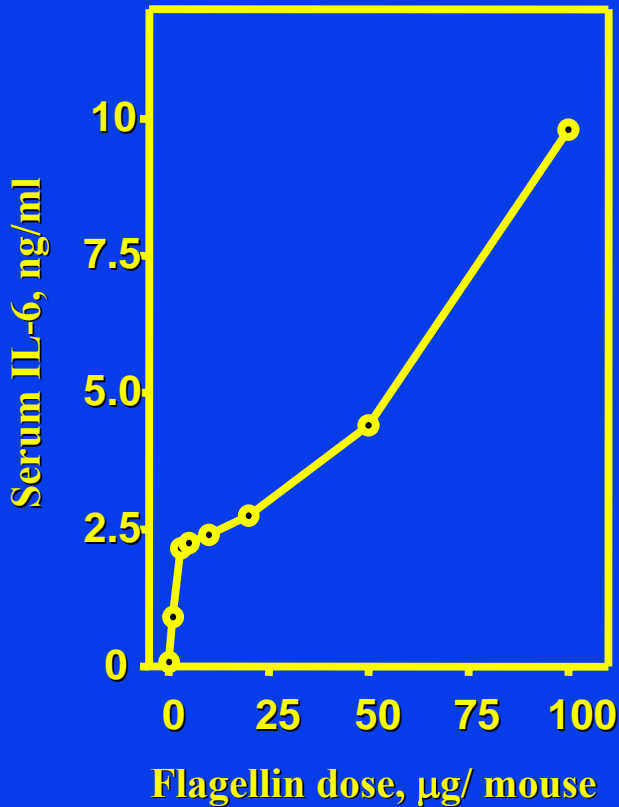
1. Administer flagellin (or HBSS as control)



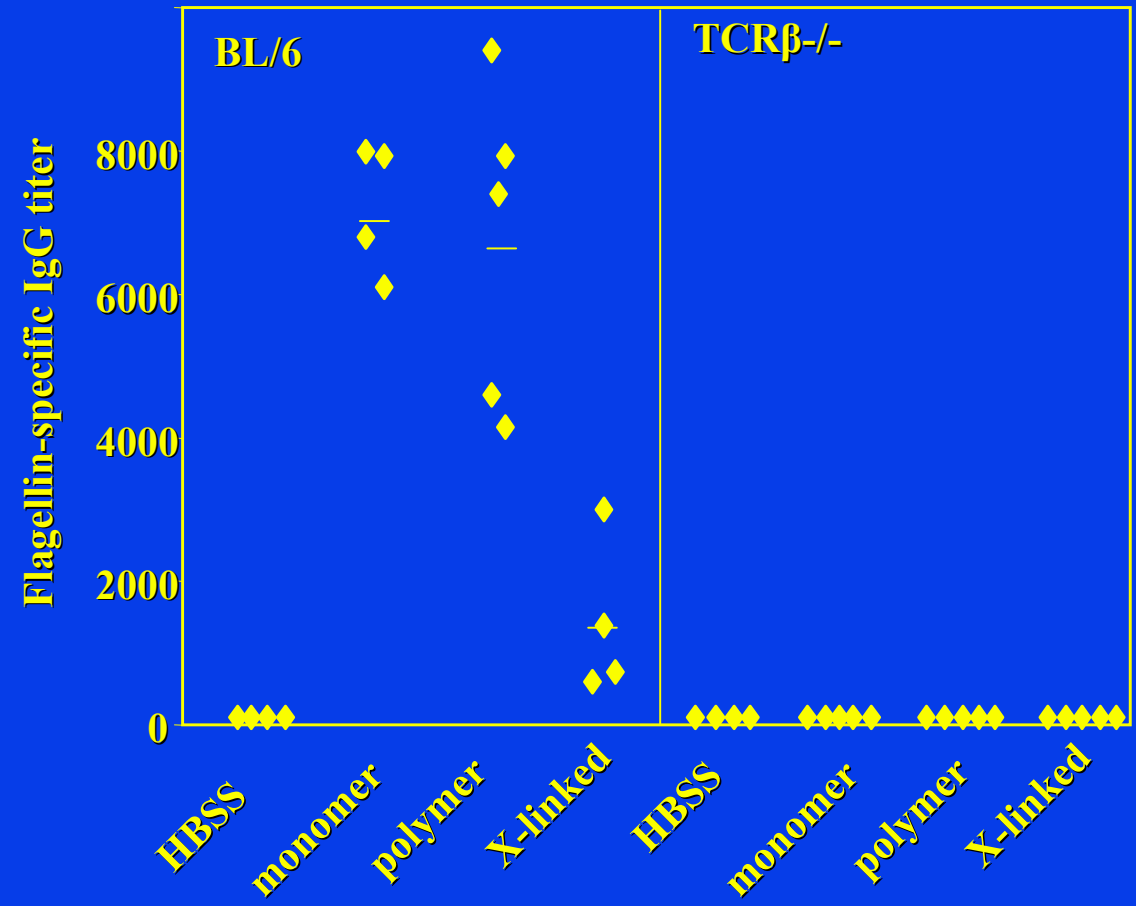
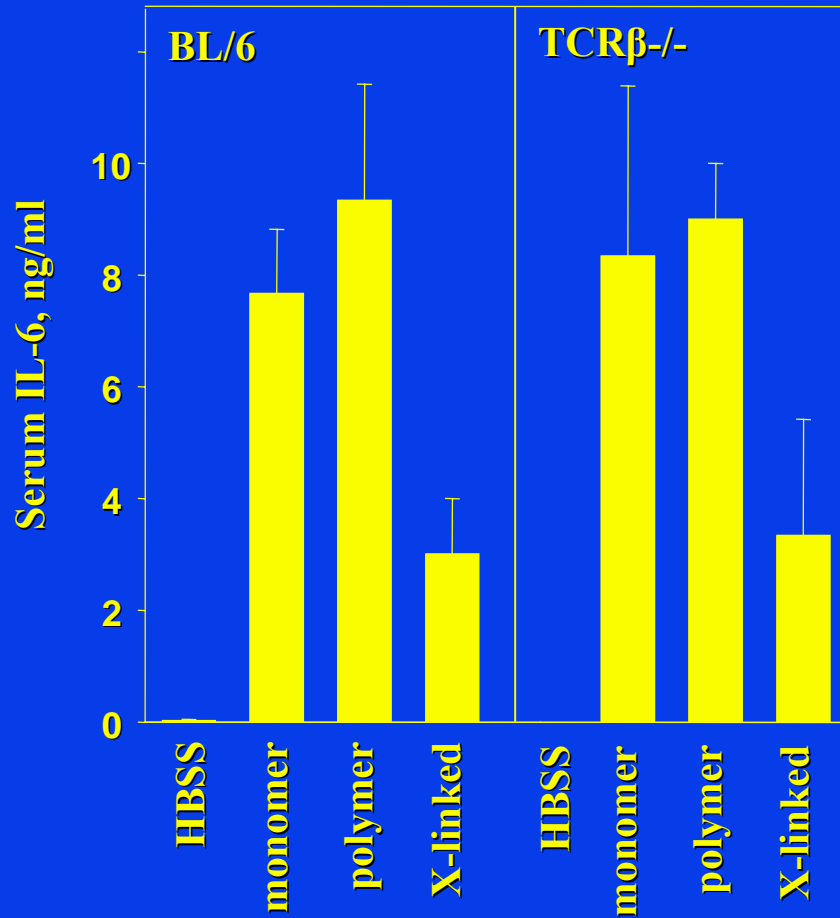
**2. Bleed at 90 minutes for
cytokine measurements**

**2. Bleed at 15 days to
measure flagellin-specific Ig**

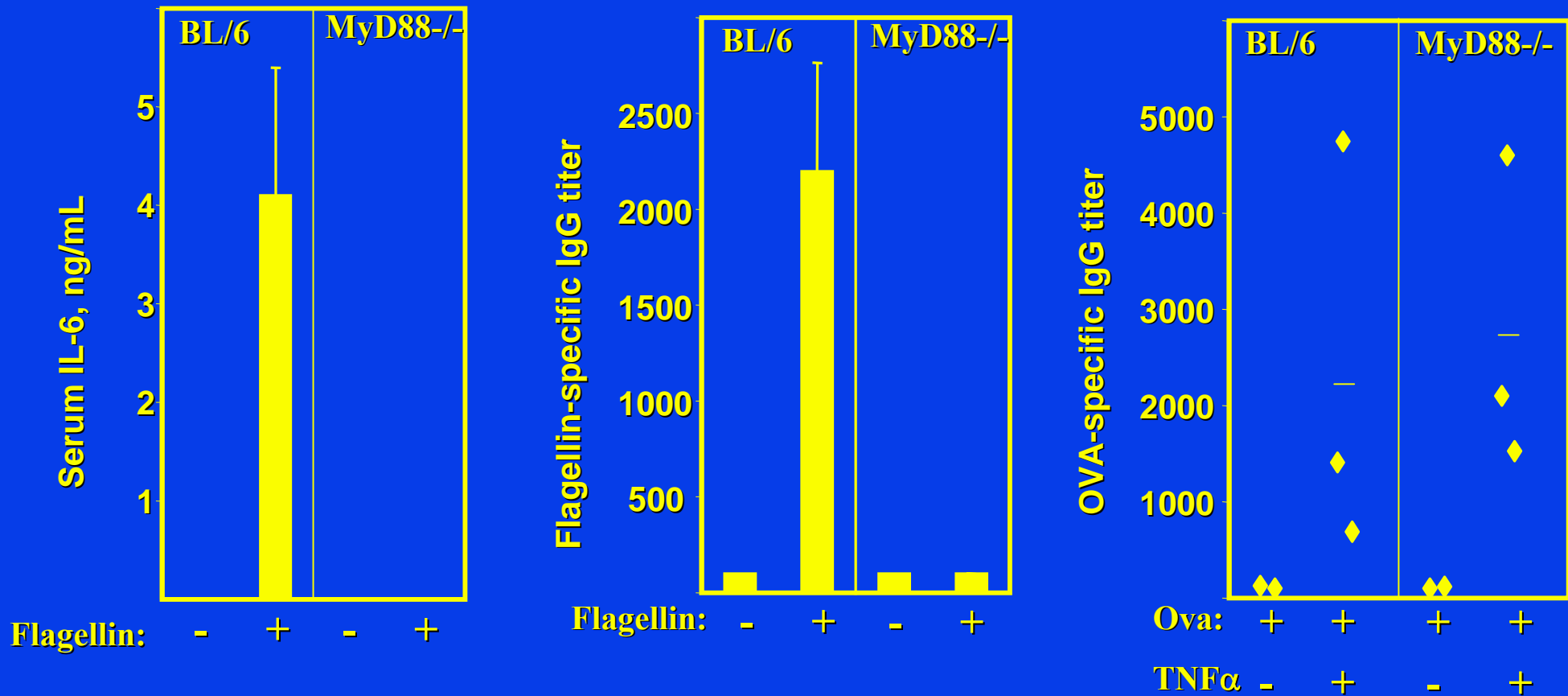
Flagellin elicits innate and adaptive immune responses in mice



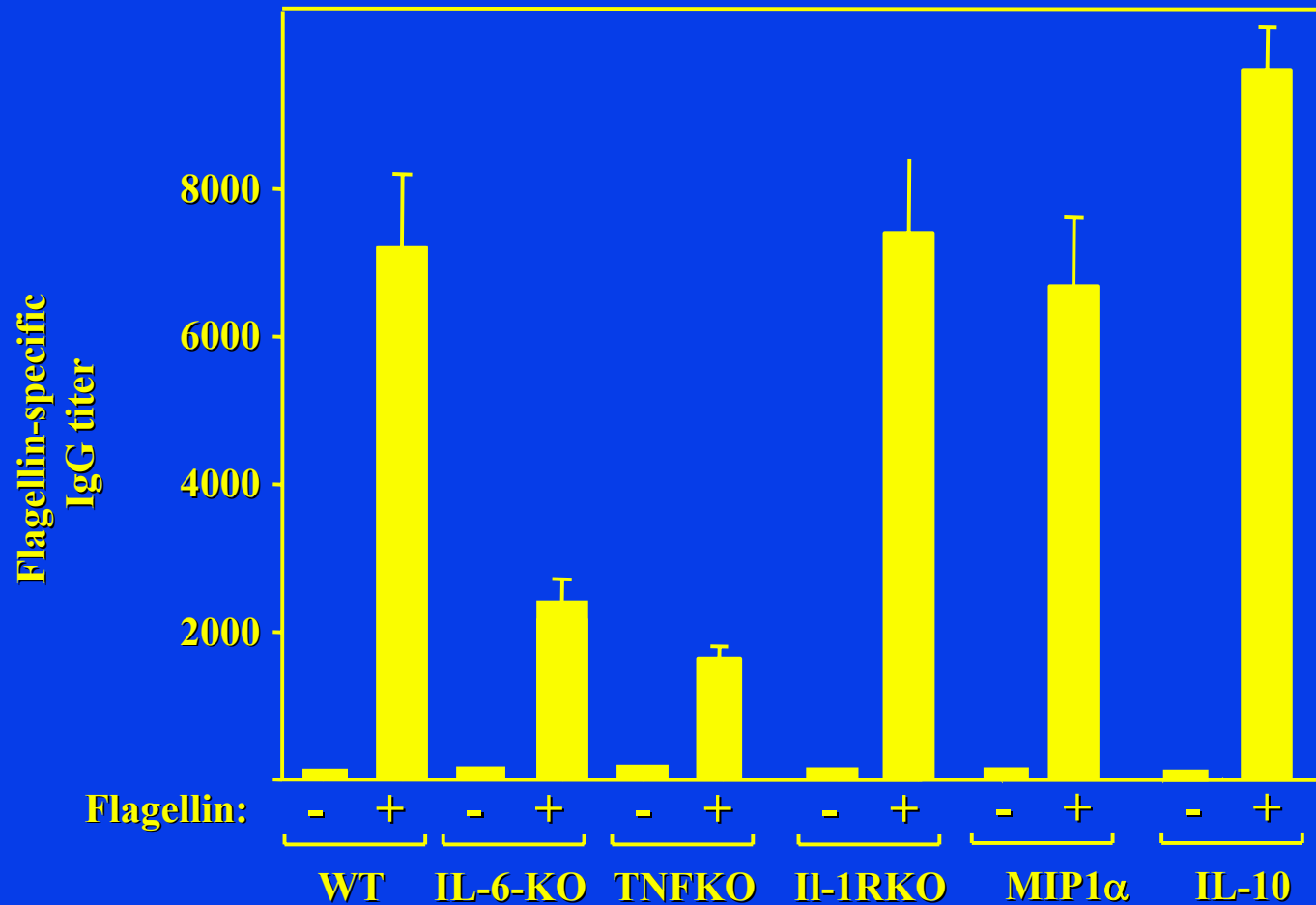
Generation of Flagellin Antibodies Requires T-cells



Generation of Flagellin Antibodies Requires Innate Immune Signaling

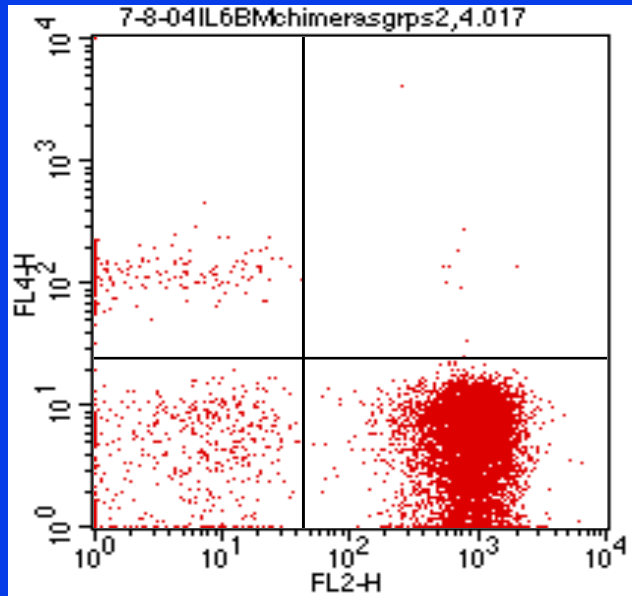


IL-6 and TNF α Play Roles in Linking Innate and Adaptive Immune Responses to Flagellin

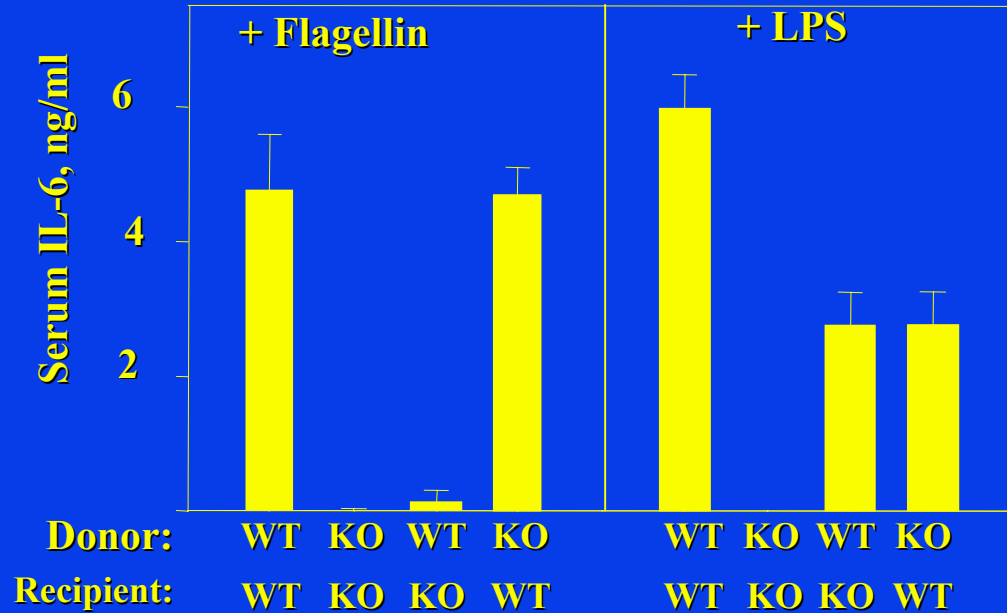


Non-hematopoietic Cells are the Primary IL-6 Producers In Response to Flagellin

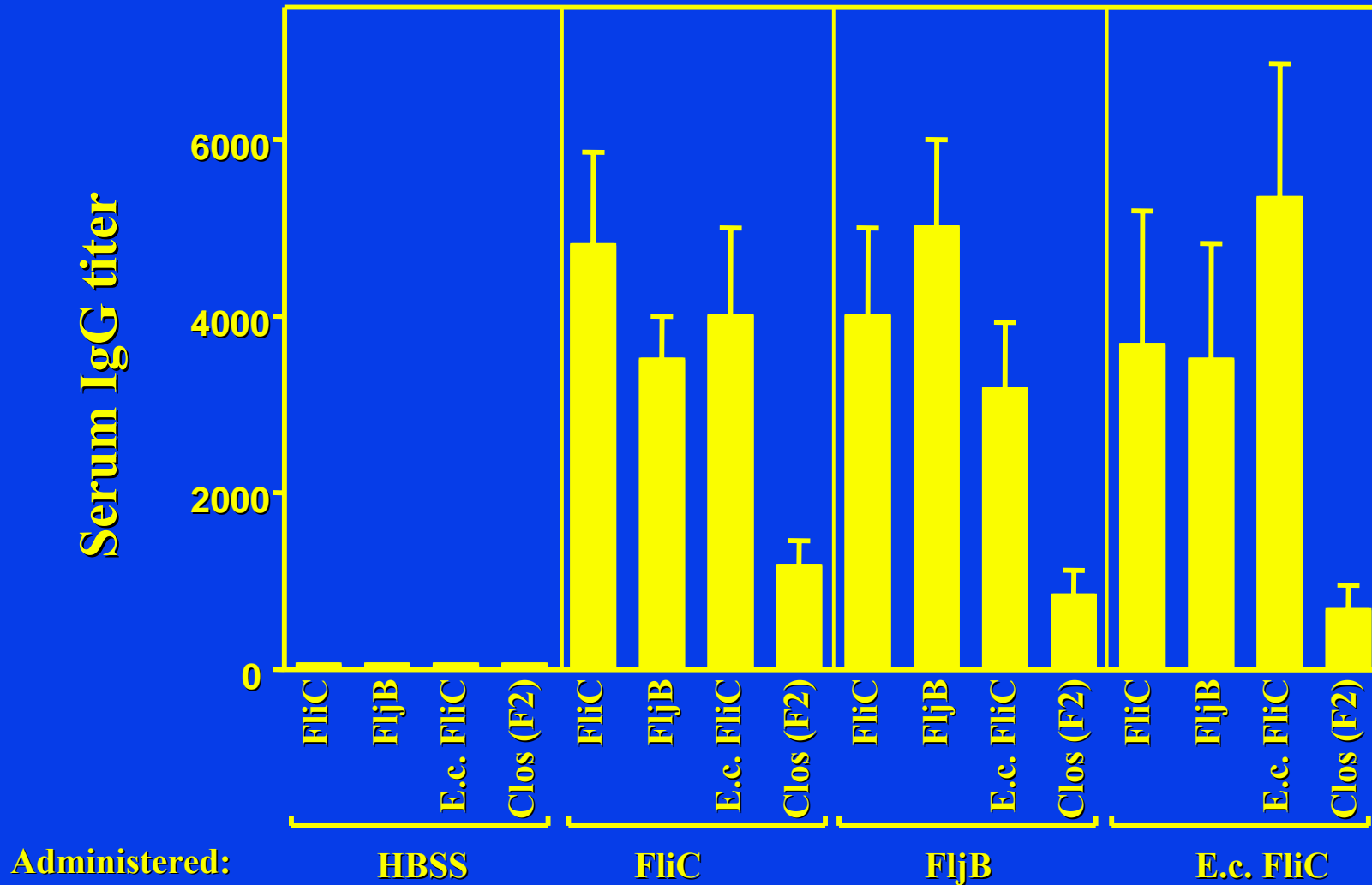
CD45.1 (host)



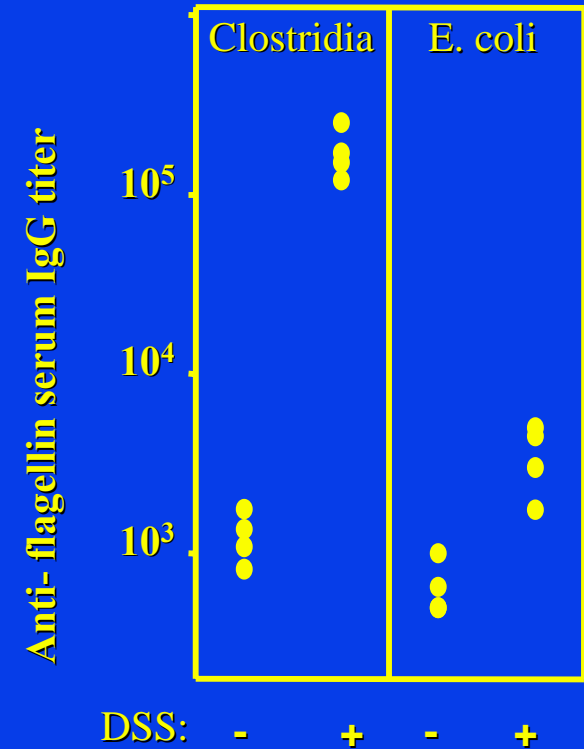
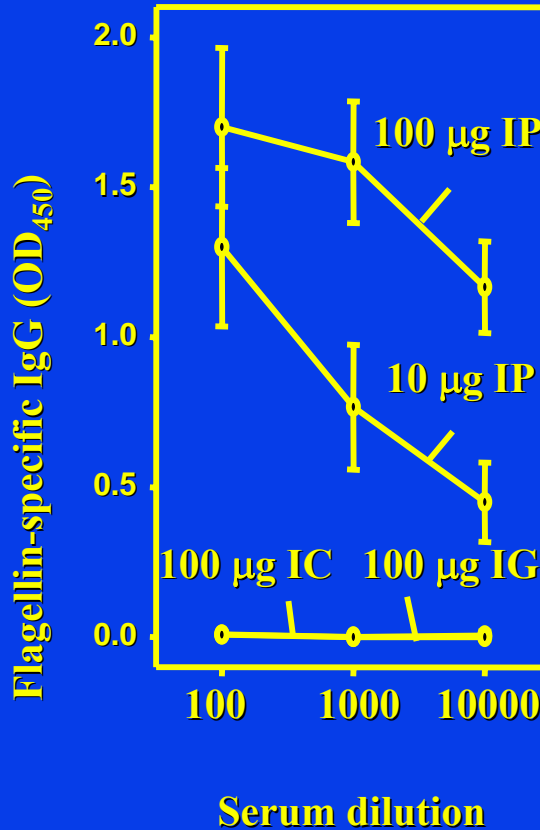
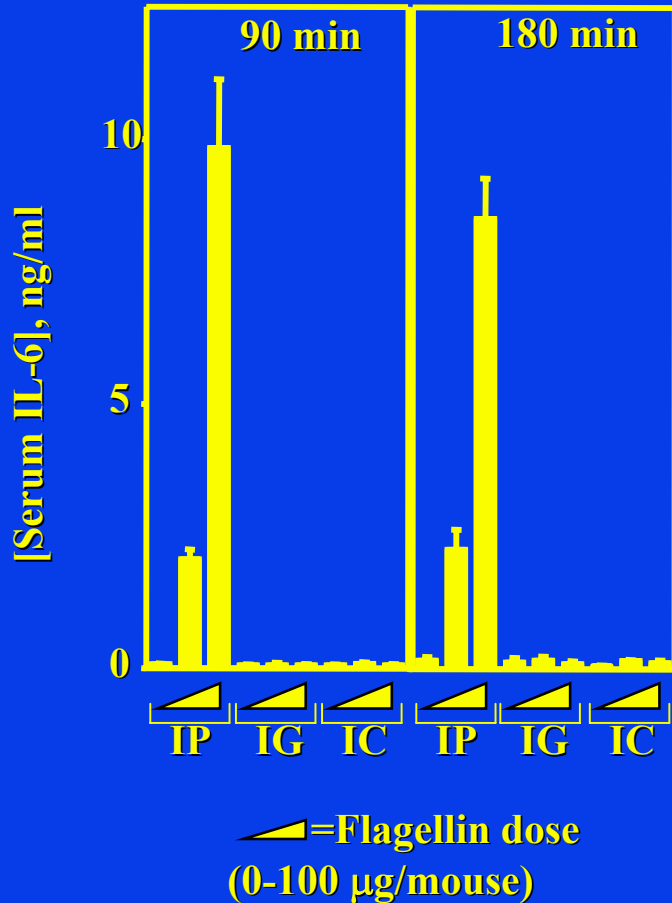
CD45.2 (donor)



Antibody Responses to Flagellin Monomers have Modest Sero-specificity



Immune Response to Gut Mucosal Flagellin Requires Barrier Disruption and/or Inflammatory Context



Conclusions

- 1. Generation of anti-flagellin IgG, IgA, and IgM is highly dependent upon T-cells.**
- 2. Adaptive immunity to flagellin is regulated by TLR signaling. Cytokines (e.g. IL-6 and TNF α) produced by non-hematopoietic cells, may link mucosal detection of flagellin to adaptive immune response**
- 3. Antibody responses to flagellin monomers are moderately specific for various flagellins.**
- 4. Generating serum antibodies to flagellin monomers via gut exposure may require barrier disruption and/or inflammation.**

Acknowledgements

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