Bioactive food compounds in immune regulation

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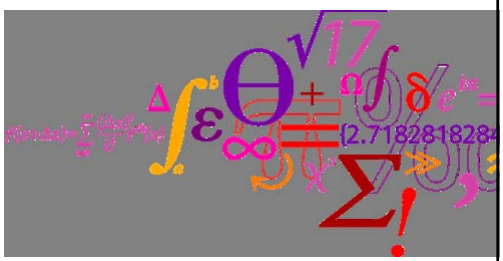


DTU Systems Biology
Department of Systems Biology

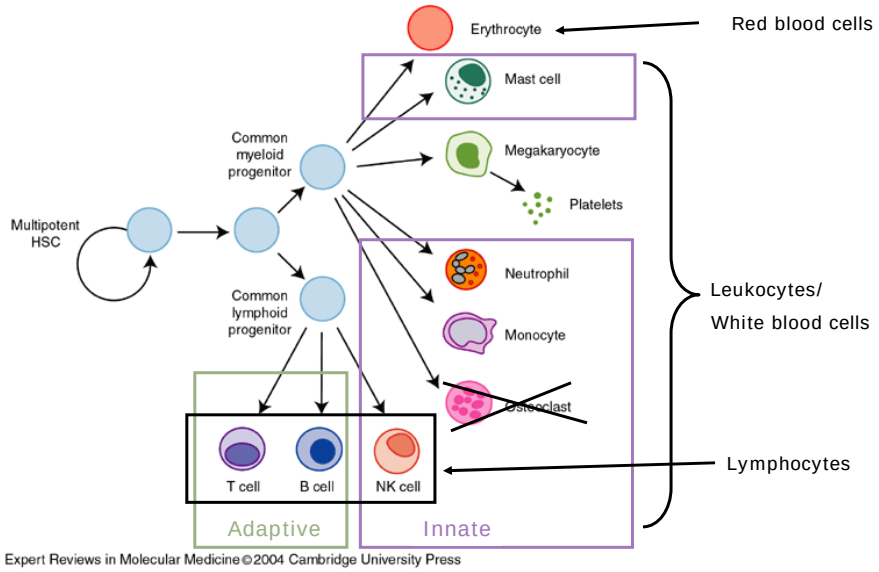
Outline

- Immune system overview
- Immune dysregulation
- Where do bioactive compounds regulate immunity?
- And how?

Example bioactive compounds:

- Flavonoids
- n-3 fatty acids
- Probiotics
- Vitamin A

Haematopoesis = creation of blood cells



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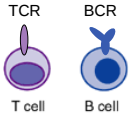
Adaptive immunity

CD4⁺ helper T cell (Th)

CD8⁺ cytotoxic T cell (Tc)



Antibodies

Innate immunity

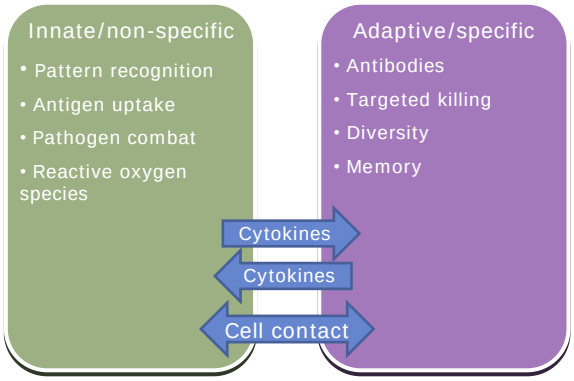

Monocyte


Macrophage

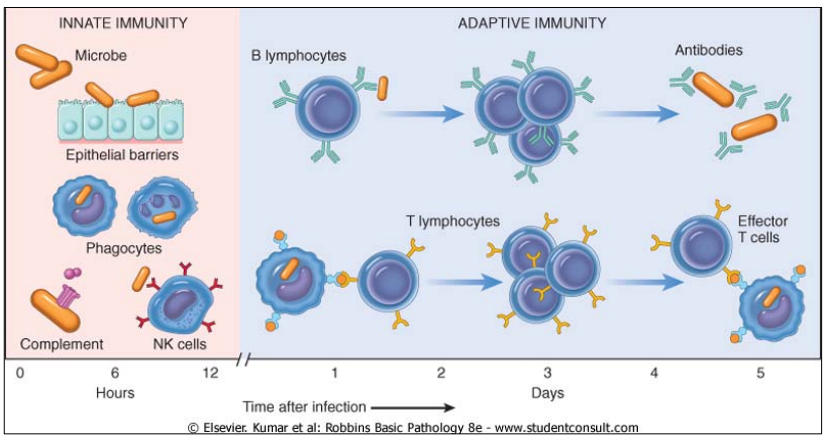

Dendritic cell

Pattern recognition receptors: TLRs, NLRs, CLRs, ???

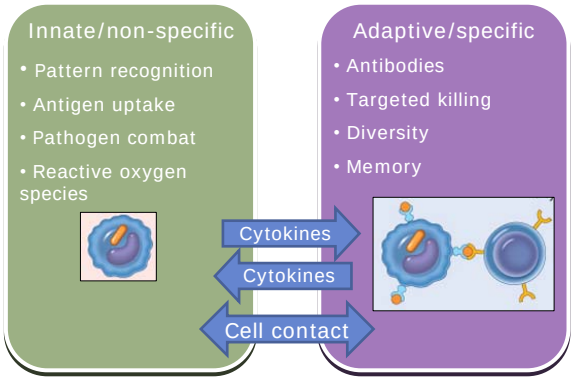
Innate and adaptive immunity



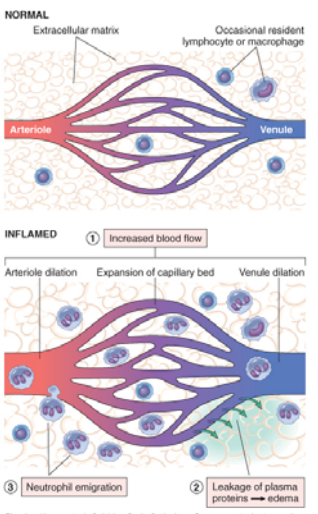
Innate and adaptive immunity

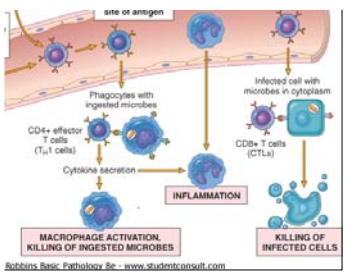


Innate and adaptive immunity

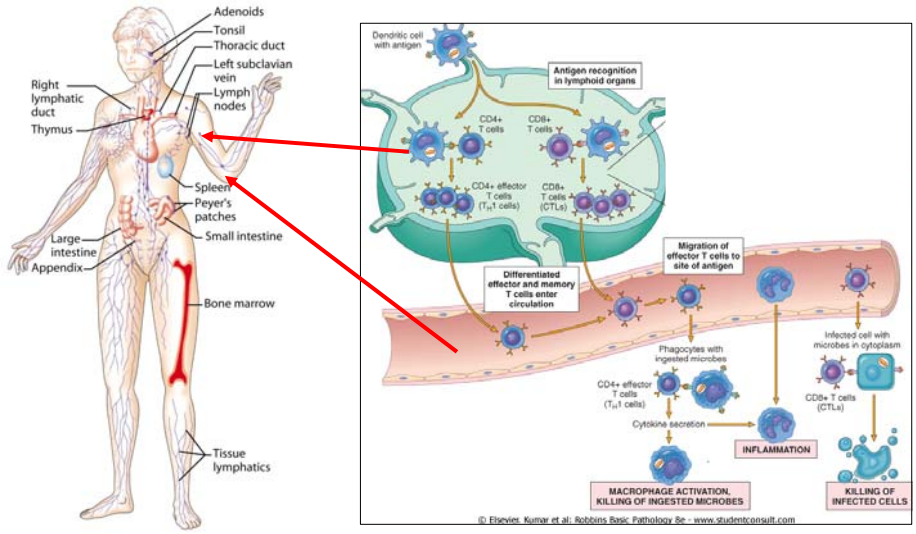


Inflammation





Meeting places (Antigen presentation)



Inflammatory mediators

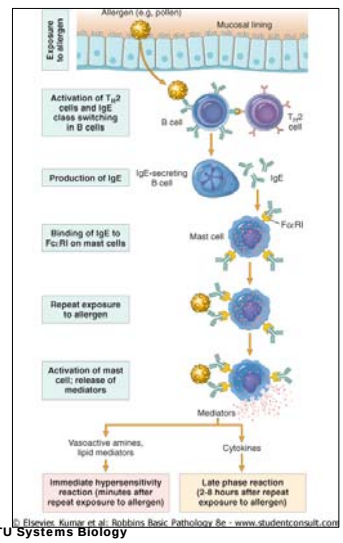
- Cytokines targeting activating receptors on immune cells and other cells
- Chemokines mediating cell migration and extravasation
- Eicosanoids (prostaglandins, leukotrienes)
- Histamine, proteases, reactive oxygen species

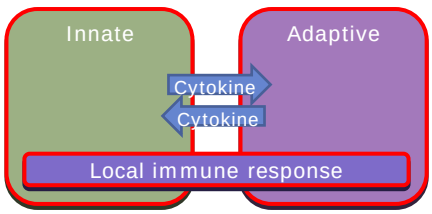
Anti-inflammation: some cytokines and eicosanoids

Immune system – important points

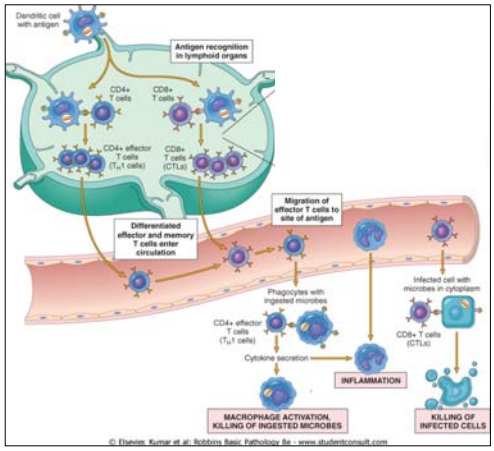
- Innate immune cells detect potential threats through pattern recognition of microbial patterns
- Adaptive immune cells recognize specific peptide epitopes
- Extensive communication between innate and adaptive cells
- Inflammation is mediated by cells and soluble factors

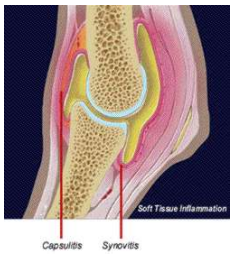
Immune dysregulation - Allergy

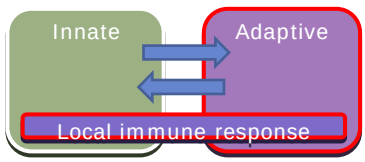




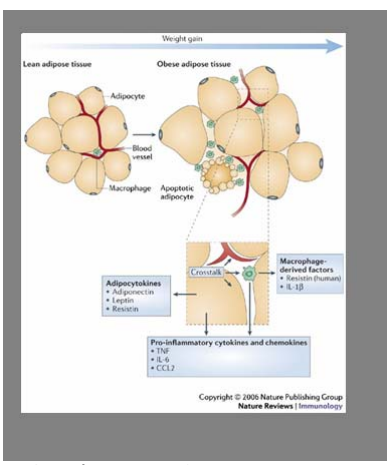
Immune dysregulation - Autoimmunity



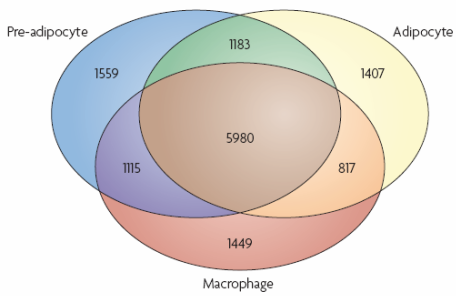




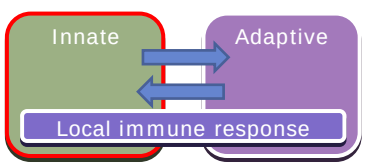
Immune dysregulation – 'Metabolic inflammation'



Causing agent?



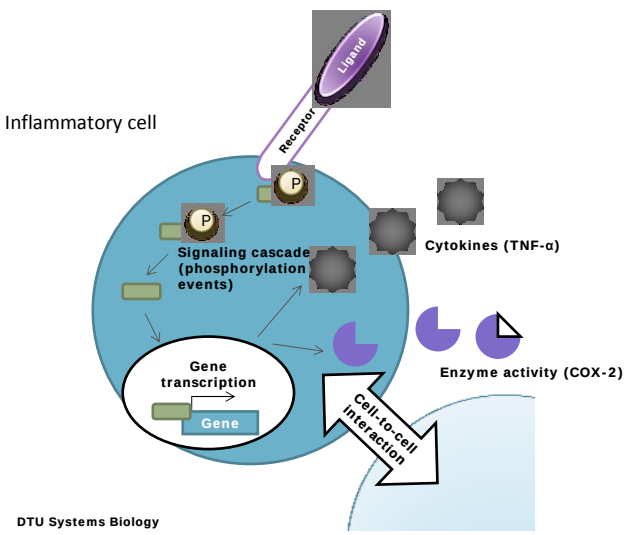
Hotamisligil and Erbay (2008)



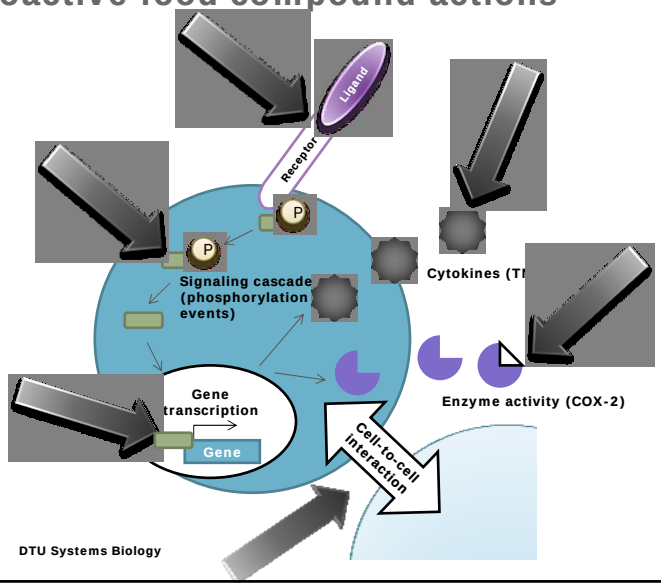
Immune dysregulation – important points

- The prevalence of these types of inflammatory diseases is increasing
- Cause: Gene–environment–food interactions
- Epigenetics, foetal imprinting?
- Targets for bioactive compounds

Bioactive food compound actions



Bioactive food compound actions



Tools for delineating mechanisms of action

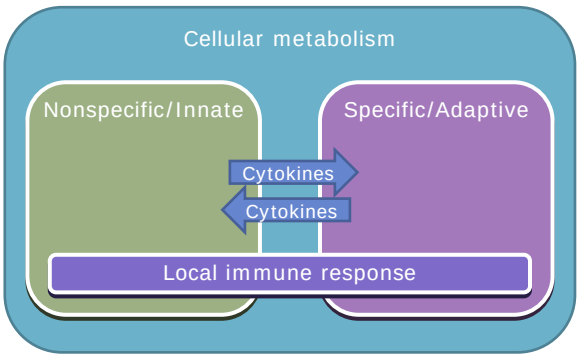
Cellular analyses

- Signalling, phosphoproteomics
- Transcription factor binding, gene transcription, miRNA
- Output: proteomics, surface protein expression, secreted proteins, metabolomics

Systems analyses

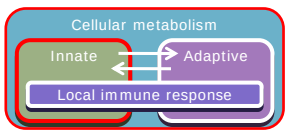
- Protein-protein interaction networks
- Protein-compound interaction networks
- Modelling of downstream events

Targets for immune regulation



Ex. 1. Flavonoids – regulation of oxidative defense

- Antioxidants of plant origin
- Regulation of cellular metabolism
- Regulation of eicosanoid synthesis (COX-1/2)
- Regulation of the production of reactive oxygen species
  - Pathogen elimination
  - Autoimmune reactions
  - Tissue damage



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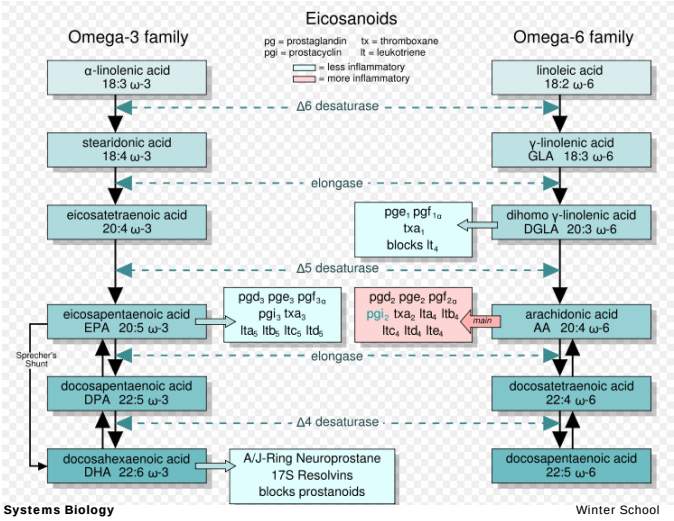
Ex. 2. n-3 fatty acids – regulating metabolic inflammation



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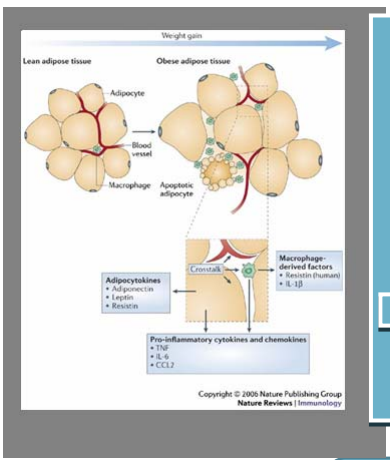
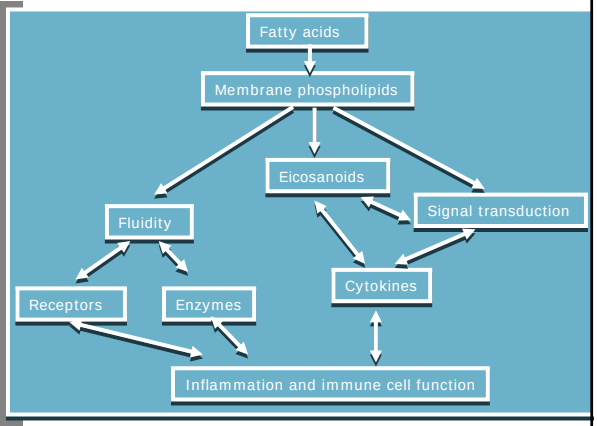
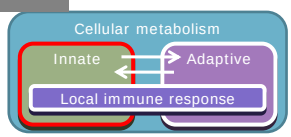
n-3 fatty acids







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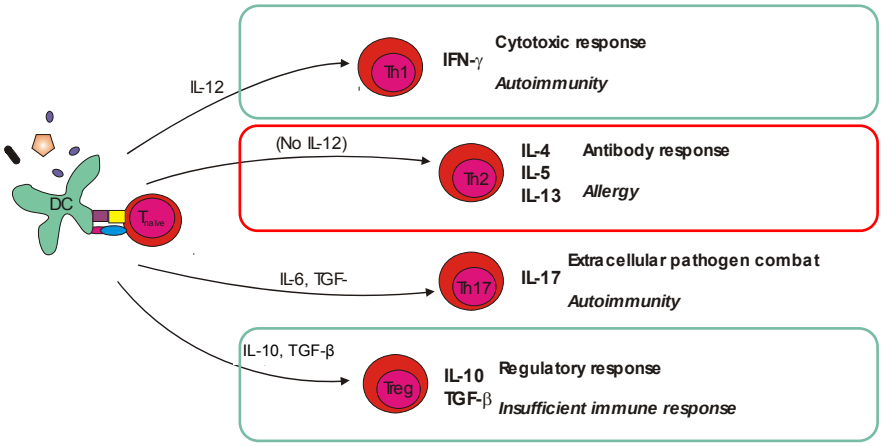
Ex. 3. Commensal bacteria (pre-/probiotics) – regulating allergic inflammation



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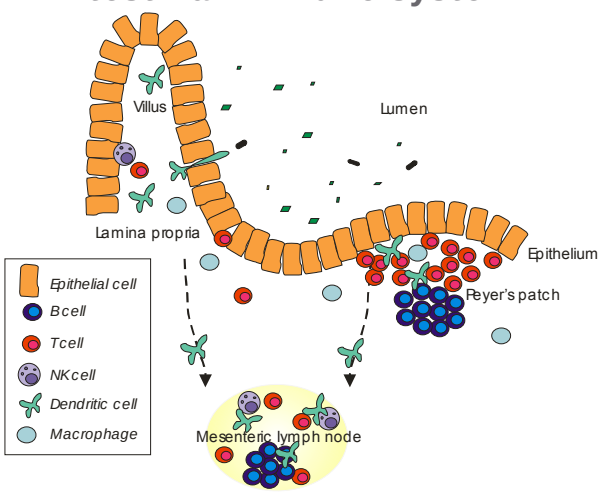
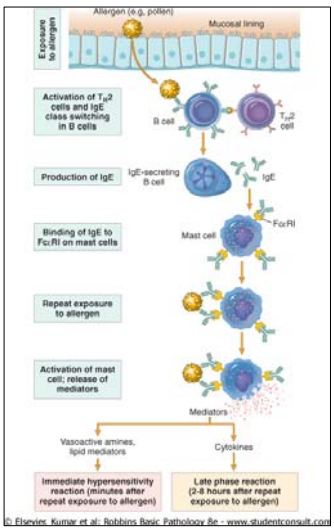
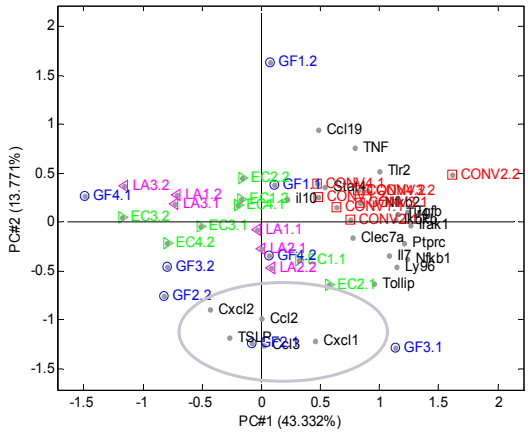
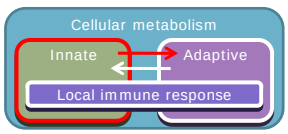
Intestinal immune system



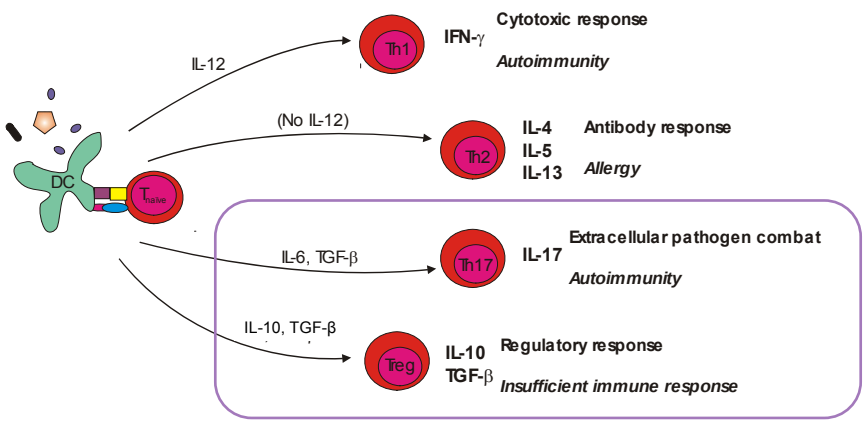


Regulatory probiotic bacteria – link to allergy

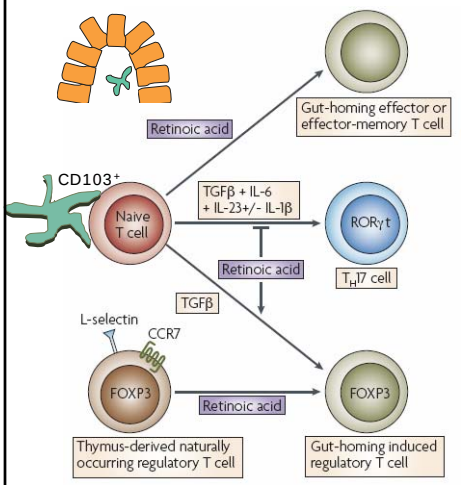


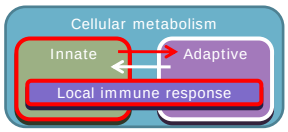


Ex. 4. Vitamin A – regulating mucosal immunity



Vitamin A in the intestine

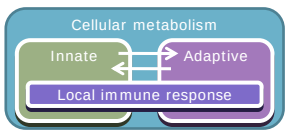




Mora, Iwata and von Andrian (2008)

Summary

- The primary task for the immune system is to eliminate pathogens while maintaining tolerance to *self* and harmless substances
- The immune system is dysregulated in allergy, autoimmunity and metabolic inflammation
- Bioactive compounds can - like drugs - regulate the immune response at different levels of immune specificity



Further readings

- Mora, Iwata and von Andrian (2008) **Vitamin effects on the immune system: vitamins A and D take centre stage**, Nature Reviews Immunology
- Hotamisligil and Erbay (2008) **Nutrient sensing and inflammation in metabolic diseases**, Nature Reviews Immunology
- Kalliomäki, Salminen, Poussa and Isolauri (2007) Probiotics during the first 7 years of life: **A cumulative risk reduction of eczema in a randomized, placebo-controlled trial**, Journal of Allergy and Clinical Nutrition

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