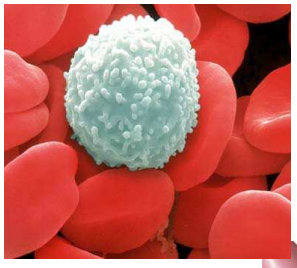
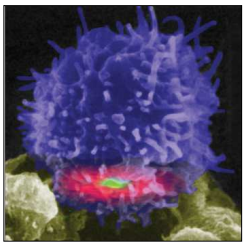
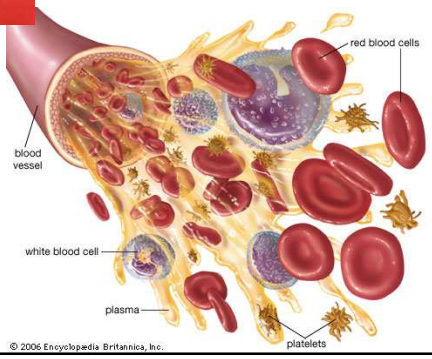
Immuuncompetentie

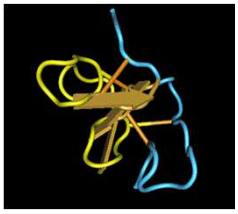


VDI-1

Huub Savelkoul







Immuuncompetentie

Definitie

- Ontwikkeling sterk gereguleerd en actief immuunsysteem op jonge leeftijd
- Effectieve reactie op infectieuze antigene stimuli en tolerantie op onschuldige (voedingsantigenen)
- goede ontwikkeling van barrièrefuncties
- Maar ook effectieve immuunrespons op antigeen dat wel door de barrières dringt

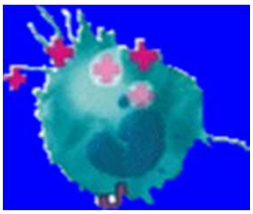
→ focus op parameters met preventieve relatie met immuuncompetentie
→ Minder nadruk op immuunstimulatie zelf

Introductie in het immuunsysteem

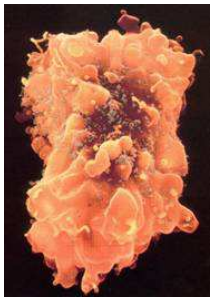
De belangrijkste functies van het immuunsysteem

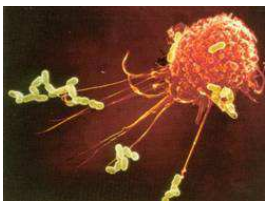
- Bescherming tegen infecties, “niet-zelf”
  - Intracellulair (virusen, somige bacterien en parasieten)
  - Extracellulair (de meeste bacterien en parasieten, fungi)
- Bescherming tegen gemodificeerd “zelf”
  - Kanker/tumor cellen of getransformeerde cellen
- Adaptatie aan omgeving, leefstijl, voeding, stress
- Normale foetale ontwikkeling

→ Moleculaire en cellulaire benadering
→ Basis voor gezondheid in praktijk

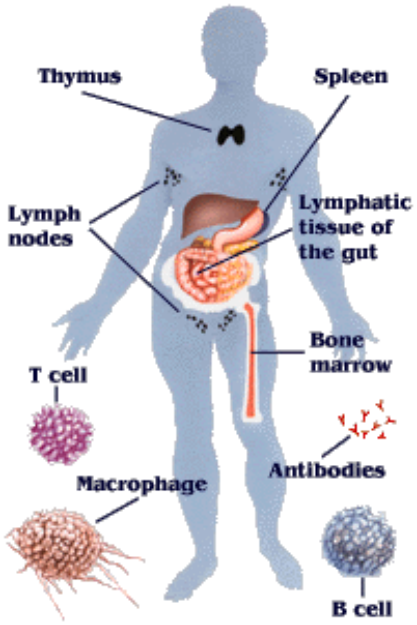


Immuunsysteem en bescherming tegen infecties

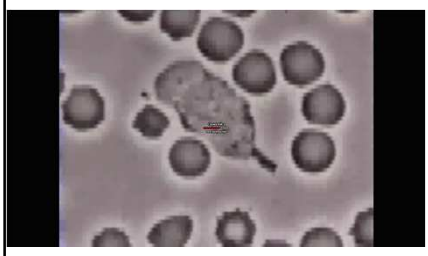


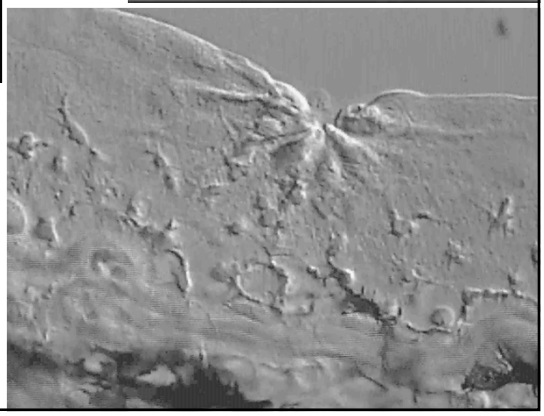


Het totale te verdedigen oppervlak bestaat uit 2 m^2 huid, 80 m^2 longweefsel en 350 m^2 darmweefsel.

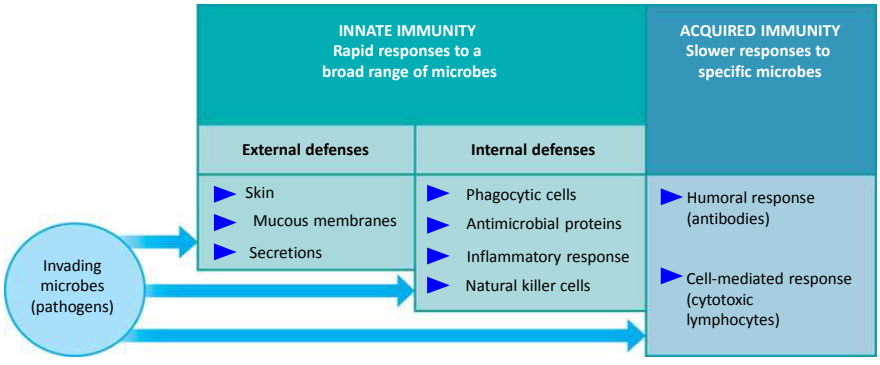


Natuurlijke weerstand



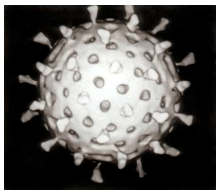
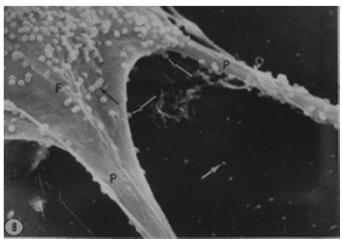


Innate en adaptieve immuniteit

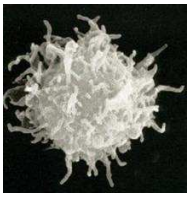
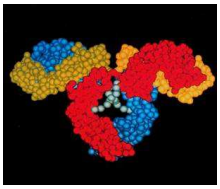
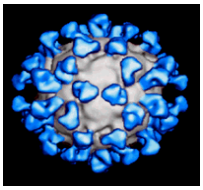
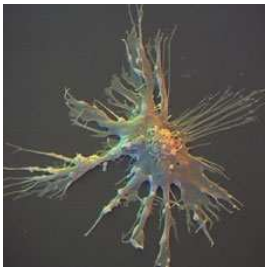


Ziekteweerstand en adaptieve immuniteit

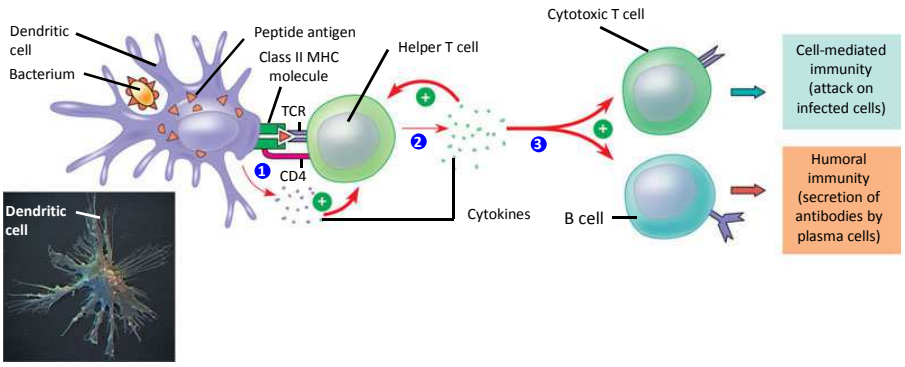
Infectie in de gastheer

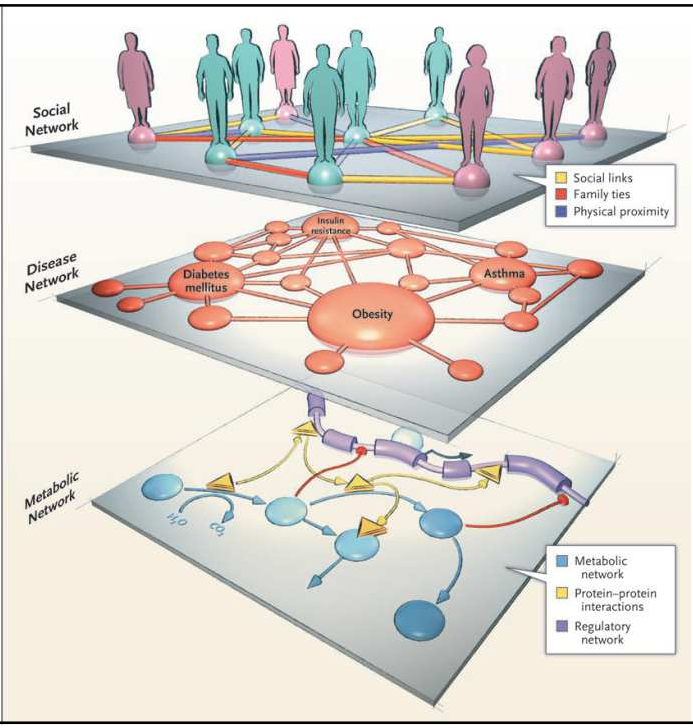
Immuunantwoord

Rol van helper T cellen in adaptieve immuniteit



Globale Genoom-wijde netwerk analyse = Systeem-biologie



Relevante discussiepunten binnen VDI-1

H1. Introductie

1) immuuncompetentie kan via voeding op positieve wijze worden versterkt
2) het mucosale immuunsysteem in de darm is bijzonder
3) de interactie tussen de darm, microbiota en voeding
4) de koppeling tussen darm- en luchtwegimmuniteit
5) wat is darmgezondheid en welke biomarkers zijn geschikt
6) wat is immuuncompetentie
7) welke nutritionele concepten beïnvloeden de immuuncompetentie

H2. Ingrediënten en functionele componenten

Prebiotica, ...

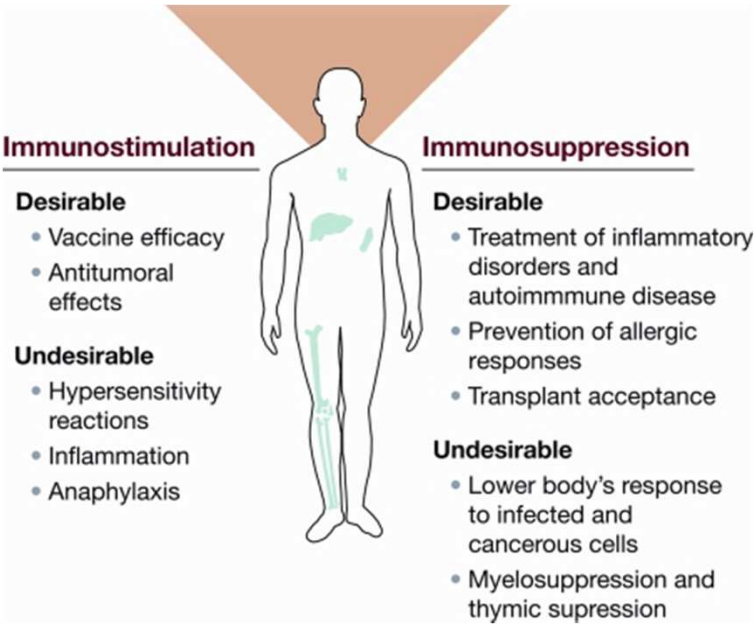
H3. Beschikbare modellen

H4. Interventie strategieën voor monogastrics

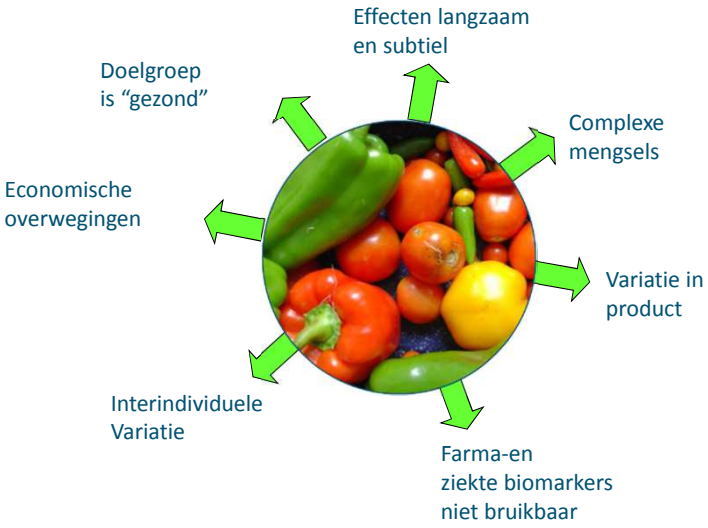
werkingsmechanismen van de nutritionele interventies

H5. Interacties tussen gastro-intestinale en luchtweg mucosale immuunsysteem

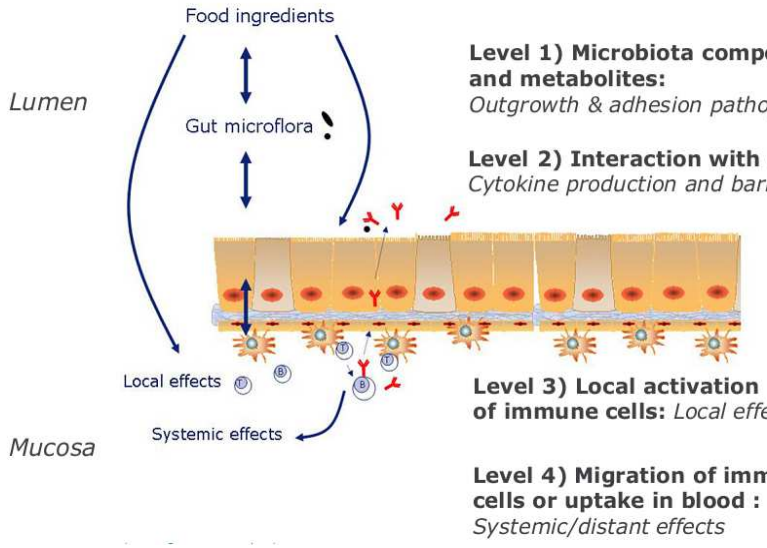
Immunomodulatie door voeding



Verandering gezondheid en gedrag via voeding?



Voeding kan immunomodulatie geven op diverse niveau's in de darm



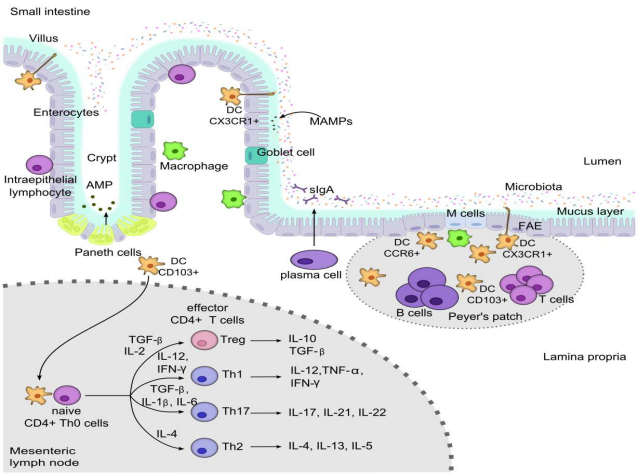
Level 1) Microbiota composition and metabolites:
Outgrowth & adhesion pathogens

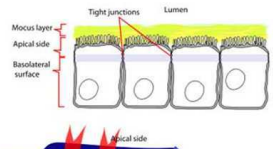
Level 2) Interaction with epithelia:
Cytokine production and barrier function

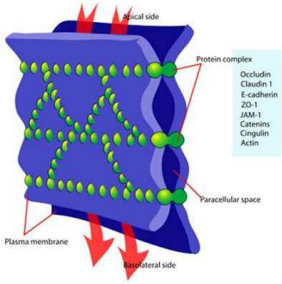
Level 3) Local activation of immune cells: *Local effects*

Level 4) Migration of immune cells or uptake in blood :
Systemic/distant effects

Voeding en immuunreactie

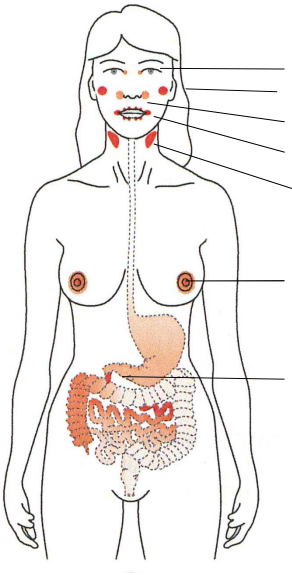






Darm: 350 m^2, 70% immuuncellen (weerstand)

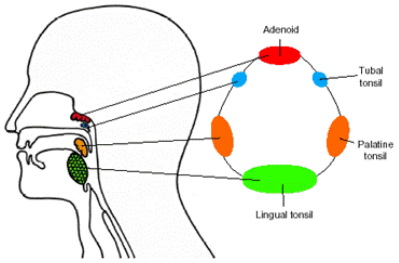
Mucosale weefsels met IgA vorming na orale immunizatie

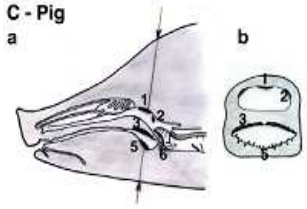


Eyes
Ears
Nose
Mouth
Throat

Breast (milk)

Upper GI tract

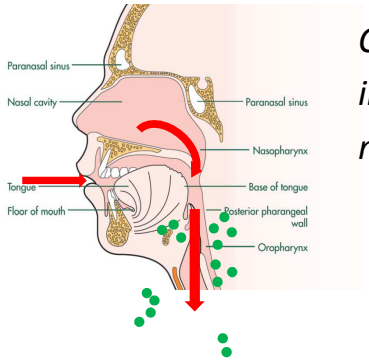




Holmgren and Czerkinsky C.
Nat Med. 2005;11:S45-53.

Elke dag slikken we luchtweg pathogenen door!

Neuspeuteren en doorslikken

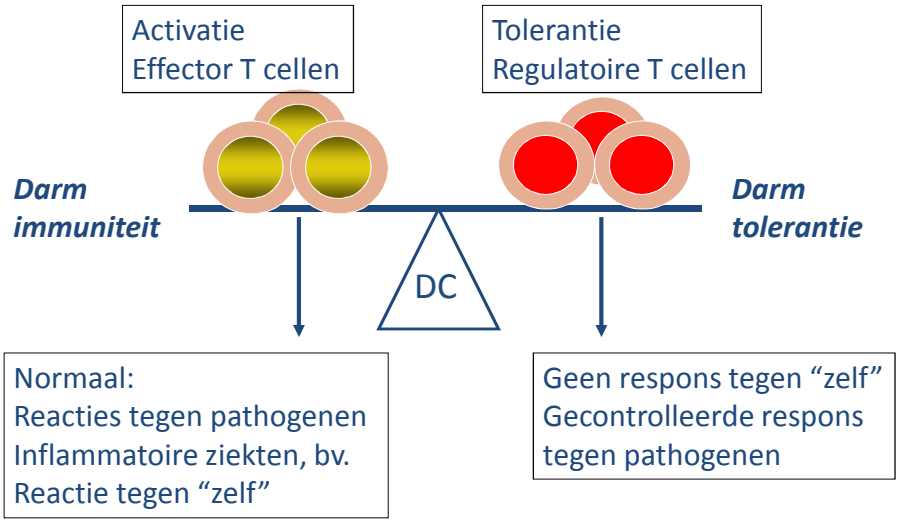


Contact met immuunweefsel in de darm

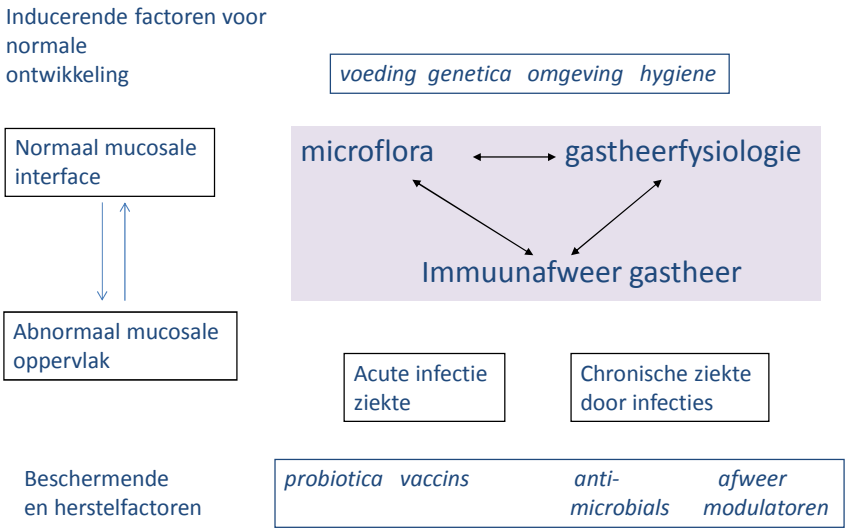
Contact met immuunweefsel in mond- en keelholte

Doorslikken nasale secreten

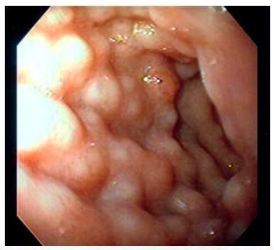
Balans in lymfocyten activatie en controle

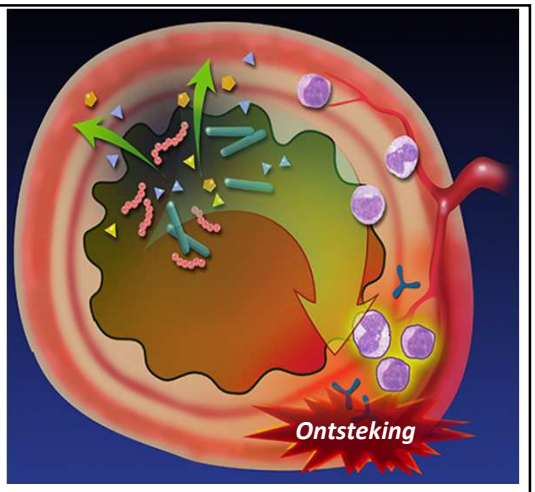


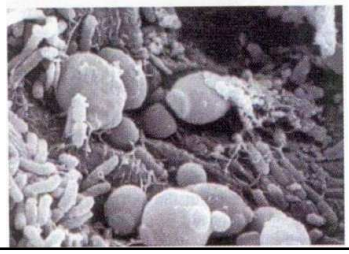
No guts, no glory!



Chronische inflammatie in de darm



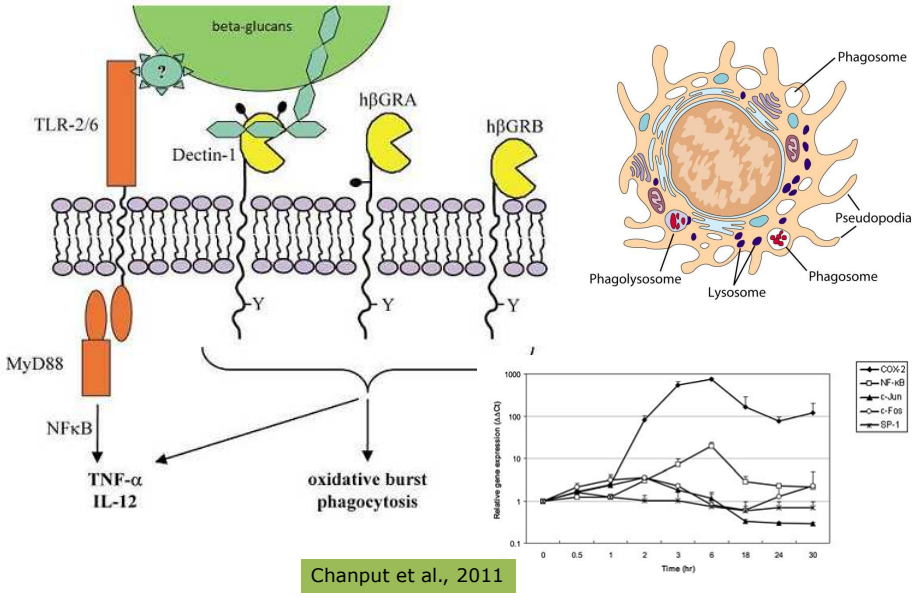




Abnormale darm

Gezonde darm

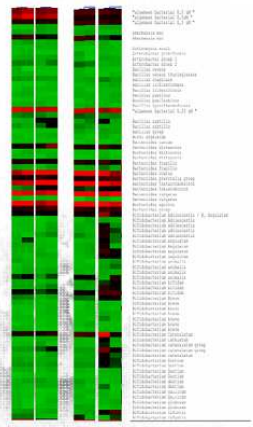
Dectine-1 en biologische effecten van β-glucanen



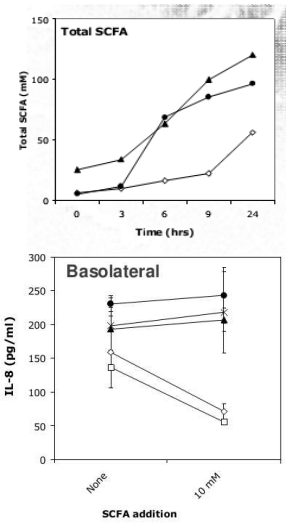
Chanput et al., 2011

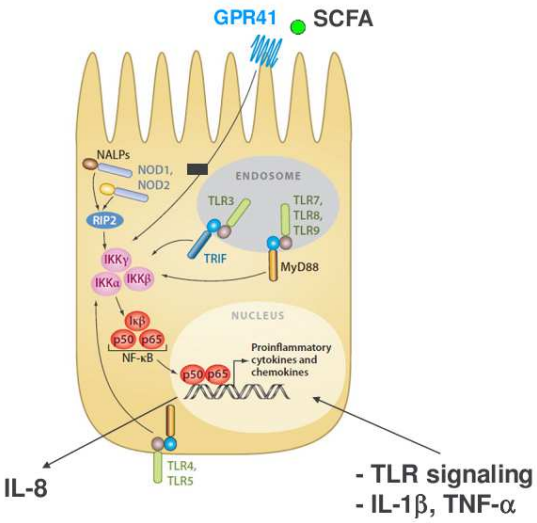
Effecten van prebiotische oligosacchariden op microbiota samenstelling en SCFA productie

	Ctrl	GOS	SL
Bacteroides fragilis	10	25	**120**
Bifidobacteriaceae	10	**100**	10
Faecalibacterium prausnitzii	2	3	**79**

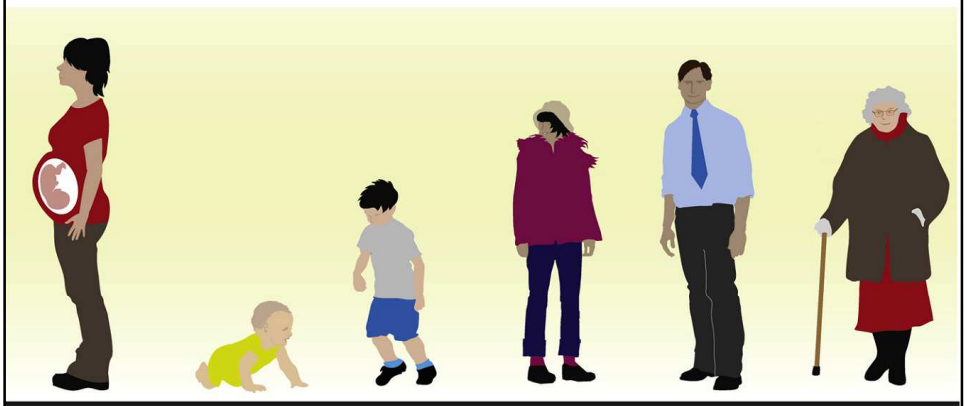


Microbiota SCFA remt NF-kB en moduleert pro-inflammatoire activiteit van epitheel





Samenstelling darm microbiota



FOETUS	BABY	CHILD	ADULTS	ELDERLY
Usually sterile	**Breast-fed-** bifidobacteria usually dominate **Bottle fed-** more diverse with more Bacteroidetes, and less bifidobacteria	Increase in microbial diversity following weaning and intake of solids	**Dominant phyla** Firmicutes Bacteroidetes Actinobacteria **Less dominant phyla** Proteobacteria Verrucomicrobia	**Compared to healthy adults-** Reduction in Firmicutes and bifidobacteria Increase in Bacteroidetes and Proteobacteria

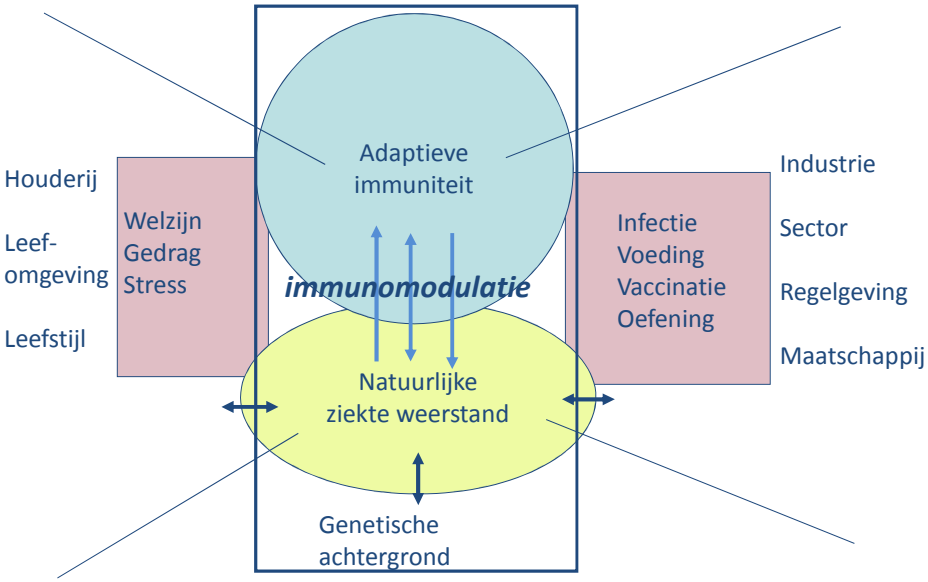
Anti-inflammatoire effecten van probiotica

Table 2 | **Bacteria shown to be protective in inflammatory bowel disease**

	Bacterial strain	Model system	Disease type or model	Mechanism of disease suppression
Probiotic strains	VSL#3*	Human and mouse	Pouchitis, ulcerative colitis and TNBS-induced colitis	Induction of IL-10- and TGFβ-expressing T cells
	Bifidobacteria lactis	Rat	TNBS-induced colitis	Decreased levels of colonic TNF and iNOS
	Bifidobacteria infantis	Mouse	*Salmonella enterica*-induced enteritis	Induction of T_{Reg} cells and inhibition of NF-κB activation
	Escherichia coli Nissle 1917	Human and mouse	Ulcerative colitis and DSS-induced colitis	Decreased colonic inflammation induced by TLR2 and TLR4 activation
	Lactobacillus rhamnosus GG	Mouse and rat	TNBS-induced colitis and HLA-B27-associated colitis	Induction of T_{Reg} cells
	Lactobacillus salivarius	Mouse	TNBS-induced colitis	Decreased colonic inflammation
	Lactobacillus reuteri	Mouse	IL-10-deficient mice	Upregulation of NGF and decreased levels of IL-8 and TNF in cell lines
	Lactobacillus plantarum 299v	Mouse	IL-10-deficient mice	Decreased levels of IFNγ and IL-12p40
	Lactobacillus fermentum	Rat	TNBS-induced colitis	Decreased levels of colonic TNF and iNOS
	Lactobacillus casei	Rat	TNBS-induced colitis	Decreased levels of colonic cyclooxygenase 2
Emerging	*Bacteriodes thetaiotaomicron*	Rat	*S. enterica*-induced enteritis	Decreased levels of IL-8 and TNF in colorectal adenocarcinoma cell line
	Bacteriodes fragilis	Mouse	T cell transfer and TNBS-induced colitis	Production of $CD4^+$ T cell-derived IL-10
	YO-MIX Y109 FRO 1000[#]	Mouse	TNBS-induced colitis	ND
	Faecalibacterium prausnitzii	Mouse	TNBS-induced colitis	Decreased levels of NF-κB, IL-8 and TNF and increased IL-10 production

Round et al
Nat Rev Immunol 2009

Immunomodulatie en natuurlijke ziekte resistentie



Voedingsinterventie en immuuncompetentie

Fundamentele en mechanistische kennisopbouw

Brede analyse

- Genoom brede kandidaatgen analyse
- Transcriptoom en proteoom analyse
- Netwerk analyse
- Epigenetische voedingseffecten

Functionele analyse

- Functionele analyse *in vitro* op cellijnen
- *Ex vivo* analyse van individuele effecten

Implementatie

- Voedings interventie cohorten *in vivo*
- *In vivo* challenge modellen en weerstand