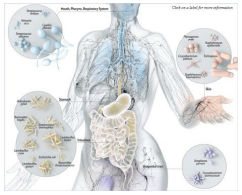
ANBI 141 Evolution of the Human Diet

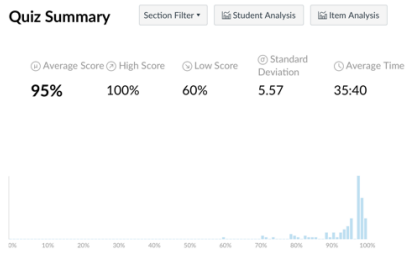
Lecture 11: The immunological Paradox of Food



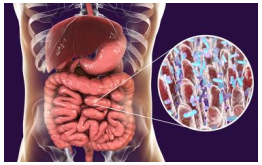
Pascal Gagneux Nov 2, 2021

Sweet potatoes from PB

Midterm Stats: Well Done!



The Human Gut is a giant surface: 300 square meters

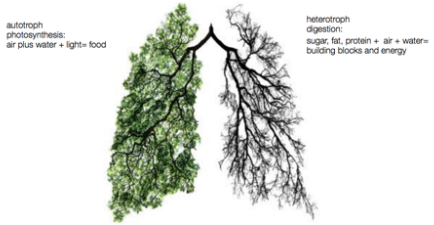


The complex structure of the gut lining with its folds and villi creates a HUGE surface for the exchange of molecules and uptake of nutrients.

Practice question: How can an organ like the human gut that is only a ~20 feet long have a surface the size of a tennis court?

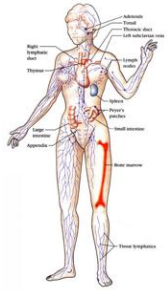
Answer:The fold and villi massively increase the surface area.

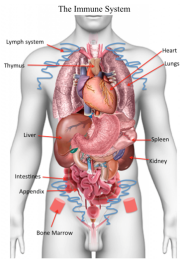
Plants: outer surface; Animals: inner surface



Animals have enormous inner surfaces: **gut** for nutrient uptake, **lungs** for gas exchange, **kidneys** for filtration, **brain** for cortical area.

Food is non-self! eating as defense





Animals have to eat, and food is non-self, how is that possible given the animals' powerful immune systems? The gastrointestinal tract is very well controlled by immune cells. Macrophages and neutrophils can "eat" foreign particles and microbes that may escape into the self. Digestion by acidity, enzymes and microbiome bacteria reduces most foreign molecules to small units: monosaccharides, fatty acids and amino acids.

Too warlike?

- Membrane Attack Complex
- Natural Killer Cells
- Bactericidal compounds
- Killing Receptors
- Suicide Bombers

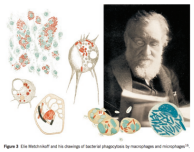
Immune responses actually represent formidably aggressive processes, so aggressive that they also form a danger to ourselves: “horror autotoxicus”

Practice question: What is horror autotoxicus?

The horror of having one’s own powerful immune system unleashed against oneself.

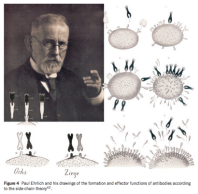
Discovery of immune responses

Elie Metchnikoff 1864-1916
Zoologist to pathologist



cells that eat……
from feeding to defense

Paul Ehrlich 1877-1915
physician with the eyes of a chemist

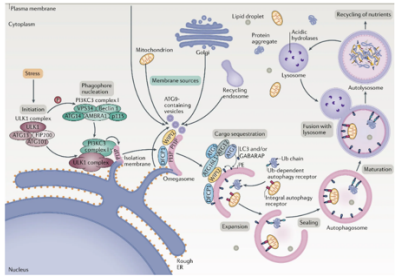


blood/serum based immunity
antibodies and colonial selection for best fitting probes

Cells fighting intruders by eating them (phagocytosis)
or by secreting “molecular probes” or beacons of destructions called antibodies.

Autophagy: protective “eating” inside the cell

cellular “booger eating”

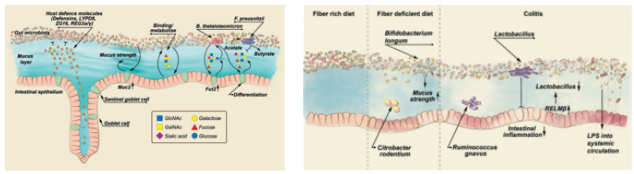


Signals that activate the autophagic process (initiation) typically originate from various conditions of stress, such as starvation, hypoxia, oxidative stress, protein aggregation, endoplasmic reticulum (ER) stress and others. Autophagy is a powerful way for cells to destroy old mitochondria, dysfunctional structures and/or intracellular parasites. Once this units have been “eaten” by an autophagosome, they are digested and recycled within the cell.

Practice question: What is autophagy?

The process by which cells can “eat” structures within the cell by sequestering these inside an autophagosome and digesting them.

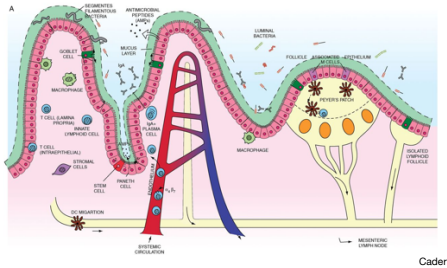
Barriers: Mucus



Schroeder, B.O. 2019 ***Gastroenterology Report***

Mucus is a highly hydrated gel consisting mostly of highly glycosylated mucin glycoproteins but also salts and anti-microbial proteins. Pathogens adapt to eat their way through the host mucin barrier. The structure of the mucus layer is affected by the gut microbiota. Gut bacteria are separated from the host epithelium by the intestinal mucus layer, which is fortified with host defense molecules, such as defensins and others.
Defects of the intestinal mucus layer exacerbate intestinal infection and inflammation. Diets lacking microbiota-accessible carbohydrates, as contained in dietary fiber, direct gut microbial species to degrade host glycans of the intestinal mucus layer (depicted by lighter mucus color), thereby deteriorating mucus strength. A defective mucus layer increases the risk for intestinal infections, for example by the mouse pathogen *Citrobacter rodentium* and a defective mucus layer may lead to increased translocation of bacterial lipopolysaccharide, thereby contributing to metabolic diseases.

Small intestine mucosal immune system landscape.



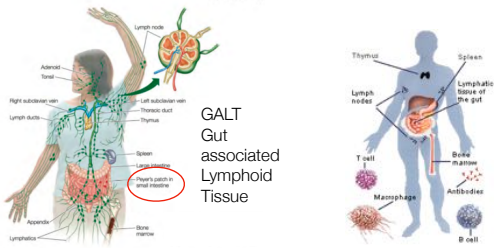
Cader MZ, et al. ***Gut*** 2013;62:1653–1664

The intestinal epithelial cell (IEC) layers form villi and crypt structures and are composed of different cell lineages. Goblet cells secrete mucus. Paneth cells, found only in the small intestine, can be found at the base of the crypts and are the main secretors of antimicrobial peptides. The base of the crypts also contains the IEC stem cell populations. Immune cells can be found in organised tissue such as Peyer's patches and throughout the lamina propria. They include macrophages, dendritic cells, intra-epithelial lymphocytes, lamina propria effector T cells, IgA secreting plasma cells, innate lymphoid cells and stromal cells such as fibroblasts. Antigen presenting cells in Peyer's patches or mesenteric lymph nodes interact with and activate local lymphocytes, which consequently upregulate expression of the integrin α4β7. Such cells then enter the systemic circulation but home towards the gut, in response to chemokine ligands such as CCL25. (B) Colon (large intestine) mucosal immune system. The colon has a much higher bacterial load and a markedly different immune cell composition. The colon contains only crypts, no villi. Also there are no Paneth cells, which mean that enterocytes have a much more important contribution to antimicrobial peptide production. However there is a high prevalence of goblet cells. The mucus forms dual layers, with a thick largely sterile inner layer and a thinner outer layer. There are no Peyer's patches. While the immune cell types present are similar to those found in the small intestine it is likely that there may be at least subtle differences. In particular natural killer T cells are found more frequently and have a more significant role in the colon.

What is the first line of defense of your gut from foreign invaders?

The Mucus layer.

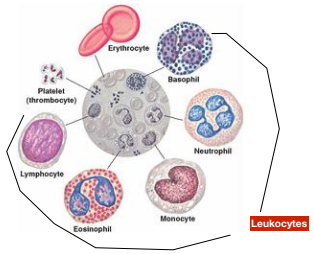
Parts of the immune system



the Immune system distributes the cells born in the bone marrow throughout the body:a distributed, information processing system.

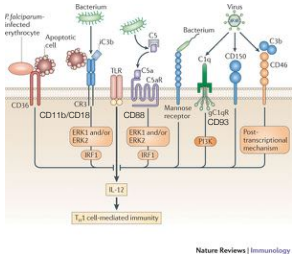
Then immune system has about as many cells as your brain:
It is a second information processing system
Unlike the brain, it is very distributed and does not have one central organ.
Practice question: What kind of information does the immune system process?
Molecular information about self and non-self, consisting of composition and shape of molecules and the patterns these form.

Types of blood cells from bone marrow



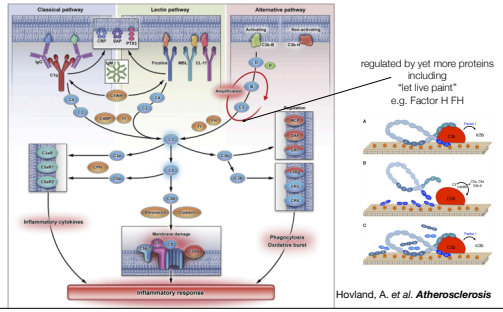
All blood cells constantly form from stem cells in the bone marrow: red and white blood cells and platelets. Lymphocytes are B, T, and NK cells, the other white cells are often called “granulocytes” because their cell nuclei look “grainy”.

Innate Receptors of Non-self



Germ-line encoded receptors for non-self molecules.
These are called innate because they do not need to “learn” about novel molecular patterns but rather have evolved over generations to target tell-tale foreign molecular patterns.
Practice question: How can the cells lining the gut detect microbes that can form a threat of infection?
By expressing innate receptors that specifically detect bacteria molecules.

More Innate Receptor, soluble “death paint”



Complement System: “paint to tag for destruction”
Classical Complement System “paint” if you see antibodies stick to a surface.
Lectin Complement System: “paint” if you detect non-human sugars.
Alternative Complement System: “paint” everything unless surface was previously painted by “paint for letting live” Complement Factor H.
Factor H binds to “self associated molecular patterns” determined by terminal silica acid sugars on healthy self cells.

Complement pathway: permanent surveillance

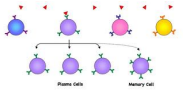
Complement
Marked for destruction

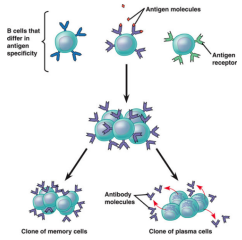
Factor H (CFH) via SIA binding
Marked for protection

Fluid phase surveillance:complement marks for destruction, factor H marks for protection.
Practice question: Do soluble innate immune proteins in the blood tag for destruction or tag for protection?
Both.

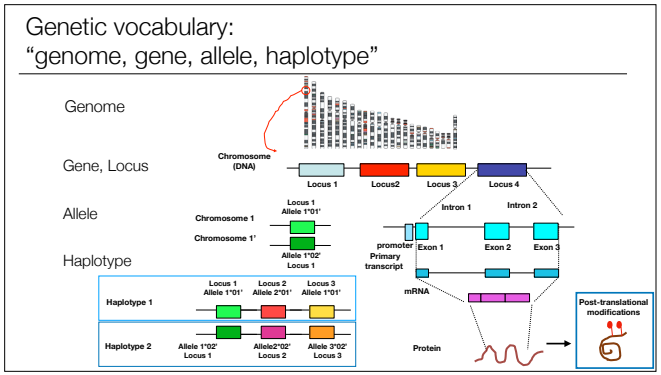
Clonal selection

white blood cells
allowed to behave like microbes….





only B-cells and T cells with fitting receptors are allowed to behave like a cancer” = clonal expansion
B-cells make antibodies (immunoglobulins)
T-cells make T-cell receptors (very similar to immunoglobulins, but attached to T-cells)
Practice question: What happens to B-cell that make antibodies specific for self molecules?
They are forced to undergo suicide.



Some key terms used in genetics: genome, gene, locus (“site” in Latin), allele, haplotype, promoter, exon, intron, mRNA, post-translational modification

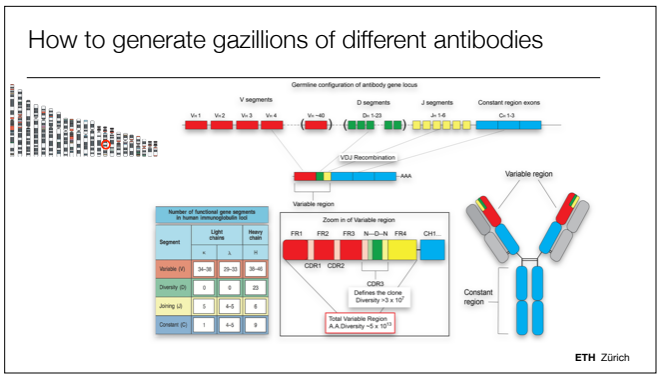
Haplotypes are long stretches of DNA that carry unique combinations of genetic variants (alleles).

Post-translational modifications of proteins include the addition of sugar (glycosylation), or phosphate (phosphorylation) etc…

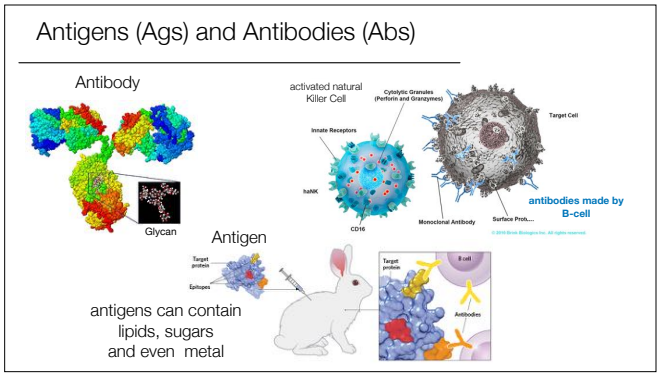
The same protein can give many different variants after it has been modified by post-translational addition of such molecules.

Practice question: how can the same gene give rise to different proteins?

Alternative splicing, or different post-translational modifications, or somatic recombination.



SOMATIC RECOMBINATION: Every time an antigen, whether natural (pathogen) or recombinant (vaccine), encounters the immune system it leaves behind a molecular imprint that encodes valuable information. This antigenic fingerprint is encoded within the immune response, more specifically in the genetic and molecular identities – the antibody and T cell receptor repertoires. For example, primary antibody diversity in B cells is generated by the recombination of non-contiguous germline gene segments, variable (V), diversity (D), and joining (J) gene segments; this process of V(D)J recombination occurs during B lymphocyte development in bone marrow. Additional antibody diversification is provided by combinatorial pairing and somatic hypermutation of the variable heavy (VH) and variable light (VL) chains. All of these diversity elements combine to generate an antibody repertoire that is estimated to be >10 to the power of 13= 10 000 000 000 000 different antibodies in humans.



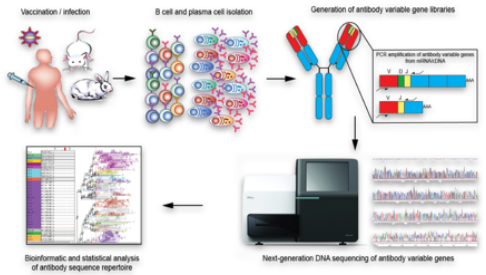
Immunoglobulin antibodies are super-precise molecular probes.

They can be generated in animals by inoculating these with a particular antigen (a foreign molecule usually presented together with a danger signal, called “adjuvant”) for later use in clinics or labs.

Practice question: What is the difference between an antigen and an antibody?

Antigens are molecules that can be recognized by the immune system, antibodies are molecular probes that recognize antigens.

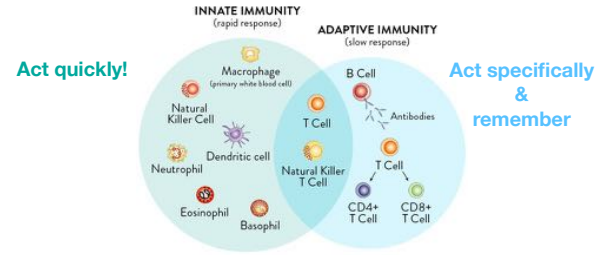
Discovery of Antibody Repertoire



ETH Zürich

Antibody repertoires can now be studied B-cell by B-cell. The strength and specificity of binding of each individual antibody variant can be determined and the DNA sequence for promising antibodies can be used to mass-produce antibodies as drugs.

Innate and Adaptive Immunity cooperate



Successful immune responses utilize both, innate (rapid) and adaptive (slower but more precise) recognition. Immunity works with cells and countless soluble proteins.

Practice question: Mention a key difference between innate and adaptive immunity.

Innate immunity acts rapidly, adaptive immunity can learn to detect new patterns and form memories.

Know Thyself!

A Tsuku-bai (蹲踞) water fountain in Ryoanji Temple, Kyoto, Japan

Self-knowledge is not just part of philosophical traditions, but it is quintessential for biological immunity.

the self knowledge targets “molecular flavor” of self cells, tissues and secretions.

Central immune tolerance is cut out for self,
but, “self” also needs to be directly perceived

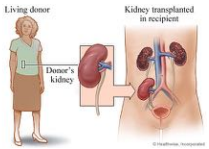
highlighting non-self

SAMPs: self-associated molecular patterns

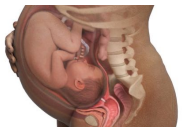
Central immune tolerance comes about by “education”/selection of B and T cells with just the right amount of reactivity against “self” and “non-self”. Further immune education happens in the gut, where resident T cells modulate reactions against food antigens.

Soba noodles from scratch

Parallels between transplantation and pregnancy?



circulating antibodies
targeting donor molecules



circulating antibodies
targeting paternal molecules

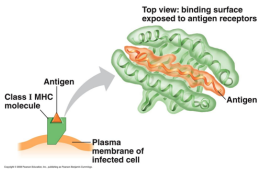
Mothers were found have circulating antibodies against molecules on the surface of white blood cells of their children’s father(s): These proteins that seemed to “insult the immune system of the mother were named: “HLA - human leukocyte antigens”. Organ transplant recipient have antibodies to the transplant (MHC). MHC turned out to be the human HLA! All mammals have their own MHC system. The HLA region on chromosome 6 is the MOST variable part of our genome!

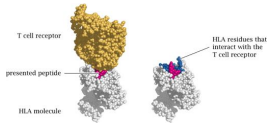
Practice question? What is the difference between HLA and MHC?

They are the same, HLA is also the other name for human MHC.

Declare Yourself! HLA/MHC

Human Leukocyte Antigen/Major Histocompatibility Complex





Most cells, constantly sample their insides and present what they sample to the outside

The sampling "probes" are called MHC or HLA
The probe and its cargo form an important signal to immune cells

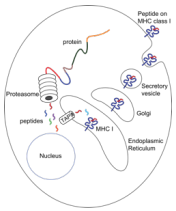
The HLA (human) /MHC (other mammals) system is a self declaration and non-self detection system in one!

Practice question: How can the immune system detect the presence of a virus that has already infected a cell?

The HLA molecules of the cell will present cellular content on the outside of the cell allowing the immune system to detect viral debris, intra-cellular parasites or cancer.

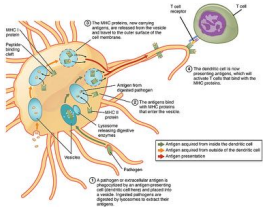
Declare Yourself! HLA/MHC

MHC CLASS 1 most cells



"keeps cells extroverted"

MHC CLASS 2 antigen presenting cell



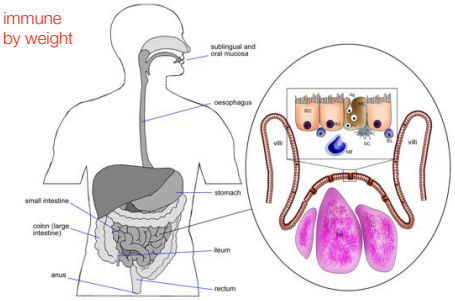
"samples extra-cellular space"

Most cells sample their own content (MHC Class I).

In addition, there are surveillance cells such as dendritic cells and macrophages that can sample molecules outside the cells (MHC Class II).

GALT: Gut Associated Lymphoid Tissue

70% of immune system by weight

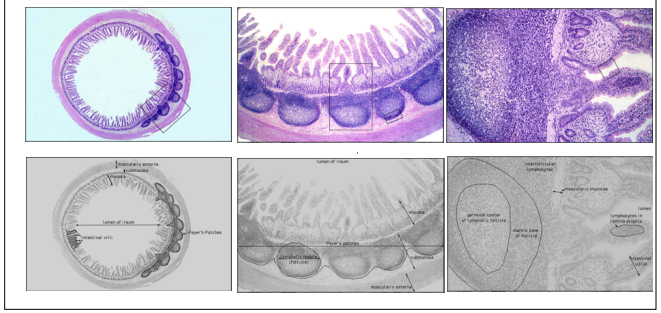


Specialized cells in the lining of the gut can take up antigens, which are then processed by immune cells.

Practice Question: What is the name of the gut immune tissue"

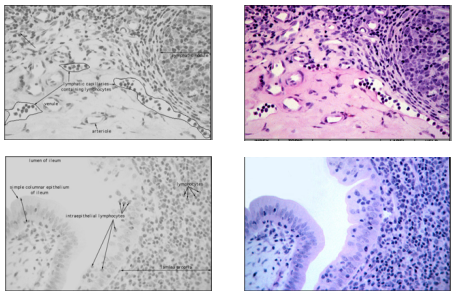
GALT.

Peyer's patches



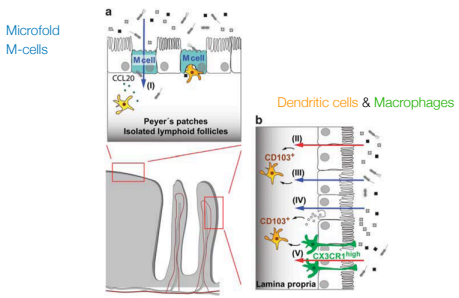
Section of an ileum (small intestine) stained with hematoxylin and eosin (H&E stain). Hematoxylin stains the DNA and RNA in the nuclei, Eosin stains the proteins in and around the cells.
A good thickness for such sections is around 5 microns which is a thousand times thinner than a pencil and about the thickness of the average cell.
Practice question: What are the lymphoid organs around the gut called?
Peyer's patches.

Peyer's patches zoomed in



Lymphocytes (B,T, and NK cells) traffic from the lumen of the gut to the lymph nodes and to the rest of the body via lymphatic an blood vessels.

Sampling soluble gut antigens: Microfold (M) cells



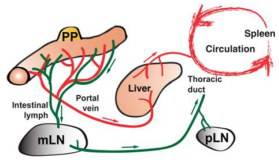
Mechanisms of antigen uptake in gut-associated lymphoid tissue (GALT) and lamina propria.
(a) In organized tissues of the GALT such as Peyer ' s patches and isolated lymphoid follicles, specialized microfold cells (M cells) in the epithelium overlying the lymphoid follicles mediate transcellular transport of particulate material including intestinal microbiota. This antigen is then passed on to dendritic cells (DCs) that lie either below the epithelium or in a " pocket " created at the basolateral surface of the M cell. Production of CCL20 by surrounding epithelial cells can attract further DCs via their expression of CCR6. Some DCs in the GALT may also take up antigen directly from the lumen.

(b) CD103 + DCs (Dendritic cells= antigen sampling and presenting cells) in the lamina propria underlying normal villus epithelium also play a critical role in presenting antigen for the induction of tolerance. They may acquire soluble antigens that have diffused through epithelial tight junctions (II), or that have been transferred across epithelial cells by transcellular routes (III). Exosomes containing antigen derived from class II MHC + enterocytes may be taken up by DCs (IV). CX3CR1 high macrophages have also been reported to capture luminal antigens by extending processes through the epithelial layer and they may pass this on to neighboring CD103 + DCs (V). There may also be a few M cells within villus epithelium (not depicted).

The **lamina propria** is the highly vascular, loose connective tissue matrix between the muscularis mucosa and epithelium. It controls mucosal shape. In the small bowel it forms the cores of the villi and in the colon it provides the structure into which the glands are embedded

Sending them out for inspection

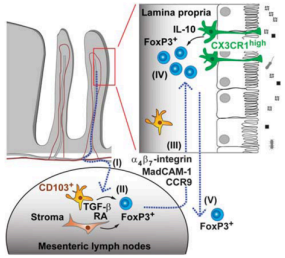
The gut associated lymphoid tissue samples gut content and "sends it out for inspection into the periphery



Routes by which intestinally derived antigen might disseminate and generate widespread systemic tolerance. Antigen taken up into Peyer ' s patches (PP) or lamina propria may enter the bloodstream via the portal vein, first reaching the liver before it becomes distributed into the wider circulation. Systemic tolerance may then occur because of antigen presentation in the liver by sinusoidal endothelial cells, tolerogenic conventional dendritic cells (DCs) or plasmacytoid DCs (pDCs), or because antigen reaching peripheral lymph nodes (pLNs) will be presented by resident DCs in the absence of costimulation. Free antigen taken up into afferent intestinal lymph will pass through the mesenteric lymph nodes (mLNs) and eventually enter the bloodstream via the thoracic duct.

Peripheral Tolerance: local immune education in the gut?

mesentery



A multistep model of oral tolerance to soluble antigens. Oral tolerance is initiated by the migration of antigen-loaded CD103 + dendritic cells (DCs) from the lamina propria (LP) into the draining mesenteric lymph nodes (mLNs; I). In the mLN, retinoic acid (RA) produced by DCs and local stromal cells induces the expression of gut-homing receptors 4 7 integrin and CCR9 on antigen-specific T cells and favors the transforming growth factor- (TGF-)-dependent differentiation of Foxp3 + induced regulatory T cells (iTregs; II). These committed Tregs home back to the intestinal lamina propria (III), where they undergo secondaryexpansion under the influence of interleukin-10 (IL-10) produced by CX3CR1 high macrophages in the lamina propria (IV). In a putative fifth step (V), some of the Tregs may exit from the mucosa via lymph and / or bloodstream, disseminating throughout the immune system, and promoting the systemic consequences of oral tolerance. Foxp3, forkhead box P3; MadCAM-1, mucosal vascular addressin cell adhesion molecule 1

Practice question: What are mesenteric lymph nodes?

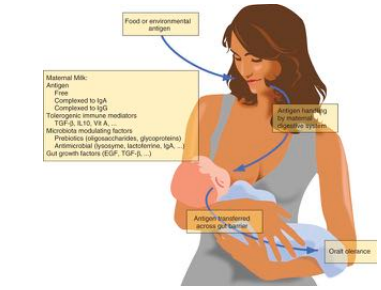
Immune organs in the mesentery, the tissue connecting the gut to the rest of the body.

Wishful Thinking?

You've got a trillion friends in low places: Bacteria in the gut may protect against viruses by signaling their presence to your immune system.
Michael DeFrayne for NPR

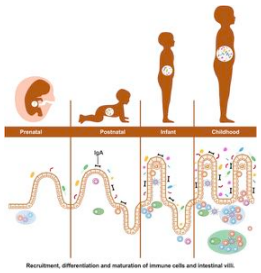
How much do our microbial partners help us? really?

Breastmilk and immunity



Before reaching the milk, ingested airborne and dietary antigens are handled by the maternal digestive system, which could contribute to the generation of tolerogenic peptides. Depending on the maternal antigen exposure and mammary gland permeability, various amounts of antigen will be found in breast milk. Maternal sensitization to the ingested allergens will dictate whether the transferred antigens will be found in the milk free or complexed to antigen-specific IgA and IgG. The presence of IgA will trap antigens and prevent their transfer to the child, whereas antigen bound to IgG will be very efficiently transferred across the gut barrier using the FcRn. Prebiotics, such as oligosaccharides, that are present in breast milk will lead to the development of a microbiota promoting immune tolerance induction.

Gut and Microbiome maturation

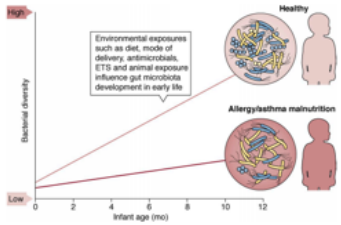


Recruitment, differentiation and maturation of immune cells and intestinal villi.

Jimenez & Torres 2017 ***Archives of Medical Research***

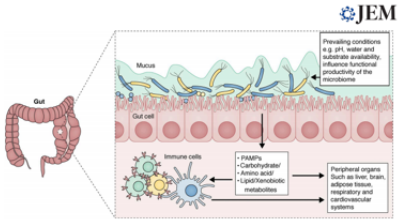
Development of microbiota in infants. The initial seeding of microbiota may occur in utero, initiating signaling of bacteria to mucosa at the fetus stage. Exposure to mother and environment microbiota is exponential after delivery and the continuous dialogue with epithelia orchestrate maturation of all, microbiota itself, immune system and specialized epithelia.

Infant gut microbiome diversification and allergy/asthma



The infant gut bacterial micro biome rapidly diversifies over the first year of life in healthy infants but is delayed in those who develop allergy or asthma or who are malnourished. A number of pre-, peri-, and postnatal environmental exposures are known to modulate risk for childhood disease, e.g., formula feeding, antimicrobial use, and exposure to environmental tobacco smoke (ETS) or animals. These same exposures also relate to gut microbiome composition at discrete developmental time points and to successional trajectories in early life.

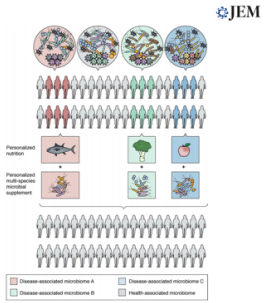
Gut-Microbiome Symbiosis



gut immunity is greatly complicated by the presence of the gut microbiome

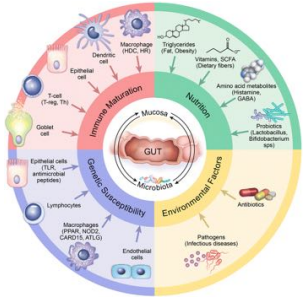
In healthy adults, the gut microbiome exists in a state of mutual symbiosis with its host. The environment of the gut dictates both the composition and functional productivity of the adult gut microbiota, which may interact with the host through presentation of various ligands such as pathogen-associated molecular patterns (PAMPs) and production of metabolites, e.g., short chain fatty acids (SCFAs). These molecules modulate immune homeostasis in the GI tract and at remote mucosal surfaces and organs via their entry into the circulation.

Microbiome manipulation via diet and microbes?



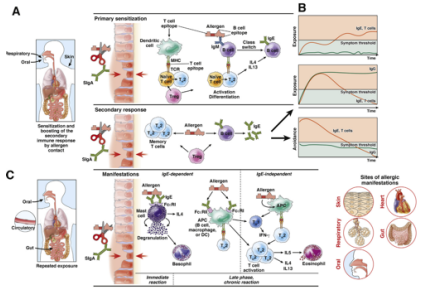
A strategic framework for a personalized integrated approach to microbiome manipulation. Due to microbial heterogeneity across populations, personalized nutrition in combination with the administration of live, functionally defined microbial strains to reengineer microbiome composition, functional gene capacity, and metabolic output may prove most effective in rehabilitating perturbed gut microbiomes for effective disease prevention or management.

Many factors influence gut immunity



Practice question: Give two examples of external influence on gut immunity.
Breast feeding, nutrition, history of infection, antibiotics treatments.

Food Allergies: Time course, pathogenesis, and manifestations of food allergies



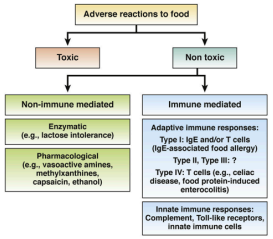
IgE-associated food allergies appear to develop early in childhood. This process is termed allergic sensitization.

(A) Allergen contact via the gastrointestinal tract, via the respiratory tract, and eventually via the skin induces IgE production (primary sensitization) in genetically predisposed individuals. Repeated allergen contact activates allergen-specific T cells and induces IgE responses during the secondary immune response. Factors that affect the epithelial barrier (red arrows) and the extent to which allergens are digested or degraded are important for primary sensitization and boosting of secondary immune responses. SIgA and T-regulatory cells may be important for exclusion of allergens from the intestinal lumen and induction of tolerance, respectively.

(B) The balance between allergen-specific IgE and blocking IgG helps determine whether or not a patient will develop symptoms. Allergen avoidance could reduce levels of allergen-specific IgE to below the threshold for symptom induction (lower panel), whereas exposure could increase production of IgE, leading to symptoms (upper panel). If allergen exposure induces allergen-specific IgG, which blocks the interaction between the allergen and IgE, then symptoms might be reduced (middle panel).

(C) Allergy symptoms are caused by repeated contact with the oral allergen, via the immediate allergic reaction (allergen-induced crosslinking of mast cell–bound IgE by allergen and then activation of allergen-specific T cells), and then by other inflammatory cells, such as eosinophils and basophils, during late-phase and chronic inflammation. Factors that affect the epithelial barrier and the extent of allergen degradation affect the amount of allergen intrusion and the magnitude and type of inflammation. After allergen ingestion, inflammation develops not only in the intestine, but in other organs, such as the skin, respiratory tract, and circulatory system (right). These allergens and allergen fragments are internalized and distributed throughout the body (left). MHC, major histocompatibility complex; T-reg, T-regulatory cell; TCR, T-cell receptor.

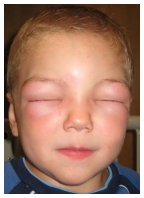
Food intolerance and Allergies

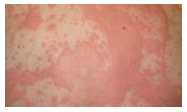


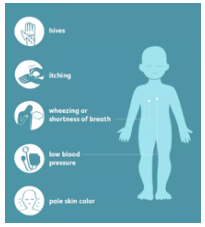
Adverse reactions to food can be classified as toxic or nontoxic reactions. Nontoxic reactions are categorized further as immune-mediated or non–immune-mediated. The most common adverse reactions are based on non–immune mediated mechanisms such as enzyme defects as observed in lactose intolerance. Hypersensitivities involving the adaptive immune system can be subdivided into 4 categories (types I–IV). Type I reactions are always associated with the formation of IgE against food allergens and therefore can be called IgE-associated food allergies. There is firm evidence for an involvement of IgG in type II or type III reactions in immune-mediated adverse reactions to food, whereas type IV reactions, which involve T cells, have important roles in disorders such as celiac disease. There is evidence that the innate immune system, which includes complement, Toll-like receptors, and innate immune cells, also mediates immune reactions against certain food components.

Food Allergies

Anaphylaxis







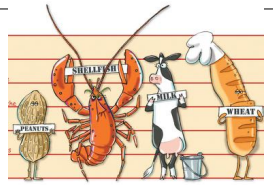
Anaphylaxis is a potentially life threatening all-out immune response.

Practice question: What is Anaphylaxis?

A potentially ice threatening, all-out immune response.

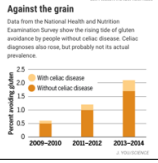
Food Allergies

8 percent of kids in the U.S. – or 6 million children – have at least one food allergy.



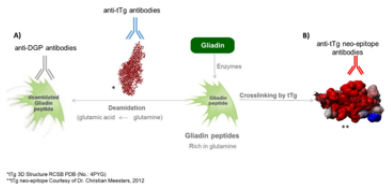
8 percent of kids in the U.S. – or 6 million children – have at least one food allergy. That means 1 in 13 children—two kids in every classroom—must avoid certain foods. And those allergies can be fatal. In fact, 40 percent of children with food allergies have suffered a life-threatening reaction.

Gluten, and bread baking

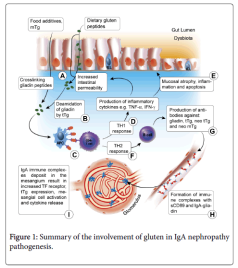


Practice question. Do most people in the USA who avoid gluten have antibodies against gluten?
No, only a minority does.

Gluten, Gliadin and tissue Transglutaminase



Lerner *et al.* 2016, ***J. Immun. Methods***



Lerner *et al.* 2017, ***J. Clin. Cell. Immun.***

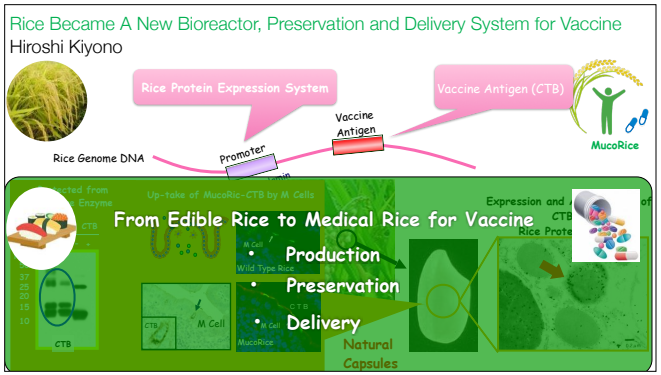
The target of celiac disease defining antibodies: gliadin and tissue transglutaminase.
Practice question: Why do patients with true celiac disease have immune reactions that attack their own guts?
Because they trigger an immune reaction against gliadin in complex with a “self” enzyme (tissue Transglutaminase).

Bamba in Israel

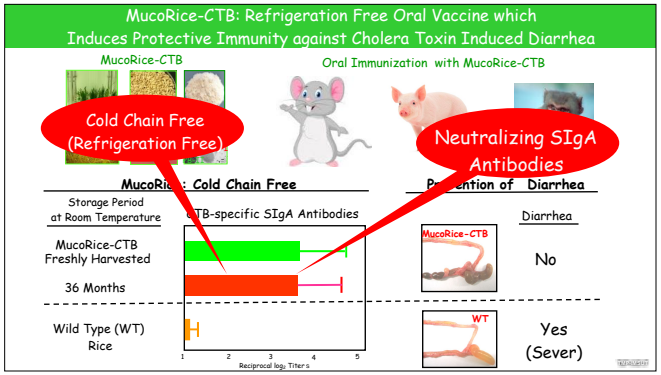
Ingredients (4)
- PEANUT BUTTER (PEANUTS)
- CORN GRITS
- HIGH-OLEIC SUNFLOWER OIL
- SALT

peanut flavored puffed maize

Israel has very low levels of peanut allergy, early exposure might actually prevent the development of allergies.



MucoRice is a rice-based oral vaccine genetically engineered to express vaccine antigens and suppress the endogenous rice storage protein, which was developed by Prof. Hiroshi Kiyono, Project Researcher Yoshikazu Yuki and their colleagues at International Research and Development Center for Mucosal Vaccines in IMSUT. MucoRice does not require the strict temperature management that is usual for the storage of biopharmaceuticals and can be stored at room temperature. The establishment of the cultivation techniques that enable efficient production should help reduce medical expenses for the vaccine.

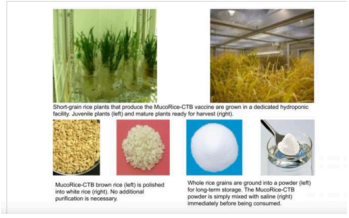


Mucorice ia an attempt to vaccinate against Cholera by creating rice that expresses a toxin of the cholera agent Vibrio cholera inside its kernels. It is an example of an edible vaccine that is in development.

There are an estimated 1·3–4·0 million cases of cholera and 20 000–140 000 cholera-related deaths worldwide each year. The rice-based cholera toxin B subunit (CTB) vaccine, MucoRice-CTB, is an oral candidate vaccine that does not require a cold chain, has shown efficacy in animal models, and could be of benefit in places where there is a paucity of medical infrastructure.

Phase 1 trial completed successfully, June 2021

Growing a new type of cholera vaccine, MucoRice-CTB (IMAGE)
UNIVERSITY OF TOKYO



Summary

The immune system is complicated and involves specialized cells made i the bone marrow as well as many secreted proteins. Cells eat and kill, secreted proteins tag for destruction and punch holes……

The immune system is very powerful and costly, it can turn on our selves! It has to learn NOT to attach self early in life.

Food is by definition non-self.

The gut has a huge amount of immune tissue termed GALT (gut associated lymphoid tissue).

Bacterial/microbiome colonization contributes to maturation of gut immunity, gut mucosa and tolerance.

The innate and adaptive immune systems work differently but cooperate.

Innate immune receptors rapidly detect foreign molecular patterns, adaptive immunity can fine tune responses and remember.

Adaptive immunity relies on "within-body-evolution" to randomly generate antibodies with millions of different types of binding pockets, and then selects the ones that best recognize non-self molecules. Self-targeted antibodies are strongly selected against and thus absent.

Food can become immunogenic depending on the genetics and experience of each individual.

Immune reaction to food are common and can sometimes be deadly.

Early life events: breastfeeding,, infection history, pets, urban vs rural life, SES, exposure to different foods can affect the risk of allergies.

Edible vaccines are currently being developed for important diseases, these could be easily delivered to vulnerable populations.

The precise reasons why some of us suffer from food allergies remain unknown, but include our genetic identity and the environmental exposures to food and other substances that shape how our immune systems.