
DESAFIE-SE
INSPIRE-SE
MOVA-SE
CENTRAL
nutrition

Intestino e imunidade

Gabriel de Carvalho
Nutricionista e Farmacêutico Bioquímico
Introdutor da Nutrição Funcional no Brasil em 1999
Co-fundador da Faculdade de Saúde Avançada

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nutrition

As 7 Funções do Sistema Gastrointestinal

1. Digestão
2. Absorção
3. Excreção
4. Neuro
5. Imuno
6. Endócrina
7. Destoxificação

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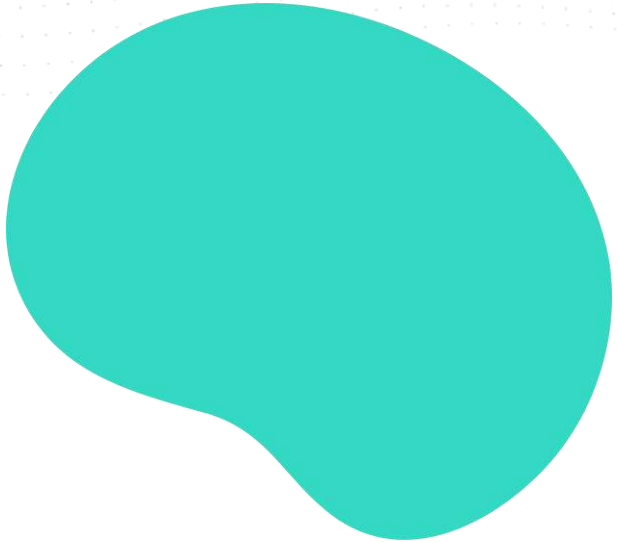
Imunológica

”70-80% dos linfócitos corporais estão no TGI”



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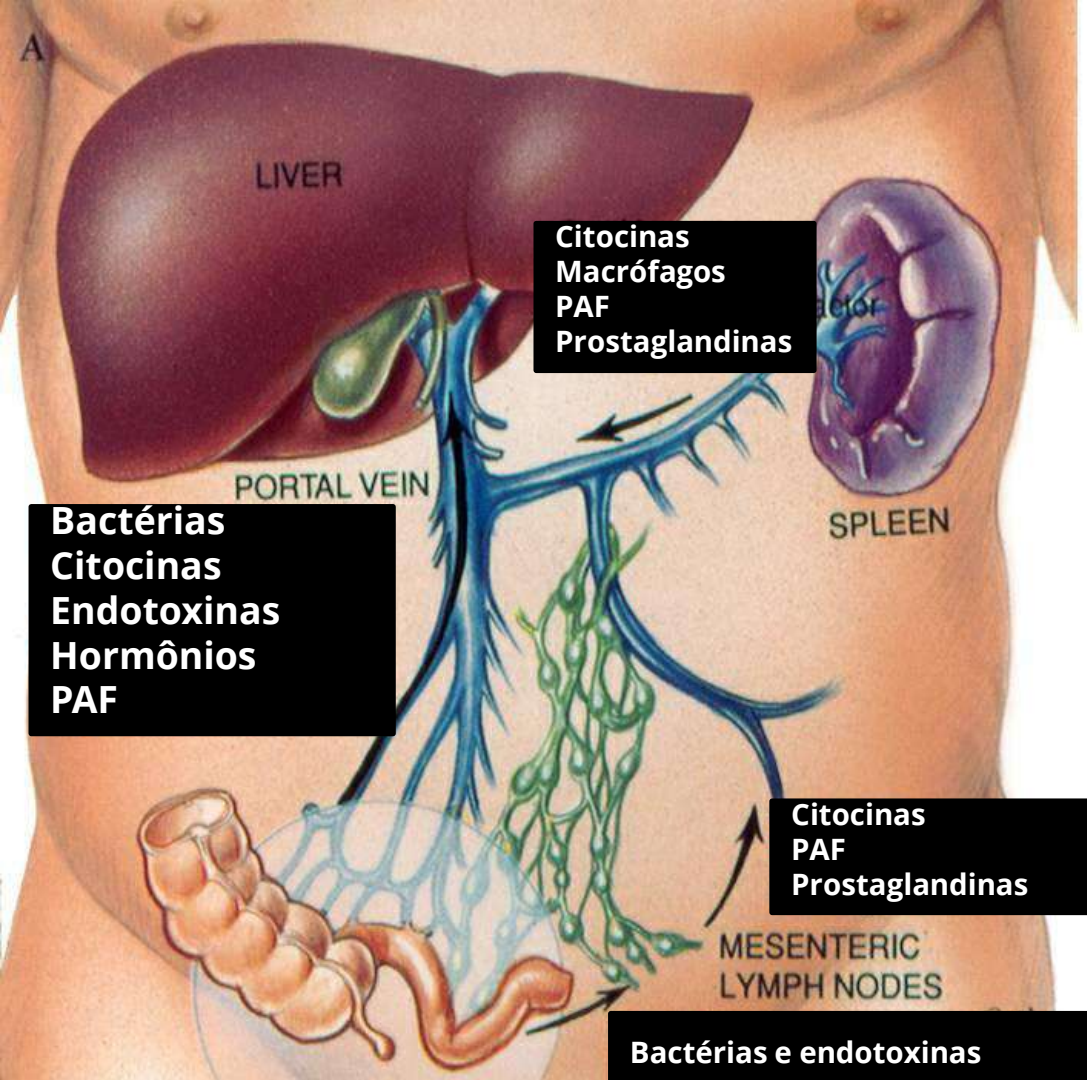

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MALT - mucosa-associated lymphoid tissue
(tecidos linfóides secundários)

1. Tec. Linfóide Associado ao Intestino - **GALT**
2. Tec. Linfóide Assoc. ao **Nariz** - NALT
3. Tec. Linf. Ass à **Laringe** – LALT;
4. Tec. Linf. Ass. aos **Brônquios** - BALT
5. Tec. Linf. Ass. à **Conjuntiva** – CALT
6. Glândulas salivares, mamárias, **ouvido médio** e trato **geniturinário**

Elia, Celeste. Atheneu: São Paulo, 2001.

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Elia, Celest. Atheneu: São Paulo, 2001.

“a circulação de linfócitos entre diferentes mucosas é um dos componentes mais importantes deste sistema, pois permite que as respostas sejam integradas em rede”

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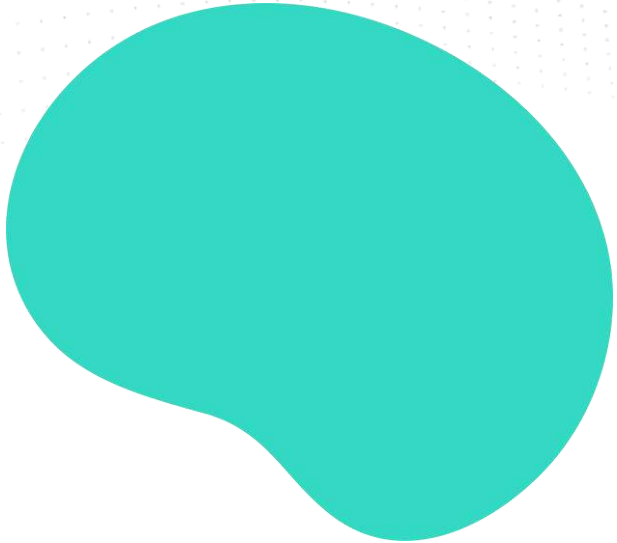
Imunidade inata e imunidade adaptativa



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Imunidade Natural (nativa ou inata)

Física

Pele, cílios, microbiota, barreira mucosa e outras

Química

Antimicrobianos diversos

Ácido graxos no suor
Lisozima e fosfolipase nas lágrimas, saliva e secreção nasal
Baixo pH do suor e estômago
Defensinas nos pulmões e TGI
Surfactante nos pulmões - opsoninas

http://pathmicro.med.sc.edu/ghaffar/innate.htm

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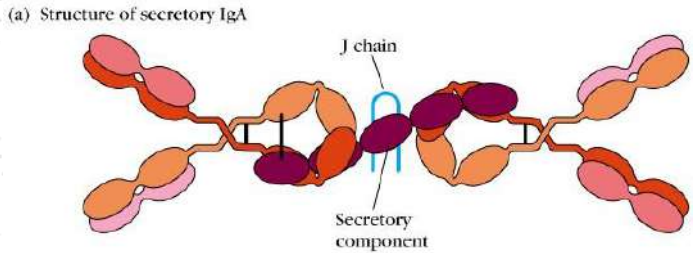

Celular

IgA Secretora

duas moléculas de IgA **+** componente secretor, síntese depende de **Retinol**

Fagócitos (4)

i.e: macrófagos, monócitos, neutrófilos

enzima elastase, depende **de Zinco**

SOD **(Zn, Cu, Mn),** catalase e mieloperoxidase **(hemo)**

Colagenase, COX, LOX, NO sintase

http://pathmicro.med.sc.edu/ghaffar/innate.htm

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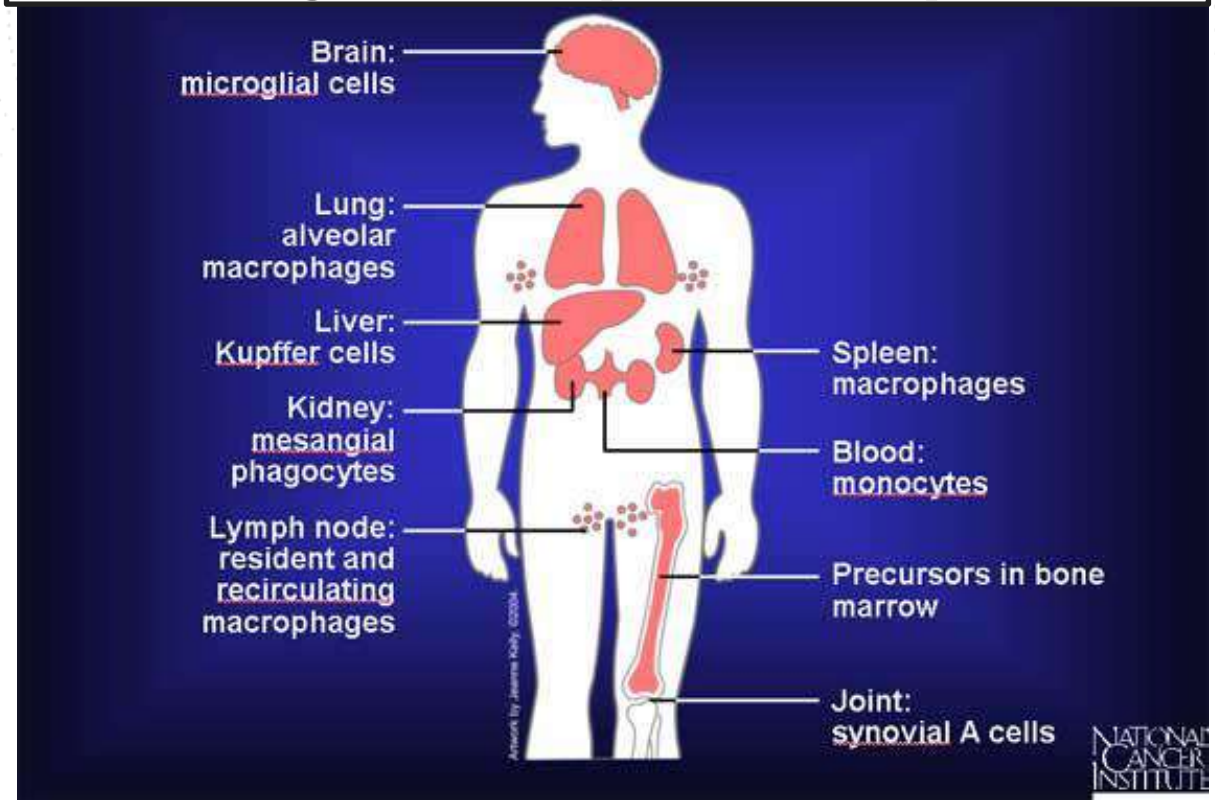
Fagócitos pelo Corpo



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Sistema de Monocítico Fagocitário
Formado por todas as células oriundas de monócitos:

- Monócito - circulante no **sangue**
- Células da Micróglia (Glia)- **SNC**
- Células de Kupfer - **fígado**
- Macrófagos Alveolares – **pulmões**
- Células Dendríticas **- linfonodos**
- Mesangio Intraglomerular – **rins**
- Macrófagos Sinusais - **baço**
- Macrófagos das serosas - **peritônio, pericárdio e pleura**
- Células de Langerhans - **pele**

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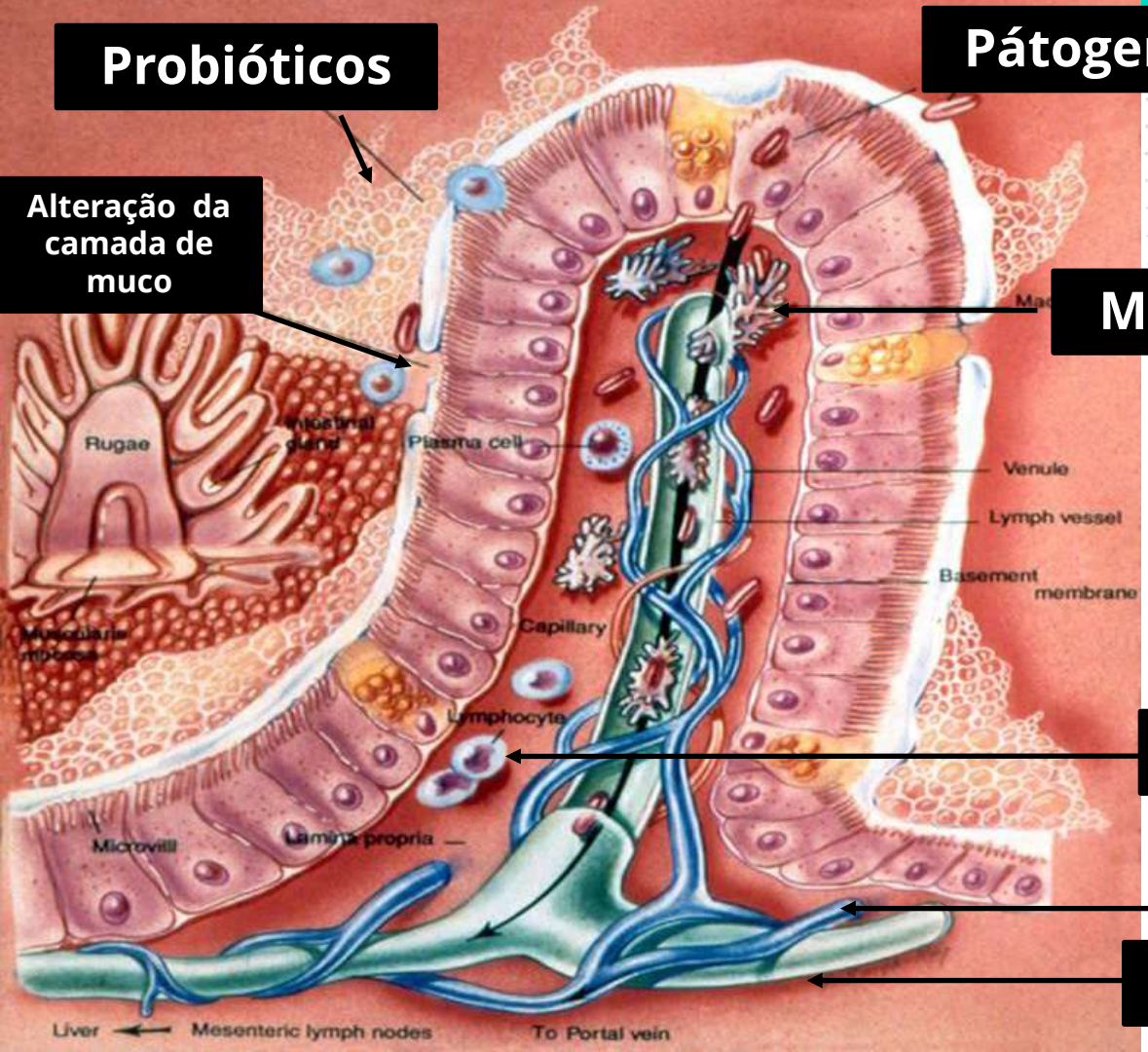
Imunidade Adquirida (ou adaptativa)
= *desenvolvida a partir de um estímulo*

- **Imunoglobulinas**
- **Imunidade Celular**
- **Sist. Complemento** (proteínas plasmáticas)
- **Citocinas**
  - *Desnutrição afeta TODOS estes pontos citados = imunodeficiência!*

Cunningham-Rundles S. Nutrient Modulation of the Immune Response. Marcel Dekker, 1993.

CENTRAL nutrition



Probióticos

Pátogeno

Alteração da camada de muco

Macrófago

Linfócito

Venula

Vaso linfático

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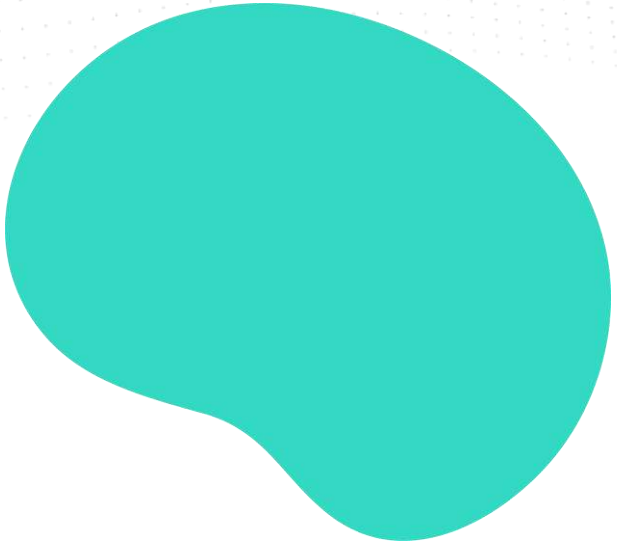
Representação esquemática da barreira intestinal



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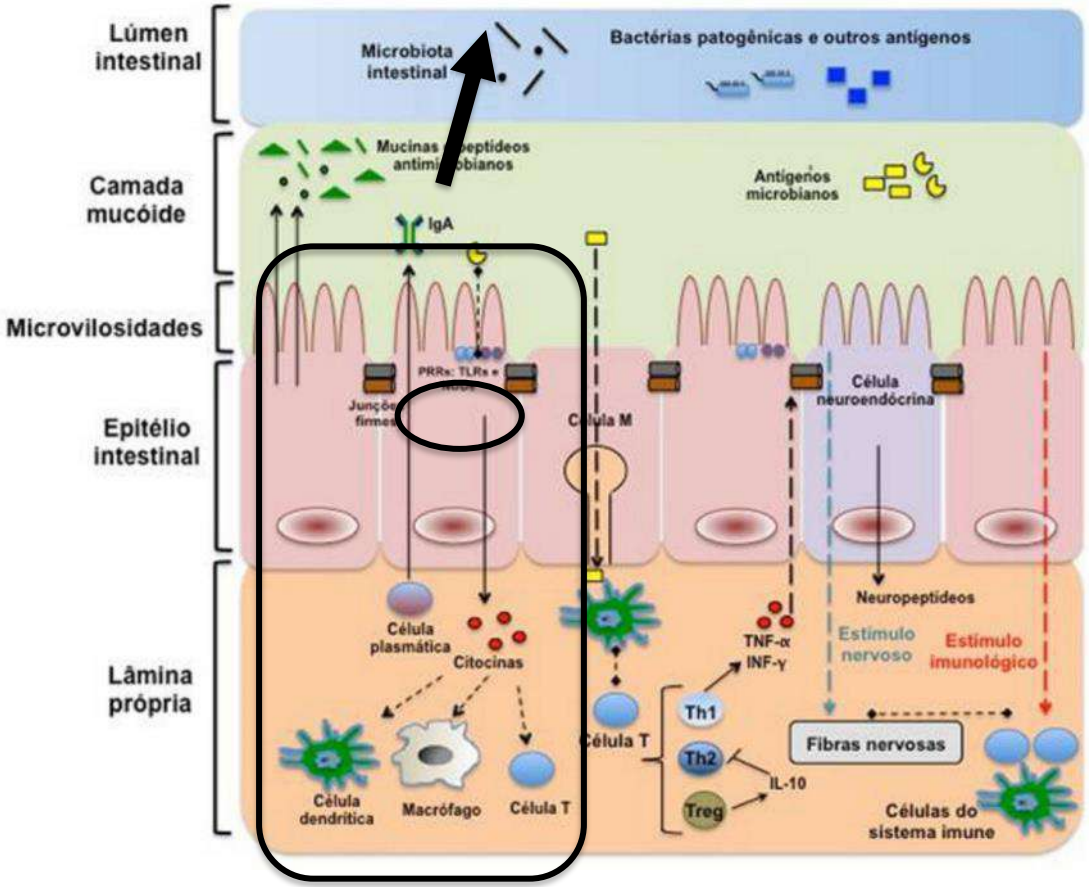
Início da regulação imunológica da barreira:

Cél. caliciformes e cél de Paneth



antígenos ativam

↓

PRR's, TLRs, NODs

↓

liberação de citocinas

↓

ativação cél. Sist. imune

PRR's - receptores de reconhecimento de padrões
TLRs - receptores toll-like
NODs - receptores de domínio de oligomerização de ligação de nucleotídeos

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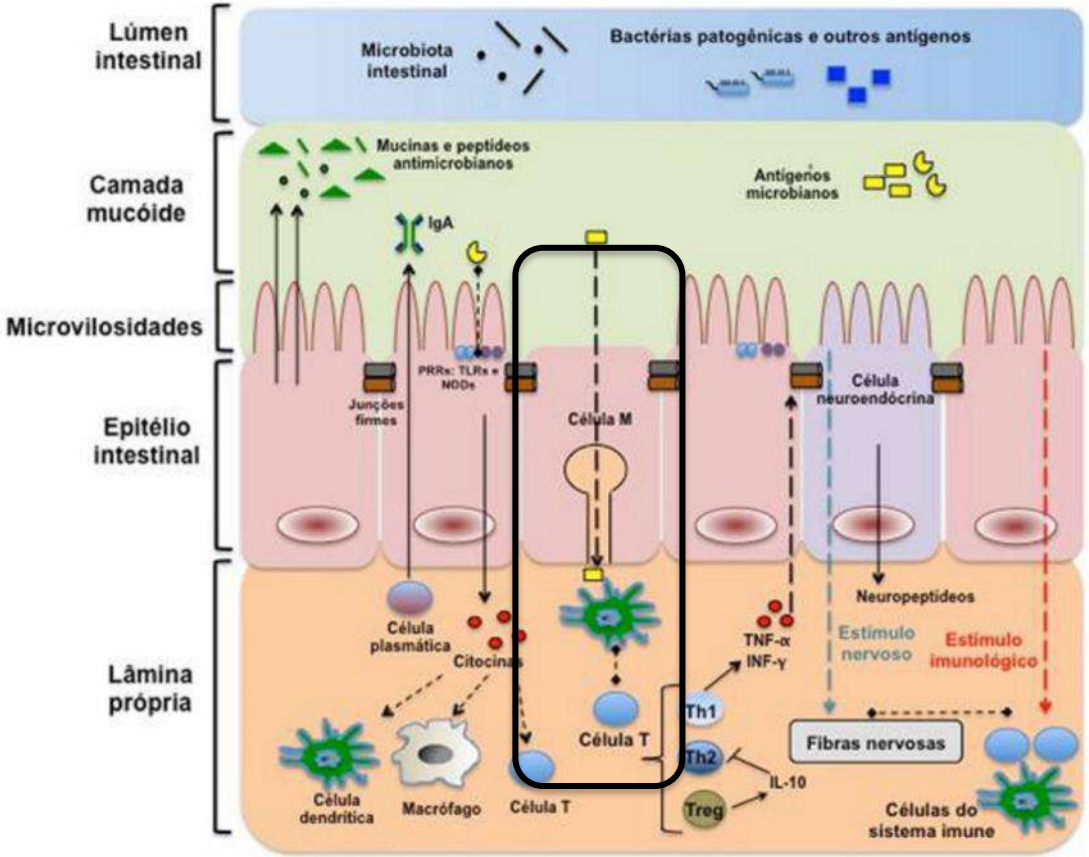
Sistema digestório : integração básico-clínica [livro eletrônico] / Reinaldo Barreto Oriá, Gerly Anne de Castro Brito (org.). -- São Paulo : Blucher, 2016.

Rota alternativa



células M *(especializadas em endocitar e transportar antígenos para a lâmina própria)*

células apresentadoras de antígenos (células dendríticas)

processamento e

indução de células T

Th1, Th2, Treg

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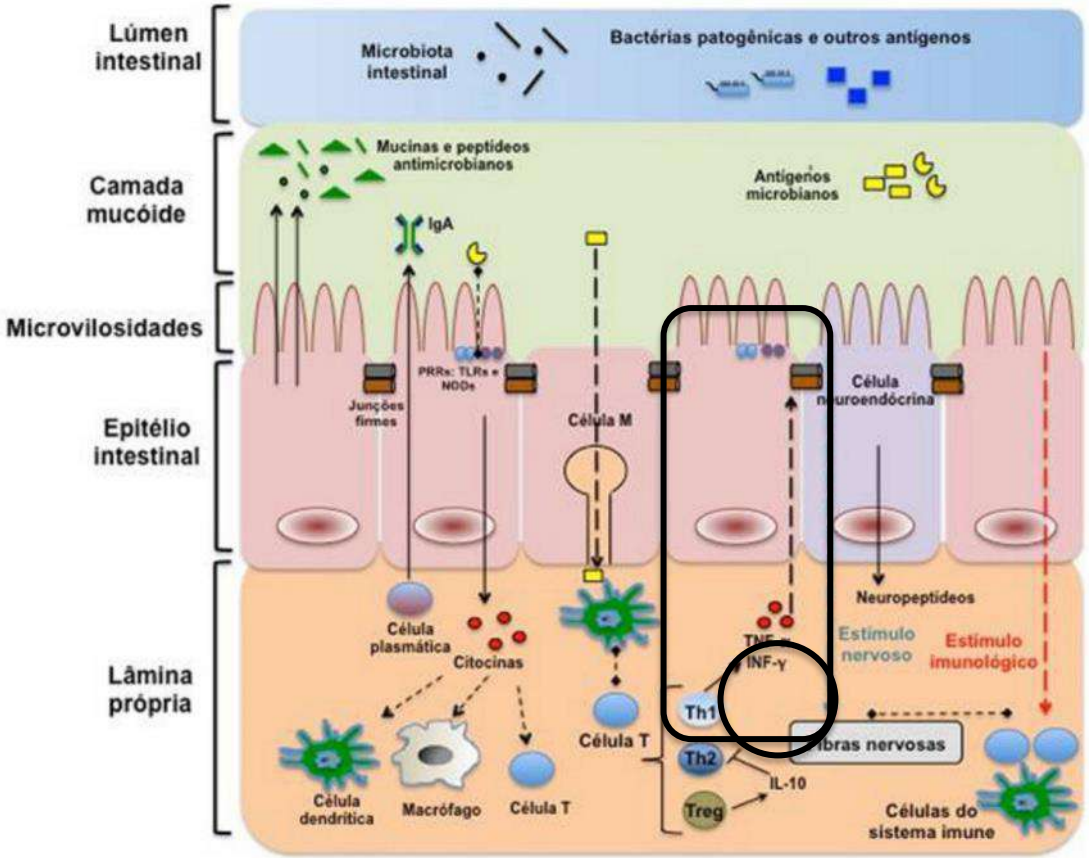
Mediadores Inflamatórios liberados



Citocinas - TNF-α e IFN-γ

↓

Modificação das funções das junções firmes

↓

↑ permeabilidade intestinal

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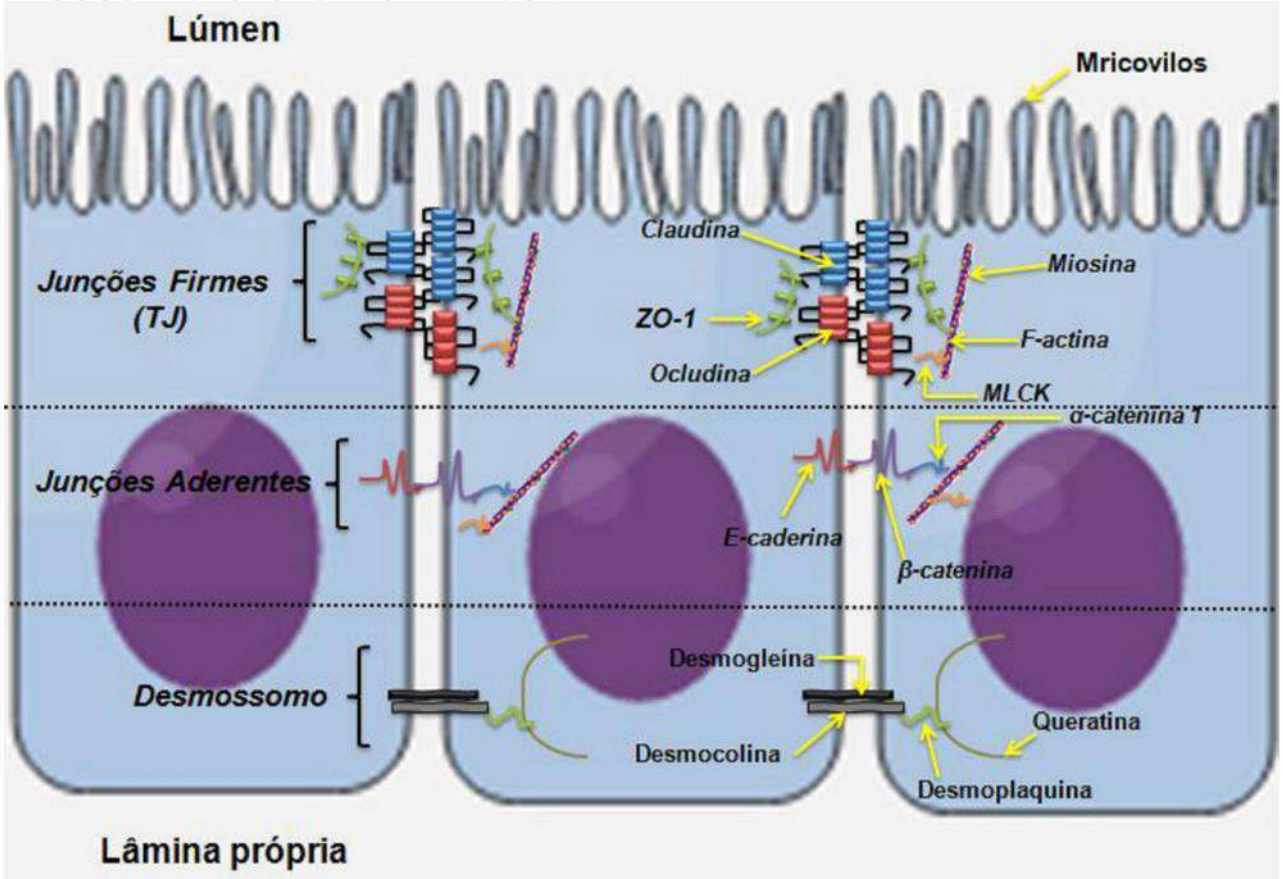
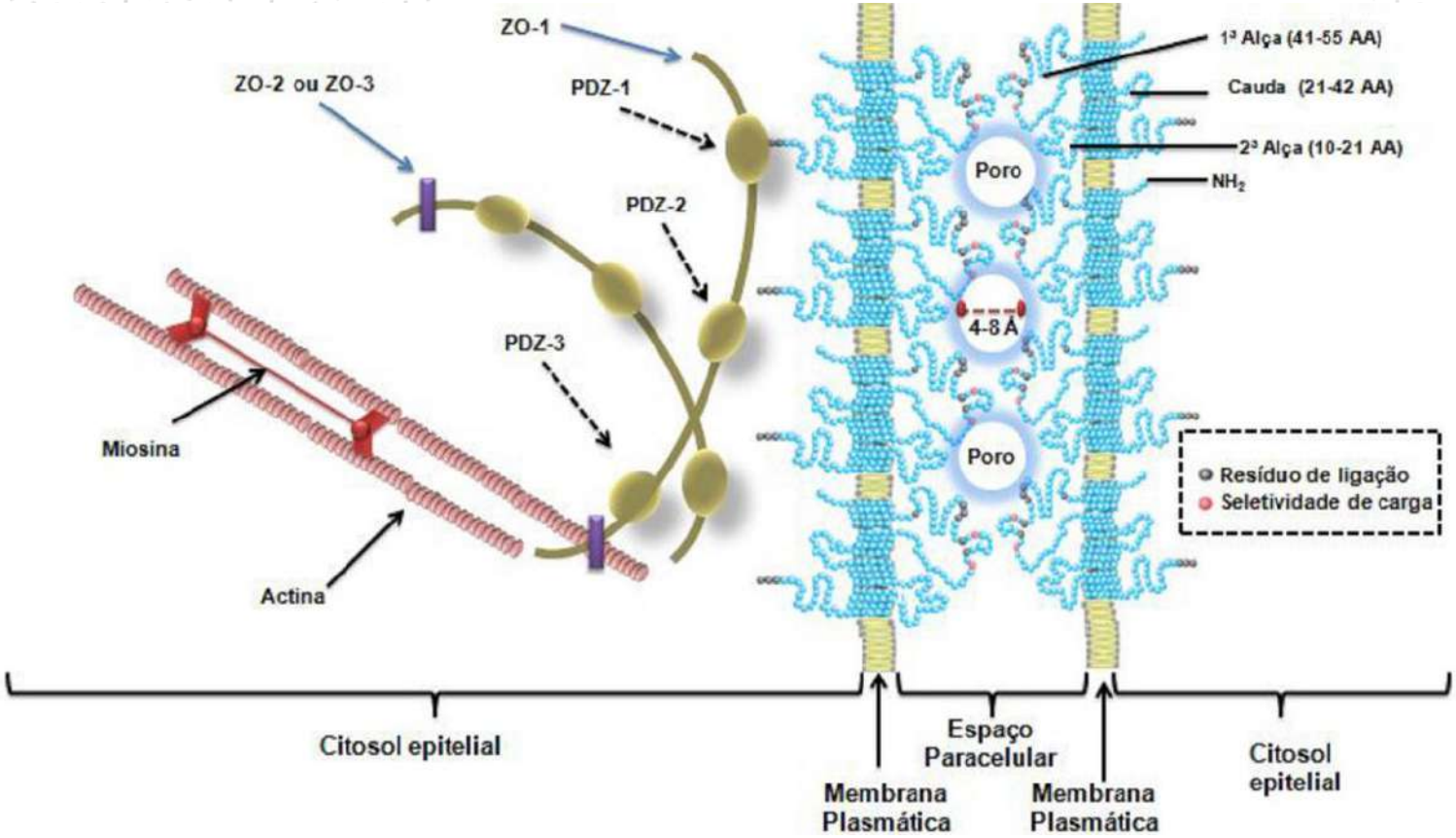
É um pouco mais complexo que isso...



Sistema digestório : integração básico-clínica [livro eletrônico] / Reinaldo Barreto Oriá, Gerly Anne de Castro Brito (org.). -– São Paulo : Blucher, 2016.

CENTRAL nutrition

Ou bem mais que isso...



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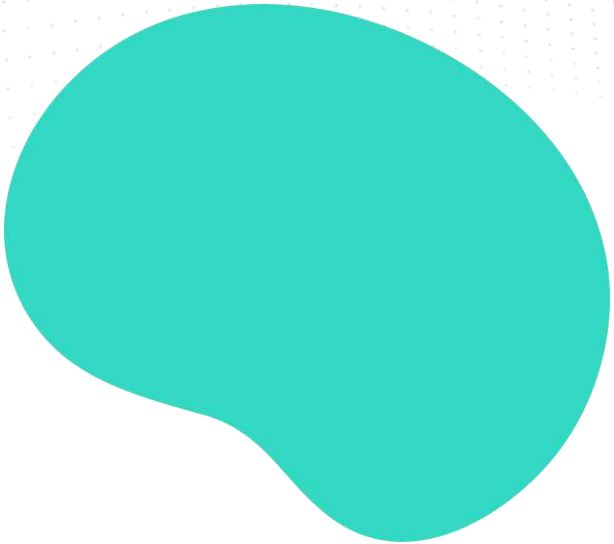
Quem pode ter alterações na permeabilidade intestinal?



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Pacientes estressados!
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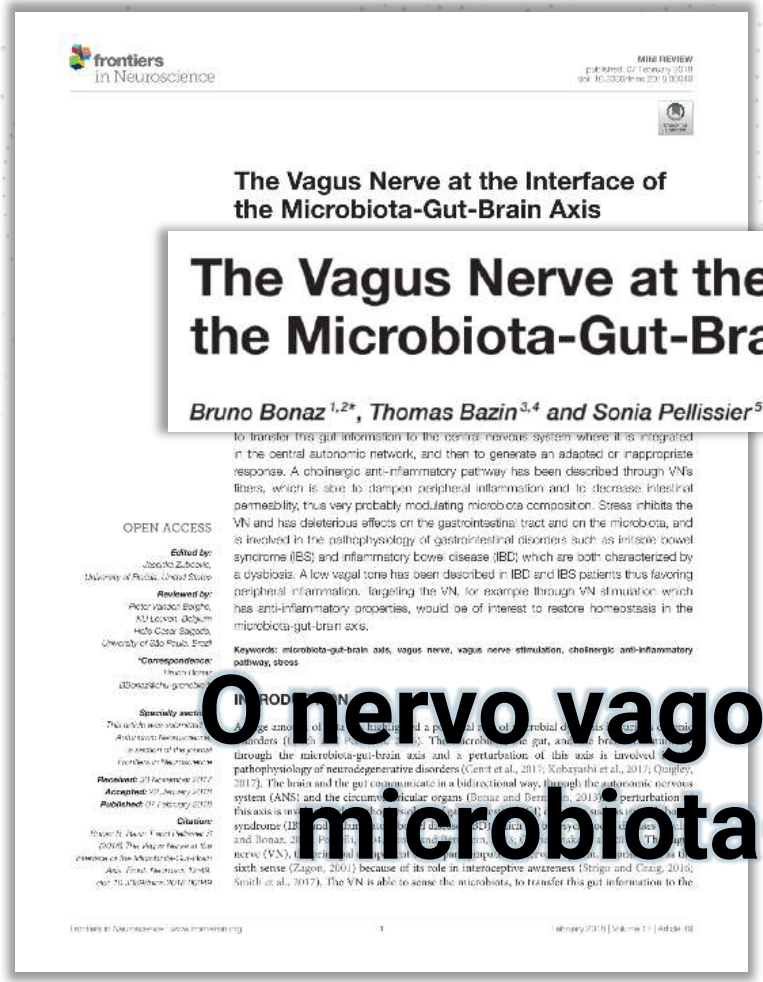
nutrition



frontiers in Neuroscience

MINI REVIEW

The Vagus Nerve at the Interface of the Microbiota-Gut-Brain Axis

The Vagus Nerve at the Interface of the Microbiota-Gut-Brain Axis

Bruno Bonaz[1,2]*, *Thomas Bazin*[3,4] *and Sonia Pellissier*[5]

to transfer this gut information to the central nervous system where it is integrated in the central autonomic network, and then to generate an adapted or inappropriate response. A cholinergic anti-inflammatory pathway has been described through VNs fibers, which is able to dampen peripheral inflammation and to decrease intestinal permeability, thus very probably modulating microbiota composition. Stress inhibits the VN and has deleterious effects on the gastrointestinal tract and on the microbiota, and is involved in the pathophysiology of gastrointestinal disorders such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) which are both characterized by a dysbiosis. A low vagal tone has been described in IBD and IBS patients thus favoring peripheral inflammation. Targeting the VN, for example through VN stimulation which has anti-inflammatory properties, would be of interest to restore homeostasis in the microbiota-gut-brain axis.

Keywords: microbiota-gut-brain axis, vagus nerve, vagus nerve stimulation, cholinergic anti-inflammatory pathway, stress

OPEN ACCESS

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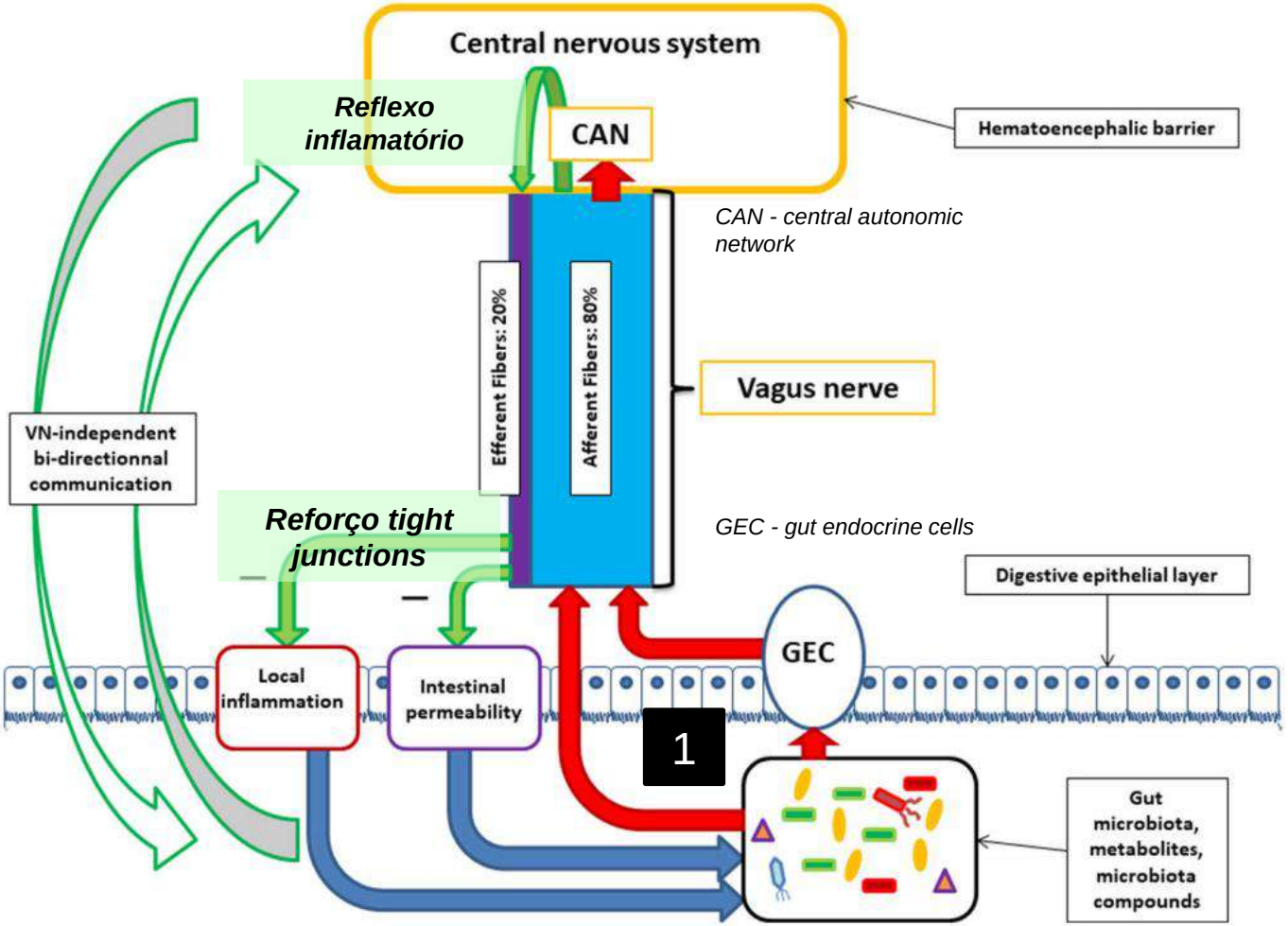
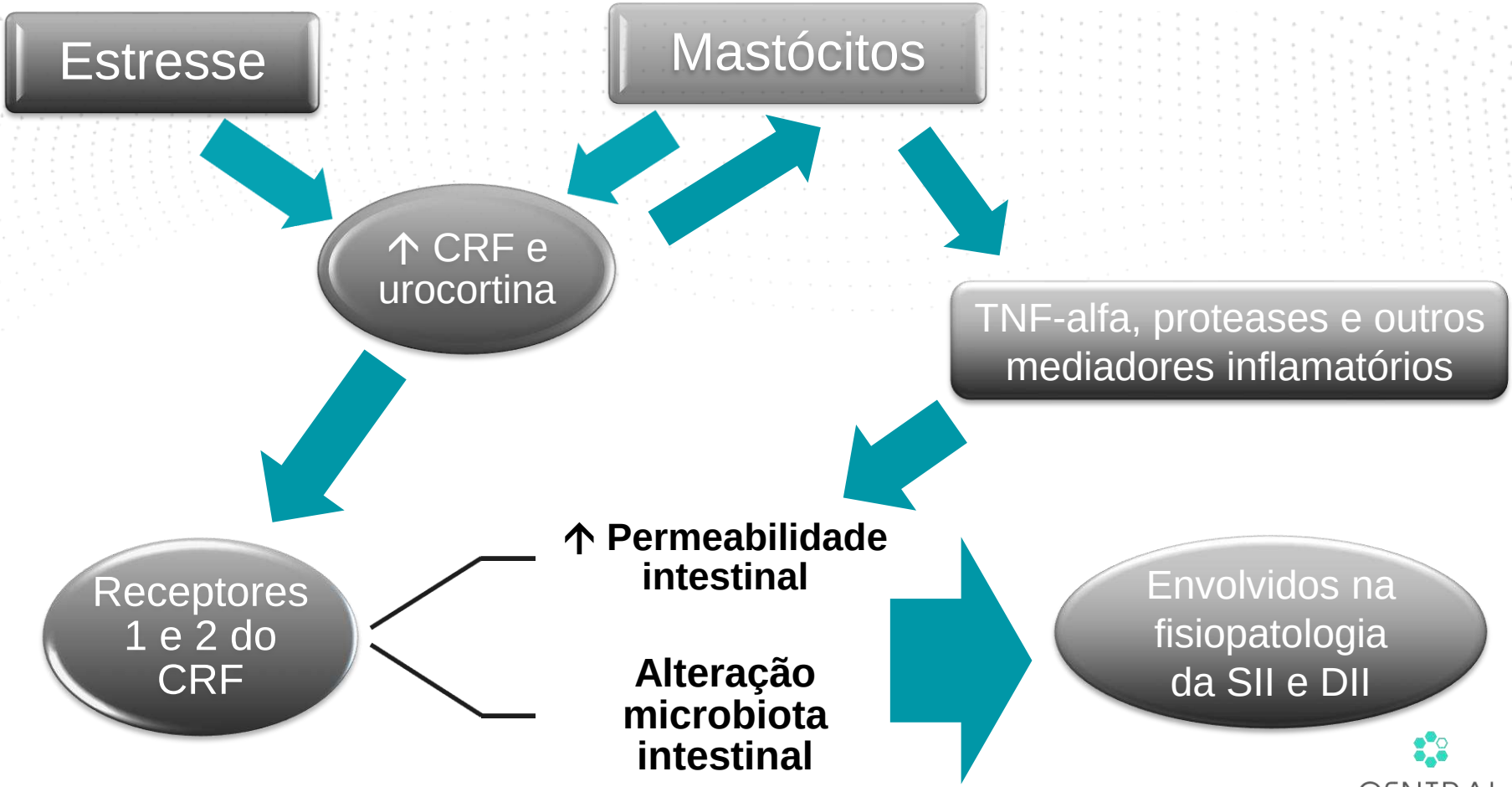
O nervo vago na interface do eixo microbiota-intestino-cérebro

CENTRAL nutrition

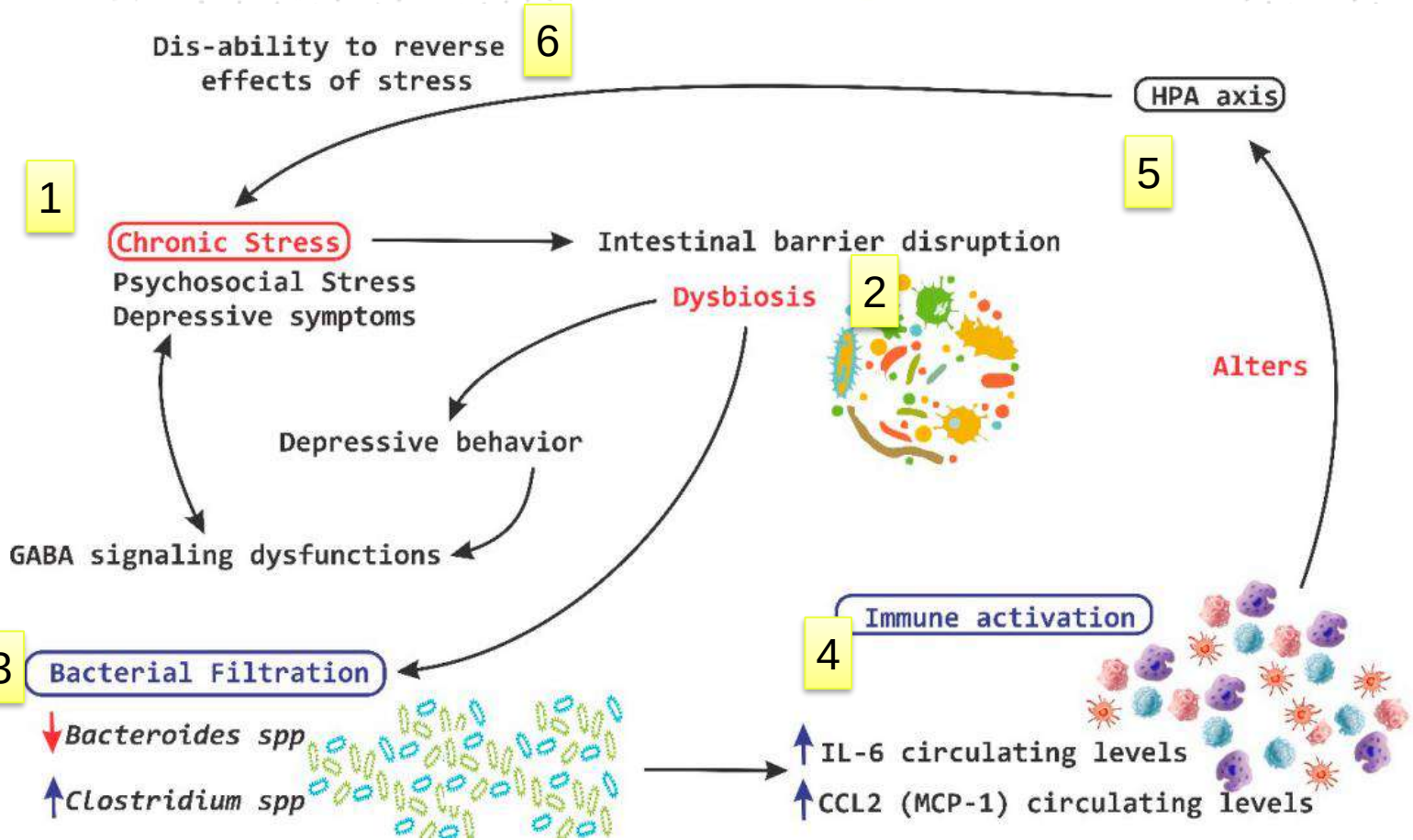


CENTRAL nutrition



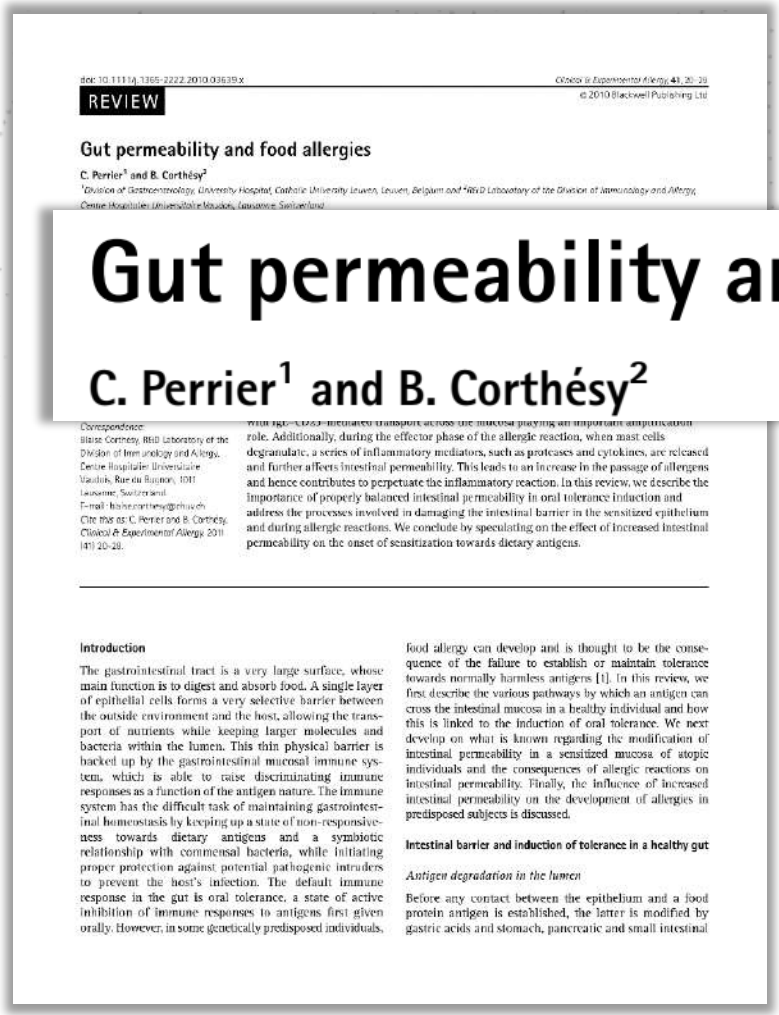
CENTRAL nutrition

Estresse crônico e suas consequências



Nutrients **2019**, *11*, 890;

CENTRAL nutrition



doi: 10.1111/j.1365-2222.2010.03639.x

REVIEW

Clinical & Experimental Allergy, 41, 20–28

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Gut permeability and food allergies

C. Perrier[1] and B. Corthésy[2]

[1]Division of Gastroenterology, University Hospital, Catholic University Leuven, Leuven, Belgium and [2]R&D Laboratory of the Division of Immunology and Allergy, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

with IgA–CD21-mediated transport across the mucosa playing an important amplification role. Additionally, during the effector phase of the allergic reaction, when mast cells degranulate, a series of inflammatory mediators, such as proteases and cytokines, are released and further affects intestinal permeability. This leads to an increase in the passage of allergens and hence contributes to perpetuate the inflammatory reaction. In this review, we describe the importance of properly balanced intestinal permeability in oral tolerance induction and address the processes involved in damaging the intestinal barrier in the sensitized epithelium and during allergic reactions. We conclude by speculating on the effect of increased intestinal permeability on the onset of sensitization towards dietary antigens.

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Introduction

The gastrointestinal tract is a very large surface, whose main function is to digest and absorb food. A single layer of epithelial cells forms a very selective barrier between the outside environment and the host, allowing the transport of nutrients while keeping larger molecules and bacteria within the lumen. This thin physical barrier is backed up by the gastrointestinal mucosal immune system, which is able to raise discriminating immune responses as a function of the antigen nature. The immune system has the difficult task of maintaining gastrointestinal homeostasis by keeping up a state of non-responsiveness towards dietary antigens and a symbiotic relationship with commensal bacteria, while initiating proper protection against potential pathogenic intruders to prevent the host's infection. The default immune response in the gut is oral tolerance, a state of active inhibition of immune responses to antigens first given orally. However, in some genetically predisposed individuals, food allergy can develop and is thought to be the consequence of the failure to establish or maintain tolerance towards normally harmless antigens [1]. In this review, we first describe the various pathways by which an antigen can cross the intestinal mucosa in a healthy individual and how this is linked to the induction of oral tolerance. We next develop on what is known regarding the modification of intestinal permeability in a sensitized mucosa of atopic individuals and the consequences of allergic reactions on intestinal permeability. Finally, the influence of increased intestinal permeability on the development of allergies in predisposed subjects is discussed.

Intestinal barrier and induction of tolerance in a healthy gut

Antigen degradation in the lumen

Before any contact between the epithelium and a food protein antigen is established, the latter is modified by gastric acids and stomach, pancreatic and small intestinal

Gut permeability and food allergies

C. Perrier[1] and B. Corthésy[2]

Pacientes com alergias alimentares

Clinical & Experimental Allergy, **41**, 20–28

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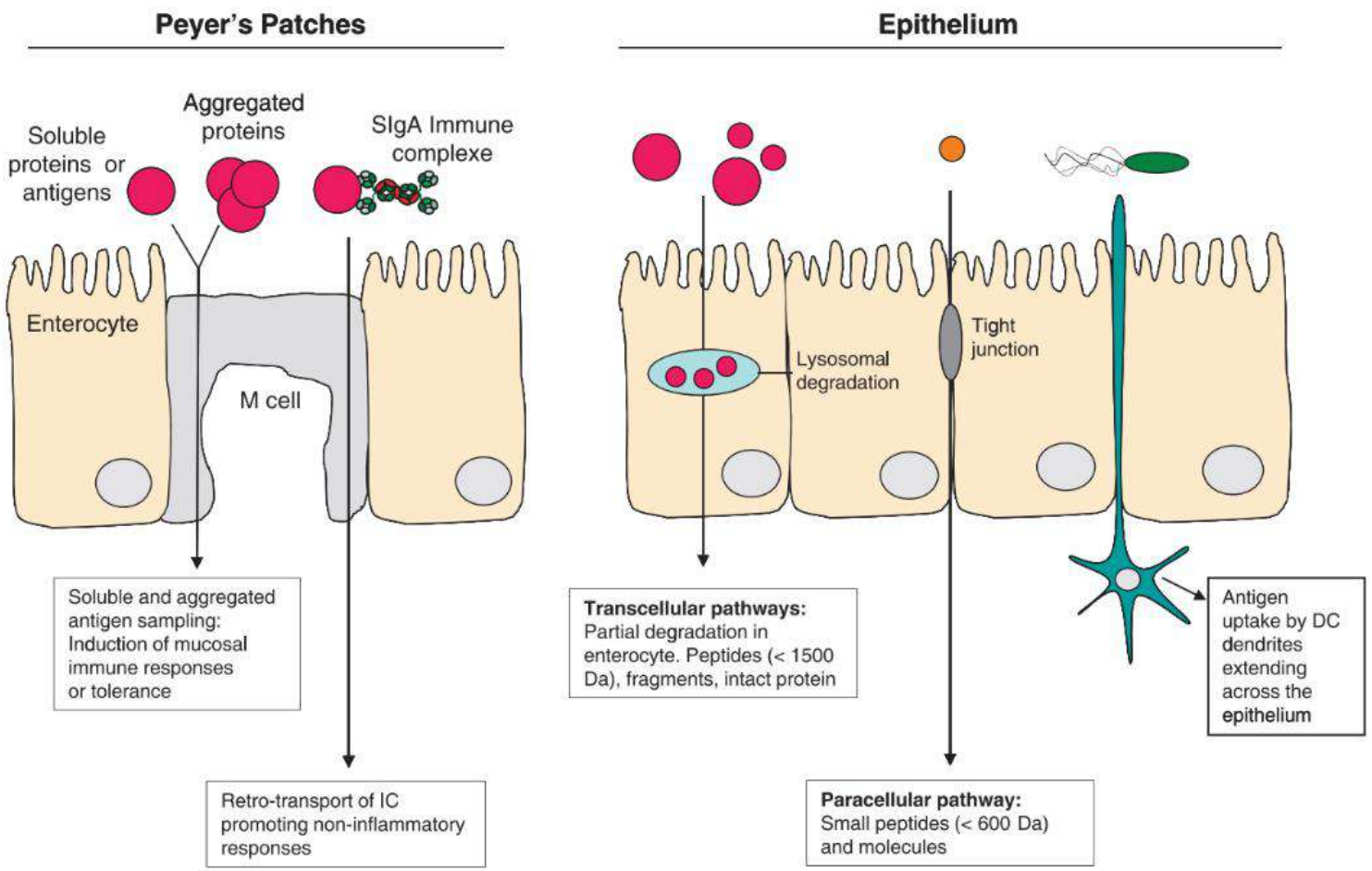

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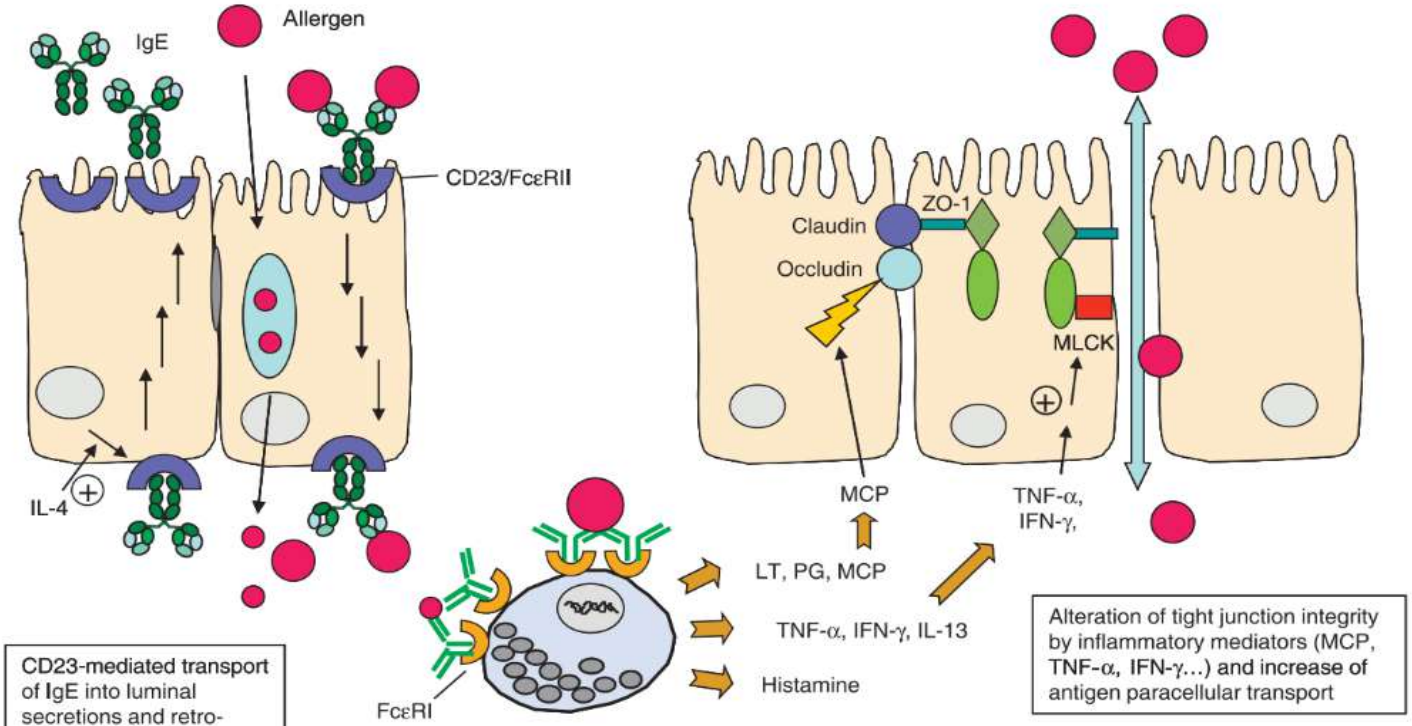
Phase 1: Increased transcellular permeability in sensitized epithelium

Phase 2: Increased paracellular permeability after degranulation of mast cells



CD23-mediated transport of IgE into luminal secretions and retro-transport of allergen-IgE complexes

Release of partially degraded and intact allergen:
- Activation of IgE-loaded mast cells
- Secretion of inflammatory cytokines and mediators

Alteration of tight junction integrity by inflammatory mediators (MCP, TNF-α, IFN-γ…) and increase of antigen paracellular transport

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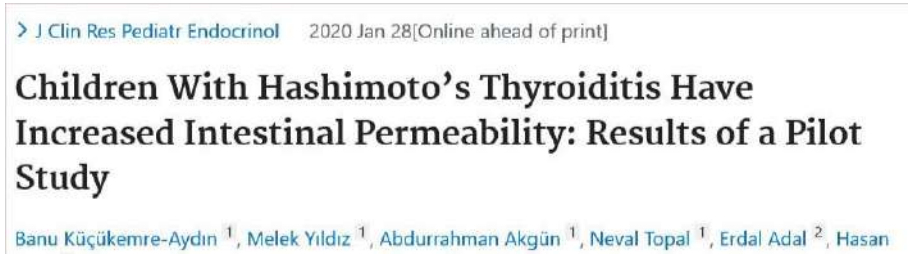
Disease	Increased Intestinal Permeability
Autoimmune Disease	
Dermatitis herpetiformis	87.5%
Ulcerative colitis	10.5-42.9%
Crohn's disease	36%
Systemic sclerosis	34.3%
Type 1 diabetes	30%
Primary biliary cirrhosis	25%



J Clin Res Pediatr Endocrinol 2020 Jan 28[Online ahead of print]

Children With Hashimoto's Thyroiditis Have Increased Intestinal Permeability: Results of a Pilot Study

Banu Küçükemre-Aydın [1], Melek Yıldız [1], Abdurrahman Akgün [1], Neval Topal [1], Erdal Adal [2], Hasan

Association between increased intestinal permeability and disease: A systematic review, *Advances in Integrative Medicine* (2018)

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Liver Related Conditions	
Chronic liver disease with type 2 diabetes	65%
Liver cirrhosis	35%
Chronic liver disease	15-35%
Non-alcoholic fatty liver disease	31%

Diabetes	
Chronic liver disease with type 2 diabetes	65%
Gestational diabetes	37.5%
Type 1 diabetes	30%

Neurological	
Autism	36.7%

Gastrointestinal	
Irritable bowel syndrome	35.6%

Association between increased intestinal permeability and disease: A systematic review, *Advances in Integrative Medicine* (2018)

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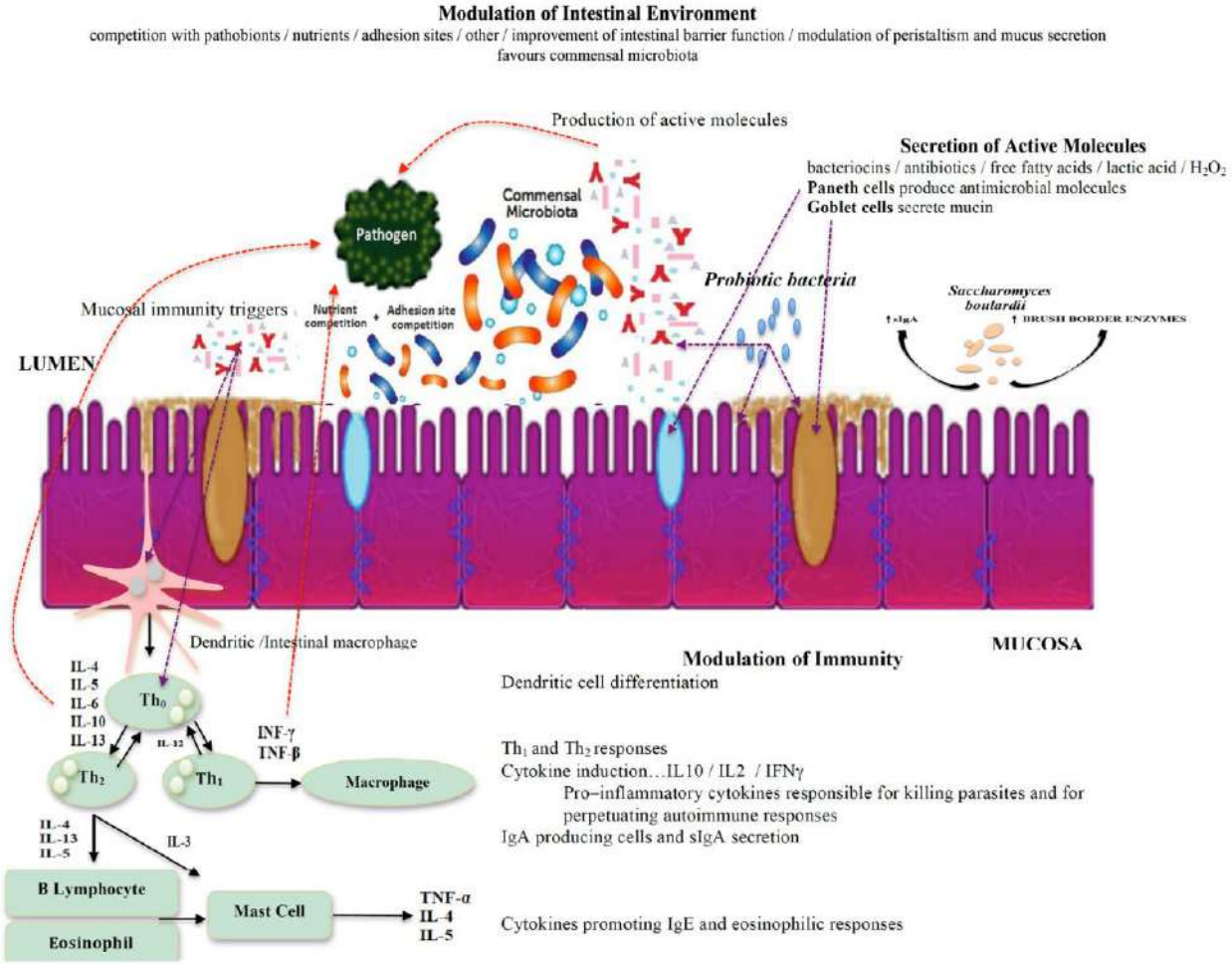
Infecções



J. Clin. Med. **2016**, *5*, 102

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DOI: 10.1111/ijcp.13385

SYSTEMATIC REVIEW

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Risk factors associated with intestinal permeability in an adult population: A systematic review

Bradley Leech | Erica McIntyre | Amie Steel | David Sibbritt

Faculty of Health, Australian Research Centre in Complementary and Integrative Medicine, University of Technology Sydney, Ultimo, New South Wales, Australia

Abstract

Background: Increased intestinal permeability (IP) involves the loss of integrity between the cells of the small intestine. IP has been suggested to contribute to the

and chronic diseases. These risk factors warrant the attention of clinicians and other healthcare providers to aid the identification of potential patients at risk of altered IP. Further research needs to examine whether the identified risk factors are homogeneous with the diagnosis of IP or whether the disease state influences the association.

1 | INTRODUCTION

Increased intestinal permeability (IP) involves the loss of integrity between the cells of the small intestine.[1] The prevalence of altered IP is estimated to be 10%-87%[2] in diseases with a known association compared to about 5% in healthy subjects.[3,4] Furthermore, approximately one in three individuals are suggested to experience IP when diagnosed with a disease associated with IP.[5] Although the concept of IP was first mentioned in the literature during the 1960s[6] and further explored in relation to disease during the 1970s[6] it was not until the 2000s that the mechanism of action for IP development was discovered, providing further clarification into the role IP plays in health and disease.[7] While IP may be considered an emerging health condition that clinicians should be aware of, the consequence of impaired barrier function remains underexamined.[8]

The loss of intestinal integrity occurs when the transmembrane proteins connecting the cells of the small intestine disassemble in response to a cascade of events involving the protein zonulin.[9] As a result of altered IP, particular aspects of disease such as clinical symptoms, severity and activity have been found to be exacerbated in the presence of IP.[9,10] In addition, preliminary evidence suggests that IP may be involved in the pathogenesis of type 1 diabetes,[11,12] Crohn's disease,[13] coeliac disease[14] and diarrhoea-predominant irritable bowel syndrome (IBS-D).[15,16] Altered IP has also

SYSTEMATIC REVIEW

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Risk factors associated with intestinal permeability in an adult population: A systematic review

Bradley Leech | Erica McIntyre | Amie Steel | David Sibbritt

Fatores de risco para Hiperpermeabilidade intestinal

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- 47 estudos
- 4935 indivíduos

“Encontramos mais de 100 fatores de risco associados a hiper permeabilidade intestinal, e muitos, parecem ser aditivos”

Int J Clin Pract. 2019;73(10):e13385.

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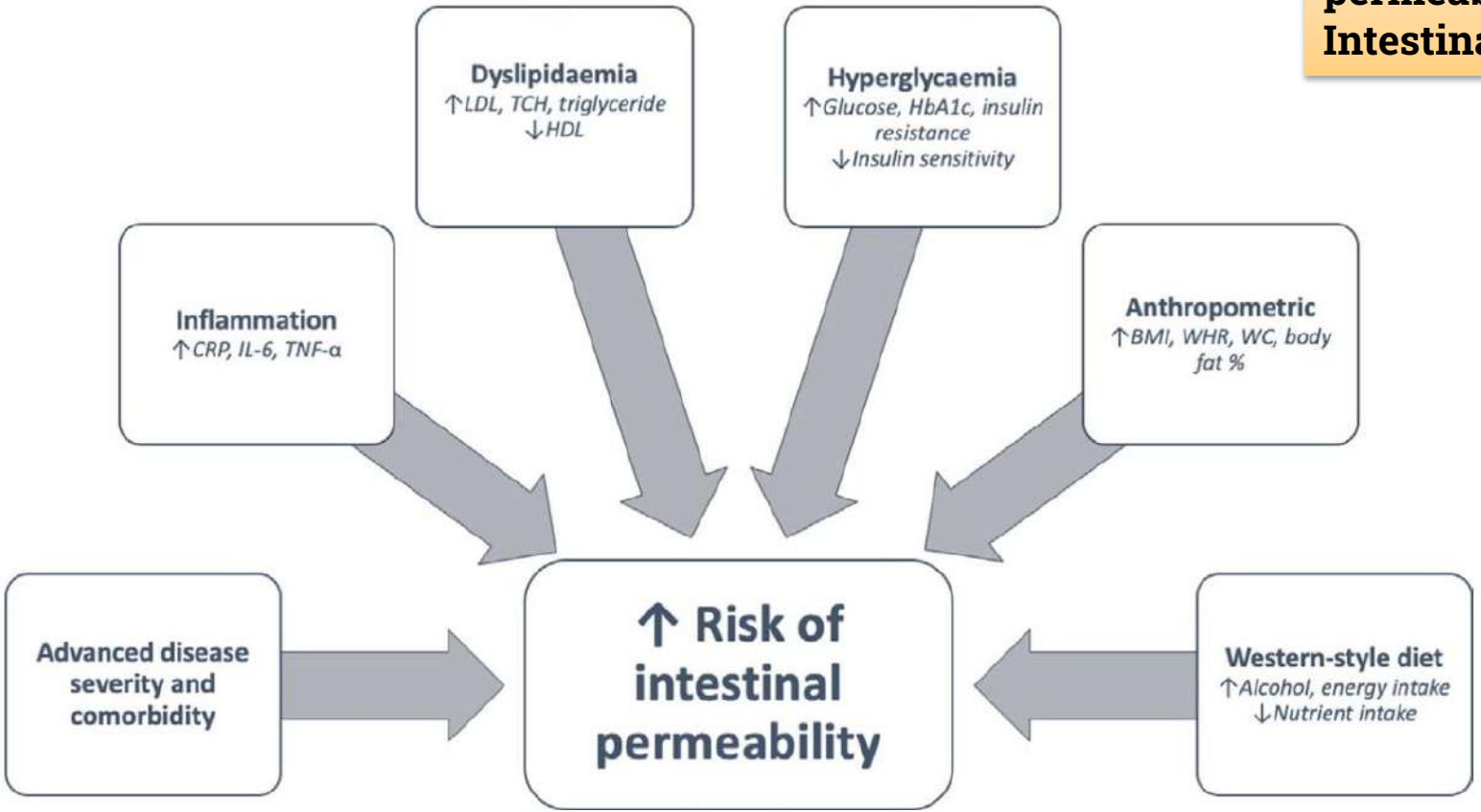
DM, D. Hepática, SM, Drenal e obesidade, SOP, D. celíaca e IMC

Os mais fortes fatores de risco para hiper permeabilidade Intestinal



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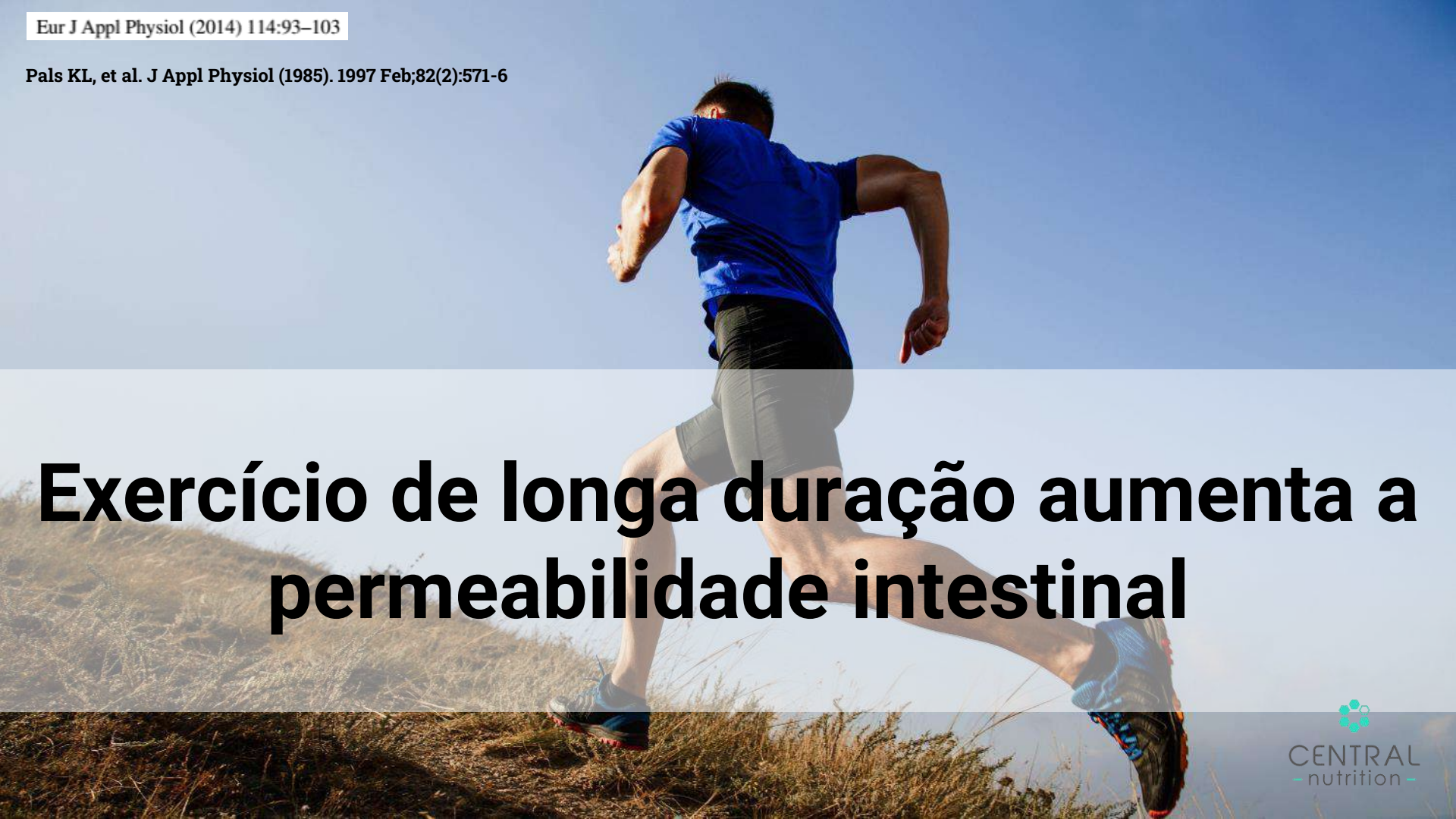

Eur J Appl Physiol (2014) 114:93–103

Pals KL, et al. J Appl Physiol (1985). 1997 Feb;82(2):571-6

Exercício de longa duração aumenta a permeabilidade intestinal

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Sports Med (2017) 47:1389–1403
DOI 10.1007/s40279-016-0654-2

SYSTEMATIC REVIEW

Association Between Exercise-Induced Hyperthermia and Intestinal Permeability: A Systematic Review

Association Between Exercise-Induced Hyperthermia and Intestinal Permeability: A Systematic Review

toxins to translocate through the intestinal barrier and reach the bloodstream. When recognized by the immune system, these endotoxins trigger a systemic inflammatory response that may affect physical performance and, in severe cases, induce heat stroke. However, it remains to be elucidated whether there is a relationship between the magnitude of exercise-induced hyperthermia and changes in intestinal permeability.

intestinal permeability.

Methods The present systematic review screened the MEDLINE/PubMed and Web of Science databases in September 2016, without any date restrictions. Sixteen studies that were performed in healthy participants, presented original data, and measured both the exercise-induced changes in T_{Core} and intestinal permeability were selected. These studies assessed intestinal permeability through the measurement of sugar levels in the urine and measurement of intestinal fatty acid binding protein or lipopolysaccharide levels in the blood.

Results Exercise increased both T_{Core} and intestinal permeability in most of the 16 studies. In addition, a positive and strong correlation was observed between the two parameters ($r = 0.793$; $p < 0.001$), and a T_{Core} exceeding 39 °C was always associated with augmented permeability.

Conclusion The magnitude of exercise-induced hyperthermia is directly associated with the increase in intestinal permeability.

W. Pires and C. E. Veneroso contributed equally to this work.

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Deveríamos parar de fazer exercício??
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Lira et al. Lipids in Health and Disease 2010, 9:82

RESEARCH Open Access

Endotoxin levels correlate positively with a sedentary lifestyle and negatively with highly trained subjects

Fabio S Lira[1*], Jose C Rosa[1], Gustavo D Pimentel[1], Hélio A Souza[2], Erico C Caperuto[3], Luiz C Carnevali Jr[2], Marília Seelaender[2], Ana R Damaso[4], Lila M Oyama[1,4], Marco T de Mello[5], Ronaldo V Santos[4*]

Endotoxemia em indivíduos sedentários e em altamente treinados

UNIFESP

USP Universidade de São Paulo

Mackenzie

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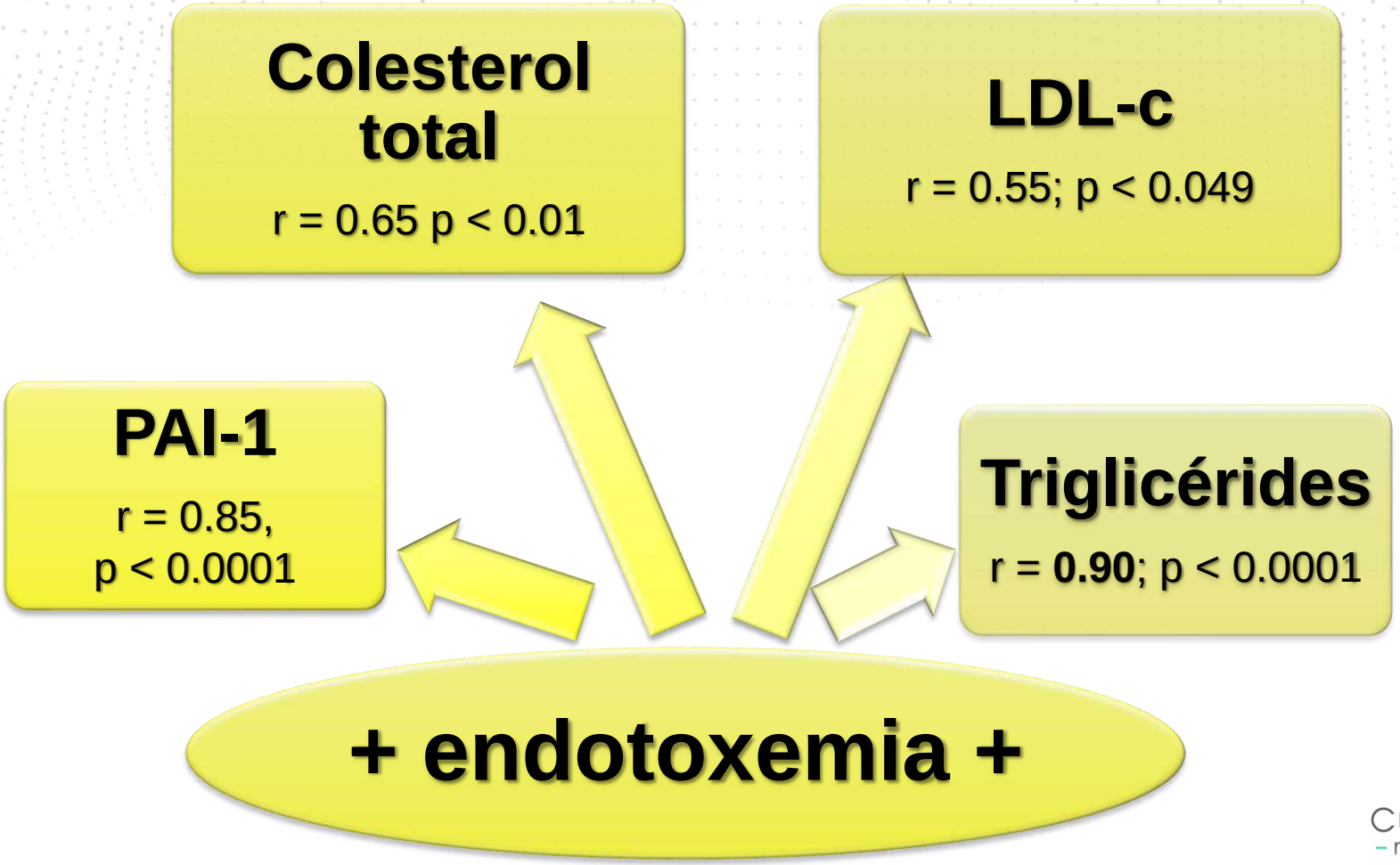

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Environ Health Perspect 118:976–981 (2010).

Polychlorinated Biphenyls Disrupt Intestinal Integrity via NADPH Oxidase-Induced Alterations of Tight Junction Protein Expression

Yean Jung Choi,[1] Melissa J. Seelbach,[1] Hong Pu,[1] Sung Yong Eum,[1] Lei Chen,[1] Bei Zhang,[1] Bernhard Hennig,[2] and Michal Toborek[1]

[1]Molecular Neuroscience and Vascular Biology Laboratory, Department of Neurosurgery, and [2]College of Agriculture, University of Kentucky, Lexington, Kentucky, USA

PCB's alteram proteínas das junções apertadas e desorganizam integridade intestinal

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› Environ Sci Pollut Res Int, 25 (23), 22529-22540 Aug 2018

Use of a Combination of in Vitro Models to Investigate the Impact of Chlorpyrifos and Inulin on the Intestinal Microbiota and the Permeability of the Intestinal Mucosa

Marina Réquilé [1 2], Dubàn O Gonzàlez Alvarez [1 2], Stéphane Delanaud [1], Larbi Rhazi [2], Véronique Bach [1], Flore Depeint [2], Hafida Khorsi-Cauet [3]

Organofosforado aumenta a permeabilidade intestinal

› PLoS One, 9 (7), e102217 2014 Jul 14 eCollection 2014

Increased Gut Permeability and Bacterial Translocation After Chronic Chlorpyrifos Exposure in Rats

Claire Joly Condette [1], Hafida Khorsi-Cauet [1], Patrice Morlière [2], Luciane Zabijak [3], Julie Reygner [1], Véronique Bach [1], Jérôme Gay-Quéheillard [1]

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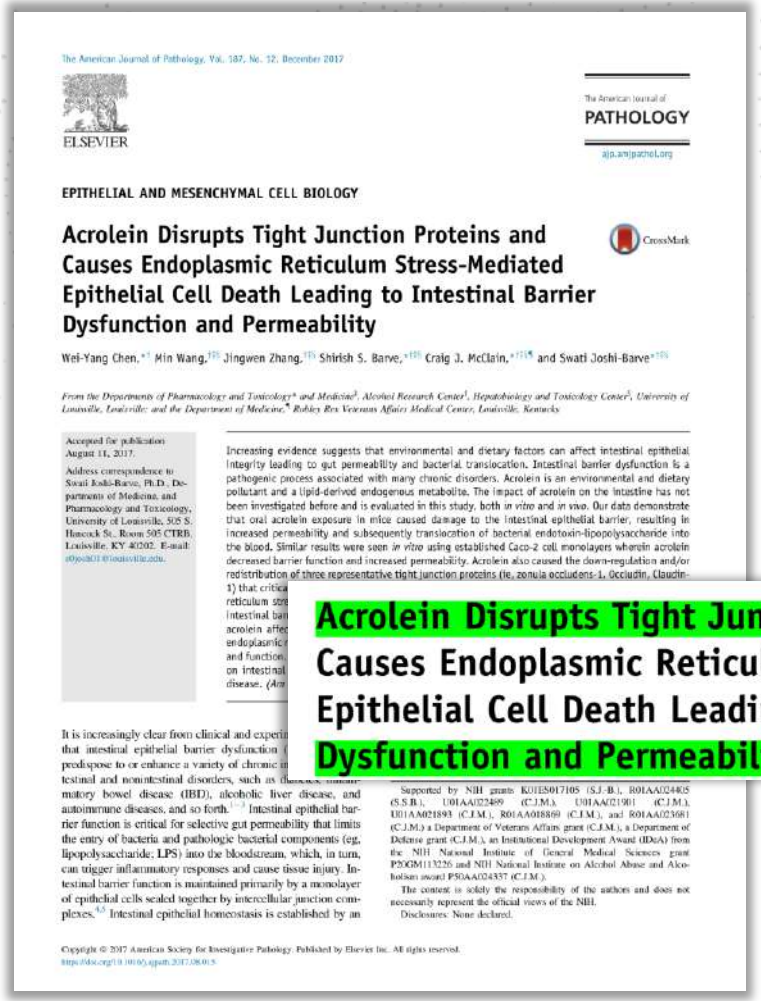

The American Journal of Pathology, Vol. 187, No. 12, December 2017

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The American Journal of PATHOLOGY

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EPITHELIAL AND MESENCHYMAL CELL BIOLOGY

Acrolein Disrupts Tight Junction Proteins and Causes Endoplasmic Reticulum Stress-Mediated Epithelial Cell Death Leading to Intestinal Barrier Dysfunction and Permeability

Wei-Yang Chen,*† Min Wang,†‡§ Jingwen Zhang,†‡§ Shirish S. Barve,*†‡§ Craig J. McClain,*†‡¶ and Swati Joshi-Barve*†‡§

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Accepted for publication August 11, 2017.

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Increasing evidence suggests that environmental and dietary factors can affect intestinal epithelial integrity leading to gut permeability and bacterial translocation. Intestinal barrier dysfunction is a pathogenic process associated with many chronic disorders. Acrolein is an environmental and dietary pollutant and a lipid-derived endogenous metabolite. The impact of acrolein on the intestine has not been investigated before and is evaluated in this study, both *in vitro* and *in vivo*. Our data demonstrate that oral acrolein exposure in mice caused damage to the intestinal epithelial barrier, resulting in increased permeability and subsequently translocation of bacterial endotoxin-lipopolysaccharide into the blood. Similar results were seen *in vitro* using established Caco-2 cell monolayers wherein acrolein decreased barrier function and increased permeability. Acrolein also caused the down-regulation and/or redistribution of three representative tight junction proteins (ie, zonula occludens-1, Occludin, Claudin-1) that critica
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intestinal bar
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and function
on intestinal
disease. (*Am*

It is increasingly clear from clinical and experi
that intestinal epithelial barrier dysfunction
predispose to or enhance a variety of chronic
testinal and nonintestinal disorders, such as
matory bowel disease (IBD), alcoholic liver disease, and autoimmune diseases, and so forth.[1–3] Intestinal epithelial barrier function is critical for selective gut permeability that limits the entry of bacteria and pathologic bacterial components (eg, lipopolysaccharide; LPS) into the bloodstream, which, in turn, can trigger inflammatory responses and cause tissue injury. Intestinal barrier function is maintained primarily by a monolayer of epithelial cells sealed together by intercellular junction complexes.[4,5] Intestinal epithelial homeostasis is established by an

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The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Disclosures: None declared.

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Acrolein Disrupts Tight Junction Proteins and Causes Endoplasmic Reticulum Stress-Mediated Epithelial Cell Death Leading to Intestinal Barrier Dysfunction and Permeability

Acroleína desorganiza proteínas das junções apertadas, levando ao aumento da permeabilidade intestinal

(Am J Pathol 2017, 187: 2686–2697;

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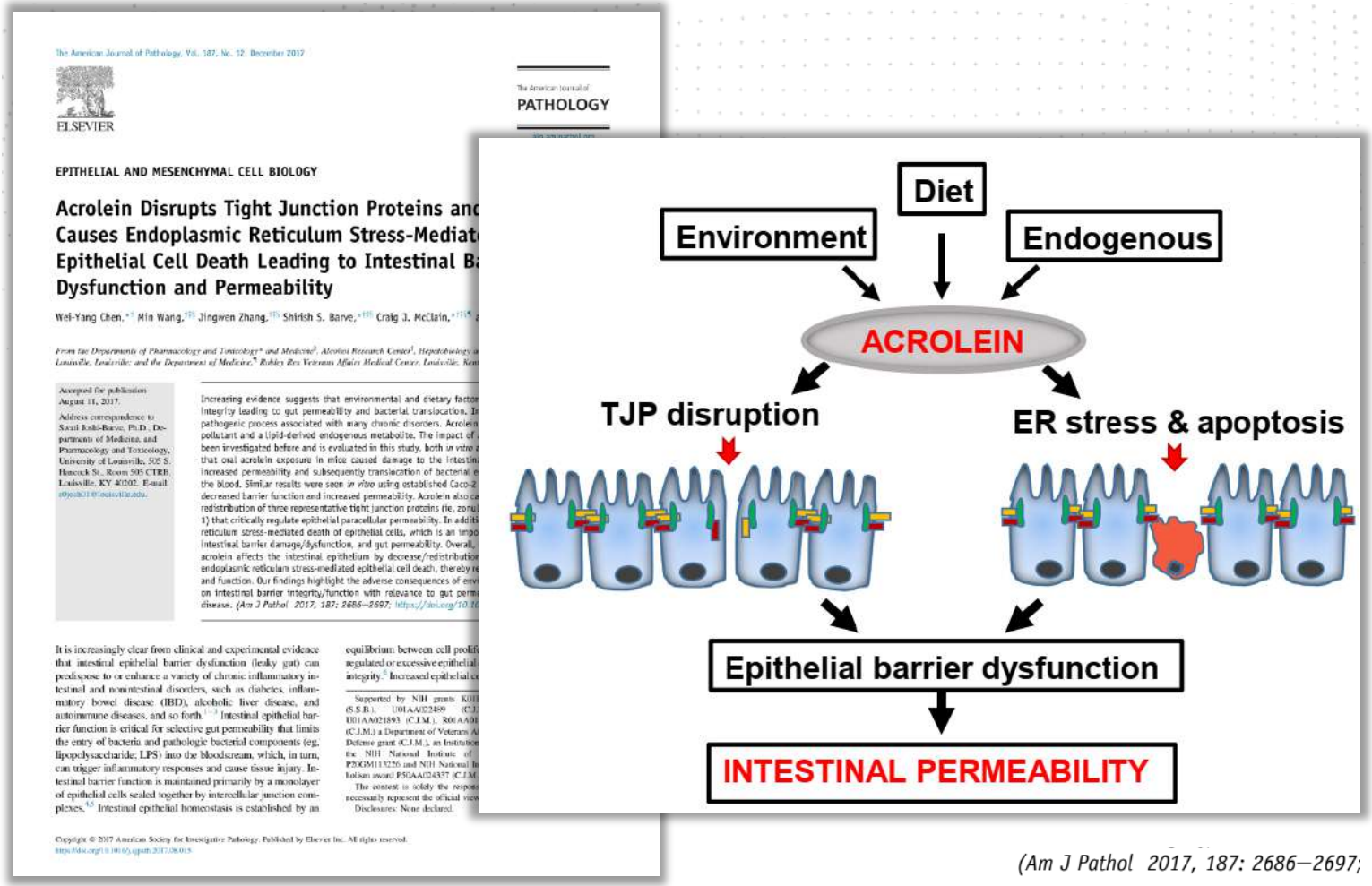

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EPITHELIAL AND MESENCHYMAL CELL BIOLOGY

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Wei-Yang Chen,* Min Wang,† Jingwen Zhang,† Shirish S. Barve,*† Craig J. McClain,*†‡

From the Departments of Pharmacology and Toxicology and Medicine†, Alcohol Research Center‡, Hepatobiology and Toxicology Center§, University of Louisville, Louisville; and the Department of Medicine,¶ Robley Rex Veterans Affairs Medical Center, Louisville, Kentucky*

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Increasing evidence suggests that environmental and dietary factors ... integrity leading to gut permeability and bacterial translocation. ... pathogenic process associated with many chronic disorders. Acrolein ... pollutant and a lipid-derived endogenous metabolite. The impact of ... been investigated before and is evaluated in this study, both *in vitro* ... that oral acrolein exposure in mice caused damage to the intestinal ... increased permeability and subsequently translocation of bacterial ... the blood. Similar results were seen *in vitro* using established Caco-2 ... decreased barrier function and increased permeability. Acrolein also ... redistribution of three representative tight junction proteins (ie, zonu... 1) that critically regulate epithelial paracellular permeability. In addit... reticulum stress-mediated death of epithelial cells, which is an impo... Intestinal barrier damage/dysfunction, and gut permeability. Overall, ... acrolein affects the intestinal epithelium by decrease/redistributio... endoplasmic reticulum stress-mediated epithelial cell death, thereby r... and function. Our findings highlight the adverse consequences of env... on intestinal barrier integrity/function with relevance to gut perm... disease. *(Am J Pathol 2017, 187: 2686–2697;* https://doi.org/10.10...

It is increasingly clear from clinical and experimental evidence that intestinal epithelial barrier dysfunction (leaky gut) can predispose to or enhance a variety of chronic inflammatory intestinal and nonintestinal disorders, such as diabetes, inflammatory bowel disease (IBD), alcoholic liver disease, and autoimmune diseases, and so forth.[1–3] Intestinal epithelial barrier function is critical for selective gut permeability that limits the entry of bacteria and pathologic bacterial components (eg, lipopolysaccharide; LPS) into the bloodstream, which, in turn, can trigger inflammatory responses and cause tissue injury. Intestinal barrier function is maintained primarily by a monolayer of epithelial cells sealed together by intercellular junction complexes.[4,5] Intestinal epithelial homeostasis is established by an equilibrium between cell proli... regulated or excessive epithelial ... integrity.[6] Increased epithelial ce...

Supported by NIH grants K01... (S.S.B.), U01AA022489 (C.J.... U01AA021893 (C.J.M.), R01AA0... (C.J.M.) a Department of Veterans A... Defense grant (C.J.M.), an Institution... the NIH National Institute of ... P30GM113226 and NIH National In... Isotsin award P50AA024337 (C.J.M.

The content is solely the respo... necessarily represent the official view...

Disclosures: None declared.

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(Am J Pathol 2017, 187: 2686–2697;

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Am J Physiol Gastrointest Liver Physiol. 2013 Jul 1;305(1):G95-G105.

Bebidas alcoólicas aumentam a permeabilidade intestinal

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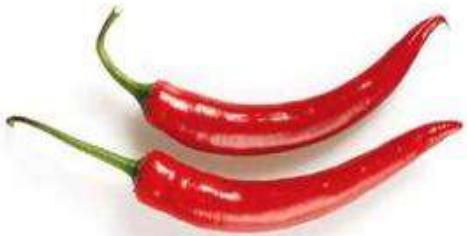
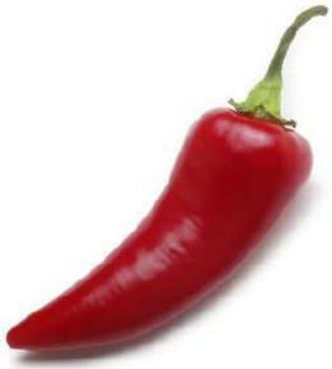
Capsaicina aumenta a permeabilidade intestinal

Pimenta caiena



Pimenta Chili



Paprica

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Dementia and Geriatric Cognitive Disorders
Dement Geriatr Cogn Disord Extra 2018;8:360–381
Published by S. Karger AG, Basel
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Review Article

Current Perspectives and Mechanisms of Relationship between Intestinal Microbiota Dysfunction and Dementia: A Review

Menizibeya O. Welcome

Department of Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Nile University of Nigeria, Abuja, Nigeria

Keywords
Dementia · Intestinal microbiota · Dysbiome repertoire · Gut-brain axis · Microbiota-brain axis

Abstract
Background: Accumulating data suggest a crucial role of the intestinal microbiota in the de-

Current Perspectives and Mechanisms of Relationship between Intestinal Microbiota Dysfunction and Dementia: A Review

Menizibeya O. Welcome

KARGER

Dement Geriatr Cogn Disord Extra 2018;8:360–381

Relação entre disfunção da microbiota intestinal, barreira intestinal e demência

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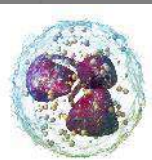
Dement Geriatr Cogn Disord Extra 2018;8:360–381

Perda de **neurônios**, **astrócitos**, **micróglia**, **células endoteliais** e **perícitos**

Alt. expressão claudinas e outros componentes da membrana da BHE, ↑ **desenvolvimento** de várias **neurodegenerativas, incluindo Alzheimer** (pela translocação desregulada de metabólitos tóxicos)



Resposta imune ↑

Dano ao endotélio da BHE (alt. expressão das claudinas)

Podem destruir os complexos juncionais do epitélio intestinal, aumentando a permeabilidade

Compostos contendo enxofre e fenol

Amônia

p-cresol sulfato

indoxil sulfato

Ác. indol-3 acético

Fenilacetilglutamina

Acroleína

Putrescina

Agmatina

N-óxido de trimetilamina

Hipurato

D-amino ácidos

Tiramina

Cadaverina

Camilleri M. *Gut* 2019;**68**:1516–1526

Resumo de doenças situações com aumento da permeabilidade intestinal

Table 3 Summary of diseases or disorders with increased intestinal permeability

Condition	Small intestinal or colonic barrier function: IP probe molecules or epithelial damage	Serum biomarkers
Ageing	No difference in LMR or most TJ protein expression, but increased claudin 2 expression and decreased transepithelial resistance in ileal biopsies ex vivo.[83]	↑ Zonulin[84]
Food allergy	↑ LMR threefold versus health.[86] ↑ LMR 38% in children with food allergy.[87]	
Eosinophilic oesophagitis	Increased small bowel IP based on lactulose absorption[57] but not LMR in adults[57 58] or in children[89]; ex vivo assessment of duodenal mucosal integrity was normal.[58]	
Liver diseases		
NAFLD/NASH	↑ LMR or ^{51}Cr-EDTA in 39% of 139 patients with NAFLD (SRMA five studies).[62]	↑ LPS in 42% of NASH[93]; ↑ LPS in NAFLD associated with SIBO.[94]
Cirrhosis		
Sclerosing cholangitis	LRR normal (83% (19/22) with quiescent IBD).[97]	Higher serum I-FABP associated with IgA a against F-actin.[98]
TPN or enteral deprivation	↑ FITC-Dextran I.P. ex vivo; ↓ ZO-1, E-cadherin and claudin-4 in unfed segments in paediatric patients[99]; ↓ ZO-1 and villus height in mice.[100]	
Neurological diseases		
Alzheimer		
Parkinson	Downregulation of occludin not ZO-1 in colonic mucosa; however, flux of sulfonic acid and horseradish peroxidase not abnormal with or without Lewy bodies[107]; LMR normal, but ↑ 24 hours urinary sucralose (marker of total intestinal permeability).[108]	Lower plasma levels of LPS binding protein indirect measure of systemic endotoxin exp
ALS	↑ LPS in most severe amyotrophic lateral sclerosis.[111]	Low diversity of the microbiome compared with healthy cohorts; low *Ruminococcus* spp. in 3/5 patients with low F/B ratio.[112]
Psychiatric diseases	Plasma levels of LPS, zonulin and FABP2 were each significantly elevated in depression/anxiety patients compared with non-depressed or anxious controls.[114]	A review documents extensive literature on cross-sectional and longitudinal studies documenting association between stool microbiota and anxiety and depression.[115] A review documents studies of the microbiome and microbial translocation in patients with schizophrenia and bipolar disorder.[116]

1. **Envelhecimento**
2. Alergia alimentar
3. Esofagite eosinofílica
4. **EHNA**
5. **Esteato hepatite**
6. **Cirrose**
7. **Colangite esclerosante**
8. Nutrição parenteral total / privação enteral
9. **Alzheimer**
10. **Parkinson**
11. Esclerose Lateral Amiotrófica
12. **Depressão / ansiedade**

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Clinical and Translational Gastroenterology (2016) 7, e196; doi:10.1038/ctg.2016.54

Citation: Clinical and Translational Gastroenterology (2016) 7, e196; doi:10.1038/ctg.2016.54

www.nature.com/ctg

Human Intestinal Barrier Function in Health and Disease

Julia König, PhD[1], Jerry Wells[2], Patrice D. Cani[3], Clara L
Jacqueline Whyte, PhD[5], Freddy Troost[1] and Robert-Jan

The gastrointestinal tract consists of an enormous s
electrolytes from food. At the same time, it needs to pro
against a reaction to omnipresent harmless compounds
disorders. In this review, the role of intestinal permea
inflammatory bowel disease, irritable bowel syndrome,
be discussed. In addition, the effect of the frequently pr
drugs on intestinal permeability, as well as commonly
Clinical and Translational Gastroenterology (2016) 7, e196

INTRODUCTION

The intestine is the main organ involved in the up
nutrients and water. At the same time, it constitu
essential barrier against harmful substances and pat
from the external environment. The intestinal barrier is
composed of the mucus layer, the epithelial layer, a
underlying lamina propria. Tight junction (TJ) proteins
the intestinal epithelial cells and regulate the para
permeability. In addition, components such as immun
the intestinal microbiota, and anti-microbial peptide
crucial roles in supporting appropriate gut barrier functi
Figure 1).

Disruption of this barrier results in increased in
permeability, which in turn facilitates translocation of
substances and pathogens to the bloodstream. The
physiology of a number of diseases is associated
dysfunctional intestinal barrier, and some of these di
and their underlying mechanisms will be discussed
review. To date, the key work has been done in animal
and *in vitro*, and little is known about the equivalent pro
in humans.

THE INTESTINAL EPITHELIAL BARRIER IN INFEC

Infectious intestinal pathogens, including various bacte
viruses, have different mechanisms of gaining access
host. Some directly adhere to and invade the in
epithelial barrier, whereas others disrupt this barrier
secretion of toxins. In either case, various common pat

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London, UK; [5]European Branch, The International Life Sciences Insti
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Correspondence: J König, PhD, Nutrition–Gut–Brain Interactions Resea
Sweden. E-mail: publications@lslseurope.be
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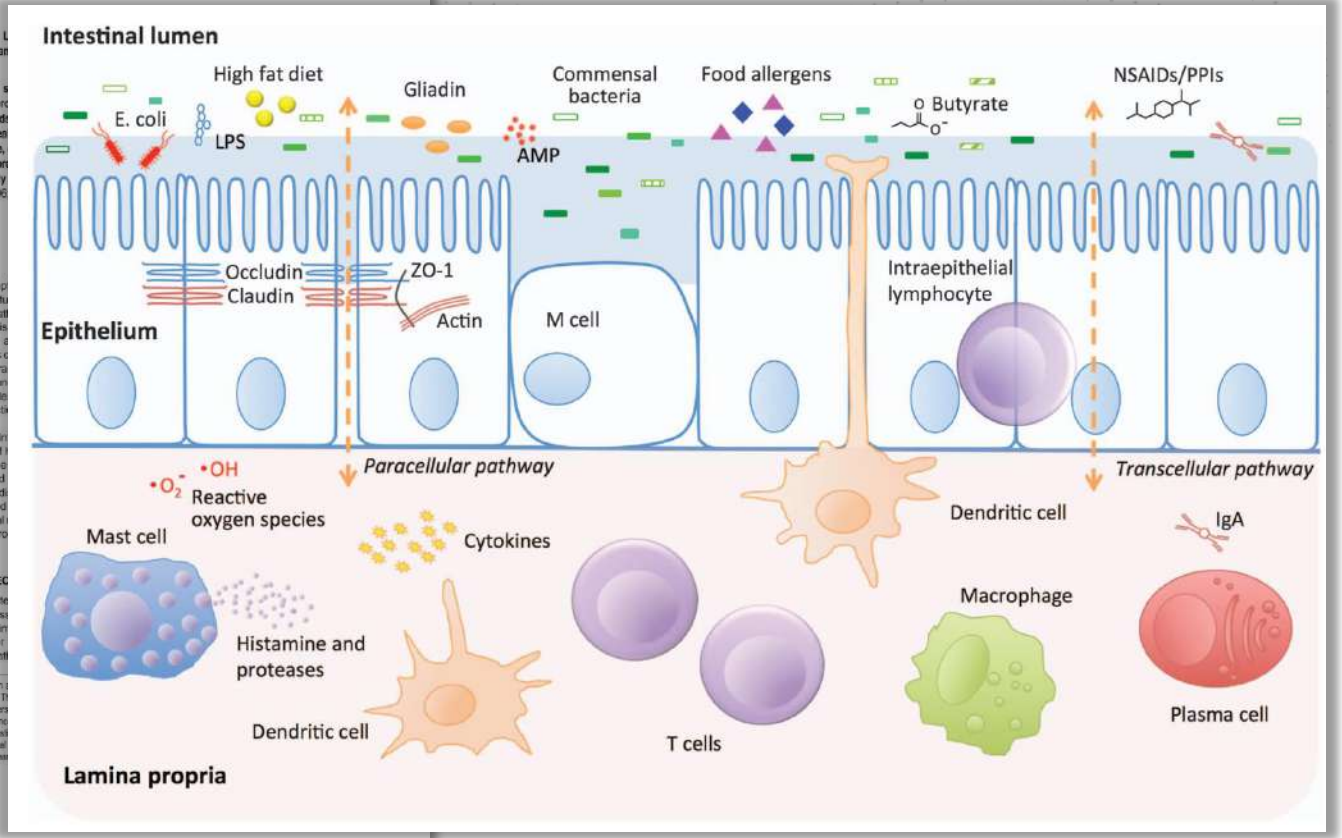

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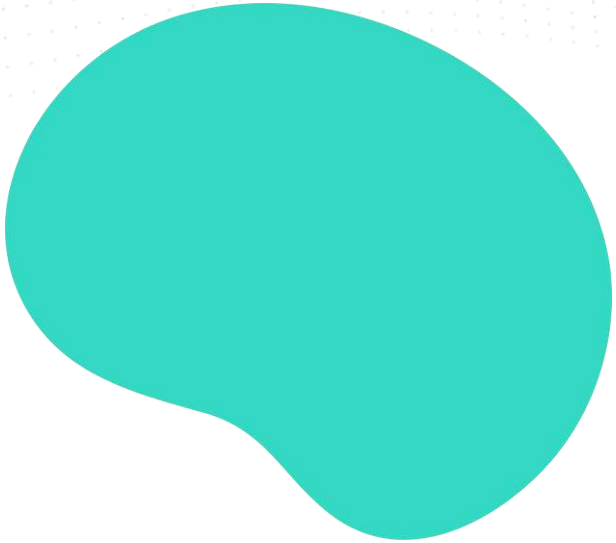
Algo mais??



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