
Immunity, Inflammation and Allergy In The Gut

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The gut (1)

- Nutrients get absorbed
 - Potential to compromise host defense
 - infection diseases are largely under control
 - But: gastrointestinal food allergies have increased
- Probably because of the absence of gut infections has upset the balance between the commensal in the gut
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The gut (2)

- High active immunsystem
 - Barrier is a single layer of epithelium
 - No completely prevent of antigens entering the tissue
 - Several mechanism how antigens get trough the epithelium
- Immunsystem gets constantly activated
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Components of the Immunsystem in the gut

- Pattern recognition receptors – recognize conserved structures
 - Severals receptors like TLR, NOD,..
 - Recognition of TLR ligands increases gut barrier function
 - Hsp25 and hsp70
 - CD4+ T cells
 - Macrophages
 - Dendritic cells
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Activation

- B and T Cells activated
 - Expression of $\alpha 4\beta 7$ integrin

 - TLR or NOD activate NF κ B
 - Leads to pro-inflammatory gene expression

 - Chemokine fine-tune the localisation of the tissue
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Crohn's disease (1)

- Complex genetic disease
 - Mucosal ulceration, ulcers penetrate into the gut wall
 - Antigen is not yet identified

 - Isolated CD 4+ T_{H1} cells produce large amount of interferon γ
 - Overexpression of transcriptionfactor T-bet
 - Macrophages produce large amount of T_{H1} inducit cytokines
 - T-cells show resistence to apoptotic signals and have an increased cell cycle
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Crohn's disease (2)

- Genes located on the chromosomes 1, 5, 6, 12, 14, 16 and 19
 - Different polymorphism in the Nod2 gene
 - Mutations in the Nod 2 can lead to a decreased ability to kill gut bacteria
 - OCTN and DGL5 gen
 - Important for epithelial permeability
 - Disruption leads to inappropriate exposure of the mucosal immunsystem to bacterial products
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Celiac disease (1)

- In some genetically susceptible individuals after ingestion of cereal products
 - Treated by adherence to a gluten free diet
 - morphological changes to the mucosa of the upper bowel – long crypts and atrophy of villi
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Celiac disease (2)

- 4 components involved
 - Gluten is prolin and glutamine rich, has negatively charged residues
 - tTG deaminates glutamin to glutamic acid and produces negatively charged residues
 - Necessary for efficient binding to HLA-DQ2 and furthermore activation of gluten specific t-cells
 - Peptides of gliadin activate gut macrophages to produce IL-15 -> increases MICA and arms IEL to kill MICA and epithelial cells
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Control of inflammation in the gut

- T-cells involved in tolerance against commensals
 - Commensals which crossed the barrier will be phagocytosed without cytokinproduction
 - The T-cells die by apoptosis
 - The epithelial permeability is genetically determined
 - Importend factor in the developement of diseases
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