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Chronic Lyme, superimposed Covid-19 infection

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Dr Piper describes one of her clinical cases presenting with symptoms attributable to M-SIDS, more commonly known as Lyme Disease. M-SIDS stands for Multiple System Infectious Diseases Syndrome.

The clinical picture develops gradually in the background of chronic family illness and bereavement, and the question of whether to treat with antibiotics or herbal treatments still remains, with the patient in question being treated with antibiotics initially, followed by herbs. However, she subsequently developed Hashimoto's autoimmune thyroiditis, following symptomatic remission which was short lived.

A multi-systems biology approach has been used throughout but subsequently utilising more herbal treatments, persistent support for the gut and micro biome throughout, with more attention to membrane therapy and fatty acid balances latterly and more focus on the combined causation of autoimmunity which is considered to be a combination of antigenic material through food & digestion, biotoxins, also that of metals and chemicals.

Introduction to the Neurolipid Foundation work with Patricia Kane, aligned with the Kennedy Kreiger Institute in America, is mentioned, plus the new lab in Germany IGL called which is looking at the effects of DNA adducts upon nuclear DNA and the functioning of mitochondria.

Throughout this case, Dr Piper, who has worked with Pol De Saedeleer of Nutrined in some of her most complex cases, utilises the resources and support of his compounding pharmacy in the supply of nasal sprays and, also, for example, organic cholestyramine. Dr Piper also thinks very highly of the Researched Nutritionals products which are so well researched for chronic complex illness under the expert research guidance of Pol De Saedeleer..

The superimposed subsequent infection in this patient of Covid 19, was diagnosed with a specific SARS Cov2, Covid-19 test carried out via video link support, by the patient at home, revealing a positive IgM test, allowed this patient to be managed in the home setting very dynamically with a systems biology approach which aimed to minimise viral replication, epigenetic insult, reducing inflammation and the risk and presence of cytokine storms. Also treating infection very actively and strongly.

In the context of a global pandemic, an example is given of a patient who was managed successfully at home.

In the context of immune suppression and pre-existing Th1 / Th2 dysregulation, she may not have done well in a hospital setting if she had required ventilation.

Some consideration should be given to the similarities between these two infections of M-SIDS (Lyme Disease) and Covid 19. There is interesting speculation about the recognition and funding behind the Covid-19 pandemic whilst Lyme disease has been largely ignored with respect to funding and research.

The post Covid syndrome involving multiple symptoms particularly mental health challenges, but also possible long-term effects on the lungs and symptoms of chronic inflammation, will require more understanding and it is suggested that a combined approach of functional medicine and integrative medical work should be considered for the future.

Medical History 1

- Female aged 61, husband died April 2015 following a long illness with lung cancer

- Two attendances for symptoms of UTI, Negative MSU, poor sleep. Followed by infrequent attendance until March 2017 , Presented for a routine check and blood tests, metabolic screen, no significant problems apart from positive thyroid antibodies TPX 97, (0 to 34) and thyroglobulin antibodies 514, (0 to 115). Vitamin D, full blood count, biochemistry, thyroid function, homocysteine, HbA1c all otherwise normal normal.

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Medical History 2

- 1st August 2017 abdominal bloating, weight gain, sluggish, tired. Spending plenty of time walking in Cornwall.
- Concern re possible tic bites
- No mold exposure
- Developed foggy brain, aching all over, depersonalisation, pains in her joints.

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Test results (infection)

Lyme disease (borrelia) antibodies IgM checked and positive.

Infection Results

Armin Labs Chronic infection results confirmed Borrelia Burgdorfei, positive Elispot 11SI
CD3 absolute measurement 788 per microlitre normal (range 900 to 1900)
CD57+ Natural killer cells low at 41 per microlitre range (100 to 360).
Bartonella negative, Babesia negative,, Anaplasma Elispot weak positive 2 SI, chlamydia pneumonia Elispot 10 SI, IgG positive, Mycoplasma pneumonia IgG positive, yersinia weak positive Elispot 2SI.

Low CD3 & CD57 indicated chronic immune suppression caused by either Borrelia Burgdorferi chlamydia pneumonia or Mycoplasma pneumonia (low Th1)

Low numbers of the CD3+T cells can be seen in viruses e.g. EBV, CMV, HSP, VZV, HHV-6, coxsackie

Marcons nose swab positive

Moderate amount of penicillium SPS

WBC 4.99 mmol/L (? Retrovirus)

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Test Results 2 (General metabolic, & gut permeability)

- Thyroid autoantibodies still high
- FBC, Metabolic screen, B12, folate, CRP, NAD

- Gut Permeability results:
- High zonulin 3.0 ng per ml, (<2)
- High histamine with low DAO/Histamine ratio (some MCAS issues; high Th2?))
- LPS IGM very high at 28.7 nanograms per ml. (<22.2)

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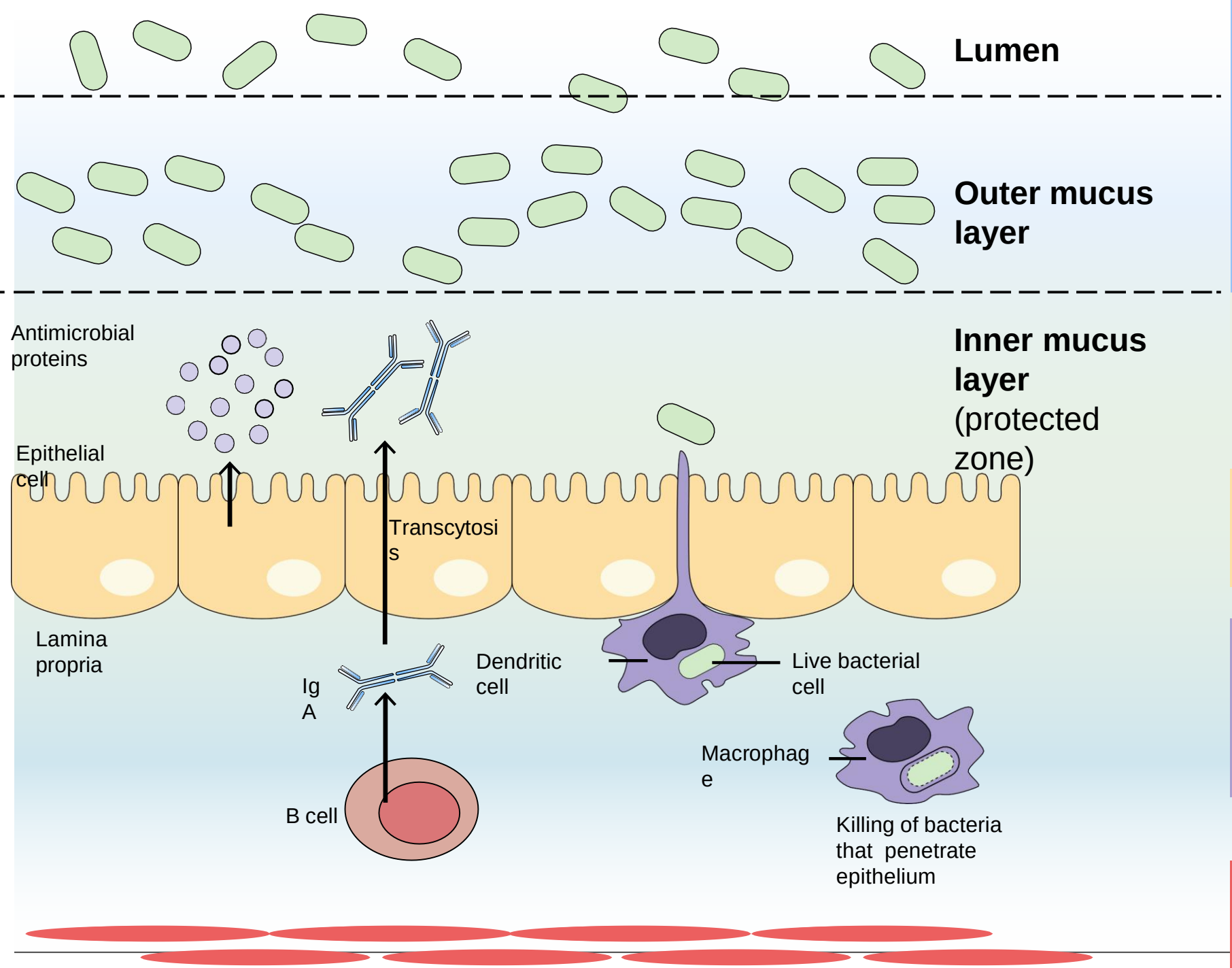


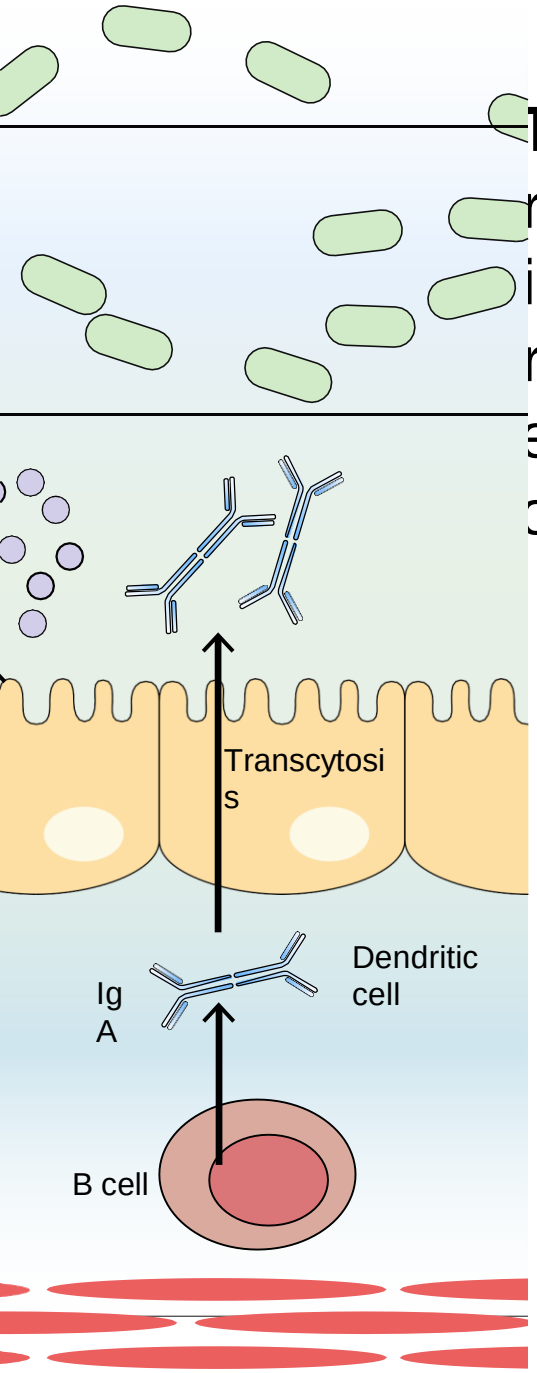
Microbial barrier
commensal bacteria

Chemical barrier
mucus layer

Physical barrier
the epithelium

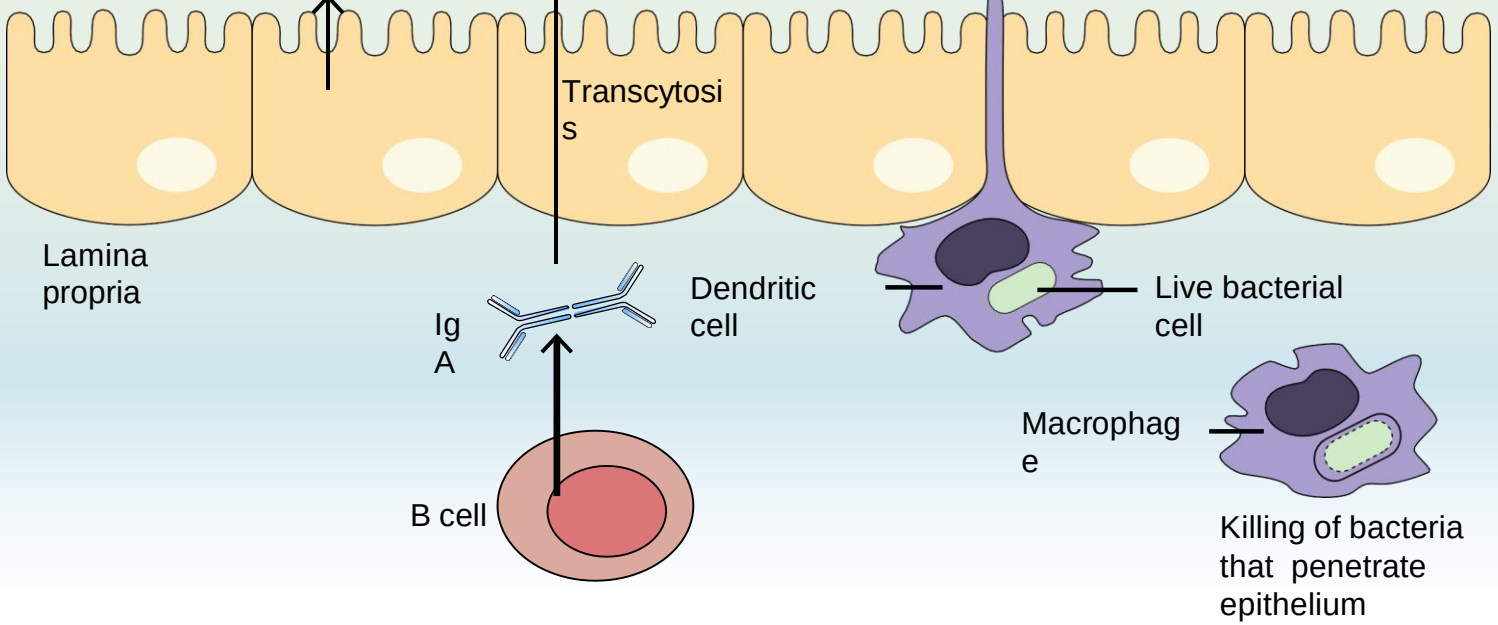
Immunological barrier
immune cells
of the lamina propria

Muscle layers
Smooth muscle intestinal wall



The intestinal barriers form a huge multi-factorial, layered and highly integrated system with high maintenance: 40% of our daily energy volume is used to maintain our gut barriers

1. **Commensal bacteria and their metabolites**
2. **Functional biochemical barrier**
   immune molecules (s IgA, antimicrobial peptides) and inflammatory mediators (cytokines) in a mucus layer
3. **External physical barrier**
   Epithelial cel lining /tight junctions
   Underlying the epithelial lining, we have the lamina propria (contains the immune system of the gut), vascular endothelium

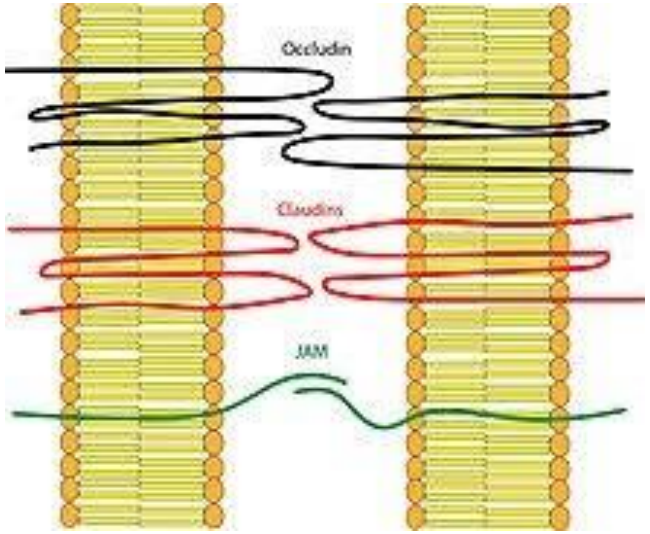


Physical barrier
the epithelium

Immunological barrier
immune cells
of the lamina propria

Epithelial cells with tight junctions Lamina propria
= connective tissue loaded with immune cells: T cells, Macrophages, Dendritic Cells

Dendritic Cells produce proinflammatory cytokines

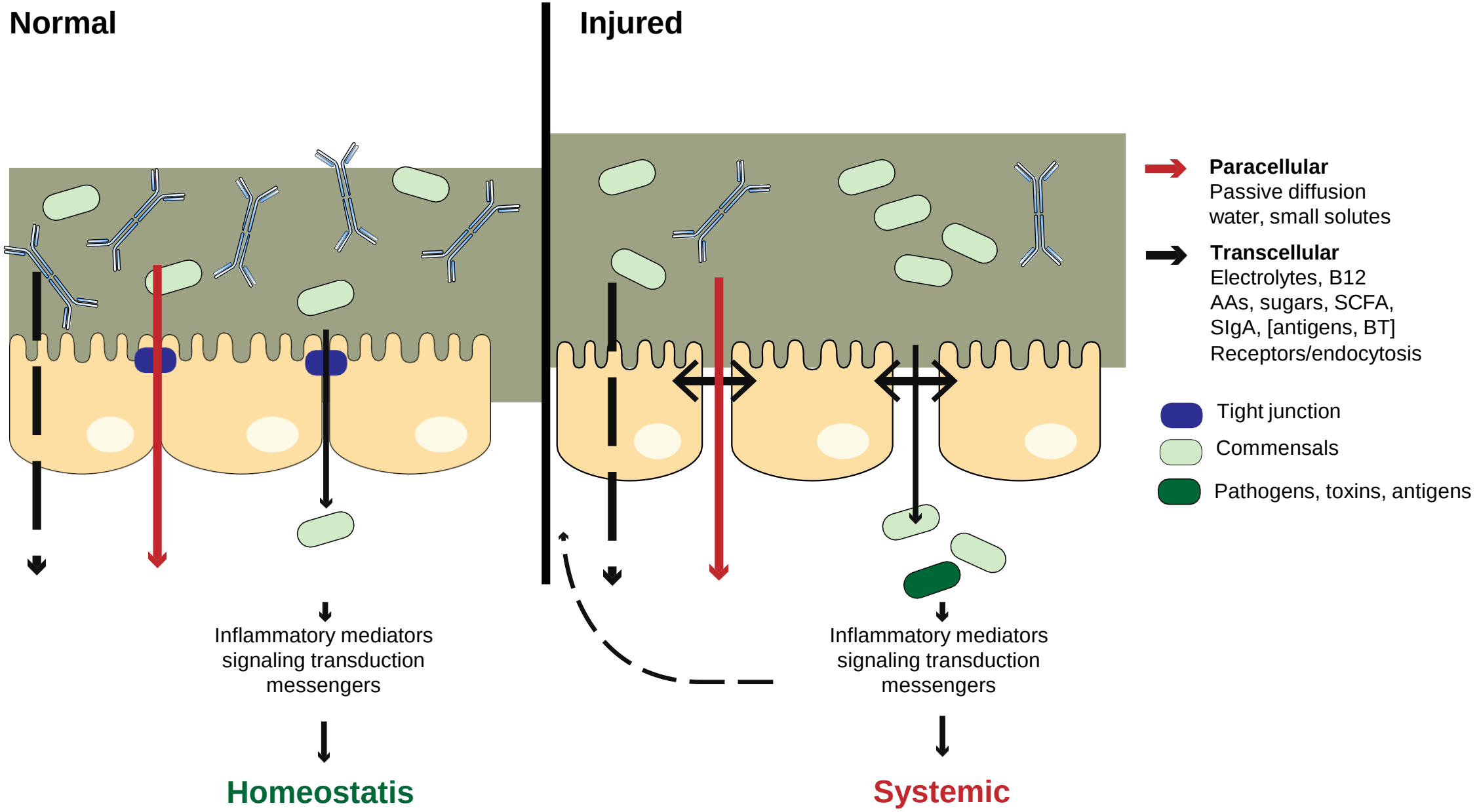


- Tight junctions are composed of a branching network of sealing strands

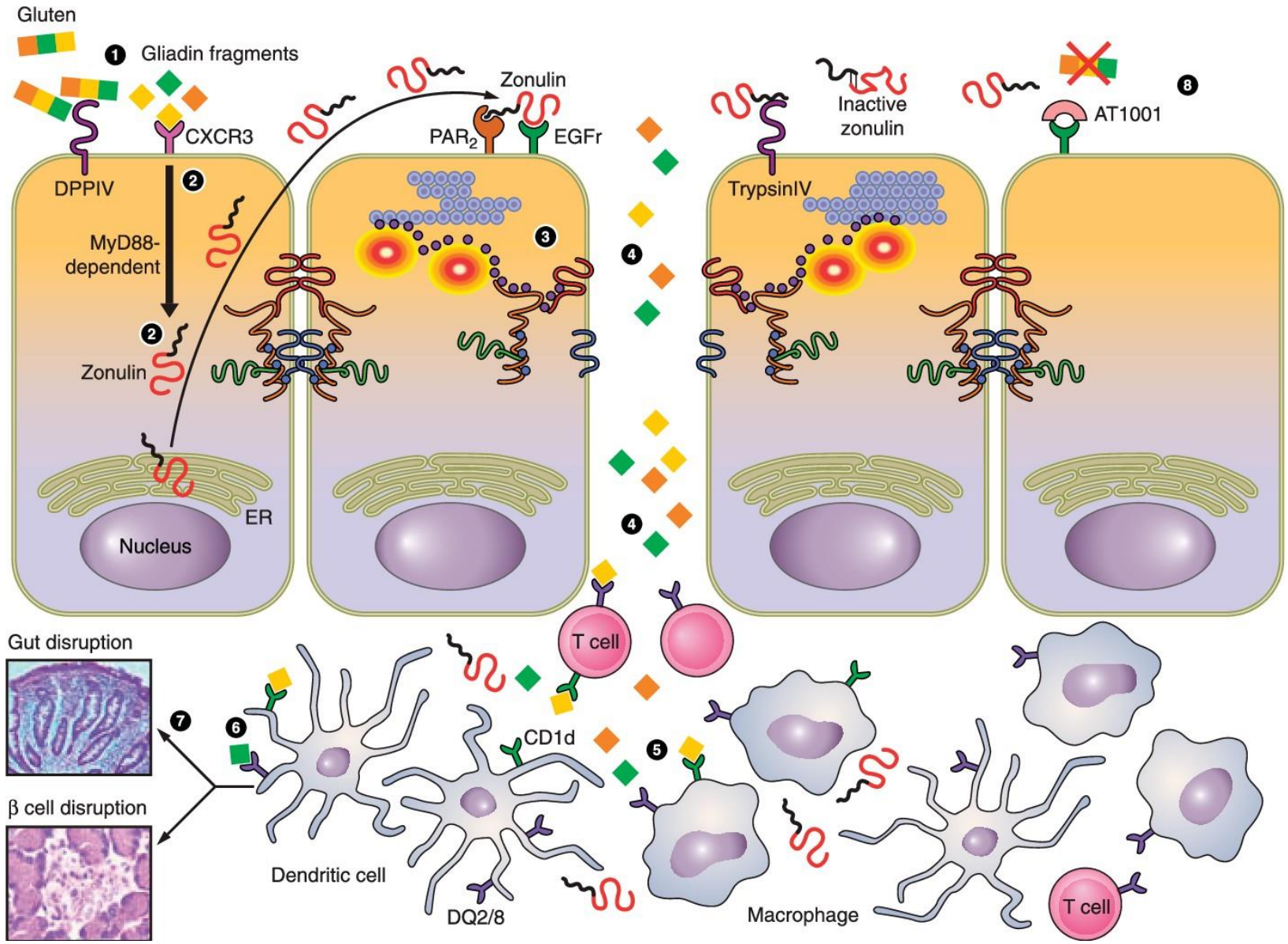
  Each strand is formed from a row of transmembrane proteins embedded in both plasma membranes

  Occludin and Adhesin are the main membrane proteins

- **Zonulin is the only physiological reversible mediator controlling the activity of the tight junctions**
  - Zonuline release is a diagnostical lab marker for leaky gut
  - Gluten/Gliadin is increasing zonulin release
- **Tight junctions regulate paracellular influx**


Normal
Injured
Paracellular
Passive diffusion
water, small solutes
Transcellular
Electrolytes, B12
AAs, sugars, SCFA,
SIgA, [antigens, BT]
Receptors/endocytosis
Tight junction
Commensals
Pathogens, toxins, antigens
Inflammatory mediators
signaling transduction
messengers
Inflammatory mediators
signaling transduction
messengers
Homeostatis
Systemic

Gliadin-induced Zonulin Release



LPS

= The major part of the outer cell membrane of Gram-negative gut bacteria

Gram-negative Cell Wall

Lipid A of LPS acts as **endotoxin**; **O polysaccharides** are antigens for typing, e.g., *E. coli* O157:H7

Gram neg. bacteria are less sensitive to medications because outer membrane acts as additional barrier.

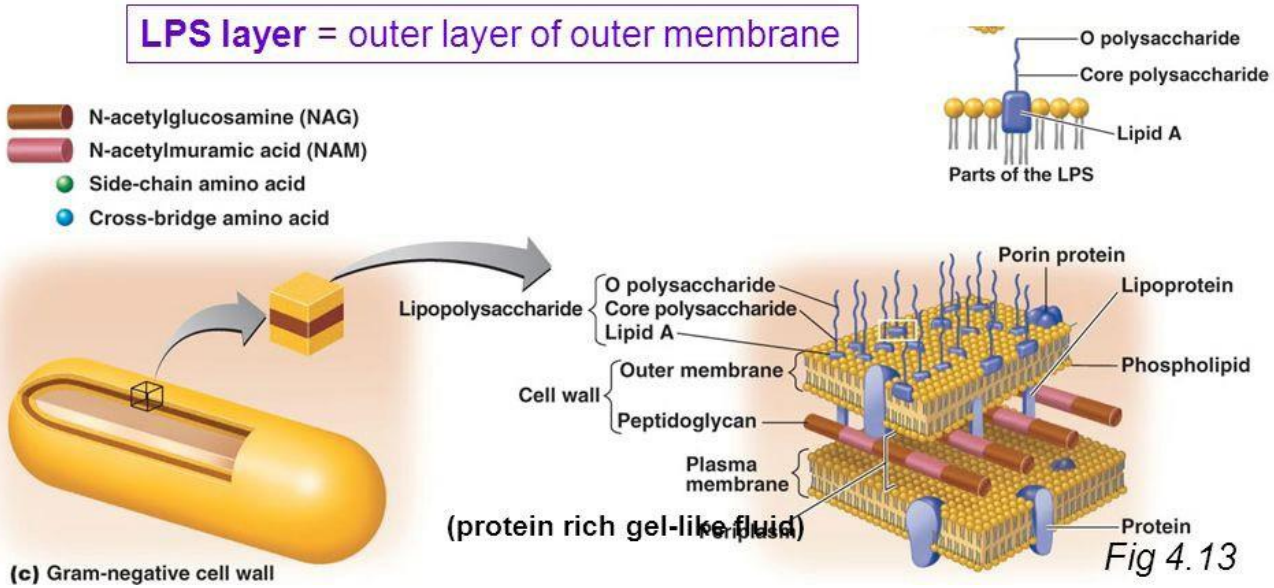


Fig 4.13

Treatment 1. Infections

The patient wished antibiotics to treat Borrelia as she recalled that she may have had a recent tic bite.

Treated for three months with amoxicillin 500 mg to 3 times a day and doxycycline 200 mg twice a day; for extracellular and intracellular cover.
Added in for 6 weeks of the 3 months: Metronidazole 500 mg three times a day.

Followed by Cowdens protocol by Nutramedix, GSH, Transfer Factors for MSIDS especially Chlamydia Pneumoniae.

For Marcons: nasal applications:
NAC nasal spray (glutathione precursor, biofilm breaker)
EDTA silver nasal spray. (Natural anti-microbial)
Amphotericin nasal spray. (Penicillium mold)

Treatment 2 Gut program

During antibiotic treatment she was treated with Corebiotics by Researched Nutritionals to support the micro biome & reduce LPS

Gut protocol with Perm Plus & DPPIV enzymes to optimise digestion especially for gluten, & help treat gut permeabilty

Advised to have a gluten & grain free diet, aiming towards a paleo/keto diet.

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DPPIV

König, Julia, et al. **““Randomized clinical trial: Effective gluten degradation by Aspergillus niger-derived enzyme in a complex meal setting.””** Scientific reports 7.1 (2017): 13100.

Gluten is a protein with a high content of proline residues (15%)

Normal enzymes in our GI tract can’t break down proline rich sides

This study shows the immunogenicity of Gluten was reduced using DPPIV enzymes

Gluten, zonulin & gut permeability

- A gluten- free diet benefits all patients with elevated serum-zonulin levels: IBS, Celiac and non-celiac Gluten sensitive Barbaro, M. R., et al.
- “Zonulin serum levels are increased in nonceliac gluten sensitivity and irritable bowel syndrome with diarrhea.” (2015): S56-S56.
- Increased Zonulin (increased permeability) Other triggers than Gliadin:
- • IL-6
- • Corticosteroids
- • Stress
- • Dietary protein fragments
- • Fructose

Microbes and toxins Fasano, Alessio. “Intestinal permeability and its regulation by zonulin: diagnostic and therapeutic implications.” Clinical Gastroenterology and Hepatology 10.10 (2012): 1096-1100

Probiotics reduce post prandial LPS

- The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: An Expanded Pilot Study Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS University of North Texas 49 Gong, Yi, Hui Li, and Yan Li.
- “Effects of Bacillus subtilis on epithelial tight junctions of mice with inflammatory bowel disease.” Journal of Interferon & Cytokine Research 36.2 (2016): 75-85. Samanya, Mongkol, and Koh-en Yamauchi.
- “Histological alterations of intestinal villi in chickens fed dried Bacillus subtilis var. natto.” Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology 133.1 (2002): 95-104. Gu, Min Jeong, et al.
- “Bacillus subtilis protects porcine intestinal barrier from deoxynivalenol via improved zonula occludens-1 expression.” Asian-Australasian journal of animal sciences 27.4 (2014): 580.

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Treatment 3 Immune support

The Low CD57 and CD3 indicated chronic immune suppression and that the problem had been there for a while, possibly also tied into the stress of her husbands illness.

Low Dose Naltrexone (improved Th1/Th2 modulation, reduces microglial activation.)

Transfer factors Multi messenger, Multi immune and L plus.

RG3 nasal spray (Ginsengoside) to reduce neuroinflammation caused by microglial activation.

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Special Dietary Usefulness for	Multimessenger	Transfer Factor L+	Messenger N° 1	Transfer Factor Enviro
Natural killer Cell - General immune support	×			
Bartonella		x		
Borrelia burgdorferi		×	×	
Babesia		×		
Ehrlichia		×		
EBV		×	×	
HHV6 B		×		
HHV6 A&B			×	
CMV	×	×	×	
Chlamydia pneumoniae			×	
Pneumocystic carinii			×	
Human TB			×	
Bovine TB			×	
Herpes 1			×	
Herpes 2			×	
Cryptosporosis			×	
Mycobacterium avian			×	
Hepatitis A,B,C			×	
Staphylcocci			×	

Special Dietary Usefulness for	Multimessenger	Transfer Factor L+	Messenger N° 1	Transfer Factor Enviro
Streptococci			×	
E. Coli			×	
Parvo virus B19			×	
Varicella Zoster			×	x
Candida (multiple strains)			×	
MMR			×	
Mycoplasma - 14 strains			×	
Ureaplasma urealyticum			×	
Nanobacterium			×	
Human Papillomaviruses			×	
Penicillium				x
Epicoccum				x
Aspergillus fumigatus				x
Aspergillus niger				x
Aspergillus versicolor				x
Cladosporium				x
Fusarium				x
Geotrichum				x
Pithomyces				x
Ustilago				x

Treatment 4 Inflammation, Bio-transformation

Inflammmation treated with Researched nutritionals Trifortify liposomal watermelon glutathione.

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Treatment 5 Hormones, & Gut Biotransformation

Developed tiredness and a low normal T3 with high reverse T3, so I treated her with half grain of nature thyroid for a few months.

White blood count under five so in view of evidence suggesting that retro viral activity may be active in these situations, I recommended Cistus incannus (Dietrich Klinghart recommendations.)

Also suffered with recurrent hot sweats and therefore I had introduced very low dose bio-identical hormones in February 2018. (Babesia negative, apyrexial, conscious to recheck for babesia if necessary, symptoms settled with combination of treatments)

In view of the mold noted on the nasal swab I also prescribed low-dose organic cholestyramine powder obtained from the Nutrined pharmacy and she gradually increased her dose to 4 gms qds to ensure a strong binder for Biotransformation of biotoxins, metals and chemicals.

TOTAL PROGRAM JUST OVER A YEAR TO HERE ie 08/2018

Follow up 1. She had stopped all Rx. Found to be hyperthyroid.

In October 2018, she was feeling extremely tired with poor sleep, previously felt that she had recovered quite well from her infections.

In view of her recurrent symptoms, I advised that she returned to her LDN and as she had stopped this.

I recommended various tests but she declined. She represented in February 2019 with abdominal pain, repeat blood tests showed her to be hyperthyroid, Successfully treated over the subsequent few months with a reducing dose of carbimazole & revert to gut protocol. Thyroid scan was normal.

Query was this as a result quite long-term treatment with antibiotics?

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Mucins, commensal microbiota, probable mechanism of antibiotic interference

Mucins are highly glycosylated proteins, polymers form a gel-like network

- Mucins are essential to maintain Gut Barrier function, mucins can be compared with biofilm
- Mucins are to the epithelial cells as the biofilm is to bacteria and yeast;
- Prevent direct bacterial binding to endothelial cells
- Mucins are regulated by commensal microbiota within the mucosa

Follow up 2. Oxidative stress, deficiencies

- – Dutch Test confirmed functional deficiencies of B12, and B6 due to high MMA and pyroglutamate, also high levels of eight hydroxy D guanidine indicating oxidative stress. Very low levels of 40H oestrogen (glutathione was helping her to biotransform oestrogen healthily)Treated her with anti-oxidants; vitamin B6, methylated B12 & folate.

- In September 2019, had weaned off of the carbimazole but we decided to do more work on her gut barrier and therefore carried out a fatty acid test at the Kennedy Kreiger Institute and neurolipid foundation in America

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Follow up 3. “Membrane medicine”

- This showed high levels of ALA (Omega 3), also LA (Omega 6) but low Arachidonic acid & very high levels of very long chain fatty acids and renegrades.

- A prescription was made to improve dietary healthy fats to include GLA, **butyrate, bile salts,** and various minerals and vitamins to aid processing of fats.

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Red Cell Lipid Biopsy. Kennedy Krieger Institute

- SATURATED ODD: Pentadecanoic 82.56 H
- VLCFA'S: Erucic 60.00 H; Lignoceric 35.34 H; Lumequic 39.90; Hexacosanoic 85.06 H

Triacontanoic 50.00 H

- RENEGADES: Mead 115.00 H; Eicosanoic 115.00 H; Phytanic 150.00 H; Pristanic 950.00
- MYELINATION: 16:0 DMA -104.65 L; 18:0 DMA -110.92 L; 18:1 DMA -109.28 L;

STRUCTURAL: Stearic -46.70 LBALANCE

- OMEGA 6

Linoleic 32.17 H; Gamma Linolenic 76.32 H; Dihomo-y Linolenic 122.46 H

Arachidonic -40.07 L; Adrenic -48.19 L

- OMEGA 3: Alpha Linolenic 134.38 H; Eicosapentaenoic 14.22; Docosapentaenoic 24.96

Docosahexaenoic 8.41

- INDEXES: Fluidity Index -55.00 L; MR Index -34.53 L; PR Index 204.69 H; Myelination Index -71.50 L; Odd Chain Index -0.63
- STABILISE IT: ITPR Index 204.69 H; Palmitic 28.33 H

Follow up 4: Mitochondrial assessment

Mitochondrial assessment at the IGL lab in Germany to look at cell-free DNA and DNA adducts to include chemicals, by toxins and metals. Showed:

- High level of cell-free DNA
- DNA adducts: diesel particles.
- low levels of phosphatidylcholine and phosphatidylethanolamine and was not biotransforming adequately as reflected by high levels of MDA.
- Low DNA associated zinc
- Low levels of red-cell glutathione. Various parameters for glutathione are measured and all were normal including glutathione S transferase
- High levels of cadmium, aluminium, benzoquinone lindane, bisphenol A , Phthalates toluene. There were no obvious challenges with the mycotoxins at this stage.
- Her metallothionein was high due to the necessity of binding higher amounts of metal and her zinc been replaced by cadmium.
- Superoxide dismutase SOD2 & SOD 3 were blocked due to oxidative stress and inflammation. SOD2 was blocked by benzoquinone and SOD3 by diesel particles.

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Adduct Benzoquinine

Consumer Uses
This substance is used in the following products: coating products and fillers, putties, plasters, modelling clay.
Other release to the environment of this substance is likely to occur from: indoor use and outdoor use resulting in inclusion into or onto a materials (e.g. binding agent in paints and coatings or adhesives).

Follow up 5: Treatment for adducts & poor biotransformation

- She was treated with the fatty acid protocol
- High amounts of phosphatidylcholine produced by BodyBio and the neurolipid foundation, as this also includes phosphatidylethanolamine.
- We also used magnesium with butyrate from Bodybio, & Neurolipid foundation, also NUTRINED now have a coated version of **Butyrate** called **BUYTFLAM** released on August 31st 2020.
- Butyrate from a research perspective is known to modulate the action of T cells via epigenetic activity.
- Dietary advice about healthy fats and digestion with ox bile
- Liquid minerals,
- Continue liposomal glutathione, + specific recommendations from the neurolipid foundation.
- NB Heat eg sunbathing, Epsom salt baths, saunas

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Butyrate modulation activities 1

(Pol de Saedeleer)

Microbial-host cross talk: " the host listens to butyrate"
=Butyrate impacts epigenetics
= Butyrate modifies genetic material → impact on gene expression and transcription

Immune modulation / anti inflammation on local level: Butyrate inhibits HDAC (histone deacetylase) – this changes gene expression in Dendritic Cells

As a result IL-12 & IL-6 are suppressed = more IL-10 = more differentiation to T reg

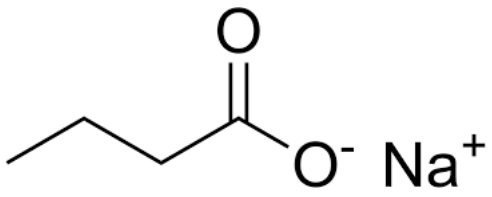
Butyrate modulation activities 2

- T regs release TGF1B causing naïve B cells to produce more sIgA

- Butyrate modulates the immune response in macrophages and makes them more tolerant towards commensal bacteria.

- Butyrate affects neutrophil chemotaxis leading to anti inflammation on local level

- Goblet Cells release more mucins



How is butyrate formed?

1. From host prebiotic

Mucin harvesting bacteria that release glycans
= mucin derived glycans are fermented by other bacteria to form butyrate

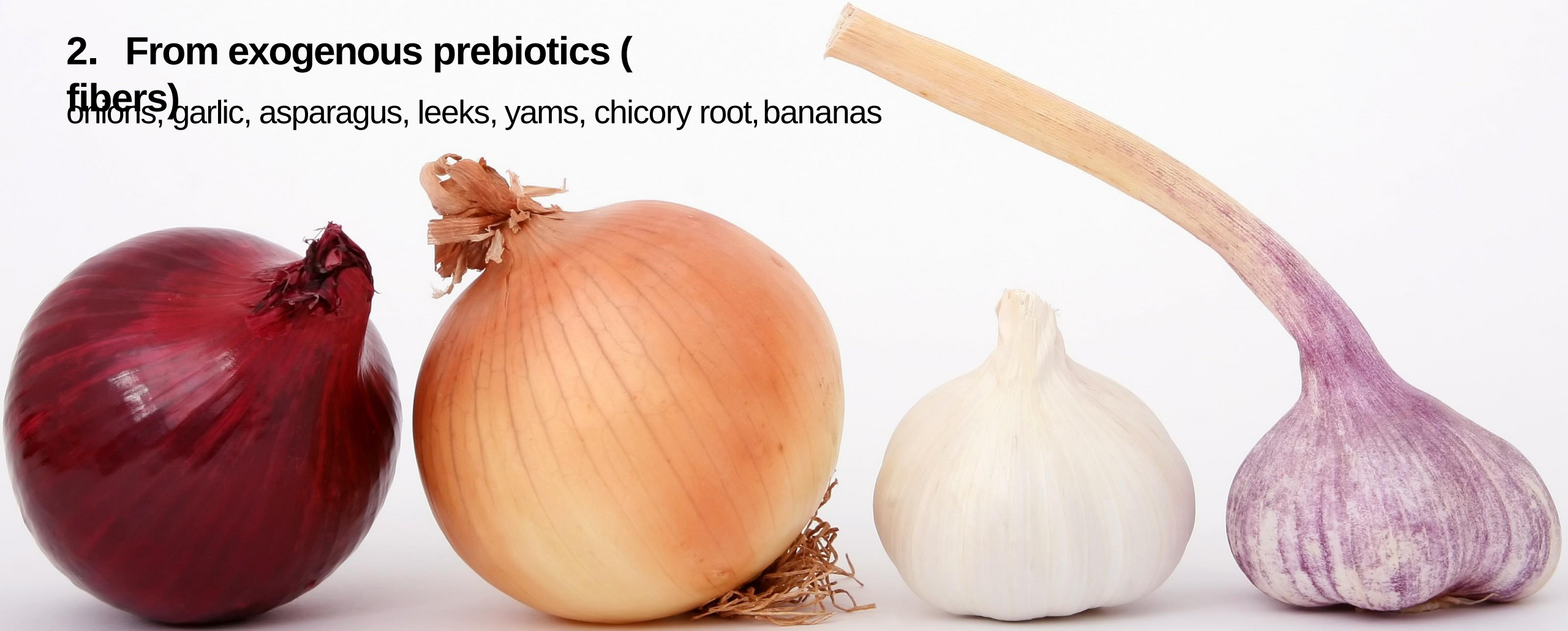
What bacteria produce butyrate?

- Clostridium spp. have a key regulatory role
  = major butyrate producers – initiating that cross talk
- Fecalibacterium prausnitzii

- we have a decreased amount of Clostridium spp. in colorectal cancer and IBD versus controls
- the more fibers, vegetables and beans we eat, the more abundant Clostridium spp. are
- Vs. we also have 5 very pathogenic spp. like C difficile
  – THE MAJORITY OF CLOSTRIDIUM spp. ARE NOT BAD

2. From exogenous prebiotics (fibers)

onions, garlic, asparagus, leeks, yams, chicory root, bananas

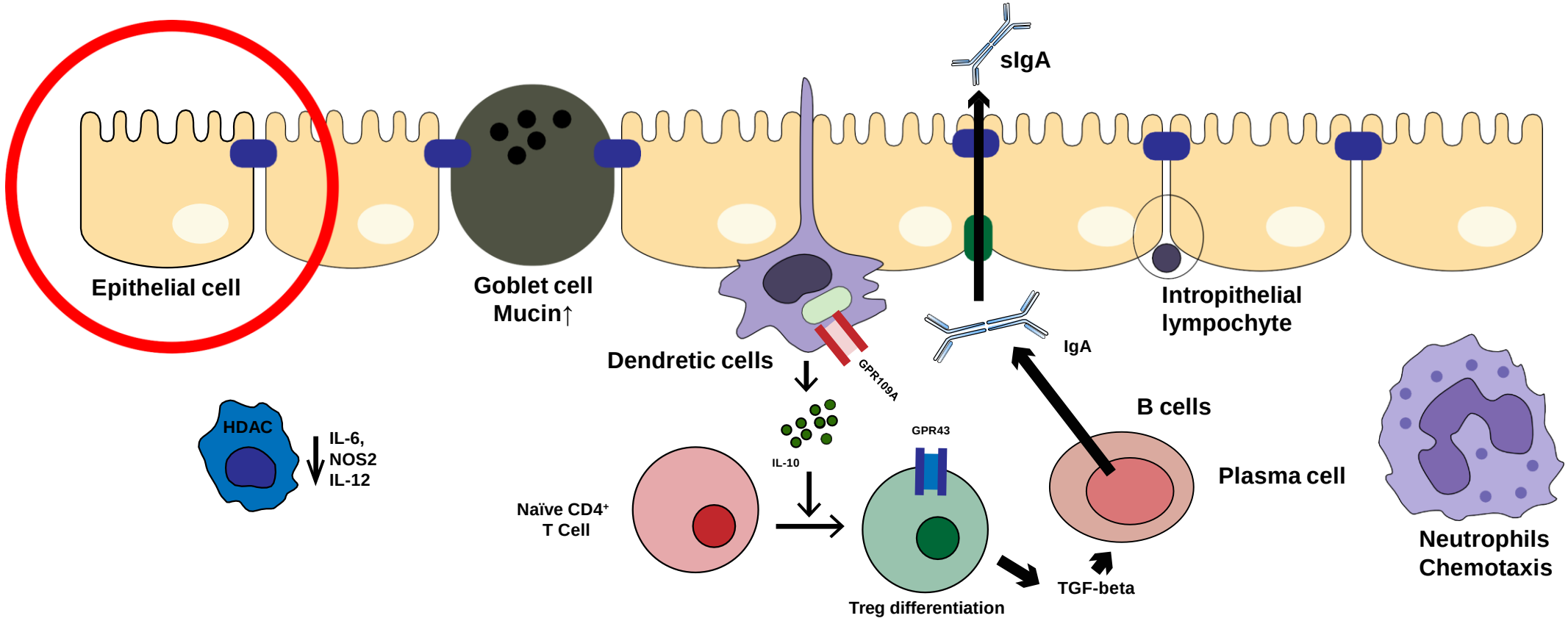


What is the role of butyrate andSCFA's?

Butyrate, acetate, propionate

Fuel to renew the intestinal epithelial cells (IEC)

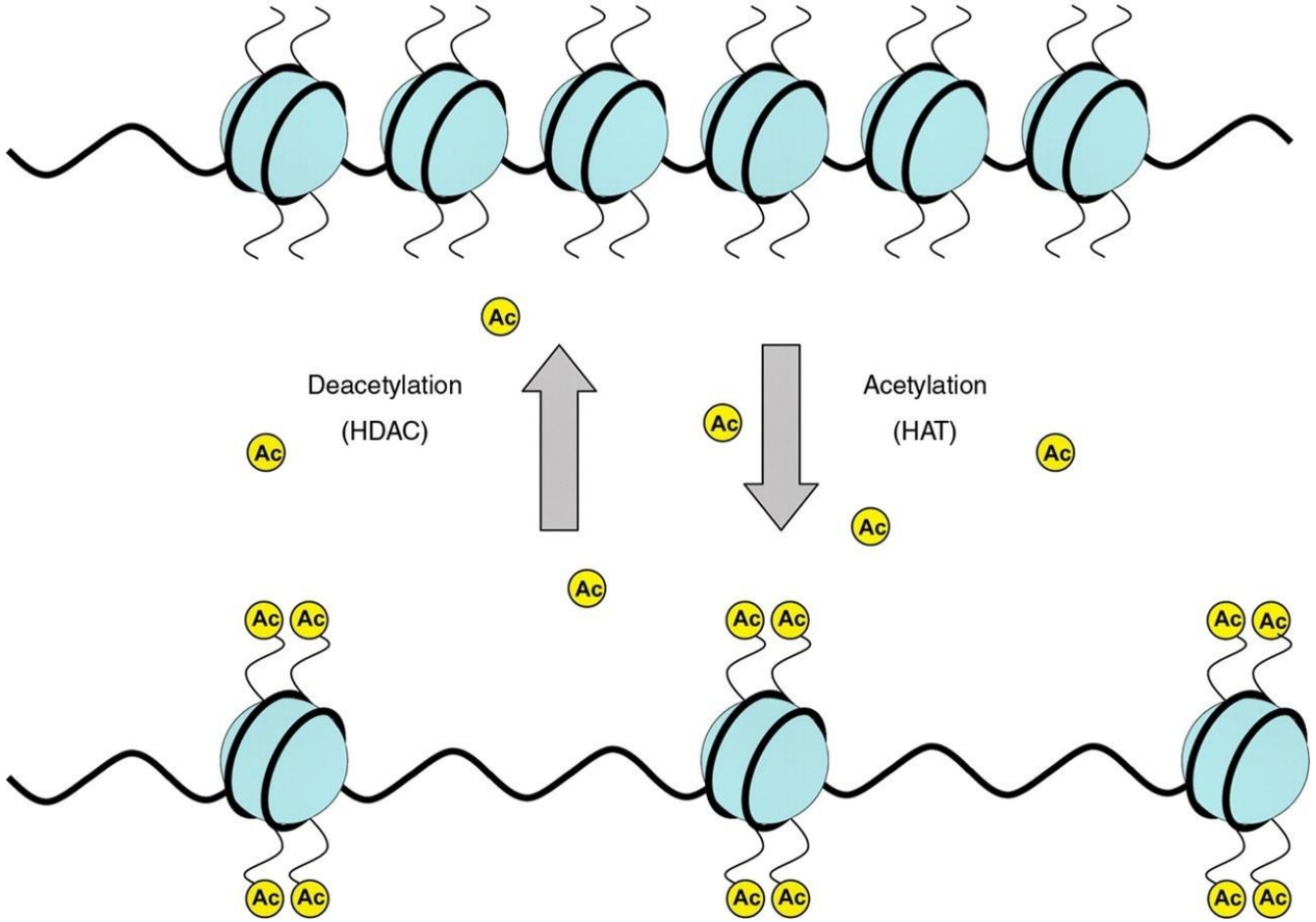
IEC need to be renewed every 3-5 days



Microbial-host cross talk: “ the host listens to butyrate”

=Butyrate impacts epigenetics
= Butyrate modifies genetic material
→ impact on gene expression and transcription

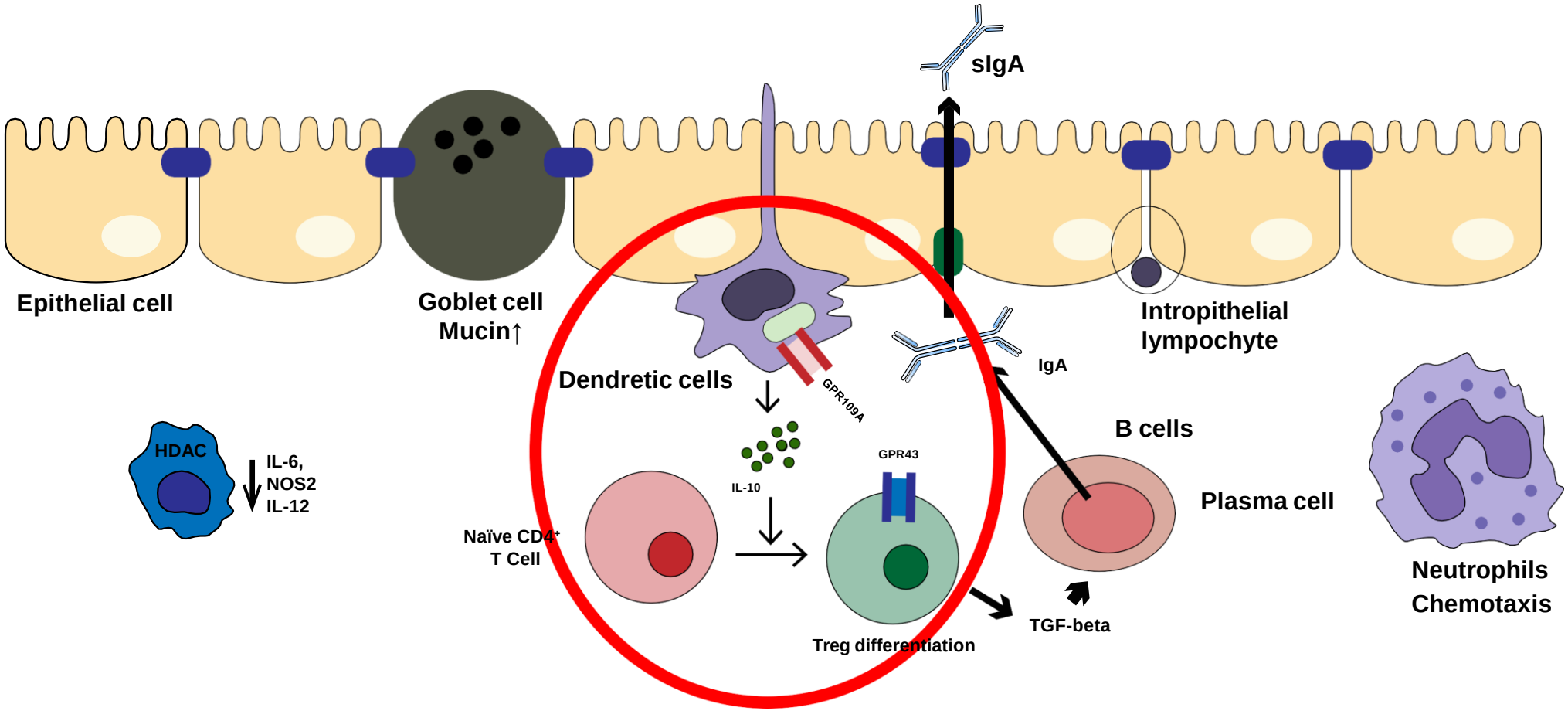
Immune modulation / anti inflammation on local level:
Butyrate inhibits HDAC (histone deacetylase) – this modification is changing the gene expression



Gene expression is modified in Dendritic Cells

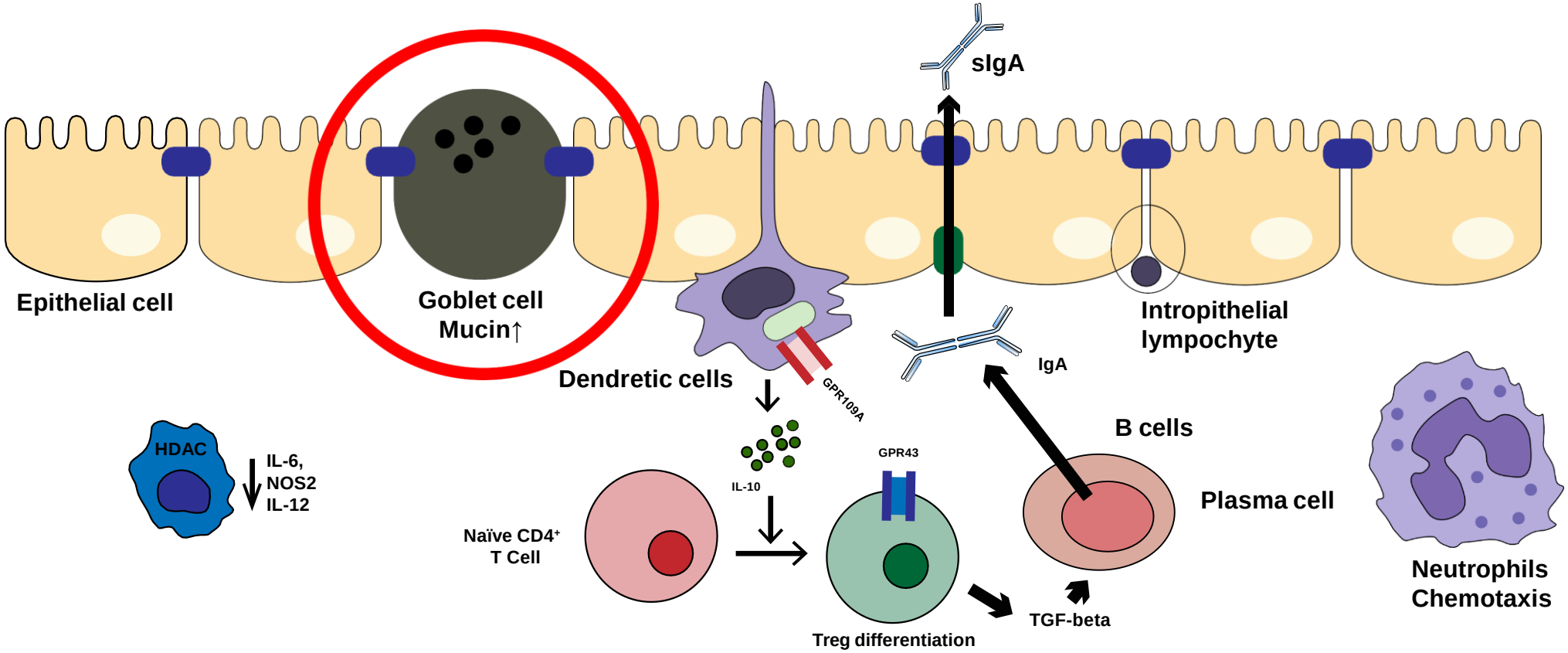
IL-6 is suppressed = more IL-10

More differentiation to T regs



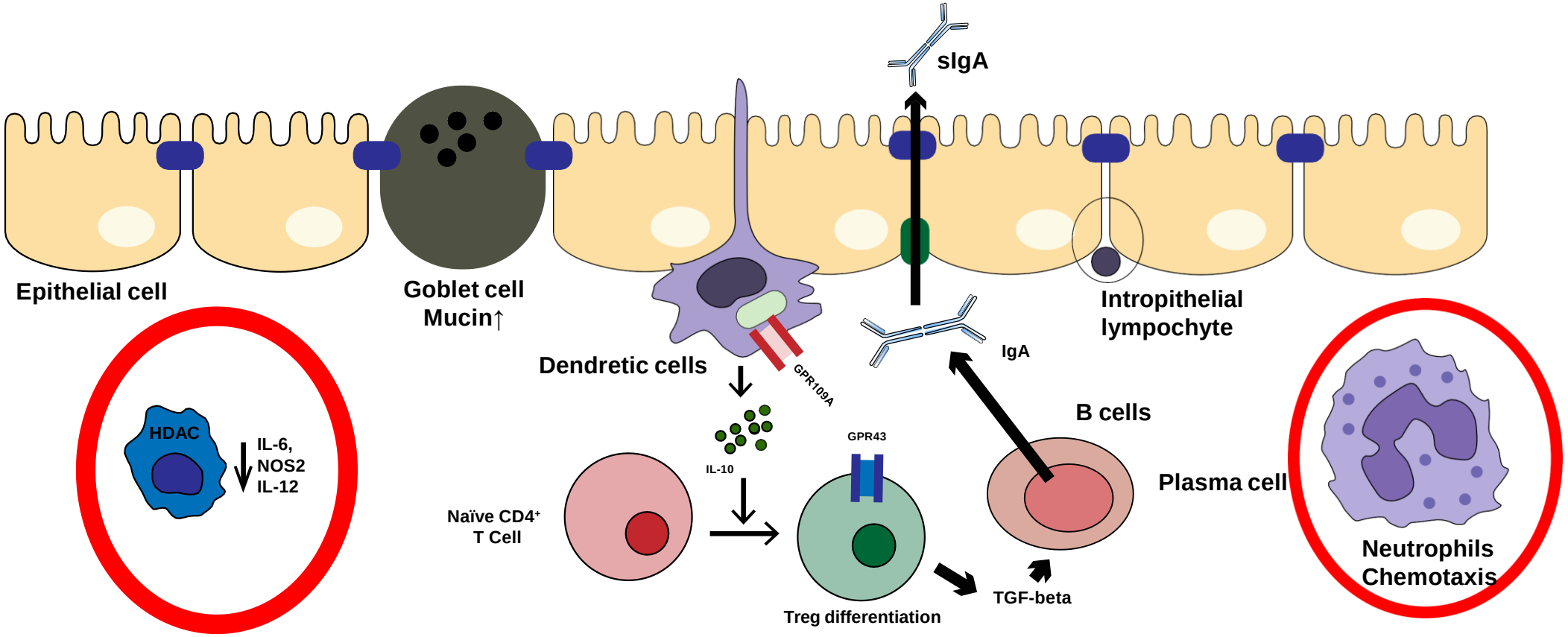
Differentiation of Goblet Cells and mucus formation

More mucin is a better immune defense against invading pathogens



Butyrate modulates the immune response in macrophages what makes macrophages more tolerant towards commensal bacteria

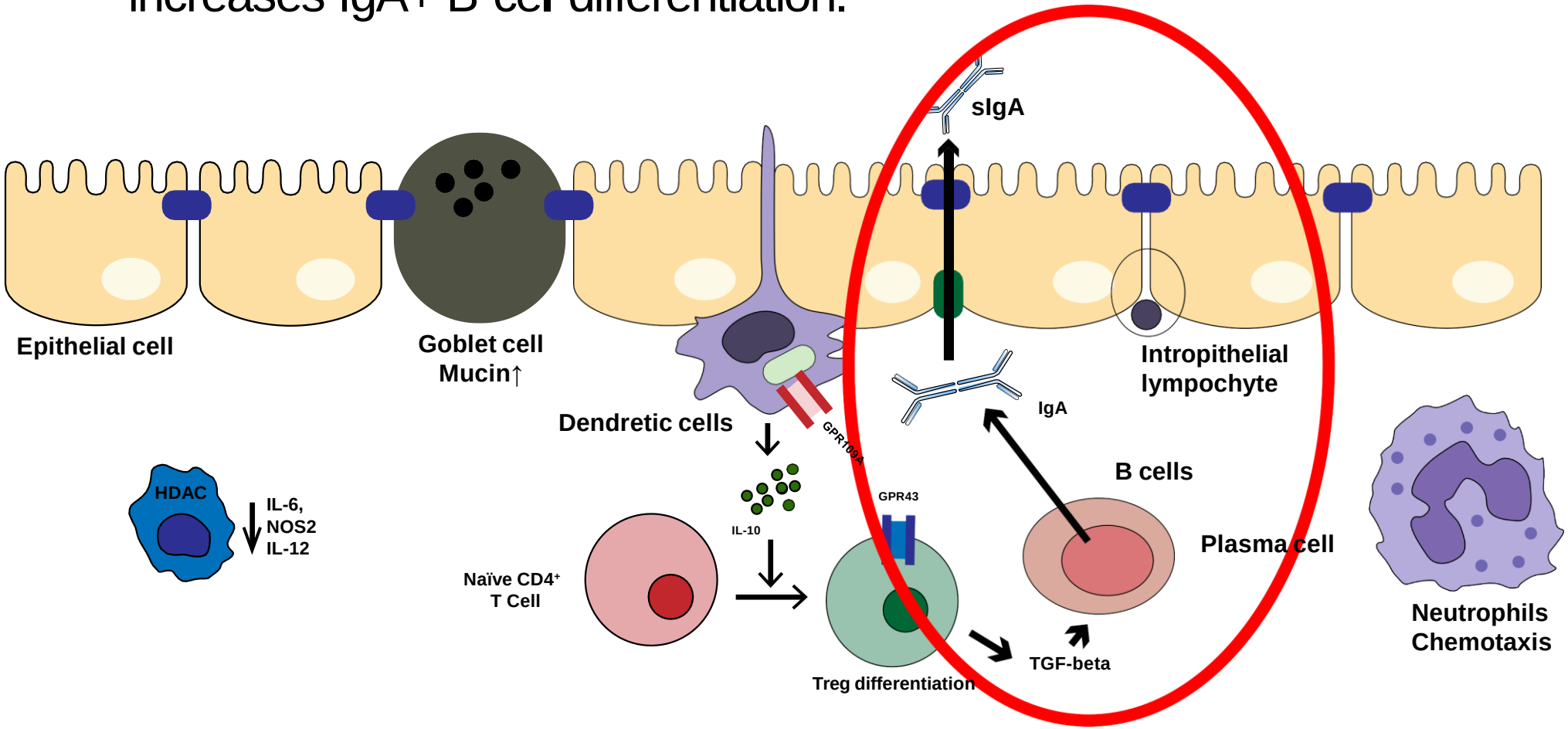
Butyrate affects neutrophil chemotaxis anti inflammation on local level



sIgA

TGF-beta produced by Treg cells drives naïve B cells to differentiate into IgA-producing cells.

IL-21 from Th17 cells accentuates the effect of TGFb and increases IgA+ B cell differentiation.



Fuel to renew epithelial cells

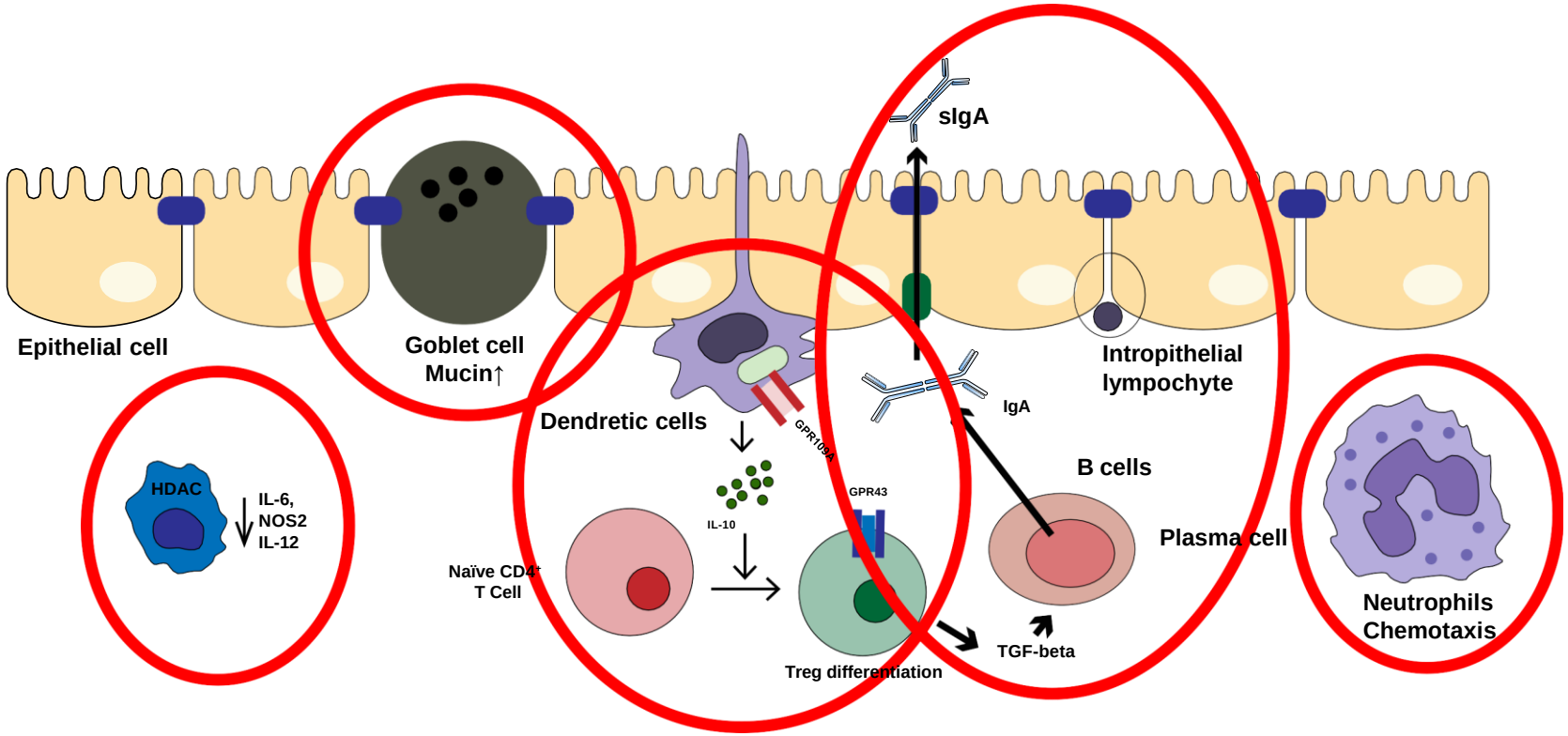
Impact on dendritic cells, more IL-10 & T regs

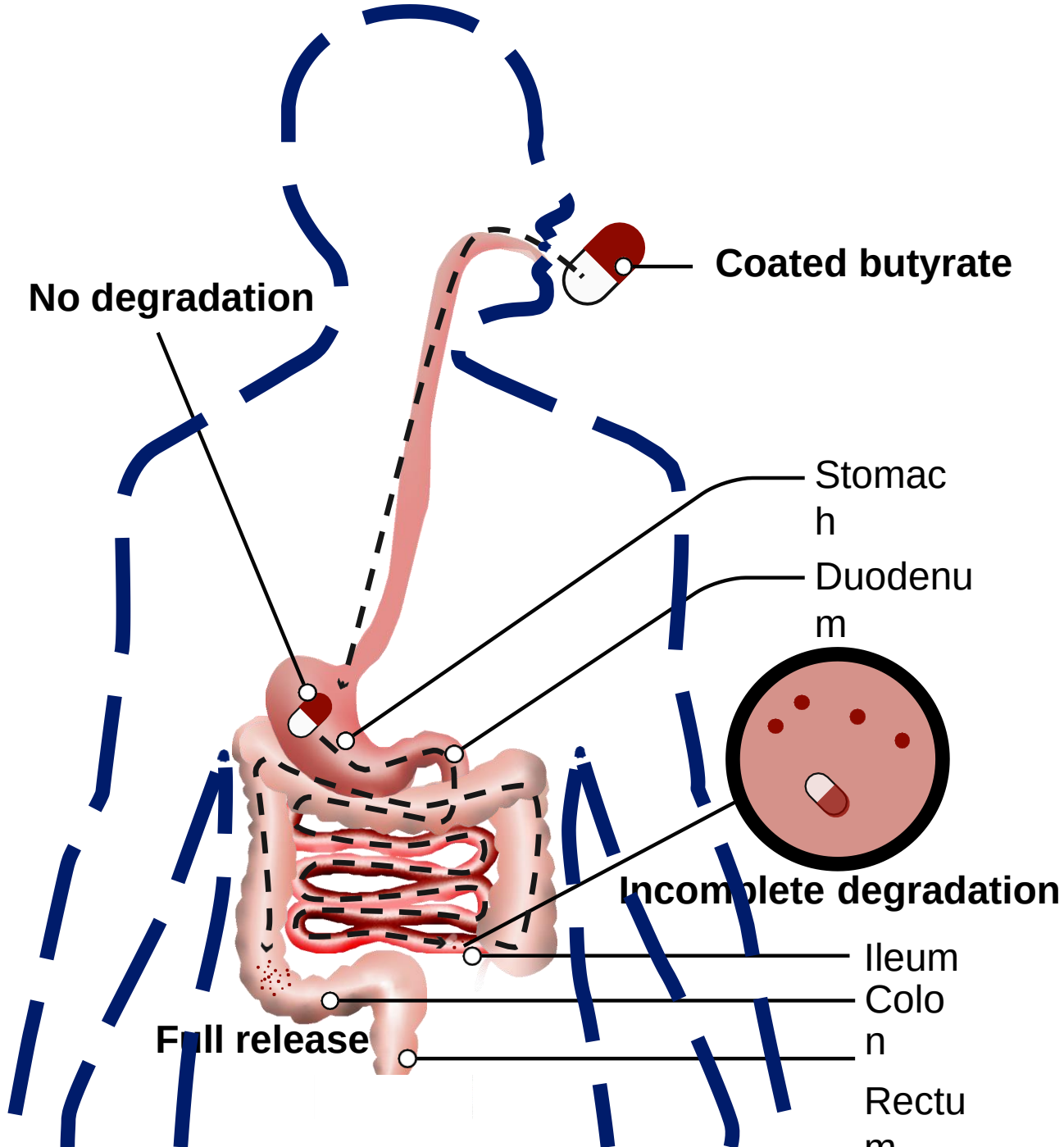
Goblet Cells release more mucins

Macrophages more tolerant towards commensal bacteria

Neutrophil chemotaxis

B cells synthesize more s IgA's





Butyrate needs coating for overall activity on different levels

- To obtain both local and systemic effect
- To avoid a premature release and absorption of butyrate
- To ensure complete release of the active ingredient at a time comparable to the oro-ilear transit time

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Gut permeability evidence for support

(by kind agreement of Pol de Saedeleer)

Support for expression of tight junctions

- • Prebiotics for butyrate production or butyrate (coated)
- • probiotics
- • Glutamine
- • Green Tea, Resveratrol, Curcumin
- • Vit D3
- • Gamma-Lineolic Acid (GLA)

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Nutrined: Butyflam Coated Indication: Dosage: Amount per 6 tablets Daily dose based on 6 tablets 180 coated tablets per container Neuroinflammation Immune modulating (T reg + IL-10 anti-inflammation) Remodeling intestinal barrier function Take 3 x 2 tablets per day Butyrate 3000 mg

Follow up 6

- Poor sleep at this time so treated with CBD slow release 50 mg at night. She did well with this.

- Repeat Armin: CD57 & CD3 were still low, positive seraspot for Borrelia, chlamydia pneumonia was now normal, Mycoplasma Pneumoniae was now high, but strongly positive HSV 1 & 2 and Coxsackie virus. Treatment was to continue immune & gut protocol, but this time use anti-microbial herbs again ie BLT and Stevia as an anti-microbial, biofilm Breaker & binder. Add Lysine 500mg 2 bd.

- Treatment added: rebuilding the gut membrane, strengthening the gut protocol with perm plus, ox bile and DPP4 enzymes, fatty acid program (Butyrate, PC,) re start TFs, continue LDN.

- At that time also developed problems with poor passing of urine and weight gain of 8 lb if she did not sleep. ? HPA axis inflammation and High ADH ? This subsequently settled with her treatments To help reduce infection and inflammation, also when she began to sleep better with the CBD this also has quite a profound anti-inflammatory effect.

COVID protection

12th of March 2020 feeling better.

Due to Covid, I discussed further protection of 5 g of vitamin C per day, 5000IU of vitamin D per day, (orthomolecular Society evidence base) to continue her transfer factors including Multimessenger and Messenger No 1, zinc 50 mg per day all to be taken with phosphatidylcholine liquid and to continue liposomal glutathione to help reduce the metals on her IGL test. Also to return to her LDN which she had again stopped.

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COVID TREATMENT

6th April 2020 called me with symptoms of probable COVID-19, present for one week, severe pain in her right shoulder, with a sudden worsening of the condition, coughing green phlegm and very short of breath. SARS Cov2 IGM/IGG test carried out at home & result sent by phone. Positive IGM.
Rx:

- Declined hospital admission.
- Urgent antibiotic azithromycin orally, 500 mg two twice a day for one day followed by One twice a day for one day, then once a day for the last four days of treatment.
- High doses of vitamin C every two hours, 5 g to bowel tolerance (Not G6PD deficient).
- Increased dose of liposomal glutathione 1 teaspoon 4 times a day.
- NAC 500mg 2 bd
- QUERCETIN 500 mg three times a day (NB Remember CYTOQUEL)
- HIGH DOSE curcumin.
- Zinc 100mg a day
- Because of previous treatment with Lyme, she had all of these to hand. After one day she felt 70% better and improved quickly after this, following which time I rang her almost every day and she has now recovered extremely well and was happy to give her consent for this presentation.

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Currently 27.06.20

- Stable and well, still taking Low Dose Naltrexone, due for review.

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Clinical Pearls

- Consider Membrane Medicine to support immune system
- Consider DNA Adducts
- Care with antibiotics; be aware of Butyrate (eg Butyflam) for additional gut membrane protection & immune optimisation
- Are you using Low Dose Naltrexone?

Thank you

Email: drpiper@privategp.com