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# Early nutrition and immunity- progress and perspectives

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# Immunological tolerance

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- Lifelong processes
- Polarization of Th cells: Th2<sup>\*</sup>, Treg ↑↑
- \* Recognition of ultra-low antigen dosis (IgE, IgA)
- Sterile GIT
- Exposure to bacteria at term and after (mother's skin, breast milk → maturation of infant's gut)



# Nutrition + immunologic development

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## Nutrition

- ...might affect ID during pregnancy, suckling period, introduction of formula and solide foods  
→
- ...source of antigens IS must become tolerant
- ...provides factors, which modulate immune maturation + responses + influences intestinal flora → antigen exposure, immune maturation, immune response

# German Infant Nutritional Intervention Study



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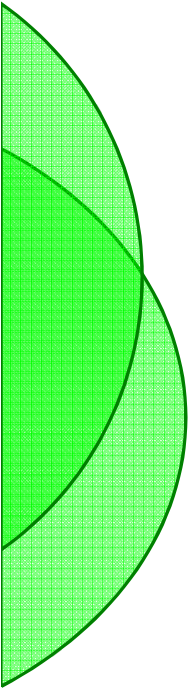
- Effects of hydrolysed and standard cow's milk formula
- → human milk feeding: ↓ allergic diseases at 1y
- → Hydrolysed formula: ↓ atopic dermatitis
- Extensively hydrolysed formula: ▣ allergy preventive effect
- Partially hydrolysed formula: + allergy preventive effect
- Keeping pets (dogs!) → atopic diseases ↓
- Caesarean section: different gut flora, antibiotics → diarrhoea, allergic sensitization ↑

# Dendritic cells + Lactobacilli

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Function of DC:

- ✓ drive differentiation of naive Th cells into Th1, Th2 or Treg cells
- **Treg cells**: prevention of autoimmunity, allergy
- **L. reuteri + L. casei** prime human DC and drive development of Treg cells by targeting **DC-SIGN**



# IMMUNOFLORA study



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- „...how early intestinal colonization affects the development of putative Treg cells and clinical allergy in Swedish infants“
- Western infants have a delayed acquisition of several gut microbes and a reduced turnover of strains in intestinal flora → Exposure ↓, variety ↓ of environmental bacteria
- Early food allergy ↔ **poor** colonization with *S. aureus* (strong T cell stimulation)

# PUFA

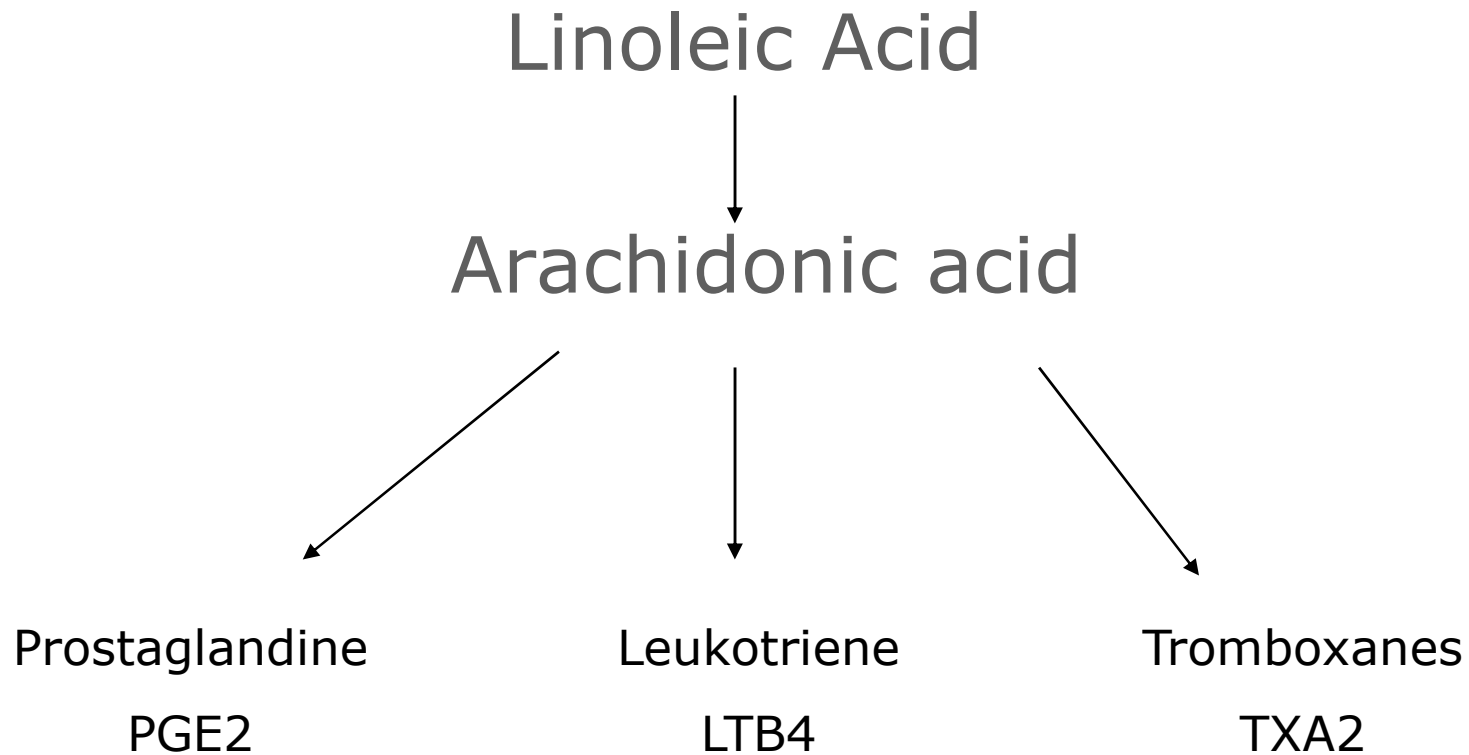
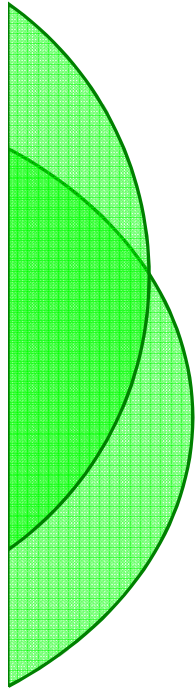
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- ↓ in the intake of saturated fatty acids
- ↑ in the intake of n-6 family of PUFA
- Linoleic acid

# N-6 family of PUFA

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# 4-series leukotrien

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= mediators of allergic inflammation:

- Vascular permeability
- Leucocyte chemotaxis
- Respiratory burst
- Production of inflammatory cytokines
- HYPOTHESIS: ↑ intake of linoleic acid ↑ prevalence of atopic disease

# n-3 family of PUFA

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- $\alpha$ -Linolenic acid

EPA                  DHA



- Increased consumption:
  - incorporation into immune cells
  - decrease the production of prostaglandin E2 and other eicosanoids
- Protective towards allergic disease
- E.g. n-3 LCPUFA status was lower in cord blood serum from pregnancy of allergic compared with non allergic mothers.



# n-3 family of PUFA

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- Positive results in patients with asthma
- n-3 LCPUFA intervention: Stronger impact on fetal and neonatal Th1/Th2 immune responses compared to immune responses beyond early infancy

# n-3 LCPUFA

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- Influence on T-cell functional responses and signalling
- First, prostaglandin E2 influence the activity of DC, differentiation of naive T-cells and activity of Th1 and Th2 cells
- Second mechanism:  
Direct alteration of gene expression through modification of transcription factor activity



# n-3 LCPUFA

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- EPA and DHA give rise to a novel family of eicosanoid-like mediators, called D- and E- resolvins
- Inhibition (in vitro):
  - T-cell proliferation,
  - Production of IL-2 and IFN- $\gamma$
  - Surface expression of CD25

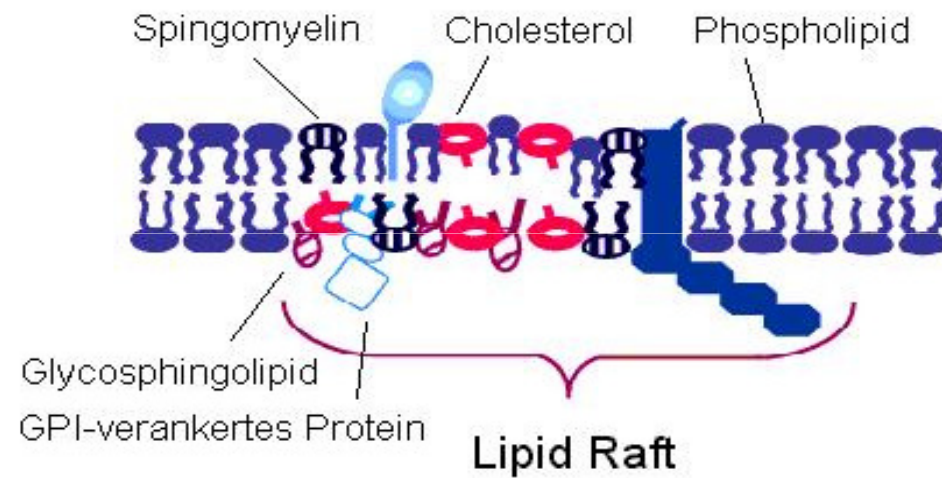
# Lipid rafts:

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- Microdomains of the plasma membrane
  - Rich in sphingolipids and cholesterol
  - Signalling processes
  - Influence by PUFA treatment
- Alter the protein composition of the inner leaflet of the plasma membrane

# Lipid rafts

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Lebensmittel, Probiotika und Nutrigenomics, Dr.  
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