AMBIENTE INTESTINAL DO PACIENTE ONCOLÓGICO: ALTERAÇÕES E SUPORTE

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MÉDICO VETERINÁRIO ONCOSPES
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PRESIDENTE DA SOCIEDADE LATINOAMERICANA DE ONCOLOGIA VETERINÁRIA - SLOVET

MV. DR. FABIO ALVES TEIXEIRA
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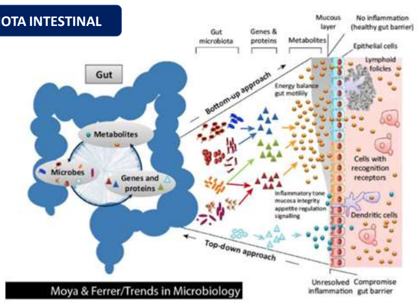
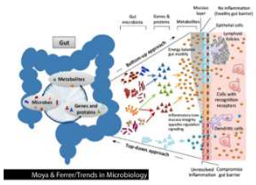
PROF. FACULDADE ANCLIVEPA
SOCIEDADE BRASILEIRA DE NUTRIÇÃO E NUTROLOGIA DE CÃES E GATOS

"A MEDICINA É A CIÊNCIA DAS ETERNAS VERDADES TRANSITÓRIAS"

MICROBIOTA INTESTINAL



MICROBIOTA INTESTINAL



VOCÊ JÁ OUVIU FALAR EM ONCOMICROBIOMA?

ONCOMICROBIOMA

CONFIGURAÇÕES DO MICROBIOMA QUE PARTICIPAM DIRETA OU INDIRETAMENTE NO DESENVOLVIMENTO DO CÂNCER PODENDO EXERCER INFLUÊNCIA POSITIVA OU NEGATIVA NA EVOLUÇÃO DA NEOPLASIA

ONCOMICROBIOMA

EFEITO PROMOTOR DE CÂNCER

- PRODUÇÃO DE METABÓLITOS CARCINOGÊNICOS
- ALTERAÇÃO DA IMUNIDADE LOCAL E SISTÊMICA

MODULAÇÃO POSITIVA OU NEGATIVA DO TRATAMENTO

- AUMENTANDO A EFICÁCIA DA TERAPIA
- DIMINUINDO A EFICÁCIA DA TERAPIA
- AUMENTANDO A TOXICIDADE DO TRATAMENTO

ONCOMICROBIOMA

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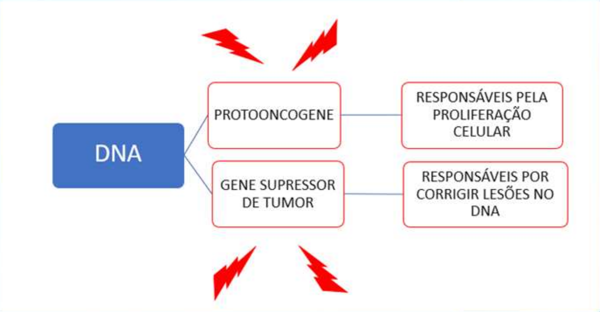
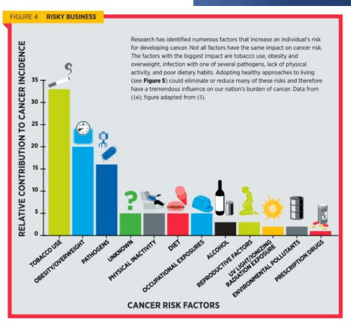
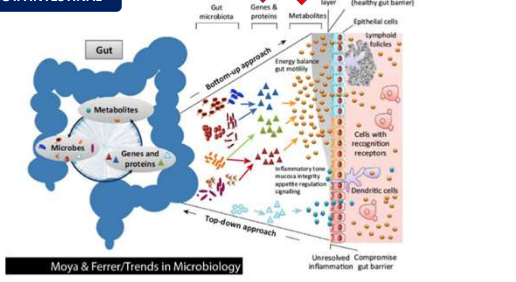


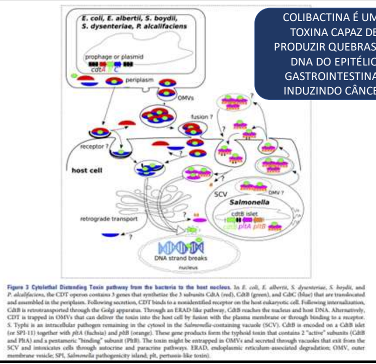
FATORES ETIOLÓGICOS NO DESENVOLVIMENTO DO CÂNCER



E AS GENOTOXINAS PRODUZIDAS DURANTE A DISBIOSE INTESTINAL PODEM INDUZIR CÂNCER?

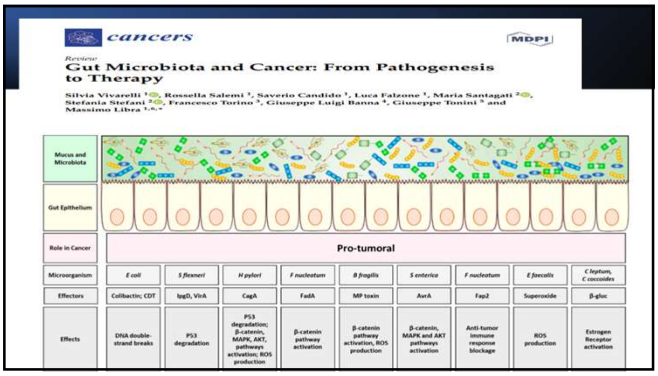
MICROBIOTA INTESTINAL

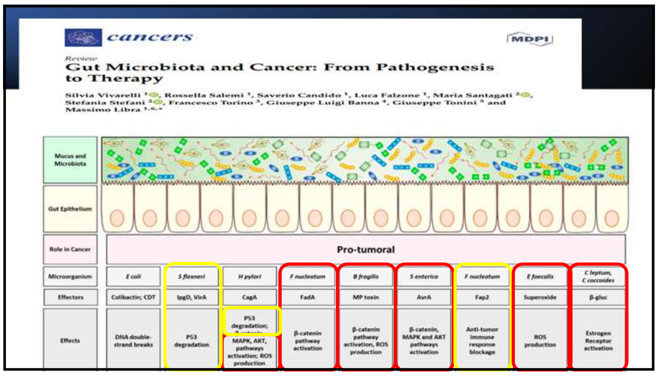




COLIBACTINA É UMA TOXINA CAPAZ DE PRODUZIR QUEBRAS NO DNA DO EPITÉLIO GASTROINTESTINAL INDUZINDO CÂNCER

ALTERAÇÃO NA MICROBIOTA E A PRODUÇÃO DE CARCINÓGENOS


cancers
MDPI
Review
Gut Microbiota and Cancer: From Pathogenesis to Therapy
Silvia Vivarelli 1, Rossella Salemi 1, Saverio Candido 1, Luca Falzone 1, Maria Santagati 2, Stefania Stefani 2, Francesco Torino 3, Giuseppe Luigi Banna 4, Giuseppe Tonini 5 and Massimo Libra 1,6,*
Mucus and Microbiota
Gut Epithelium
Role in Cancer
Pro-tumoral
Microorganism
E coli
S flexneri
H pylori
F nucleatum
B fragilis
S enterica
F nucleatum
E faecalis
C leptum, C coccoides
Effectors
Colibactin; CDT
IpgD, VirA
CagA
FadA
MP toxin
AvrA
Fap2
Superoxide
β-gluc
Effects
DNA double-strand breaks
P53 degradation
P53 degradation; β-catenin, MAPK, AKT, pathways activation; ROS production
β-catenin pathway activation
β-catenin pathway activation, ROS production
β-catenin, MAPK and AKT pathways activation
Anti-tumor immune response blockage
ROS production
Estrogen Receptor activation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Colibactin; CDT
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DNA double-strand breaks
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P53 degradation; β-catenin, MAPK, AKT, pathways activation; ROS production
β-catenin pathway activation
β-catenin pathway activation, ROS production
β-catenin, MAPK and AKT pathways activation
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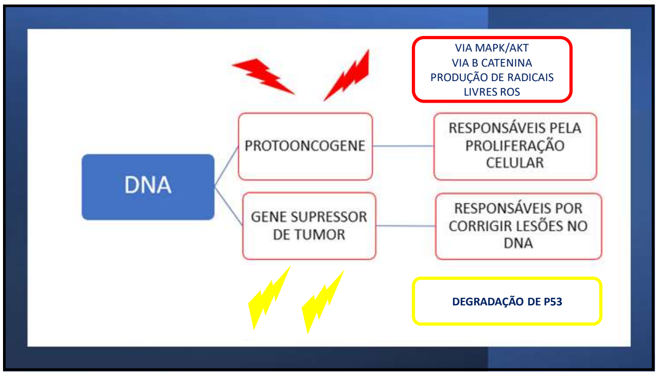
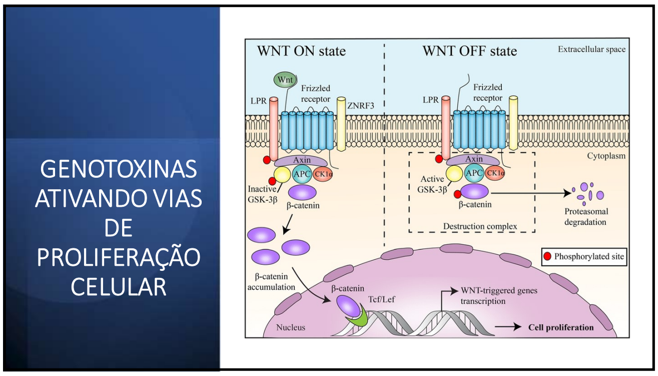
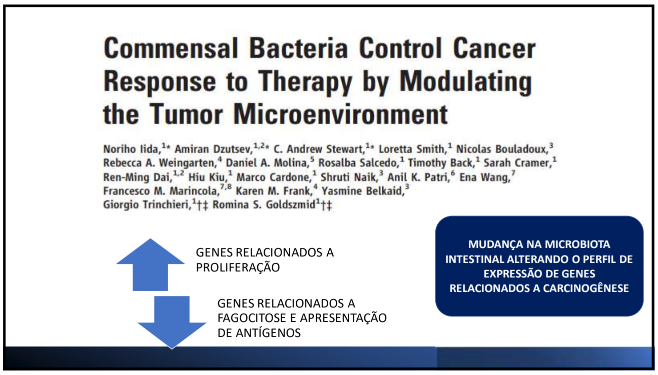
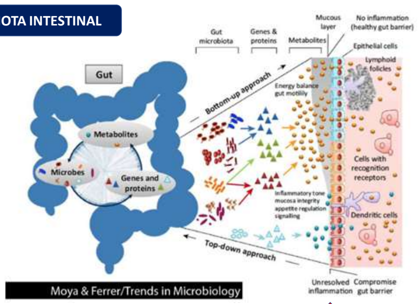

VIA MAPK/AKT
VIA Β CATENINA
PRODUÇÃO DE RADICAIS LIVRES ROS
DNA
PROTOONCOGENE
RESPONSÁVEIS PELA PROLIFERAÇÃO CELULAR
GENE SUPRESSOR DE TUMOR
RESPONSÁVEIS POR CORRIGIR LESÕES NO DNA
DEGRADAÇÃO DE P53


GENOTOXINAS ATIVANDO VIAS DE PROLIFERAÇÃO CELULAR
WNT ON state
WNT OFF state
Extracellular space
Wnt
Frizzled receptor
LPR
ZNRF3
Axin
APC
CK1α
Inactive GSK-3β
Active GSK-3β
β-catenin
Cytoplasm
Destruction complex
Proteasomal degradation
Phosphorylated site
β-catenin accumulation
Tcf/Lef
WNT-triggered genes transcription
Nucleus
Cell proliferation

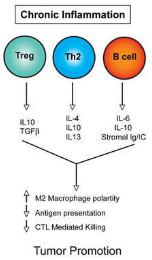

Commensal Bacteria Control Cancer Response to Therapy by Modulating the Tumor Microenvironment
Noriho Iida, Amiran Dzutsev, C. Andrew Stewart, Loretta Smith, Nicolas Bouladoux, Rebecca A. Weingarten, Daniel A. Molina, Rosalba Salcedo, Timothy Back, Sarah Cramer, Ren-Ming Dai, Hiu Kiu, Marco Cardone, Shruti Naik, Anil K. Patri, Ena Wang, Francesco M. Marincola, Karen M. Frank, Yasmine Belkaid, Giorgio Trinchieri, Romina S. Goldszmid
GENES RELACIONADOS A PROLIFERAÇÃO
GENES RELACIONADOS A FAGOCITOSE E APRESENTAÇÃO DE ANTÍGENOS
MUDANÇA NA MICROBIOTA INTESTINAL ALTERANDO O PERFIL DE EXPRESSÃO DE GENES RELACIONADOS A CARCINOGÊNESE


FEBS openbio
FEBS PRESS
science publishing by scientists
Helicobacter pylori induces somatic mutations in TP53 via overexpression of CHAC1 in infected gastric epithelial cells
Yuriko Wada, Kosuke Takemura, Padmaja Tummala, Keisuke Uchida, Keisuke Kitagaki, Asuka Furukawa, Yuuki Ishige, Takashi Ito, Yukichi Hara, Takashige Suzuki, Hitomi Mimuro, Philip G. Board and Yoshinobu Eishi
• Infeccção por H. pilory pode induzir a mutação em p53 e aumentar a degradação da glutationa e levar ao aumento de radicais livres favorecendo o desenvolvimento de câncer gástrico
ALTERAÇÃO EM GENES SUPRESSORES DE TUMOR

MICROBIOTA INTESTINAL



INFLAMAÇÃO E CÂNCER



- ESTÍMULO A PROLIFERAÇÃO CELULAR
- ESTÍMULO A ANGIOGÊNESE
- ESTÍMULO A MIGRAÇÃO TECIDUAL

60% DOS GATOS COM LINFOMA INTESTINAL T E 33% DOS GATOS COM LINFOMAS DE GRANDES LINFÓCITOS GRANULARES INTESTINAIS TINHAM HISTÓRICO DE DOENÇA INFLAMATÓRIA INTESTINAL PREVIA

41% DOS GATOS COM LINFOMA DE PEQUENAS CÉLULAS APRESENTARAM ENTERITE LINFOPLASMOCITÁRIA PRÉVIA

LINFOMA INTESTINAL FELINO
X
DIIC

ONCOMICROBIOMA

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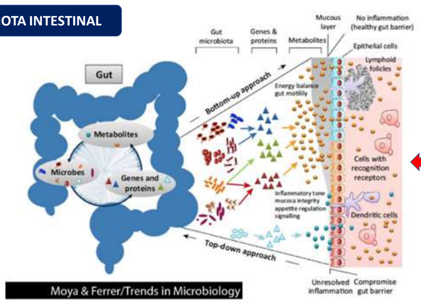
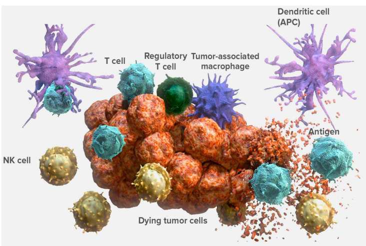
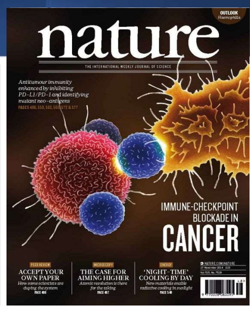
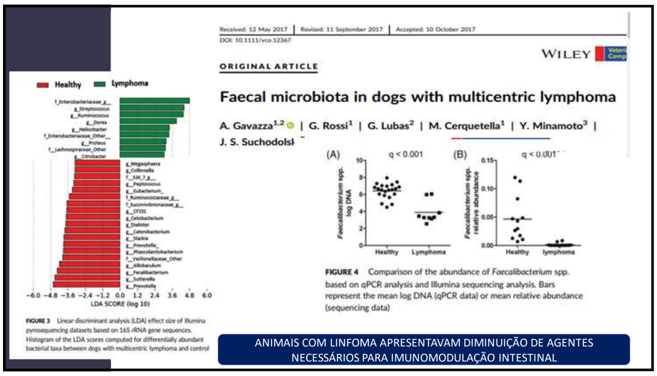
MICROBIOTA INTESTINAL

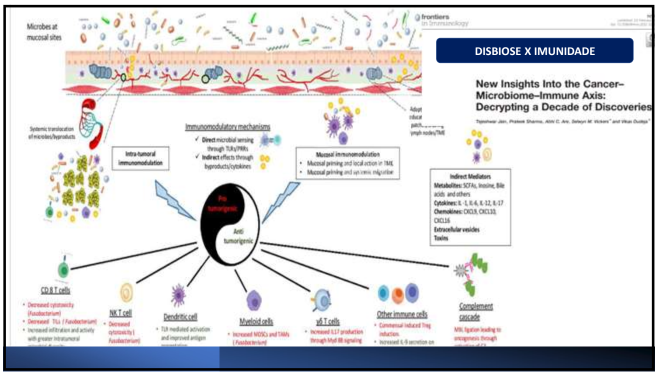


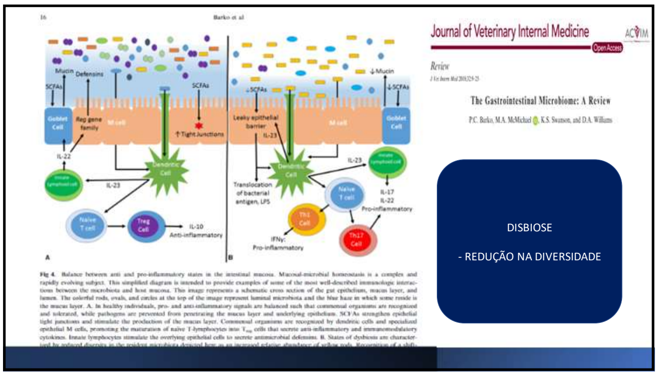
IMUNIDADE E CÂNCER

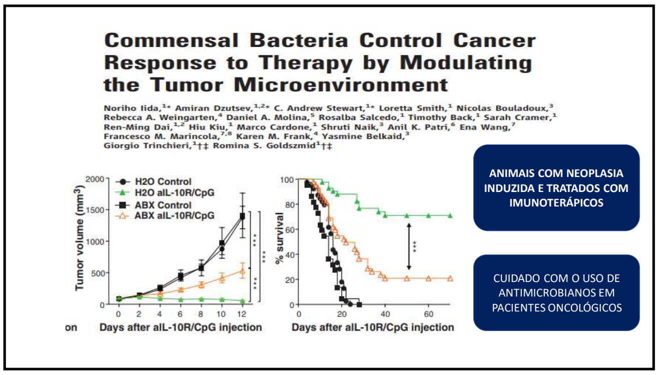












ONCOMICROBIOMA

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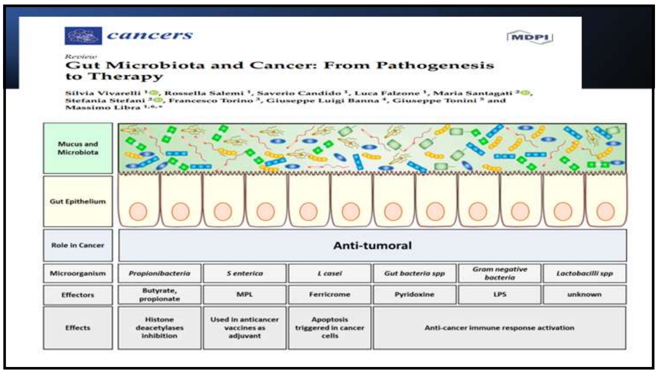

ANTICANCER RESEARCH 39: 4659-4666 (2019)
doi:10.21873/anticanres.13647

Antiproliferative Effects of Short-chain Fatty Acids on Human Colorectal Cancer Cells *via* Gene Expression Inhibition

TADASHI OHARA[1] and TSUTOMU MORI[2]

MICROBIOTA PODE PRODUZIR METABÓLITOS COMO ÁCIDOS GRAXOS DE CADEIA CURTA DURANTE A FERMENTAÇÃO DE DIETAS RICAS EM FIBRAS (A NATUREZA DESSES PRODUTOS DEPENDE DA DIETA E DOS COMPONENTES DA MICROBIOTA)

ESSES ÁCIDOS GRAXOS PODEM TER ATIVIDADE ANTITUMORAL

MICROBIOTA NO COMBATE AO CÂNCER

ONCOMICROBIOMA

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DIMINUIÇÕA DA EFICÁCIA DA TERAPIA

CICLOFOSFAMIDA ALTERA A COMPOSIÇÃO DA MICROBIOTA INTESTINAL E INDUZ A TRANSLOCAÇÃO DE BACTERIAS GRAM + ESPECÍFICAS PARA O TECIDO LINFÓIDE LOCAL

ESSAS BACTERIAS ESTIMULAM A PRODUÇÃO DE CÉLULAS THELPER E DE MEMÓRIA RESPONSÁVEIS PELA RESPOSTA IMUNE CONTRA O TUMOR

COBAIAS QUE NÃO APRESENTAM ESSAS BACTERIAS, APRESENTAM DIMINUIÇÃO DE RESPOSTA IMUNE E SEUS TUMORES SÃO RESISTENTES A CICLOFOSFAMIDA

The intestinal microbiota modulates the anticancer immune effects of cyclophosphamide

Sophie Viaud[1,3], Fabiana Saccheri[1], Grégoire Mignot[4,5], Takahiro Yamazaki[1], Romain Daillère[1,3], Dalil Hannani[1], David P. Enot[7,8], Christina Pfirschke[9], Camilla Engblom[9], Mikael J. Pittet[9], Andreas Schlitzer[10], Florent Ginhoux[10], Lionel Apetoh[4,5], Elisabeth Chachaty[11], Paul-Louis Woerther[11], Gérard Eberl[12], Marion Bérard[13], Chantal Ecobichon[14,15], Dominique Clermont[16], Chantal Bizet[16], Valérie Gaboriau-Routhiau[17,18], Nadine Cerf-Bensussan[17,18], Paule Opolon[19,20], Nadia Yessaad[21,22,23,24], Eric Vivier[21,22,23,24], Bernhard Ryffel[25], Charles O. Elson[26], Joël Doré[17,27], Guido Kroemer[7,8,28,29,30], Patricia Lepage[17,27], Ivo Gomperts Boneca[14,15], François Ghiringhelli[4,5,6,†], and Laurence Zitvogel[1,2,3,*,†]

CICLOFOSFAMIDA É DEPENDENTE DA MICROBIOTA PARA EXERCER UMA DAS SUAS FUNÇÕES DE ESTIMULO DO SISTEMA IMUNE

DIMINUIÇÕA DA EFICÁCIA DA TERAPIA

Mycoplasma hyorhinis É UMA BACTERIA PATOGÊNICA DA MICROBIOTA QUE PRODUZ UMA ENZIMA CHAMADA TIMIDINA FOSFORILASE

ESSA ENZIMA DIMINUI A AÇÃO DE ALGUNS QUIMIOTERÁPICOS ANTIMETABÓLITOS COMO ALGUNS DERIVADOS DO 5-FLUORACIL

ScienceDirect

The cytostatic activity of pyrimidine nucleosides is strongly modulated by *Mycoplasma hyorhinis* infection: Implications for cancer therapy

*Annelies Bronckaers, Jan Balzarini *, Sandra Liekens **

MAIS UM EXEMPLO DE ALTERAÇÃO NA MICROBIOTA DIMINUINDO A EFICÁCIA DA QUIMIOTERAPIA

ONCOMICROBIOMA

EFEITO PROMOTOR DE CÂNCER

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AUMENTO DA TOXICIDADE A QUIMIOTERAPIA

DIARRÉIA EM PACIENTES EM QUIMIOTERAPIA

QUIMIOTERAPIA DESTROI CÉLULAS EM RÁPIDA MULTIPLICAÇÃO PORTANTO AS MICROVILOSIDADES SÃO AFETADAS OCASIONANDO DÉFICIT ABSORTIVO E DIARREIA

ORIGINAL ARTICLE

Substantial decreases in the number and diversity of microbiota during chemotherapy-induced gastrointestinal mucositis in a rat model

DIARRÉIA EM PACIENTES EM QUIMIOTERAPIA

PACIENTES TRATADOS COM METOTREXATO TIVERAM DIMINUIÇÃO SIGNIFICATIVA NA MICROBIOTA INTESTINAL COM REDUÇÃO DE AGENTES ANAERÓBICOS (13X MENOS) E SYTREPTOCOCCI (296X MENOS) COM AUMENTO DE BACTEROIDES E ESSSAS ALTERAÇÕES CONTRIBUIRAM PARA QUADROS DE DIARRÉIA E DIMINUIÇÃO DA MICROVILOSIDADE INTESTINAL

AUMENTO DA TOXICIDADE A QUIMIOTERAPIA

Support Care Cancer
DOI 10.1007/s00520-014-2457-6
ORIGINAL ARTICLE

Substantial decreases in the number and diversity of microbiota during chemotherapy-induced gastrointestinal mucositis in a rat model

Margot Fijlstra · Mithila Ferdous · Anne M. Koning · Edmond H. H. M. Rings · Hermie J. M. Harmsen · Wim J. E. Tissing

REVIEWS

Gut microbiota modulation of chemotherapy efficacy and toxicity

James L. Alexander[1-3], Ian D. Wilson[3], Julian Teare[1], Julian R. Marchesi[1-3], Jeremy K. Nicholson[3] and James M. Kinross[1,3]

ONDE ESTAMOS NA MEDICINA VETERINÁRIA?

Received: 19 February 2021 | Revised: 8 April 2021 | Accepted: 20 April 2021
DOI: 10.1111/vcp.13031
REVIEW ARTICLE
Veterinary Clinical Pathology WILEY

Analysis of the gut microbiome in dogs and cats

Jan S. Suchodolski

Journal of Veterinary Internal Medicine
Open Access
ACVIM
Review
J Vet Intern Med 2018;32:9–25

The Gastrointestinal Microbiome: A Review

P.C. Barko, M.A. McMichael, K.S. Swanson, and D.A. Williams

MICROBIOMA EM CÃES E GATOS

Phylum	Class	Order	Family	Genus
Firmicutes	Clostridia	Clostridiales	*Clostridiaceae*	*Clostridium*
			Ruminococcaceae	*Ruminococcus*
				Faecalibacterium
			Eubacteraceae	*Eubacterium*
	Bacilli	Lactobacilliales	*Lactobacillaceae*	*Lactobacillus*
			Streptococcaceae	*Streptococcus*
				Enterococcus
	Erysiphelotrichia	Erisophelotrichales	*Erysiphelotrichaceae*	*Turicibacter*
				Catenibacterium
				Coprobacillus
				Allobaculum
	Negativicutes	Selenomonadales	*Selenomonadaceae*	*Megamonas*
		Veillonellales	*Veillonellaceae*	*Dialister*
				Megasphaera
				Veillonella
Bacteroidetes	Bacteroidia	Bacteroidales	*Prevotellaceae*	*Prevotella*
			Bacteroidaceae	*Bacteroides*
Actinobacteria	Coriobacteriia	Coriobacteriales	*Coriobacteriaceae*	*Collinsella*
			Atopobiaceae	*Olsenella*
				Slackia

frontiers in Microbiology
REVIEW
published: 25 June 2020
doi: 10.3389/fmicb.2020.01266

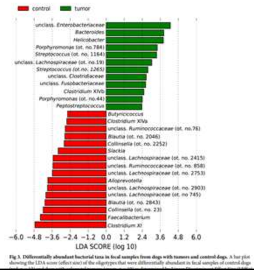
The Effects of Nutrition on the Gastrointestinal Microbiome of Cats and Dogs: Impact on Health and Disease

Susan M. Wernimont[1*], Jennifer Radosevich[1], Matthew I. Jackson[1], Eden Ephraim[1], Dayakar V. Badri[1], Jennifer M. MacLeay[1], Dennis E. Jewell[2] and Jan S. Suchodolski[3]

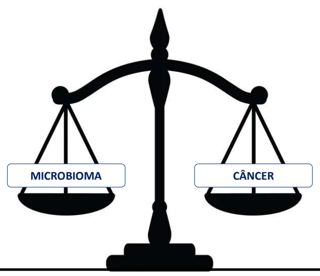
MICROBIOMA X NUTRIÇÃO X DOENÇA

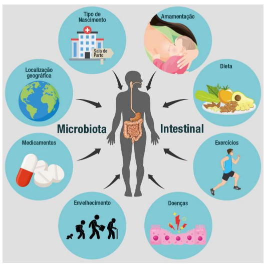
- CÂNCER
- OBESIDADE
- ALERGIAS
- NEFROPATIAS
- ENTEROPATIAS
- CONSTIPAÇÃO
- DOENÇAS DE CAVIDADE ORAL

DIFERENÇAS NO MICROBIOMA DE CÃES SAUDÁVEIS E CÃES COM NEOPLASIAS COLORETAIS



ONCOMICROBIOMA





COMO MODULAR O AMBIENTE INTESTINAL?

Quais os focos?

MICROBIOTA
- Remover
- Acrescentar
- Maximizar

ESTRUTURA
- Menos lesão
- Redução do risco de translocação

RESPOSTA/PRODUTOS
- Posbióticos
- Imunidade
- Qualidade fecal

MODULAÇÃO DA MICROBIOTA INTESTINAL

- Antibióticos
- Transplante fecal
- Probióticos
- Prebióticos

ANTIBIÓTICOS nas gastroenterites agudas

STANDARD ARTICLE — Journal of Veterinary Internal Medicine

Effect of amoxicillin-clavulanic acid on clinical scores, intestinal microbiome, and amoxicillin-resistant *Escherichia coli* in dogs with uncomplicated acute diarrhea

Melanie Werner | Jan S. Suchodolski | Reinhard K. Straubinger | Georg Wolf | Jörg M. Steiner | Jonathan A. Lidbury | Katrin Hartmann | Stefan Unterer

Evaluating the effect of metronidazole plus amoxicillin-clavulanate *versus* amoxicillin-clavulanate alone in canine haemorrhagic diarrhoea: a randomised controlled trial in primary care practice

- Tratamento com antibióticos não demonstra benefícios direto aos quadros de diarreia aguda
- Sem melhora na mortalidade ou desfecho clínico
- Sem indicação quando não há evidências de possível sepse
- Aumenta a resistência

ANTIBIÓTICOS nas gastroenterites agudas

OPEN ACCESS Freely available online — PLOS ONE

Effect of Oral Administration of Metronidazole or Prednisolone on Fecal Microbiota in Dogs

Hirotaka Igarashi, Shingo Maeda, Koichi Ohno, Ayako Horigome, Toshitaka Odamaki, Hajime Tsujimoto

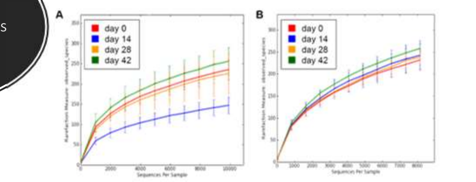


Figure 2. Rarefraction analysis of V4 16S rRNA gene sequences obtained from fecal samples. Results from dogs administered metronidazole (A) and prednisolone (B). Lines represent the average of each time point and the error bars represent standard deviations. This analysis was performed using a randomly selected subset of 9,915 (A) or 8,153 (B) sequences per sample. Operational Taxonomical Units (OTUs) in this analysis were defined by 97–100% similarity.
doi:10.1371/journal.pone.0107909.g002

ANTIBIÓTICOS nas gastroenterites agudas

STANDARD ARTICLE — Journal of Veterinary Internal Medicine

Effects of metronidazole on the fecal microbiome and metabolome in healthy dogs

Impact of Changes in Gastrointestinal Microbiota in Canine and Feline Digestive Diseases

Vet Clin Small Anim 51 (2021) 155–169

Anna-Lena Ziese, Dr med vet, Jan S. Suchodolski, Dr med vet, PhD

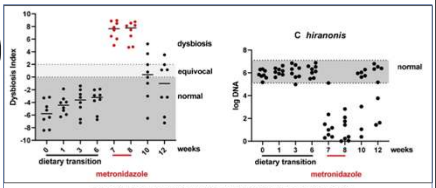


Fig. 1. Effect of diet and metronidazole on intestinal microbiome in healthy dogs. Diet (hydrolyzed protein diet) has only a minor effect on intestinal microbiota as assessed by the quantitative polymerase chain reaction–based dysbiosis index (*left*) and abundance of the primary to secondary BA-converting bacterium *C hiranonis* (*right*). In contrast, metronidazole treatment induces significant dysbiosis and reduction of *C hiranonis*, which is associated with improper BA conversion. One month after metronidazole cessation, some dogs did not recover their proper microbiome composition (week 12). This is 1 potential explanation for why a subset of clinically healthy dogs lack the important beneficial bacterium *C hiranonis*. Data based on Pilla and colleagues.[11]

ANTIBIÓTICOS

Contents lists available at ScienceDirect — The Veterinary Journal — journal homepage: www.elsevier.com/locate/tvjl

Oral tylosin administration is associated with an increase of faecal enterococci and lactic acid bacteria in dogs with tylosin-responsive diarrhoea

Susanne Kilpinen, Merja Rantala, Thomas Spillmann, Johanna Björkroth, Elias Westermarck

- Diarreias recorrentes e idiopáticas respondem a tilosina em poucos dias
- Aumenta contagem de *Enterococcus spp* e bactérias acido lácticas
- "Melhora" no perfil de microbiota pode ser a causa do melhor desfecho clínico
- Não é usado em humanos

MODULAÇÃO DA MICROBIOTA INTESTINAL

- Antibióticos
- Transplante fecal
- Probióticos
- Prebióticos

TRANSPLANTE FECAL

Fecal Microbiota Transplantation in Dogs

Jennifer Chaitman, VMD, Frédéric Gaschen, Dr med vet, Dr habil

Vet Clin Small Anim 51 (2021) 219–233
https://doi.org/10.1016/j.cvsm.2020.09.012

- Transferência de fezes de um doador **saudável** para o intestino de um receptor doente
- Enema, colonoscopia, duodenoscopia, sonda nasogástrica/nasojejunal ou ingestão de cápsulas
- Sem estudos com animais com câncer
- Dificuldade de seleção do doador

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Vet Clin Small Anim 51 (2021) 219–233
https://doi.org/10.1016/j.cvsm.2020.09.012
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SELEÇÃO DO DOADOR

- 1 a 10 anos de idade
- Preferencialmente sem mudanças/viagens
- 6 a 12 meses sem problemas de saúde
- Sem doenças crônicas TGI, alergia ou doenças imunomediadas
- Mínimo 12 meses sem antibioticoterapia
- Vacinação adequada (seguindo guia/consenso)
- Alimentação completa e balanceada (exclusão de alimentação crua)
- ECC 4 a 6/9
- Consistência fecal adequada
- Exame físico = ok
- Sangue: hemograma, bioquímicos básicos, T4 e cortisol
- Fezes: pesquisa por parasitas (ELISA giárdia)
- Índice de disbiose < 0

MODULAÇÃO DA MICROBIOTA INTESTINAL

- Antibióticos
- Transplante fecal
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- Prebióticos

PROBIÓTICOS

Value of Probiotics in Canine and Feline Gastroenterology

Silke Salavati Schmitz, Drmedvet, PhD, FHEA, MRCVS

Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, The Roslin Institute, College of Medicine and Veterinary Medicine, University of Edinburgh, Easter Bush, Midlothian EH25 9RG, UK
E-mail address: Silke.Salavati@ed.ac.uk

Vet Clin Small Anim 51 (2021) 171–217
https://doi.org/10.1016/j.cvsm.2020.09.011
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Diferentes cepas, "concentrações" e períodos de fornecimento

- Microrganismos vivos que, na quantidade adequada, geram benefícios ao hospedeiro
- Benefícios para quadros agudos/parvovirose
- Poucos benefícios nas enteropatias caninas responsivas a dieta e antibióticos, mas parece ser válido nos quadros inflamatórios
- Tritrichomonas e constipação dos felinos
- Cada situação um grupo?
- *Lactobacillus spp, Bifidobacterium spp, Saccharomyces boulardi.*

Supportive Care in Cancer (2018) 26:2503–2509
https://doi.org/10.1007/s00520-018-4216-z

REVIEW ARTICLE

Systematic review and meta-analysis investigating the efficacy and safety of probiotics in people with cancer

Hadeel Hassan · M. Rompola · A. W. Glaser · S. E. Kinsey · R. S. Phillips

- Redução na diarreia
- Redução no tempo de febre
- Benéfico, mas há vieses e poucos estudos

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Current Opinion

Prophylactic probiotics for cancer therapy-induced diarrhoea: a meta-analysis

Hannah R. Wardill, Ysabella Z.A. Van Sebille, Matthew A. Ciorba, and Joanne M. Bowen

- Não preveniu ocorrência de diarreia
- Não reduziu episódios de diarreia
- Sem evidência para indicação

Supportive Care in Cancer (2018) 26:2503–2509
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Medicine

SYSTEMATIC REVIEW AND META-ANALYSIS

OPEN

Effects of Probiotics on Intestinal Mucosa Barrier in Patients With Colorectal Cancer after Operation

Meta-Analysis of Randomized Controlled Trials

Dun Liu, Xiao-Ying Jiang, Lan-Shu Zhou, MD, PhD, Ji-Hong Song, and Xuan Zhang, MD

- Melhora na permeabilidade
- Menor risco de translocação
- Melhor secreção IgA
- Menos proteína C reativa, igual IL-6

Supportive Care in Cancer (2018) 26:2503–2509

REVIEW ARTICLE

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Meta-Analysis of Randomized Controlled Trials

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- Melhor secreção IgA
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International Journal of Colorectal Disease (2019) 34:459–469

ORIGINAL ARTICLE

Probiotics for preventing postoperative infection in colorectal cancer patients: a systematic review and meta-analysis

Xiaojing Ouyang · Qingfeng Li · Mengjing Shi · Dongsheng Niu · Wenjing Song · Qinggong Nian · Xiangda Li · Zhonghui Ding · Xianyin Ai · Jian Wang

- Menos infecções no geral
- Menos pneumonia
- Melhora no tempo para primeira flatulência (motilidade)
- Sem efeito: infecção urinária, extravasamento na anastomose e febre

Vet Record Open

RESEARCH ARTICLE

Preliminary evaluation of probiotic effects on gastrointestinal signs in dogs with multicentric lymphoma undergoing multi-agent chemotherapy: A randomised, placebo-controlled study

Maria C. Jugan | Raelene M. Wouda | Mary Lynn Higginbotham

Probiótico – dose: 200 × 10^9 cfu/10 kg
- *Streptococcus thermophiles*
- *Bifidobacterium breve*
- *B. longum*
- *B. infantis*
- *Lactobacillus acidophilus*
- *L. plantarum*
- *L. paracasei*
- *L. delbrueckii bulgaricus*

Placebo (maltodextrina em cápsula gelatinosa) – n de cáps equivalente a dose de probiótico dose

Preliminary evaluation of probiotic effects on gastrointestinal signs in dogs with multicentric lymphoma undergoing multi-agent chemotherapy: A randomised, placebo-controlled study

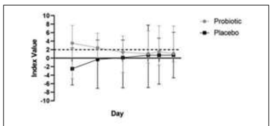
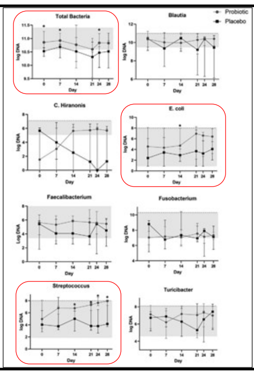


FIGURE 2 Dysbiosis index values, 10 dogs undergoing CHOP-based chemotherapy for multicentric lymphoma and receiving either probiotic or placebo. An index value of <0 is considered normal. Dashed line indicates the dysbiosis index value, at or above which was considered abnormal. Abbreviation: CHOP, cyclophosphamide doxorubicin vincristine prednisone.



Vet Record Open

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- *Lactobacillus acidophilus*
- *L. plantarum*
- *L. paracasei*
- *L. delbrueckii bulgaricus*

Placebo (maltodextrina em cápsula gelatinosa) – n de cáps equivalente a dose de probiótico dose

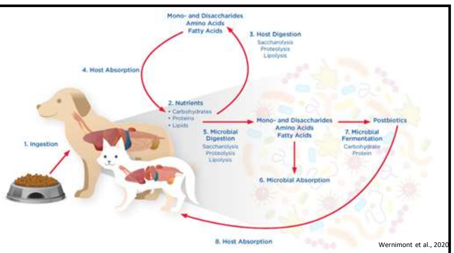
Mais Streptococcus fecal
Mais bactérias totais
Mais *E. coli*
Menos diarreia (avaliação clínica)
Sem efeitos colaterais

Limitações:
N (5 em cada grupo)
Não-cego, dieta e histórico não padronizados

MODULAÇÃO DA MICROBIOTA INTESTINAL

- Antibióticos
- Transplante fecal
- Probióticos
- Prebióticos

PREBIÓTICOS



Wernimont et al., 2020

- Compostos não digeridos que promovem crescimento de grupos específicos de microrganismos e seus metabólitos, interferindo na relação com o hospedeiro
- Carboidratos não digestíveis
- Dependem da presença de microrganismos benéficos

PREBIÓTICOS
na oncologia

in vivo 19: 201-204 (2005)

Possible Adjuvant Cancer Therapy by Two Prebiotics - Inulin or Oligofructose

HENRYK S. TAPER and MARCEL B. ROBERFROID

Unité de Pharmacocinétique, Métabolisme, Nutrition et Toxicologie, Université Catholique de Louvain, PMNT 73.69, 1200 Bruxelles, Belgium

- Redução a incidência de tumor de mama (após indução)
- Inibe o crescimento de tumor transplantado
- Menos metástase (implantado)
- Potencialização dos efeitos do quimioterápicos
- Potencialização dos efeitos da radioterapia

PREBIÓTICOS
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in vivo 19: 201-204 (2005)

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Unité de Pharmacocinétique, Métabolisme, Nutrition et Toxicologie, Université Catholique de Louvain, PMNT 73.69, 1200 Bruxelles, Belgium

Posbióticos e modificação imune

- Redução a incidência de tumor de mama (após indução)
- Inibe o crescimento de tumor transplantado
- Menos metástase (implantado)
- Potencialização dos efeitos do quimioterápicos
- Potencialização dos efeitos da radioterapia

The Journal of Veterinary Medical Science

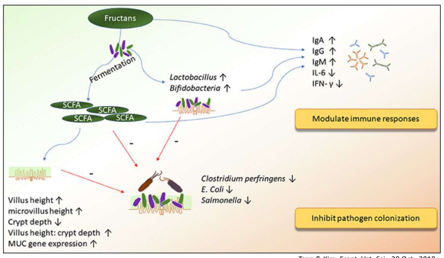
FULL PAPER
Internal Medicine

Analysis of fecal short chain fatty acid concentration in miniature dachshunds with inflammatory colorectal polyps

Hirotaka IGARASHI[1,2]*, Koichi OHNO[1], Naoaki MATSUKI[3], Aki FUJIWARA-IGARASHI[1,4], Hideyuki KANEMOTO[3], Kenjiro FUKUSHIMA[1], Kazuyuki UCHIDA[5] and Hajime TSUJIMOTO[1]

- Menor concentração de ácidos graxos de cadeia curta
- Inflamação e não necessariamente câncer
- Sem padronização de dietas

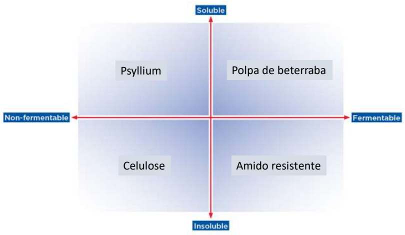
PREBIÓTICOS
aumentar
AGCC (SCFA)



Teng & Kim, Front. Vet. Sci., 30 Oct, 2018

- Inclusão de 1 a 2%
  - FOS
  - GOS
  - Fibras fermentáveis

PREBIÓTICOS
aumentar
AGCC (SCFA)



Evaluation of fermentable oligosaccharides in diets fed to dogs in comparison to fiber standards

I. S. Middelbos, N. D. Fastinger, and G. C. Fahey Jr.[1]

Department of Animal Sciences, University of Illinois, Urbana 61801

ABSTRACT: Blends of fermentable oligosaccharides in combination with nonfermentable fiber, cellulose, were evaluated for their ability to serve as dietary fibers in dog foods. Using a 6 × 6 Latin square design, 6 diets were evaluated that contained either no supplemental fiber, beet pulp, cellulose, or blends of cellulose, fructooligosaccharides, and yeast cell wall added at 2.5% of the diet. Six ileal-cannulated dogs were fed 175 g of their assigned diet twice daily. Chromic oxide served as a digestibility marker. Nutrient digestibility, fecal microbial populations, fermentative end products, and immunological indices were measured. Total tract DM and OM digestibilities were lowest ($P < 0.05$) for the cellulose treatment. Crude protein digestibility was lower ($P < 0.05$) for the treatments containing carbohydrate blends. The cellulose treatment had the lowest ($P < 0.05$) concentration of bacteria, and all diets containing fermentable fiber had greater ($P < 0.05$) fecal bifidobacteria concentrations compared with the diets without supplemental fermentable fiber. Lactobacilli concentrations tended to be greater ($P < 0.08$) in treatments containing fermentable fiber compared with the cellulose treatment. Bifidobacteria and lactobacilli concentrations were similar for the beet pulp treatment compared with the fermentable oligosaccharide blends. Total fecal short-chain fatty acid concentration was greater for the beet pulp treatment ($P < 0.05$) compared with the control and cellulose treatments. The treatments containing fermentable fiber had greater ($P < 0.05$) fecal butyrate concentrations compared with cellulose and control treatments. Immune indices were not affected by treatment. Our results suggest that dog foods containing blends of fermentable and nonfermentable carbohydrates produce similar physiological results as dog food containing beet pulp as a fiber source. Therefore, blends of these carbohydrates could be useful substitutes for beet pulp in dog foods.

Key words: beet pulp, dietary fiber, dog, intestinal microbiota, oligosaccharide

J. Anim. Sci. 2007. 85:3033–3044
doi:10.2527/jas.2007-0080

Table 5. Fecal microbial populations for dogs fed diets containing select dietary fiber sources

Item	Treatment: Control	Cellulose	Beet pulp	CF[1]	CFY1[2]	CFY2[3]	SEM
Population (plating)	cfu log_{10}/g of fecal DM						
Bifidobacteria	10.1[ab]	10.0[b]	10.3[ab]	10.6[a]	10.2[ab]	10.5[ab]	0.13
Clostridium perfringens	9.8	9.9	9.8	9.8	9.9	10.0	0.19
Escherichia coli	8.0	8.1	8.4	8.0	8.7	7.9	0.25
Lactobacilli	9.3	9.4	9.6	10.4	9.8	10.1	0.34
Total aerobes	9.0[ab]	8.9[b]	9.6[ab]	10.0[a]	9.8[ab]	9.8[ab]	0.28
Total anaerobes	10.7[ab]	10.5[b]	10.8[ab]	11.0[a]	10.9[ab]	11.0[a]	0.11
Population (quantitative PCR)							
Bifidobacteria	7.7[b]	7.8[b]	8.9[a]	8.7[a]	9.1[a]	8.7[a]	0.30
C. perfringens	10.7	10.2	11.3	11.2	11.2	11.0	0.38
Lactobacilli	11.3[ab]	11.2[b]	12.0[ab]	12.2[a]	12.1[ab]	12.1[a]	0.23
E. coli	10.3	10.1	10.6	10.7	10.7	10.1	0.32

[a,b]Means in the same row not sharing common superscript letters are different ($P < 0.05$).
[1]CF = 1% cellulose + 1.5% fructooligosaccharides.
[2]CFY1 = 1% cellulose + 1.2% fructooligosaccharides + 0.3% yeast cell wall.
[3]CFY2 = 1% cellulose + 0.9% fructooligosaccharides + 0.6% yeast cell wall.

Table 1. Composition of diets containing select dietary fiber sources and fed to adult dogs (as-fed basis)

Ingredient, %	Treatment: Control	Cellulose	Beet pulp	CF[1]	CFY1[2]	CFY2[3]
Brewers rice	45.22	42.72	42.72	42.72	42.72	42.72
Poultry by-product meal	37.00	37.00	37.00	37.00	37.00	37.00
Poultry fat	14.00	14.00	14.00	14.00	14.00	14.00
Dried egg	2.40	2.40	2.40	2.40	2.40	2.40
Salt	0.45	0.45	0.45	0.45	0.45	0.45
Potassium chloride	0.56	0.56	0.56	0.56	0.56	0.56
Choline chloride[4]	0.13	0.13	0.13	0.13	0.13	0.13
Vitamin mix[5]	0.12	0.12	0.12	0.12	0.12	0.12
Mineral mix[6]	0.12	0.12	0.12	0.12	0.12	0.12
Cellulose	—	2.50	—	1.00	1.00	1.00
Beet pulp	—	—	2.50	—	—	—
Fructooligosaccharides[7]	—	—	—	1.50	1.20	0.90
Yeast cell wall[8]	—	—	—	—	0.30	0.60

[1]CF = 1% cellulose + 1.5% fructooligosaccharides.
[2]CFY1 = 1% cellulose + 1.2% fructooligosaccharides + 0.3% yeast cell wall.
[3]CFY2 = 1% cellulose + 0.9% fructooligosaccharides + 0.6% yeast cell wall.
[4]Provided the following per kilogram of diet: choline, 2,284.2 mg.
[5]Provided the following per kilogram of diet: vitamin A, 11,000 IU; vitamin D_3, 900 IU; vitamin E, 57.5 IU; vitamin K, 0.6 mg; thiamin, 7.6 mg; riboflavin, 11.9 mg; pantothenic acid, 18.5 mg; niacin, 93.2 mg; pyridoxine, 6.6 mg; biotin, 12.4 mg; folic acid, 1,142.1 µg; and vitamin B_{12}, 164.9 µg.
[6]Provided the following per kilogram of diet: manganese ($MnSO_4$), 17.4 mg; iron ($FeSO_4$), 284.3 mg; copper ($CuSO_4$), 17.2 mg; cobalt ($CoSO_4$), 2.2 mg; zinc ($ZnSO_4$), 166.3 mg; iodine (KI), 7.5 mg; and selenium (Na_2SeO_3), 0.2 mg.
[7]Nutraflora P-95, GTC Nutrition, Golden, CO.
[8]Safmannan, LeSaffre Yeast Corp., Milwaukee, WI.

Table 7. Fecal pH, score, and concentrations of ammonia, short-chain fatty acids, branched-chain fatty acids, phenols, and indoles for dogs fed diets containing select dietary fiber sources

Item	Treatment: Control	Cellulose	Beet pulp	CF[1]	CFY1[2]	CFY2[3]	SEM
pH	6.7	6.5	6.3	6.5	6.4	6.3	0.14
Score[4]	2.9	2.7	2.7	2.9	2.7	2.6	0.18
Fecal output (as-is), g/d	73.2	87.6	89.6	80.1	69.0	76.6	7.7
Ammonia, µmol/g of DM	164	132	191	177	169	175	15.1
Short-chain fatty acids, µmol/g of DM							
Acetate	172[b]	127[b]	276[a]	187[ab]	196[ab]	187[ab]	24.3
Propionate	63[bc]	49[c]	93[a]	70[bc]	84[ab]	85[ab]	6.2
Butyrate	28[b]	21[b]	42[a]	40[a]	41[a]	42[a]	4.6
Total	262[b]	197[b]	411[a]	297[ab]	321[ab]	314[ab]	33.2
Branched-chain fatty acids, µmol/g of DM							
Isobutyrate	5.6	4.8	6.6	6.5	6.9	6.0	0.7
Isovalerate	10.4[ab]	8.3[b]	12.2[ab]	13.4[a]	13.5[a]	11.8[ab]	1.3
Valerate	12.7[ab]	9.6[b]	16.1[ab]	18.7[a]	16.9[a]	16.3[ab]	2.0
Phenols and indoles,[5] µg/g of DM							
Phenol	20.1	9.1	4.7	7.4	6.9	Trace	8.0
p-Cresol	79.9	50.5	30.6	40.6	73.7	19.7	17.0
Indole	224.1	193.3	254.5	238.9	173.7	201.2	28.4

[a–c]Means in the same row not sharing common superscript letters are different ($P < 0.05$).
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[3]CFY2 = 1% cellulose + 0.9% fructooligosaccharides + 0.6% yeast cell wall.
[4]Score based on the following scale: 1 = hard, dry pellets; small, hard mass; 2 = hard-formed, dry stool; remains firm and soft; 3 = soft, formed, and moist stool; retains shape; 4 = soft, unformed stool; assumes shape of container; and 5 = watery; liquid that can be poured.
[5]4-Ethyl-phenol, 7-methyl-indole, 3-methyl-indole, 2-methyl-indole, and 2,3-dimethyl-indole were not detected in any sample.

Received: 3 April 2016 | Accepted: 8 February 2017
DOI: 10.1111/jpn.12711

ORIGINAL ARTICLE

WILEY

Effect of resistant starch on the intestinal health of old dogs: fermentation products and histological features of the intestinal mucosa*

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Summary
The effects of resistant starch (RS) intake on nutrient digestibility, microbial fermentation products, faecal IgA, faecal pH, and histological features of the intestinal mucosa of old dogs were evaluated. The same formulation was extruded in two different conditions: one to obtain elevated starch cooking degree with low RS content (0.21%) and the other lower starch cooking with high RS content (1.46%). Eight geriatric Beagles (11.5 ± 0.38 years old) were fed each diet for 61 days in a crossover design. Food intake, nutrient digestibility, fermentation products, faecal pH, and faecal IgA were examined via variance analysis. Histological results of intestinal biopsies were assessed via Wilcoxon test for paired data. The morphometric characteristics of large intestine crypts were evaluated via paired t tests ($p < .05$). Protein, fat, and energy digestibilities were higher for the low-RS diet ($p < .05$). Dogs receiving the high-RS diet had lower faecal pH and higher values for propionate, butyrate, total volatile fatty acids, and lactate ($p < .05$). No differences between diets were found in the histological parameters of the gut mucosa, and only a tendency for deeper crypts in the descending colon was observed for dogs fed the high-RS diet ($p = .083$). The intake of a corn-based kibble diet manufactured with coarse ground raw material and low starch gelatinization to obtain 1.4% of RS affected microbial fermentation products and faecal pH and tended to increase crypt depth in the descending colon of old dogs.

KEYWORDS

TABLE 1 Analysed chemical composition and resistant starch content of the same formulation to dogs, extruded to obtain high and low resistant starch content

Item	Diets[a]: Low-RS[b]	High-RS[c]
Chemical composition (%)		
Dry matter	95.2	95.2
Ash	8.2	7.9
Crude protein	26.6	26.6
Acid-Hydrolized fat	16.2	17.2
Crude fiber	1.9	2.1
Starch	42.5	41.6
Mean geometric diameter (µm)[d]	224	312
Geometric standard deviation (µm)	1.5	1.7
Starch gelatinization degree (%)	99.9	62.6
Resistant starch content (%)	0.21	1.46
Bulk density (g/l)	300	505

[a]Ingredient composition: corn, 54.30%; poultry by-product meal, 25%; poultry fat, 9%; corn gluten meal (60% protein), 5%; sugarcane fibre, 2%; palatant enhancer 3%; vitamin–mineral premix, 0.30%; salt, 0.50%; potassium chloride, 0.48%; choline chloride, 0.20%; antioxidant, 0.10%; mold inhibitor 0.04%; L-lysine 0.03%.
[b]Low-RS—small raw material particle size and extruded with high implementation of specific mechanical energy to obtain elevated starch gelatinization degree and low resistant starch content.
[c]High-RS—coarse raw material particle size and extruded with low implementation of specific mechanical energy to obtain reduced starch gelatinization degree and high resistant starch content.
[d]Calculated according to Zanotto and Bellaver (1996).

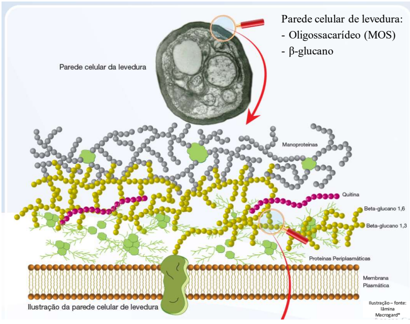
TABLE 3 Faecal production, fermentation products, and IgA content of old dogs fed the same formulation extruded to obtain high and low resistant starch content

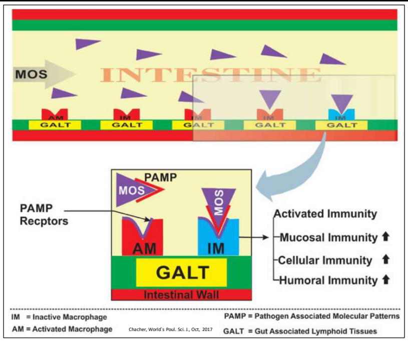
Item	Diets[a]: Low-RS	High-RS	S.E.M.	*p* value
Faeces				
g/dog/day (As is)	79.7	85.5	2.88	.333
g/dog/day (DM basis)	34.9	36.3	0.90	.428
Moisture (%)	55.8	57.3	0.91	.457
Score	3.9	3.9	0.05	.859
pH	7.17	6.76	0.08	<.001
Fermentation products (mMol/g of faecal DM)				
Acetic acid	208.6	249.6	11.22	.082
Propionic acid	92.7	154.3	10.05	<.001
Butyric acid	40.4	59.9	3.54	.003
Total SCFA	341.7	463.8	23.40	.006
Isobutyric acid	8.3	7.3	0.38	.256
Isovaleric acid	12.6	11.4	0.57	.327
Valeric acid	1.01	1.55	0.21	.228
Total BCFA	21.9	20.3	0.97	.447
Total VFA	363.7	484.1	23.65	.008
Ammonia	253.9	219.1	10.24	.051
Lactate	0.40	1.76	0.33	.043
IgA (mg/g of faecal DM)	1.92	2.31	0.26	.467

S.E.M., standard error of the mean (n = 8 dogs per treatment); SCFA, short-chain fatty acids; BCFA, branched-chain fatty acids; VFA, volatile fatty acids.
[a]Low-RS—small raw material particle size and extruded with high implementation of specific mechanical energy to obtain elevated starch gelatinization degree and low resistant starch content. High-RS—coarse raw material particle size and extruded with low implementation of specific mechanical energy to obtain reduced starch gelatinization degree and high resistant starch content.

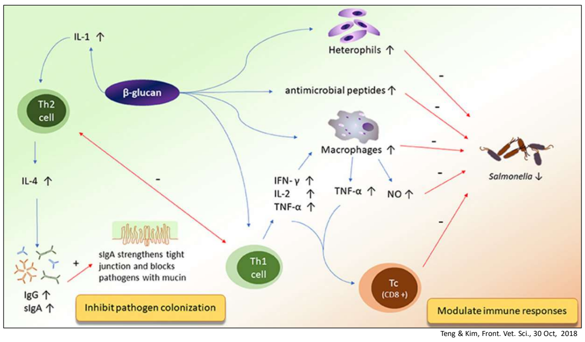
Sem modificações estruturais e inflamatórias

PREBIÓTICOS
IMUNIDADE





Mecanismo involvido na melhoria da resposta imune pelo MOS



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Glycan complexity dictates microbial resource allocation in the large intestine

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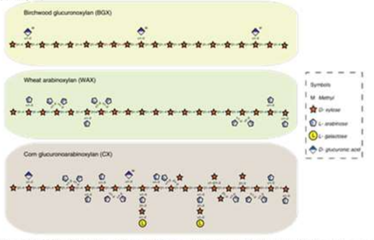


Figure 1 | Schematic of the structures of the main classes of xylan.

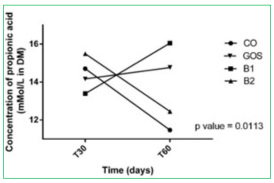
microorganisms

MDPI

Article

Duration of Prebiotic Intake Is a Key-Factor for Diet-Induced Modulation of Immunity and Fecal Fermentation Products in Dogs

Mariana P. Perini, Mariana F. Rentas, Raquel Pedreira, Andressa R. Amaral, Rafael V. A. Zafalon, Roberta B. A. Rodrigues, Lucas B. F. Henriquez, Lucca Zanini, Thiago H. A. Vendramini, Júlio C. C. Balieiro, Cristiana F. F. Pontieri and Marcio A. Brunetto



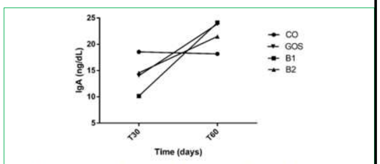


Figure 2. Increased fecal IgA at T60. Despite having no effects, at T60, IgA increased in CO, GOS, and B1 treatments. CO: control food, without the addition of prebiotic; GOS: control food with addition of 0.38% galactooligosaccharides; B1: control food with addition of 0.5% YES GOLF® prebiotic blend; B2: control food with the addition of 1% YES GOLF® prebiotic blend; T30: 30-day period; T60: 60-day period.

MODULAÇÃO DA MICROBIOTA INTESTINAL

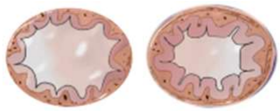
- Antibióticos
- Transplante fecal
- Probióticos
- Prebióticos

} Simbióticos

ESTRUTURA INTESTINAL

- Pre- Pro- Sim- Posbióticos

Acréscimo de 1 a 5% de fibras fermentáveis



- "Dietas complexas"

ESTRUTURA INTESTINAL

- Pre- Pro- Sim- Posbióticos
- "Dietas complexas"

Dietary composition alters methotrexate toxicity without changing its pharmacokinetic parameters in cats

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- 6 gatos recebendo alimentação complexa

Todos os animais alertas e responsivos
Diarreia – n = 1
Vômito – n = 0

- 6 gatos recebendo alimentação purificada
(amido + glicose + aminoácidos + vitaminas + gorduras)

Prostração/letargia
Diarreia – n = 4
Vômito – n = 2

21 dias

3 dias

Uma aplicação IV; 10mg/kg (160 mg/m²)

Am J Vet Res. 1997 Sep;58(9):989-96.

Dietary modulation of methotrexate-induced enteritis in cats.

Marks SL[1], Cook AK, Griffey S, Kass PH, Rogers QR.

	Dieta complexa	Dieta purificada
Cultura linfonodo mesentérico	0/6	3/6
Translocação	0%	50%
E. Coli	-	4000 ufc/g
Enterococcus fecalis	-	300 ufc/g
Salmonella infantis	-	3000 ufc/g

Am J Vet Res. 1997 Sep;58(9):989-96.

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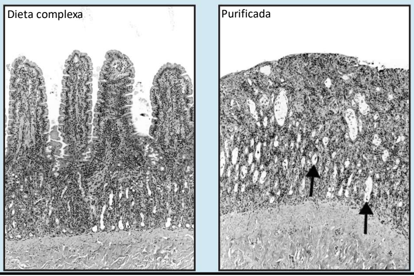

Saker, 2010

Effects of glutamine supplementation of an amino acid-based purified diet on intestinal mucosal integrity in cats with methotrexate-induced enteritis

Stanley L. Marks, BVSc, PhD; Audrey K. Cook, BVMS; Rachel Reader, BVMS; Philip H. Kass, DVM, PhD; Alain P. Théon, DVM, MS; Carl Greve, PhD; Quinton R. Rogers, PhD

AVALIAÇÕES:
- Permeabilidade
- Proliferação e morfometria celular
- Translocação

Conclusions—Feeding of a glutamine-supplemented amino acid-based purified diet was unable to preserve intestinal function in cats with MTX-induced enteritis.

Amino acid composition (g/kg) of the complex, glutamine-supplemented (Gln+), and glutamine-free (Gln–) diets

Amino acid*	Complex	Gln+	Gln–
Essential			
Arginine	22.0	22.5	22.5
Histidine	9.0	6.8	6.8
Isoleucine	12.0	11.2	11.2
Leucine	25.0	27.0	27.0
Lysine	19.0	22.5	22.5
Methionine	6.0	8.9	8.9
Cystine	4.0	7.9	7.9
Taurine	1.2	1.5	1.5
Phenylalanine	14.0	8.9	8.9
Tyrosine	9.0	7.9	7.9
Threonine	14.0	13.6	13.6
Tryptophan	2.0	3.4	3.4
Valine	15.0	13.6	13.6
Dispensable			
Alanine	16.0	15.0	50.0
Glycine	22.0	15.0	40.0
Glutamine	20.0†	70.0	0.0
Asparagine	30.0	10.0	30.0
Proline	20.0	15.0	20.0
Aspartate	17.0	15.0	0.0
Serine	13.0	0.0	0.0
Glutamate	20.0†	0.0	0.0
Total—dispensable	158.0	140.0	140.0

*Amino acids provided by Ajinomoto USA Inc, Teaneck, NJ. †Estimated as an equal amount of glutamine and glutamate from the glutamate analysis of an acid hydrolysate of the diet.

RESUMINDO

AMBIENTE INTESTINAL "ONCOPATA"

Modulação

- Evitar antibioticoterapia
- Transplante fecal – não prático
- Probióticos – mais estudos e melhores produtos
- Prebióticos – mais aplicável na rotina clínica e industrial

Obrigado!

ONConnectionVet

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