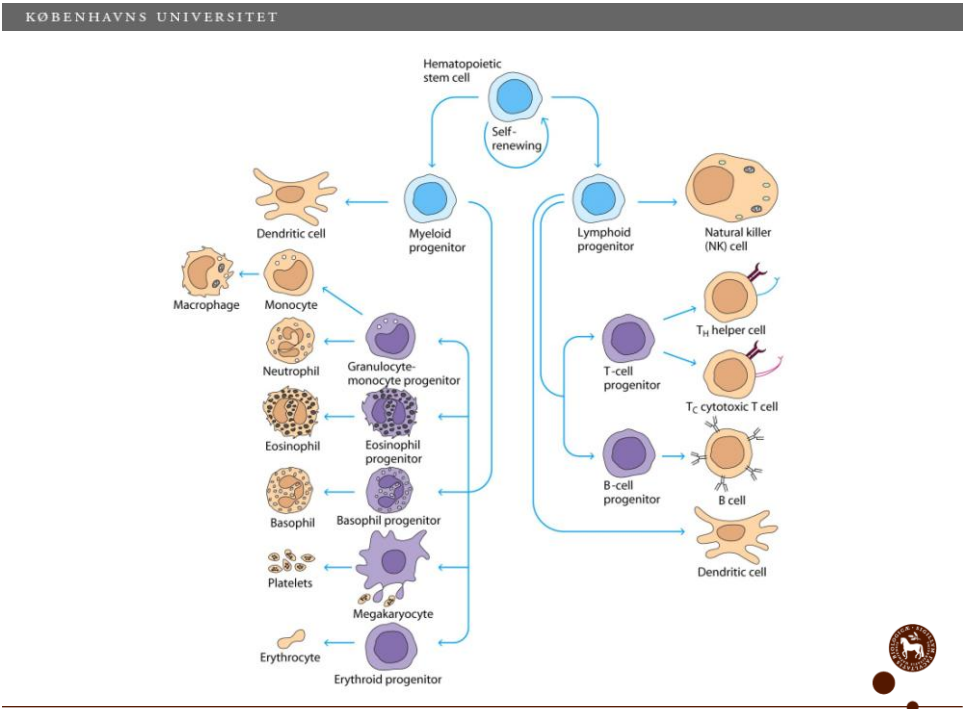
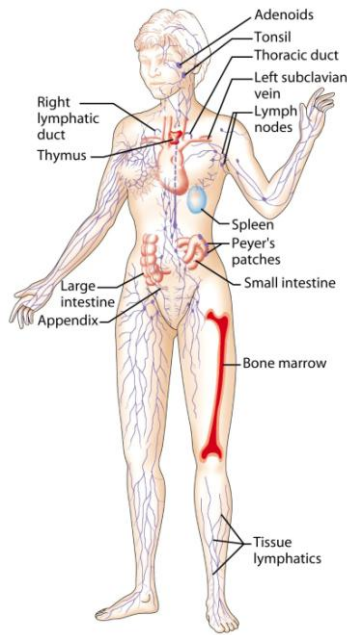


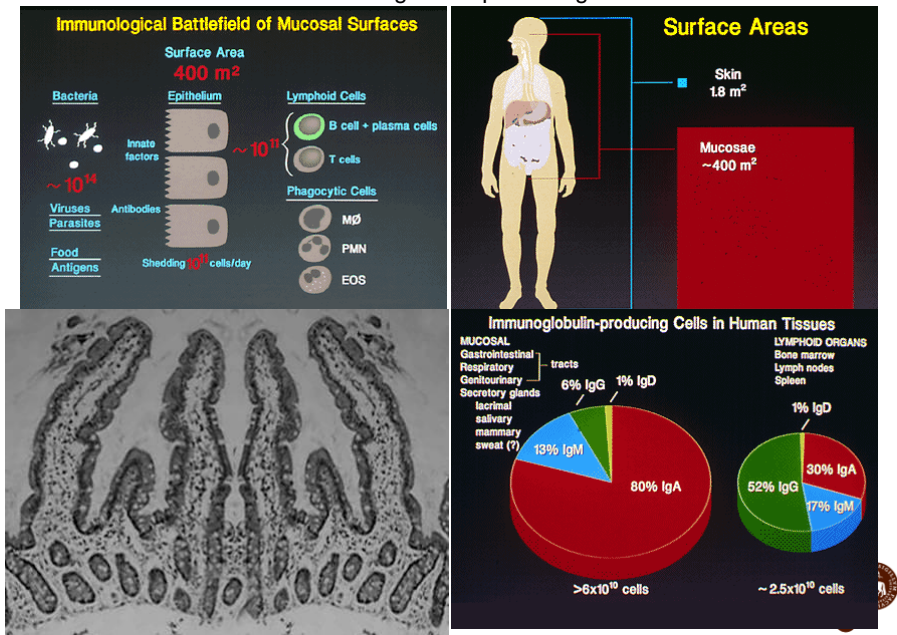
# The immune system of the gut: Development, homeostasis, and response

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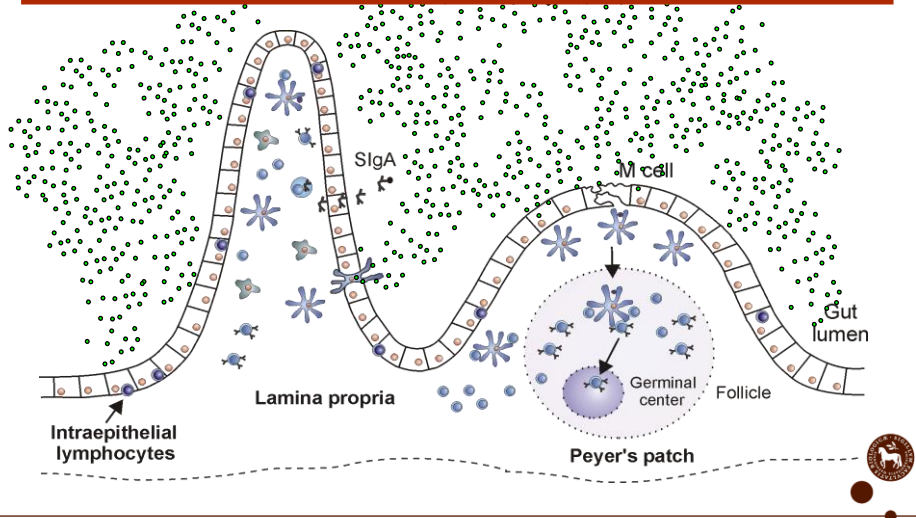




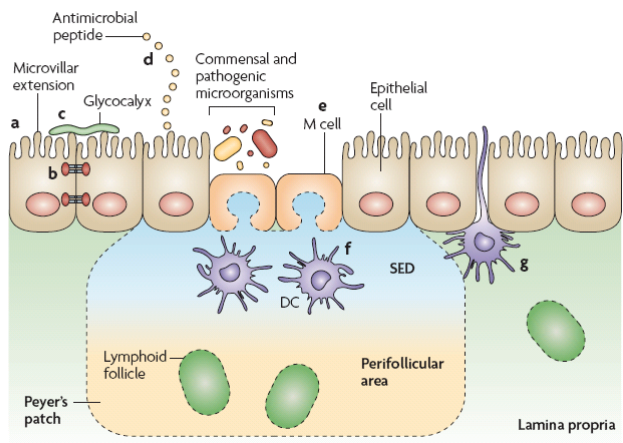
Mucosa and immunoglobulin producing cells



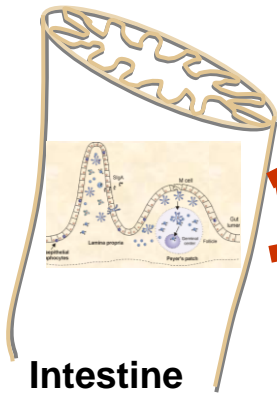
# Influence of the intestinal microbiota on the immune system



# The intestinal epithelial-cell barrier



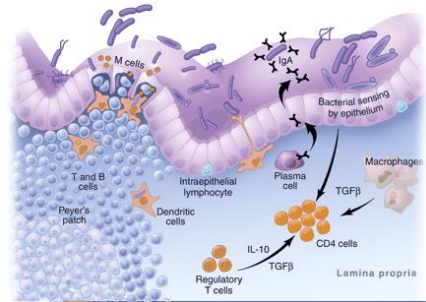
Artis, Nature rev. 2008



Intestine

- ➔ Inflammation
- ➔ Tolerance ( $T_R$ )
- ➔ Mucosal response (IgA)

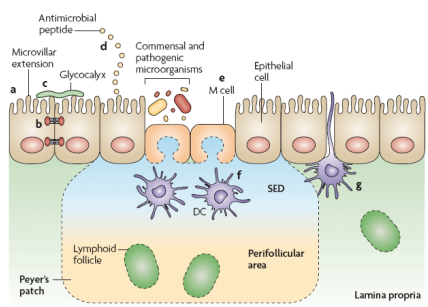
What determines the type of response ?



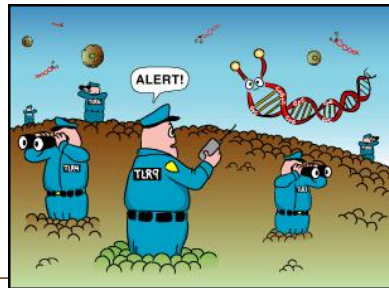
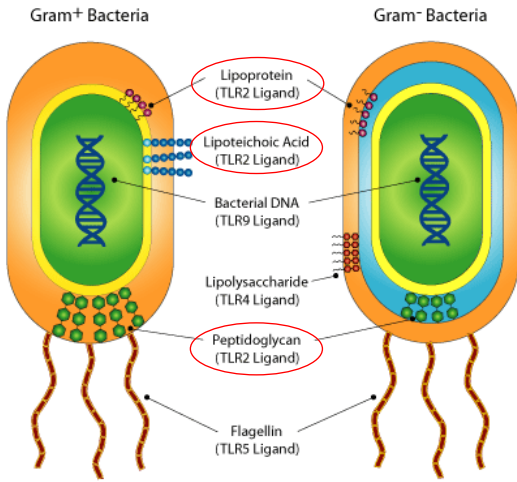
KØBENHAVNS UNIVERSITET

## What determines the type of immune response?

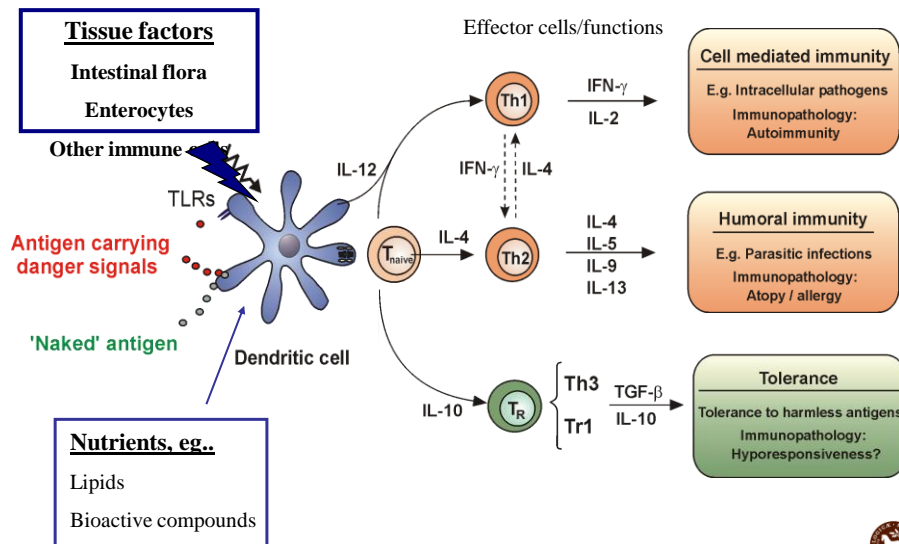
- Presence/absence of microorganisms
- Site where antigen encounters antigen presenting cells
- The state of the local environment.



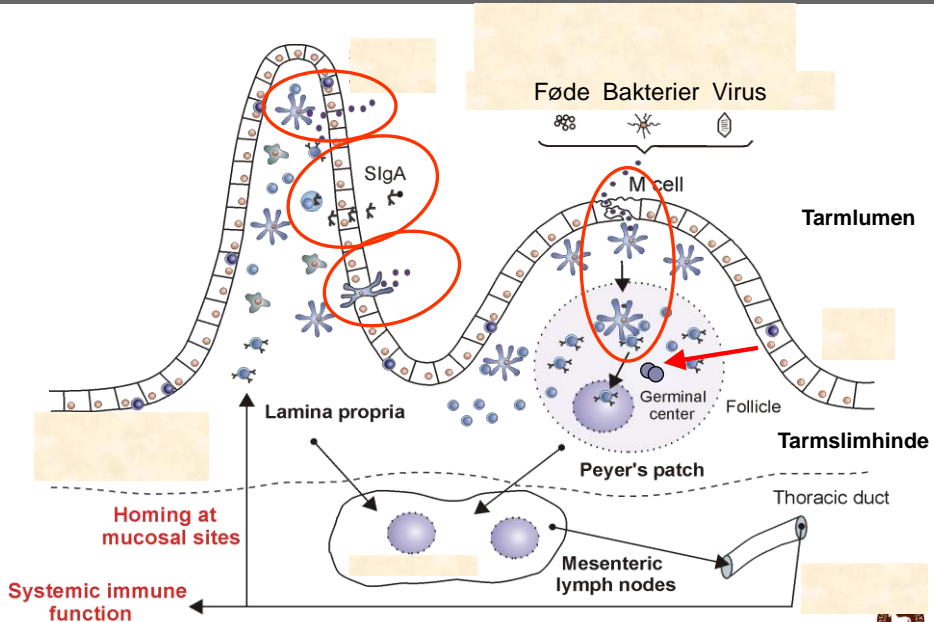
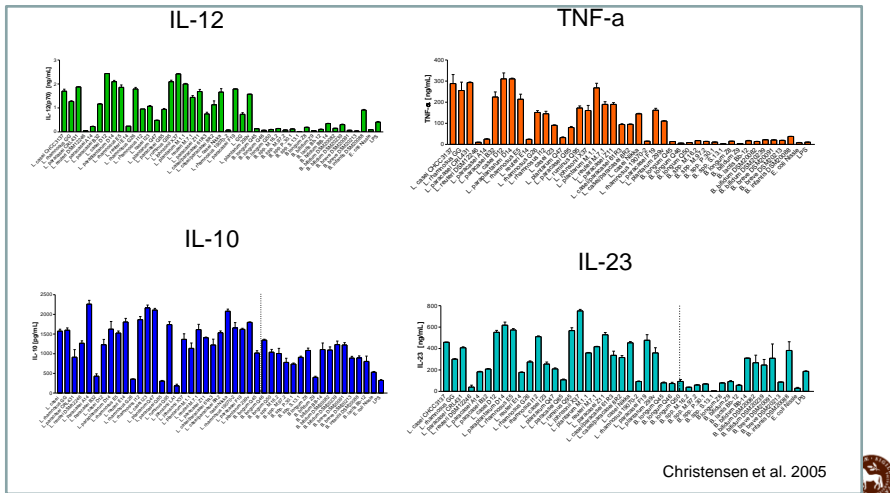
## Toll-like receptors - microbial recognition



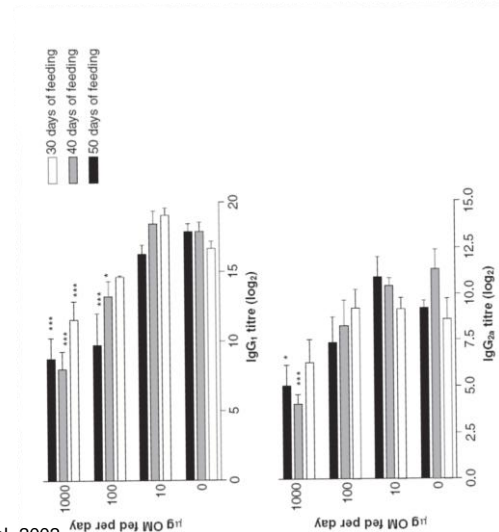
## Polarization of the immune response



## Screening of LAB strains in a murine DC in vitro model



## Induction of oral tolerance towards egg white proteins



Kjær & Frøkiær scand.J.Immunol. 2002

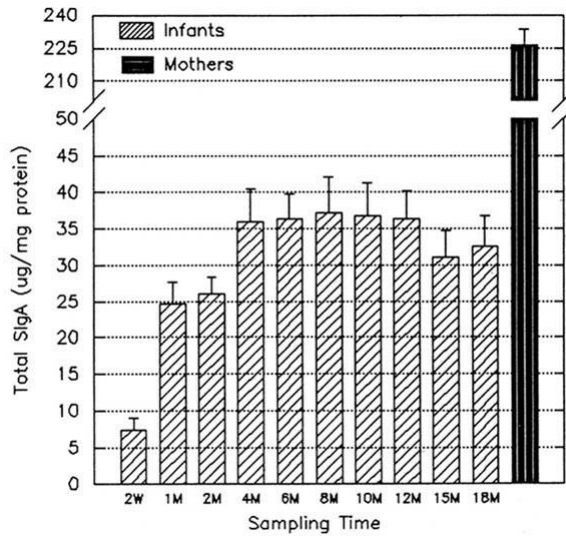


## Development of the immune system: Role of microorganisms

### Germ-free animals have a less developed immune system

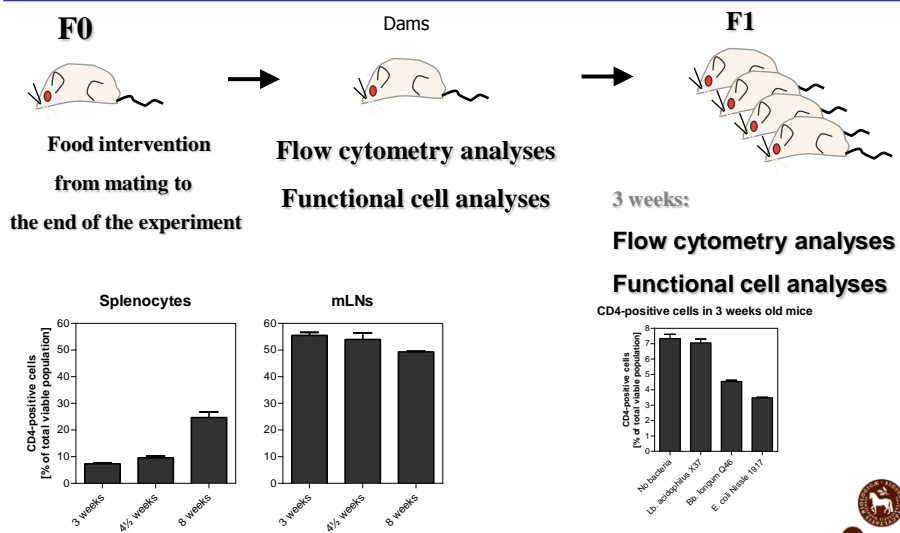
- Decreased size of spleen, lymph nodes
- Decreased size of Peyer's patches
- Decreased number/absence of lymphocytes in lamina propria
- Decrease phagocytotic activity and macrophage mobility
- Decrease IgA and IgG production
- Decreased IELs

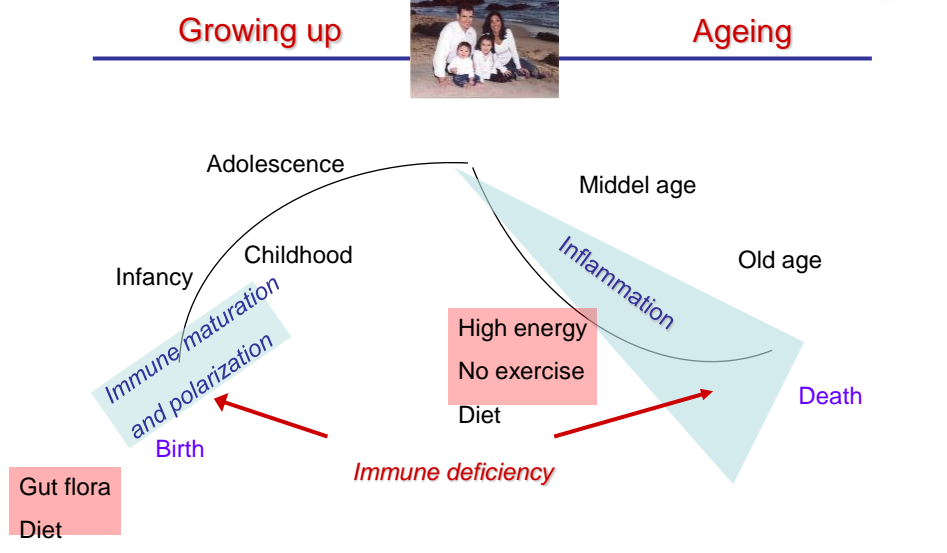




## Animal Experiments:

### Example: Immune maturation

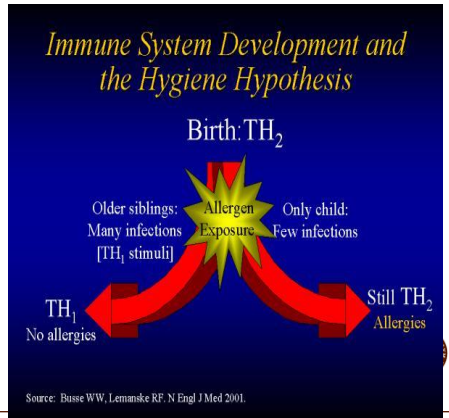




### The Hygiene Hypothesis

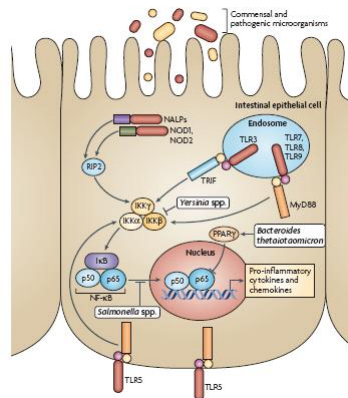
The Hygiene Hypothesis suggests that improved hygiene in industrialized societies, with improved public health measures and the use of vaccines and antibiotics, has reduced the incidence of infections that would normally stimulate the immune system in some way that mitigates against asthma and other allergies (and autoimmune diseases)

- Family size
- Early placement in day care settings
- Exposure to infectious agents
- Farm animal exposure
- Exposure to raw milk
- Exposure to pets



## How is immune homeostasis maintained in the gut?

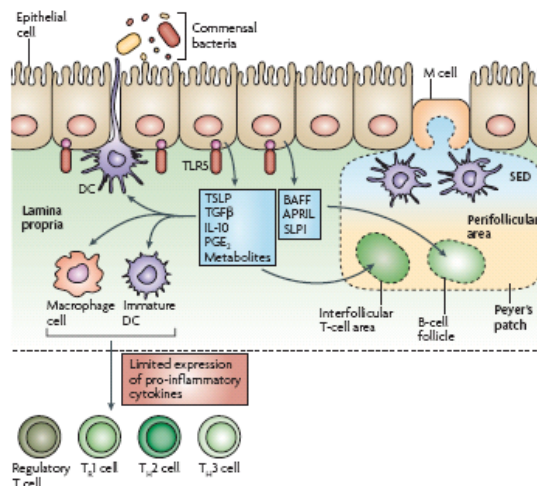
Commensal bacteria regulate intestinal epithelial-cell gene expression



Artis, Nature rev. 2008

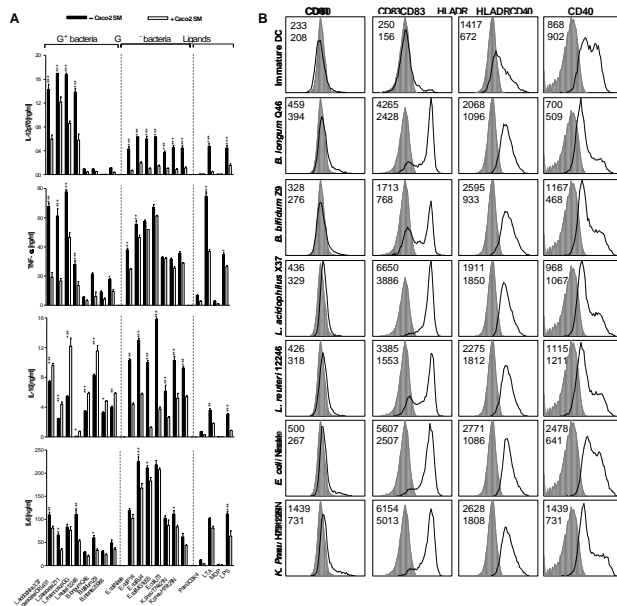
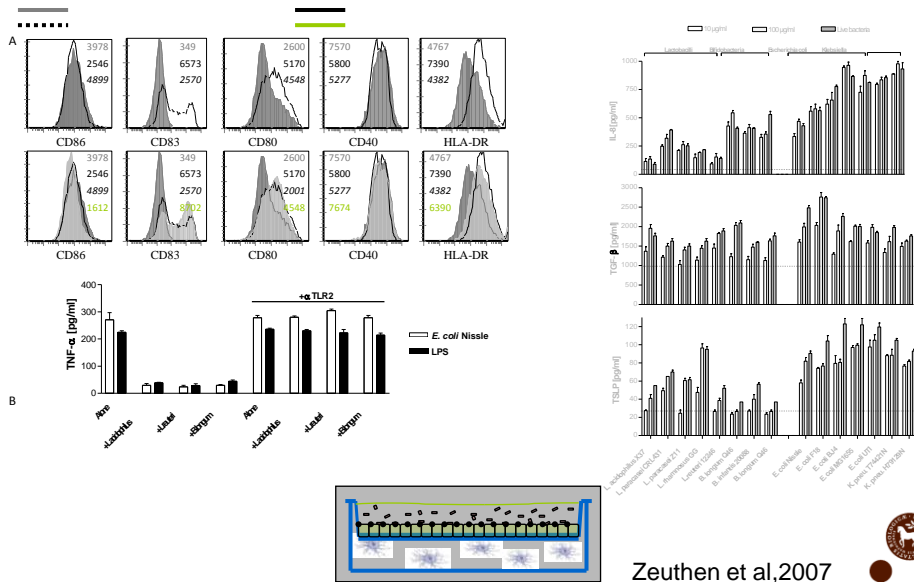


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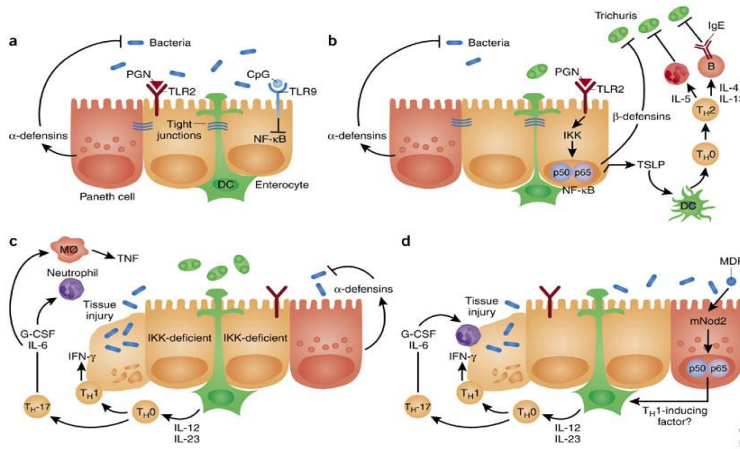


Artis, Nature Rev. 2008





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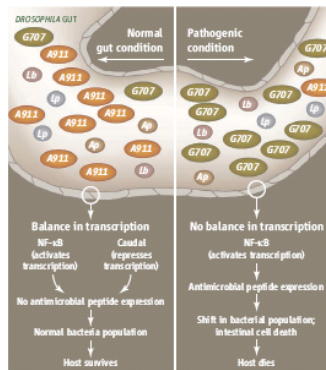


Ben-Neriah & Schmidt-Supprian, 2007



## Why is it so difficult to change disease state by e.g. Probiotic bacteria?

*Drosophila* express genes in the gut that maintains the specific microbiota



Nature rev. 2008



## Encounter with 'old friends' a prerequisite for a proper maturation of the immune system?

