Escuela de Osteopatía de Madrid Internacional

INTESTINO
BIOQUÍMICA POR ALIMENTACIÓN
Parte 5

OSTEOPATÍA E INTESTINOS

EL SISTEMA GASTROINTESTINAL ES SENSIBLE A LAS FUERZAS DE CONPRESIÓN Y CIZALLAMIENTO, LAS CÉLULAS ENTEROCROMAFINES SON MECANOSENSIBLES.

Front Endocrinol (Lausanne). 2019 Jan 15;9:804. doi: 10.3389/fendo.2018.00804. eCollection 2018.

In Pursuit of the Epithelial Mechanosensitivity Mechanisms.

Beyder A[1,2].

Author information

Abstract

Mechanosensation is critical for normal gastrointestinal (GI) function. Disruption in GI mechanosensation leads to human diseases. Mechanical forces in the GI tract are sensed by specialized mechanosensory cells, as well as non-specialized mechanosensors, like smooth muscle cells. Together, these cellular mechanosensors orchestrate physiologic responses. GI epithelium is at the interface of the body and the environment. It encounters a variety of mechanical forces that range from shear stress due to flow of luminal contents to extrinsic compression due to smooth muscle contraction. Mechanical forces applied to the GI mucosa lead to a large outflow of serotonin, and since serotonin is concentrated in a single type of an epithelial cell, called enterochromaffin cell (ECC), it was assumed that ECC is mechanosensitive. Recent studies show that a subset of ECCs is indeed mechanosensitive and that Piezo2 mechanosensitive ion channels are necessary for coupling force to serotonin release. This review aims to place this mechanism into the larger context of ECC mechanotransduction.

KEYWORDS: enteric nervous system; enteroendocine cells; mechanosensitive ion channel; mechanosensitivity; serotonin

PMID: 30697191 PMCID: PMC6340920 DOI: 10.3389/fendo.2018.00804

Y LLEGARON LOS ESCÉPTICOS DEL TRATAMIENTO VISCERAL ….

Berne Levy (TRATADO DE FISIOLOGÍA MÉDICA).

GRACIAS A MIS ESTUDIOS EN MEDICINA Y FARMACOLOGÍA PUEDO DOCUMENTAR QUE:

1.-CADA VEZ QUE TRABAJAMOS CON COMPRESIÓN UNA VÍSCERA SE LIBERA SEROTONINA QUE FACILITA LA MOTILIDAD VISCERAL .

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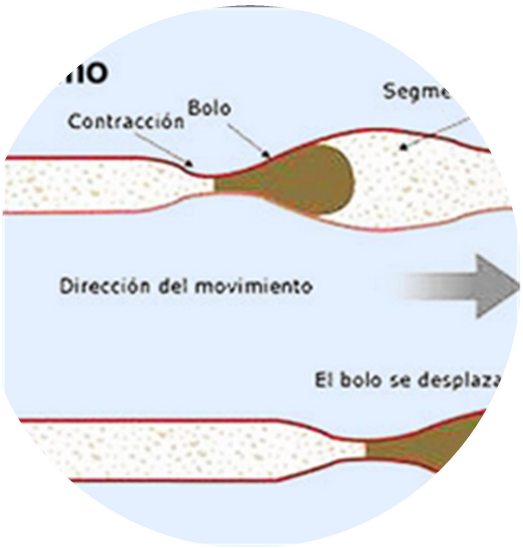
LA ACTUAL EVIDENCIA SUGIERE QUE LA SEROTONINA NO INFLUYE SOLAMENTE EN LA MOTILIDAD INTESTINAL SINO EN LA HEMATOPOYESIS, HOMEOSTASIS METABÓLICA Y METABOLISMO ÓSEO Y ES INFLUENCIADA , A SU VEZ , POR LA MICROBIOTA INTESTINAL.



LA SEROTONINA SE USA EN EL TRATAMIENTO FARMACOLÓGICO DE LA NAUSEA, DIARREA Y ESTREÑIMIENTO.

LA ACTUAL EVIDENCIA SUGIERE QUE LA SEROTONINA NO INFLUYE SOLAMENTE EN LA MOTILIDAD INTESTINAL SINO EN LA HEMATOPOYESIS, HOMEOSTASIS METABÓLICA Y METABOLISMO ÓSEO Y ES INFLUENCIADA , A SU VEZ , POR LA MICROBIOTA INTESTINAL.

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Nat Rev Gastroenterol Hepatol. 2017 Jul;14(7):412-420. doi: 10.1038/nrgastro.2017.51. Epub 2017 May 10.

Non-conventional features of peripheral serotonin signalling - the gut and beyond.

Spohn SN[1,2], Mawe GM[1].

Author information

Abstract

Serotonin was first discovered in the gut, and its conventional actions as an intercellular signalling molecule in the intrinsic and extrinsic enteric reflexes are well recognized, as are a number of serotonin signalling pharmacotherapeutic targets for treatment of nausea, diarrhoea or constipation. The latest discoveries have greatly broadened our understanding of non-conventional actions of peripheral serotonin within the gastrointestinal tract and in a number of other tissues. For example, it is now clear that bacteria within the lumen of the bowel influence serotonin synthesis and release by enterochromaffin cells. Also, serotonin can act both as a pro-inflammatory and anti-inflammatory signalling molecule in the intestinal mucosa via activation of serotonin receptors ($5\text{-}HT_7$ or $5\text{-}HT_4$ receptors, respectively). For decades, serotonin receptors have been known to exist in a variety of tissues other than the gut, but studies have now provided strong evidence for physiological roles of serotonin in several important processes, including haematopoiesis, metabolic homeostasis and bone metabolism. Furthermore, evidence for serotonin synthesis in peripheral tissues outside of the gut is emerging. In this Review, we expand the discussion beyond gastrointestinal functions to highlight the roles of peripheral serotonin in colitis, haematopoiesis, energy and bone metabolism, and how serotonin is influenced by the gut microbiota.

PMID: 28487547 PMCID: PMC5672796 DOI: 10.1038/nrgastro.2017.51

EL TRACTO GASTROINTESTINAL ES EL MAYOR PRODUCTOR DE SEROTONINA , TANTO MUCOSA , COMO NEURONAL. LA PRIMERA GENERA MEDIADORES PROINFLAMATORIOS Y LA SEGUNDA NEUROPROTECCIÓN

ACS Chem Neurosci. 2017 May 17;8(5):920-931. doi: 10.1021/acschemneuro.6b00414. Epub 2017 Mar 27.

Diverse Effects of Gut-Derived Serotonin in Intestinal Inflammation.

Shajib MS[1,2], Baranov A[1,2], Khan WI[1,2,3].

Author information

Abstract

The gut is the largest producer of serotonin or 5-hydroxytryptamine (5-HT) in the human body, and 5-HT has been recognized as an important signaling molecule in the gut for decades. There are two distinct sources of enteric 5-HT. Mucosal 5-HT is predominantly produced by enterochromaffin (EC) cells of the gastrointestinal (GI) tract, and neuronal 5-HT in the gut is produced by serotonergic neurons of the enteric nervous system (ENS). The quantity of mucosal 5-HT produced vastly eclipses the amount of neuronal 5-HT in the gut. Though it is difficult to separate the functions of neuronal and mucosal 5-HT, in the normal gut both types of enteric 5-HT work synergistically playing a prominent role in the maintenance of GI functions. In inflammatory conditions of the gut, like inflammatory bowel disease (IBD) recent studies have revealed new diverse functions of enteric 5-HT. Mucosal 5-HT plays an important role in the production of pro-inflammatory mediators from immune cells, and neuronal 5-HT provides neuroprotection in the ENS. Based on searches for terms such as "5-HT", "EC cell", "ENS", and "inflammation" in pubmed.gov as well as by utilizing pertinent reviews, the current review aims to provide an update on the role of enteric 5-HT and its immune mediators in the context of intestinal inflammation.

KEYWORDS: 5-hydroxytryptamine (5-HT); enteric 5-HT; enteric nervous system (ENS); enterochromaffin (EC) cells; inflammation; inflammatory bowel disease (IBD)

PMID: 28288510 DOI: 10.1021/acschemneuro.6b00414

[Indexed for MEDLINE]

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Behav Brain Res. 2015 Jan 15;277:32-48. doi: 10.1016/j.bbr.2014.07.027. Epub 2014 Jul 29.

Serotonin, tryptophan metabolism and the brain-gut-microbiome axis.

O'Mahony SM[1], Clarke G[2], Borre YE[3], Dinan TG[4], Cryan JF[1].

Author information

Abstract

The brain-gut axis is a bidirectional communication system between the central nervous system and the gastrointestinal tract. Serotonin functions as a key neurotransmitter at both terminals of this network. Accumulating evidence points to a critical role for the gut microbiome in regulating normal functioning of this axis. In particular, it is becoming clear that the microbial influence on tryptophan metabolism and the serotonergic system may be an important node in such regulation. There is also substantial overlap between behaviours influenced by the gut microbiota and those which rely on intact serotonergic neurotransmission. The developing serotonergic system may be vulnerable to differential microbial colonisation patterns prior to the emergence of a stable adult-like gut microbiota. At the other extreme of life, the decreased diversity and stability of the gut microbiota may dictate serotonin-related health problems in the elderly. The mechanisms underpinning this crosstalk require further elaboration but may be related to the ability of the gut microbiota to control host tryptophan metabolism along the kynurenine pathway, thereby simultaneously reducing the fraction available for serotonin synthesis and increasing the production of neuroactive metabolites. The enzymes of this pathway are immune and stress-responsive, both systems which buttress the brain-gut axis. In addition, there are neural processes in the gastrointestinal tract which can be influenced by local alterations in serotonin concentrations with subsequent relay of signals along the scaffolding of the brain-gut axis to influence CNS neurotransmission. Therapeutic targeting of the gut microbiota might be a viable treatment strategy for serotonin-related brain-gut axis disorders.

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KEYWORDS: Anxiety; Kynurenine; Microbiome; Pain; Serotonin; Tryptophan

PMID: 25078296 DOI: 10.1016/j.bbr.2014.07.027

EL EJE CEREBRO –INTESTINO ES UN SISTEMA DE COMUNICACIÓN BIDIRECCIONAL ENTRE EL SISTEMA NERVIOSO CENTRAL Y EL TRACTO GASTROINTESTINAL , EL MODULADOR DE ESTA RED ES LA SEROTONINA , CONDICIONADA POR LA MICROBIOTA Y SU INFLUENCIA EN EL METABOLISMO DEL TRIPTÓFANO

A SU VEZ LA SEROTONINA INFLUYE EN LA MICROBIOTA INTESTINAL

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Cell Mol Gastroenterol Hepatol. 2019;7(4):709-728. doi: 10.1016/j.jcmgh.2019.01.004. Epub 2019 Feb 1.

Modulation of Gut Microbiota Composition by Serotonin Signaling Influences Intestinal Immune Response and Susceptibility to Colitis.

Kwon YH[1], Wang H[1], Denou E[2], Ghia JE[3], Rossi L[4], Fontes ME[4], Bernier SP[4], Shajib MS[1], Banskota S[1], Collins SM[5], Surette MG[4], Khan WI[6].

Author information

Abstract

BACKGROUND & AIMS: Serotonin (5-hydroxytryptamine [5-HT]) is synthesized mainly within enterochromaffin (EC) cells in the gut, and tryptophan hydroxylase 1 (Tph1) is the rate-limiting enzyme for 5-HT synthesis in EC cells. Accumulating evidence suggests the importance of gut microbiota in intestinal inflammation. Considering the close proximity of EC cells and the microbes, we investigated the influence of gut-derived 5-HT on the microbiota and the susceptibility to colitis.

METHODS: Gut microbiota of Tph1$^{-/-}$ and Tph1$^{+/-}$ mice were investigated by deep sequencing. Direct influence of 5-HT on bacteria was assessed by using in vitro system of isolated commensals. The indirect influence of 5-HT on microbiota was assessed by measuring antimicrobial peptides, specifically β-defensins, in the colon of mice and HT-29 colonic epithelial cells. The impact of gut microbiota on the development of dextran sulfate sodium-induced colitis was assessed by transferring gut microbiota from Tph1$^{-/-}$ mice to Tph1$^{+/-}$ littermates and vice versa, as well as in germ-free mice.

RESULTS: A significant difference in microbial composition between Tph1$^{-/-}$ and Tph1$^{+/-}$ littermates was observed. 5-HT directly stimulated and inhibited the growth of commensal bacteria in vitro, exhibiting a concentration-dependent and species-specific effect. 5-HT also inhibited β-defensin production by HT-29 cells. Microbial transfer from Tph1$^{-/-}$ to Tph1$^{+/-}$ littermates and vice versa altered colitis severity, with microbiota from Tph1$^{-/-}$ mice mediating the protective effects. Furthermore, germ-free mice colonized with microbiota from Tph1$^{-/-}$ mice exhibited less severe dextran sulfate sodium-induced colitis.

CONCLUSIONS: These findings demonstrate a novel role of gut-derived 5-HT in shaping gut microbiota composition in relation to susceptibility to colitis, identifying 5-HT-microbiota axis as a potential new therapeutic target in intestinal inflammatory disorders.

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KEYWORDS: 5-Hydroxytryptamine (5-HT); Colitis; Microbiota; Tph1; β-defensins

PMID: 30716420 PMCID: PMC6462823 DOI: 10.1016/j.jcmgh.2019.01.004

Functional brain imaging of gastrointestinal sensation in health and disease

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Lukas Van Oudenhove, Qasim Aziz, Division of Neuroscience & Medicine, Department of GI Sciences, Hope Hospital, University of Manchester, United Kingdom

Steven J Coen, Centre for Neuroimaging Sciences, Institute of Psychiatry, London, United Kingdom

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Received: 2007-03-09 Accepted: 2007-03-12

patients will be highlighted.

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Key words: Functional brain imaging; Functional gastro-intestinal disorders; Visceral hypersensitivity; Gastrointestinal sensation; Psychological factors

Van Oudenhove L, Coen SJ, Aziz Q. Functional brain imaging of gastrointestinal sensation in health and disease. *World J Gastroenterol* 2007; 13(25): 3438-3445

http://www.wjgnet.com/1007-9327/13/3438.asp

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Resumen:

- Desde hace mucho tiempo se sabe, desde la experiencia cotidiana, así como desde estudios animales y humanos, que los procesos psicológicos, tanto afectivos como cognitivos, influyen en la función sensoriomotora gastrointestinal.
- Más específicamente, se ha sugerido un vínculo entre los factores psicológicos y la hipersensibilidad visceral, principalmente basado en la investigación en pacientes con trastorno gastrointestinal funcional.
- Sin embargo, hasta hace poco, la naturaleza exacta de esta relación putativa seguía siendo poco clara, principalmente debido a la falta de métodos no invasivos para estudiar los mecanismos (neurobiológicos) subyacentes a esta relación en los seres humanos no dormidos.

RESUMEN:

En este artículo, se da una visión general de la evidencia de imágenes cerebrales sobre la sensación gastrointestinal, con especial énfasis en los mecanismos cerebrales subyacentes a la interacción entre los procesos afectivos y cognitivos y la sensación visceral.

Gastroenterol Clin North Am. 2017 Mar;46(1):77-89. doi: 10.1016/j.gtc.2016.09.007. Epub 2017 Jan 4.

The Microbiome-Gut-Brain Axis in Health and Disease.

Dinan TG[1], Cryan JF[2].

Author information

1 APC Microbiome Institute, University College Cork, Cork, Ireland; Department of Psychiatry and Neurobehavioural Science, University College Cork, Cork, Ireland. Electronic address: t.dinan@ucc.ie.

2 APC Microbiome Institute, University College Cork, Cork, Ireland; Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland.

Abstract

Gut microbes are capable of producing most neurotransmitters found in the human brain. Evidence is accumulating to support the view that gut microbes influence central neurochemistry and behavior. Irritable bowel syndrome is regarded as the prototypic disorder of the brain-gut-microbiota axis that can be responsive to probiotic therapy. Translational studies indicate that certain bacteria may have an impact on stress responses and cognitive functioning. Manipulating the gut microbiota with psychobiotics, prebiotics, or even antibiotics offers a novel approach to altering brain function and treating gut-brain axis disorders, such as depression and autism.

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KEYWORDS: GABA; Microbiota; Psychobiotics; Serotonin; Short-chain fatty acids; Vagus nerve

PMID: 28164854 DOI: 10.1016/j.gtc.2016.09.007

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Chin Med J (Engl). 2016 Oct 5;129(19):2373-80. doi: 10.4103/0366-6999.190667.

Gut Microbiota-brain Axis.

Wang HX[1], Wang YP[2].

Author information

1 Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China.
2 Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing 100053; Center of Epilepsy, Beijing Institute for Brain Disorders, Laboratory of Brain Disorders, Capital Medical University, Beijing 100069, China.

Abstract

OBJECTIVE: To systematically review the updated information about the gut microbiota-brain axis.

DATA SOURCES: All articles about gut microbiota-brain axis published up to July 18, 2016, were identified through a literature search on PubMed, ScienceDirect, and Web of Science, with the keywords of "gut microbiota", "gut-brain axis", and "neuroscience".

STUDY SELECTION: All relevant articles on gut microbiota and gut-brain axis were included and carefully reviewed, with no limitation of study design.

RESULTS: It is well-recognized that gut microbiota affects the brain's physiological, behavioral, and cognitive functions although its precise mechanism has not yet been fully understood. Gut microbiota-brain axis may include gut microbiota and their metabolic products, enteric nervous system, sympathetic and parasympathetic branches within the autonomic nervous system, neural-immune system, neuroendocrine system, and central nervous system. Moreover, there may be five communication routes between gut microbiota and brain, including the gut-brain's neural network, neuroendocrine-hypothalamic-pituitary-adrenal axis, gut immune system, some neurotransmitters and neural regulators synthesized by gut bacteria, and barrier paths including intestinal mucosal barrier and blood-brain barrier. The microbiome is used to define the composition and functional characteristics of gut microbiota, and metagenomics is an appropriate technique to characterize gut microbiota.

CONCLUSIONS: Gut microbiota-brain axis refers to a bidirectional information network between the gut microbiota and the brain, which may provide a new way to protect the brain in the near future.

PMID: 27647198 PMCID: PMC5040025 DOI: 10.4103/0366-6999.190667

¿QUÉ VENTAJAS TIENE LA MEJORA DEL TRÁNSITO?

Microorganisms. 2019 Jan 31;7(2). pii: E41. doi: 10.3390/microorganisms7020041.

Potential Role for the Gut Microbiota in Modulating Host Circadian Rhythms and Metabolic Health.

Parkar SG[1], Kalsbeek A[2,3], Cheeseman JF[4].

Author information

Abstract

This article reviews the current evidence associating gut microbiota with factors that impact host circadian-metabolic axis, such as light/dark cycles, sleep/wake cycles, diet, and eating patterns. We examine how gut bacteria possess their own daily rhythmicity in terms of composition, their localization to intestinal niches, and functions. We review evidence that gut bacteria modulate host rhythms via microbial metabolites such as butyrate, polyphenolic derivatives, vitamins, and amines. Lifestyle stressors such as altered sleep and eating patterns that may disturb the host circadian system also influence the gut microbiome. The consequent disruptions to microbiota-mediated functions such as decreased conjugation of bile acids or increased production of hydrogen sulfide and the resultant decreased production of butyrate, in turn affect substrate oxidation and energy regulation in the host. Thus, disturbances in microbiome rhythms may at least partially contribute to an increased risk of obesity and metabolic syndrome associated with insufficient sleep and circadian misalignment. Good sleep and a healthy diet appear to be essential for maintaining gut microbial balance. Manipulating daily rhythms of gut microbial abundance and activity may therefore hold promise for a chrononutrition-based approach to consolidate host circadian rhythms and metabolic homeorhesis.

KEYWORDS: chronodisruption; clock genes; gut microbiome; plant food; prebiotics; sleep/wake rhythm

PMID: 30709031 PMCID: PMC6406615 DOI: 10.3390/microorganisms7020041

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La disbiosis altera el metabolismo de la triptofanasa, la calidad del sueño y el sistema inmunitario.

El **triptófano** se transforma en **serotonina**, una molécula que regula la motilidad intestinal (SÓLO CON COMPRIMIR LA VISCERA).

pero algunos estudios han descubierto que está vinculado con la producción de melatonina (la hormona del sueño).

Asimismo, se ha revelado la existencia de un nuevo mecanismo de transporte del triptófano hacia el cerebro, con el correspondiente impacto en las funciones cerebrales como el sueño.

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¿QUÉ VENTAJAS TIENE LA MEJORA DEL TRÁNSITO?

Maturitas. 2017 Sep;103:45-53. doi: 10.1016/j.maturitas.2017.06.025. Epub 2017 Jun 23.

Estrogen-gut microbiome axis: Physiological and clinical implications.

Baker JM[1], Al-Nakkash L[2], Herbst-Kralovetz MM[3].

Author information

Abstract

Low levels of gonadal circulating estrogen observed in post-menopausal women can adversely impact a diverse range of physiological factors, with clinical implications for brain cognition, gut health, the female reproductive tract and other aspects of women's health. One of the principal regulators of circulating estrogens is the gut microbiome. This review aims to shed light on the role of the gut microbiota in estrogen-modulated disease. The gut microbiota regulates estrogens through secretion of β-glucuronidase, an enzyme that deconjugates estrogens into their active forms. When this process is impaired through dysbiosis of gut microbiota, characterized by lower microbial diversity, the decrease in deconjugation results in a reduction of circulating estrogens. The alteration in circulating estrogens may contribute to the development of conditions discussed herein: obesity, metabolic syndrome, cancer, endometrial hyperplasia, endometriosis, polycystic ovary syndrome, fertility, cardiovascular disease (CVD) and cognitive function. The bi-directional relationship between the metabolic profile (including estrogen levels) and gut microbiota in estrogen-driven disease will also be discussed. Promising therapeutic interventions manipulating the gut microbiome and the metabolic profile of estrogen-driven disease, such as bariatric surgery and metformin, will be detailed. Modulation of the microbiome composition subsequently impacts the metabolic profile, and vice versa, and has been shown to alleviate many of the estrogen-modulated disease states. Last, we highlight promising research interventions in the field, such as dietary therapeutics, and discuss areas that provide exciting unexplored topics of study.

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KEYWORDS: Cancer; Dysbiosis; Estrobolome; Fertility; Metabolic syndrome; Phytoestrogen

PMID: 28778332 DOI: 10.1016/j.maturitas.2017.06.025

Uno de los principales reguladores de los estrógenos circundantes es la microbiota intestinal.

Cuando este proceso es alterado debido a la disbiosis intestinal (que como hemos visto mejora con el tratamiento osteopático), la reducción de la desconjugación resulta en la reducción de los estrógenos circulantes.

Esto favorece la obesidad , el síndrome metabólico, el cáncer, la hiperplasia endometrial, la endometriosis, el síndrome de ovario poliquístico, el cáncer, la hiperplasia endometrial, la enfermedad cardiovascular y el empeoramiento dela función cognitiva.

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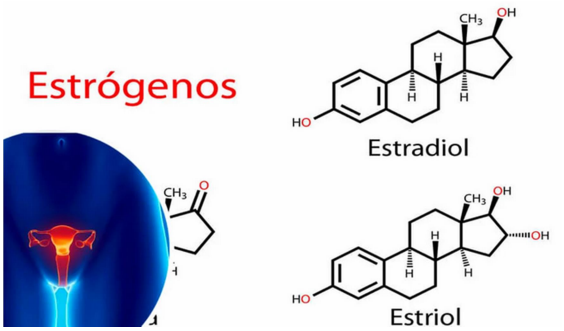

¿ QUÉ VENTAJAS TIENE LA MEJORA DEL TRÁNSITO

Environ Toxicol Pharmacol. 2015 Jul;40(1):241-58. doi: 10.1016/j.etap.2015.06.009. Epub 2015 Jun 9.

A review on endocrine disruptors and their possible impacts on human health.

Kabir ER[1], Rahman MS[2], Rahman I[3].

Author information

Abstract

Endocrine disruption is a named field of research which has been very active for over 10 years, although the effects of endocrine disruptors in wildlife have been studied mainly in vast since the 1940s. A large number of chemicals have been identified as endocrine disruptors and humans can be exposed to them either due to their occupations or through dietary and environmental exposure (water, soil and air). Endocrine disrupting chemicals are compounds that alter the normal functioning of the endocrine system of both humans and wildlife. In order to understand the vulnerability and risk factors of people due to endocrine disruptors as well as the remedies for these, methods need to be developed in order to predict effects on populations and communities from the knowledge of effects on individuals. For several years there have been a growing interest on the mechanism and effect of endocrine disruptors and their relation with environment and human health effect. This paper, based on extensive literature survey, briefly studies the progress mainly in human to provide information concerning causative substances, mechanism of action, ubiquity of effects and important issues related to endocrine disruptors. It also reviews the current knowledge of the potential impacts of endocrine disruptors on human health so that the effects can be known and remedies applied for the problem as soon as possible.

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KEYWORDS: Chemicals; Endocrine disruption; Hormones; Organs; Toxicity

PMID: 26164742 DOI: 10.1016/j.etap.2015.06.009

EMUNTORIO-> elminamos tóxicos y disruptores encocrinos.

CIRCULACIÓN ENTEROHEPÁTICA-> reducción del colesterol exógeno (importante reducir con dieta la síntesis endógena para no empeorar al paciente).

NANCE, DM; SANDERS, VM(2007)AUTONOMIC INNERVATION AND REGULATIONOF THE INMUNE SYSTEM. BRAIN BEHAV INMUN 21,736-745.

- CUALQUIER ESTÍMULO SENSORIAL O INMUNE, DESDE LE CÓRTEX, ACTIVA EL SNS. LA NORADRENALINA TIENE UN EFECTO SOBRE LA MÉDULA ÓSEA, EL TIMO, LOS GANGLIOS LINFÁTICOS, EL BAZO Y EL GALT. Y TODOS ESTOS SOBRE LA CÉLULA INMUNE.

¿ QUÉ VENTAJAS TIENE LA MEJORA DEL TRÁNSITO?

Competición por la vitamina B12: **o Síndrome de intestino ciego**.

El alimento se demora o deja de movilizarse a través de los intestinos . Esto causa proliferación bacteriana excesiva. Lleva también a que se presentes problemas en la absorción de nutrientes (vit liposolubles o b12)

VITAMINAS A (RETINOPATÍAS),D (INMUNOSUPRESIÓN, OSTEOPOROSIS),E(ALT EN REG EPITELIOS Y PROPIOCEPCIÓN),K (OSTEOPOROSIS POR DÉFICIT DE OSTEOCALCINA Y ALTERACIONES COAGULACIÓN).

Teodorczyk-Injeyan et al. OBSERVARON REDUCCIÓN DEL TNF ALFA TRAS LA MANIPULACIÓN OSTEOPÁTICA

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Ther. 2006 Jan;29(1):14-21.

lative therapy reduces inflammatory cytokines but not substance F ts.

, Injeyan HS, Ruegg R.

ion

earch, Canadian Memorial Chiropractic College, Toronto, Ontario, Canada.

nine the effect of a single spinal manipulation therapy (SMT) on the in vitro production of inflamr
, and interleukin (IL) 1beta, in relation to the systemic (in vivo) levels of neurotransmitter substa

asymptomatic subjects were assigned to SMT, sham manipulation, or venipuncture control gr
ustment in the thoracic spine. Blood and serum samples were obtained from subjects before
ervention. Whole-blood cultures were activated with lipopolysaccharide (LPS) for 24 hours. Cyto
and serum SP levels were assessed by specific immunoassays.

tudy period, a significant proportion (P </= .05) of sham and control subjects demonstrated pro
or necrosis factor alpha and IL-1beta. Conversely, in a comparable proportion of cultures from S
h cytokines decreased gradually. Normalization of the observed alterations to reflect the change
ated that, within 2 hours after intervention, the production of both cytokines increased significan
rast, a significant (P < .001 to .05) reduction of proinflammatory cytokine secretion was observe
all study groups, serum levels of SP remained unaltered within 2 hours after intervention.

-treated subjects show a time-dependent attenuation of LPS-induced production of the inflamn
c levels of SP. This suggests SMT-related down-regulation of inflammatory-type responses via

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Microcirculation. 2000 Dec;7(6 Pt 1):411-8.

TNF-alpha modulates arteriolar reactivity secondary to a change in intimal permeability.

Matsuki T[1], Duling BR.

Author Information

1 Department of Molecular Physiology & Biological Physics, University of Virginia Health Sciences Center, Charlottesville 22906-0011, USA.

Abstract

OBJECTIVE: Inflammatory stimuli are often associated with marked changes in vascular reactivity. Tumor necrosis factor-alpha (TNF-alpha) is and important inflammatory cytokine with diverse effects including the ability to increase vascular endothelial cell permeability and to alter the structure of the endothelial cell glycocalyx. We have previously shown that arteriolar sensitivity to vasoactive materials is influenced by a barrier property of the arteriolar endothelium, and here we test the hypothesis that TNF-alpha might increase intimal permeability and thereby increase the access of circulating arginine-vasopressin (AVP) to vascular smooth muscle. Our objective in the current work was to show that TNF-alpha-mediated modulation of intimal cell permeability may produce both quantitative and qualitative alterations in vascular reactivity to arginine-vasopressin.

METHODS: Hamster cheek pouch arterioles (approximately 65 microm, I.d.) were double-cannulated and perfused. [Arg8]-vasopressin was applied selectively to either the luminal or the adventitial surface of isolated cannulated arterioles. The reactivity of the arterioles to vasopressin was determined in the presence and absence of TNF-alpha (0.625 microg/mL; 1 hour).

RESULTS: Adventially applied AVP induced a concentration-dependent vasoconstriction with a threshold of approximately 1 pM, and a maximal constriction at 10 nM. In contrast, luminally applied AVP induced a biphasic response, showing a modest vasodilation in the range of 1 to 100 pM, and constrictions at doses higher than 1 nM. Maximal constrictions were not obtained with luminal doses of AVP as high as 1 microM; (i.e., at doses 100-fold higher than those that produced maximal responses with adventitial application). Dilations induced by luminal application of AVP were significantly attenuated by 10 microM Nomega-nitro-L-arginine methyl ester (L-NAME), but were not altered by 10 microM indomethacin. After treatment with TNF-alpha, the concentration-response curve for luminally applied AVP showed a more pronounced constriction and the dilator component of the agonist was eliminated. There was no change in the reactivity to adventitially applied AVP or to adventitial applications of acetylcholine. Nonspecific increases in endothelial cell permeability induced by 3-[(3-chloroamino-dopropyl)-dimethylamino]-1-propanesulfonate (CHAPS) also eliminated the potency differences between luminal and adventitial drug application. Following TNF-alpha treatment and loss of the dilator component of the response to AVP, L-NAME was still capable of reducing the arteriolar sensitivity to ACh, thus showing that the endothelial cell machinery for NO production was intact following TNF-alpha treatment.

CONCLUSION: Our findings show that the reactivity of intact resistance vessels to agonists that have both endothelial-dependent and smooth muscle cell-dependent components will be complex. Reactivity is the summation of: 1) the relative sensitivities of smooth muscle and endothelial cells to AVP, 2) the release of nitric oxide or other mediators from endothelium, and 3) the restricted access of intraluminal AVP to arteriolar smooth muscle cells. Thus, cytokines, and perhaps other materials that regulate endothelial cell permeability, can modify arteriolar reactivity by altering transendothelial cell access of luminal stimuli to the smooth muscle cells, as well as by acting directly on smooth muscle or by influencing the production of endothelial cell-derived vasoactive materials. In the case of agonists that have an endothelial cell dilator component as well as a smooth muscle constrictor component, this may result in a qualitative change in response as is shown here with AVP.

PMID: 11142338

Implicaciones Osteopáticas:

- El tratamiento osteopático incide a nivel vegetativo en la regulación de la tensión arterial y frecuencia cardiaca: **Knutson G. 2001**
- Holt et al. 2010
- Campos and Burrel 2012
- Welch A.2008
- Da Silva et al 2018

- Amoroso Borges et al 2018Budgell and Hirano 2001
- Roy et al. 2009
- MODIFICAR Frecuencia Cardiaca/ TA (VFC)
- Win et al. 2015
- Younes M 2017

Sampath et al (2017) demostraron que la manipulación involucra al sistema nervioso simpático y al sistema endocrino

TOMADO DE F. RICARD: Mecanismo de acción biológico de las manipulaciones vertebrales con HVT.

¿ QUÉ VENTAJAS TIENE LA MEJORA DEL TRÁNSITO

Las bacterias intestinales ***comensales presentes en el GALT del intestino delgado contribuyen a la formación de una célula inmunitaria*** *«linfocito intraepitelial doble-positivo» (DP IEL),* ***que permite al huésped tolerar las sustancias inofensivas de su entorno.***

Atenuando las respuestas inmunitarias y reduciendo la inflamación.

Cervantes-Barragan L, Chai JN, Tianero MD, DiLuccia B, Ahern PP, Merriman J, Cortez VS, Caparon MG, Donia MS, Gilfillan S, Cella M, Gordon JI, Hsieh C-S, Colonna M.

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Lactobacillus reuteri induces gut intraepithelial CD4 CD8 alpha alpha T cells. Science. 2017 ; 357 (6353) : 806-810. doi : 10.1126/science.aah5825

- *A través del uso de técnicas de inmunotinción con anticuerpos específicos, se encontraron iTregs para expresar moléculas CD25, un marcador de superficie del antígeno que se experimentó en Células T, lo que indica que los iTregs se desarrollan a través de ciertas respuestas inflamatorias.*
- *De hecho, iTregs son específicamente abundantes en el tracto digestivo, tracto respiratorio, y otros sitios inflamatorios, donde la afluencia de materiales exógenos es común.*
- *Es bien sabido que una variedad de microbiota que viven en el tracto intestinal descarga una enorme cantidad de productos microbianos como lipopolisacáridos, flagellinas, ARN de doble cadena, y fragmentos de ADN ricos en citosina y guanina .*
- *Existe , pues, vía entérico-nutricional una regulación del sistema inmunitario para mantener adecuadamente las defensas del huésped mientras se suprimen las respuestas inflamatorias crónicas*

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Review

Advances in Nutritional Research on Regulatory T-Cells

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Received: 29 July 2013; in revised form: 17 October 2013 / Accepted: 22 October 2013 / Published: 28 October 2013

Abstract: Many clinical and animal studies have shown that certain dietary components exert anti-inflammatory properties that aid in the amelioration of chronic inflammatory diseases. Among the various proposed channels through which dietary components affect immune responses, regulatory T-cells (Tregs) are emerging as key targets for the dietary prevention of chronic inflammatory diseases. In this review, immunoregulation by Tregs is briefly described, followed by a summary of recent advances and possible applications of techniques for the study of Tregs. In addition, this review provides an overview of the current knowledge on Treg regulation by certain dietary components, including vitamins, omega-3 polyunsaturated fatty acids, and polyphenols. The caveats of previous studies are also discussed in order to highlight the distinctions between dietary studies and immunological approaches. Consequently, this review may help to clarify the means by which nutritional components influence Tregs.

Keywords: nutrition; immunology; regulatory T-cells; Tregs; anti-inflammatory

Defensa del tracto gastrointestinal y sistema nervioso entérico: importancia del stress

- *Los mastocitos pueden ser activados por varios agentes incluyendo antígenos (AG), CCK (a través del receptor CCK2), neurotensina, sustancia P (SP) y neurokinina A (NKA) liberada por los terminales de las neuronas aferentes espinales.*

(Yu and Perdue 2001).

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Am J Physiol Gastrointest Liver Physiol. 2001 Jan;280(1):G7-G13.

Stress and gastrointestinal tract. II. Stress and intestinal barrier function.

Söderholm JD[1], Perdue MH.

Author information

1 Intestinal Disease Research Program, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada.

Abstract

The influence of stress on the clinical course of a number of intestinal diseases is increasingly being recognized, but the underlying mechanisms are largely unknown. This themes article focuses on recent findings related to the effects of stress on mucosal barrier function in the small intestine and colon. Experiments using animal models demonstrate that various types of psychological and physical stress induce dysfunction of the intestinal barrier, resulting in enhanced uptake of potentially noxious material (e.g., antigens, toxins, and other proinflammatory molecules) from the gut lumen. Evidence from several studies indicates that in this process, mucosal mast cells play an important role, possibly activated via neurons releasing corticotropin-releasing hormone and/or acetylcholine. Defining the role of specific cells and mediator molecules in stress-induced barrier dysfunction may provide clues to novel treatments for intestinal disorders.

PMID: 11123192 DOI: 10.1152/ajpgi.2001.280.1.G7

Defensa del tracto gastrointestinal y sistema nervioso entérico: implicaciones nutricionales sobre la HISTAMINOSIS.

- *Los mastocitos activados pueden liberar muchas moléculas de señalización, como leucotrienos, interleucinas, prostaglandinas, TNF, triptamina, histamina y 5-HT.*
- *Están bajo el control de las neuronas entéricas del plexo submucoso, probablemente influenciado por neuronas posganglionares simpáticas noradrenérgicas y posiblemente bajo control neuroendocrino*

Immunol Rev. 2001 Feb;179:61-73.

Role of mast cells in intestinal mucosal function: studies in models of hypersensitivity and stress.

Yu LC[1], Perdue MH.

Author information

1 Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada.

Abstract

A single layer of epithelial cells lines the gastrointestinal tract, forming a critical barrier between the lunminal contents, which includes antigens and other noxious substances, and the body proper. It has become clear in recent years that the role of mast cells in the gastrointestinal mucosa is not only to react to antigens, but also to actively regulate the barrier and transport properties of the intestinal epithelium. Mucosal mast cells respond to both IgE/antigen-dependent and non-IgE-dependent stimulation, releasing bioactive mediators into adjacent tissues where they induce physiological responses. Studies in models of hypersensitivity and stress have provided evidence that changes in mucosal function are due to either direct action of mast cell mediators on epithelial receptors and/or indirect action via nerves/neurotransmitters.

PMID: 11292029 DOI: 10.1034/j.1600-065x.2001.790107.x

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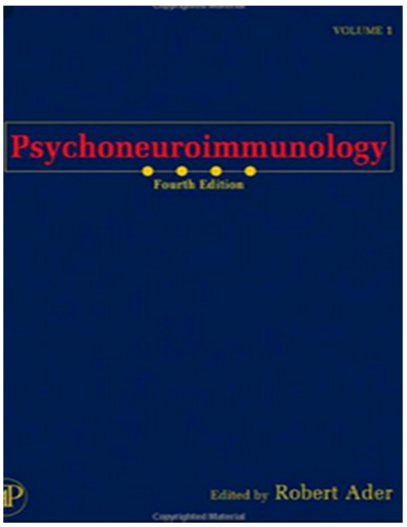
Defensa del tracto gastrointestinal y sistema nervioso entérico:

Su activación sensibiliza las fibras nerviosas aferentes extrínsecas, p.ej. mediante la liberación de histamina y otros compuestos, estimula las neuronas entéricas, estimula la extravasación leucocitaria y genera directamente la secreción de fluidos por la mucosa (por ejemplo, por liberación del factor activador de plaquetas [PAF] y leucotrieno C4.
Se considera que los mastocitos median los defectos de barrera inducidos por el estrés generados por el estrés psicológico. W.Janig.

IMPLICACIONES OSTEOPÁTICAS : INDUCIR UNA RESPUESTA PARASIMPÁTICOTÓNICA : ***DEGENHART ET AL 2007*** *"tras el tratamiento osteopáticos aumentan las Beta endorfinas y se evidencia una activación parasimpática durante 5 días".*

Control del Sistema immune por el SNS.

- *Implica que el telencéfalo influye, vía hipotalámica ,en las respuestas inmunes.*
- *Sabemos que una situación de estrés emocional importante puede inmunosuprimirnos durante , al menos , una semana.*



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Front Neuroendocrinol. 1992 Jan;13(1):61-94.

Immune-neuroendocrine circuits: integrative role of cytokines.

Besedovsky HO[1], del Rey A.

Author information

1 Department of Research, University Hospital, Basel, Switzerland.

Abstract

Several efficient autoregulatory mechanisms confer a certain degree of autonomy to the immune system. However, increasing evidence shows that immune processes operate in a coordinated fashion with other body systems. In this article, we discuss concepts and facts concerning interactions between immune and neuroendocrine mechanisms. There are clear examples that immune cells can be influenced by hormones, neurotransmitters, and neuropeptides and also by alterations in brain functions. Conversely, immune-derived products such as lymphokines and monokines can affect endocrine, autonomic, and central mechanisms. Neuroendocrine responses occur during the activation of the immune system. These responses can be elicited by innocuous antigens; they can also be detected during pathological conditions involving immune activation, and in many cases are dissociable from the effects of the disease itself and from the stress of being sick. On this basis, we emphasize the multidirectional nature of the communication processes between the immune, endocrine, and nervous systems. The role of lymphokines and monokines as messengers able to convey information to neuro and endocrine structures about the present state of activity of the immune system is stressed. The relevance of immune-neuroendocrine interactions for immunoregulation and host defenses is discussed as well as the active role of the immune system in mediating metabolic and homeostatic adjustments or derangements during the course of certain infectious, inflammatory, and neoplastic processes. The evidence available suggests that complex immune-neuroendocrine networks operate under both physiological and pathological conditions.

PMID: 1468599

EFECTOS DEL SIMPÁTICO SOBRE EL SISTEMA INMUNE: EVIDENCIAS QUE RESPALDAN LA HIPÓTESIS.

- *Los tejidos linfoides primarios y secundarios son inervados por neuronas simpáticas noradrenérgicas postganglionares.*
- *Las varicosidades de los terminales simpáticos se pueden encontrar en estrecha proximidad con linfocitos T y macrófagos.*

Front Horm Res. 2017;48:1-18. doi: 10.1159/000452902. Epub 2017 Feb 28.

Immune-Neuro-Endocrine Reflexes, Circuits, and Networks: Physiologic and Evolutionary Implications.

Del Rey A, Besedovsky HO.

Abstract

The existence of a network of interactions between the immune and nervous systems that influences host defenses and brain functions is now well-established. Here we discuss how immune and classical neuro/sensorial signals are processed in the brain and how neuro-endocrine immunoregulatory and behavioral responses are integrated. Considering the ability of brain cells to produce cytokines, originally described as immune cell products, we propose that the tripartite synapse plays a central role in the integration of neuro-endocrine-immune interactions. We also propose that the immune-neuro-endocrine responses that influence the course of transmissible and other diseases predisposing to infections can be relevant for evolution, either by restoring health or by mediating an active process of negative selection.

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PMID: 28245448 DOI: 10.1159/000452902

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EFECTOS DEL SIMPÁTICO SOBRE EL SISTEMA INMUNE: EVIDENCIAS QUE RESPALDAN LA HIPÓTESIS. ***EL BAZO.***

- ***El bazo está inervado por neuronas simpáticas postganglionares que son numéricamente en relación al peso del órgano, tres veces mayores que la inervación simpática renal.***
- ***Además: La simpatectomía altera las respuestas inmunitarias esplénicas (por ejemplo, aumento de la citotoxicidad natural de las células asesinas, respuestas de proliferación de linfocitos a la estimulación mitógena y producción de interleucina-1***
- ***La estimulación del nervio esplénico reduce las respuestas inmunes esplénicas mediadas por alfa-adrenoceptores.***
- ***La lesión o estimulación del núcleo ventromedial del hipotálamo activa respuestas inmunes esplénicas. Estos cambios no están presentes después tras denervación del bazo***

Neuroimmunomodulation. 1995 Jul-Aug;2(4):203-15.

The autonomic nervous system as a communication channel between the brain and the immune system.

Hori T[1], Katafuchi T, Take S, Shimizu N, Niijima A.

Author information

1 Department of Physiology, Kyushu University Faculty of Medicine, Fukuoka, Japan.

Abstract

Much evidence from various fields has revealed multiple channels of communication between the brain and the immune system. Among the routes of signal transmission, this review focuses on the roles and mechanisms of neural communication between the two systems. As for the centrifugal neural pathway by which the brain modulates immunity, there are various requirements for the noradrenergic sympathetic innervation of the primary and secondary lymphoid organs. In addition to the presence of beta- and alpha-adrenergic receptors on different types of immunocompetent cells, histological studies have demonstrated direct contact between tyrosine-hydroxylase-positive nerve terminals and lymphocytes in the spleen and thymus. The exposure of lymphocytes and macrophages to adrenergic agonists in vitro modulates their functions. A surgical or chemical sympathectomy is known to alter the immune responses in rodents. Recent data from the rat show that stress-induced immunosuppression is only slightly affected, if at all, by hypophysectomy or adrenalectomy, whereas it is largely dependent on sympathetic innervation. The splenic sympathetic nerve alters the firing rate by an ablation or stimulation of the hypothalamus, the administration of cytokines or neuropeptides, and an exposure to stress. Furthermore, such procedures provoke the increase in the release of noradrenaline in the rat spleen as assessed by in vivo microdialysis. The altered activities of the splenic sympathetic nerves mentioned above have been found to be causally related to the alteration in immunological responses including natural killer cytotoxicity. The splenic sympathetic nerve may thus constitute a communication channel that mediates central modulation of peripheral cellular immunity. Although the roles and mechanisms of parasympathetic control of lymphoid organs still remain obscure, recent data suggest that the thymic vagal efferent nerve may be involved in central modulation of immunity. Finally, electrophysiological studies have shown that hepatic vagal afferents may be one of the pathways through which blood-borne cytokines signal the brain.

PMID: 8963749 DOI: 10.1159/000097198

¿ QUÉ MÁS SABEMOS?: ¿ QUÉ DICE LA EVIDENCIA CIENTÍFICA SOBRE LA MANIPULACIÓN OSTEOPÁTICA

- *WALKOWSKI ET AL 2014*

1.-MEJOR RESPUESTA INMUNE DE LOS INDIVIDUOS

2.-INCREMENTO DE LOS ANTICUERPOS Y REGULACIÓN DE LEUCOCITOS CIRCULANTES.

3.-MEJORA PERFIL INMUNOLÓGICO DE LOS INDIVIDUOS.

Leucocitos	5.746
Linfocitos	1.363
Linfocitos T	881
Linfocitos B	130
Linfocitos CD4+	231
Linfocitos CD8+	513
CD4/CD8	0.58
IgA	1.195
IgG	2.285
IgM	264

Walkowski S et al . Osteopathic manipulative therapy induces early plasma citoquine reléase and mobilization of a population of blood dendritic cells. PloS One 2014 Mar 10;9(3)e90132.

EFECTOS DEL SIMPÁTICO SOBRE EL SISTEMA INMUNE: EVIDENCIAS QUE RESPALDAN LA HIPÓTESIS.

- *Muchas neuronas simpáticas postganglionares que se proyectan en los nervios de la piel no muestran actividad espontánea y reflejo. Estas neuronas no se dirigen a vasos, glándulas sudoríparas o erectores del pelo, sino que se asocian al sistema inmune de la piel.*

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Life Sci. 1996;58(18):1485-507.

Immunity at the surface: homeostatic mechanisms of the skin immune system.

Williams IR[1], Kupper TS.

Author information

1 Harvard Skin Disease Research Center, Brigham and Women's Hospital, Boston, MA 02115, USA.

Abstract

The coordinated function of multiple epidermal and dermal cell populations allows the skin immune system to respond rapidly and effectively to a wide variety of insults occurring at the interface of the organism and its environment. Keratinocytes are the first line of defense in the skin immune system, and keratinocyte-derived cytokines are pivotal in mobilizing leukocytes from blood and signaling other cutaneous cells. Cytokine-mediated cellular communication also enables dermal fibroblasts and endothelial cells lining the cutaneous vasculature to participate in immune and inflammatory responses. Skin is an important site for antigen presentation, and both epidermal Langerhans cells and dermal dendritic cells play pivotal roles in T cell-mediated immune responses to antigens encountered in skin. Proinflammatory signaling pathways are necessarily balanced by a variety of regulatory pathways that help maintain the homeostatic functioning of the skin immune system.

PMID: 8649179 DOI: 10.1016/0024-3205(96)00042-2

La piel como órgano inmunológico(en endocrino se habla de la piel como órgano endocrino).

- *Barrera poderosa contra patógenos contiene mastocitos, macrófagos y células de Langerhans así como el doble de linfocitos T que los encontrados en la circulación.*

Immunol. 2006 Apr 1;176(7):4431-9.

The vast majority of CLA+ T cells are resident in normal skin.

lark RA[1], Chong B, Mirchandani N, Brinster NK, Yamanaka K, Dowgiert RK, Kupper TS.

Author information

Department of Dermatology, Brigham and Women's Hospital and Harvard Skin Disease Research Center, Boston, MA 02115, US

bstract

here are T cells within normal, noninflamed skin that most likely conduct immunosurveillance and are implicated in the developme soriasis. We isolated T cells from normal human skin using both established and novel methods. Skin resident T cells expressed f CLA, CCR4, and CCR6, and a subset expressed CCR8 and CXCR6. Skin T cells had a remarkably diverse TCR repertoire and v h1 memory effector cells with smaller subsets of central memory, Th2, and functional T regulatory cells. We isolated a surprisin onexpanded T cells from normal skin. To validate this finding, we counted T cells in sections of normal skin and determined that t pproximately 1 x 10(6) T cells/cm(2) normal skin and an estimated 2 x 10(10) T cells in the entire skin surface, nearly twice the r ells in the circulation. Moreover, we estimate that 98% of CLA(+) effector memory T cells are resident in normal skin under restir onditions. These findings demonstrate that there is a large pool of memory T cells in normal skin that can initiate and perpetuate i eactions in the absence of T cell recruitment from the blood.

omment in

omment on "The vast majority of CLA+ T cells are resident in normal skin". [J Immunol. 2006]

MID: 16547281 DOI: 10.4049/jimmunol.176.7.4431

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BIOQUÍMICA POR ALIMENTACIÓN

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REVIEW

Dendritic cells: Vehicles for tolerance induction and prevention of autoimmune diseases

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[a]*Department of Rheumatology, Leiden University Medical Center, The Netherlands*
[b]*Department of Ophthalmology, Leiden University Medical Center, The Netherlands*

Abstract

Adaptive immune responses are orchestrated by specialized professional antigen-presenting cells (APC dendritic cells (DCs), which play crucial roles as initiators and modulators of adaptive immune responses. feature of DCs is their phenotypic and functional plasticity. In the absence of any inflammation or patl elements, most DCs in peripheral tissues and lymphoid organs have a resting, immature phenotype character high endocytic capacity and low surface expression of MHC- and costimulatory molecules. However, upon inte with microbial ligands, pro-inflammatory cytokines or CD40Ligand, DCs rapidly acquire an activated phe These mature DCs have a very efficient T cell-priming ability as a consequence of upregulation of MH costimulatory molecules on their cell surface. For this reason, DC-based vaccines have been used successf combat infections and malignancies. Nonetheless, evidence is accumulating that, especially immature, o matured, DCs also have a potent ability to tolerize T cells or prevent undesired immune reactions. Therefore, and prospective strategies to promote the inherent tolerogenic potential of DCs are a rational approach for the t of autoimmune diseases such as rheumatoid arthritis (RA). This review summarizes some aspects of the int ability of DCs to steer the outcome of immunity and their potency to modulate the outcome of various patho conditions.
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Keywords: Autoimmunity; Dendritic cells; Immune regulation; Rheumatoid arthritis; Tolerance induction

Generation of regulatory dendritic cells and $CD4^+Foxp3^+$ T cells by probiotics administration suppresses immune disorders

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[a]Department of Life Sciences, Gwangju Institute of Science and Technology, Gwangju 500-712, Korea; [b]Chonnam National University Medical School, Gwangju 501-749, Korea; [c]Cardiovascular Research Institute, Yonsei University College of Medicine, Seoul 120-752, Korea; and [d]Center for Distributed Sensor Network, Gwangju Institute of Science and Technology, Gwangju 500-712, Korea

Edited by Anjana Rao, Harvard Medical School, Boston, MA, and approved December 8, 2009 (received for review April 15, 2009)

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The beneficial effects of probiotics have been described in many diseases, but the mechanism by which they modulate the immune system is poorly understood. In this study, we identified a mixture of probiotics that up-regulates $CD4^+Foxp3^+$ regulatory T cells (Tregs). Administration of the probiotics mixture induced both T-cell and B-cell hyporesponsiveness and down-regulated T helper (Th) 1, Th2, and Th17 cytokines without apoptosis induction. It also induced generation of $CD4^+Foxp3^+$ Tregs from the $CD4^+CD25^-$ population and increased the suppressor activity of naturally occurring $CD4^+CD25^+$ Tregs. Conversion of T cells into $Foxp3^+$ Tregs is directly mediated by regulatory dendritic cells (rDCs) that express high levels of IL-10, TGF-β, COX-2, and indoleamine 2,3-dioxygenase. Administration of probiotics had therapeutical effects in experimental inflammatory bowel disease, atopic dermatitis, and rheumatoid arthritis. The therapeutical effect of the probiotics is associated with enrichment of $CD4^+Foxp3^+$ Tregs in the inflamed regions. Collectively, the administration of probiotics that enhance the generation of rDCs and Tregs represents an applicable treatment of inflammatory immune disorders.