Universidade Federal do Rio de Janeiro
Centro de Ciências da Saúde
Instituto de Ciências Biomédicas

Prova Didática

Morfologia e função do eixo neuro-entérico

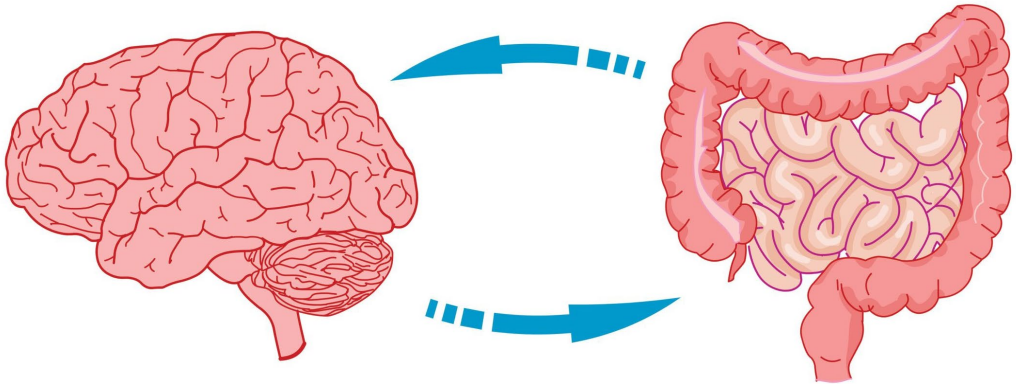
Candidato: Vanderlei Fraga Junior

Concurso público – Edital Nº 54 para Professor Adjunto

Vaga: MC-046 – Anatomia: Integração Sistêmica

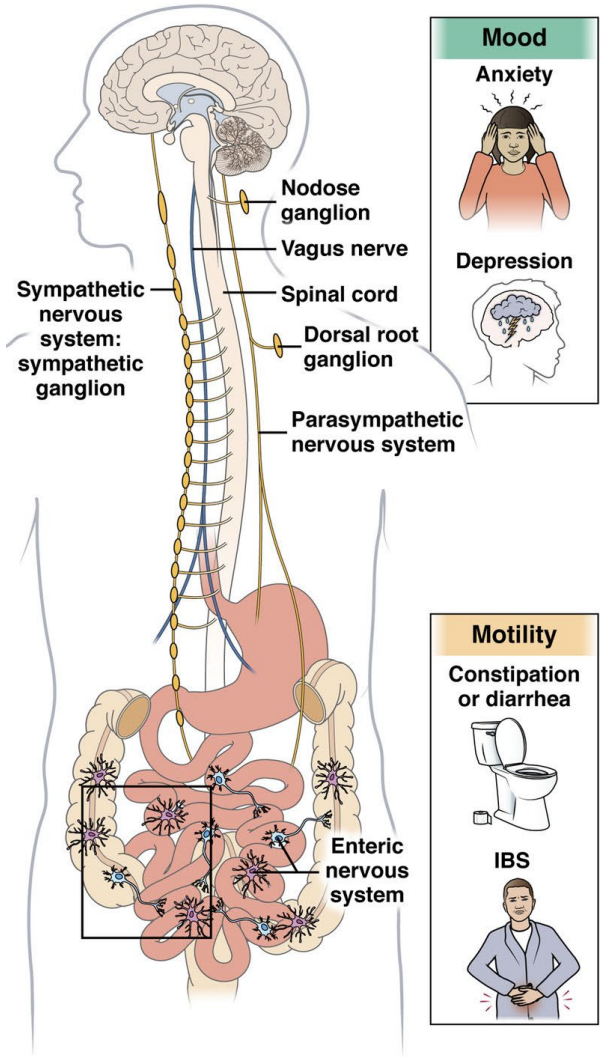
Rio de Janeiro, 2025

Roteiro de aula



- Definição do conceito de “eixo neuro-endócrino”;
- Anatomia e fisiologia do Sistema Nervoso Entérico;
- Vias de comunicação (ascendentes e descendentes);
- Papel do hipotálamo dentro do eixo;
- Relevância clínica;
- Revisão dos principais pontos abordados.

Eixo neuro-entérico



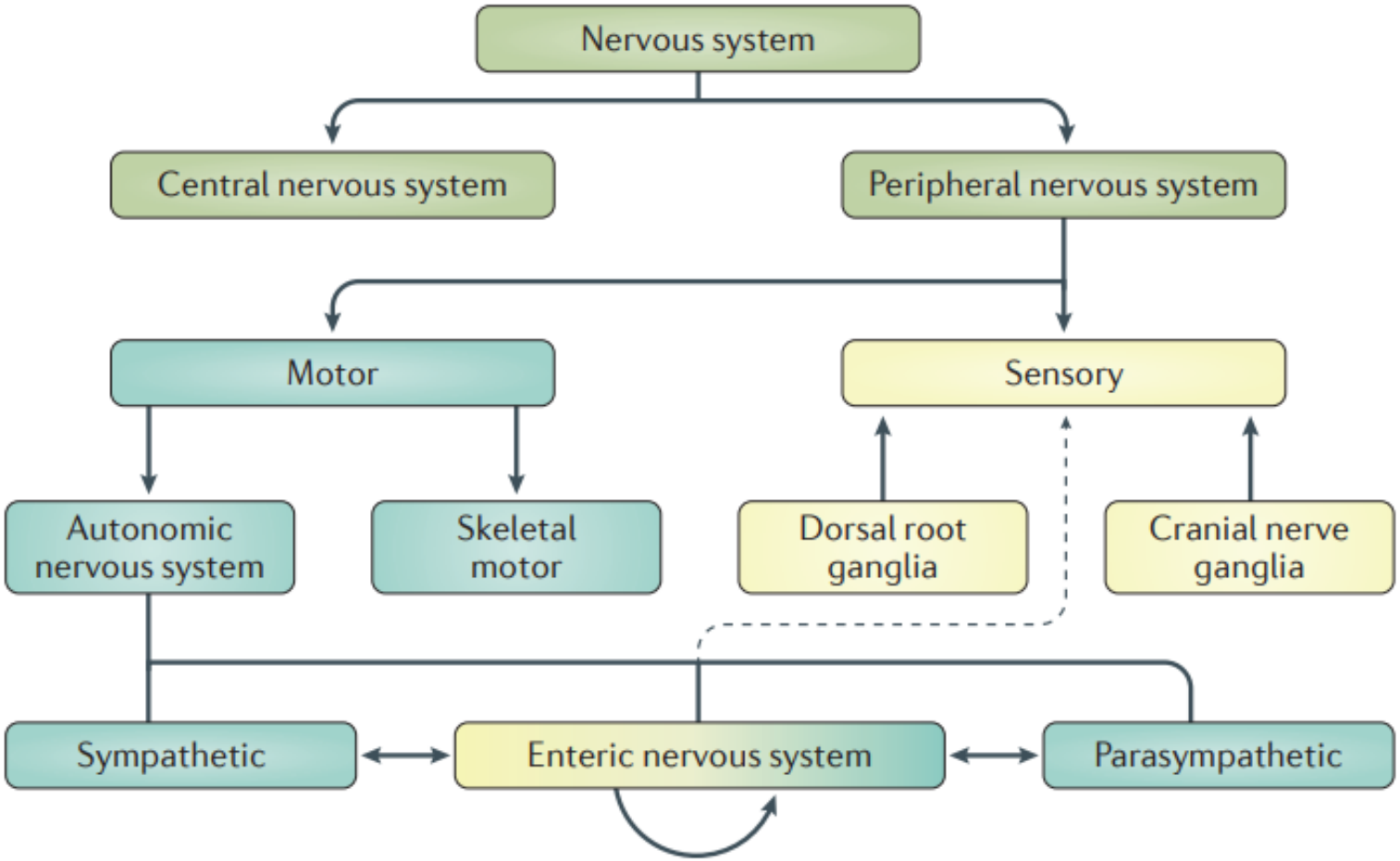
Conceito

"O termo eixo neuro-entérico refere-se às conexões funcionais e anatômicas que permitem que o intestino e o cérebro "conversem" de maneira direta ou indireta".

- Sistema Nervoso Entérico
- Sistema Nervoso Central
  (Sistema Límbico e o Hipotálamo)

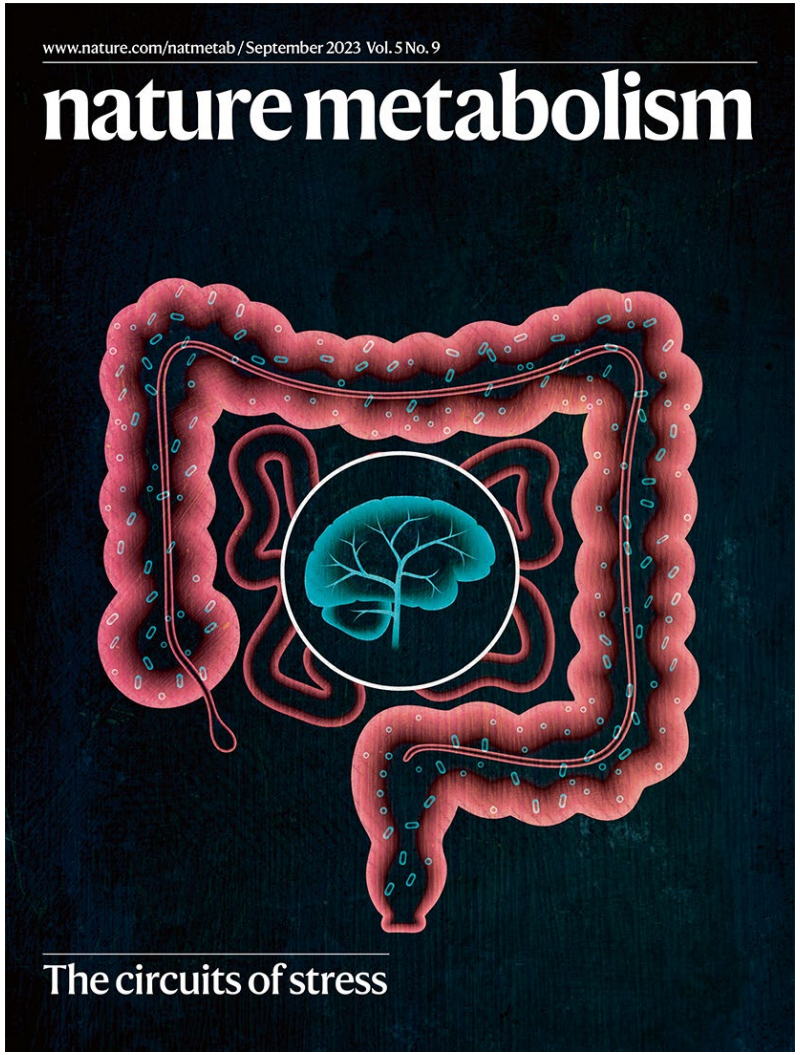
(Margolis, Cryan, Mayer. Gastroenterology, 2021).

Subdivisões do Sistema Nervoso



(Rao & Gershon. Nature Reviews – Gostroenterology and Hepathology , 2016).

Segundo cérebro?

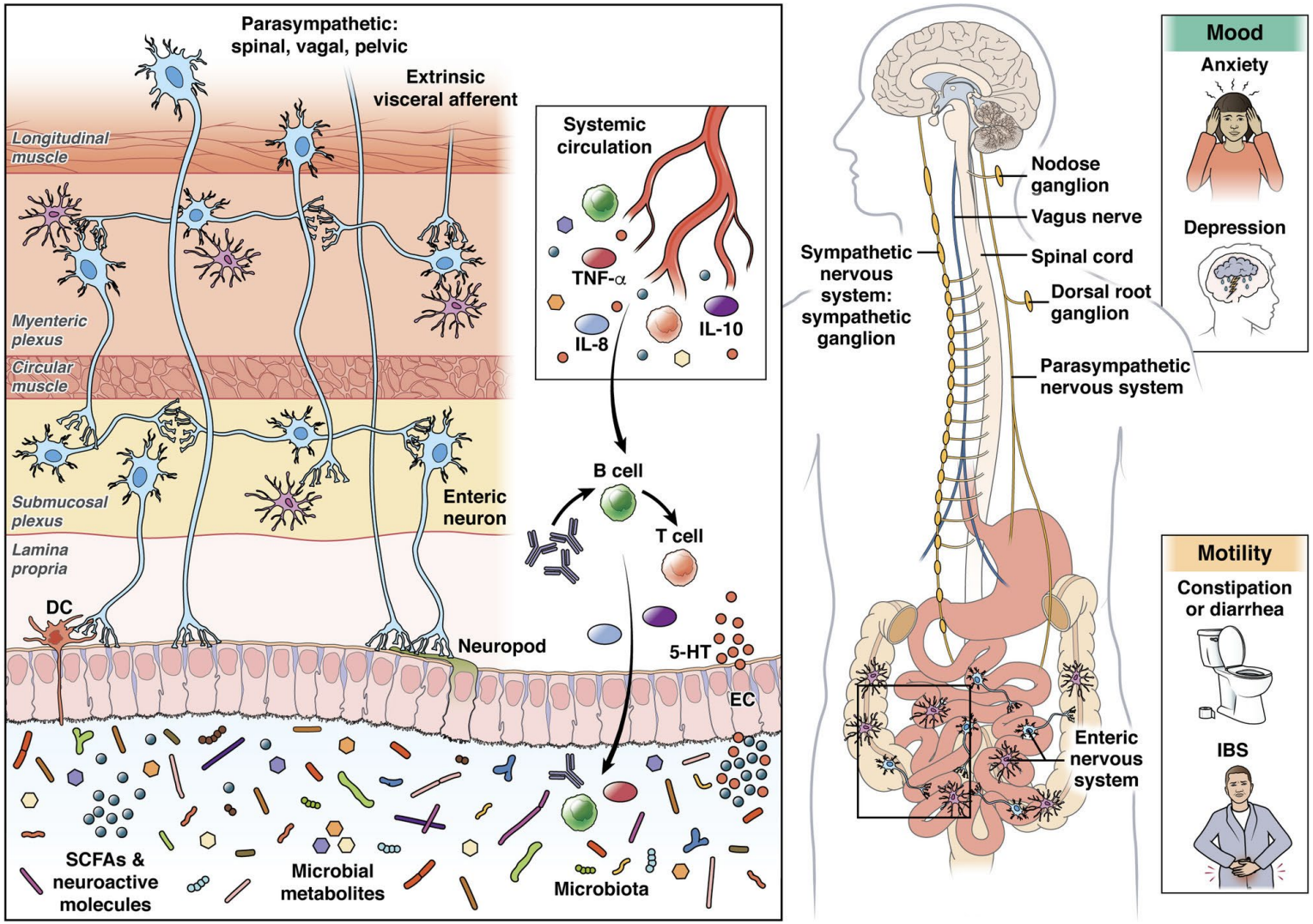


Por que essa fama toda?

- Mesma quantidade de neurônios que a medula espinal (cerca de 500 milhões);
- Produz mais de 70% da serotonina presente no nosso organismo;
- Funciona de maneira independente do SNC;
- É diretamente modulado pelo sistema nervoso autônomo.

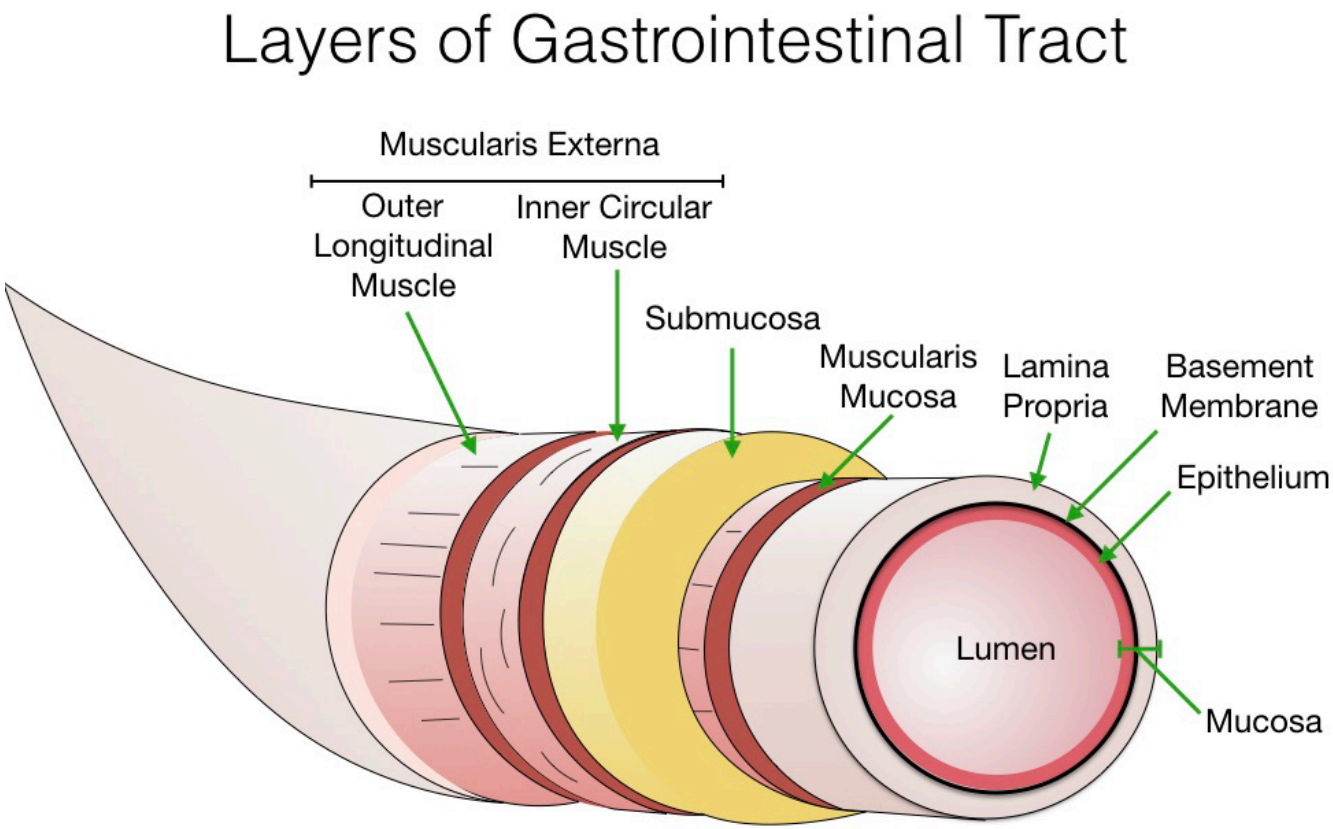
(Cover Nature Metabolism, 2023).

Muito além das vias anatômicas



(Margolis, Cryan, Mayer. Gastroenterology, 2021).

Camadas do TGI



(National University of Singapore, 2025).

Camadas do TGI

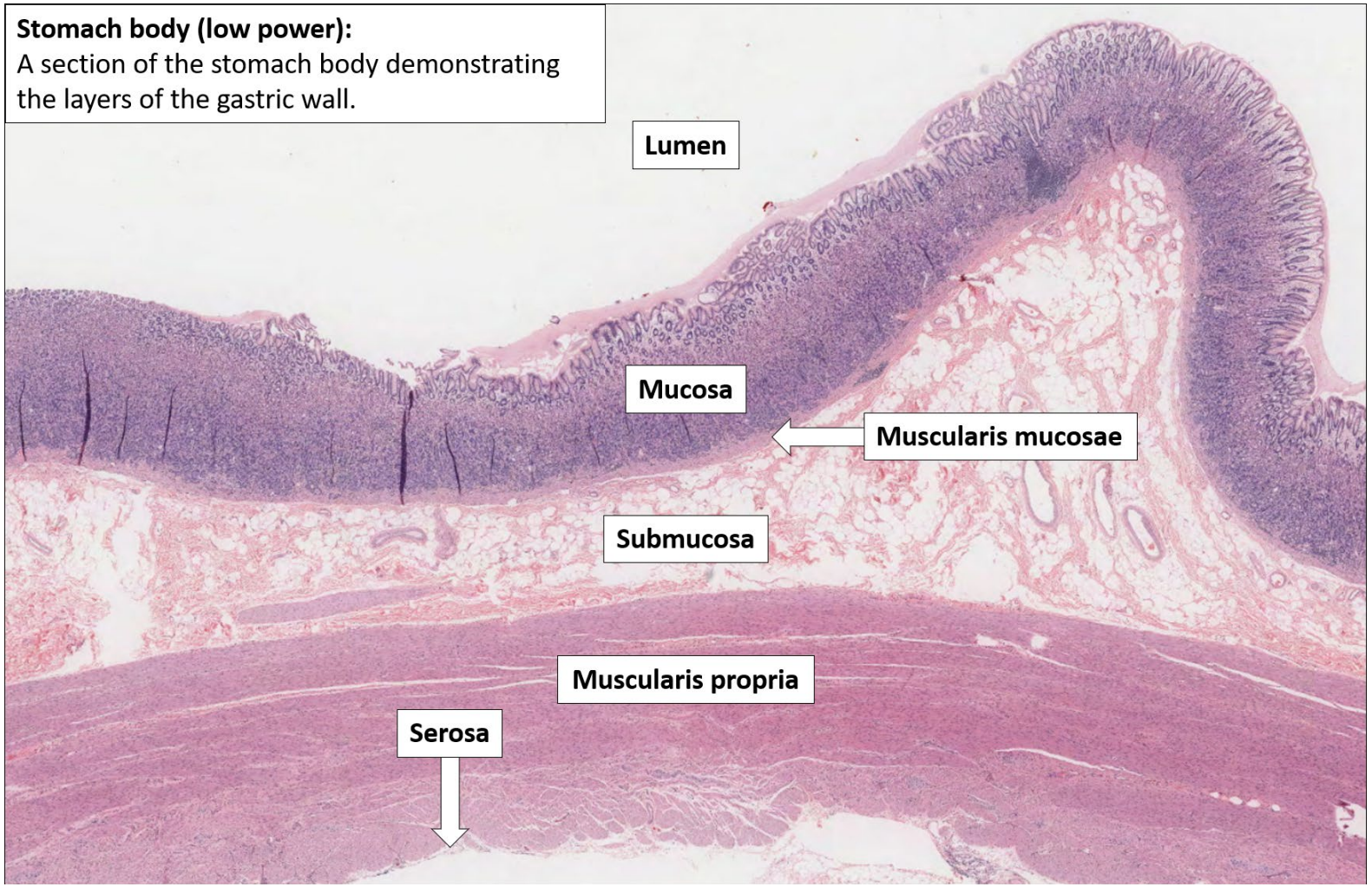
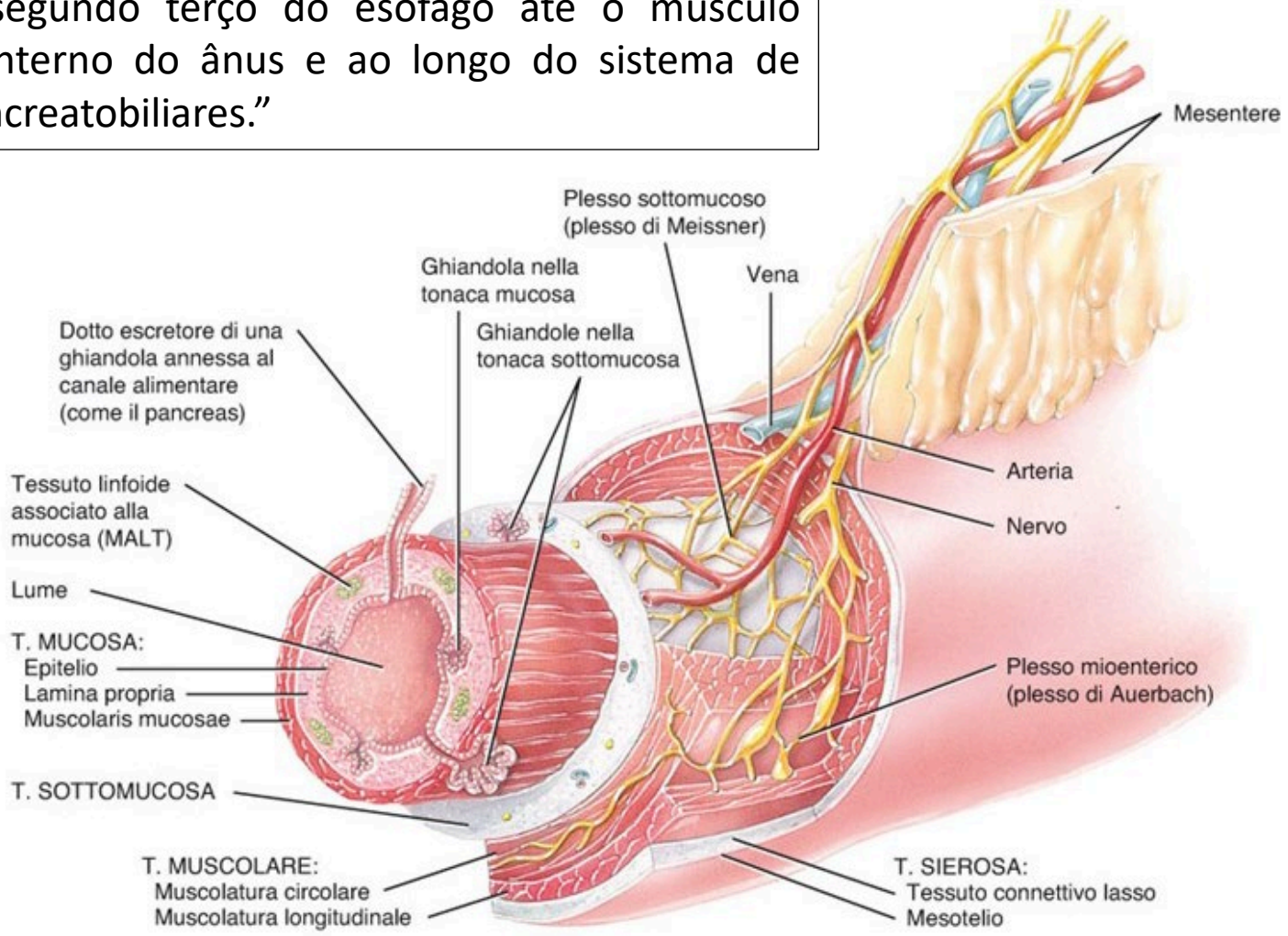


Foto micrografia corada com HE.

(National University of Singapore, 2025).

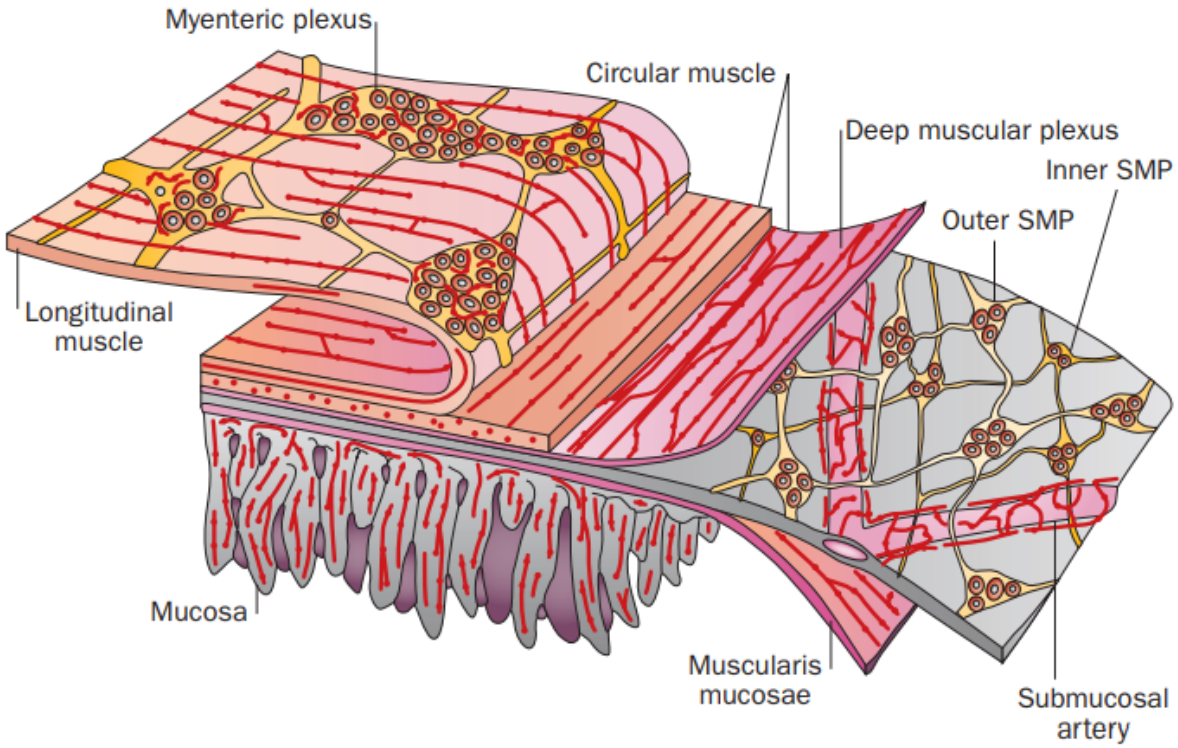
Localização no TGI

"Plexos ganglionares intrínsecos do sistema digestório, desde o segundo terço do esôfago até o músculo esfíncter interno do ânus e ao longo do sistema de ductos pancreatobiliares."



(Moore – Anatomia Orientada Para a Clínica, VIII edição , 2019).

Sistema nervoso entérico

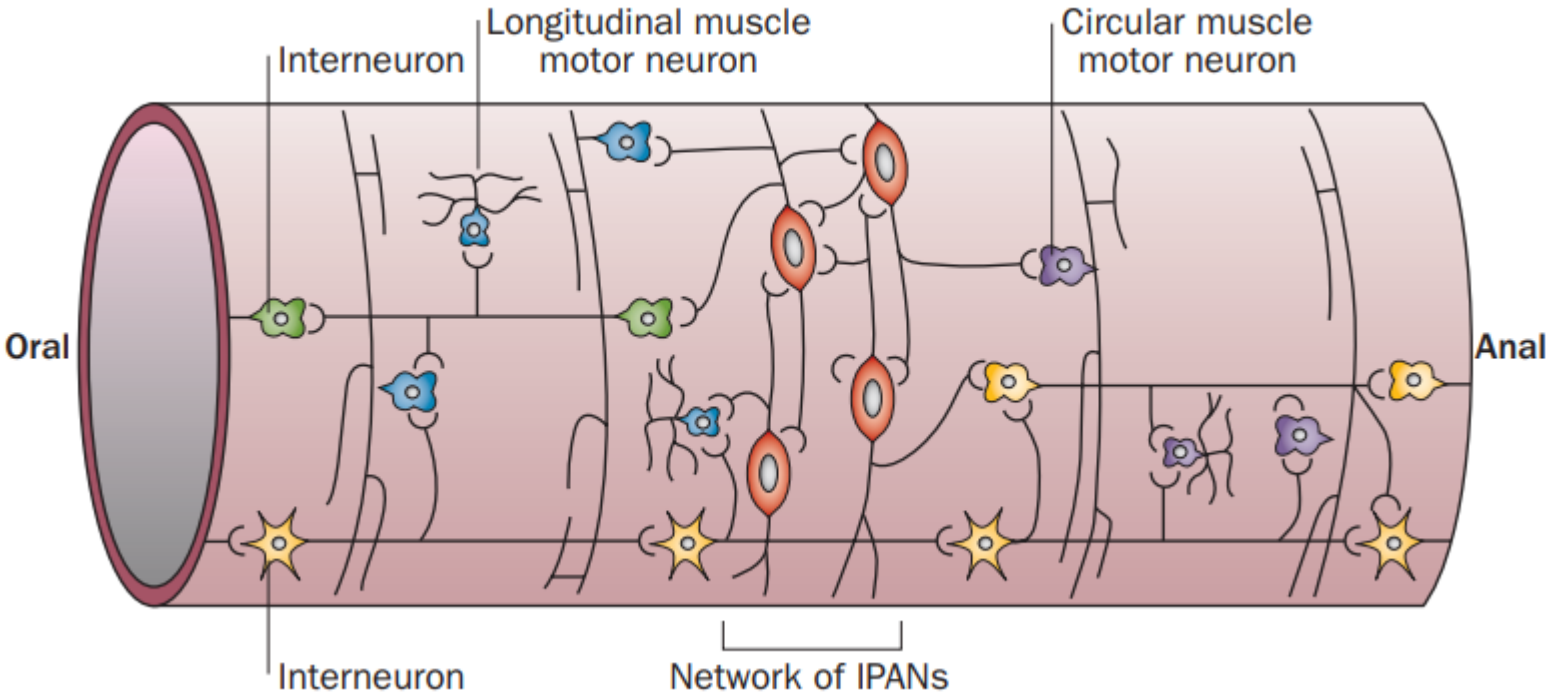


- Plexo mioentérico (de Aerbach);
- Plexo submucoso (de Meissner).

(Furness – Nat. Rev. Gastroenterol. Hepatol., 2012).

Plexo mioentérico

Composição:

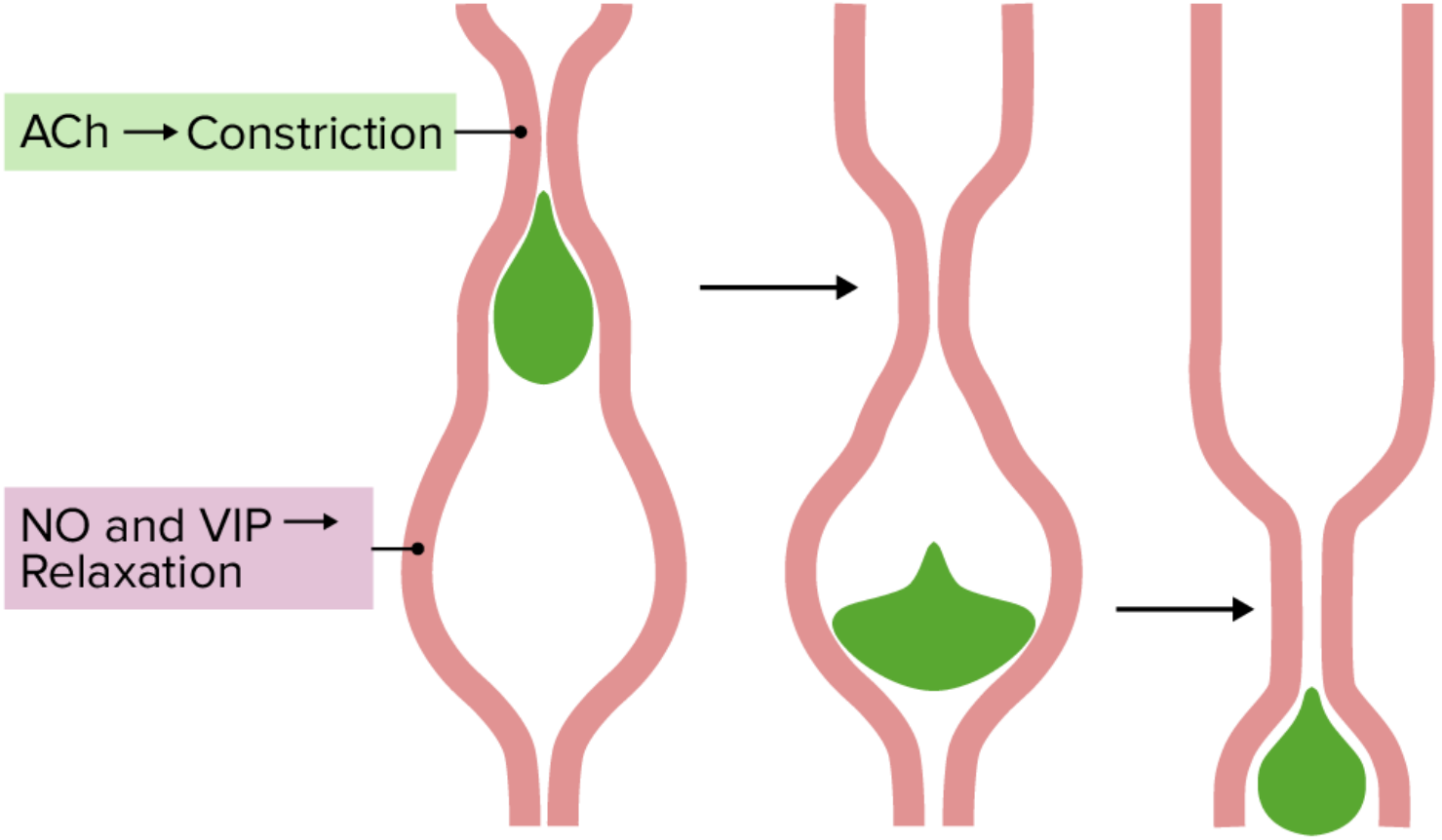


- Neurônios motores – excitatórios (Substância P e Acetilcolina);
- Neurônios motores – inibitórios (NO e VIP);
- Interneurônios e Neurônios sensoriais.

(Furness – Nat. Rev. Gastroenterol. Hepatol., 2012).

Plexo mioentérico

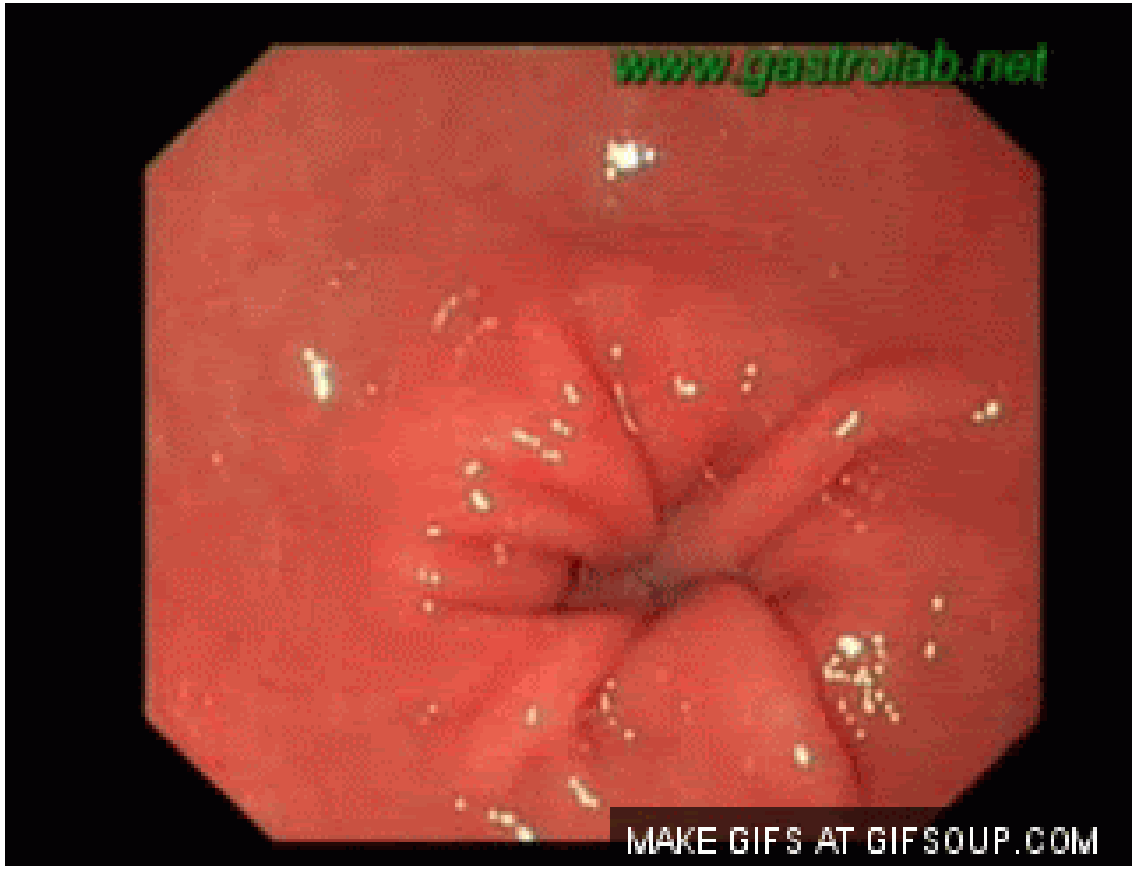
Motilidade:



(Concise Medical Images, 2025).

Plexo mioentérico

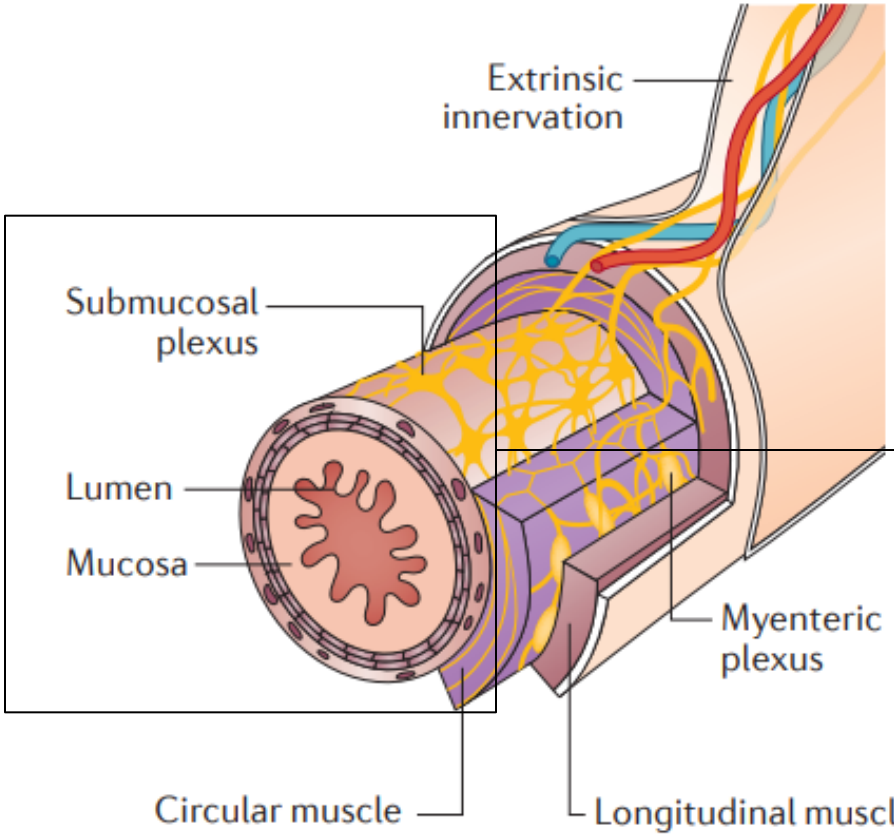
Funções principais:



- Transporte;
- Tônus basal;
- Reflexos motores.

(Vídeo – GastroLab.net, 2019)

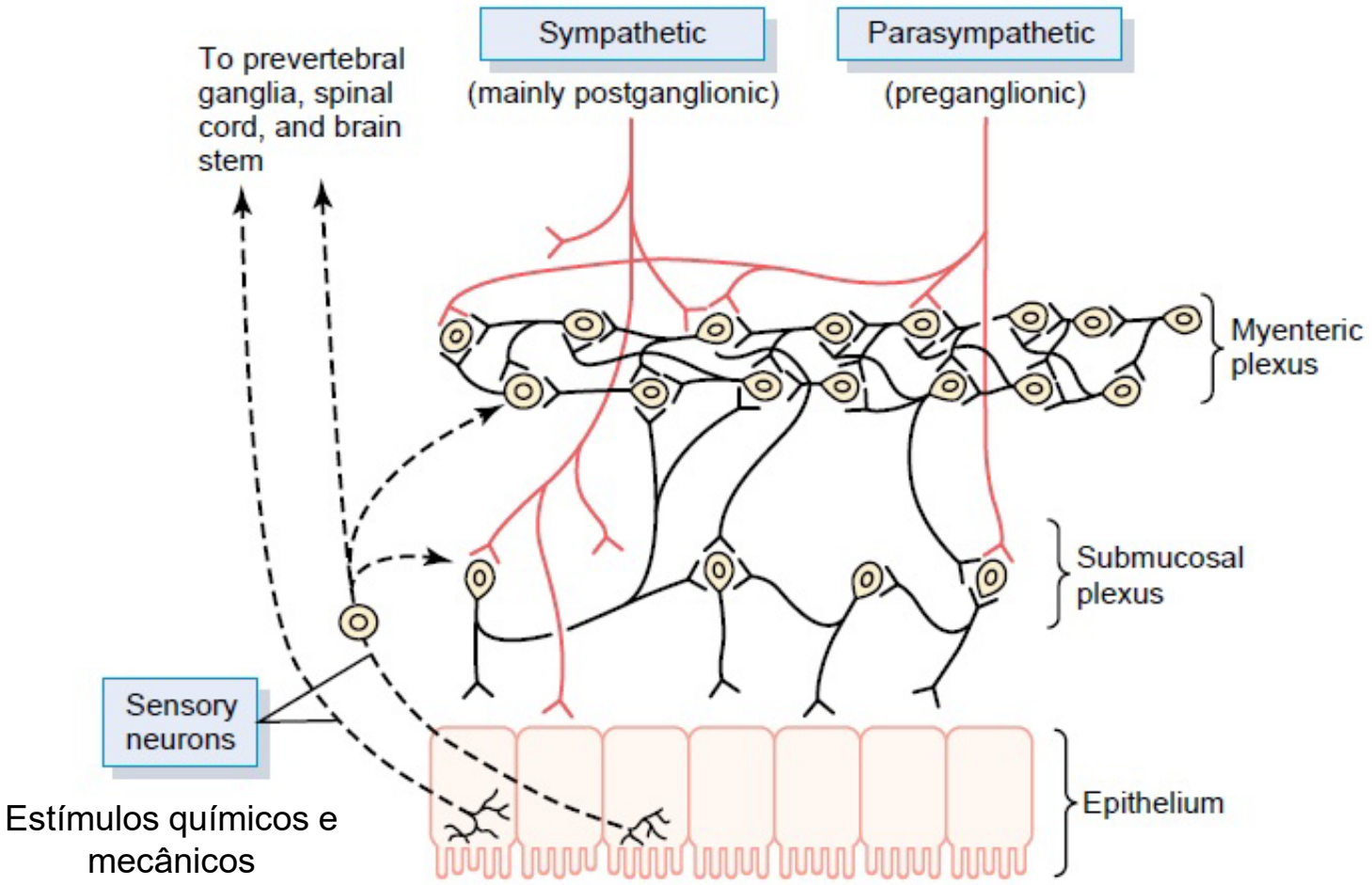
Plexo submucoso



- Regula as funções secretoras do TGI;
- Controla o fluxo sanguíneo intestinal;
- Regula o transporte de água e eletrólitos;
- Modula a secreção de enzimas digestivas.

(Rao & Gershon. Nature Reviews – Gastroenterology and Hepathology , 2016).

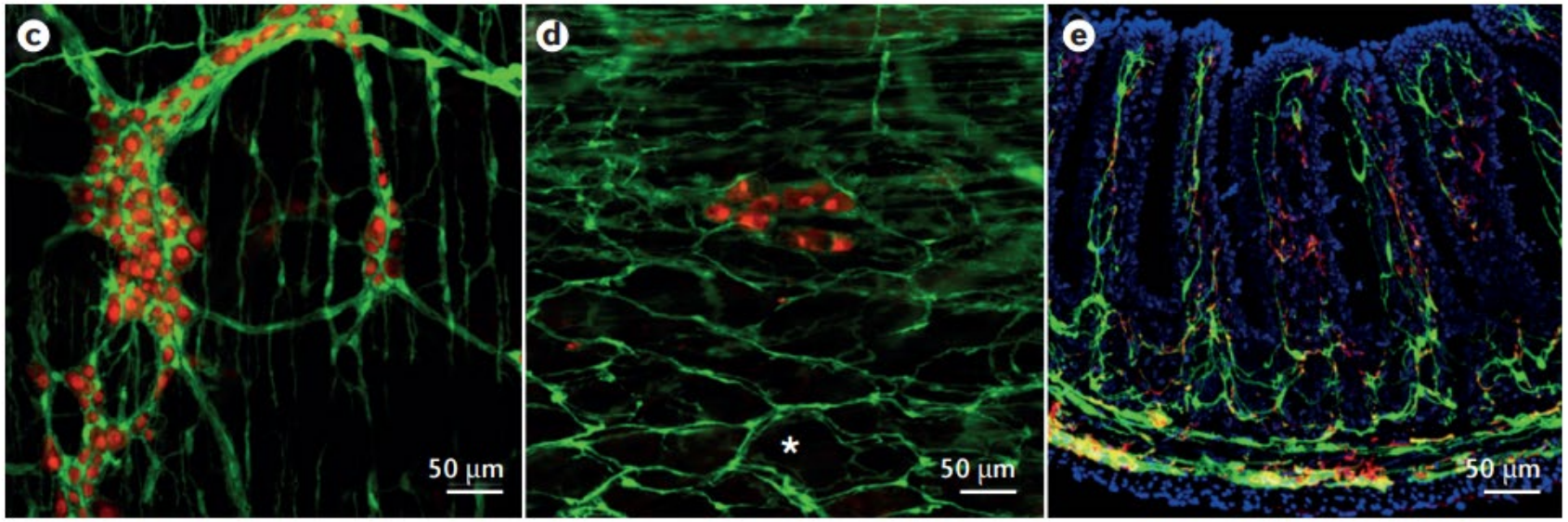
Plexo submucoso



(Kandel – Principios de Neurosciência, 2014).

Organização do SNE

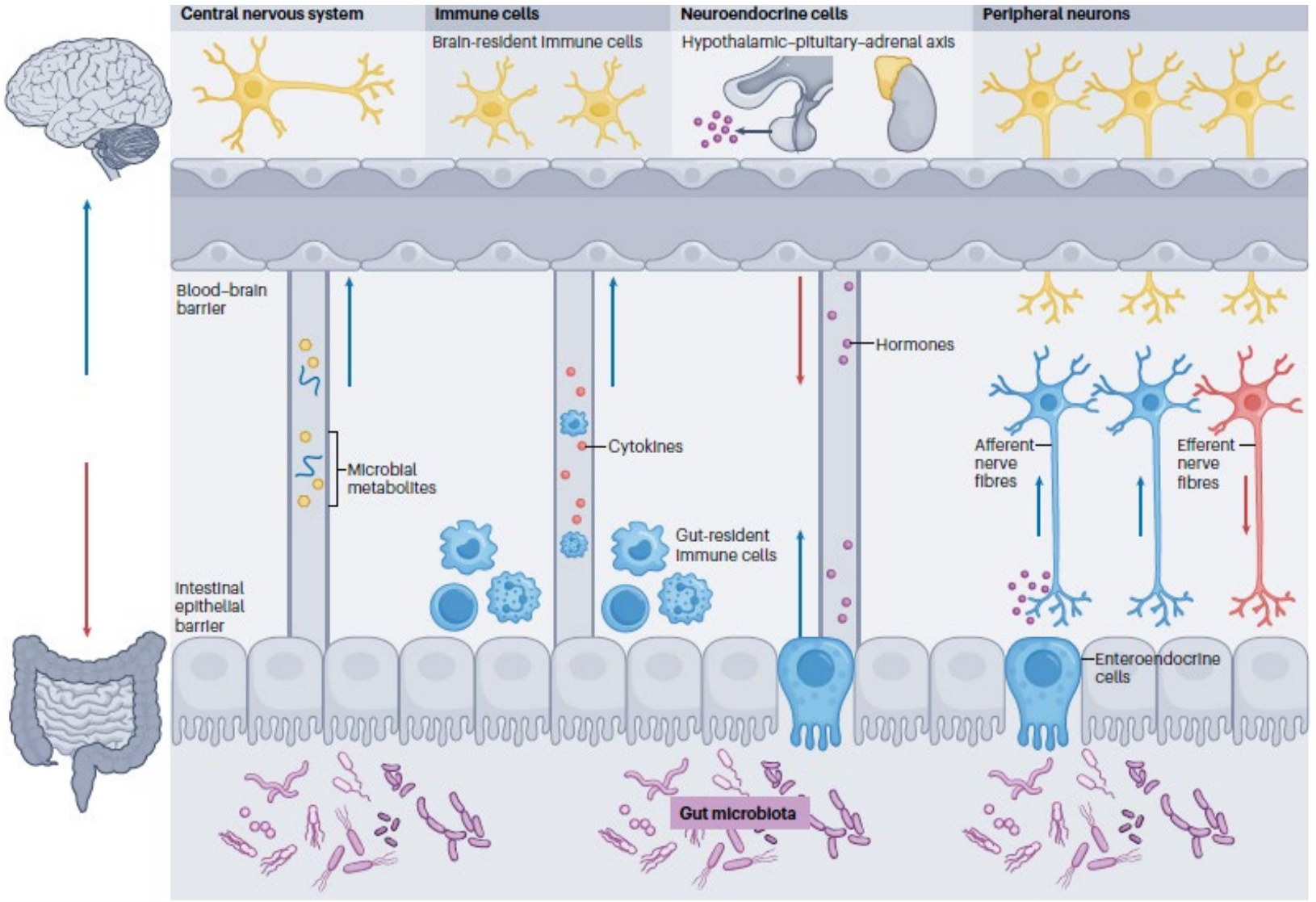
As células gliais entéricas:



ANNA1: corpo do neurônio
PLP1-eGFP: corpo do neurônio
DAPI: núcleos

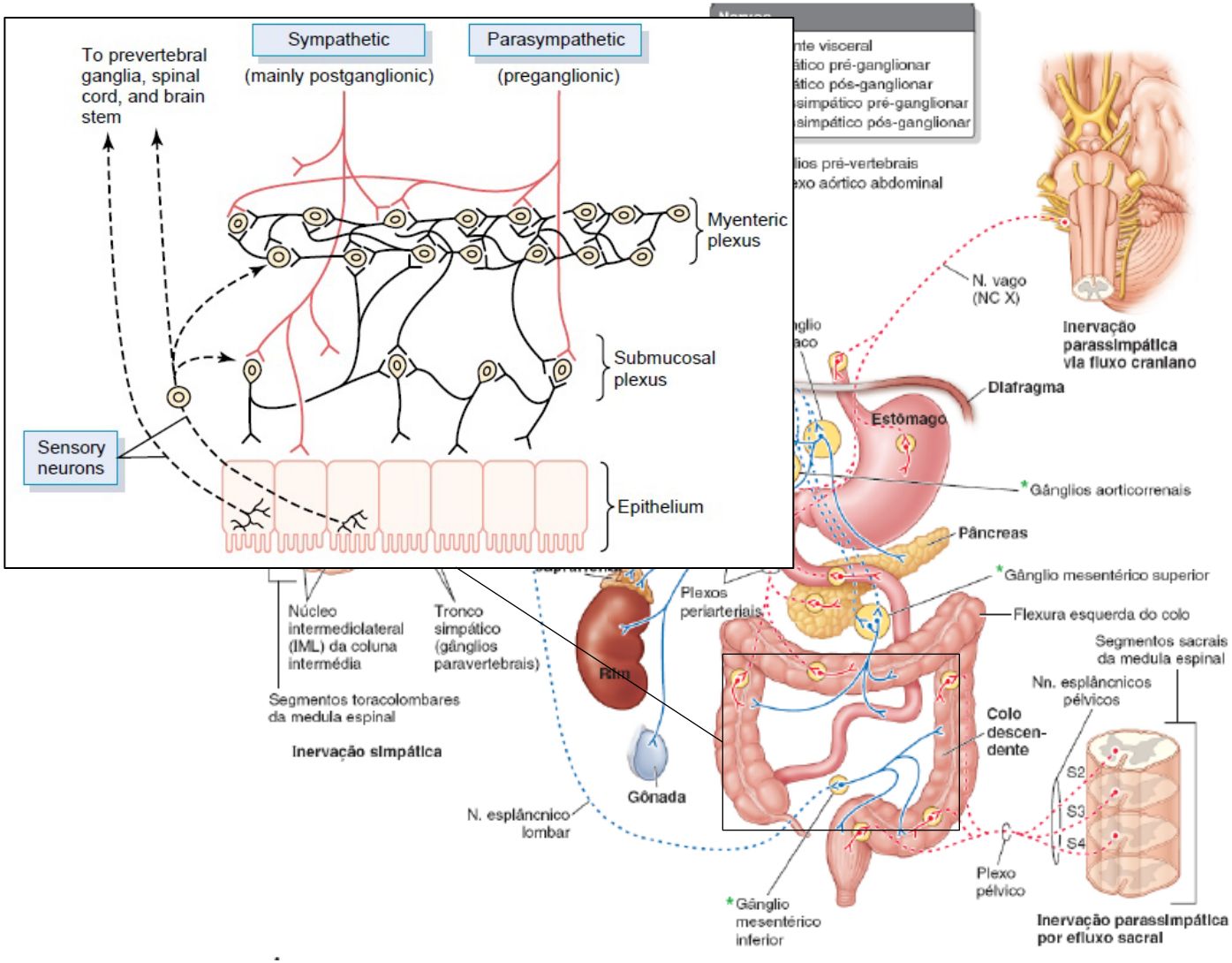
(Rao & Gershon. Nature Reviews – Gastroenterology and Hepathology, 2016).

Comunicação bidirecional



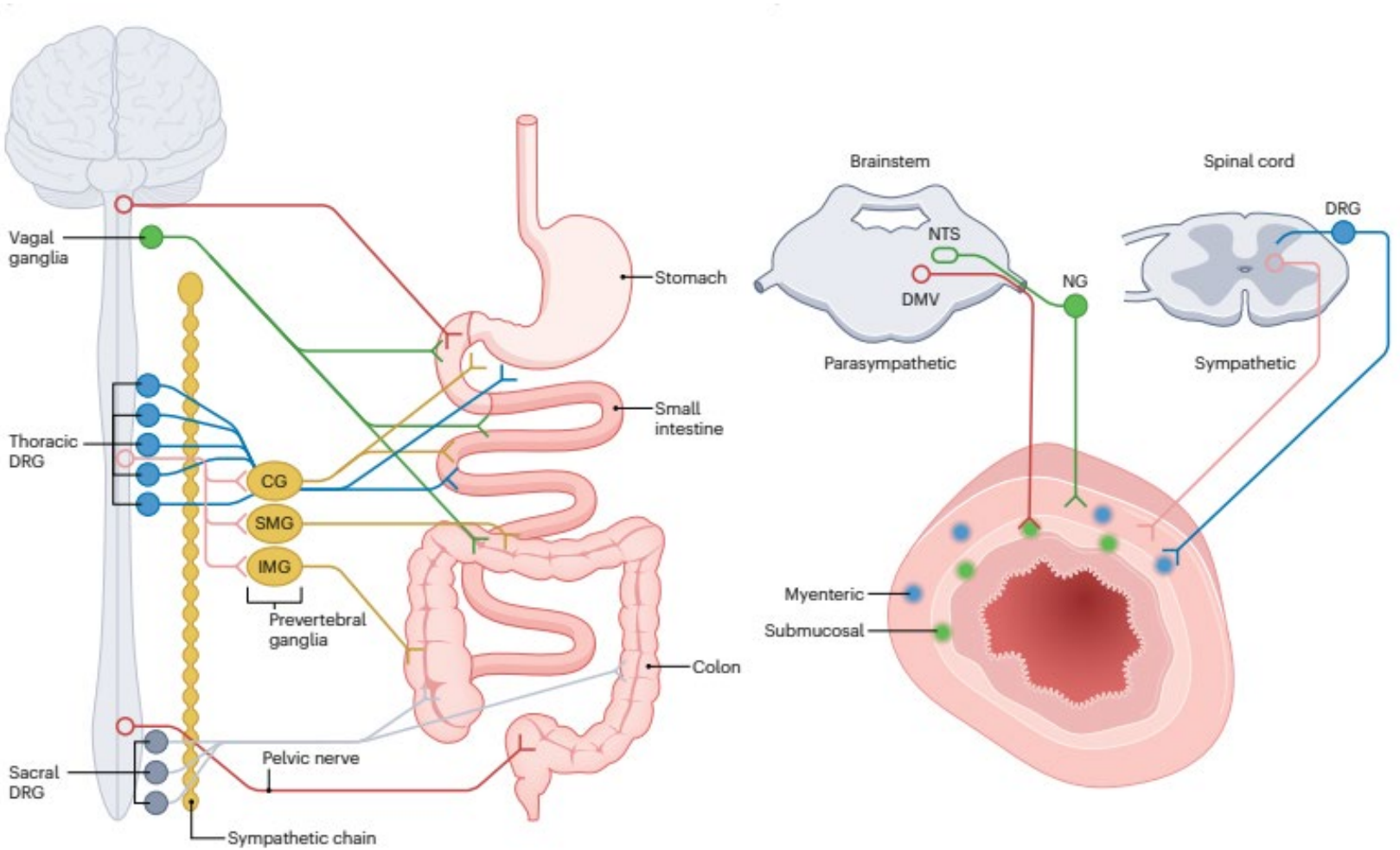
(Ohara & Hsiao. Nature Reviews – Microbiology, 2025).

Vias autonômicas periféricas



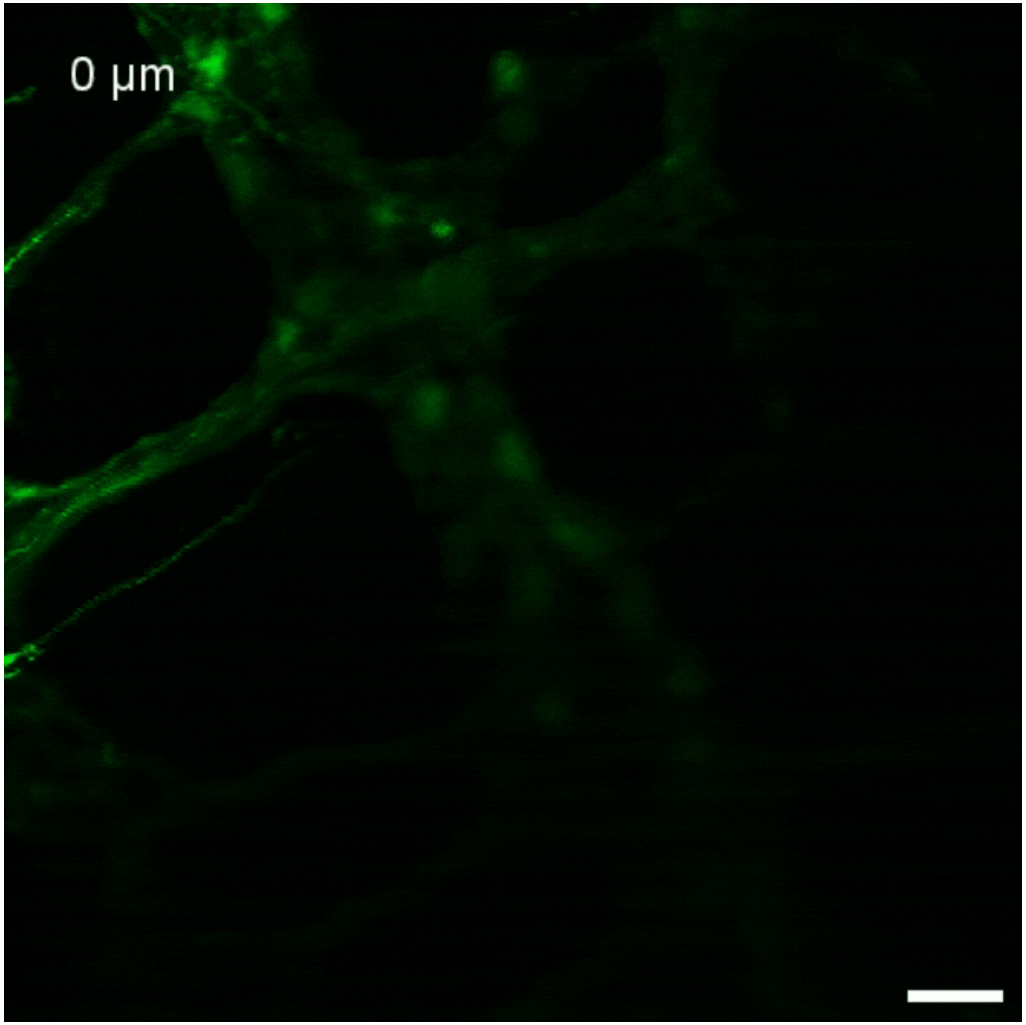
(Moore – Anatomia Orientada Para a Clínica, VIII edição , 2019).

Vias bidirecionais



(Meerschaert & Chiu. Nature Reviews - Gastroenterology & Hepatology, 2024.).

Vago em ação



(Jiang et al. Nature Communications, 2024).

Efeito do SNA no SNE

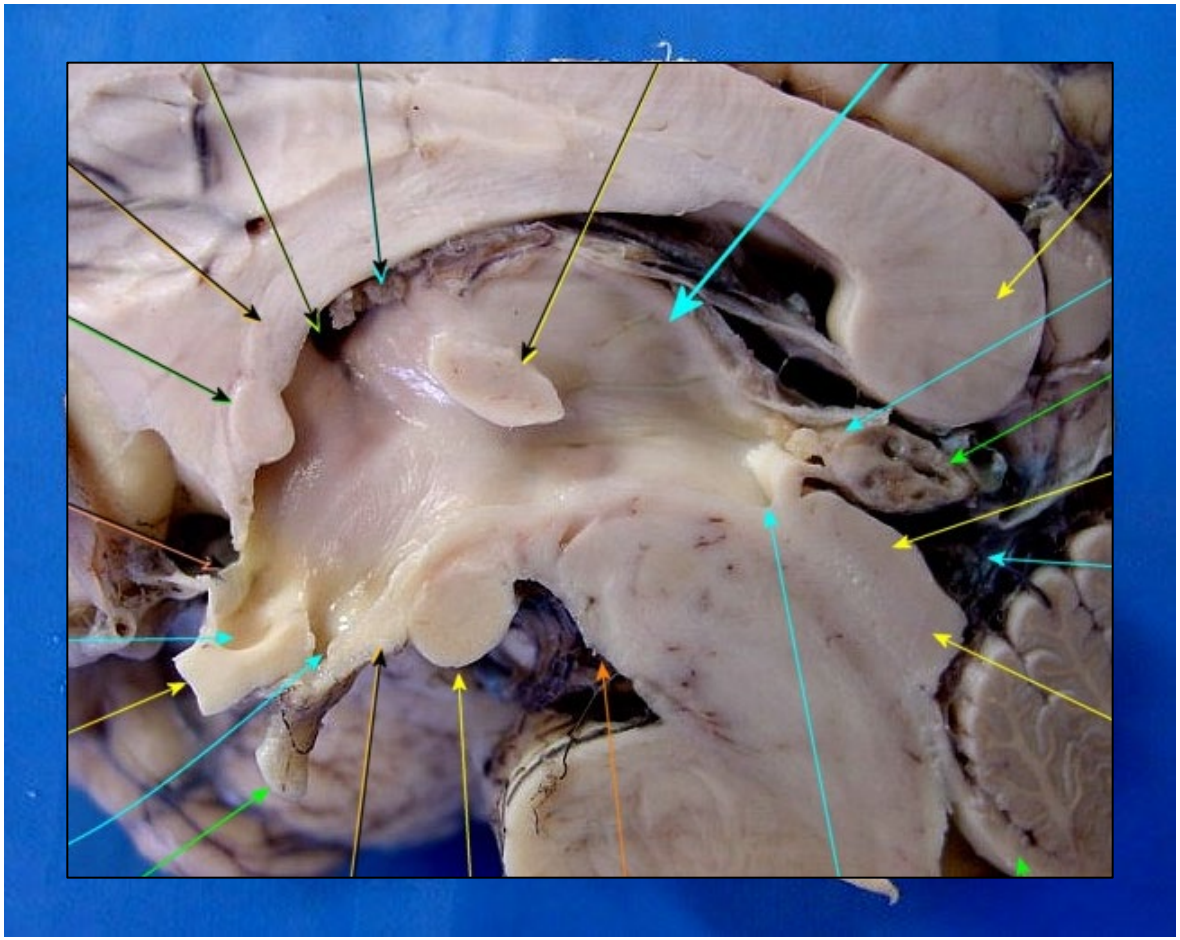
Parassimpático

- Aumenta a motilidade intestinal;
- Aumenta a secreção glandular;
- Favorece o aporte sanguíneo para o TGI.

Simpático

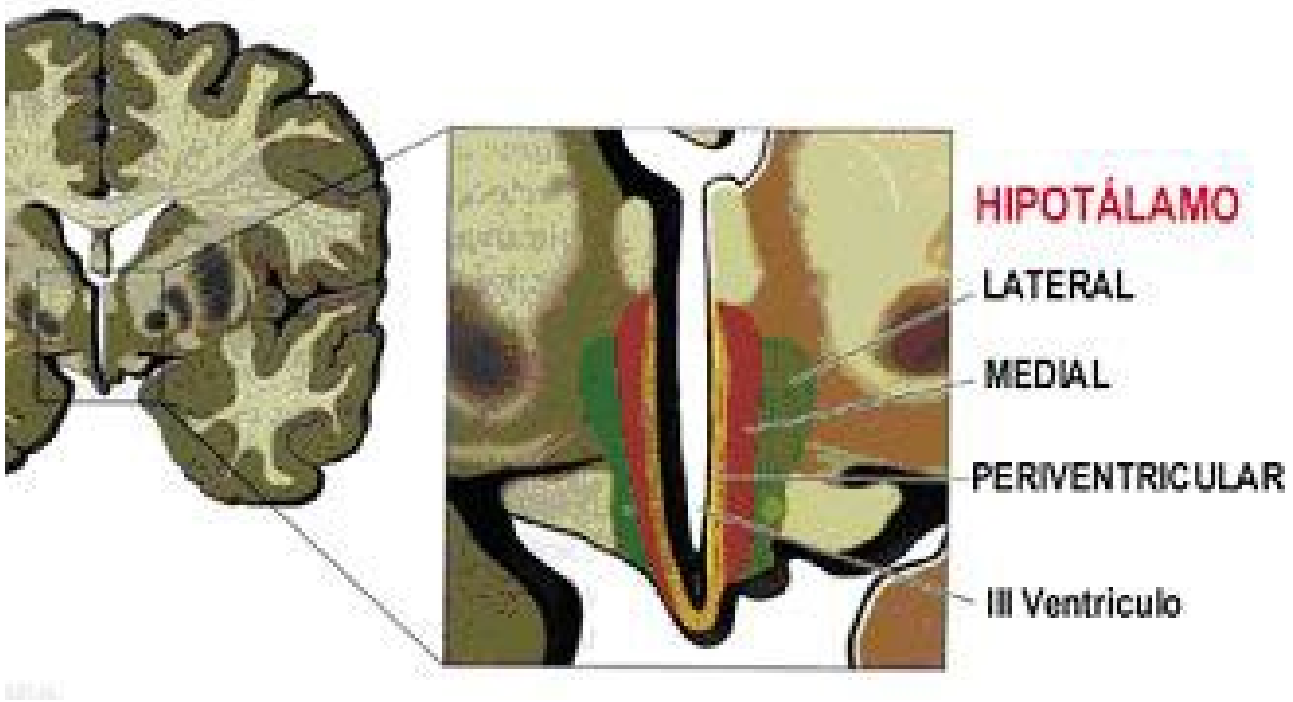
- Diminui a motilidade intestinal;
- Diminui a secreção glandular;
- Desvie o aporte sanguíneo para o músculo esquelético.

Centro de Controle - SNC



(Atlas de Neuroanatomia para Patologista - UNICAMP).

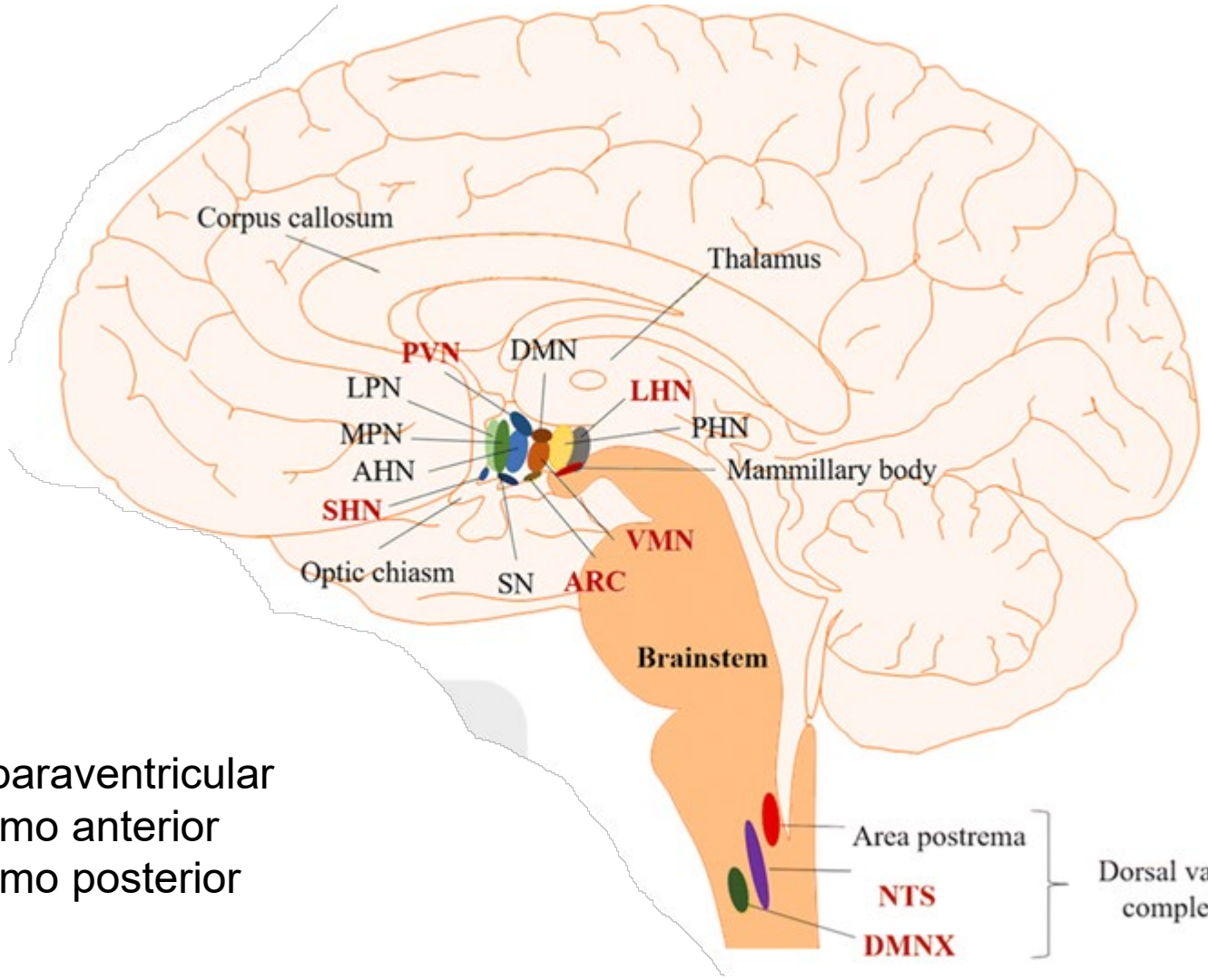
Hipotálamo



- Controle do SNA;
- Controle do Sistema Endócrino;
- Conexão com o sistema límbico.

(Anatomia Clínica de Netter – I Edição, 2006).

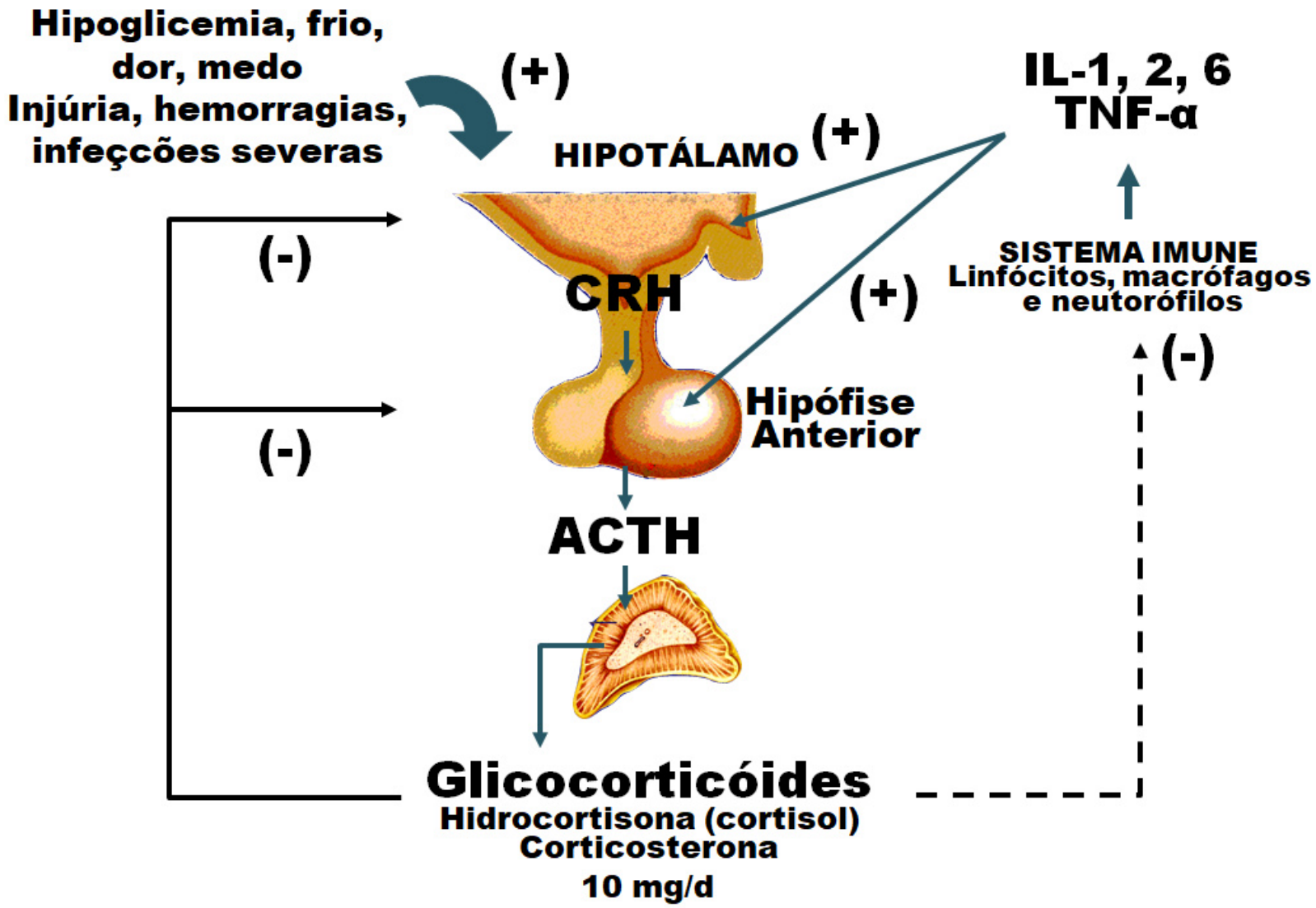
Núcleos Hipotalâmicos



- ✓ Núcleo paraventricular
- ✓ Hipotálamo anterior
- ✓ Hipotálamo posterior

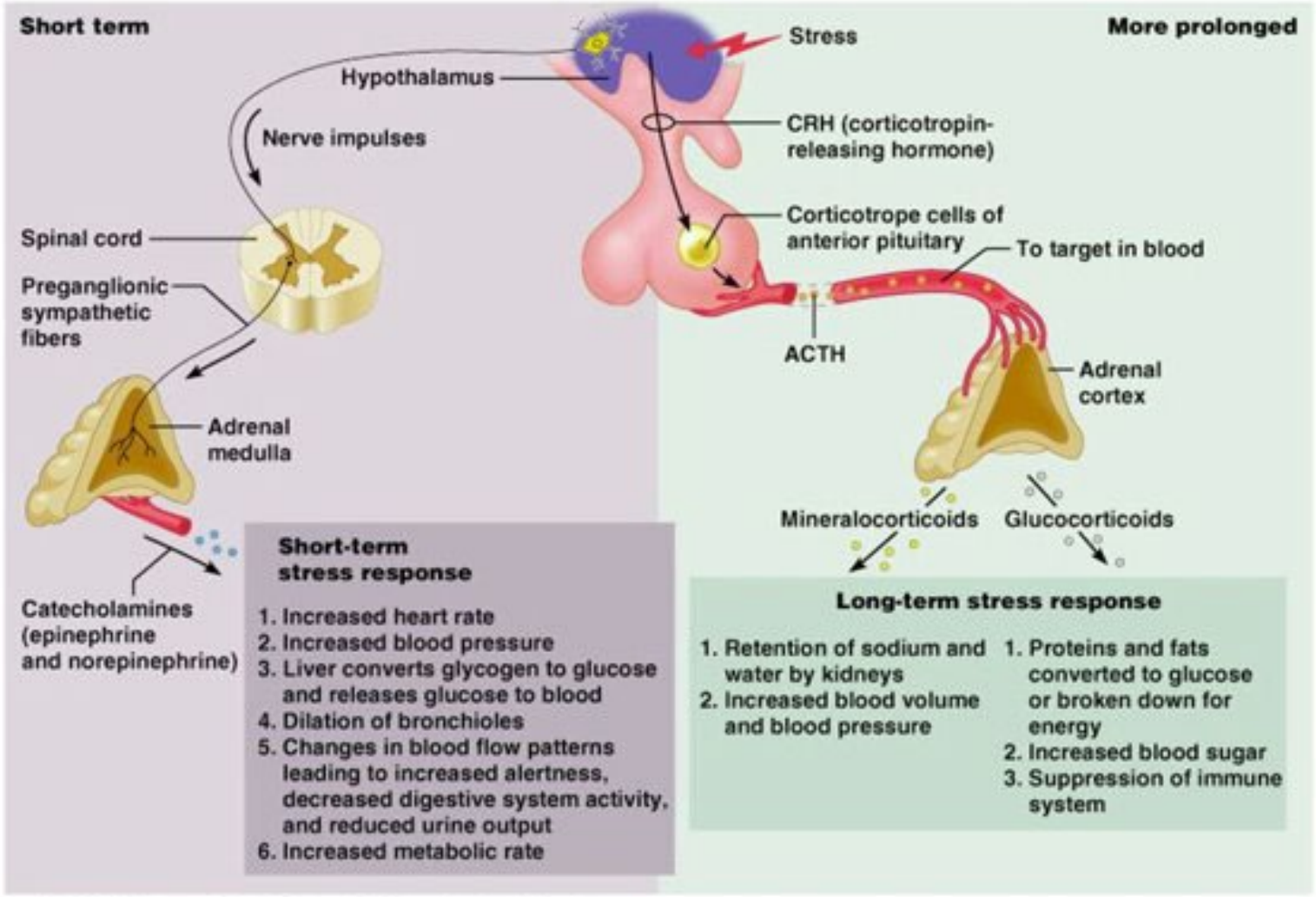
(Intuitive Neuroanatomy Schemes, 2006).

Eixo H-P-A



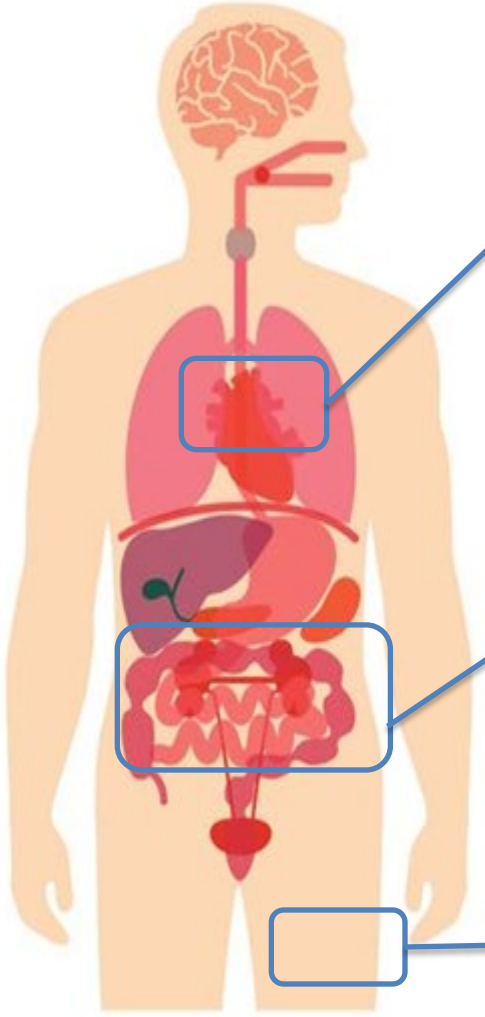
(Intuitive Neuroanatomy Schemes, 2006).

Estresse Agudo e Crônico



Via local de produção de cortisol

Produção extra-adrenal de glicocorticoides



JEM Journal of Experimental Medicine
Rockefeller University Press
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Thymus-derived Glucocorticoids Regulate Antigen-specific Positive Selection

By Melanie S. Vacchio* and Jonathan D. Ashwell‡

J Exp Med. 1997 Jun 2; 185(11): 2033–2038.

JEM Journal of Experimental Medicine
Rockefeller University Press
This article at JEM.org | Editors | Contact | Instructions for Authors

Intestinal Epithelial Cells Synthesize Glucocorticoids and Regulate T Cell Activation

Igor Cima,[1] Nadia Corazza,[1] Bernhard Dick,[2] Andrea Fuhrer,[1] Simon Herren,[1] Sabine Jakob,[1] Erick Ayuni,[3] Christoph Mueller,[1] and Thomas Brunner[1]

J Exp Med. 2004 Dec 20; 200(12): 1635–1646.

THE FASEB JOURNAL

FJ Express Summaries

Human hair follicles display a functional equivalent of the hypothalamic-pituitary-adrenal axis and synthesize cortisol

Natsuho Ito, Taisuke Ito, Arno Kromminga, Albrecht Bettermann, Masahiro Takigawa, Frieder Kees, Rainer H. Straub, and Ralf Paus

Published Online: 9 Jun 2005 | https://doi.org/10.1096/fj.04-1968fje

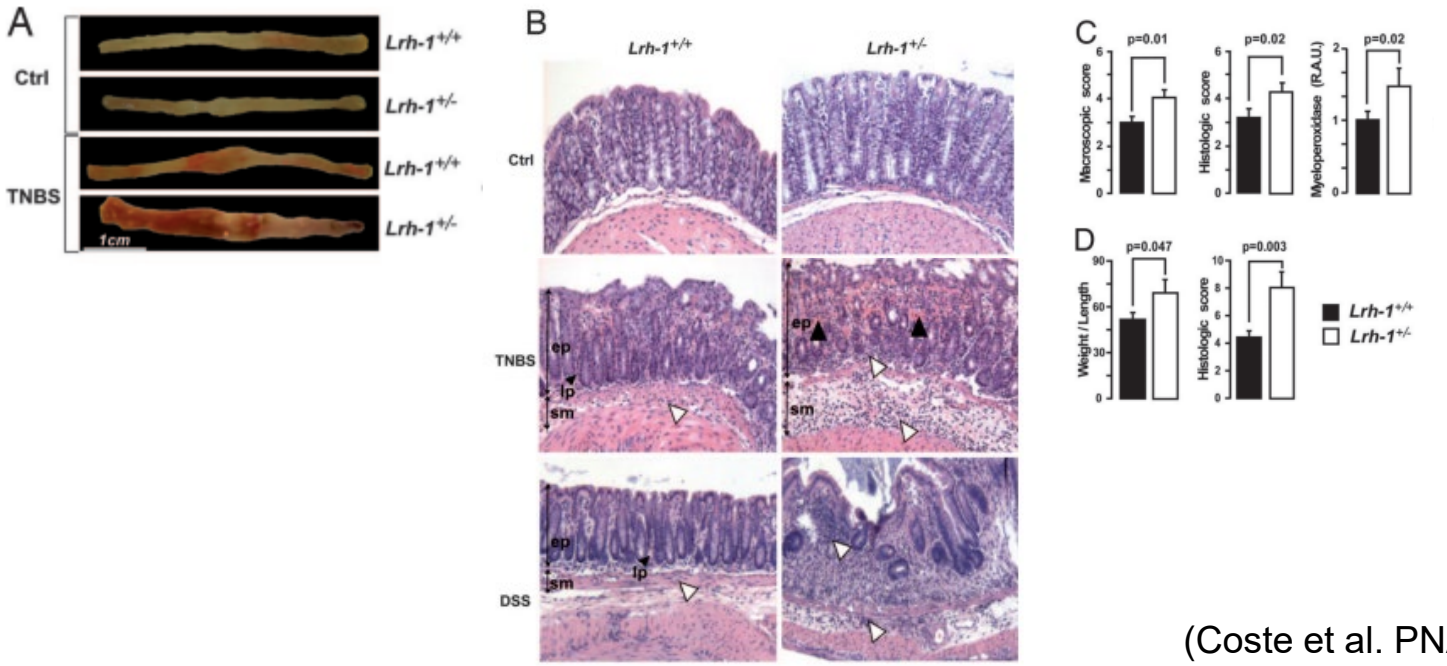
Via local de produção de cortisol

PNAS

LRH-1-mediated glucocorticoid synthesis in enterocytes protects against inflammatory bowel disease

Agnes Coste*, Laurent Dubuquoy*†, Romain Barnouin*, Jean-Sebastien Annicotte*, Benjamin Magnier*, Mario Notti‡, Nadia Corazza‡, Maria Cristina Antal§, Daniel Metzger*, Pierre Desreumaux†, Thomas Brunner‡, Johan Auwerx*§, and Kristina Schoonjans*¶

*Institut de Génétique et de Biologie Moléculaire et Cellulaire, Centre National de la Recherche Scientifique (CNRS), Institut National de la Santé et de la Recherche Médicale (INSERM), Université Louis Pasteur, 67404 Illkirch, France; †INSERM U795 Université de Lille 2 et Service des Maladies de l'Appareil Digestif et de la Nutrition, Hôpital Huriez, Centre Hospitalier Régional Universitaire Lille, 59037 Lille, France; ‡Division of Immunopathology, Institute of Pathology, University of Bern, 3010 Bern, Switzerland; and §Institut Clinique de la Souris, Génopole de Strasbourg, 67404 Illkirch, France



(Coste et al. PNAS, 2007).

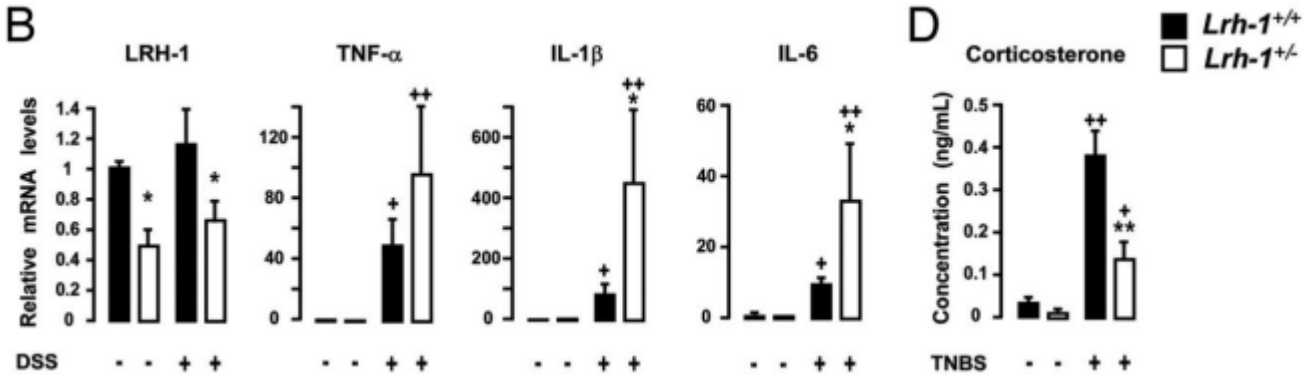
Via local de produção de cortisol

PNAS

LRH-1-mediated glucocorticoid synthesis in enterocytes protects against inflammatory bowel disease

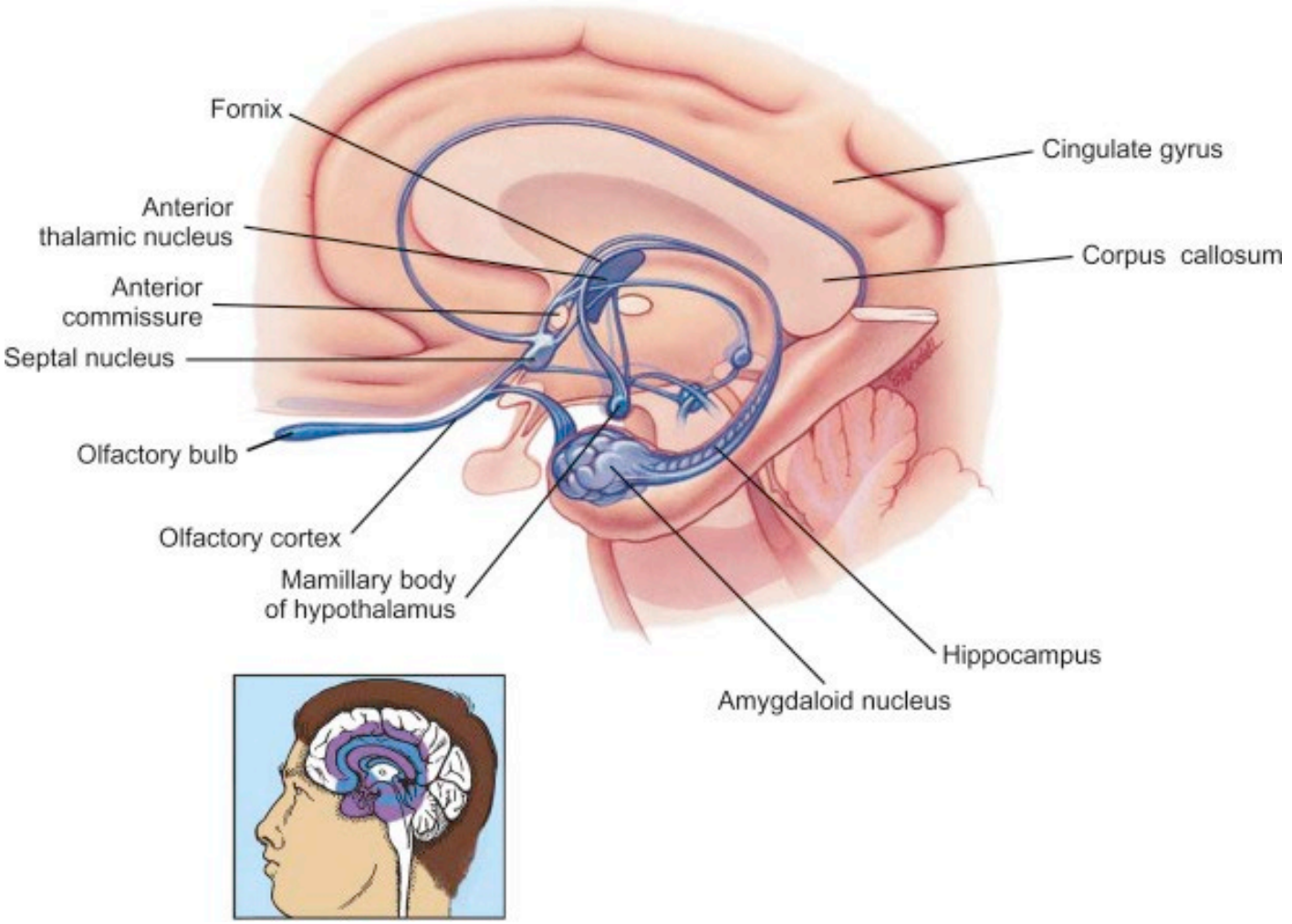
Agnes Coste*, Laurent Dubuquoy*†, Romain Barnouin*, Jean-Sebastien Annicotte*, Benjamin Magnier*, Mario Notti‡, Nadia Corazza‡, Maria Cristina Antal§, Daniel Metzger*, Pierre Desreumaux†, Thomas Brunner‡, Johan Auwerx*§, and Kristina Schoonjans*¶

*Institut de Génétique et de Biologie Moléculaire et Cellulaire, Centre National de la Recherche Scientifique (CNRS), Institut National de la Santé et de la Recherche Médicale (INSERM), Université Louis Pasteur, 67404 Illkirch, France; †INSERM U795 Université de Lille 2 et Service des Maladies de l'Appareil Digestif et de la Nutrition, Hôpital Huriez, Centre Hospitalier Régional Universitaire Lille, 59037 Lille, France; ‡Division of Immunopathology, Institute of Pathology, University of Bern, 3010 Bern, Switzerland; and §Institut Clinique de la Souris, Génopole de Strasbourg, 67404 Illkirch, France



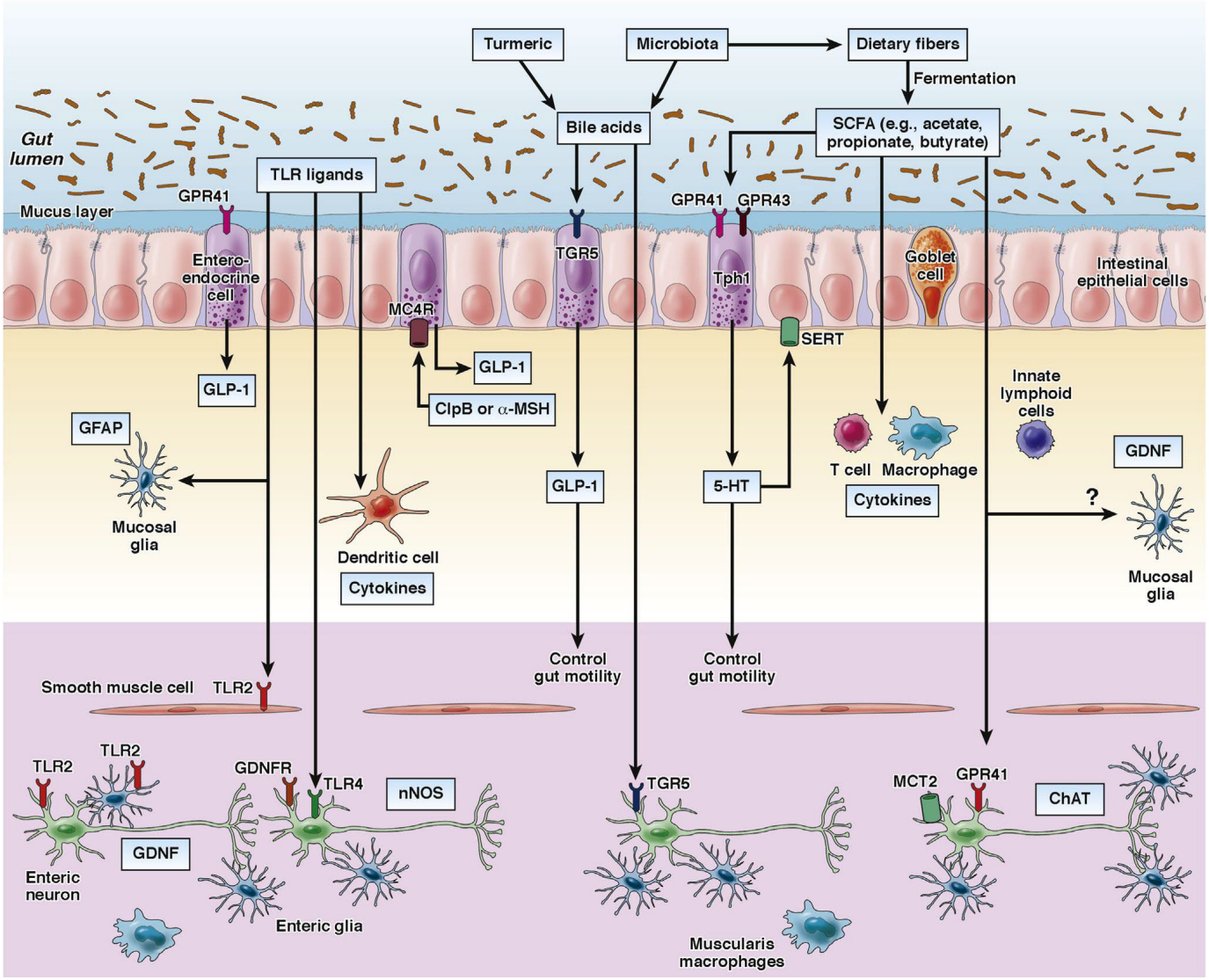
(Coste et al. PNAS, 2007).

Hipotálamo



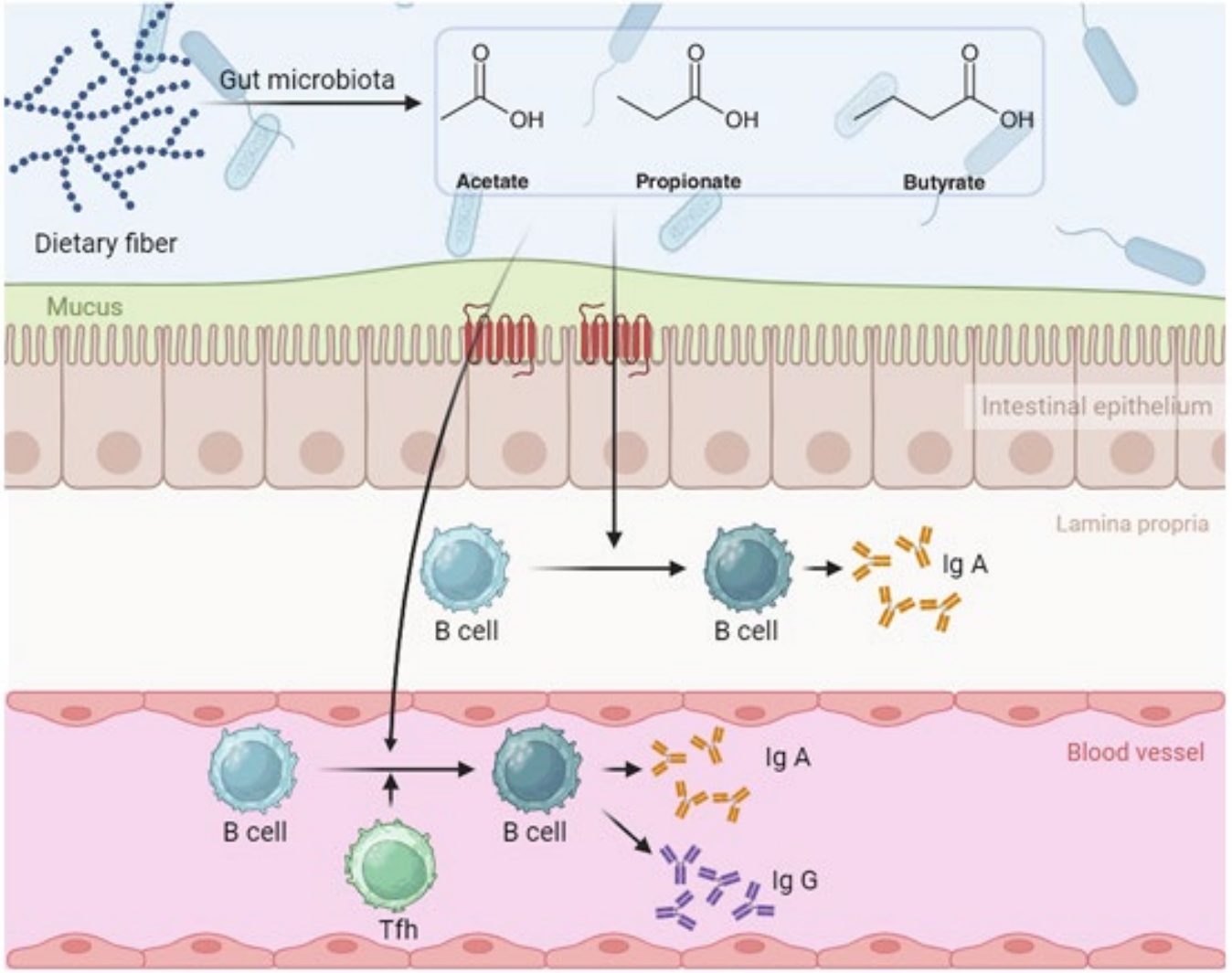
(Kandel – VI Edição, 2023).

Microbiota



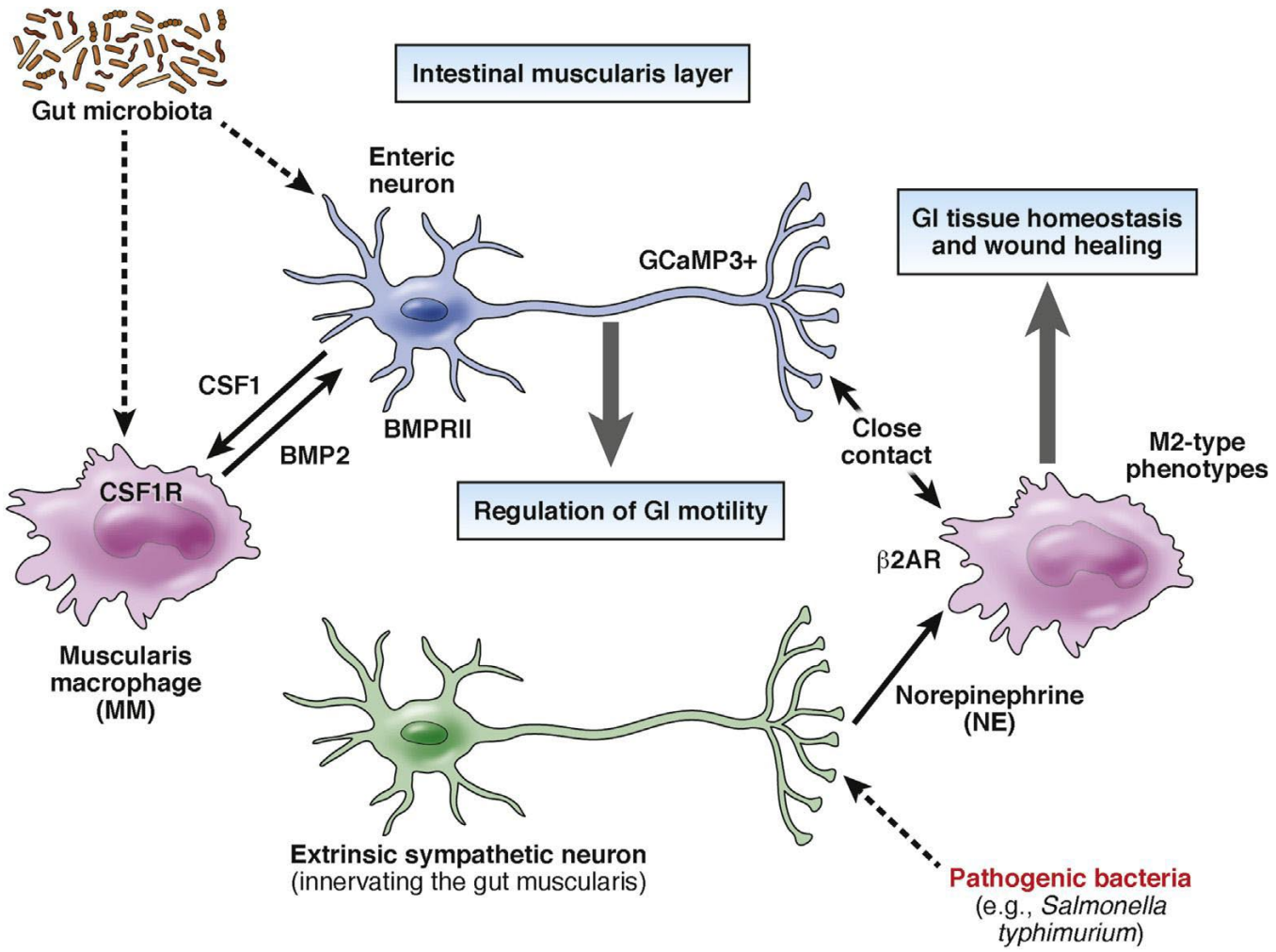
(Obata & Pachnis. Gastroenterology, 2016).

Microbiota x Sistema Imune



(Qu et al. Biomedicine and Pharmacoterapy, 2023).

Microbiota



(Obata & Pachnis. Gastroenterology, 2016).

Article

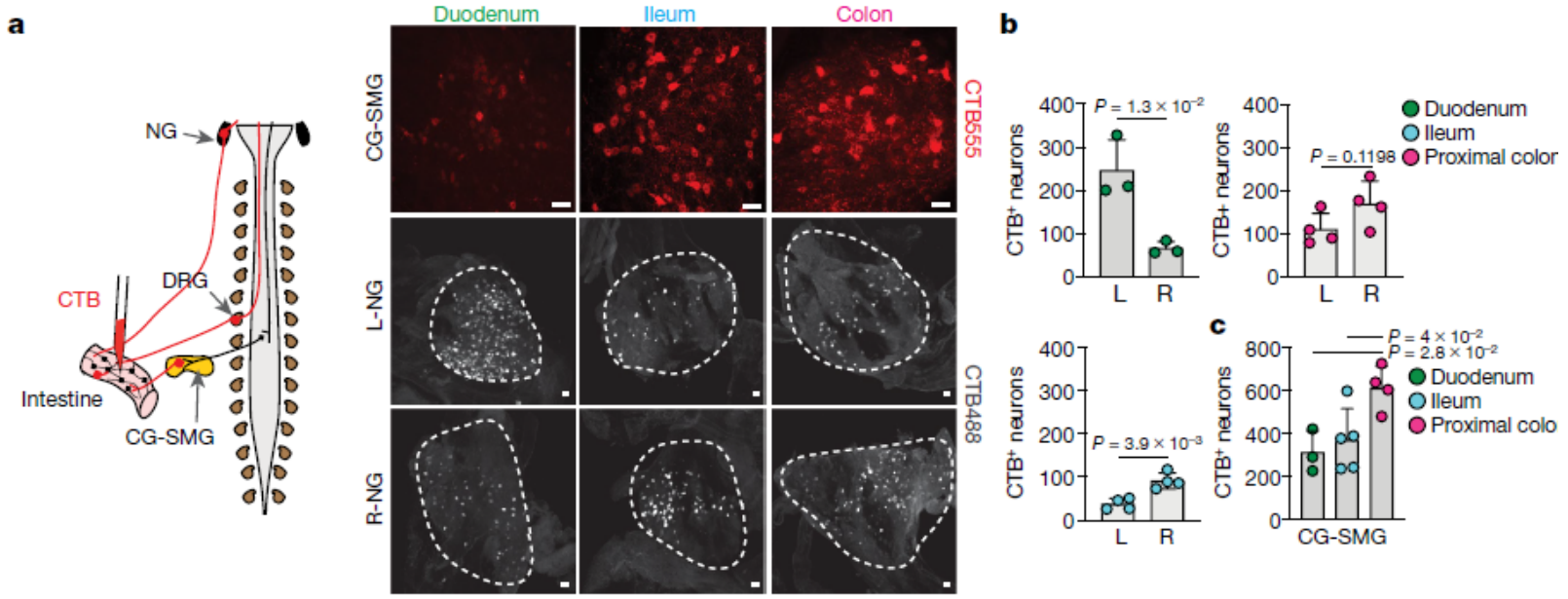
Microbiota modulate sympathetic neurons via a gut–brain circuit

https://doi.org/10.1038/s41586-020-2474-7

Received: 29 May 2018

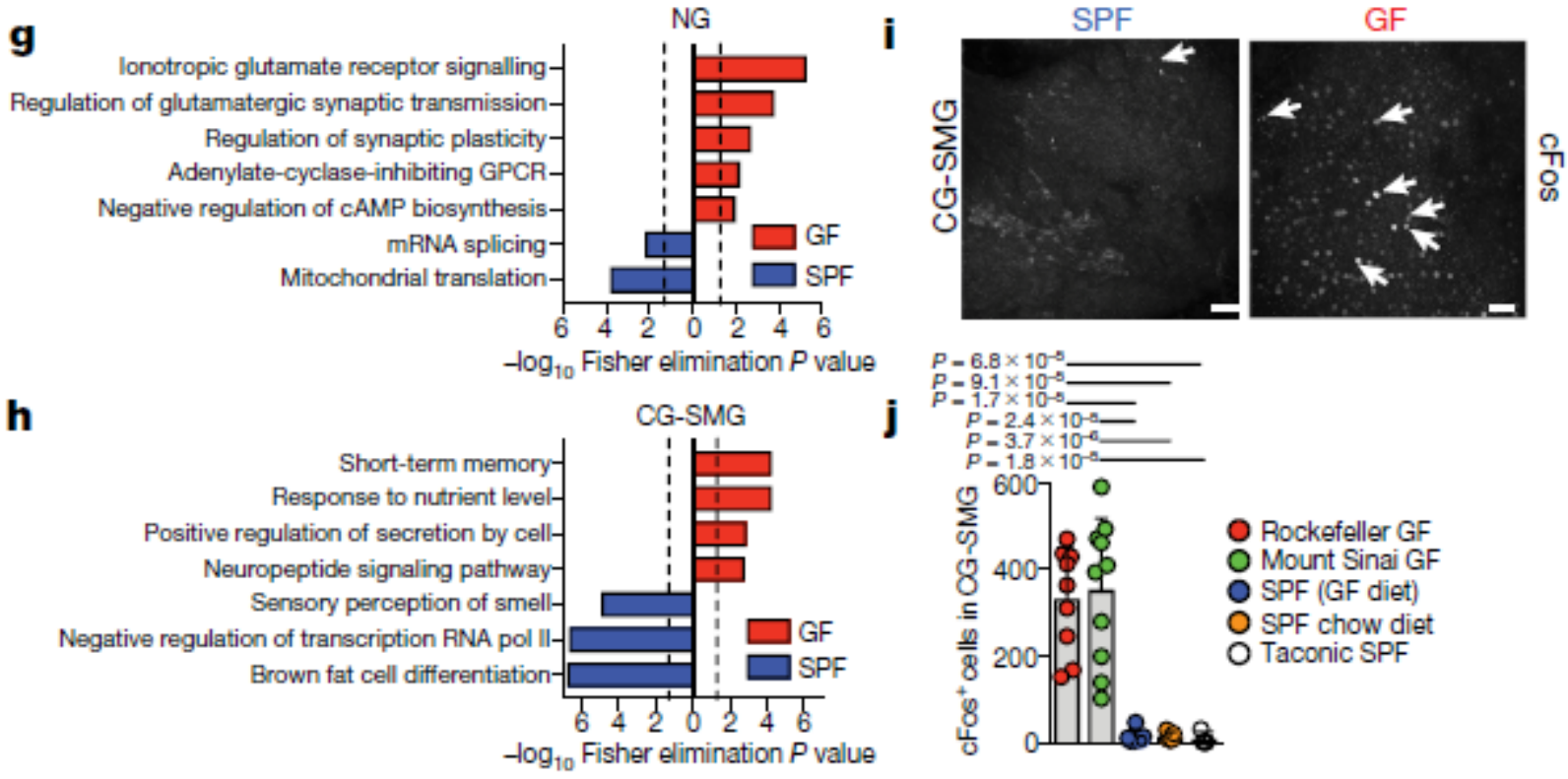
Accepted: 2 April 2020

Paul A. Muller[1,7]✉, Marc Schneeberger[2,8], Fanny Matheis[1,8], Putianqi Wang[2,8], Zachary Kerner[1], Anoj Ilanges[2], Kyle Pellegrino[2], Josefina del Mármol[3], Tiago B. R. Castro[1], Munehiro Furuichi[4], Matthew Perkins[5], Wenfei Han[5], Arka Rao[6], Amanda J. Pickard[6], Justin R. Cross[6], Kenya Honda[4], Ivan de Araujo[5] & Daniel Mucida[1]✉



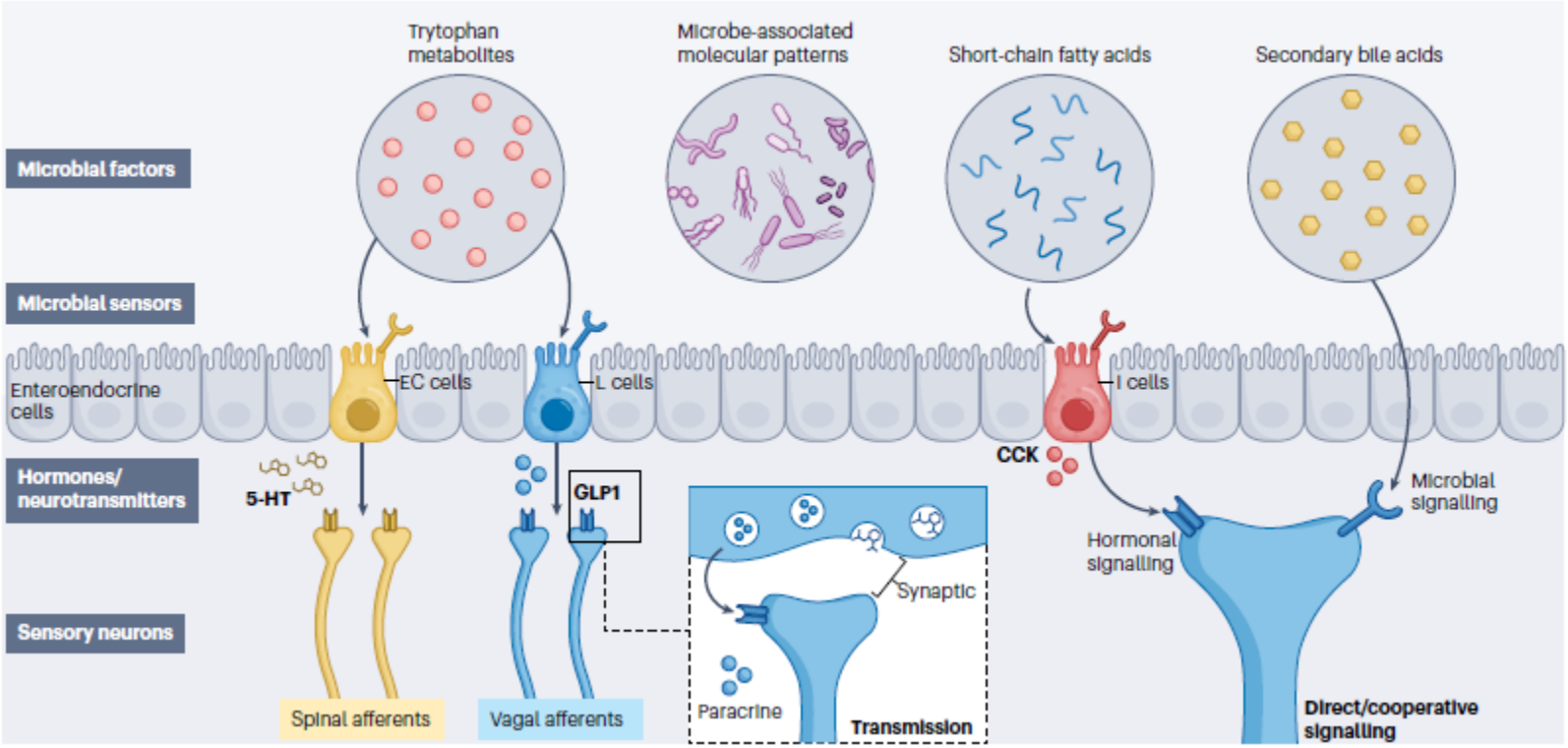
(Muller et al. Nature, 2020).

Microbiota



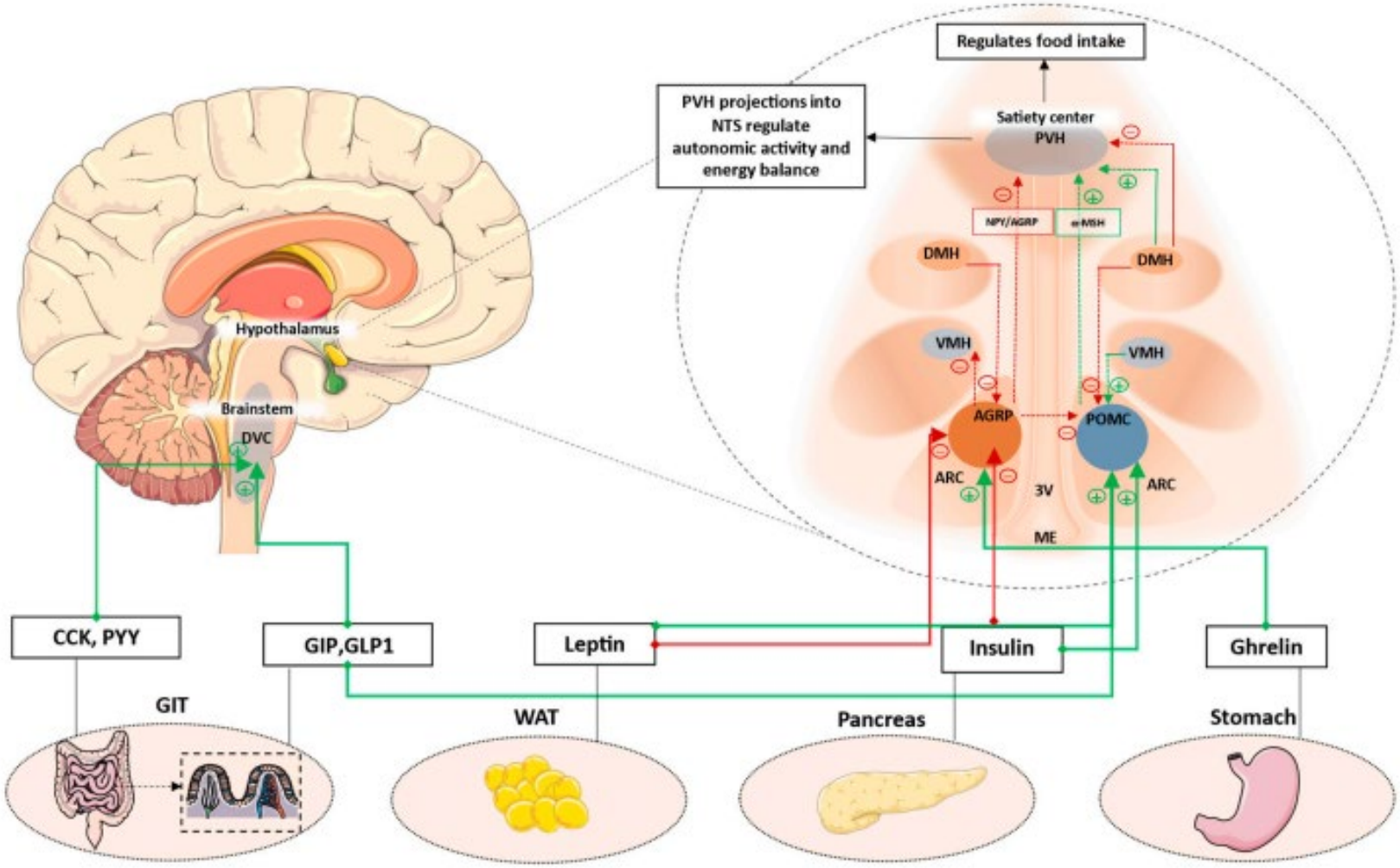
(Muller et al. Nature, 2020).

Microbiota x células enteroendócrinas



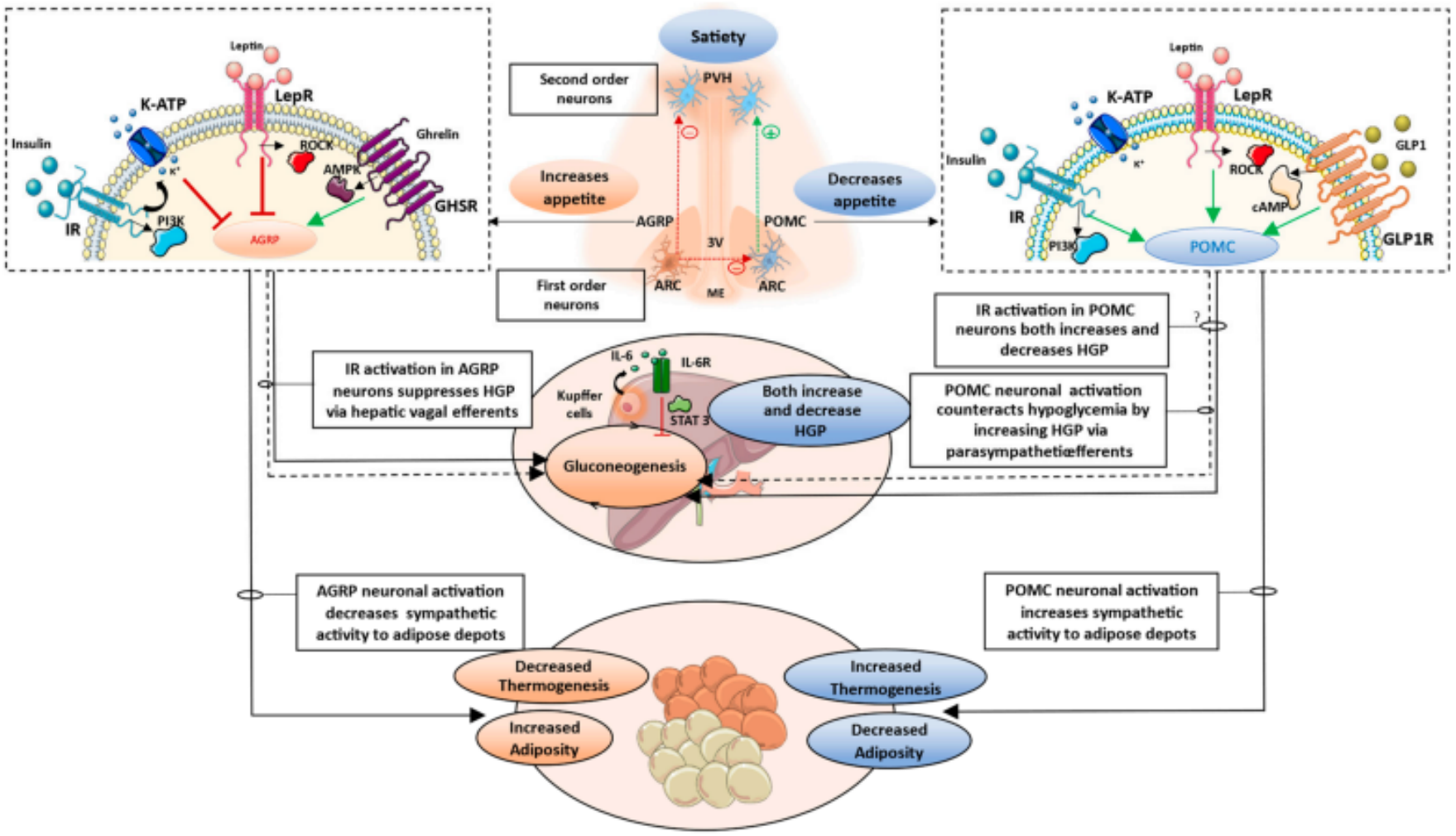
(Ohara & Hsiao. Nature Reviews – Microbiology, 2025).

Hormônios Intestinais x SNC



(Haspula & Cui. Cells, 2023).

Hormônios Intestinais x SNC



(Haspula & Cui. Cells, 2023).

Ação do GLP-1

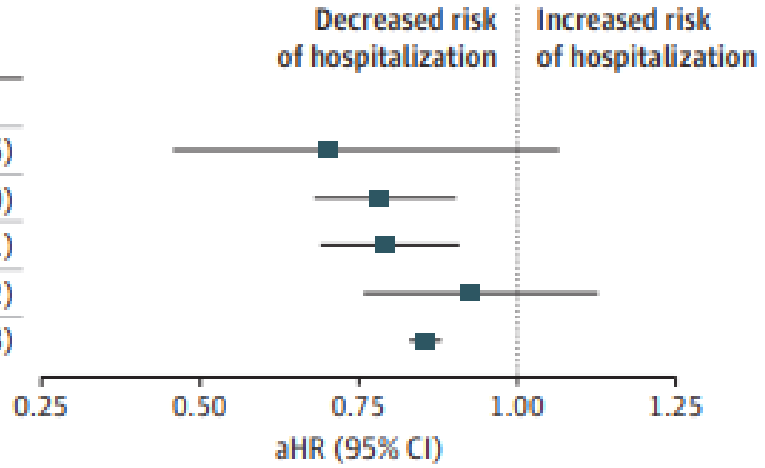
JAMA Psychiatry | Brief Report

Repurposing Semaglutide and Liraglutide for Alcohol Use Disorder

Markku Lähteenvuo, MD, PhD; Jari Tiihonen, MD, PhD; Anssi Solismaa, MD, PhD; Antti Tanskanen, PhD; Ellenor Mittendorfer-Rutz, PhD; Heidi Taipale, PhD

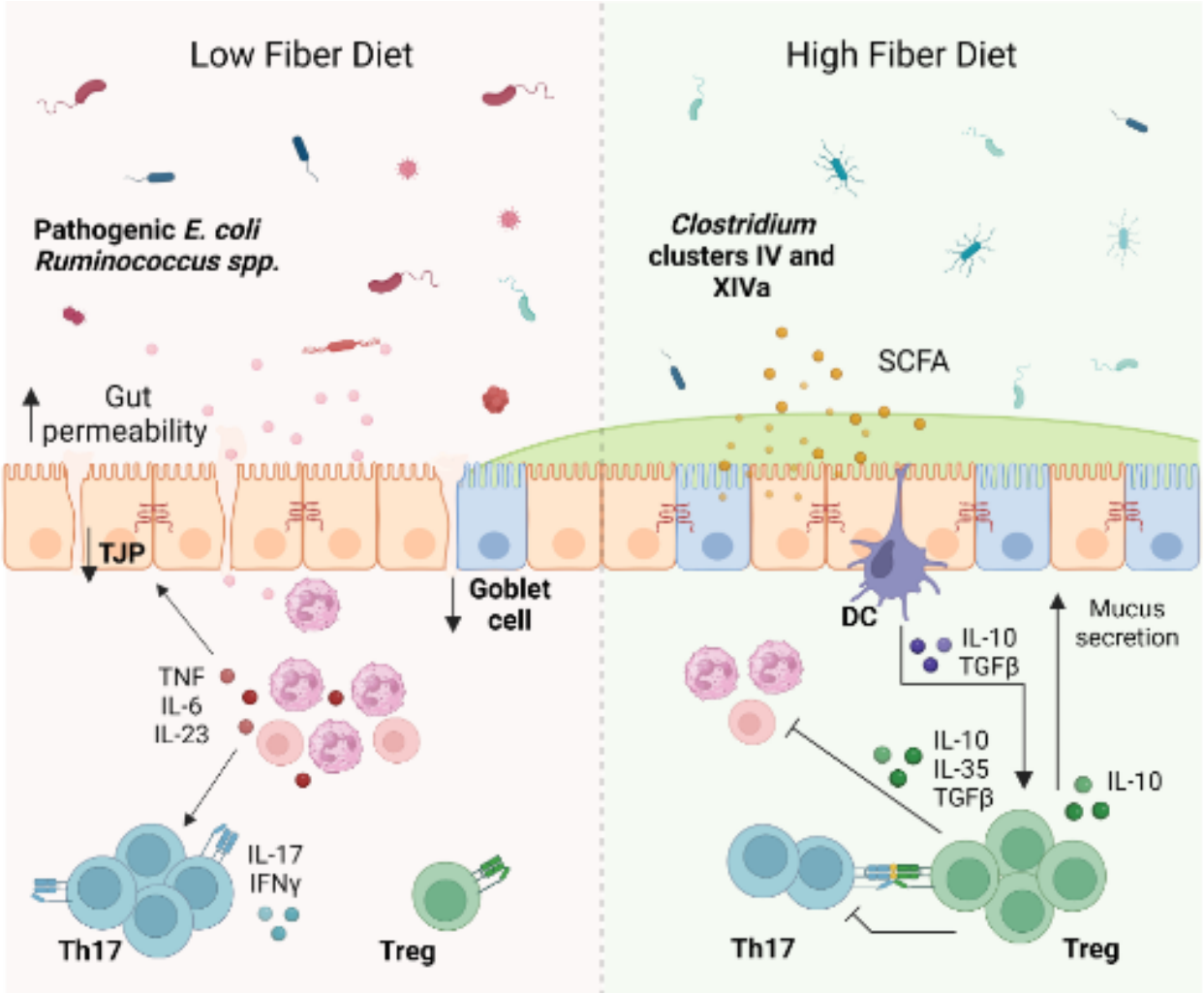
A Risk of somatic hospitalization associated with use of GLP-1 agonists and medications for AUD in within-individual model of persons with AUD

Drug	No. Users	Events	PYs	aHR (95% CI)
GLP-1 agonists				
Exenatide	98	50	167	0.70 (0.46-1.06)
Semaglutide	4321	708	4677	0.78 (0.68-0.90)
Liraglutide	2509	613	3076	0.79 (0.69-0.91)
Dulaglutide	1118	362	1443	0.92 (0.76-1.12)
AUD medications	75454	9995	73222	0.85 (0.83-0.88)



(Lähteenvuo et al. JAMA Psychiatry, 2025).

Doença Inflamatória Intestinal

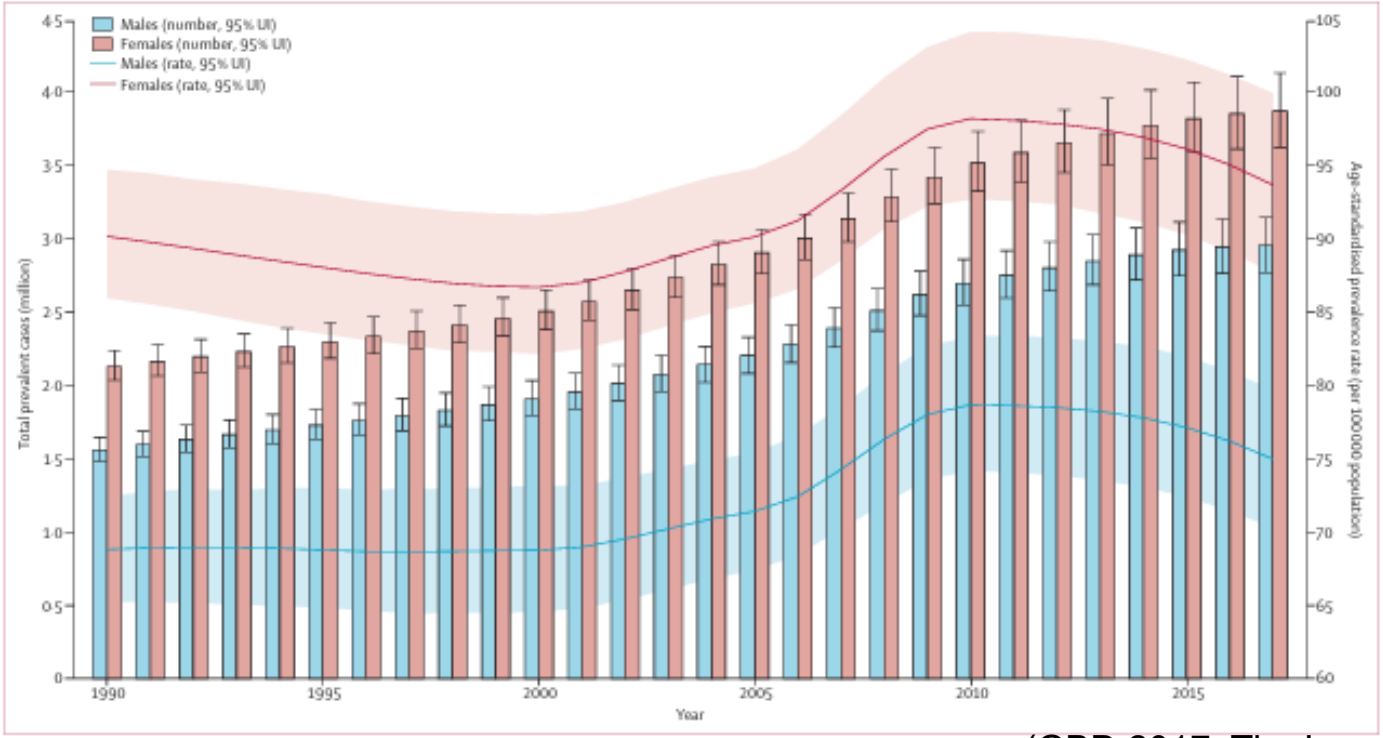


(Kunar, Ooi & Goldberg. Frontiers in Microbiology, 2023).

Doença Inflamatória Intestinal

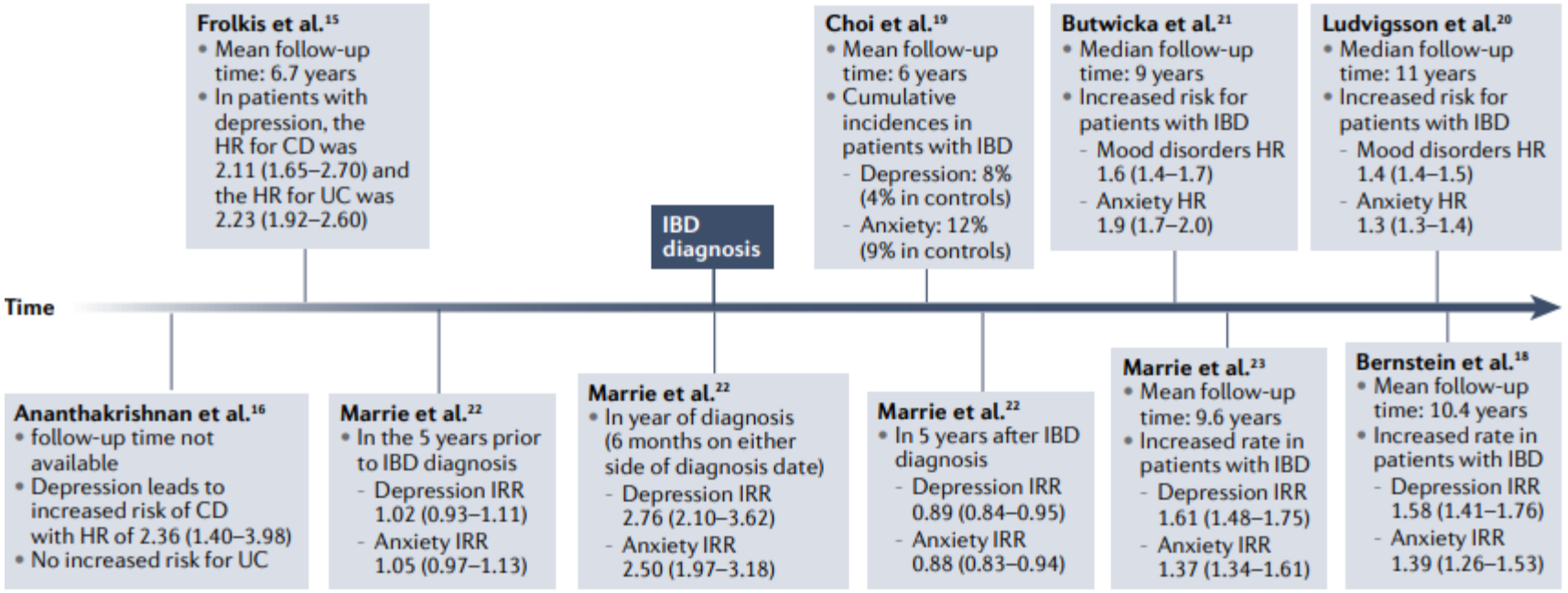
The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017

*GBD 2017 Inflammatory Bowel Disease Collaborators**



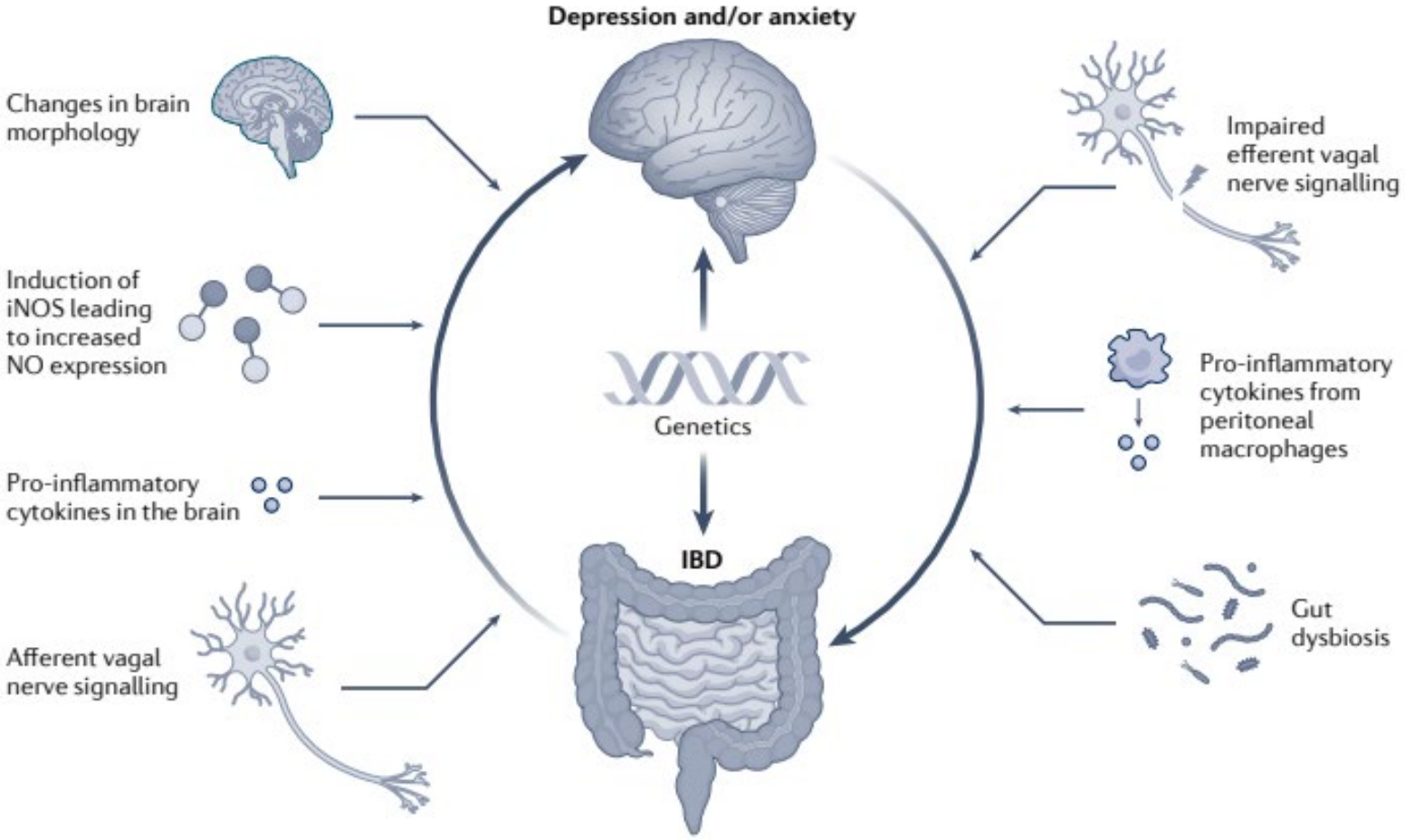
(GBD 2017. The Lancet, 2020).

Depressão e DII



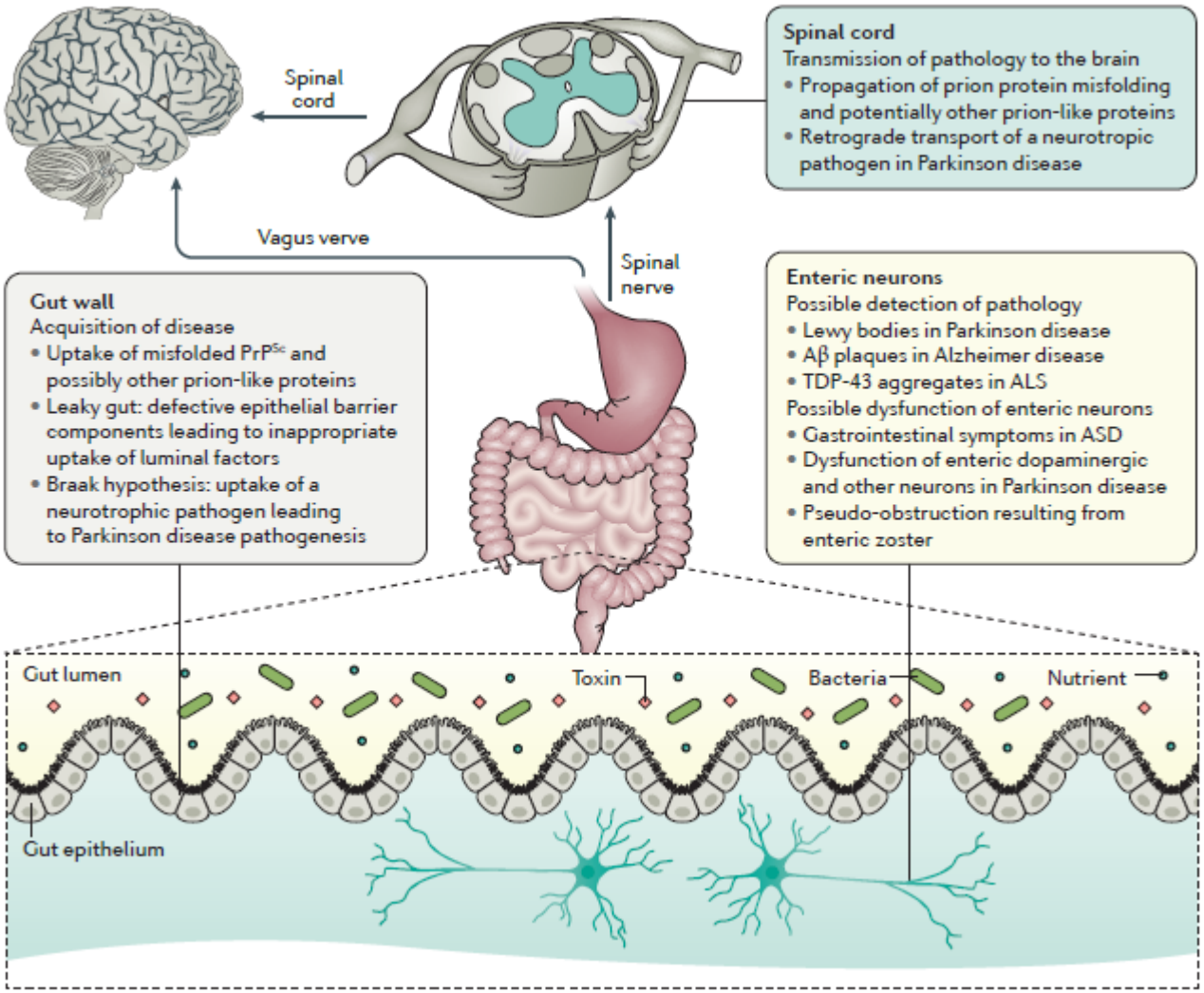
(Bisgaard et al. Nature Reviews – Gastroenterology and Hepathology, 2022).

Depressão e DII



(Bisgaard et al. Nature Reviews – Gastroenterology and Hepathology, 2022).

Implicações clínicas



(Rao & Gershon. Nature Reviews – Gastroenterology and Hepathology, 2016).

Varicella zoster virus

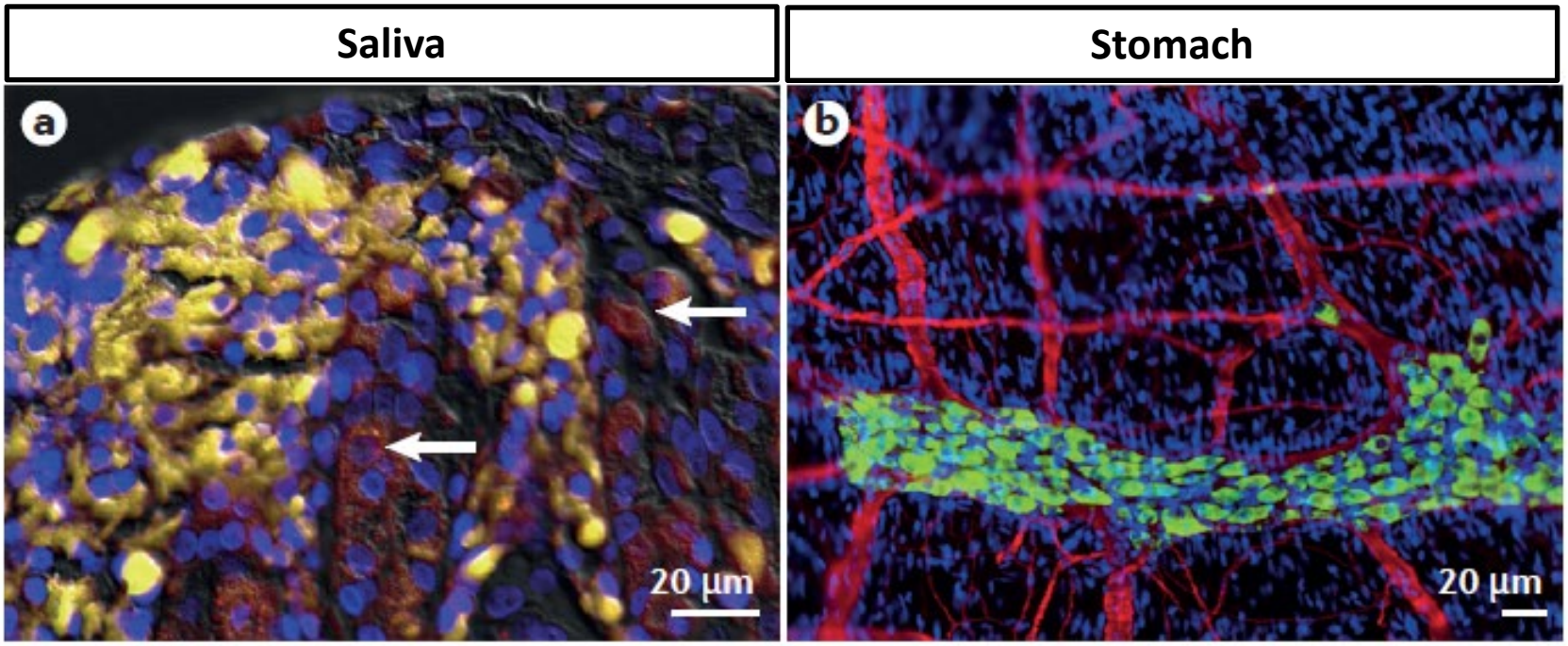
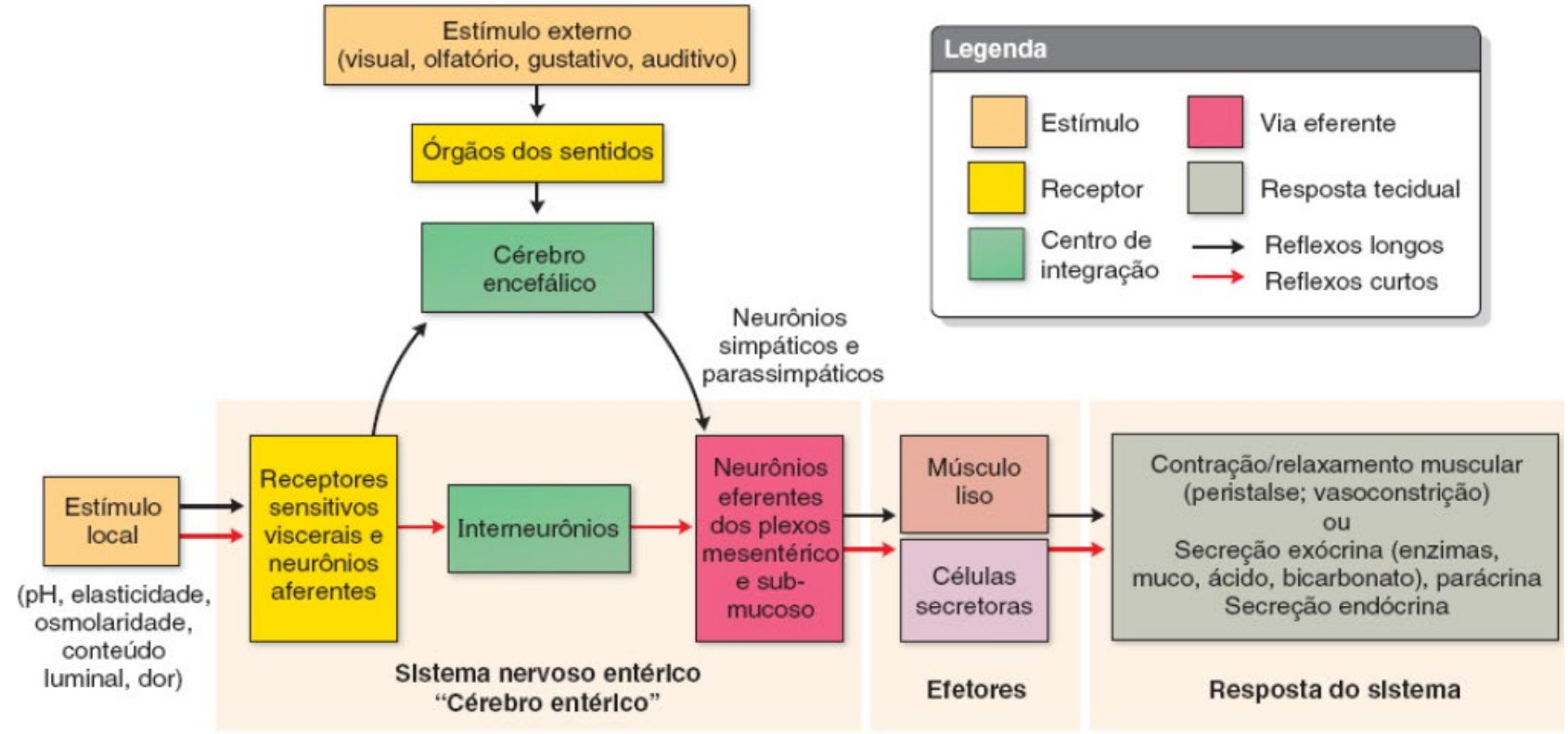


Figure 5 | **Enteric manifestations of lytic VZV infection of the mucosa and latent VZV**

(Rao & Gershon. Nature Reviews – Gastroenterology and Hepathology , 2016).

Revisão



(Moore – Anatomia Orientada Para a Clínica, VIII edição , 2019).

Obrigado!