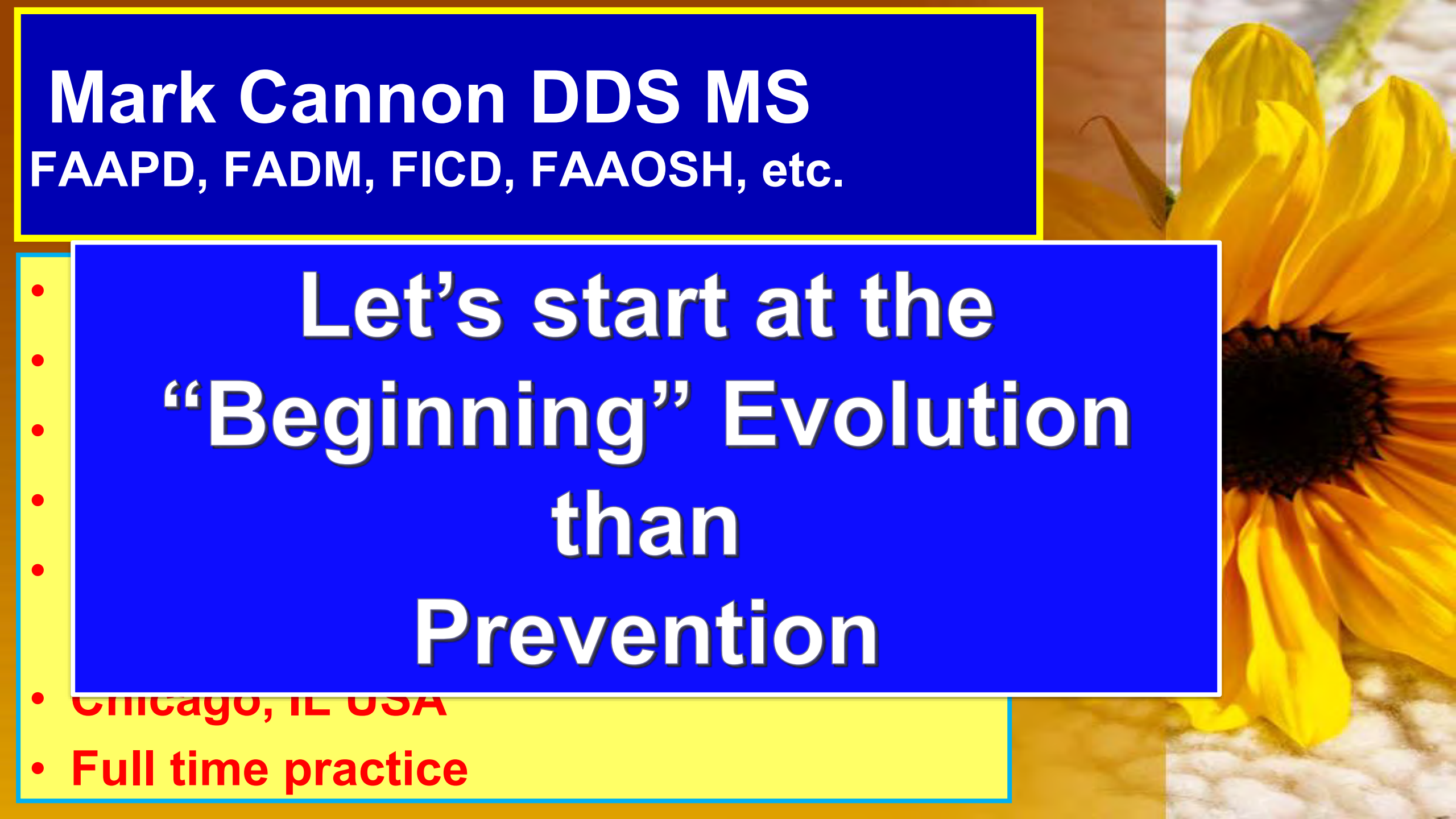
Pediatric Oral Medicine

Geyserville, CA

September 2019

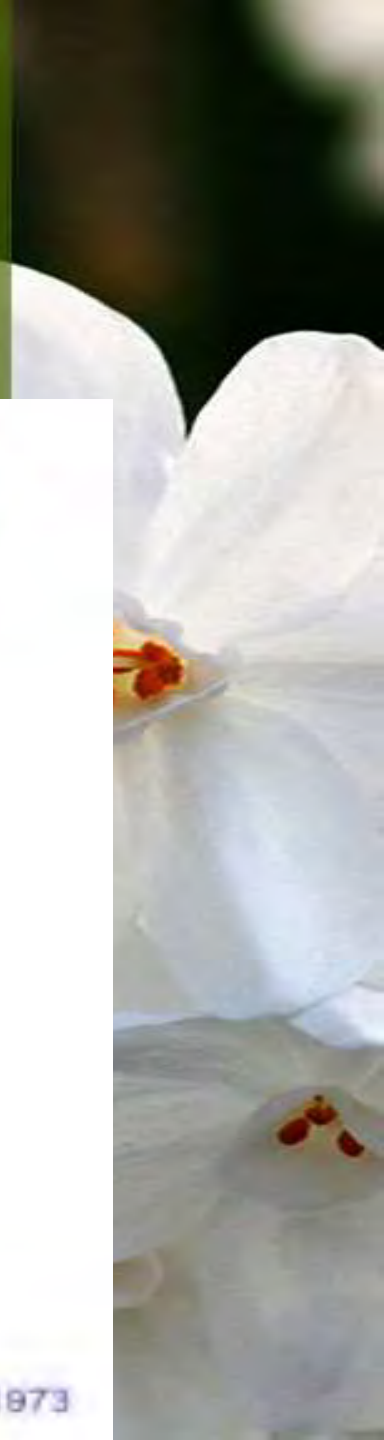
Mark Cannon DDS MS
FAAPD, FADM, FICD, FAAOSH, etc.



- Chicago, IL USA
- Full time practice

Let's start at the "Beginning" Evolution than Prevention

The "Gateway" Microbiomes



"Nothing in biology makes sense except in the light of evolution."

—Theodosius Dobzhansky

Dobzhansky TG: Nothing in biology makes sense except in the light of evolution. *Am Biol Teacher* 35:125-129, 1973

Dental Calculus- Fossils

nature genetics

ARTICLE PREVIEW

view full access options ▸

NATURE GENETICS | LETTER

日本語要約

Sequencing ancient calcified dental plaque shows changes in oral microbiota with dietary shifts of the Neolithic and Industrial revolutions

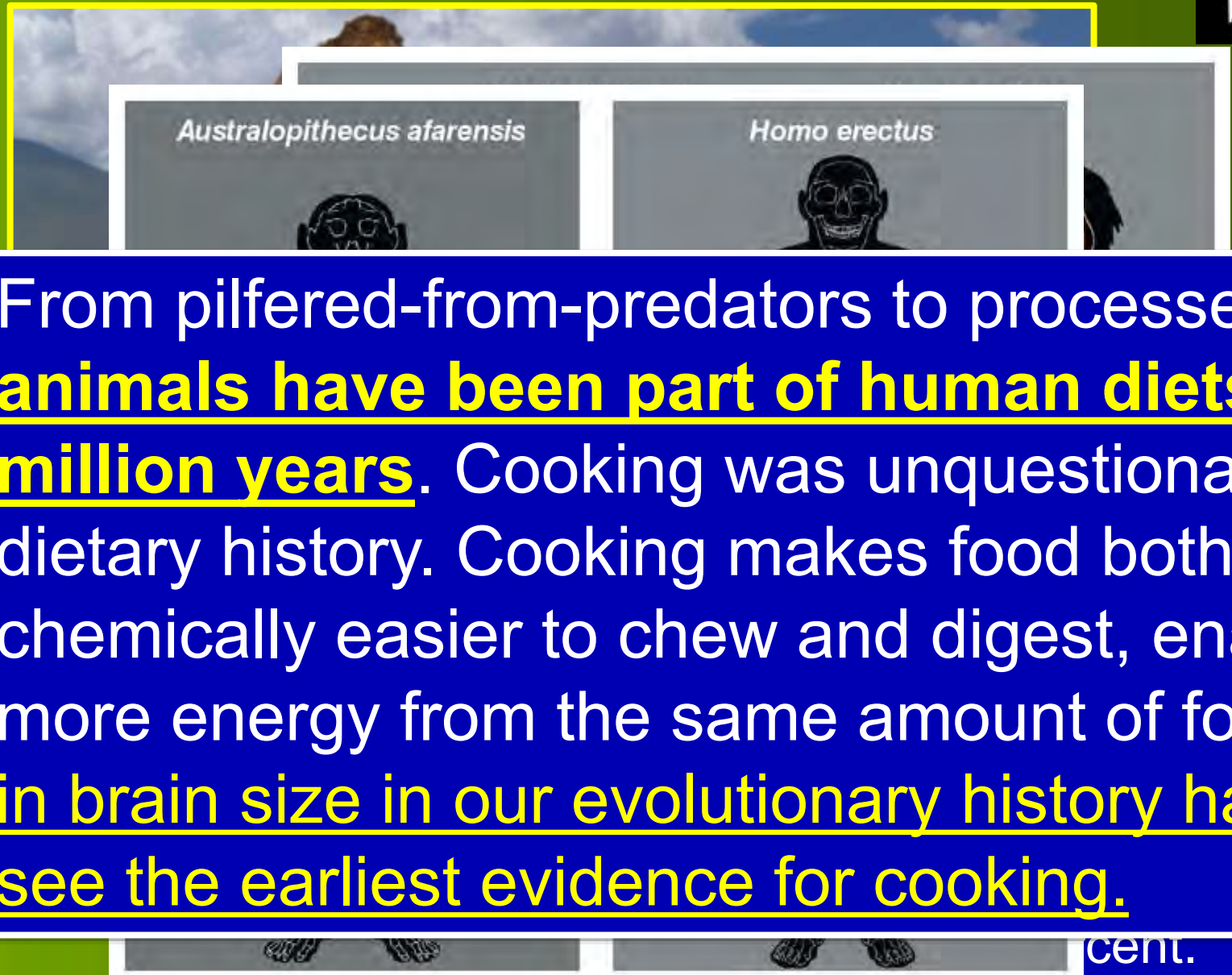
Christina J Adler, Keith Dobney, Laura S Weyrich, John Kaidonis, Alan W Walker, Wolfgang Haak, Corey J A Bradshaw, Grant Townsend, Arkadiusz Sołtysiak, Kurt W Alt, Julian Parkhill & Alan Cooper

Dental Calculus- Fossils

ecosys… …ss diverse than historic
popula… …contributing to chronic oral
(and other) disease in post…dustrial lifestyles.

Dense Nutrient Food

AMERICAN Scientist



From pilfered-from-predators to processed-and-packaged, **animals have been part of human diets for more than 3 million years**. Cooking was unquestionably a revolution in our dietary history. Cooking makes food both physically and chemically easier to chew and digest, enabling the extraction of more energy from the same amount of food. The biggest increase in brain size in our evolutionary history happened right after we see the earliest evidence for cooking.

cent.

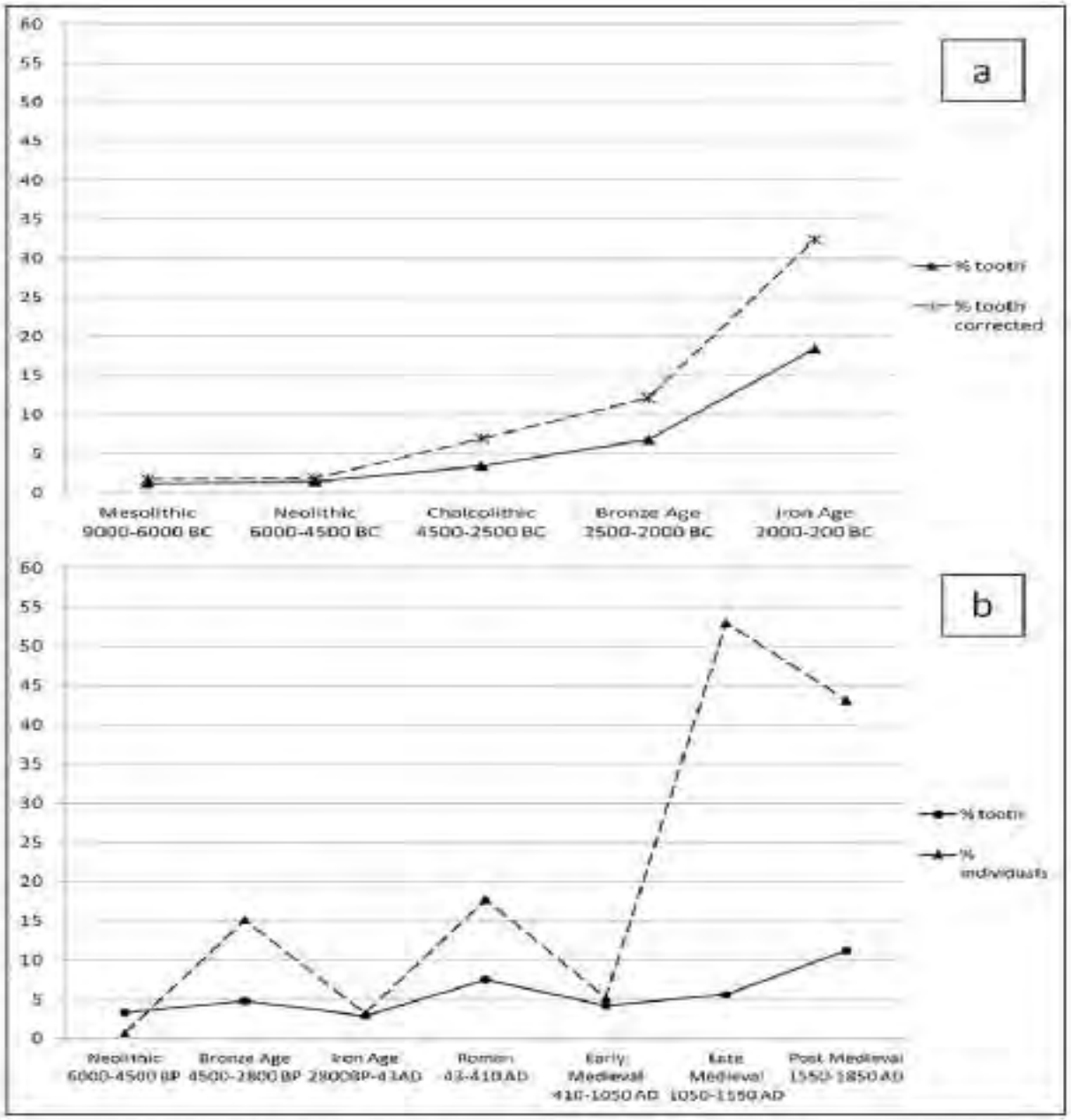
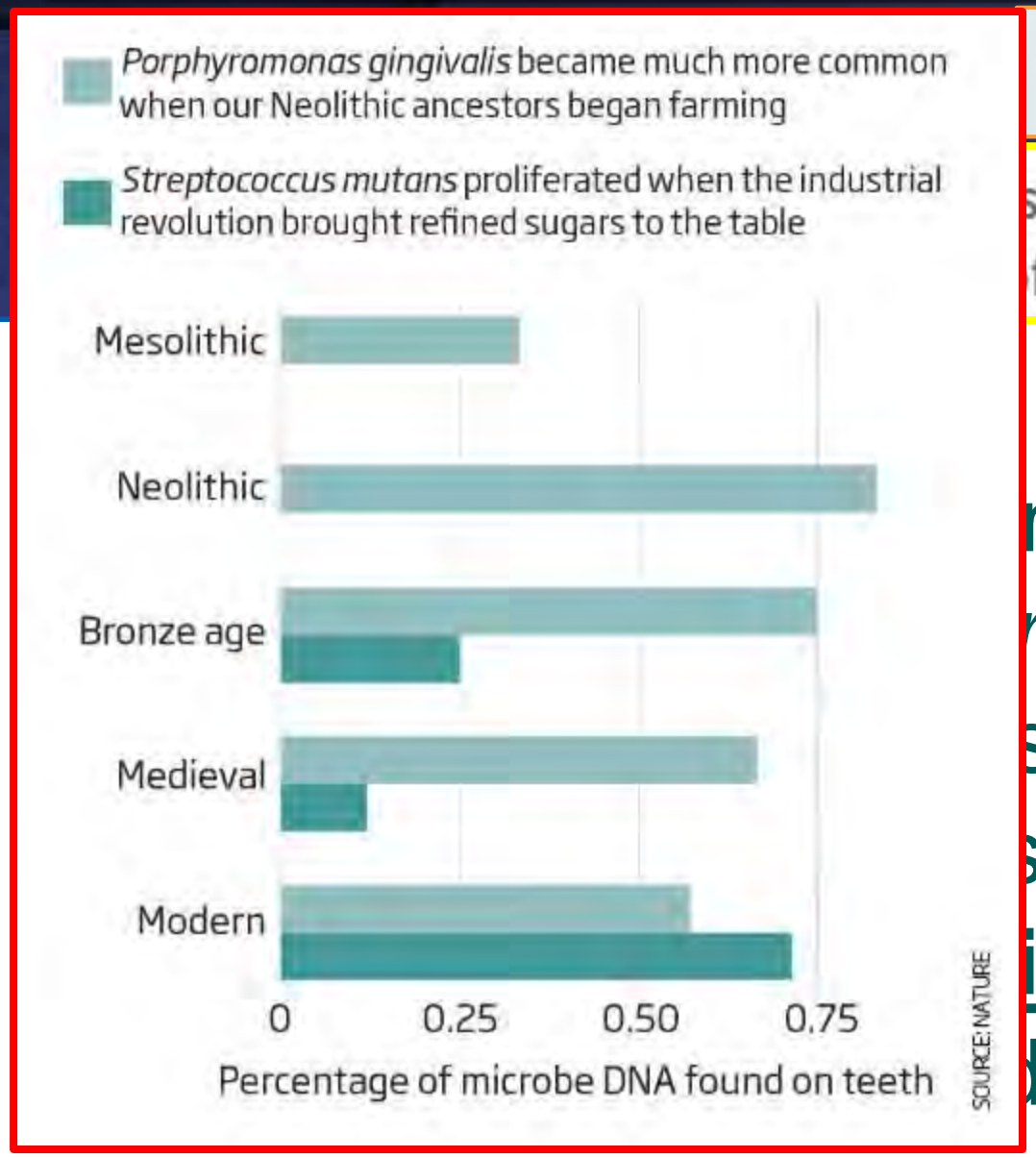


Fig. 2. **Caries trends in the Old World across time.** a) Indus valley civilization sequence, caries frequency versus corrected frequency (Lukacs, 1996). b) Britain sequence, caries frequency versus prevalence (Roberts & Cox, 2007).

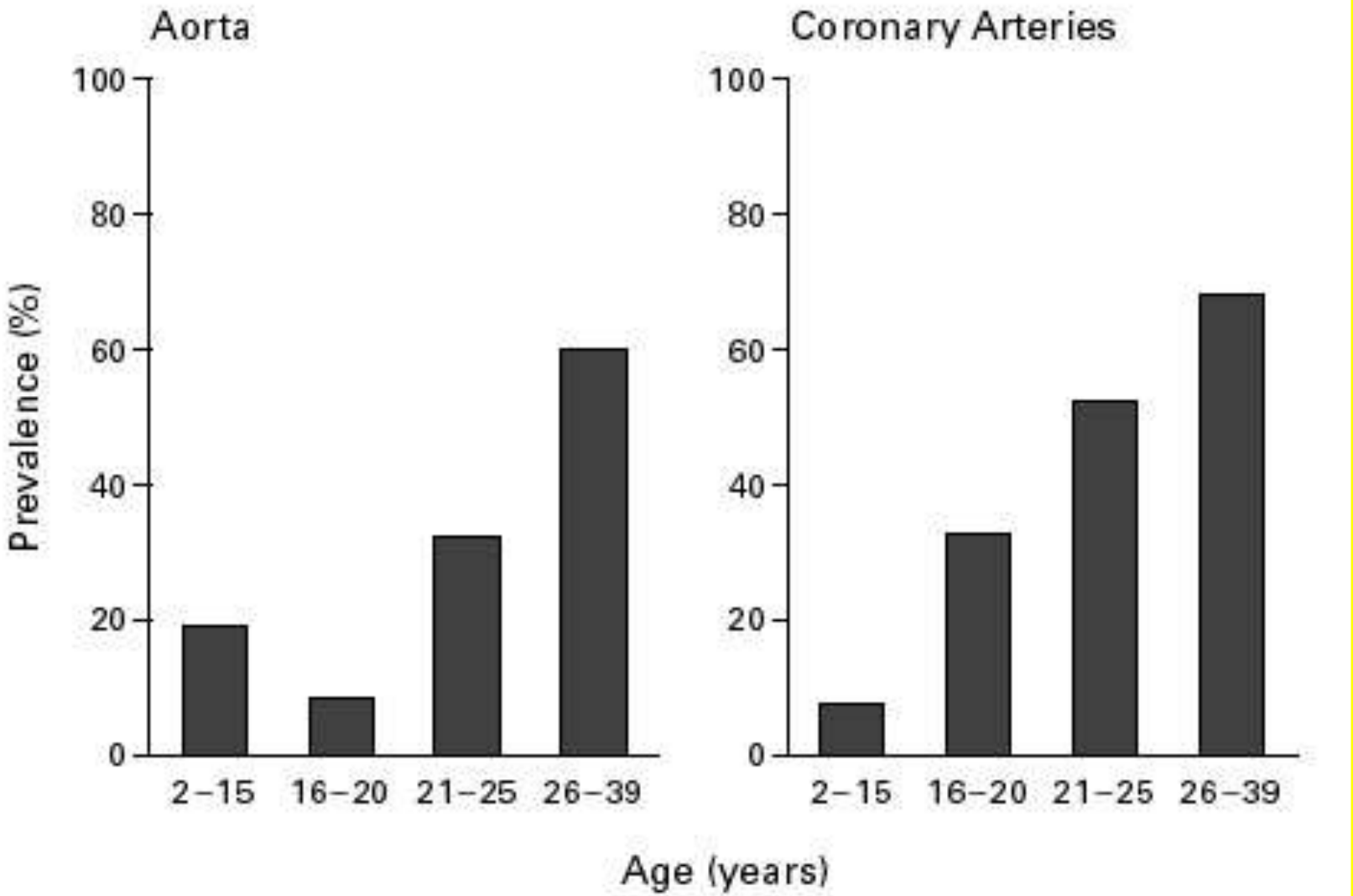
Fig. 1. T
Picture

paleontological record.
s 2010.

What Do Mummies Tell Us?



Children and Atherosclerosis



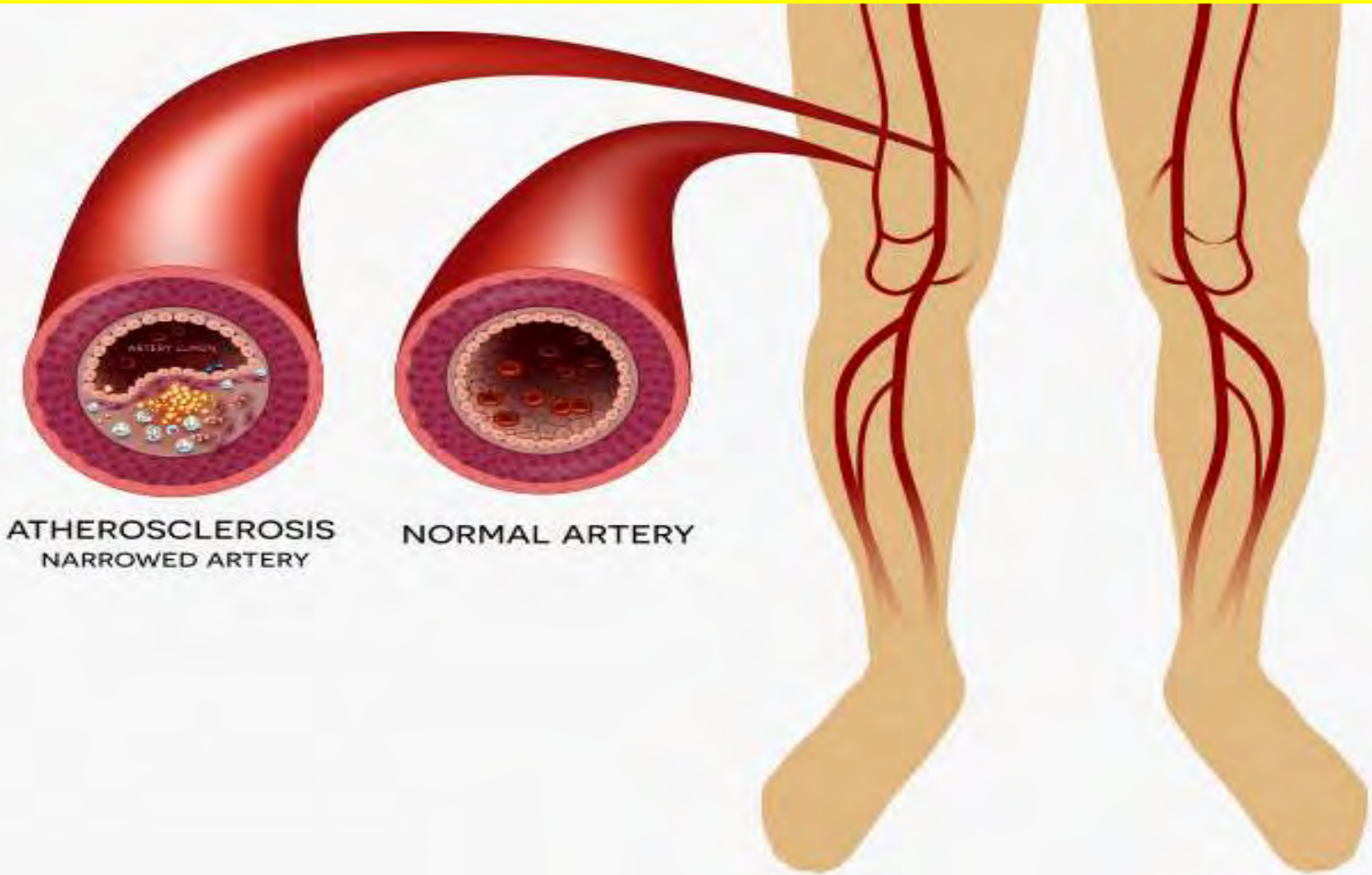
D
CINE

ctors and
s

racy, M.D., Ph.D., and Wendy A.

erformed
2 to 39 years of
auses, principally

Heart Disease and “Fries”



deposition and metabolism in artery walls.

8 years ago- it was missed

PLOS ONE | TENTH ANNIVERSARY

RESEARCH ARTICLE

Phosphorylated Dihydroceramides from Common Human Bacteria Are Recovered in Human Tissues

Frank C. Nichols, Xudong Yao, Bekim Bajrami, Julia Downes, Sydney M. Finegold, Erica Knee, James J. Gallagher, William J. Housley, Robert B. Clark

Cell Reports

Volume 18, Issue 9, 28 February 2017, Pages 2269-2279

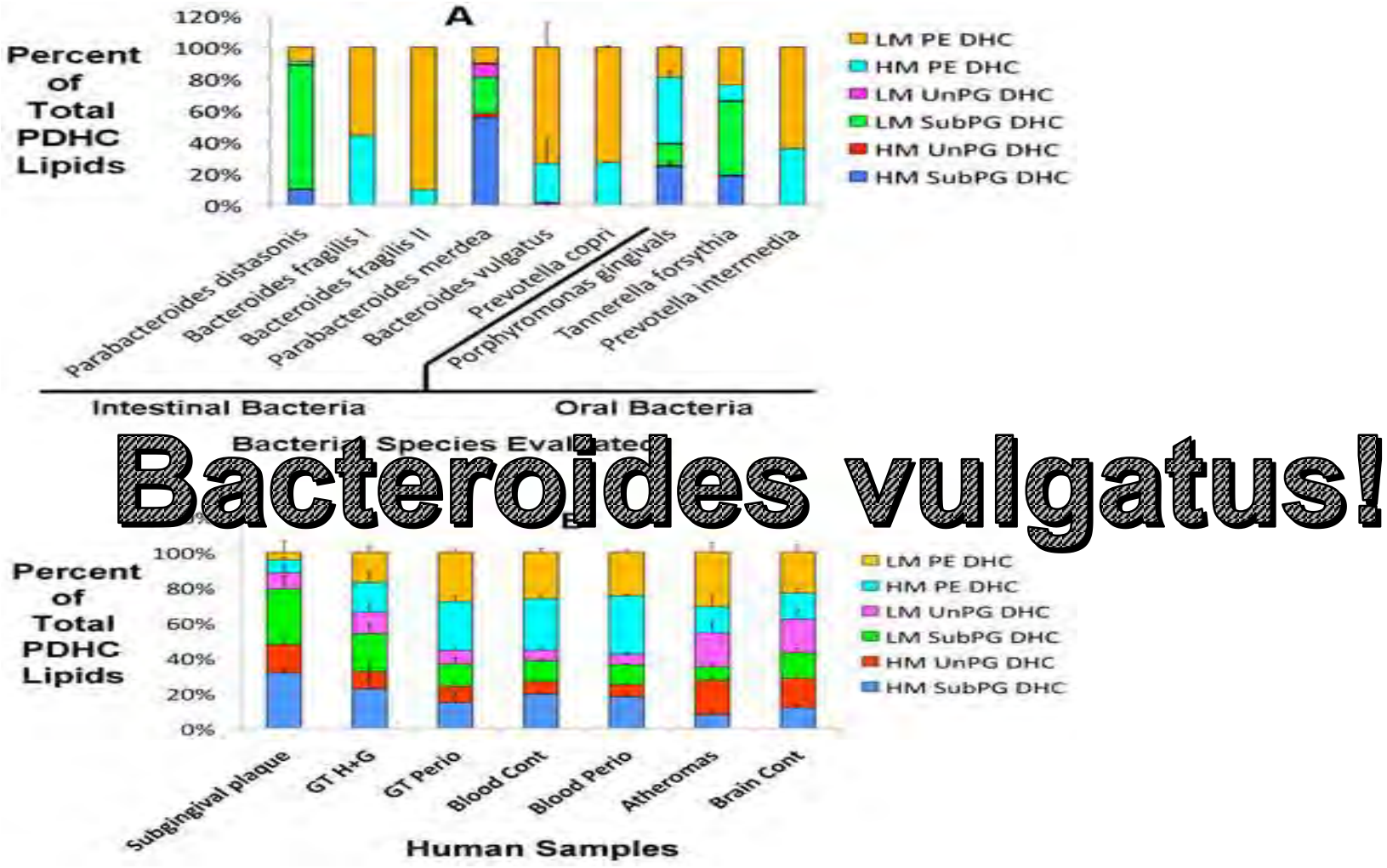
open access

Article

Plasma Dihydroceramides Are Diabetes Susceptibility Biomarker Candidates in Mice and Humans

Leonore Wigger [1, 2], Céline Cruciani-Guglielmacci [3], Anthony Nicolas [4, 5, 6, 7], Jessica Denom [3], Neïké Fernandez [3], Frédéric Fumeron [4, 5, 6, 7], Pedro Marques-Vidal [8], Alain Ktorza [9], Werner Kramer [10], Anke Schulte [11], Hervé Le Stunff [3, 12], Robin Liechti [1], Ioannis Xenarios [1], Peter Vollenweider [8], Gérard Waeber [8], Ingo Uphues [13], Ronan Roussel [4, 5, 6, 7], Christophe Magnan [3] ... Bernard Thorens [2, 14]

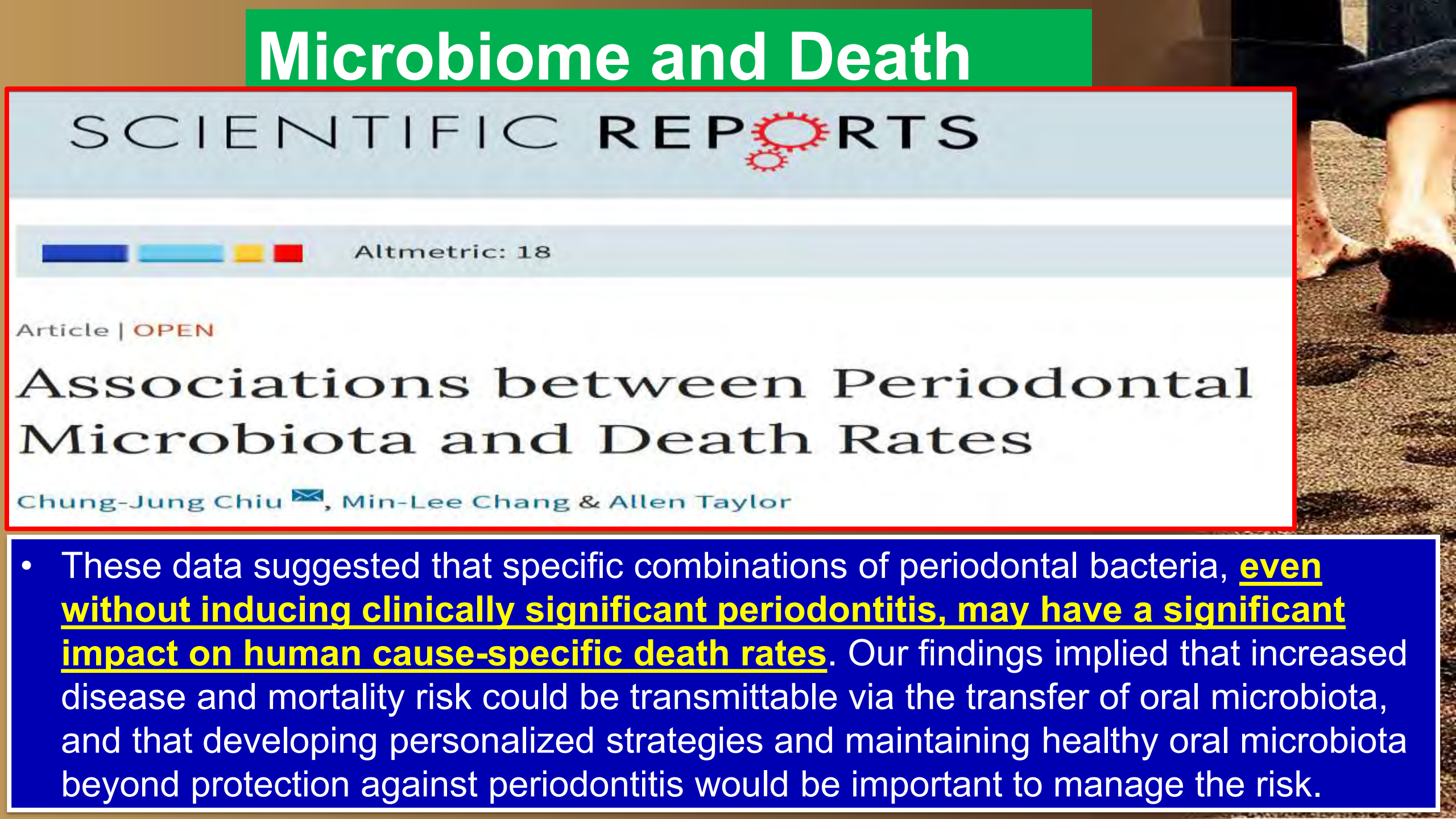
Figure 2. Recovery of bacterial phosphorylated dihydroceramides in intestinal and oral bacteria, subgingival plaque samples, blood plasma, atheroma and brain samples.



Nichols FC, Yao X, Bajrami B, Downes J, Finegold SM, et al. (2011) Phosphorylated Dihydroceramides from Common Human Bacteria Are Recovered in Human Tissues. PLOS ONE 6(2): e16771. https://doi.org/10.1371/journal.pone.0016771
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0016771

PLOS ONE
TENTH ANNIVERSARY

Microbiome and Death



SCIENTIFIC REPORTS

Altmetric: 18

Article | OPEN

Associations between Periodontal Microbiota and Death Rates

Chung-Jung Chiu ✉, Min-Lee Chang & Allen Taylor

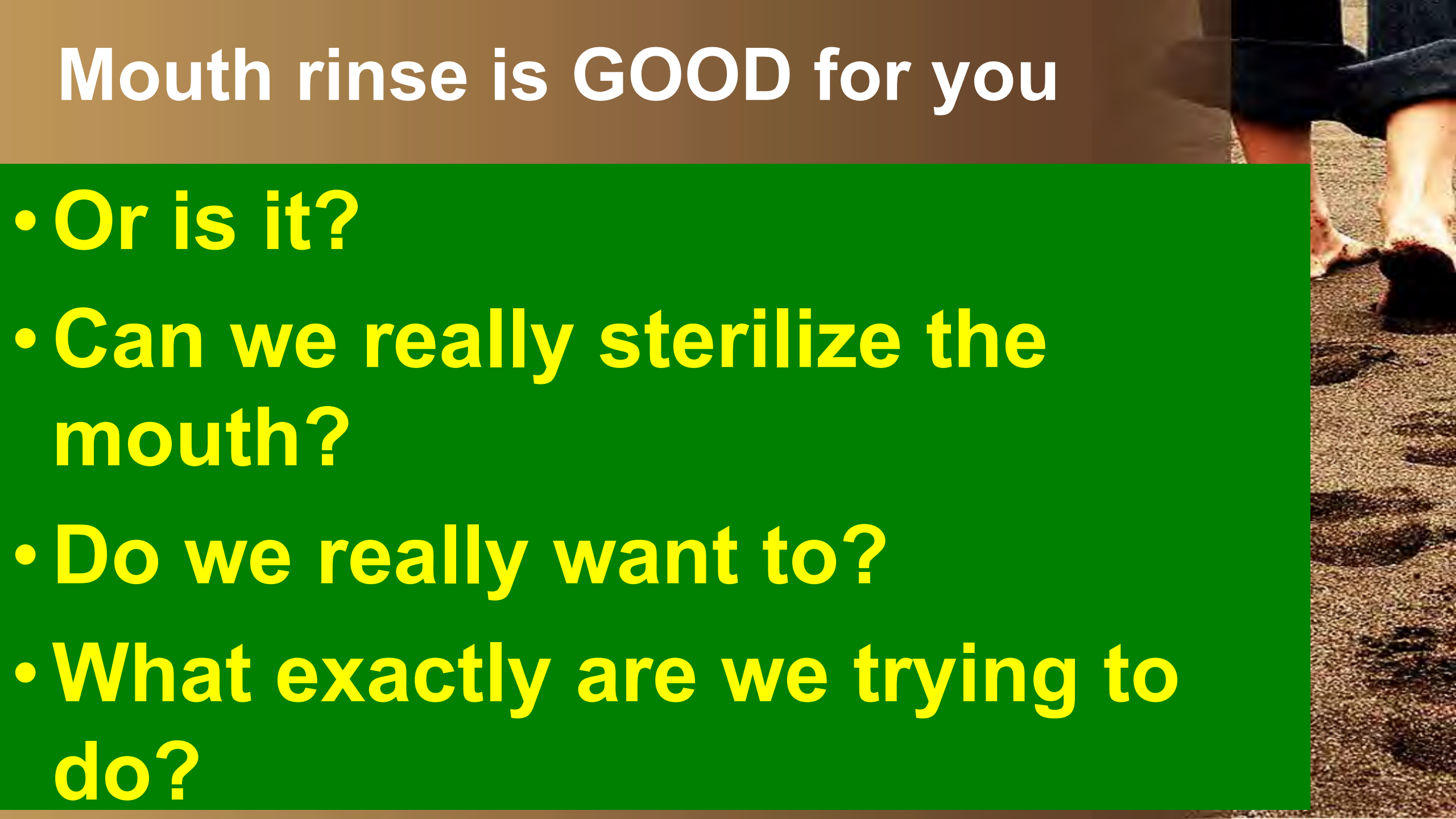
- These data suggested that specific combinations of periodontal bacteria, **even without inducing clinically significant periodontitis, may have a significant impact on human cause-specific death rates**. Our findings implied that increased disease and mortality risk could be transmittable via the transfer of oral microbiota, and that developing personalized strategies and maintaining healthy oral microbiota beyond protection against periodontitis would be important to manage the risk.

Pediatric Oral Health and Adult CVD

Just have everyone use an anti-microbial mouth rinse???

risk factor for adult cardiovascular disease.

Mouth rinse is GOOD for you



- Or is it?
- Can we really sterilize the mouth?
- Do we really want to?
- What exactly are we trying to do?

Nitrate Reducing Bacteria

- **But if you kill nitrate reducing bacteria? 2004 Article**

ssue TOC
12, Issue 5
er 2004
424-428

"Nitrate reducing commensals limit growth of cariogenic bacteria"

g capacity
The
ccus
ontrol

subjects, a significant reduction in caries experience was found in patients with high salivary nitrate and high nitrate-reducing ability. Production of nitrite from salivary nitrate by commensal nitrate-reducing bacteria may limit the growth of cariogenic bacteria as a result of the production of antimicrobial oxides of nitrogen, including nitric oxide.

Curr Hypertens Rep (2017) 19:33
DOI 10.1007/s11906-017-0725-2

GUT MICROBIOME, SYMPATHETIC NERVOUS SYSTEM, AND HYPERTENSION (M RAIZADA AND E M. SUMNERS, SECTION EDITORS)

Oral Microbiome and Nitric Oxide: the Missing Link in the Management of Blood Pressure

Nathan S. Bryan[1] · Gena Tribble[2] · Nikola Angelov[2]

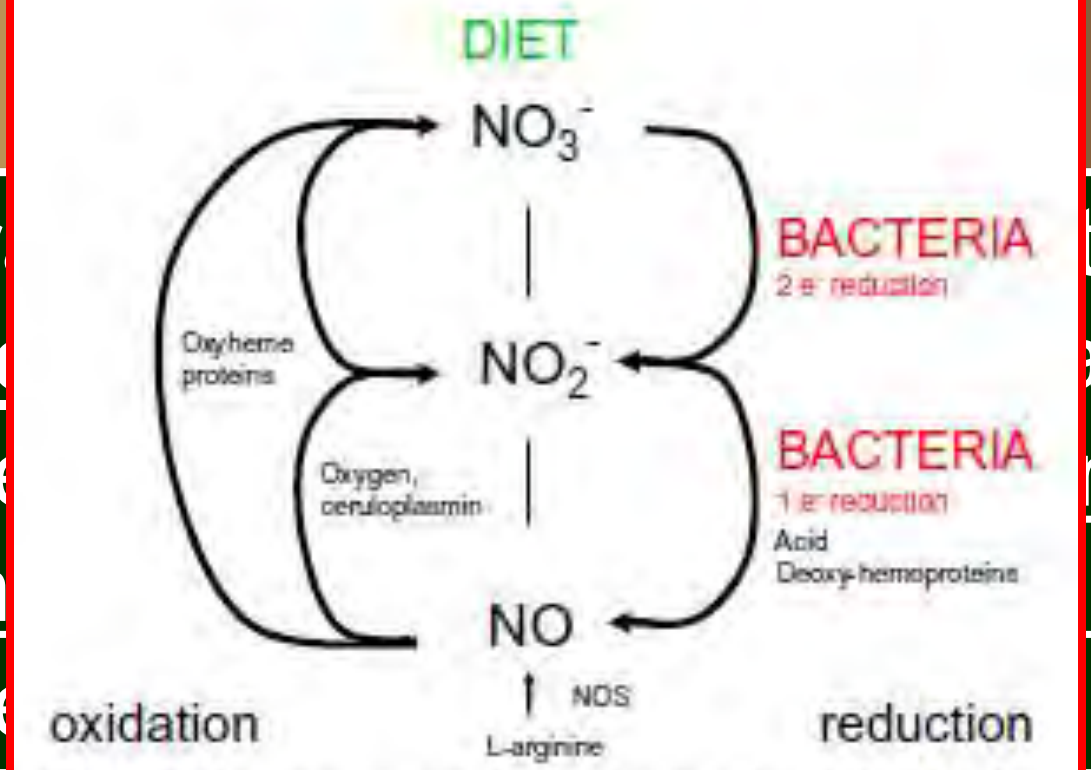


Fig. 1 The human nitrogen cycle whereby nitrate is serially reduced to nitrite and NO providing the host with a source of bioactive NO

In various animal models and in humans, dietary nitrate supplementation has shown numerous beneficial effects, including a **reduction in blood pressure, protection against ischemia reperfusion damage, restoration of NO homeostasis with associated cardioprotection, increased vascular regeneration after chronic ischemia, and a reversal of vascular dysfunction in the elderly**

Long Term Clinical Study

ELSEVIER

Nitric Oxide

Volume 71, 1 December 2017, Pages 14-20

P. Patel [d]

Loss of enterosalivary nitrate reduction by oral bacteria?

- (SOALS)
  l 40–65,
  seases-
  was

associated with increased risk of developing pre-diabetes/diabetes in this population.

Nitrate reducers and exercise

Free Radical Biology and Medicine
Volume 143, 1 November 2019, Pages 252-259

Original article

Post-exercise hypotension and skeletal muscle oxygenation is regulated by nitrate-reducing activity of oral bacteria

C. Cutler [a], M. Kiernan [b], J.R. Willis [c], L. Gallardo-Alfaro [d], P. Casas-Agustench [a], D. White [a], M. Hickson [a], T. Gabaldon [c, e, f], R. Bescos [a]

- The SBP-lowering effect of exercise was attenuated by 61% at 1 h in the recovery period, and it was fully attenuated 2 h after exercise with antibacterial mouthwash. This was associated with a lack of changes in circulatory nitrite ($P > 0.05$), and impaired microvascular response These findings show that nitrite synthesis by oral commensal bacteria is a key mechanism to induce the vascular response to exercise over the first period of recovery thereby promoting lower blood pressure and greater muscle oxygenation.

Nitrate reducers and vegans

- **vegetables are the main source of this anion. Dietary nitrate is reduced to nitrite by commensal bacteria in the mouth,** which in turn leads to increased circulatory nitrite availability. Nitrite can form nitric oxide by several pathways promoting a reduction in the vascular tone and lower blood pressure.

Nitrate

View

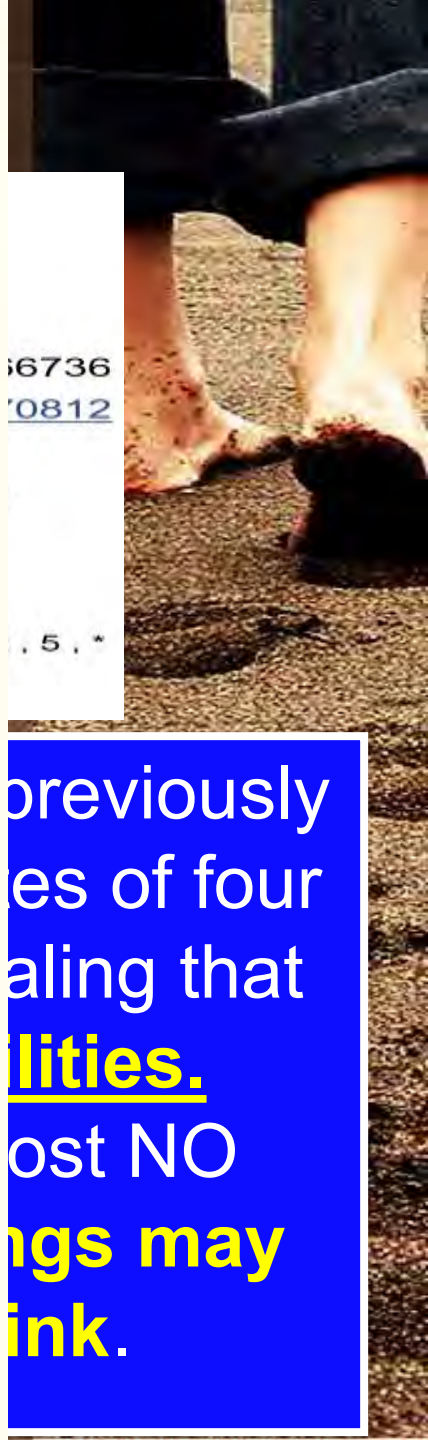
PLoS One. 2014; 9
Published online 20

Metagenomi
Implications

Embriette R. Hyde,
Deepa K. Parthasa
and Nathan S. Bry

The 14 candidate species detected through WGS sequencing and analysis of one representative sample from each group are listed.

	Best nitrate reducer	*Intermediate nitrate reducer*	*Worst nitrate reducer*
Species	% abundance	% abundance	% abundance
Neisseria flavescens	3.65	1.40	0.004
Haemophilus parainfluenzae	3.12	0.93	0.017
Neisseria mucosa	2.53	0.792	0.001
Prevotella melaninogenica	2.22	1.35	0.020
Granulicatella adiacens	1.56	1.16	0.941
Veillonella dispar	1.34	0.587	0.002
Veillonella atypica	0.816	0.301	0.002
Veillonella parvula	0.566	0.256	0.009
Neisseria sicca	0.369	0.146	0.0004
Prevotella salivae	0.189	0.071	0
Actinomyces odontolyticus	0.162	0.068	0.006
Actinomyces viscosus	0.124	0.064	0.002
Actinomyces oris	0.124	0.072	0.0003
Neisseria subflava	0.119	0.043	0



- We identi
believed t
candidate
they have
Colonizat
homeosta
also prov

previously
es of four
aling that
lities.
ost NO
gs may
ink.

Nitrate reducers and PERFORMANCE

ELSEVIER

Nitric Oxide

Volume 87, 1 June 2019, Pages 43-51

The oral nitrate-reducing capacity correlates with peak power output and peak oxygen uptake in healthy humans

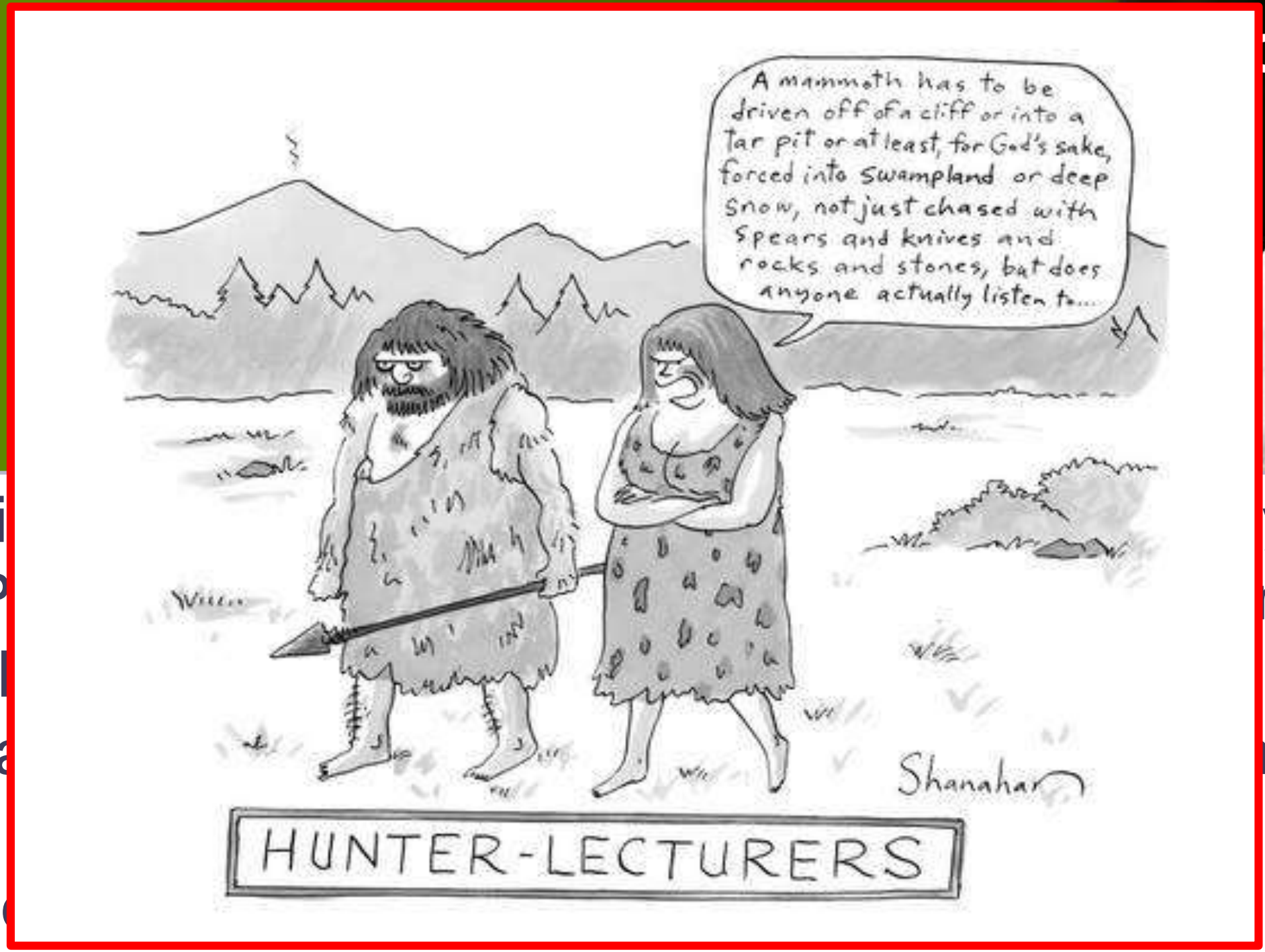
B. Thomas [a], S. Smallwood [a], C. Cutler [a], R. Bescos [a, b]

What influence diet had on early man? The hunter gatherer.

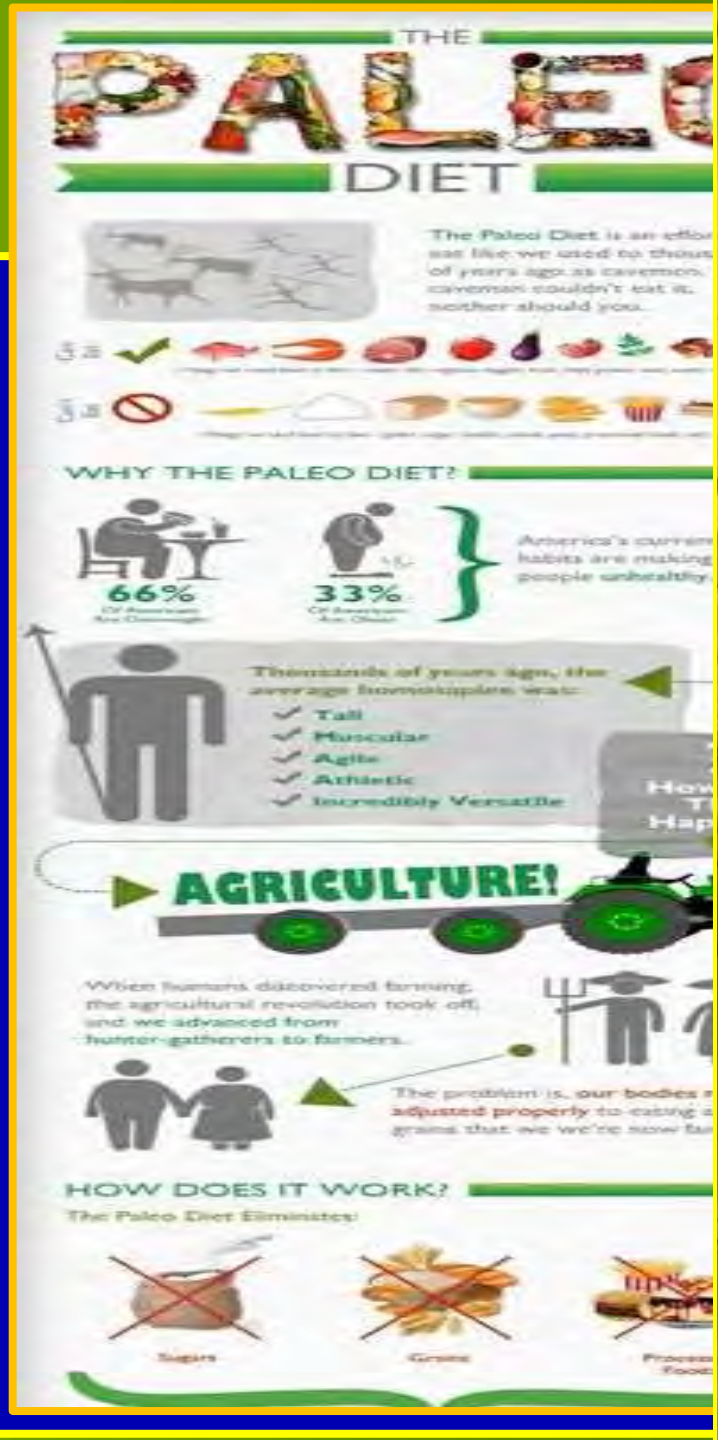
Dental Calculus- Fossils

Average height went down from ***5'10" (178 cm) for men and 5'6" (168 cm) for women to 5'5" (165 cm) and 5'1" (155 cm), respectively,*** *and it took until the twentieth century for average human height to come back to the pre-Neolithic Revolution* levels. ***Agriculturalists had more anemias and vitamin deficiencies, more spinal deformations and more dental pathologies***.

Natufian



- The Natufi
  Late Epi-P
  region of t
  10,200 yea
  as emmer
  gazelle, d



cestors of Pre-

Natufian Period - Hunter-Gathe
of Pre-Pottery Neolit

Dental Calculus- Fossils

Journal of Human Evolution xxx (2014) 1–6

Contents lists available at ScienceDirect

Journal of Human Evolution

journal homepage: www.elsevier.com/locate/jhevol

Ancient DNA analysis of dental calculus

Laura S. Weyrich [a], Keith Dobney [b], Alan Cooper [a,*]

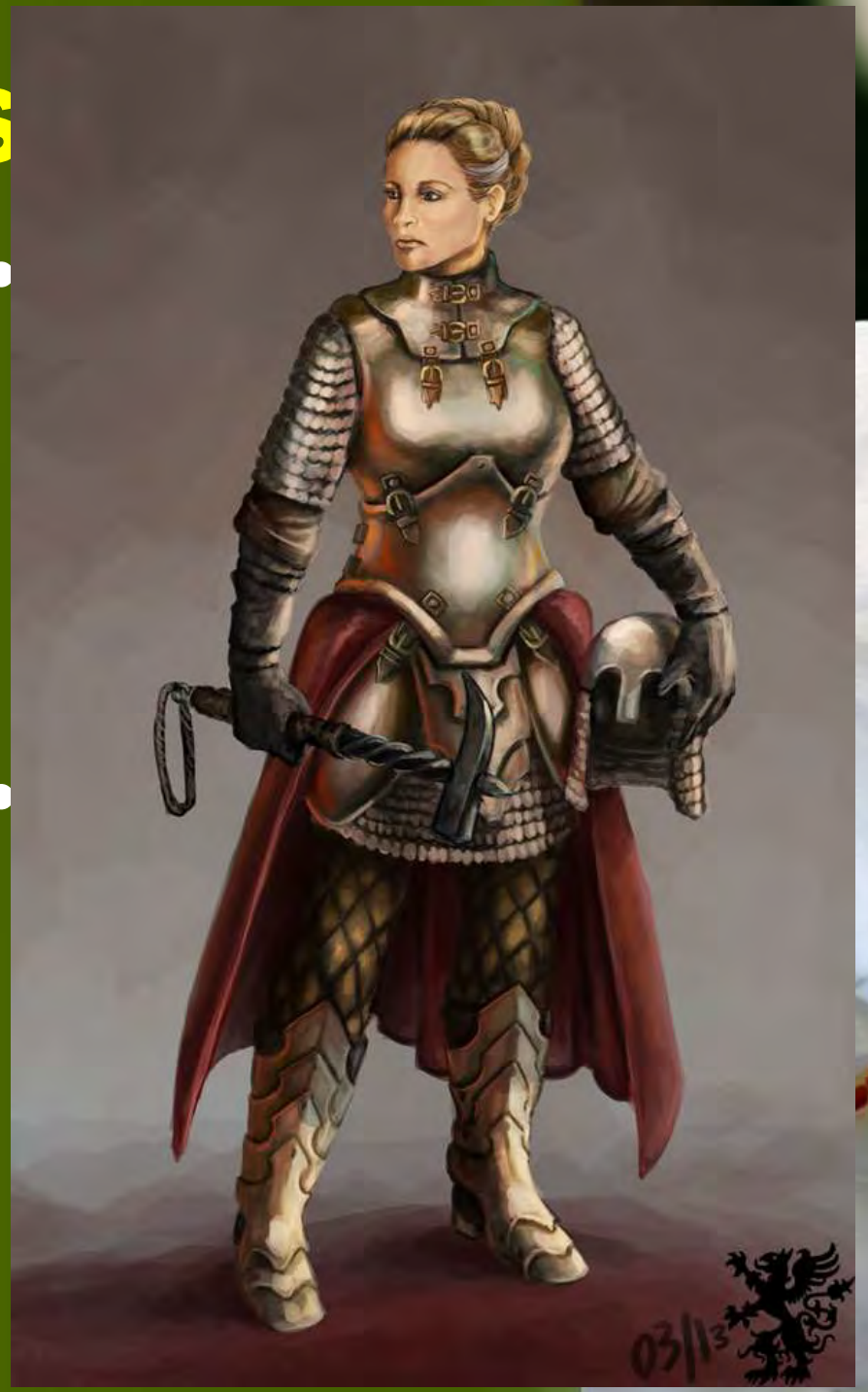
[a] The Australian Centre for Ancient DNA, The University of Adelaide, Adelaide, Australia
[b] Department of Archaeology, School of Geosciences, University of Aberdeen, Aberdeen, UK

- **Dental calculus preserves DNA of oral microbiome…**

Dental Calculus- Foss

Figure 1. Supra-gingival dental calculus is identifiable in a concave ring on a lower molar from a Medieval specimen, York, UK.

-
-



Dental Calculus- Fossils

- Calcified dental plaque (dental calculus) preserves for millennia and entraps biomolecules from all domains of life and viruses. We characterize (i) the ancient oral microbiome in a diseased state, (ii) **40 opportunistic pathogens**, **(iii) ancient human–associated putative antibiotic resistance genes**, **(iv) a genome reconstruction of the periodontal pathogen Tannerella forsythia**, **(v) 239 bacterial and 43 human proteins**, allowing confirmation of a long-term association between host immune factors, **'red complex' pathogens and periodontal disease**, and (vi) DNA sequences **matching dietary sources**.

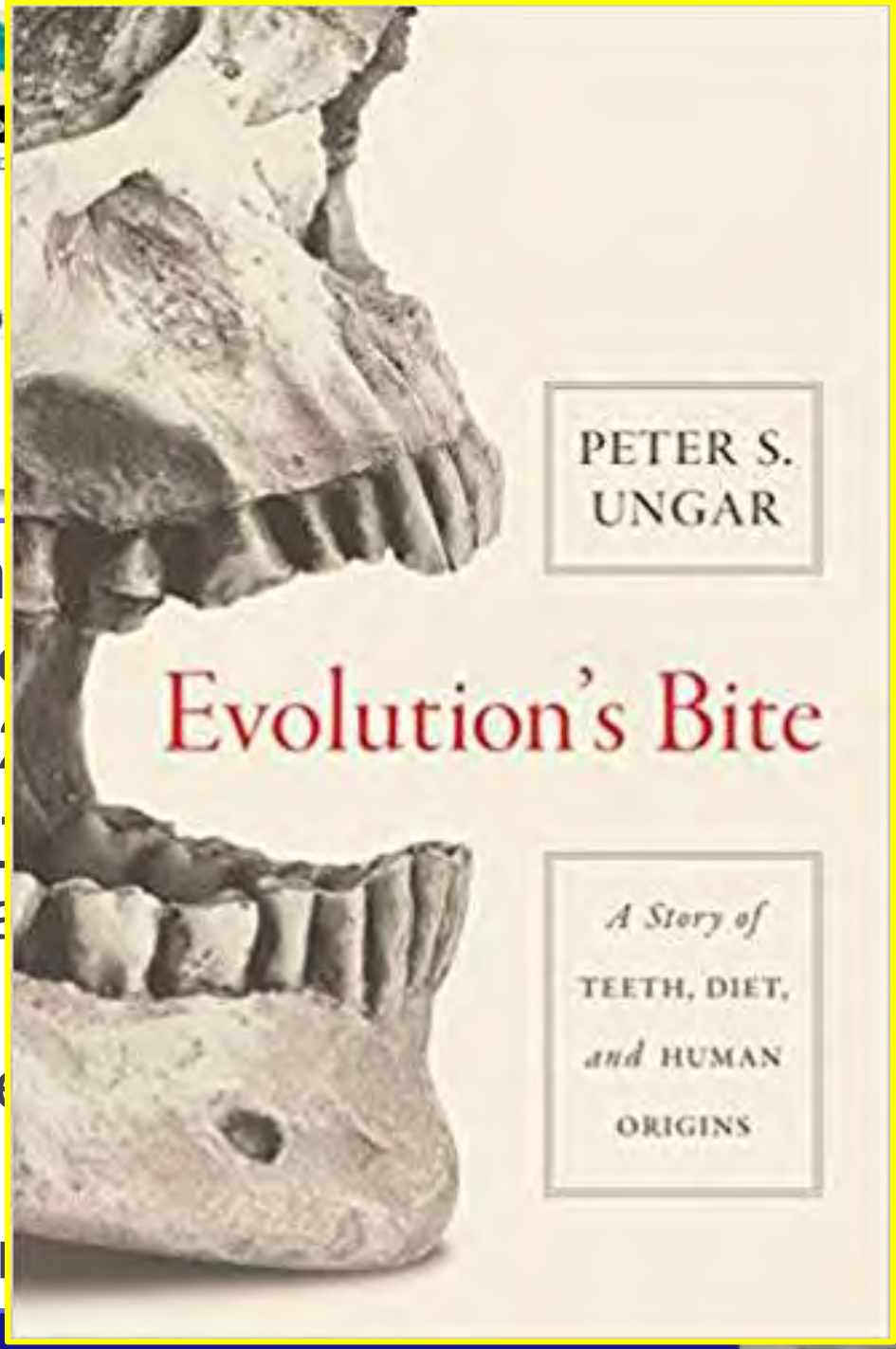
American Journal of
PHYSICAL ANTHROPOLOGY
The Official Journal of the American Association of Physical Anthropo
Explore this jo

Research Article/Section III: Case Studies in Extant Primates

Tubers as fallback foods and their imp
hunter-gatherers

Frank W. Marlowe ✉, Julia C. Berbesque

Tubers are present within the latitudes that hom
their inception through the first **expansion of H**
(O'Connell et al., 1999; Laden and Wrangham, 2
show dental features (e.g., thick enamel) tha
as adaptations to eating USOs (Hatley and Ka
and Ungar, 2000; Laden and Wrangham, 2005)
Brittain (2003) and Wrangham et al. (1999) have
implicated in the transition to Homo and that
because tubers are usually roasted before eate



Tubers and Polyols

American Journal of
PHYSICAL ANTHROPOLOGY
The Official Journal of the American Association of Physical Anthropol
Explore this jo

Research Article/Section III: Case Studies in Extant Primates

**Tubers as fallback foods and their imp
hunter-gatherers**

Frank W. Marlowe ✉, Julia C. Berbesque

In the majority of plants, the main glu
saccharose. **However in a large nu
other compounds, such as polyols
transported. Polyols (or sugar alco**
saccharose, primary products of phot
include mannitol, sorbitol, dulcitol, ga
myo-inositol, ribitol, **xylitol** and more

Cellulose and Xylan Hydrolysis

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo[a], Duccio Cavalieri[a], Monica Di Paola[b], Matteo Ramazzotti[c], Jean Baptiste Poullet[d], Sebastien Massart[d], Silvia Collini[b], Giuseppe Pieraccini[e], and Paolo Lionetti[b,1]

- Compared the fecal microbiota of European children (EU) and that of children from a rural African village of Burkina Faso (BF), where the diet, high in fiber content, is similar to that of early human settlements at the time of the birth of agriculture. **By using high-throughput 16S rDNA sequencing and biochemical analyses, we found significant differences in gut microbiota between the two groups.**

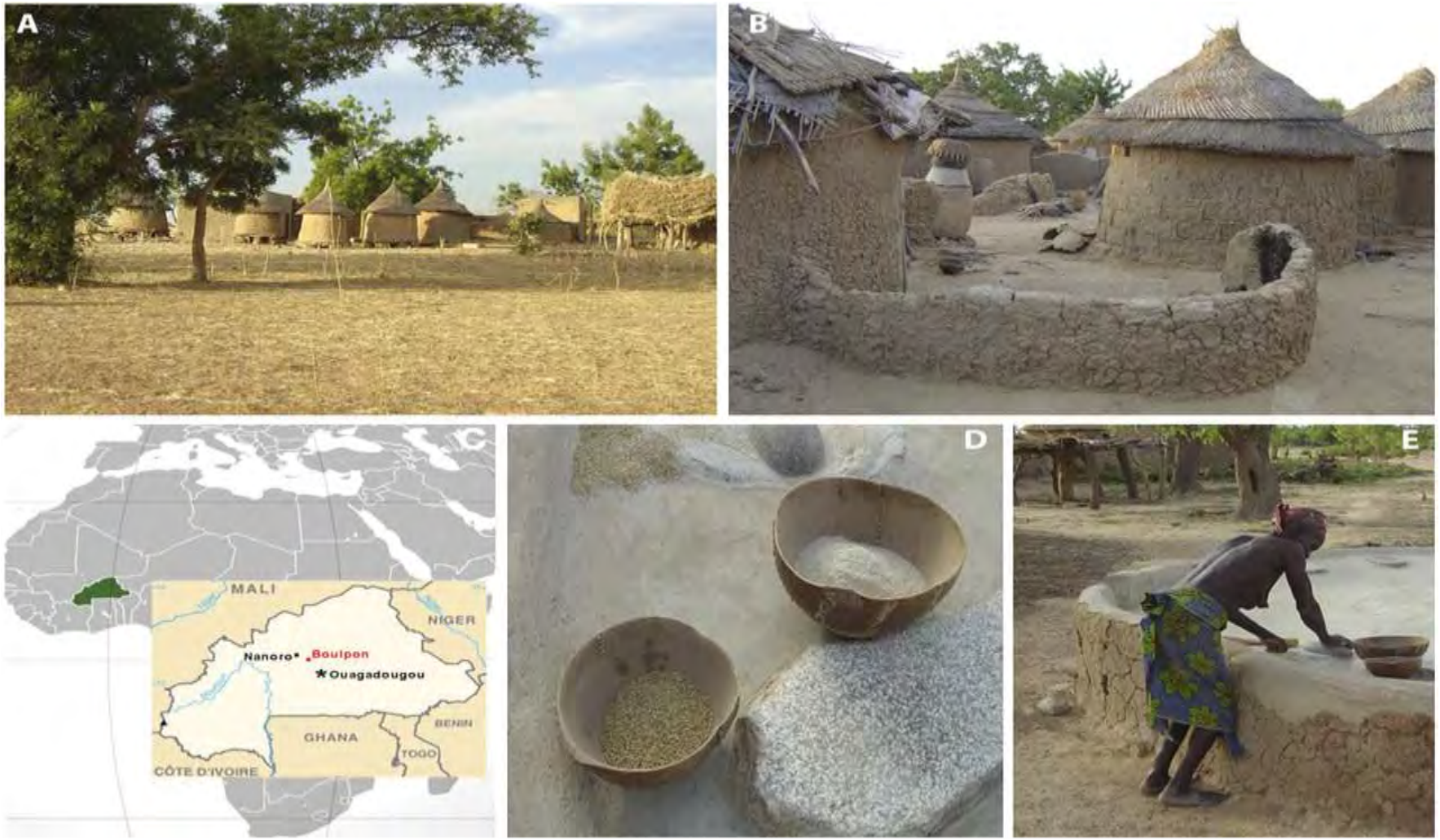
Cellulose and Xylan Hydrolysis

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo[a], Duccio Cavalieri[a], Monica Di Paola[b], Matteo Ramazzotti[c], Jean Baptiste Poullet[d], Sebastien Massart[d], Silvia Collini[b], Giuseppe Pieraccini[e], and Paolo Lionetti[b,1]

- BF children showed a significant enrichment in Bacteroidetes and depletion in Firmicutes ($P < 0.001$), with a unique abundance of bacteria from the genus **Prevotella and Xylanibacter, known to contain a set of bacterial genes for cellulose and xylan hydrolysis, completely lacking in the EU children**.

Life in a rural village of Burkina Faso.



Carlotta De Filippo et al. PNAS 2010;107:14691-14696

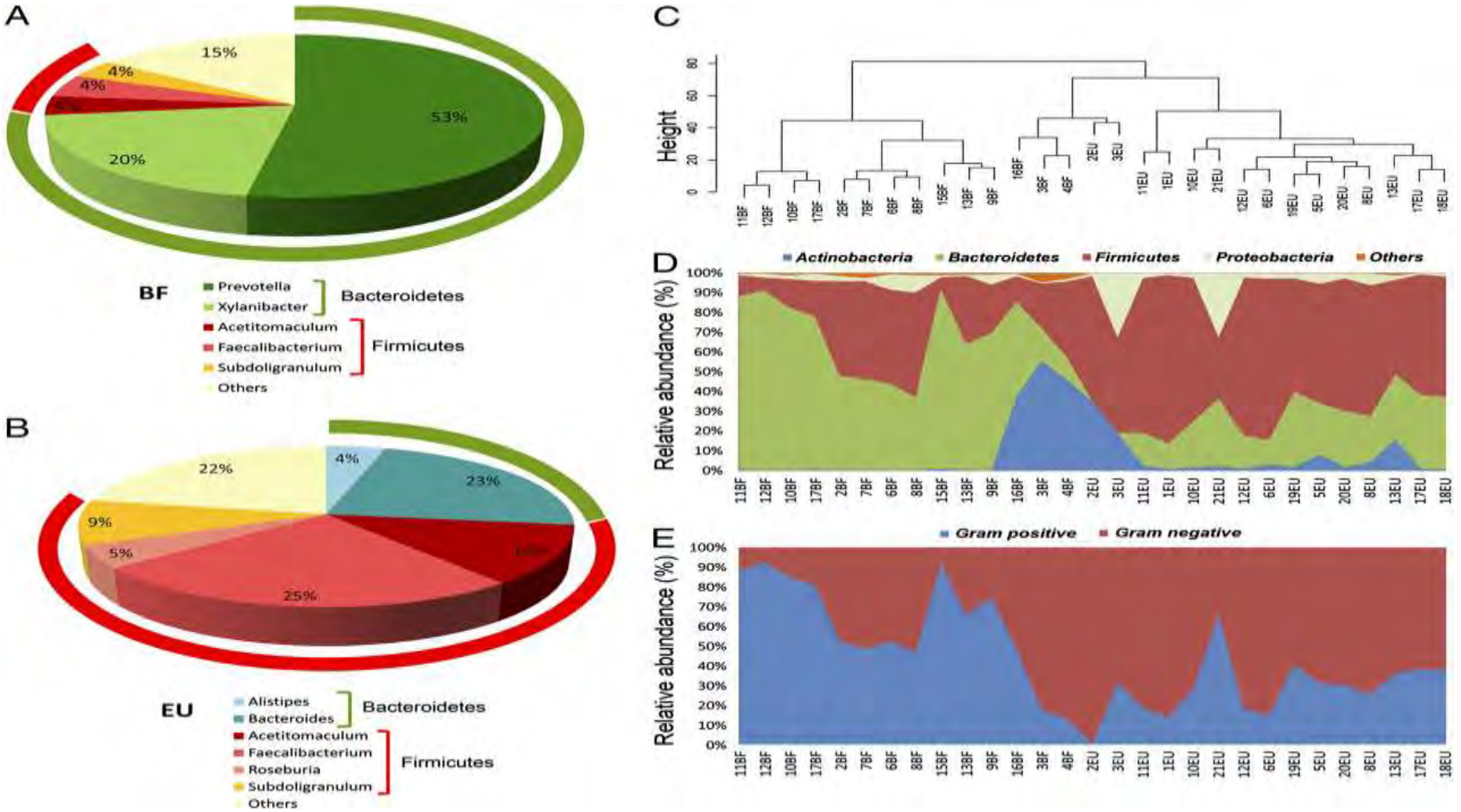
©2010 by National Academy of Sciences

Cellulose and Xylan Hydrolysis

- e to the BF
  xylane,

xylose, and carboxymethylcellulose to produce high levels of SCFAs whose protective role against gut inflammation has been well proven .

16S rRNA gene surveys reveal a clear separation of two children populations investigated.



Carlotta De Filippo et al. PNAS 2010;107:14691-14696

©2010 by National Academy of Sciences

Cellulose and Xylan Hydrolysis

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo[a], Duccio Cavalieri[a], Monica Di Paola[b], Matteo Ramazzotti[c], Jean Baptiste Poullet[d], Sebastien Massart[d], Silvia Collini[b], Giuseppe Pieraccini[e], and Paolo Lionetti[b,1]

- The SCFA-producing bacteria that are abundant in the BF children's gut possibly help to prevent the establishment of some potentially pathogenic intestinal microbes causing diarrhea, as seen by the fact that Enterobacteriaceae, such as Shigella and Escherichia, were significantly underrepresented in BF than in EU children. **Increased gut microbial diversity and reduced quantities of potentially pathogenic strains in BF would agree with the "old friend" hypothesis, indicating a role of microbiota in protecting children from pathogens as well as from gastrointestinal diseases.**

No guts, No glory! GUT

BMJ Journals
Gut

The microbiome of professional athletes differs from that of more sedentary subjects in composition and particularly at the functional metabolic level

- Athletes had relative increases in pathways (eg, amino acid and antibiotic biosynthesis and carbohydrate metabolism) and faecal metabolites (eg, microbial produced **short-chain fatty acids (SCFAs) acetate, propionate and butyrate**) associated with enhanced muscle turnover (fitness) and overall health when compared with control groups. **Differences in faecal microbiota between athletes and sedentary controls show even greater separation at the metagenomic and metabolomic than at compositional levels** and provide added insight into the diet–exercise–gut microbiota paradigm.

No guts, No glory! GUT

BMJ Journals
Gut

Exercise and associated dietary extremes impact on gut microbial diversity FREE

Siobhan F Clarke[1, 2, 3], Eileen F Murphy[2, 4], Orla O'Sullivan[1], Alice J Lucey[5], Margaret Humphreys[6], Aileen Hogan[2], Paula Hayes[2], Maeve O'Reilly[2, 4], Ian B Jeffery[2, 3], Ruth Wood-Martin[7], David M Kerins[8, 9], Eamonn Quigley[2], R Paul Ross[1, 2], Paul W O'Toole[3], Michael G Molloy[10], Eanna Falvey[10, 11], Fergus Shanahan[2, 10, 12], Paul D Cotter[1, 2]

When does the protection start? How do children develop the protective microbiome? Before birth!

accompanying dietary extremes.

Pre-natal microbiome

- **The Maternal Effect-**

everyone knows!

BE

SCIENTIFIC AMERICAN

English Cart

HE SCIENCES MIND HEALTH TECH SUSTAINABILITY EDUCATION VIDEO PODCASTS BLOGS STOR

HEALTH

How Bacteria in the Placenta Could Help Shape Human Health

The placenta is full of microbes, a new study finds, raising questions about how that ecosystem and mothers' oral health influence the risk of preterm birth

By Dina Fine Maron on May 21, 2014 2

Pre-natal microbiome

- **The Maternal Effect**

Science Translational Medicine

Vol 6, Issue 237
21 May 2014

Table of Contents

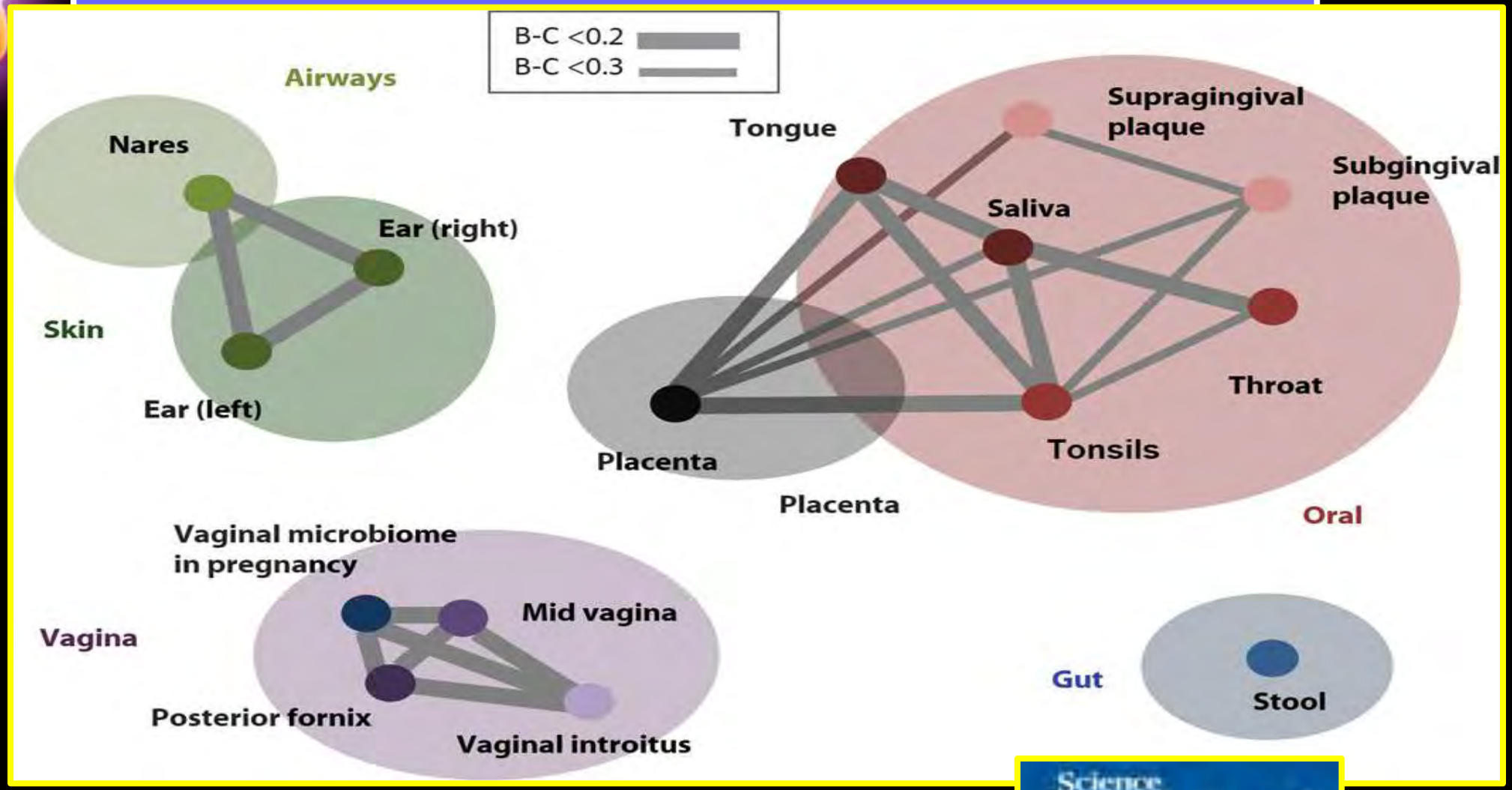
The Placenta Harbors a Unique Microbiome

Kjersti Aagaard[1,2,3,*], Jun Ma[1,2], Kathleen M. Antony[1], Radhika Ganu[1], Joseph Petrosino[4] and James Versalovic[5]
+ See all authors and affiliations

Science Translational Medicine 21 May 2014:
Vol. 6, Issue 237, pp. 237ra65
DOI: 10.1126/scitranslmed.3008599

We characterized a unique placental microbiome niche, composed of nonpathogenic commensal microbiota from the Firmicutes, Tenericutes, Proteobacteria, Bacteroidetes, and Fusobacteria phyla. **In aggregate, the placental microbiome profiles were most akin (Bray-Curtis dissimilarity <0.3) to the human oral microbiome.** 16S-based operational taxonomic unit analyses revealed associations of the placental microbiome with a remote history of antenatal infection (permutational multivariate analysis of variance, $P = 0.006$), such as urinary tract infection in the first trimester, as well as with preterm birth <37 weeks ($P = 0.001$).

Fig. 1. The placental microbiome has a taxonomic profile that is similar to the oral microbiome.

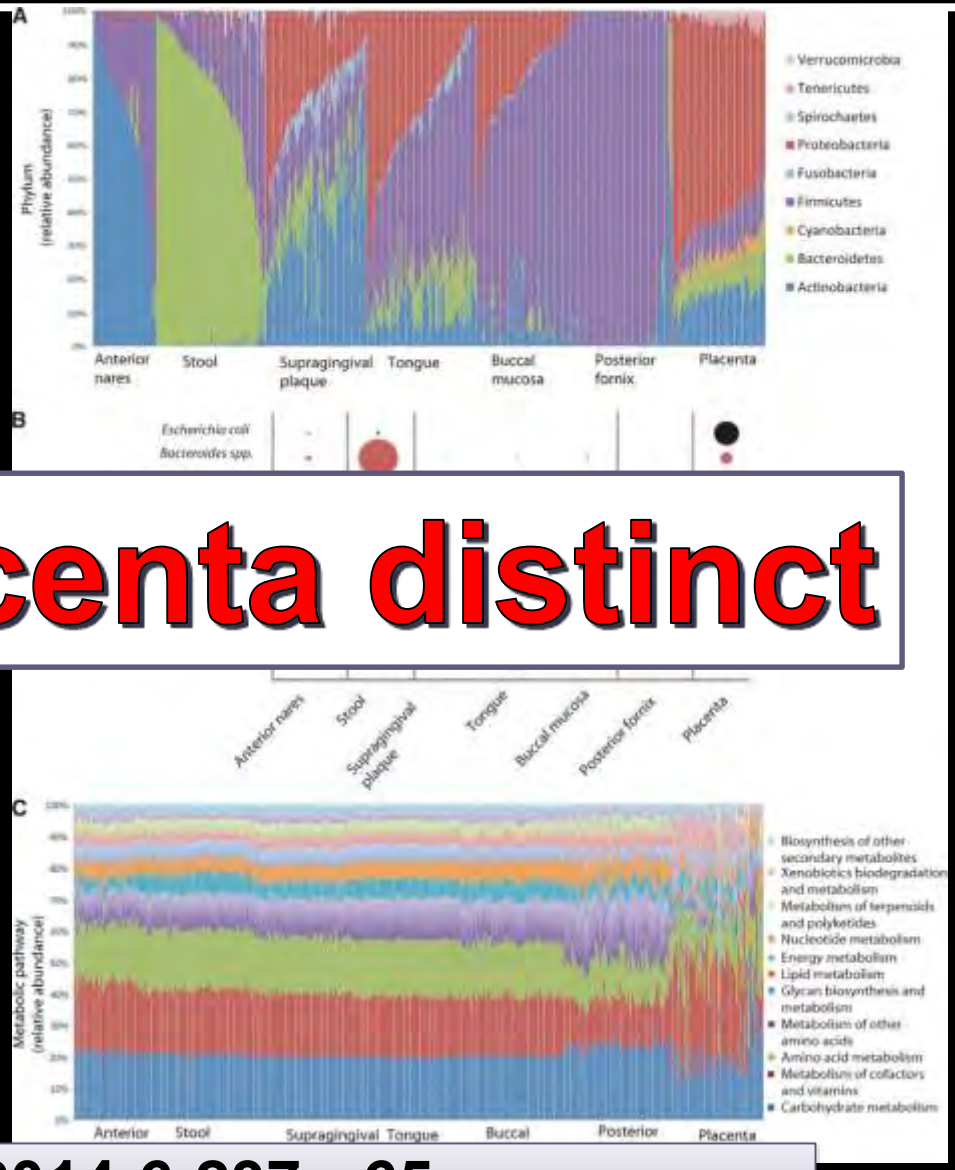


Kjersti Aagaard et al., Sci Transl Med 2014;6:237ra65

Published by AAAS

Science Translational Medicine
AAAS

Fig. 2. Comparison of WGS-generated taxa and metabolic capacity among body sites reveals distinct features of the placental microbiome.



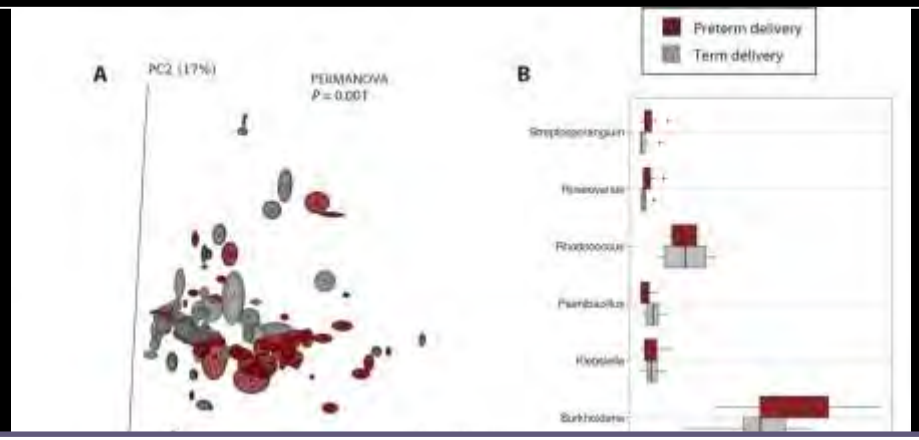
Science Translational Medicine AAAS

Published by AAAS

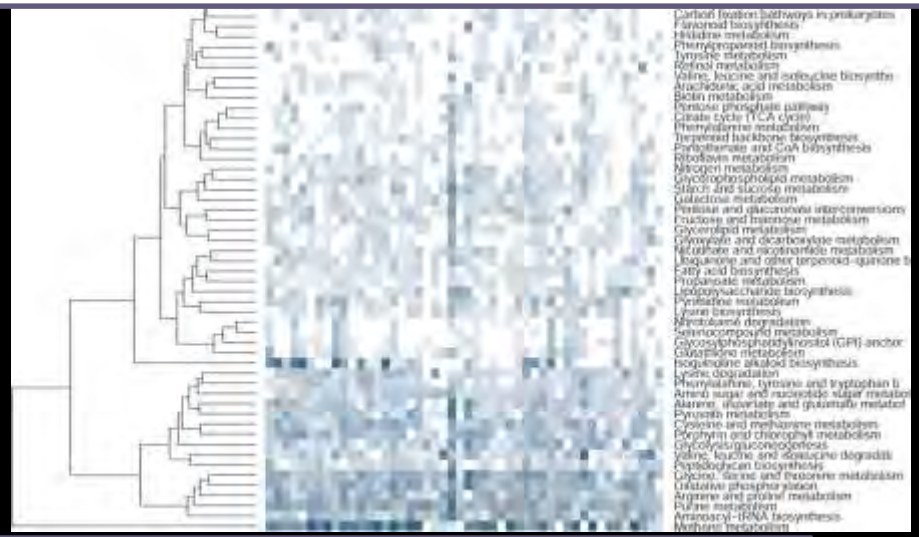
Placenta distinct

Kjersti Aagaard et al., Sci Transl Med 2014;6:237ra65

Fig. 3. The placental microbiome from pregnancies complicated by a preterm delivery demonstrates discrete taxonomic profiles and variations in metabolic pathways.



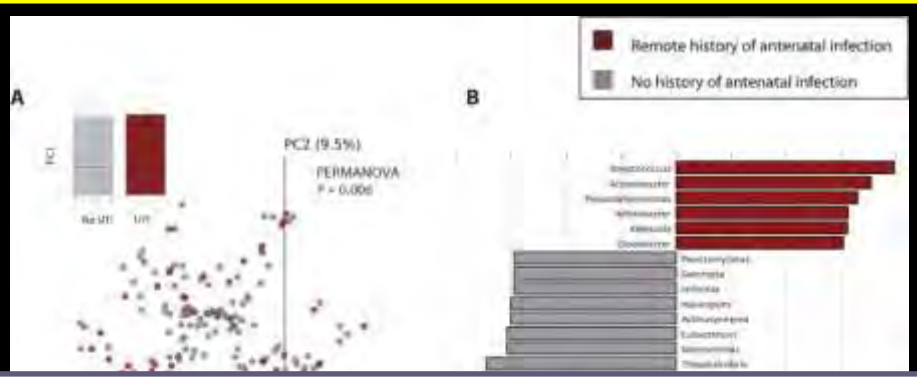
Pre-term are different



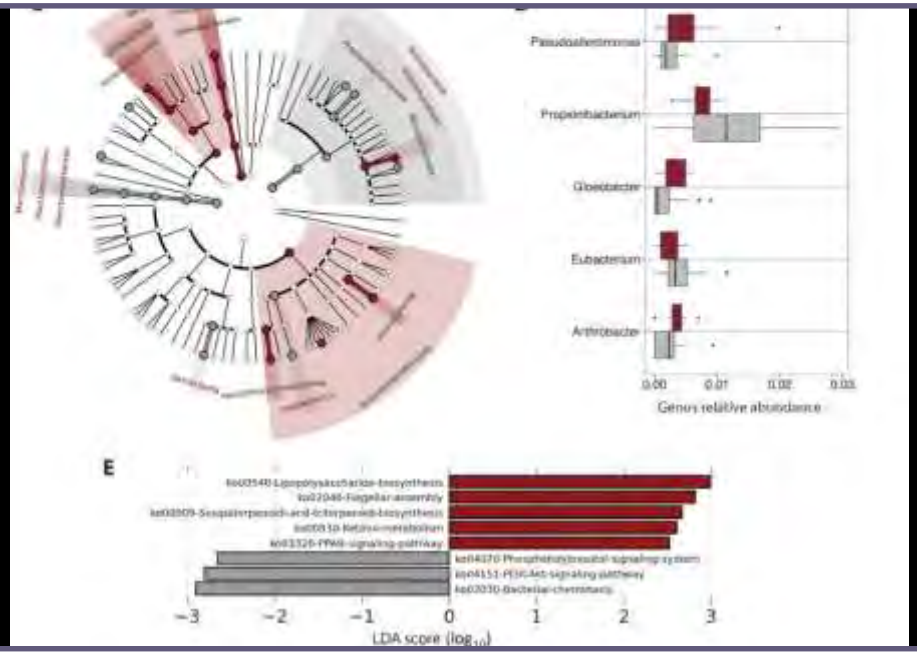
Science Translational Medicine
AAAS

Kjersti Aagaard et al., Sci Transl Med 2014;6:237ra65

Fig. 4. A remote history of maternal antenatal infection correlates with the placental microbiome community.



Antibiotics again!



Science Translational Medicine AAAS

Published by AAAS

Kjersti Aagaard et al., Sci Transl Med 2014;6:237ra65

Epigenetics- fetal

Current Microbiology

October 2005, Volume 51, Issue 4, pp 270–274 | Cite as

Isolation of Commensal Bacteria from Umbilical Cord Blood of Healthy Neonates Born by Cesarean Section

Authors | Authors and affiliations

Esther Jiménez, Leonides Fernández, María L. Marín, Rocío Martín, Juan M. Odriozola, Carmen Nueno-Palop, Arjan Narbad, Mónica Olivares, Jordi Xaus, Juan M. Rodríguez

- In a pre
  obtain
  sugges
  to-chil
  such ba
  electiv
  submit
  the ide
  Strepto

Later, a group of pregnant mice were orally inoculated with a **genetically labeled E. faecium strain** previously isolated from **breast milk** of a healthy woman. The **labeled strain** could be isolated and **polymerase chain reaction detected from the amniotic fluid of the inoculated animal.**

Pre-natal intervention

ClinicalTrials.gov

Saving Live … ntal Disease in Relation to Preterm Birth in Malawi (PPaX)

This study i … nd Locations)

Verified July 2…

Sponsor:
Baylor Coll…

ClinicalTrials.gov Identifier:
NCT02333227

First received: December 23, 2014
Last updated: July 18, 2016
Last verified: July 2016

In rodents, … eriodontal pathogens cause dose-dependent decreases … atory responses that can trigger preterm birth when pres… defined as a destructive inflammation of the periodontiu… eater in women of child bearing age. By definition, … e periodontium, which stimulates a chronic inflammato… , and the production of cytokines and prostaglan… irth. It is the same production of prostaglan… isk of preterm birth. **The investigators' overarchi… nsive primary preterm birth prevention, inclusive … ol chewing gum (the intervention), will reduce th… l caries, preterm birth prevalence, and neonatal mortality.**

Prevention:

- Diagnosis
- What is missing?

Prebiotics and Probiotics

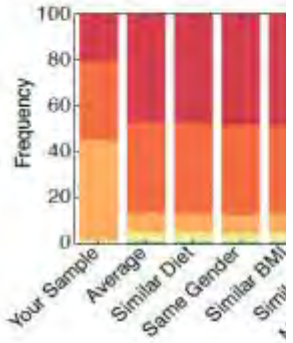
american gut

american gut

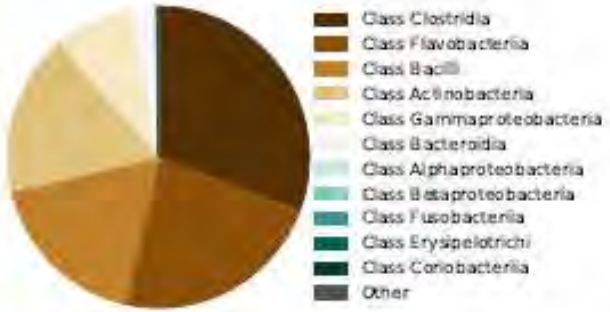
YOUR AMERICAN GUT SAMPLE

MARK CANNON

What's in your A



What's in your oral sample?



Your most abundant microbes:

Taxonomy	Sample
Genus *Veillonella*	29.1%
Genus *Chryseobacterium*	22.7%
Genus *Rothia*	15.7%
Genus *Streptococcus*	15.7%

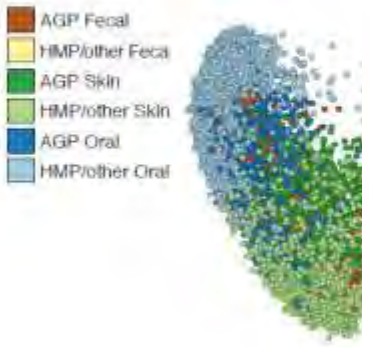
Your most enriched microbes:

Taxonomy	Sample	Population	Fold
Genus *Conchiformibius*	0.02%	0.00%	7x
Genus *Chryseobacterium*	22.72%	0.57%	40x
Genus *Amaricoccus*	0.00%	0.00%	39x
Genus *Skermanella*	0.00%	0.00%	27x

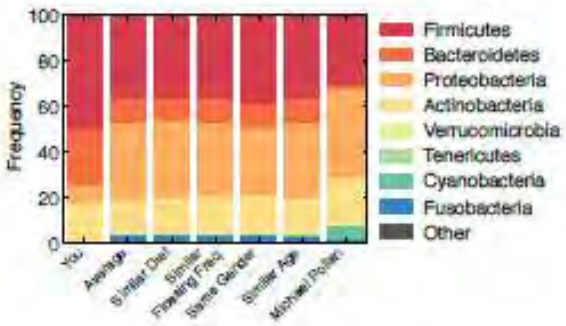
Your sample contained 9 rare taxa, including the following: Genus *Microbacterium*, Unclassified Family Solirubrobacteraceae, Genus *Jeotgalicoccus*, Genus *Peptostreptococcus*, Genus *Megamonas*.

This sample was registered on unknown at 11:00.

How do your gut



How do your oral microbes compare to others?



Different Subpopulations

Different Body Sites

The American Gut Population

You • Others • Missing metadata

90	1852384	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Ruminococcaceae		Ruminococcaceae bacterium Marseille-P2963
91	821	species	Bacteria	Bacteroide	Bacteroidia	Bacteroida	Bacteroida	Bacteroide	Bacteroides vulgatus
92	823	species	Bacteria	Bacteroide	Bacteroidia	Bacteroida	Porphyrom	Parabacter	Parabacteroides distasonis
93	84026	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Ruminococ	Ruminiclos	[Clostridium] methylpentosum
94	84112	species	Bacteria	Actinobact	Coriobacte	Eggerthella	Eggerthella	Eggerthella	Eggerthella lenta
95	853	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Ruminococ	Faecalibact	Faecalibacterium prausnitzii
96	88431	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Lachnospir	Dorea	Dorea longicatena
97	1118061	species	Bacteria	Bacteroide	Bacteroidia	Bacteroida	Rikenellace	Alistipes	Alistipes obesi
98	1870991	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Clostridiac	Massilioclc	Massilioclostridium coli
99	1188792	species	Viruses	dsRNA viruses			Endornavir	Endornavir	Phaseolus vulgaris endornavirus 1
100	1871035	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Ruminococ	Ruminococ	Ruminococcus sp. Marseille-P3213
101	1226324	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Lachnospir	Blautia	Blautia sp. KLE 1732
102	1352	species	Bacteria	Firmicutes	Bacilli	Lactobacill	Enterococc	Enterococc	Enterococcus faecium
103	1226325	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Clostridiac	Clostridium	Clostridium sp. KLE 1755
104	1308	species	Bacteria	Firmicutes	Bacilli	Lactobacill	Streptococ	Streptococ	Streptococcus thermophilus
105	1163670	species	Bacteria	Bacteroide	Bacteroidia	Bacteroida	Bacteroida	Bacteroide	Bacteroides sp. 14(A)
106	1232453	species	Bacteria	Firmicutes	Clostridia	Clostridiales			Clostridiales bacterium VE202-21
107	1550024	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Ruminococ	Ruthenibac	Ruthenibacterium lactatiformans
108	1499682	species	Bacteria	Bacteroide	Bacteroidia	Bacteroida	Rikenellace	Alistipes	Alistipes sp. AL-1
109	1574264	species	Bacteria	Verrucomi	Verrucomi	Verrucomi	Akkermans	Akkermans	Akkermansia sp. KLE1797
110	1531	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Lachnospir	Lachnoclos	[Clostridium] clostridioforme
111	1761477	species	Viruses	ssRNA viruses			Virgavirida	Tobamovir	Tomato brown rugose fruit virus
112	1776382	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Ruminococ	Neglecta	Neglecta timonensis
113	1697787	species	Bacteria	Firmicutes	Clostridia				Clostridia bacterium UC5.1-1D10
114	1468449	species	Bacteria	Firmicutes	Erysipelotr	Erysipelotr	Erysipelotr	Holdemani	Holdemania massiliensis
115	204516	species	Bacteria	Bacteroide	Bacteroidia	Bacteroida	Bacteroida	Bacteroide	Bacteroides massiliensis
116	1871020	species	Bacteria	Firmicutes	Clostridia	Clostridiale	Clostridiac	Clostridium	Clostridium sp. Marseille-P3244

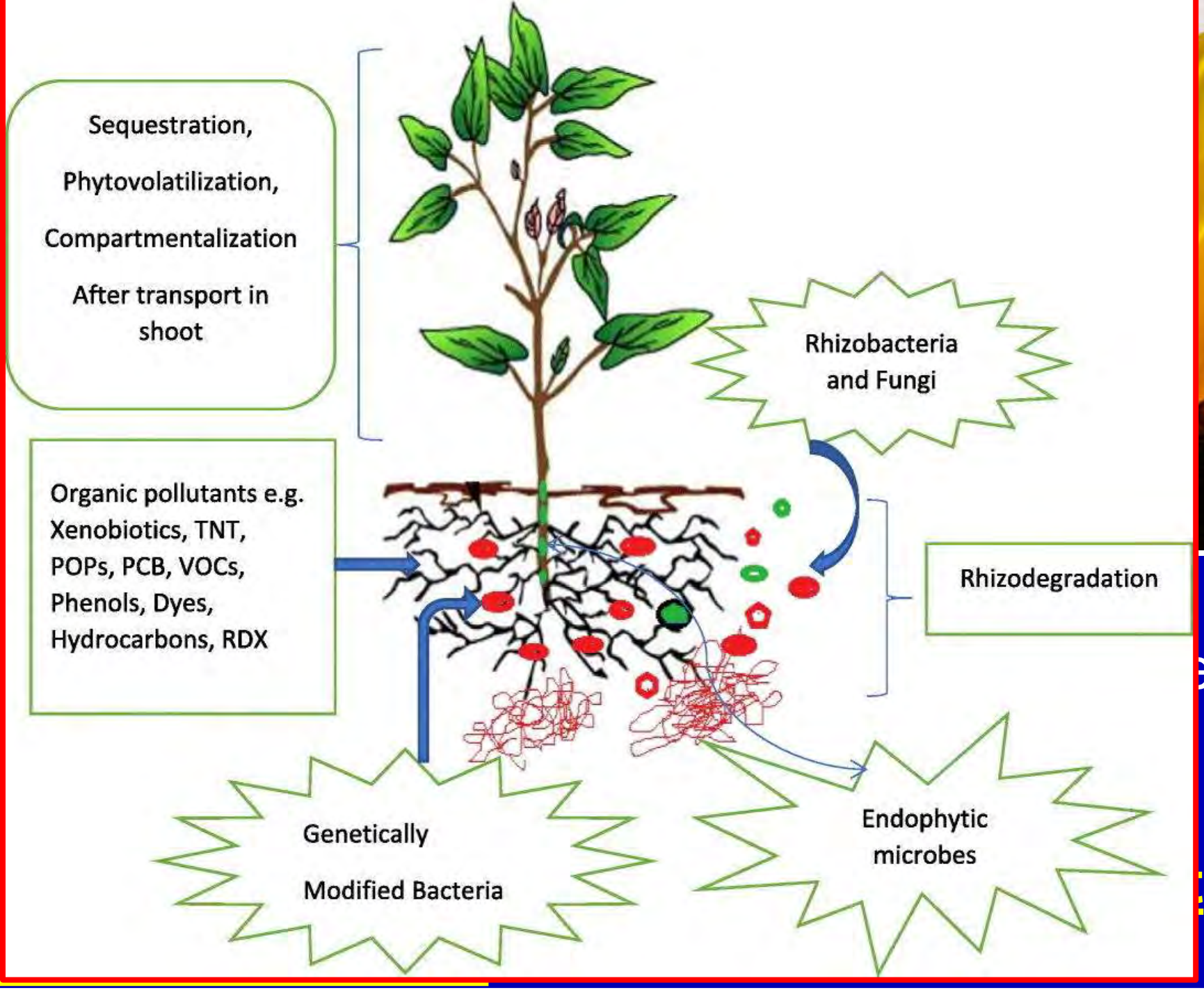
GMO

Review

Microbe a
organic xe
genetically
technolog

Imran Hussain [a, b, 1], G
Mahmudur Rahman [c],

- Synergist
and gene
restoratio
pollutants
modified
does pos

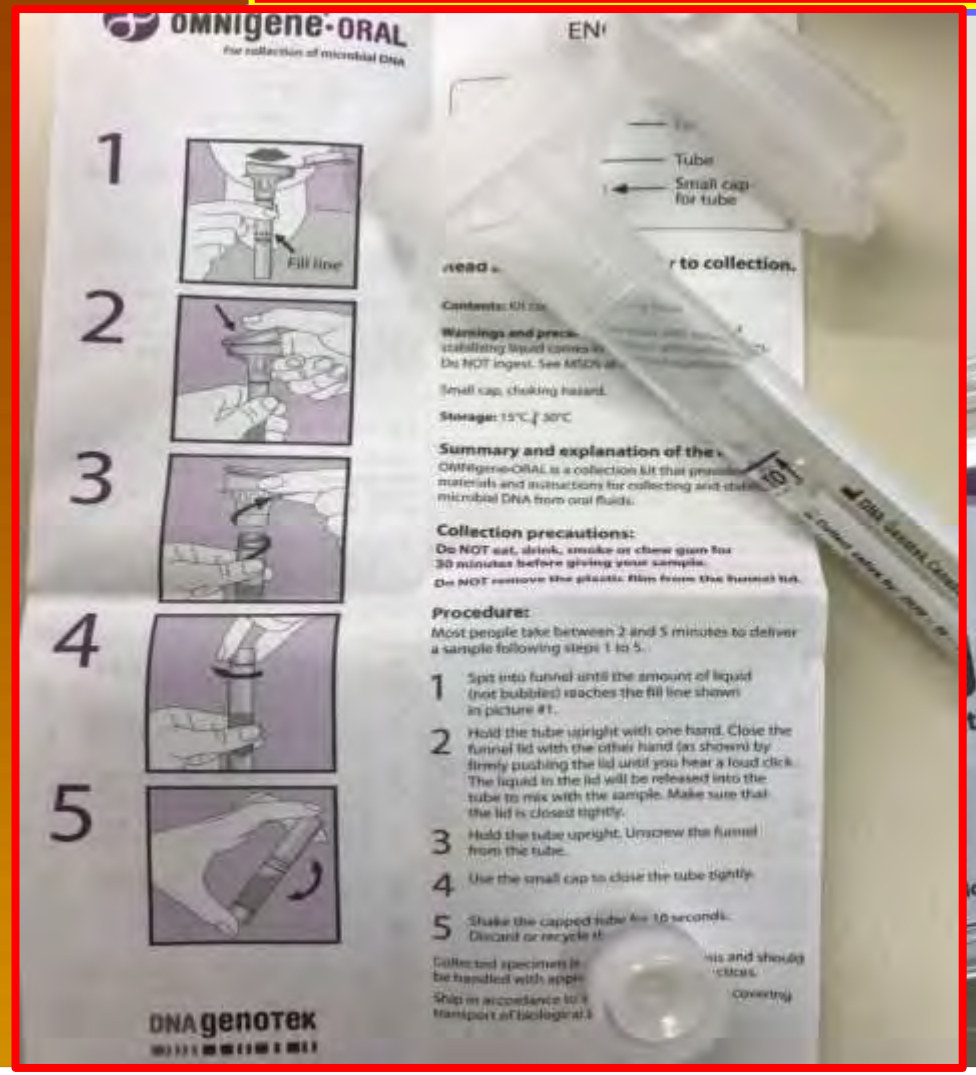


Prebiotics and Probiotics

- **Diagnosis:**

  –Salivary- oral microbiome genetic info

Diagnostic tests



- DNA GenoTek – OMNIgene Oral
- OM-501

MITOswab test analysis reveals -

-The overall content of mitochondria is significantly higher than - 'normal range' as indicated by the citrate synthase activity valu (265% of the normal mean activity level) in test buccal sample

- The activity of Resp
range.

- The activity of Resp

Powered by RELIGEN

MITOSWAB

Interpretation-

- Biochemical analysi
RC-IV.

- Although the RC-I a
suggest a compensat
present.

- Periodic mitochond
compensatory/corre

- Microbi th
reflects

Shows up before clinical signs

Mitochondrial DNA sequencing

Journal of Indian Society of Periodontology
Wolters Kluwer -- Medknow Publications

Identical mitochondrial somatic mutations unique to chronic periodontitis and coronary artery disease

Tokala Pallavi, Rampalli Viswa Chandra, [...], and Anumala Naveen

- Among the complete mtDNA sequences, a total of 162 variations were spread across the whole mitochondrial genome and *present only in the coronary artery and the gingival tissue samples* but not in the blood samples. Among the 162 variations, **12 were novel and four of the 12 novel variations were found in mitochondrial NADH dehydrogenase subunit 5 complex I gene (33.3%).**

Viome- transcriptomics

Entire gut or oral microbiome

The term can be applied to the total set of transcripts in a given organism, or to the specific subset of transcripts present in a particular cell type. Unlike the genome, which is roughly fixed for a given cell line (excluding mutations), the transcriptome can vary with external environmental conditions. Because it includes all mRNA transcripts in the cell, the *transcriptome reflects the genes that are being actively expressed at any given time*, with the exception of mRNA degradation phenomena such as transcriptional attenuation.

gut ?

Prevention:

- Prebiotics

and

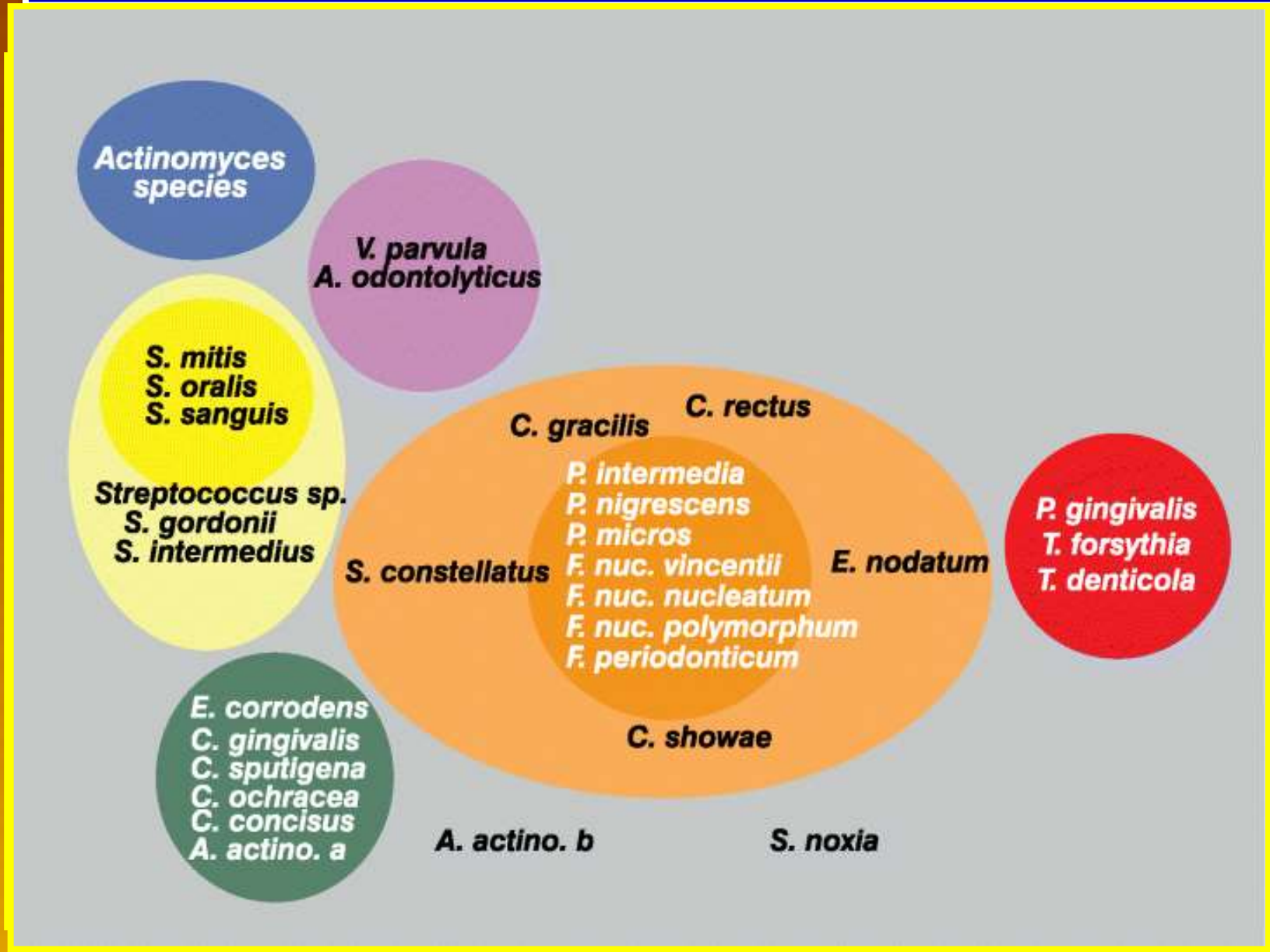
- Probiotics

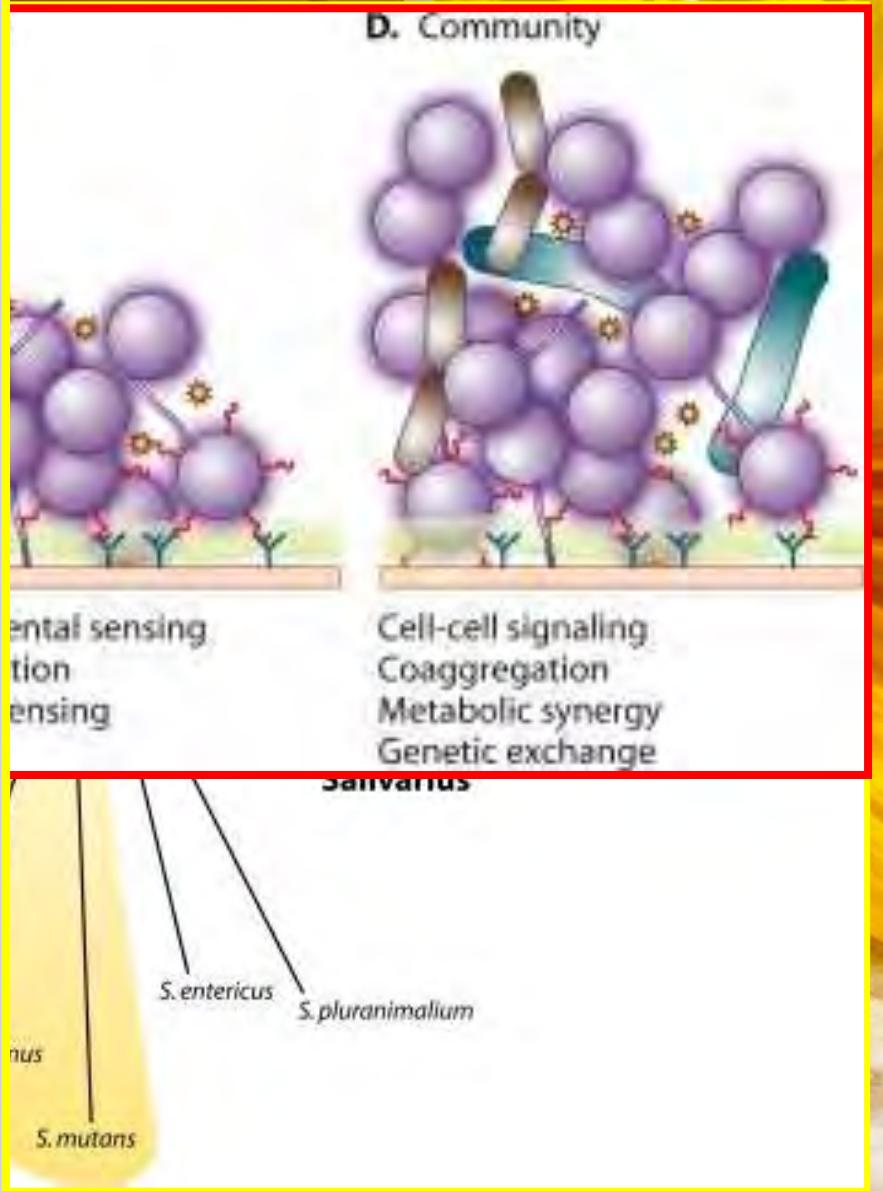
Dental Disease- Dysbiosis

- Disease, bacterial, fungal, yeast, and probably viral, are due to **“dysbiosis”.**
- Bacteria protect from, and cause dental decay, and periodontal disease.
- Esthetic dentistry may also be needed because of trauma, or genetic causes, or iatrogenic reasons

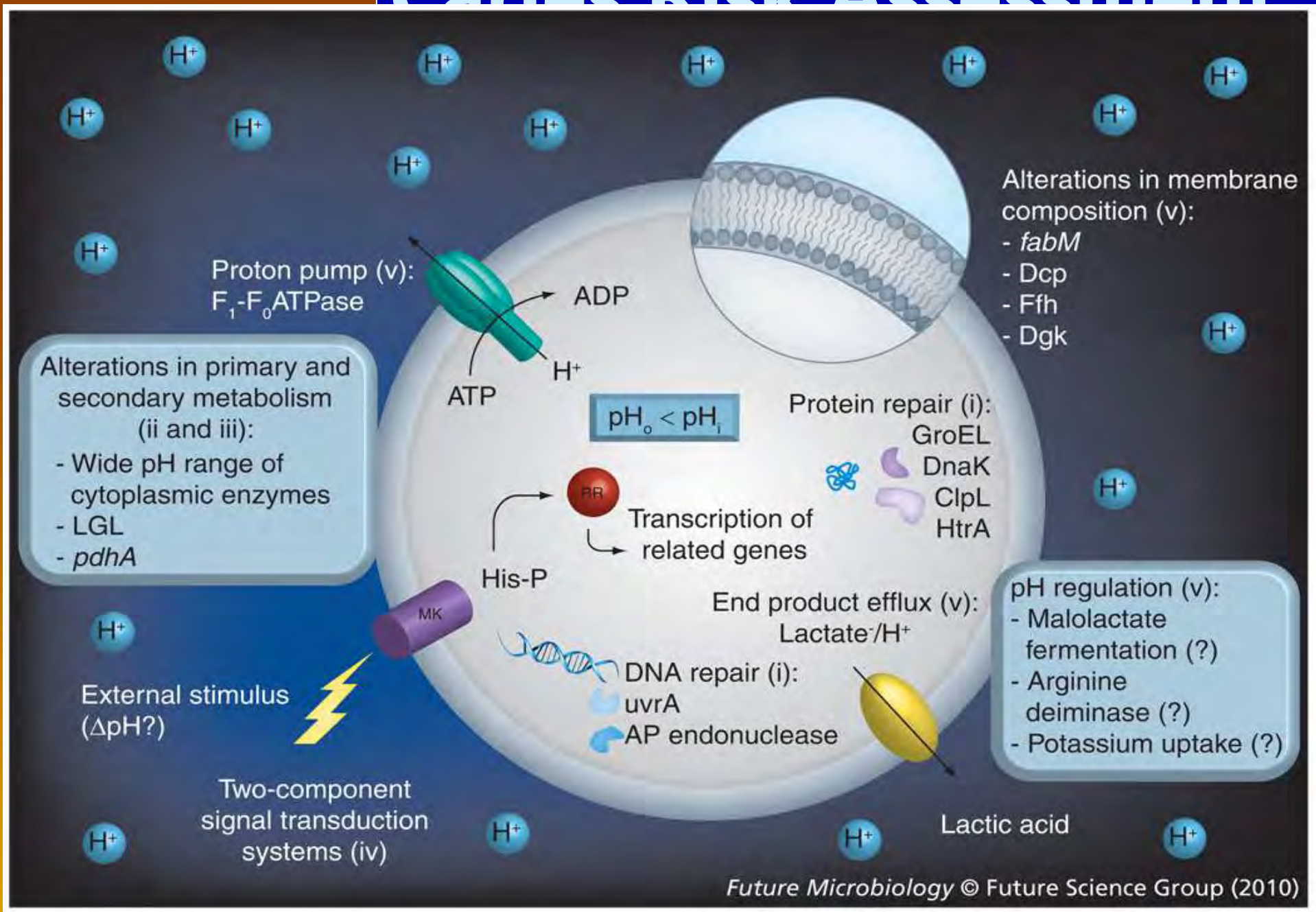
Principles of Prevention

Streptococci- Plaque Kingdoms





Caries Risk Assessment



s in
4 h)
f
l
s of
od

ned
er
e to

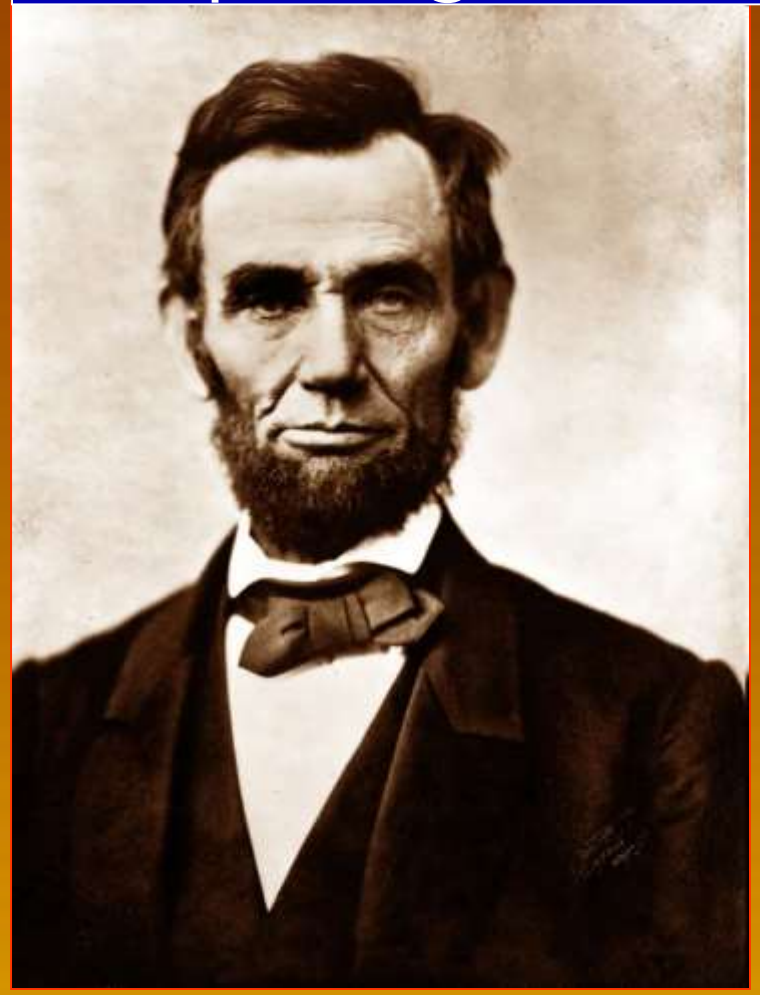
e

ely to

e use

Caries Risk Assessment

Interpreting the Results



Risk Indication Values (RLU's)

- 0-1500 = low risk
- 1501-3500 = moderate risk
- 3501-9999 = high risk

"And in the end it's not the years in your life that count. It's the life in your years."

Caries Risk Assessment

Interpreting the Results

Probiotics- Replacing Nature

Necessary for today and TOMORROW

Ilyich M
(Elie Metch

Gary B. Huffnag
Microbiology, ar
His research on
and has been fe

otics
er"
illus
bulgaricus

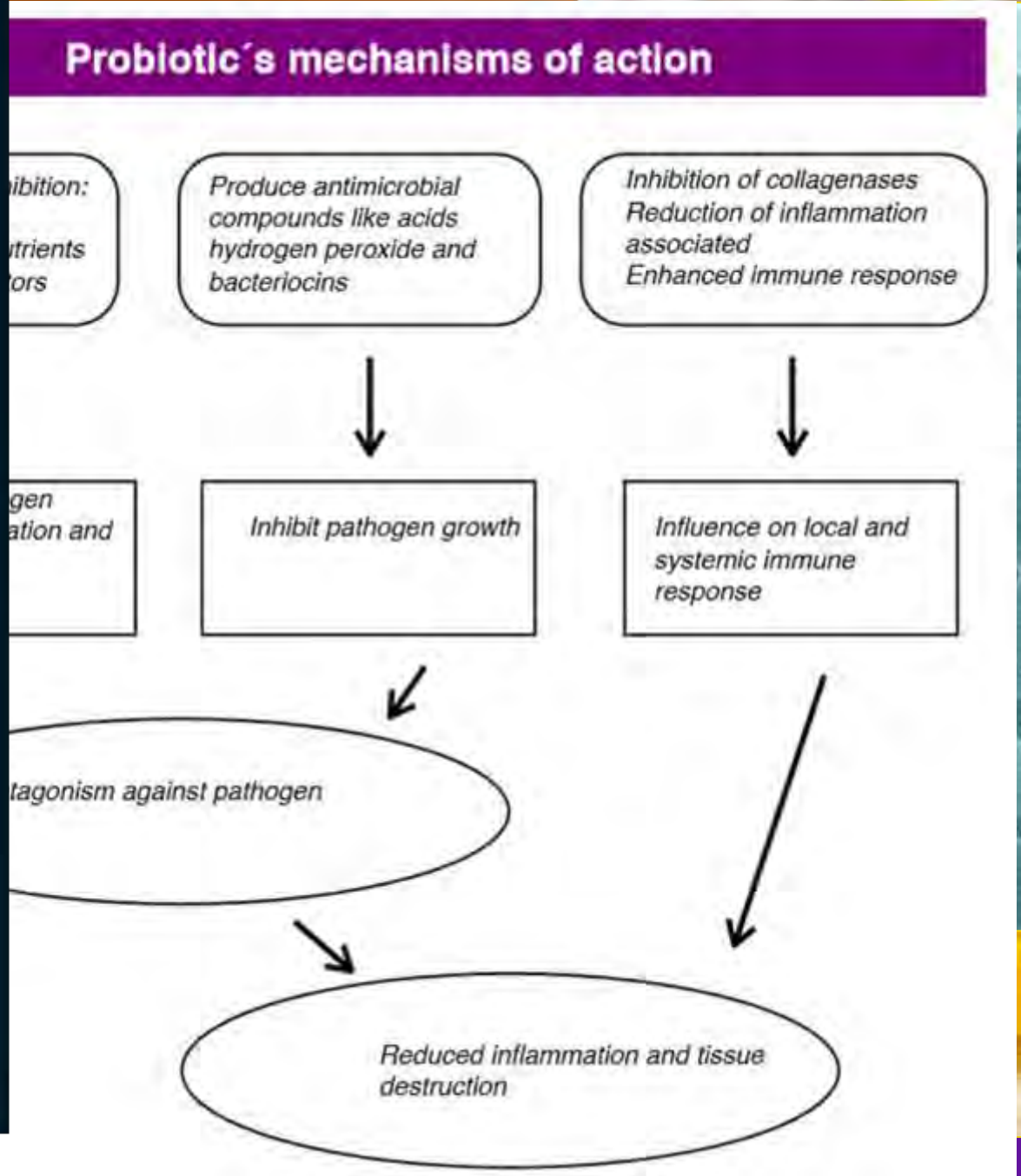
"A general belief is that microbes are harmful. This belief is erroneous. There are many useful microbes....."

Pathogen= bacteria in the wrong place at the wrong time

Probiotic= bacteria in the right place at the right time

- Dr. Cannon's Definition

on the host"



FAO/WHO (2002) Joint Working Group Guidelines for Probiotics in Food

Probiotics – great interest in research

The number of published studies investigating probiotics has increased 15 fold in as many years, and 2011 looks set to be a record year with more than 1300 publications anticipated.

An analysis of publications posted to the NIH PubMed database reveals strong growth in the number of publications featuring the keyword 'probiotic'. In 1997 there were roughly 80 publications globally per year referencing probiotics, today that figure is over 1200 per year or 100 publications per month.

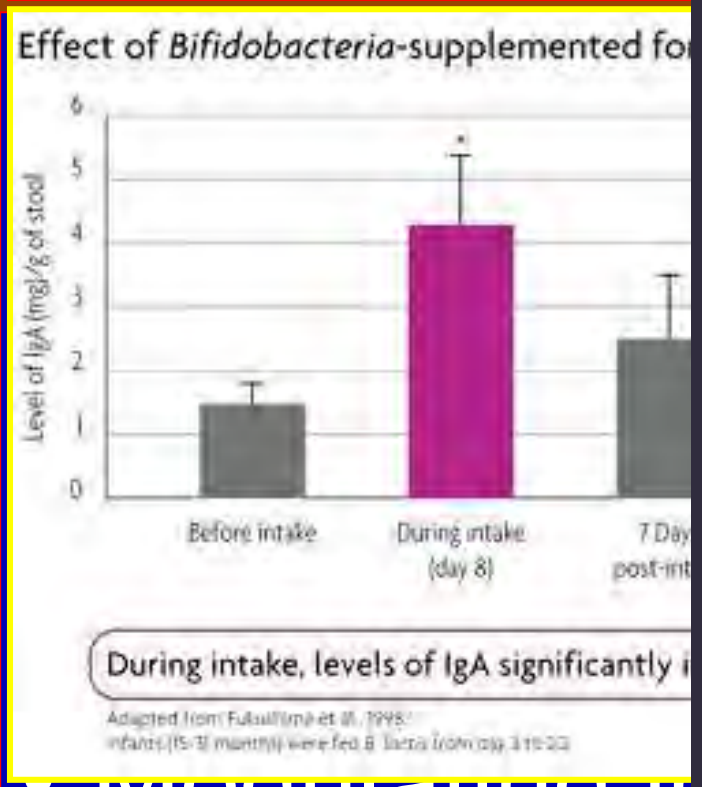
- PubMed data base hits for "probi
- Key
- Lim
  -
  -
- 200
  -
  -
  - pu
- 2015
  - Many new Journals

Preservation of Antibiotics for Medical Treatment Act

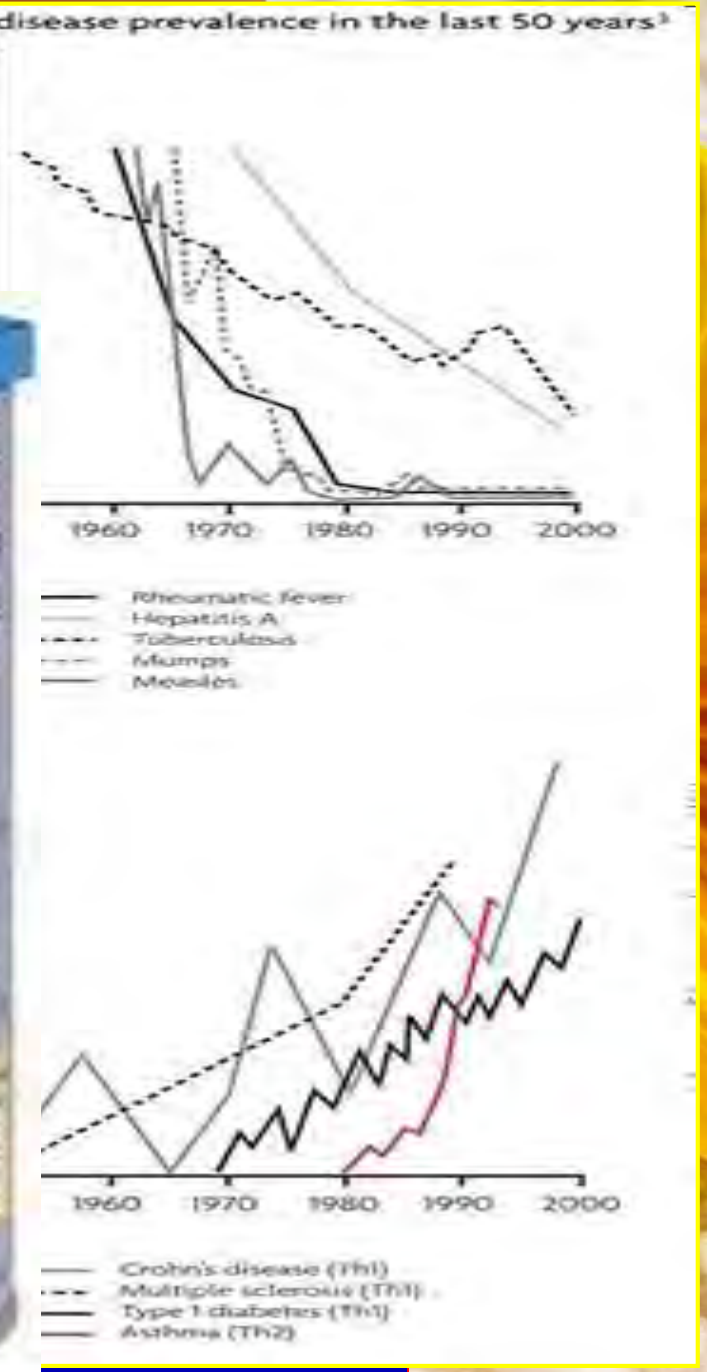
H.R. 1549/S. 619

How do probiotics work?

- Modulating i
- health

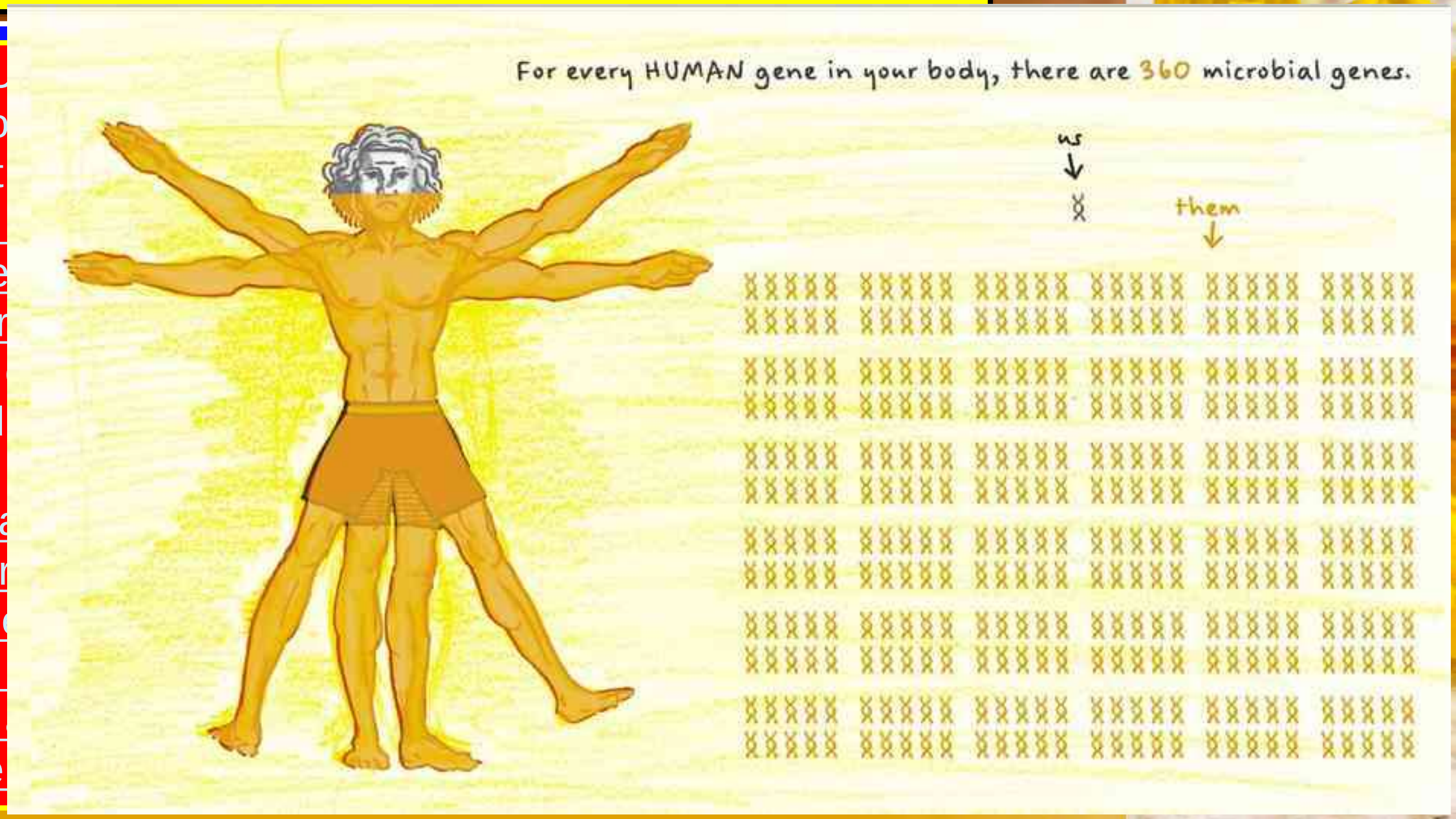


5. **Saavedra** JM, Abi-Hanna A, Moore N, Yolken RH. Long-term consumption of infant formulas containing live probiotic bacteria: tolerance and safety. *Am J Clin Nutr* 2004;79:261–7.
6. **St**
Skou
supp
infan
7. **Wa**
pedia
8. **We**
form
probi
9. **Yo**
intes
infan
10. **S**
mech
2007
11. **F**
follo
and f
1997
12. **K**
comp
bifid
13. **M**
intes
2004
14. **A**
enter
Revi
15. **K**
Paed
16. **S**
Gast
Evide
75.



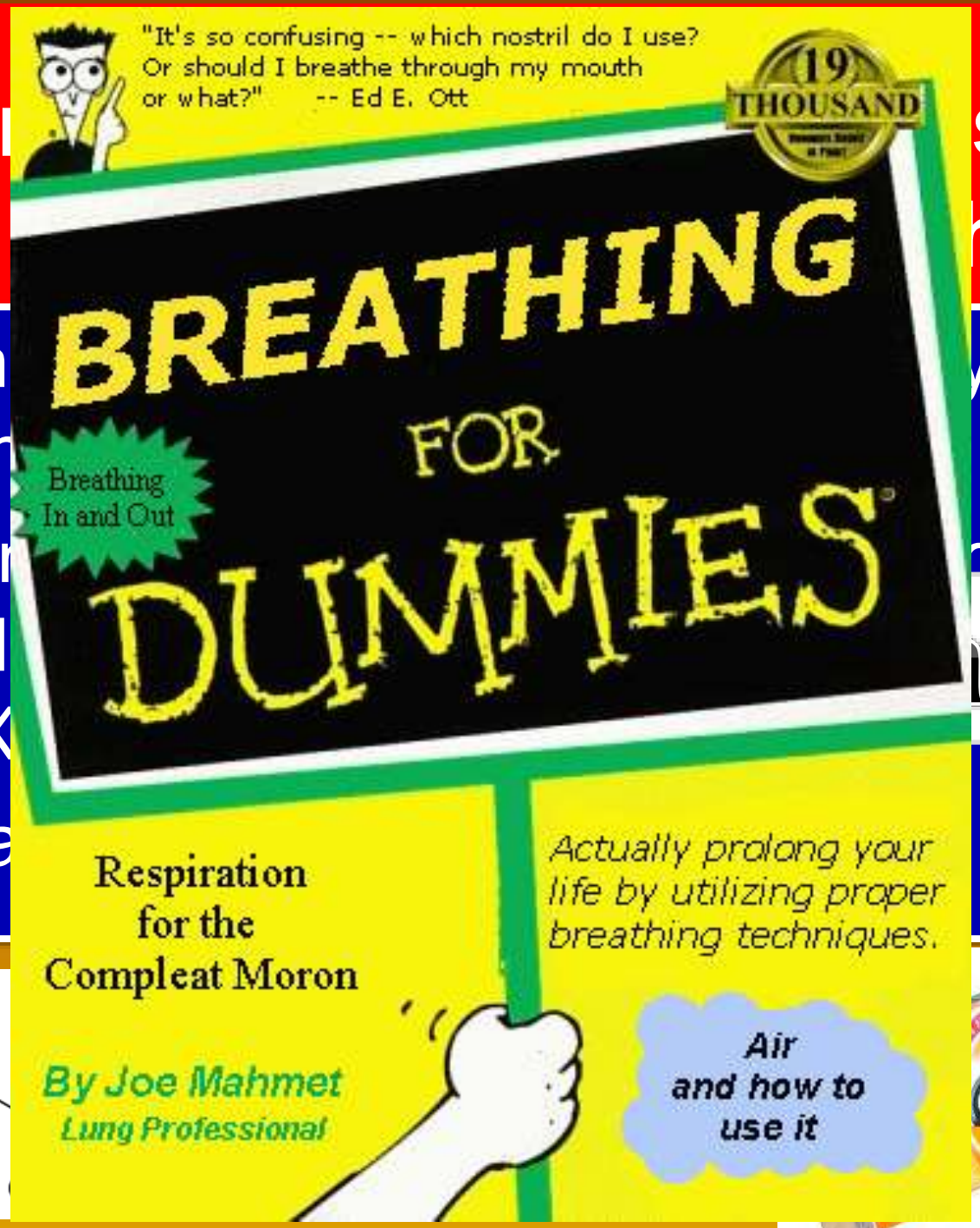
MATERNAL IMPRINTING

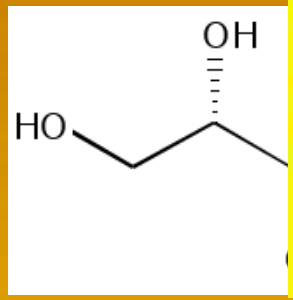
CONCLU
physiolo
and lact
contain
of bacte
peripher
blood m
than did
women.
intestina
transpor
cells. W
immune
molecul
pathoge

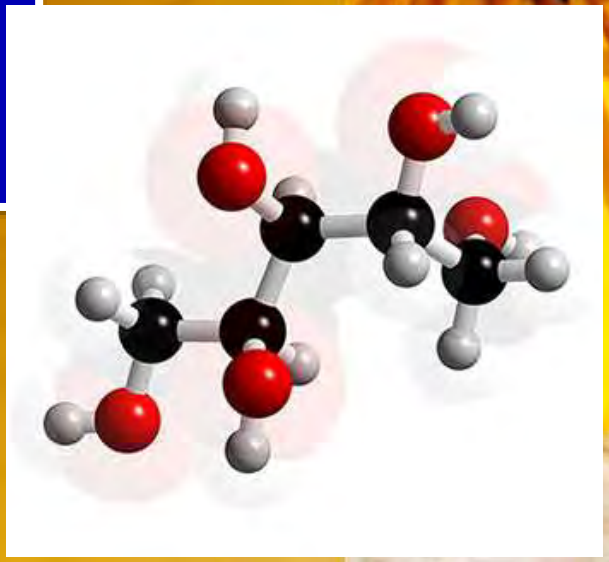


Treat… sulted in … hild

- Moth… years begin…
- Wher… d the need… asses the X…
- Isoka…







Pediatric Dental Care Protocols

Maternal

Discuss with mother xylitol gum or mint use and why, encourage use.

Give copy of maternal use of xylitol/child protection from decay research article. Ask mother to share with pediatrician. Explain probiotic use to mother, give informati on Klaire Lab products, and oral probiotics, such as Evora Plus and Spry probiotic.

Twice yearly dental visits stressed for themselves and gooc home care practices.

Pediatric Dental Care Protocols

Infect Immun. 2009 Jul;77(7):3075-9. doi: 10.1128/IAI.00209-09. Epub 2009 Apr 27.

Complementation of the fadA mutation in Fusobacterium nucleatum demonstrates that the surface-exposed adhesin promotes cellular invasion and placental colonization.

Ikegami A[1], Chung P, Han YW.

Author information

Promotes cell invasion and colonization

Abstract

Fusobacterium nucleatum is a gram-negative oral anaerobe implicated in periodontal disease and adverse pregnancy outcome. The organism colonizes the mouse placenta, causing localized infection and inflammation. The mechanism of placental colonization has not been elucidated. Previous studies identified a novel adhesin from F. nucleatum, FadA, as being involved in the attachment and invasion of host cells. The fadA deletion mutant F. nucleatum 12230 US1 was defective in host cell attachment and invasion in vitro, but it also exhibited pleiotropic effects with altered cell morphology and growth rate. In this study, a fadA-complementing clone, F. nucleatum 12230 USF81, was constructed. The expression of FadA on USF81 was confirmed by Western blotting and immunofluorescent labeling. USF81 restored host cell attachment and invasion activities. The ability of F. nucleatum 12230, US1, and USF81 to colonize the mouse placenta was examined. US1 was severely defective in placental colonization compared to the wild type and USF81. Thus, FadA plays an important role in F. nucleatum colonization in vivo. These results also represent the first complementation studies for F. nucleatum. FadA may be a therapeutic target for preventing F. nucleatum colonization of the host.

Colorectal Cancer- *Fusibacterium nucleatum*

International Cancer Screening Network

Sponsored by the National Cancer Institute

North America				
Canada	45.4	14.4	31.8	9.4
United States	34.1	9.9	25.0	7.7

Fusobacterium nucleatum Promotes Colorectal Carcinogenesis by Modulating E-Cadherin/β-Catenin Signaling via its FadA Adhesin

Mara Roxana Rubinstein[7], Xiaowei Wang[7], Wendy Liu, Yujun Hao, Guifang Cai, Yiping W. Han

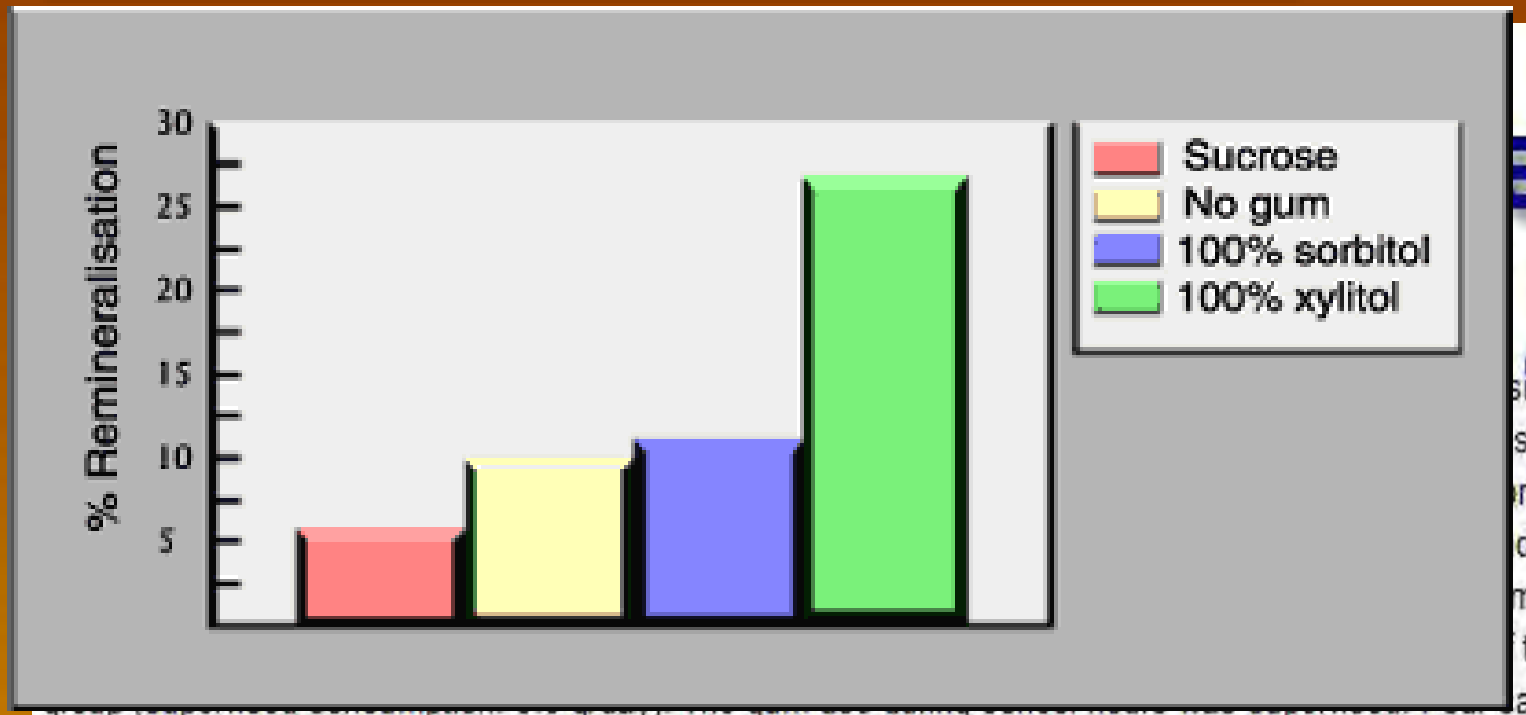
Summary

Fusobacterium nucleatum (*Fn*) has been associated with colorectal cancer (CRC), but causality and underlying mechanisms remain to be established. We demonstrate that *Fn* adheres to, invades, and induces oncogenic and inflammatory responses to stimulate growth of CRC cells through its unique FadA adhesin. FadA binds to E-cadherin, activates β-catenin signaling, and differentially regulates the inflammatory and oncogenic responses. The FadA-binding site on E-cadherin is mapped to an 11-amino-acid region. A synthetic peptide derived from this region of E-cadherin abolishes FadA-induced CRC cell growth and oncogenic and inflammatory responses. The *fadA* gene levels in the colon tissue from patients with adenomas and adenocarcinomas are >10–100 times higher compared to normal individuals. The increased FadA expression in CRC correlates with increased expression of oncogenic and inflammatory genes. This study unveils a mechanism by which *Fn* can drive CRC and identifies FadA as a potential diagnostic and therapeutic target for CRC.

Xylitol- 5 carbon chai

- From Xylon (wood) a
(sugar alcohol). Xylit
in the fibers of many
vegetables, and can
extracted from variou
oats, and mushrooms
as fibrous material su
corn husks and sugar cane
bagasse, and birch.

Xylitol- research



siderable hea
s simultaneo
rt study on t
d two hundre
m use), four
total polyols
alibrated den

registrations by means of a modified WHO procedure. The primary endpoint was the development of an unequivoc
tooth surface. Compared with the no-gum group, sucrose gum usage resulted in a marginal increase in the caries
confidence interval,0.96 to 1.49; p = 0.1128). Sorbitol gum significantly reduced caries rates (relative risk 0.74; 95
= 0.0074). The four xylitol gums were most effective in reducing caries rates, the most effective agent being a 100
0.27; 95% confidence interval, 0.20 to 0.36; p = 0.0001). This gum was superior to any other gum (p < 0.01). The
effective than xylitol, but they reduced caries rates significantly compared with the no-gum group. DMFS analyses
conclusions. The results suggest that systematic usage of polyol-based chewing gums reduces caries rates in young subjects, with xylitol gums being more effective than sorbitol gums.

Xylitol- research

J Dent Res. 2000 Mar;79(3):882-7.

Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants.

Söderling E, Isokangas P, Pienihäkkinen K, Tenovuo J.

Institute of Dentistry, University of Turku, Finland. eva.soderling@utu.fi

classic 2000

Abstract

Xylitol is effective as a non-cariogenic sugar substitute. Habitual xylitol consumption appears to select for mutans streptococci (MS) with impaired adhesion properties, i.e., they shed easily to saliva from plaque. One hundred sixty-nine mother-child pairs participated in a two-year study exploring whether the mothers' xylitol consumption could be used to prevent mother-child transmission of mutans streptococci. All mothers showed high salivary levels of mutans streptococci during pregnancy. The mothers in the xylitol group (n = 106) were requested to chew xylitol-sweetened gum (65% w/w) at least 2 or 3 times a day, starting three months after delivery. In the two control groups, the mothers received either chlorhexidine (n = 30) or fluoride (n = 33) varnish treatments at 6, 12, and 18 months after delivery. The children did not chew gum or receive varnish treatments. MS were assessed from the mothers' saliva at half-year intervals and from the children's plaque at the one- and two-year examinations. The MS were cultured on Mitis salivarius agars containing bacitracin. The salivary MS levels of the mothers remained high and not significantly different among the three study groups throughout the study. At two years of age, 9.7% of the children in the xylitol, 28.6% in the chlorhexidine, and 48.5% in the fluoride varnish group showed a detectable level of MS. In conclusion, therefore, habitual xylitol consumption by mothers was associated with a statistically significant reduction of the probability of mother-child transmission of MS assessed at two years of age. The effect was superior to that obtained with either chlorhexidine or fluoride varnish treatments performed as single applications at six-month intervals.

Mutans strep detectable-
9.7% of xylitol group
28.6% of chlorhexidine group
48.5% of fluoride varnish group

Xylitol- resea

Archives of Oral Biology (2004) 49, 161–164

ELSEVIER

Available

s

SHORT COMMUNICATION

Adaptation of saliv to xylitol

C. Badet*, B. Richard, M.

Smart targeting- negligible ef many probiotic bacteria whil greatly reducing mutans streptococci.

Table 1 Acid production after exposure to xylitol.

Strain	Species	Time of acid production in M2 medium (days)	Final pH	Rate of pH change (U per day)
ATCC 4356	*Lact. acidophilus*	20	5.3	0.11
HK 21	*Lact. salivarius*	8	4.9	0.25
DO2	*Lact. delbrüeckii*	6	5.3	0.13
ATCC 334	*Lact. casei*	–	6.2	–
ATCC 393	*Lact. casei*	6	5.5	0.16
FP	*Lact. paracasei*	6	5.4	0.18
BHS2	*Lact. paracasei*	–	6.3	–
ATCC 8014	*Lact. plantarum*	–	7.0	–
PS2	*Lact. plantarum*	–	6.4	–
PJ3	*Lact. plantarum*	15	5.1	0.05
NF1	*Lact. plantarum*	–	6.4	–
AS5	*Lact. paracasei*	–	6.8	–
NFA	*Lact. pentosus*	8	5.1	0.22
AAG	*Lact. rhamnosus*	5	5.0	0.27
PAM1	*Lact. rhamnosus*	15	5.2	0.08
DPB5	*Lact. rhamnosus*	6	5.2	0.23
LL1	*Lact. rhamnosus*	10	5.3	0.12
CN	*Lact. rhamnosus*	27	5.3	0.06
BNS4	*Lact. rhamnosus*	20	5.4	0.05
PCP	*Lact. rhamnosus*	27	5.1	0.05
XX1	*Lact. rhamnosus*	27	5.5	0.03
BR1	*Lact. rhamnosus*	–	6.5	–
GDM2	*Lact. rhamnosus*	27	5.2	0.06
BMP9	*Lact. rhamnosus*	3	5.5	0.15
LC1	*Lact. rhamnosus*	3	5.4	0.20
AAC	*Lact. rhamnosus*	3	5.4	0.20
DM5	*Lact. rhamnosus*	6	5.3	0.16
SF1	*Lact. rhamnosus*	–	7.3	–
YDS2	*Lact. rhamnosus*	–	6.7	–
ATCC 7469	*Lact. rhamnosus*	20	5.2	0.07
YA3	*Lact. cellobiosus*	–	6.4	–
DS2	*Lact. cellobiosus*	–	6.6	–
GMD3	*Lact. fermentum*	–	6.8	–
ATCC 14869	*Lact. brevis*	–	6.5	–

Xylit s

- Xlear (Clear)

WHISKEY Tooth Paste!

Genuine 6 Proof Stuff
SCOTCH • BOURBON

Why fight oral hygiene—enjoy it! Here's real he-man toothpaste, best argument yet for brushing 3 times a day. 2½ oz. tubes flavored with the real thing—Scotch or Bourbon. Night-before feeling on the morning after. Rinse with soda instead of water if you prefer. Per tube ppd. $1

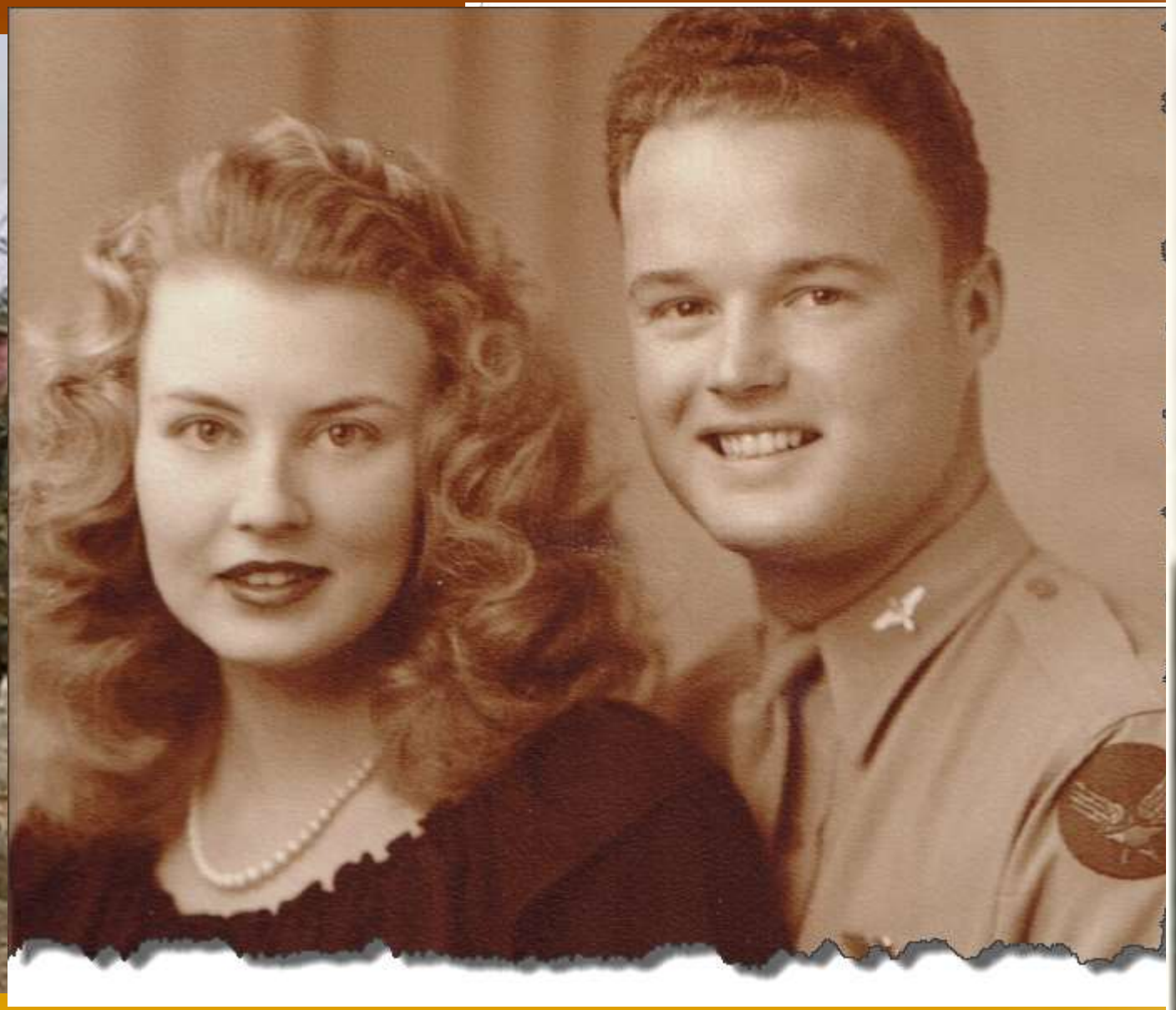
Greenland Studios
DEPT. HG-114, MIAMI 47, FLORIDA

New Xylitol Products

For Special Needs!

- Children's Mouthwash- safe for all ages

MRE- xylitol gum- G.I. issue



Xylitol and Dentistry

PEDIATRIC DENTISTRY V 39 / NO 2 MAR / APR 17

SYSTEMATIC REVIEW AND META-ANALYSIS

Effectiveness of Xylitol in Reducing Dental Caries in Children

Abdullah A. Marghalani, BDS, MSD, DrPH[1] • Emilie Guinto, DDS[2] • Minhthu Phan, DDS[3] • Vineet Dhar, BDS, MDS, PhD[4] • Norman Tinanoff, DDS, MS[5]

- **Abstract: The purpose of this study was to evaluate the**

Scheinin A, Mäkinen KK, Tammisalo E, Rekola M. **Turku sugar studies**. XVIII. Incidence of dental caries in relation to 1-year consumption of xylitol chewing gum. Acta Odontol Scand 1975;33(5):269-78.

Scheinin A, Mäkinen KK, Ylitalo K. **Turku sugar studies**. V. Final report on the effect of sucrose, fructose and xylitol diets on caries incidence in man. Acta Odontol Scand 1976;34(4):179-216.

January 1, 1995 through Sept. 28, 2016 for randomized and controlled trials on children consuming xylitol for at least 12 months. The primary endpoint was caries reduction measured by mean decayed, missing, and filled primary and permanent surfaces/teeth (dmfs/t, DMFS/T, respectively).

Xylitol and Dentistry

Effectiveness
Abdullah A. Marghalani,

- Only te
basicall
and on
togethe
polyols

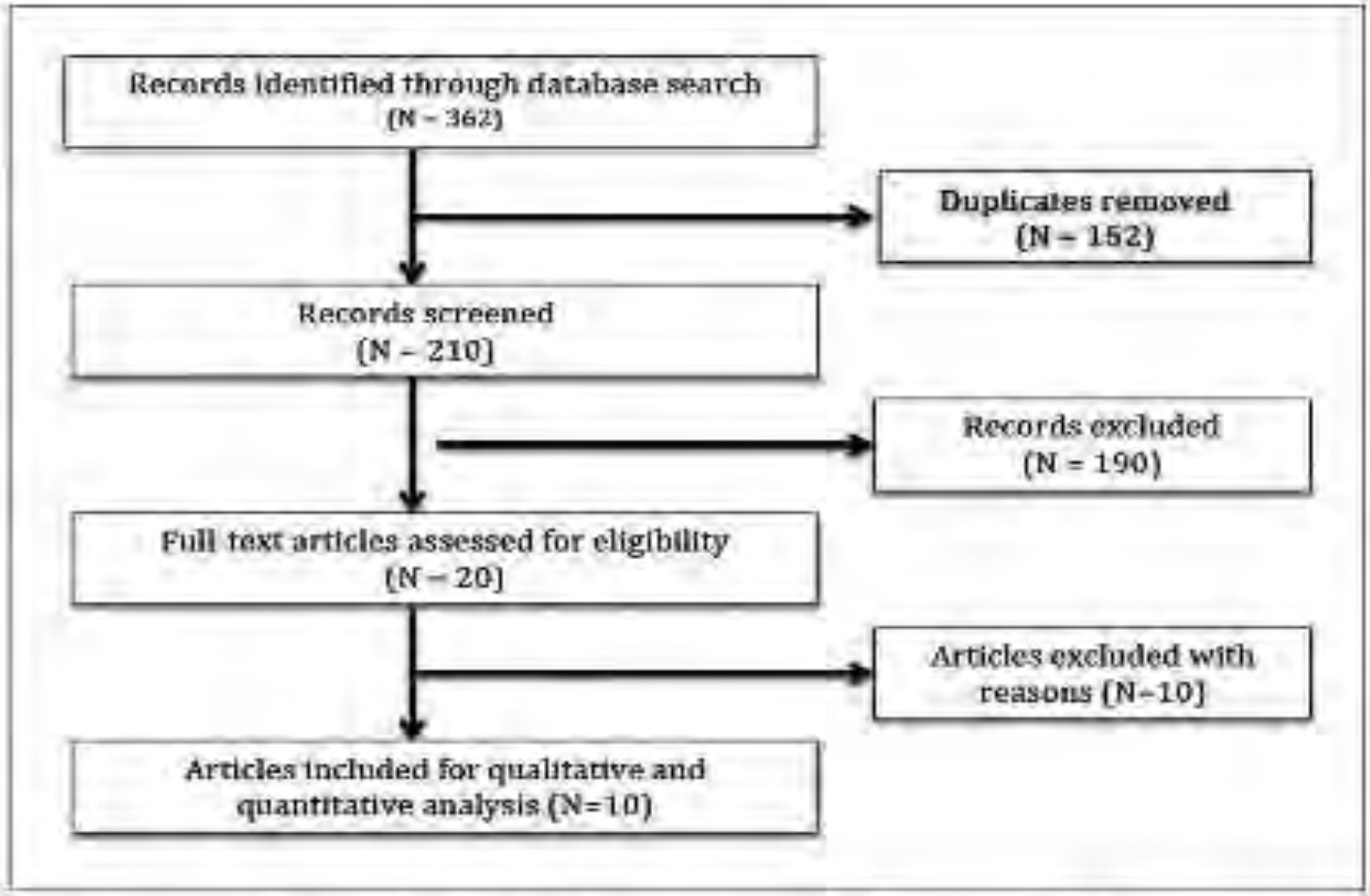


Figure 1. Flowchart of the trial selection process and elimination of studies.

Xylitol and Dentistry

PEDIATRIC DENTISTRY V 39 / NO 2 MAR / APR 17

SYSTEMATIC REVIEW AND META-ANALYSIS

Effectiveness of Xylitol in Reducing Dental Caries in Children

Abdullah A. Marghalani, BDS, MSD, DrPH[1] • Emilie Guinto, DDS[2] • Minhthu Phan, DDS[3] • Vineet Dhar, BDS, MDS, PhD[4] • Norman Tinanoff, DDS, MS[5]

- **Toothpaste works, wipes work, but gum had a varied result.**

Xylitol dentifrice-840/840 Control dentifrice-837/837	3 years from when the children were 7-12 years old	Significant reduction in DFS 5.0±3.7 vs. 5.7±4.1	High risk
Xylitol dentifrice-1280/1280 Control dentifrice-1259/1259	30 months from when the children were 7-12 years old	Significant reduction in DFS 1.30±1.89 vs. 1.51±2.00 and in DFT 0.69±1.10 vs. 0.81±1.21	High risk

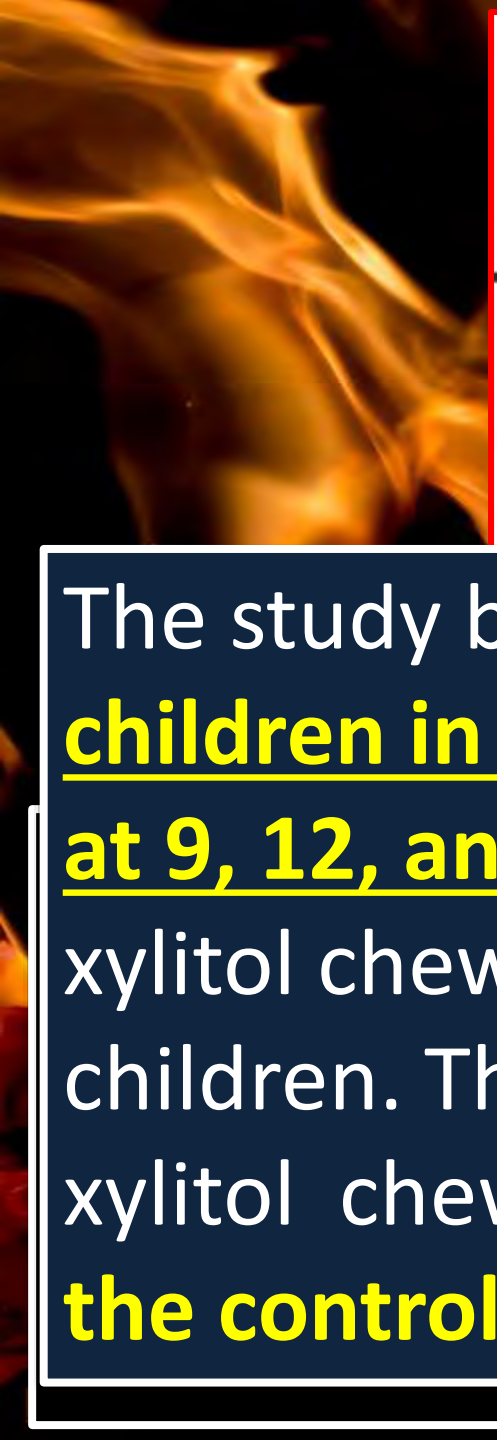
Xylitol and Dentistry

- Stecken-Blicks (sic) changes the Forest plot of results and Alanen inconsistently

The fluoride content in the pipe drinking water was ≤0.3 p.p.m. !!!

elected. After
informed consent, they were randomly assigned into a **xylitol and a xylitol/ fluoride group. They were instructed to take two tablets three times a day (total xylitol and fluoride dose 2.5 g and 1.5 mg, respectively). The dropout rate was 28%, and 41% exhibited a good compliance** with the study protocol. No statistically significant differences in caries incidence could be found between the study groups ($P > 0.05$). **Huge non-compliance rate of 59%! Plus 28% dropout??**

EXIT
Criticism of the Cochrane review and some recent clinical studies
Riley P, Moore D, Ahmed F, Sharif MO, Worthington HV (2015): Xylitol-containing products for preventing dental caries in children and adults. *Cochrane Database Syst Rev.* 3:CDO010743
Spry



Caries Research

Caries Res
DOI: 10.1159/000495187

Received: July 26, 2018
Accepted after revision: October 31, 2018
Published online: January 10, 2019

Prenatal Oral Health Care and Early Childhood Caries Prevention: A Systematic Review and Meta-Analysis

The study by Nakai et al. [2010] showed that significantly more **children in the xylitol chewing group remained S. mutans free at 9, 12, and 24 months**. Furthermore, pre- and perinatal xylitol chewing by mothers delayed S. mutans carriage in children. The children's S. mutans acquisition age in the xylitol chewing group was **8.8 months later than that of the control group (mean age 20.8 vs. 12.0 months old).**

Cervitec Plus- Ivoclar

- FDA approved in 2008
- Used in Europe for many years
- 1% chlorhexidine and 1% thymol varnish

Cervitec Plus- Ivoclar

- Swollen and inflamed gingival tissues
- Periodontal Classification Type I- gingivitis

Cervitec Plus- Ivoclar

Unit dose and bulk packaging

Cervitec Plus- Ivoclar

- Apply to gingival third of dentition

Inside Dentistry

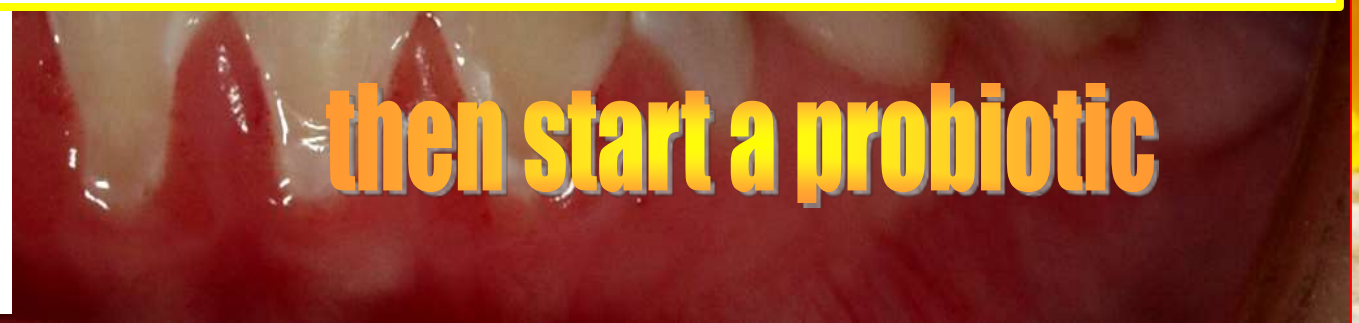
June 2011, Volume 7, Issue 6

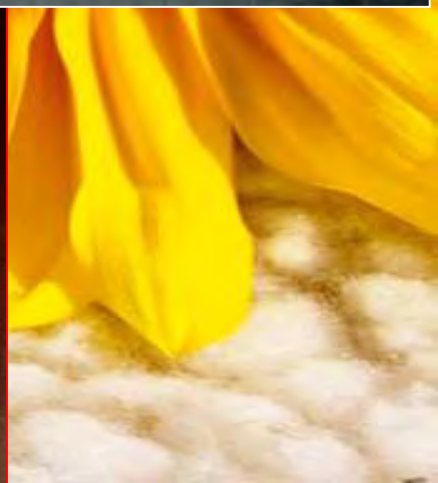
Published by AEGIS Communications

Clinical Application of Probiotic Therapy

New adjunctive therapies offer new alternatives for treatment.

By Mark L. Cannon, DDS, MS





DNA-PCR and CRT Results in Children After Probiotic use

Children's Memorial Hospital
Where kids come first.

THE PRIMARY OBJECTIVE OF THIS CLINICAL STUDY IS TO DETERMINE THE EFFECT, IF ANY, OF "OVER THE COUNTER" PROBIOTIC SUPPLEMENTS ON THE DNA-PCR And CRT ANALYSIS

DNA-PCR and CRT Results in Children After Probiotic use

Children's Memorial Hospital
Where kids come first.

Methods

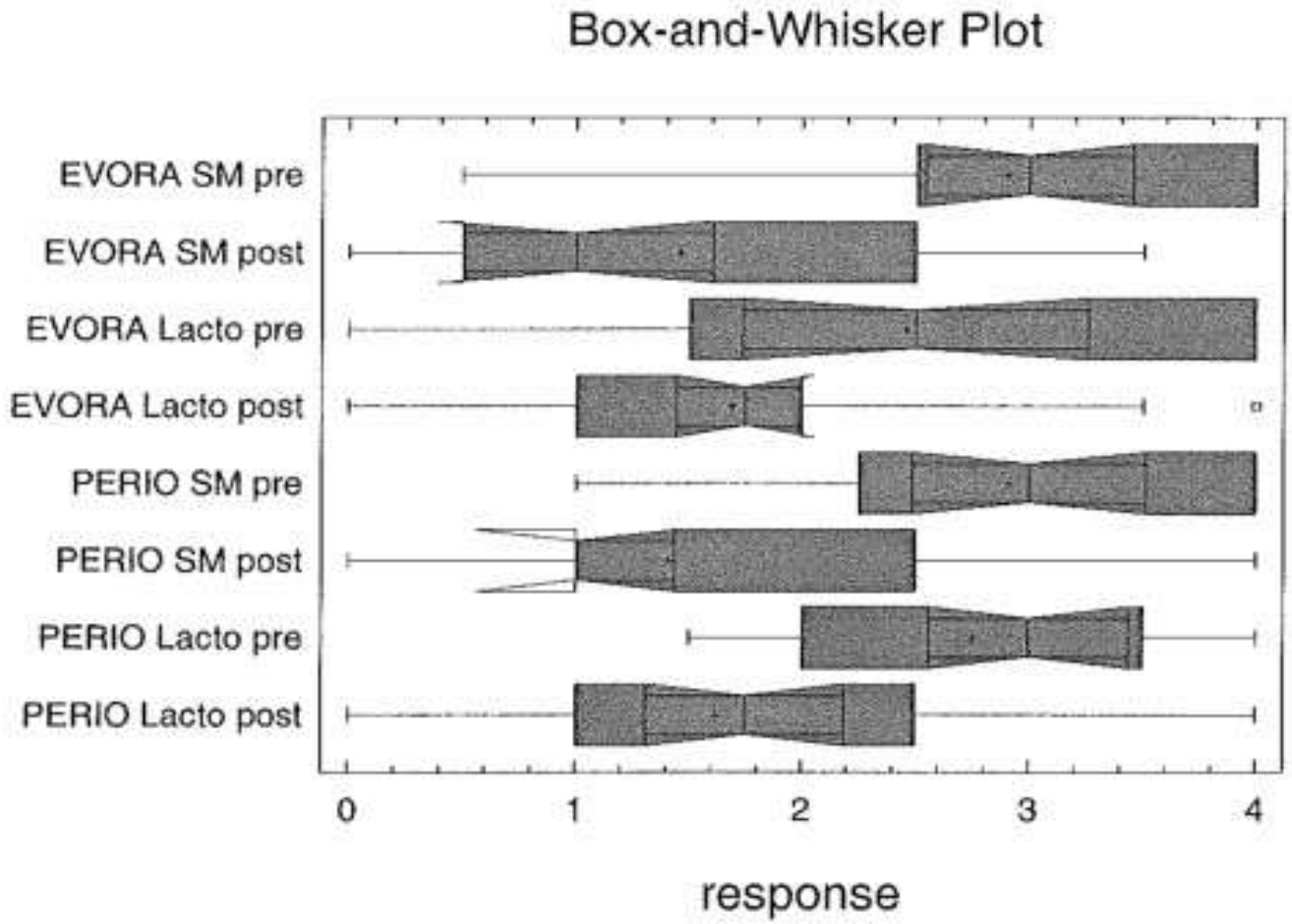
-60 patients 6 to 12 years of age- caries prone with 4 or more restorations and /or lesions
-CRT collected before and after probiotic use
-8 week (60 day) experimental time period- considered optimal to see effect

DNA-PCR and CRT Results in Children After Probiotic use

Children's Memorial Hospital
Where kids come first.

Statistics

Two separate statisticians in different institutions



Conclusions:

Children's Memorial Hospital
Where kids come first.

Effectiveness of CRT at Measuring the Salivary Level of Bacteria in Caries Prone Children with Probiotic Therapy

Cannon M* / Trent B** / Vorachek A*** / Kramer S**** / Esterly R*****

Aim: *This IRB approved clinical trial was to determine the effect of "over the counter" probiotic supplements on the Caries Risk Test- CRT- (Ivoclar) results of the oral microflora in high caries risk children.* ***Study design:*** *Sixty subjects 6 to 12 years old with a caries risk assessment (CAMBRA) of moderate to high (caries prone) were evaluated by an analysis of the difference in the salivary levels of pathogenic bacteria (mutans streptococci and Lactobacilli). The subjects were randomly selected by randomizing software and assigned to two different Groups. Group A used PerioBalance (Lactobacilli reuteri-CFU of 200 million) lozenges for 28 days. Group B used the EvoraKids (Streptococcus uberis KJ2, Streptococcus oralis KJ3, Streptococcus rattus JH145, ≥ 100 million) probiotics chewable tablets for 30 days. Salivary samples were collected then incubated for 48 hours for colony counting and ranking. Follow up testing with the CRT was performed after 60 days at a follow up visit.* ***Results:*** *There was a statistically significant difference in the CRT results between the pre and post use of the probiotics. PerioBalance; SM results t= -6.78 p< .0001 Lactobacilli results t= -5.762, p< .0001, EvoraKids SM results t= -7.33, p< .0001, Lactobacilli results t= -2.952, p= .0068.* ***Conclusions:*** *The CRT values obtained with caries prone children may be significantly affected by probiotic use. Based on this study's results the following conclusions can be made: Both EvoraKids and PerioBalance affected the CRT results by significantly decreasing the number of S. mutans and lactobacilli present in the salivary samples.*

voraKids
erioBalance
ed the CRT
s.
eduction in
tans and
bacilli was
ically
cant.

Further Research

Children's Memorial Hospital
Where kids come first.

Retrospective Review of Probiotic Therapy.

ML Cannon DDS MS
A Vorachek DDS
K White DMD
C Le DMD

An IRB Approved Study

Does EvoraKids and PerioBalance affected the caries proneness of the subjects?

Is the reduction in *dental caries* was statistically significant?

Materials and Methods:

Dental records of 60 patients that were enrolled in the Institutional Review Board approved study, "A clinical trial to evaluate the effectiveness of DNA-PCR and CRT at measuring the salivary level of bacteria in caries prone children with PerioBalance or EvoraKids Plus therapy" were reviewed as to current caries activity status with measurement of the Decay Missing Filled Teeth index and Caries By Risk Assessment (CAMBRA) determination. The current Oral health status was compared to the prior-to-study enrollment status and then analyzed in respect to published national norms.

Children's Memorial Hospital
Where kids come first.

Results:

Of the **53 subjects** available for follow up, only 4 had remained caries active with a grand total of 17 caries lesions being detected and subsequently restored in this group. Of the original total of 60 patients with 292 initial carious lesions, after probiotic therapy and dental restoration, 36 total restorations were place in the subject group over the following three years. Approximately half of these restorations were required in teeth that had initially presented with smaller lesions and had been placed in a “watch” category. Two of the patients that developed further carious lesions had been randomly assigned to the probiotic PerioBalance, what the other two caries active patients were assigned EvoraKids probiotic.

Of the original group of caries active patients, 23 did not present with any further carious involvement. Another 26 could be categorized as Caries static, as the restorations required were substantially less than before probiotic therapy had been begun.

Further Research

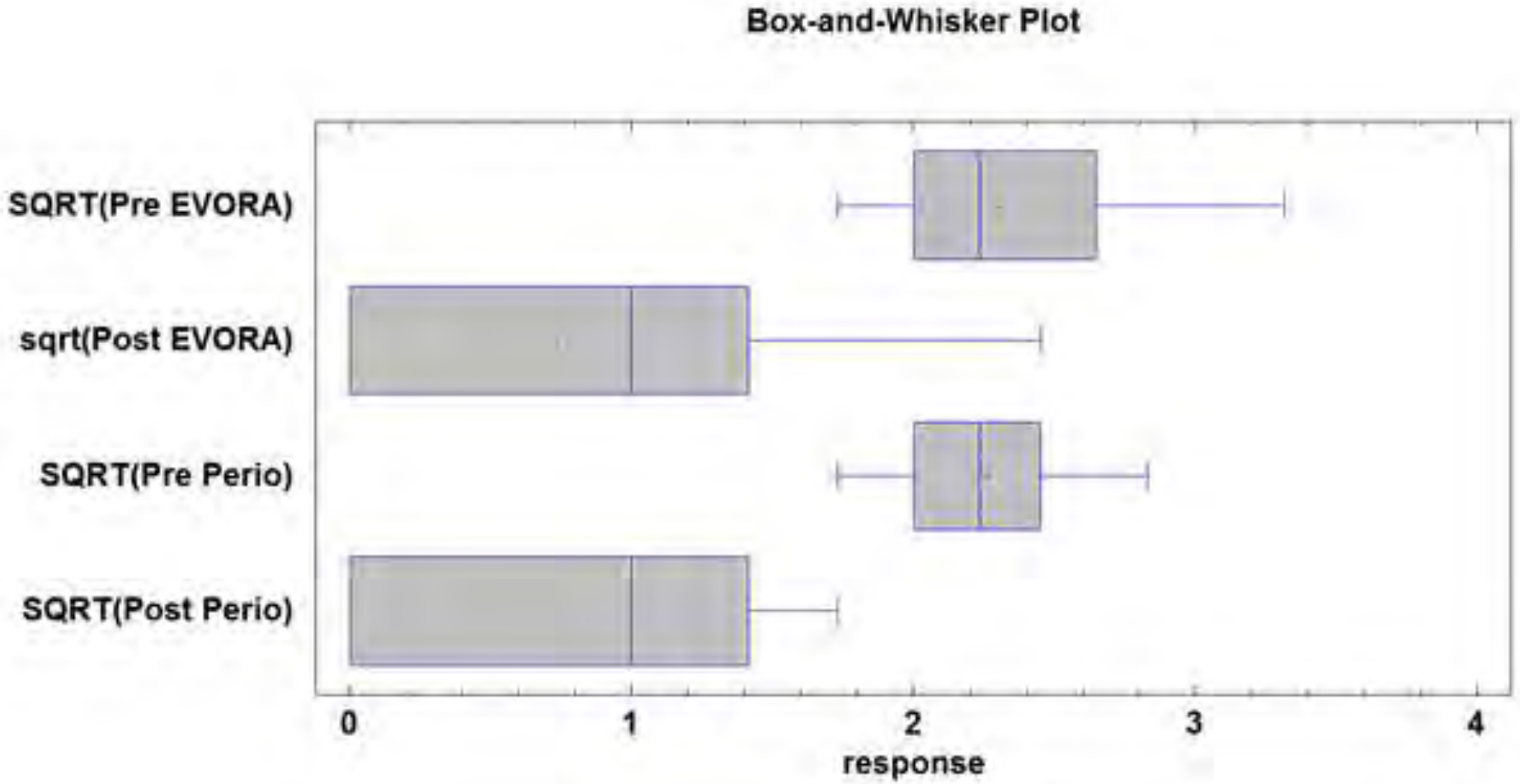
Children's Memorial Hospital
Where kids come first.

Conclusion:
Within the limitations of this retrospective IRB approved study, the tested probiotic supplements had a statistically significant effect on the caries experience of the enrolled subjects.

Table 3. Caries History Compared to Nationally Reported Values.

Caries Experience	Pre Probiotic	National Average	Post Probiotic
Per patient- 3 years	5.51	1.84	0.75
	Caries Active	Caries Resistant	Caries Static
PerioBalance	2	12	15
EvoraKids	2	11	11
Caries Count	17	0	36

Table 1. Caries active, Caries resistant and Caries static patients.


Box-and-Whisker Plot
SQRT(Pre EVORA)
sqrt(Post EVORA)
SQRT(Pre Perio)
SQRT(Post Perio)
0
1
2
3
4
response

The ANOVA table decomposes the variance

Validation Study (I told you so!)

Low caries rate To begin with!

112 doi:10.1186/s12903-015-0096-5

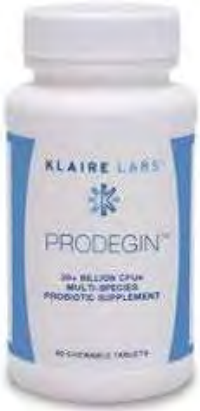
Results

0.2 versus 0.8 cavity rate-

The groups were balanced at baseline and the attrition rate was 20 %. Around 2/3 of the children in both groups reported an acceptable compliance. The caries increment (Δds) was significantly lower in the test group when compared with the placebo group, 0.2 *vs.* 0.8 ($p < 0.05$). The risk reduction was 0.47 (95 % CI 0.24–0.98) and the number needed to treat close to five. No differences were displayed between the groups concerning presence of visible plaque or bleeding-on-brushing. No side effects were reported.

Oral Health Probiotics- what to use?

- Periobalance
- Probiora
- Biogaia
- ProlacSan
- BLIS K12
- Prodegin
- Gluten metabolizers

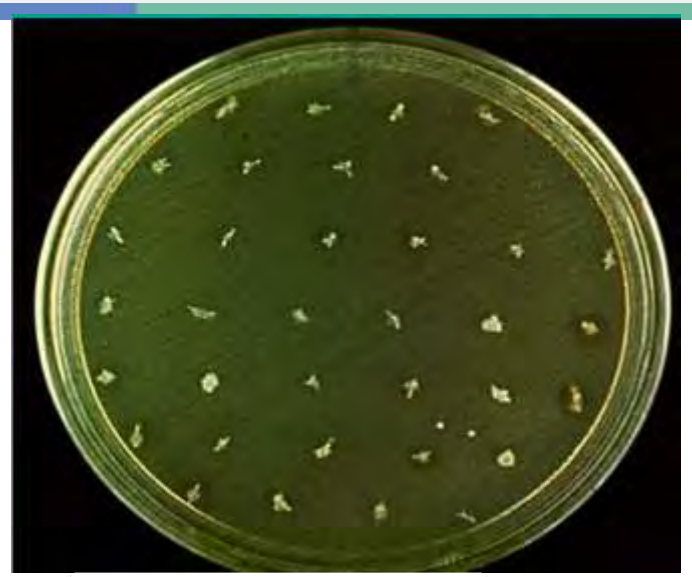


ProBioraPro Product Overview

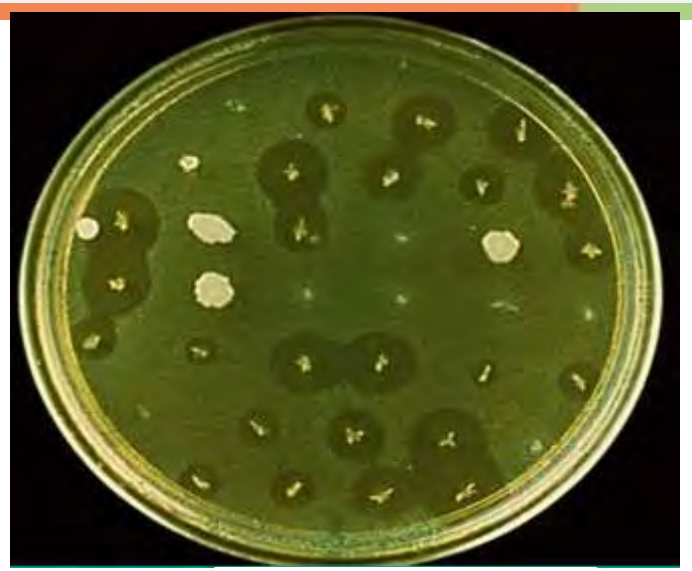
- Distributed exclusively by dental professionals
- Extra-strength blend of ProBiora3® crowds out harmful bacteria
- Use once daily for 90 days after a dental hygiene visit
- Extends the benefits of a dental hygiene visit

ProBioraPro

About ProBioraPro



Diseased



Healthy

The hazy background on these petri dishes is due to the growth of *Aggregatibacter actinomycetemcomitans, or (Aa)*. *In the petri dish to the right, the clear zone surrounding* ***S. oralis KJ3 and S. uberis KJ2 colonies*** *indicate that these beneficial bacteria are producing hydrogen peroxide which inhibits the* growth of undesirable bacteria and naturally whitens teeth.

Infant Probiotics- Necessary?

- Depends on the maternal microbiome- probably YES!

Probiotics- Bio-kult for Infants

- 7 probio
- Omega-
- Vitamin
- Preplex
- No suga
- Gluten f
- Made in

Probiotic Strains:

- *Lactobacillus casei* PXN® 37™
- *Lactobacillus rhamnosus* PXN® 54™
- *Streptococcus thermophilus* PXN® 66™
- *Lactobacillus acidophilus* PXN® 35™
- *Bifidobacterium breve* PXN® 25™
- *Lactobacillus delbrueckii* ssp. *bulgaricus* PXN® 39™
- *Bifidobacterium infantis* PXN® 27™

Each sachet contains:

- Minimum 1 billion microorganisms per sachet (1×10^9 CFU/g), guaranteed throughout the shelf life

Probiotics- BioGaia Protectis

- Establishing a healthy microbiota, filled with protective bacteria, is

BioGaia Protectis baby drops is a food supplement containing the patented lactic acid bacterium **Lactobacillus reuteri Protectis®/™ (L. reuteri DSM 17938) L. reuteri Protectis has been tested in more than 130 clinical trials and proven effective and safe for children.**

Lifeway Kefir-

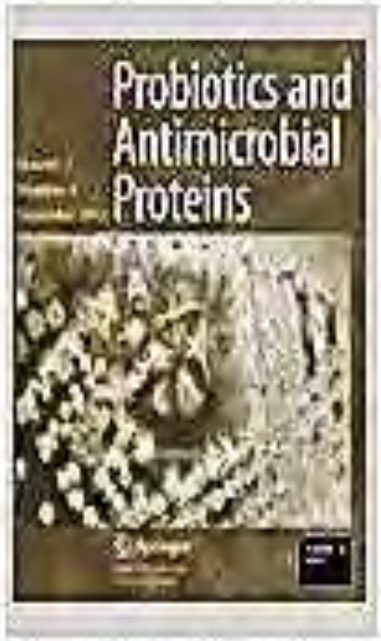
- Lifeway Kefir is a tart and tangy cultured milk smoothie that is high in protein, calcium and vitamin D. Due to their exclusive blend of kefir cultures, each cup of kefir contains 12 live and active cultures and 15 to 20 billion beneficial CFUs.

Lifeway Kefir- ProBugs

- Frozen kefir for kids
- Great dessert item or health treat after a lot of outside play

Probiotics? Some caution necessary!

PROBIOTICS AND ANTIMICROBIAL PROTEINS
Volume 3, Number 2, 63-67, DOI: 10.1007/s12602-011-9072-9



A Review of Probiotic Therapy in Preventive Dental Practice

Mark L. Cannon

ted with
ed bacteremia
m blood
sease can be
ut should serve

What is changing? What needs to change?
Requires understanding.

Probiotics often forgotten

acillus subtilis

Probiotics and Microbiome

- Autism Spectrum Disorder

Special Care for Special Patients

AUTISM SPEAKS®

CDC estimate of autism prevalence increases to 15%. Now 1 in 59 children.

Autism Speaks calls on nations' leaders to adequately fund critical research and resources

NEW YORK (April 26, 2018) The Centers for Disease Control and Prevention (CDC) today released its biennial update of autism's estimated prevalence among the nation's children, based on an analysis of 2014 medical and/or school records of 8-year-olds from 11 monitoring sites across the United States. The report demonstrates that while progress has been made on some fronts, there is still critical work to do.

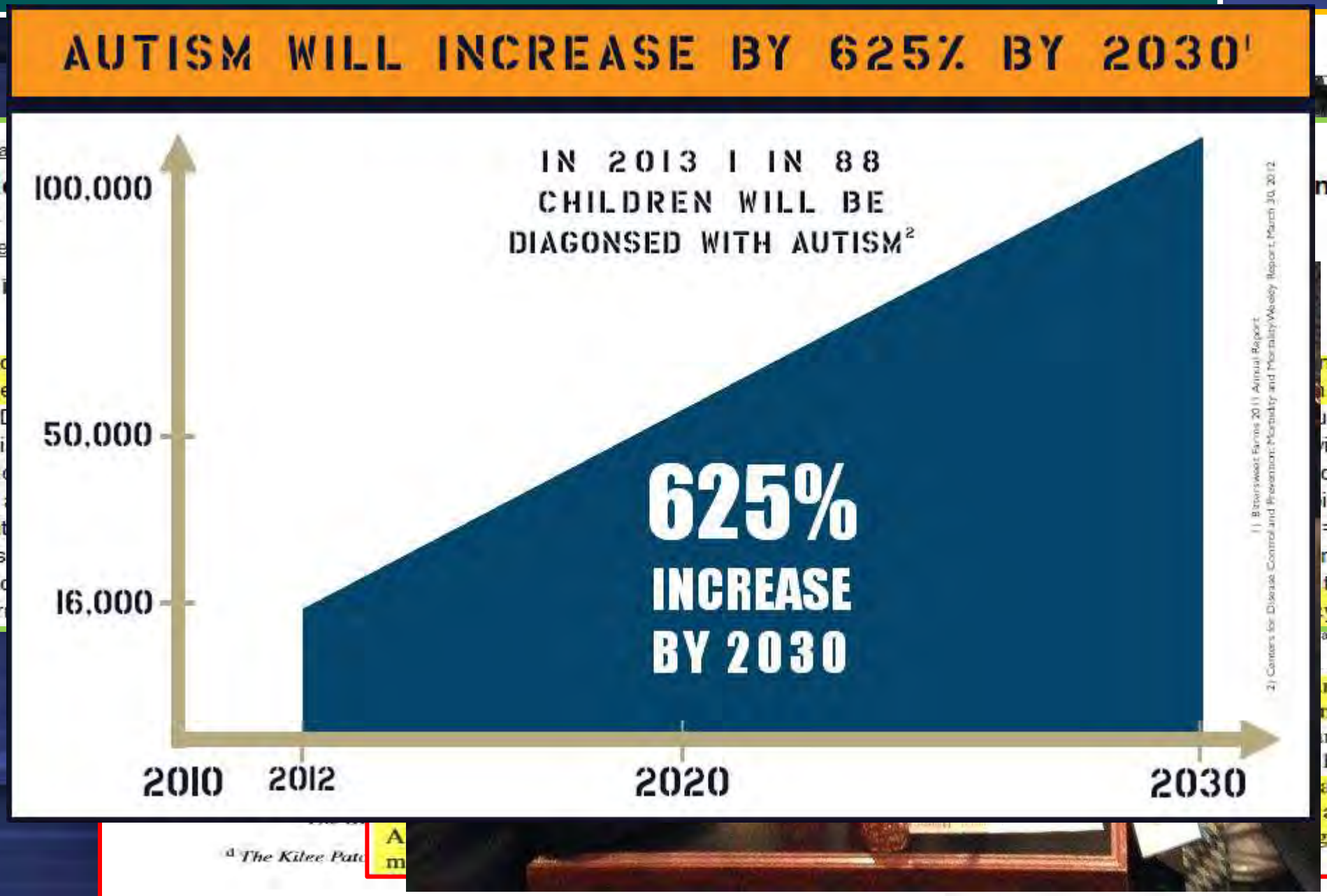
lining up
ccasionally
uals with

ecial

- The diagn
require tha
become a
child is thr

A young
who has
toys in c

Probiotics- Neurologic Implications



Autism- and other dilemmas

Microbial Ecology in Health and Disease

Taylor & Francis
Taylor & Francis Group

Microb Ecol Health Dis. 2015; 26: 10.3402/mehd.v26.26914.
Published online 2015 Mar 12. doi: 10.3402/mehd.v26.26914

PMCID: PMC4359272

Gut bacteria in children with autism spectrum disorders: challenges and promise of studying how a complex community influences a complex disease

Rosa Krajmalnik-Brown,[1,2,*] Catherine Lozupone,[3] Dae-Wook Kang,[1] and James B. Adams[4]

Here we first summarize previously published data supporting **that GI dysfunction is common in individuals with ASD and the role of the microbiota in ASD.** Second, by comparing with other publically available microbiome datasets, we provide some **evidence that the shifted microbiota can be a result of westernization and that this shift could also be framing an altered immune system**. Third, we explore the **possibility that gut–brain interactions could also be a direct result of microbially produced metabolites.**

Microbial Ecology in Health and Disease

Taylor & Francis
Taylor & Francis Group

Microb Ecol Health Dis. 2015; 26: 10.3402/mehd.v26.26914.
Published online 2015 Mar 12. doi: 10.3402/mehd.v26.26914

PMCID: PMC4359272

Gut bacteria in children with autism spectrum disorders: challenges and promise of studying how a complex community influences a complex disease

Rosa Krajmalnik-Brown,[1,2,*] Catherine Lozupone,[3] Dae-Wook Kang,[1] and James B. Adams[4]

Prevotella, is highly enriched in the fecal microbiota in populations in Africa including agrarian societies in **Malawi and Burkina Faso , and the Hadza hunter–gatherers in Tanzania** intrigued us and inspired us to perform comparative analyses. Since Prevotella is only one genus in the very diverse gut microbiota and has a tendency to co-occur with a complex collection of other bacteria species, we wanted to determine whether **Prevotella depletion in children with ASD** is an indicator that the gut microbiome of children with ASD who live in the United States differs even more from individuals in the developing world than does the gut microbiome of neurotypical children in the US, **providing evidence of the gut microbiota as an environmental factor that may correlate with increased rates of ASD in industrialized countries.**

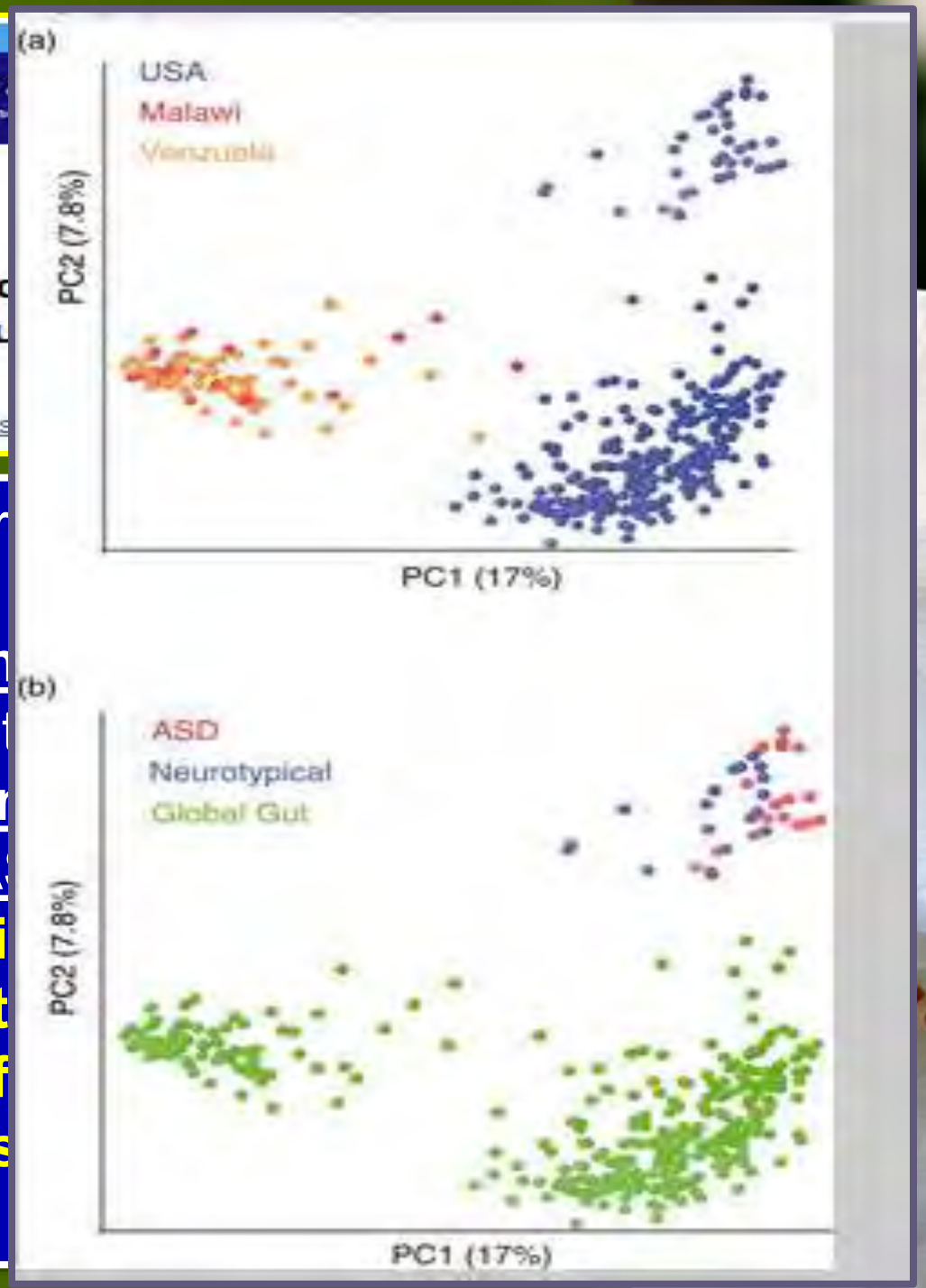
Microbial Ecology in Health and Disease

Microb Ecol Health Dis. 2015; 26: 10.3402/mehd.v26.26914.
Published online 2015 Mar 12. doi: 10.3402/mehd.v26.26914

**Gut bacteria in children with autism spectrum disorc
promise of studying how a complex community influ
disease**

Rosa Krajmalnik-Brown,[1,2,*] Catherine Lozupone,[3] Dae-Wook Kang,[1] and James

A high rate of GI problems in children with ASD, cor
symptom severity and GI symptoms within children
profiles of gut microbes and their metabolites in
growing appreciation of a link between the gut and t
neurological disorders**, all point towards the poter
microbiota in the presentation and severity of A**
Furthermore, our observation of a **'hyper-Westerni
microbiota of children with ASD could indicate t
differences that are driven by unique aspects of
compared to the developing world lead to the as
microbiota composition with ASD.**



Autism S

Neuroglial activa
autism

Diana L. Vargas MD[1]
Nascimbene MD[1,2,3]
MHS[1], Andrew W. Zi
and Carlos A. Pardo

Article first published

DOI: 10.1002/ana.20

Copyright © 2003 Amer
Association

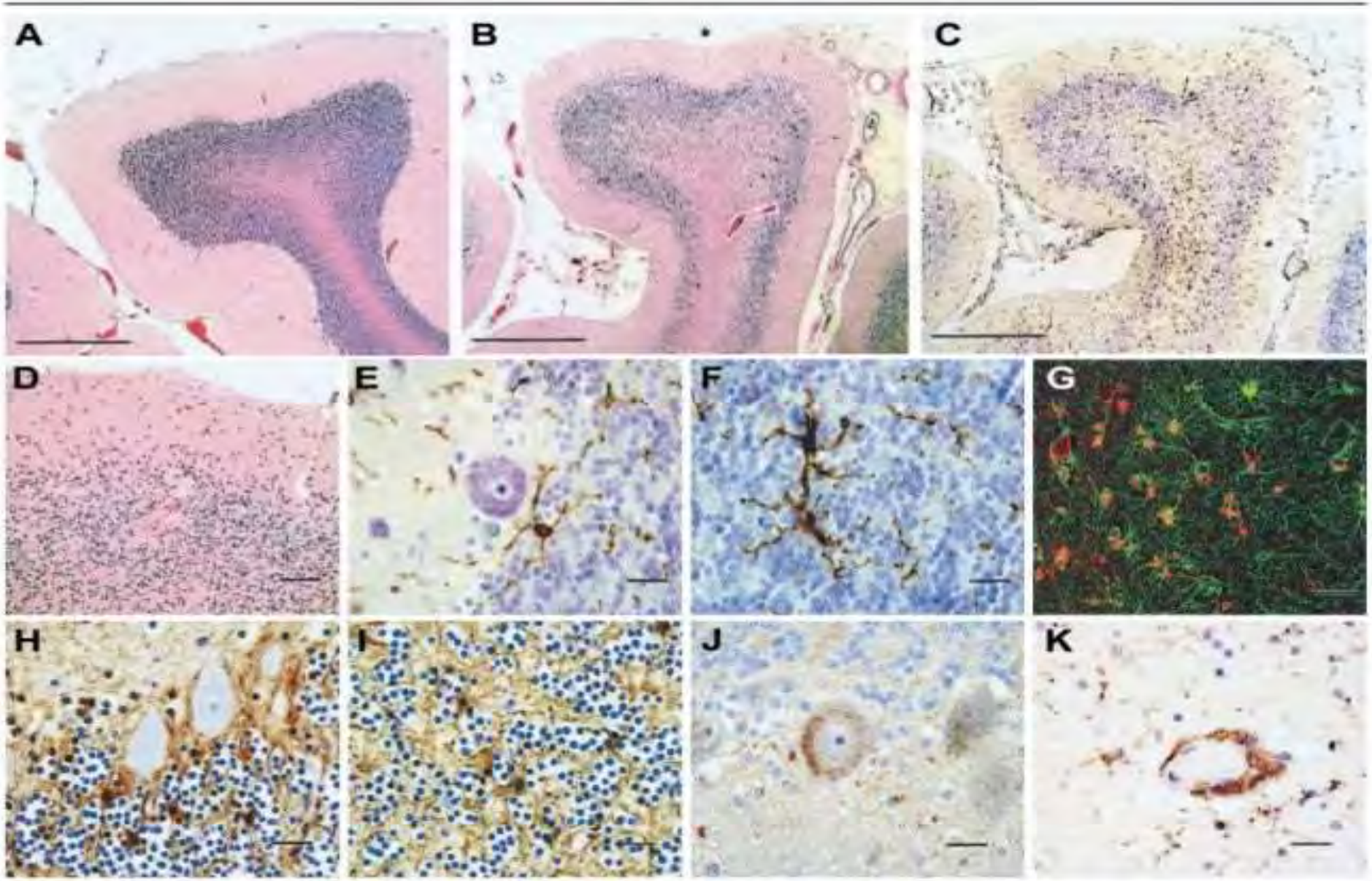


Fig 1. Cerebellar pathology in autism. (A) Normal cerebellar folia in a control brain (H and E staining). (B) Patchy loss of Purkinje cell layer (PCL) and granular cell layer (GCL) neurons (H and E) and (C) marked activation of microglia (immunostained with anti–HLA-DR antibody) are seen in the cerebellar folia of a patient with autism. Bar in A–C = 500μm. (D) High-magnification detail of a cerebellar region with marked PCL and GCL neuronal loss (H and E). Bar = 50μm. (E, F) Activated microglia around

Probiotics- Neurologic Implications

Autism Spectrum Disorders

Valproate Model for Autism- tells all!

Neurosci Lett. 2010 Feb 5;470(1):55-9. doi: 10.1016/j.neulet.2009.12.054. Epub 2009 Dec 28.

Behavior and serotonergic disorders in rats exposed prenatally to valproate: a model for autism.

Dufour-Rainfray D[1], Vourc'h P, Le Guisquet AM, Garreau L, Ternant D, Bodard S, Jaumain E, Gulhan Z, Belzung C, Andres CR, Chalon S, Guilloteau D.

JAMA. 2013 Apr 24;309(16):1696-703. doi: 10.1001/jama.2013.2270.

Prenatal valproate exposure and risk of autism spectrum disorders and childhood autism.

Christensen J[1], Grønborg TK, Sørensen MJ, Schendel D, Parner ET, Pedersen LH, Vestergaard M.

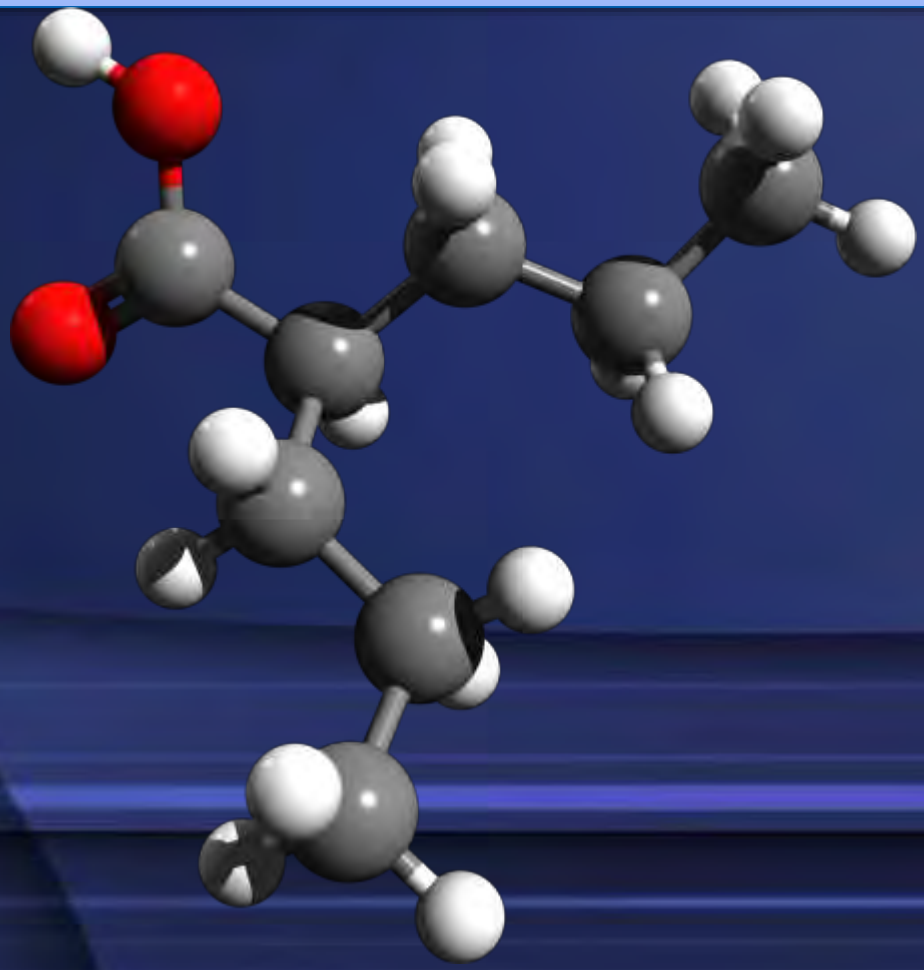
Anat Rec (Hoboken). 2010 Nov;293(11):1947-53. doi: 10.1002/ar.21232.

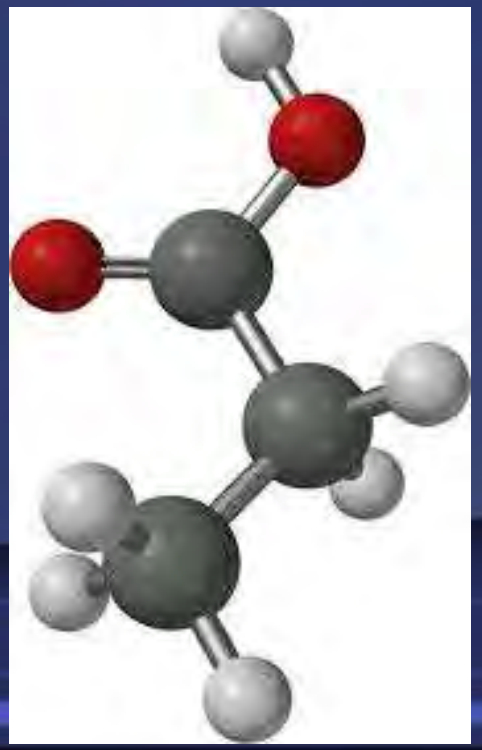
Demethylation of specific Wnt/β-catenin pathway genes and its upregulation in rat brain induced by prenatal valproate exposure.

Wang Z[1], Xu L, Zhu X, Cui W, Sun Y, Nishijo H, Peng Y, Li R.

Autism Spectrum Disorders

Valproic and Propionic structures





American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

1 in 40 children- ASD

Dec 2018

AUTISM RESEARCH

INSAR
International Society for Autism Research

Research Article

Assessing autistic traits: cross-cultural validation of the social responsiveness scale (SRS)

Sven Bölte ✉, Fritz Poustka, John N. Constantino

First published: 23 December 2008 | https://doi.org/10.1002/aur.49 | Cited by: 134

Table 1. Evidence for the link between Clostridium bacteria and autism spectrum conditions. Table summarizing the main results of nine studies included in the systematic review. The table is organized by year of publication.

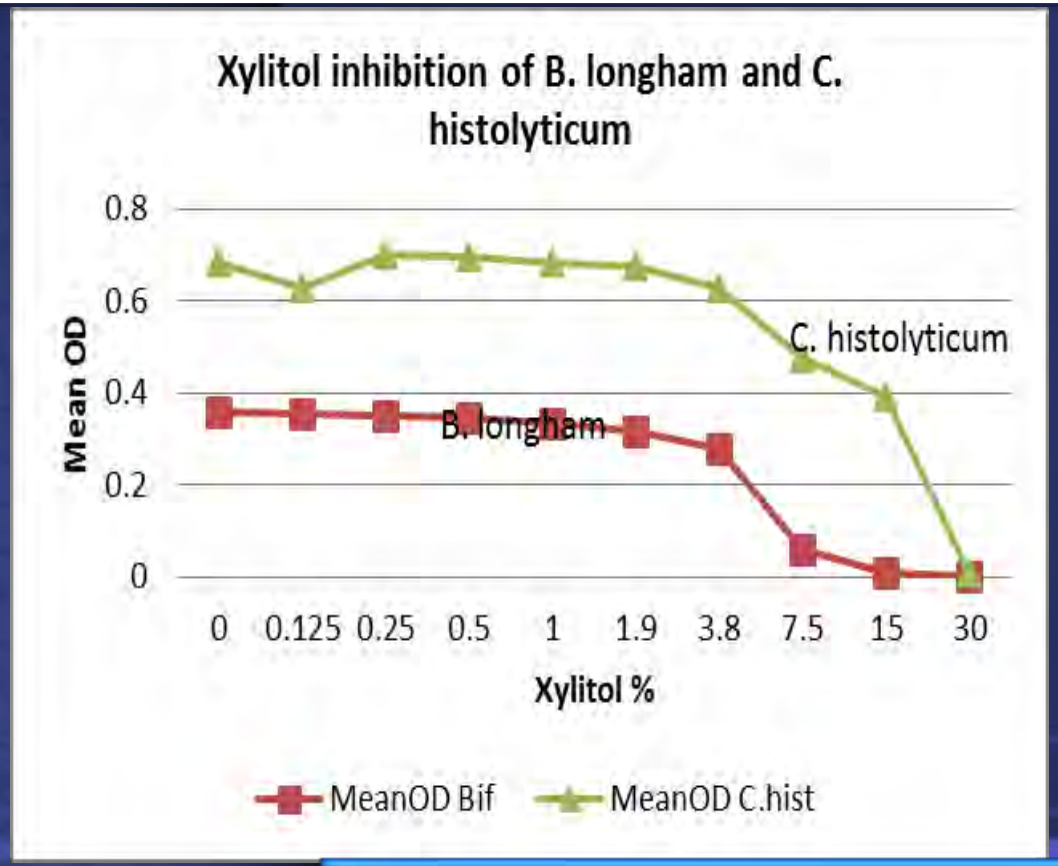
TITLE	AUTHOR / YEAR	PMID	MATERIAL	Nº PATIENTS / CONTROLS	CONCLUSIONS
Gastrointestinal microflora studies in late-onset autism	Finegold *et al.*, 2002	12173102	Human (Stools)	13 ASD / 8 controls	Children with autism had nine species of Clostridium not found in controls, with significant alterations in the upper and lower intestinal flora of children with late-onset autism
Real-time PCR quantitation of clostridia in feces of autistic children	Song *et al.*, 2004	15528506	Human (Stools)	15 ASD / 8 controls	Analysis of the real-time PCR data showed cell count differences between autistic and control children for *Clostridium boltae*
Differences between the gut microflora of children with autistic spectrum disorders and that of healthy children	Parracho *et al.*, 2005	16157555	Human (Stools)	58 ASD / 22 controls (2 groups)	The fecal flora of autism spectrum disorder (ASD) patients contained a higher incidence of the *Clostridium histolyticum* group (Clostridium clusters I and II) of bacteria than that of healthy children
Fecal lactoferrin and *Clostridium* spp. in stools of autistic children	Martirosian *et al.*, 2011	21167951	Human (Stools)	41 ASD / 10 controls	Elevated level of fecal lactoferrin was demonstrated in 24.4% stools, all from boys (31.25%). No toxins were detected. *Clostridium spp.* was isolated with similar frequency from all samples. *Clostridium perfringens* were isolated significantly often from the autistic stools
Fecal microbiota and metabolome of children with autism and pervasive developmental disorder not otherwise specified	De Angelis *et al.*, 2013	24130822	Human (Stools)	20 ASD / 10 controls	The highest microbial diversity was found in ASD children. Based on 16S-rRNA and culture-dependent data, Faecalibacterium and Ruminococcus were present at the highest level in fecal samples of pervasive developmental disorder not otherwise specified (PDD-NOS) and healthy children. Caloramator, Sarcina and Clostridium genera were the highest in ASD children
Urinary 3-(3-Hydroxyphenyl)-3-hydroxypropionic Acid, 3-Hydroxyphenylacetic Acid, and 3-Hydroxyhippuric Acid Are Elevated in Children with Autism Spectrum Disorders	Xiong *et al.*, 2016	27123458	Human (Urine)	62 ASD / 62 controls	Measurement of these three compounds (aromatic metabolites in autism patients are presumably derived from overgrown Clostridium species in gut) are strong predictors of ASDs and support the potential clinical utility for identifying a subgroup of ASD subjects
Intestinal Dysbiosis and Yeast Isolation in Stool of Subjects with Autism Spectrum Disorders	Iovene *et al.*, 2017	27655151	Human (Stools)	47 ASD / 33 controls	Significant linear correlation was found between disease severity and calprotectin and *Clostridium spp.* presence in the stool of subjects with ASD
Analysis of the Duodenal Microbiome in Autistic Individuals: Association with Carbohydrate Digestion	Kushak *et al.*, 2017	27811623	Human (Intestinal biopsies)	21 ASD / 19 controls	A positive correlation was found between the abundance of Clostridium species and disaccharidase activity in autistic individuals
Detection of *Clostridium perfringens* toxin genes in the gut microbiota of autistic children	Finegold *et al.*, 2017	28215985	Human (Stools)	33 ASD / 13 controls	The author's results indicate that autistic subjects with gastrointestinal disease harbor statistically significantly higher counts of C. *perfringens* and β2-toxin gene-producing C. *perfringens* in their gut when compared to control children. In addition, the incidence of β2-toxin gene-producing C. *perfringens* is also significantly higher in these autistic subjects

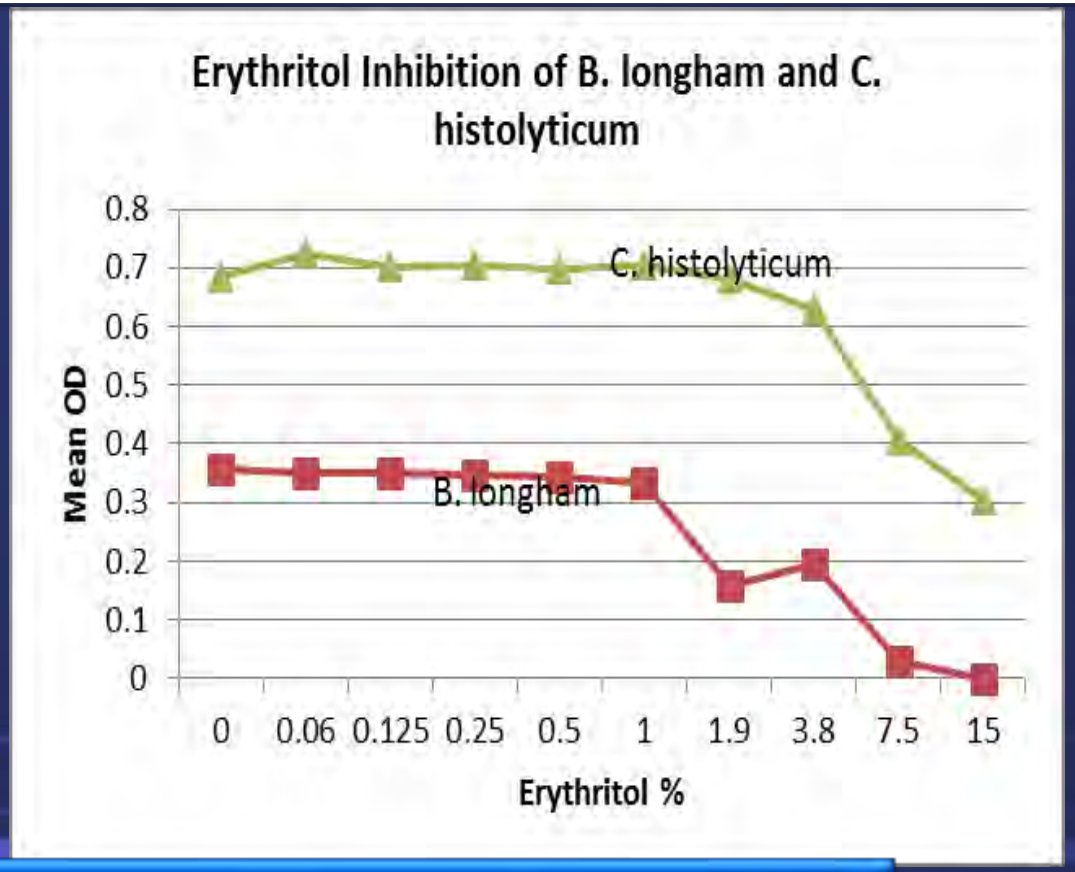
Ann and Robert Lurie Children's Hospital- Autism Spectrum Disorder
Microbiome Research

- Results: Eight strains were tested for polyol inhibitory activity C. histolyticum, B. vulgatis, C. bolteae (x2), C. suggested polyol activity but did not reach a level of discernable growth to be able to assess the assays appropriately. Detailed OD values vs. polyol concentration are plotted as follows with relative inhibition inflection points.

Eight Strains- Two Polyols

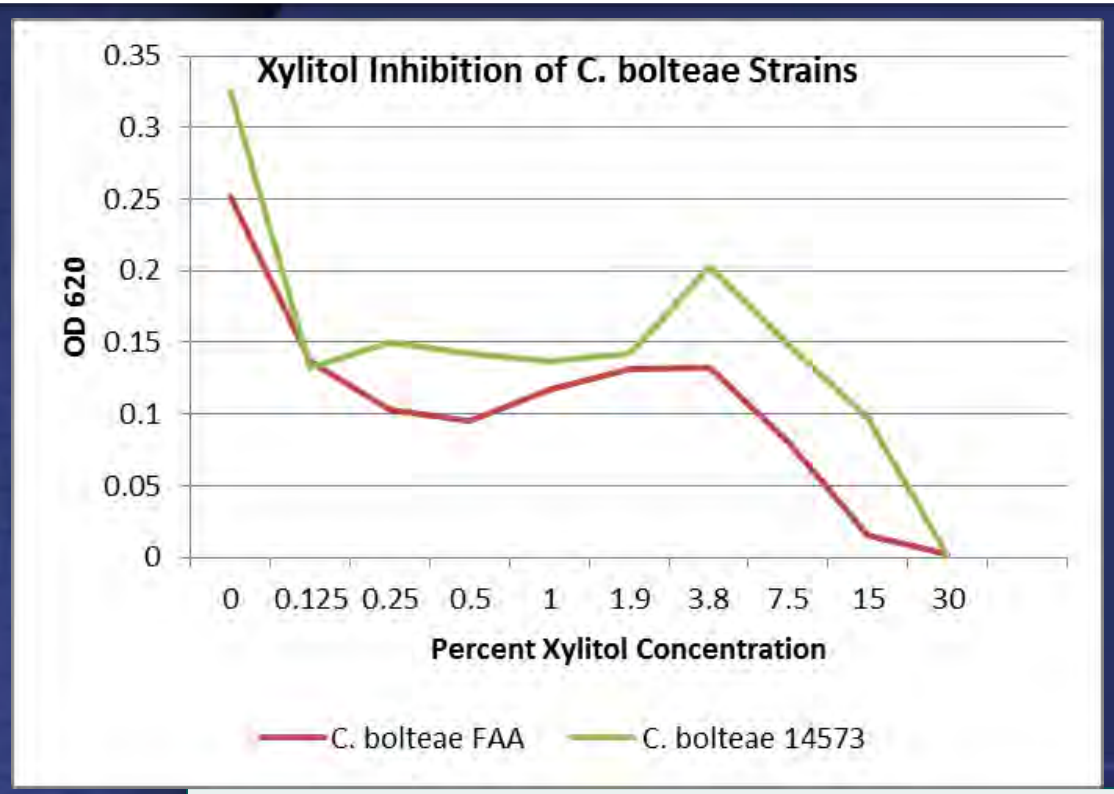
Ann and Robert Lurie Children's Hospital- Autism Spectrum Disorder Microbiome Research

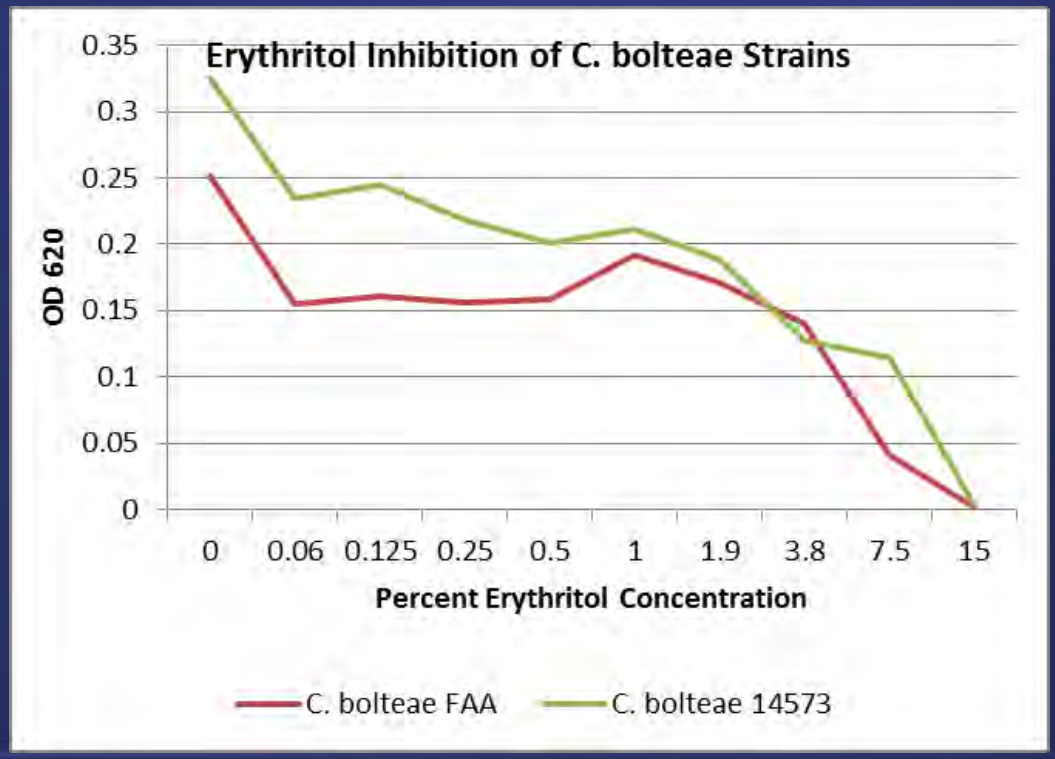




Erythritol more effective

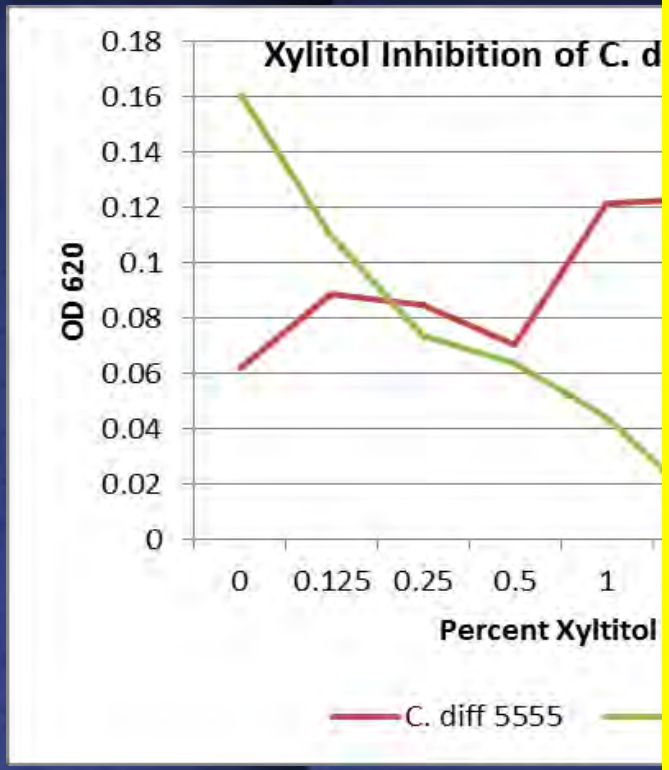
Ann and Robert Lurie Children's Hospital- Autism Spectrum Disorder Microbiome Research





- Erythritol seems better suited to inhibit Clostridia bolteae

Ann and Rob
Autis
Mi



- Xylitol may be b
- Perhaps we sho

CDC puts C difficile burden at 453,000 cases, 29,000 deaths

Filed Under: Antimicrobial Resistance; Clostridium difficile

Robert Roos | News Editor | CIDRAP News | Feb 25, 2015

Share Tweet LinkedIn Email Print & PDF

On the basis of a 2011 study, the Centers for Disease Control and Prevention (CDC) has increased its estimate of the annual burden of *Clostridium difficile* infections in the United States, putting it at 453,000 cases per year, with 29,300 associated deaths.

CDC

Clostridium difficile bacteria, highly magnified

The agency, which released the findings in the *New England Journal of Medicine* (*NEJM*), said they point up the need for better antibiotic stewardship and rigorous infection control in healthcare facilities.

C diff infections occur when someone is exposed to the pathogen while receiving antibiotic treatment for some other illness. Antibiotics suppress the normal bacteria in the colon, allowing *C diff* to flourish, producing toxins that cause severe diarrhea. Damage to the colon can cause bacteria to leak into the bloodstream.

The CDC found that about two thirds of the 453,000 cases were related to a stay in a hospital or nursing home and the other third were community-associated cases, involving people with no recent hospital or nursing home exposure. Most of those who died were elderly.

Nobel Fo

The Gut-Brain
Early life progr
of brain functio
behavior

Microbiome and Epigenetics- so many ?s

And so many publications…

REVIEW ARTICLE

Front. Neurol., 26 May 2015 | http://dx.doi.org/10.3389/fneur.2015.00107

The role of epigenetic change in autism spectrum disorders

Yuk Jing Loke[1], Anthony John Hannan[2] and Jeffrey Mark Craig[1]*

[1]Murdoch Childrens Research Institute, Royal Children's Hospital and Department of Paediatrics, University of Melbourne, Parkville, VIC, Australia

[2]Melbourne Brain Centre, Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Parkville, VIC, Australia

epigenetic dysregulation.

CONCLUSION: Data reviewed in this article highlight a variety of situations in which epigenetic dysregulation is associated with the development of ASD, thereby supporting a role for epigenetics in the multifactorial etiologies of ASD.

Epigenetics

DNA methylation and Autism

Molecular Psychiatry **19**, 862-871 (August 2014) | doi:10.1038/mp.2013.

Common DNA methylation alterations in multiple brain regions in autism

C Ladd-Acosta, K D Hansen, E Briem, M D Fallin, W E Kaufmann and A P Feinberg

DNA methylation (DNAm) in a pilot study of postmortem brain tissue from **19 autism cases and 21 unrelated controls,** among three brain regions including dorsolateral prefrontal cortex, temporal cortex and cerebellum.

The DMRs identified in this study represent suggestive evidence for commonly altered methylation sites in ASD and provide several promising new candidate genes.

DNA methylation

Molecular Psychiatry (2014) **19**, 495–503; doi:

Methylomic analysis of mo
autism spectrum disorder a

C C Y Wong[1], E L Meaburn[1,2], A Ronal
C Schalkwyk[1], R Plomin[1] and J Mill[1,4]

Genome-wide analysis of DNA methylation in a sample of **50 MZ twin pairs (100 individuals)** sampled from a representative population cohort that included twins discordant and concordant for ASD, ASD-associated traits and no autistic phenotype.

Significant correlations between DNA methylation and quantitatively measured autistic trait scores across our sample cohort. This study represents the first systematic epigenomic analyses of MZ twins discordant for ASD and implicates a role for altered DNA methylation in autism.

frontiers in Immunology

ORIGINAL RESEARCH
published: 22 December 2017
doi: 10.3389/fimmu.2017.01670

Modulation of Immunological Pathways in Autistic and Neurotypical Lymphoblastoid Cell Lines by the Enteric Microbiome Metabolite Propionic Acid

Richard E. Frye[1,2], Bistra Nankova[3], Sudeepa Bhattacharyya[1,2], Shannon Rose[1,2], Sirish C. Bennuri[1,2] and Derrick F. MacFabe[4]*

Propionic acid (PPA) is a ubiquitous short-chain fatty acid which is a fermentation product of the enteric microbiome and present or added to many foods. PPA modulates mitochondrial dysfunction differentially in subsets of lymphoblastoid cell lines (LCLs) derived from patients with ASD. Specifically, PPA significantly increases mitochondrial function in LCLs that have mitochondrial dysfunction at baseline [individuals with autistic disorder with atypical mitochondrial function (AD-A) LCLs] as compared to ASD LCLs with normal mitochondrial function [individuals with autistic disorder with normal mitochondrial function (AD-N) LCLs] and control (CNT) LCLs.

Rose et al. Translational Psychiatry (2018)8:42
DOI 10.1038/s41398-017-0089-z

Translational Psychiatry

ARTICLE Open Access

Butyrate enhances mitochondrial function during oxidative stress in cell lines from boys with autism

Shannon Rose[1], Sirish C. Bennuri[1], Jakeira E. Davis[1], Rebecca Wynne[1], John C. Slattery[1], Marie Tippett[1], Leanna Delhey[1], Stephan Melnyk[1], Stephen G. Kahler[1], Derrick F. MacFabe[2] and Richard E. Frye[1,3]

In general, these data suggest that **BT can enhance mitochondrial function** in the context of physiological stress and/or mitochondrial dysfunction, and may be an important metabolite that can help **rescue energy metabolism during disease states.** Thus, insight into this metabolic modulator may have wide applications for both health and disease since **BT has been implicated in a wide variety of conditions including ASD**.

Oral Microbiome- Autism

Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.intl.elsevierhealth.com/journals/jden

Effect of three-year consumption of erythritol, xylitol and sorbitol candies on various plaque and salivary caries-related variables

Riina Runnel [a,*], *Kauko K. Mäkinen* [b], *Sisko Honkala* [c], *Jana Olak* [a], *Pirkko-Liisa Mäkinen* [b], *Rita Nõmmela* [a], *Tero Vahlberg* [d], *Eino Honkala* [b,c], *Mare Saag* [a]

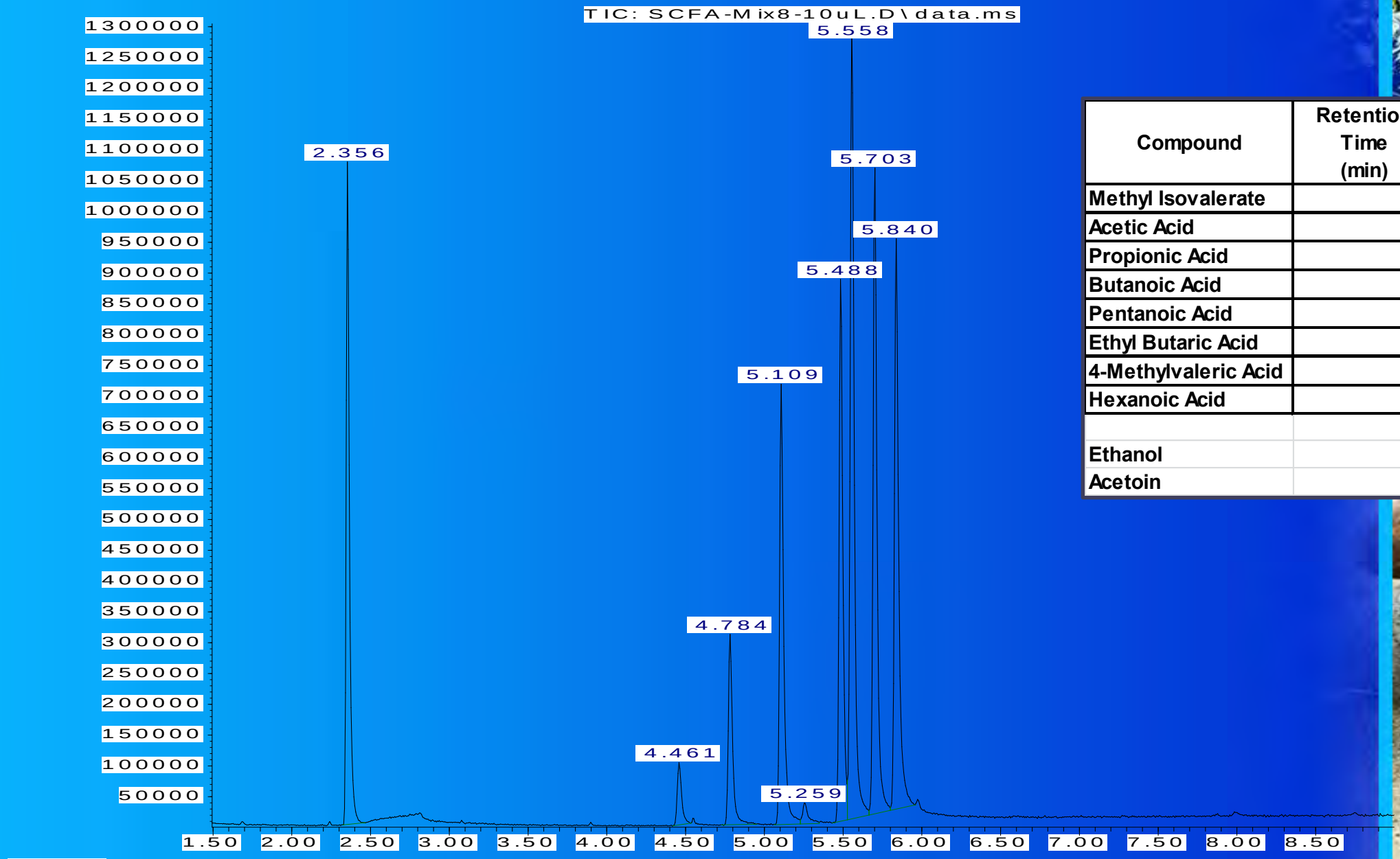
- Three-year consumption of erythritol-containing candies by initially 7- to 8-year old children was associated with reduced plaque growth**, lower levels of plaque, acetic acid and propionic acid,** and reduced oral counts of mutans streptococci compared with the consumption of xylitol or sorbitol candies.

SCFA- microbiome

- Pilot study of the SCFA Headspace Analysis of Bacterial Metabolites in Media with and without Polyols

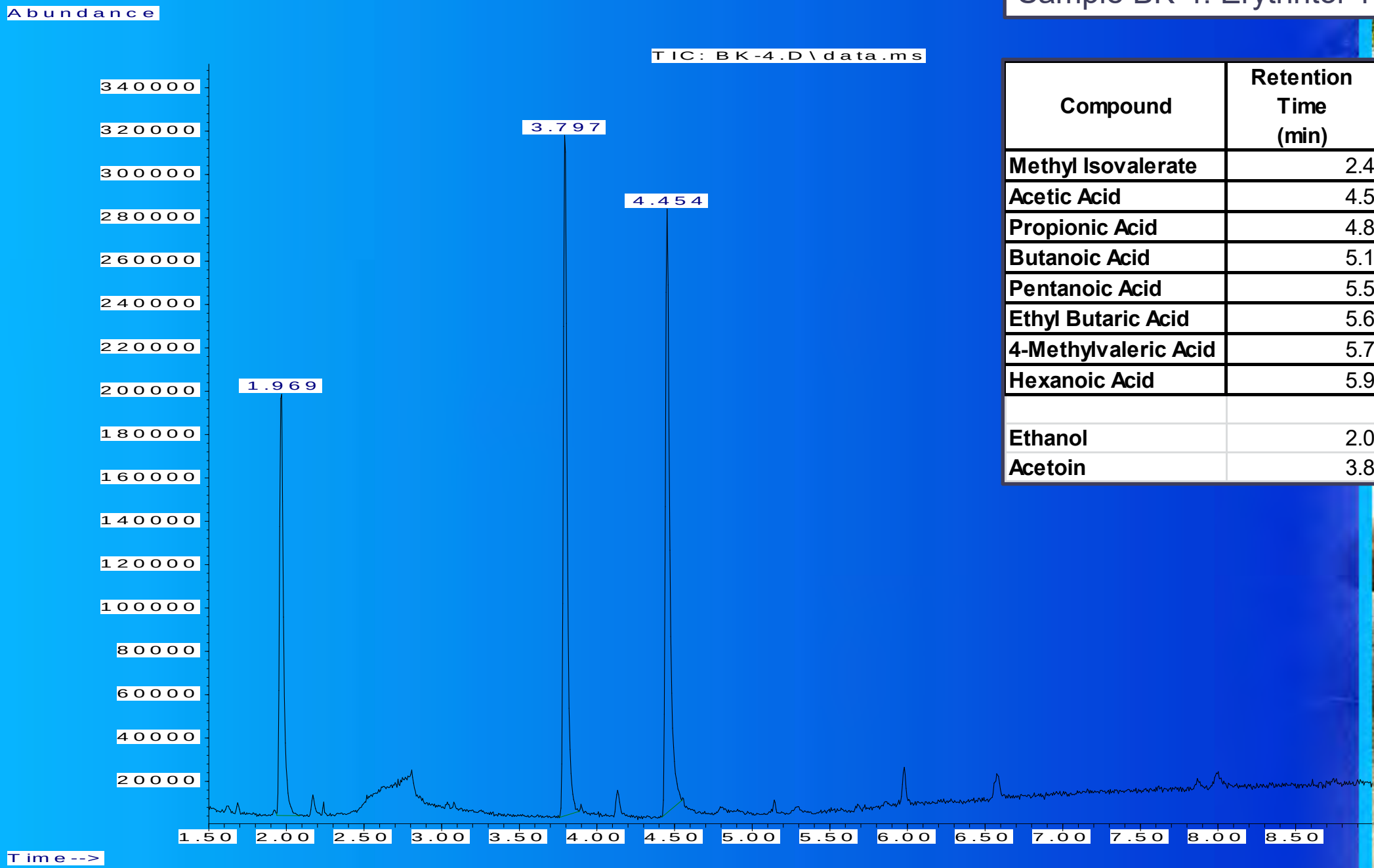
- MacFabe, D., Habibi, Kabat, B., Cannon, M., Gashkoff, M., Zurek, R.

Standard Mix: 52 ng on column



Compound	Retention Time (min)	m/z
Methyl Isovalerate	2.4	74
Acetic Acid	4.5	60
Propionic Acid	4.8	74
Butanoic Acid	5.1	60
Pentanoic Acid	5.5	60
Ethyl Butaric Acid	5.6	88
4-Methylvaleric Acid	5.7	57
Hexanoic Acid	5.9	60
Ethanol	2.0	45
Acetoin	3.8	45

Sample BK-4: Erythritol-1.25mg



Compound	Retention Time (min)	m/z
Methyl Isovalerate	2.4	74
Acetic Acid	4.5	60
Propionic Acid	4.8	74
Butanoic Acid	5.1	60
Pentanoic Acid	5.5	60
Ethyl Butaric Acid	5.6	88
4-Methylvaleric Acid	5.7	57
Hexanoic Acid	5.9	60
Ethanol	2.0	45
Acetoin	3.8	45

SCFA- microbiome

- ***Constituents of media effect the bacterial metabolite production***, possibly shifting from benign or protective to more pathogenic. Additional laboratory study is required testing other species, specifically the propionic producing *Clostridium histolyticum* and *boltae* plus *Bacteroides vulgatus*.

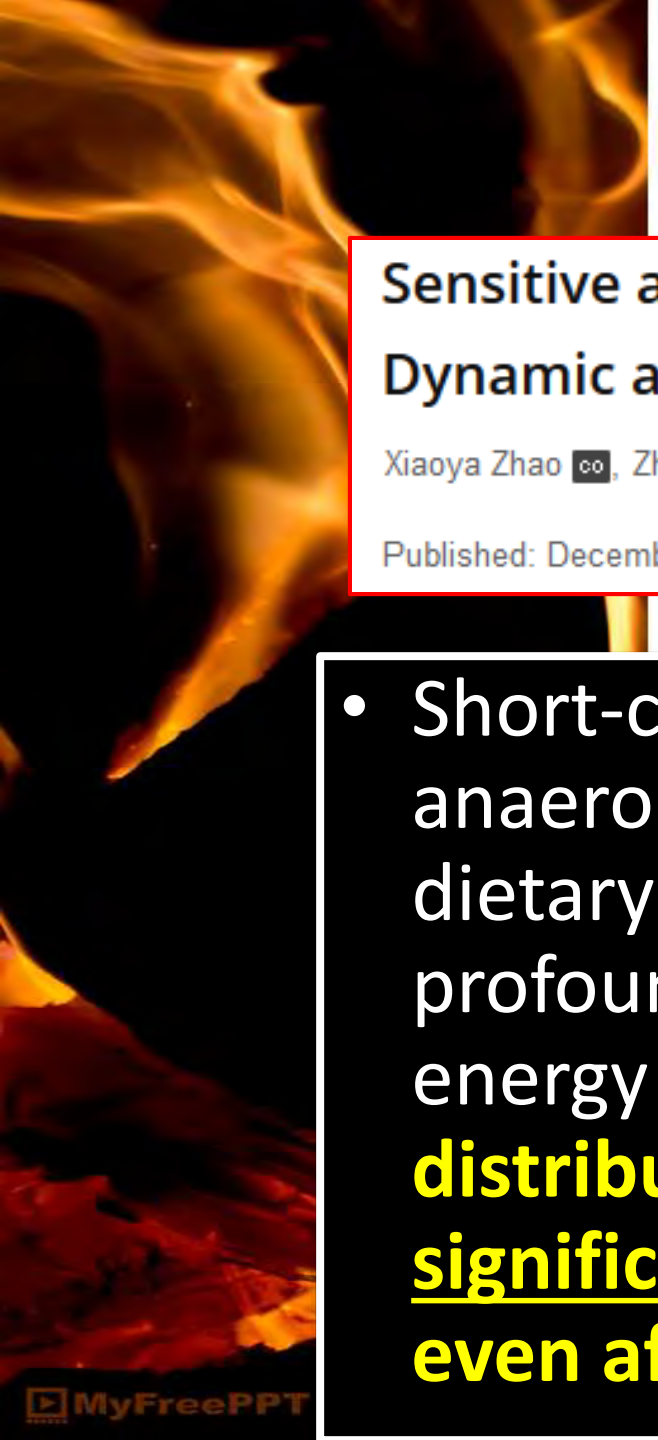
SCIENTIFIC REPORTS

Alterations of oral microbiota distinguish children with autism spectrum disorders from healthy controls

Yanan Qiao, Mingtao Wu, Yanhuizhi Feng, Zhichong Zhou, Lei Chen & Fengshan Chen

Scientific Reports **8**, Article number: 1597 | Received: 23 February 2017

- Moreover, pathogens such as Haemophilus in saliva and Streptococcus in plaques showed significantly higher abundance in ASD patients, whereas commensals such as Prevotella, Selenomonas, Actinomyces, Porphyromonas, and Fusobacterium were reduced. Specifically, an overt depletion of Prevotellaceae co-occurrence network in ASD patients was obtained in dental plaques. The distinguishable bacteria were also correlated with clinical indices, reflecting disease severity and the oral health status. **Finally, diagnostic models based on key microbes were constructed, with 96.3% accuracy in saliva.**



Epigenetics- antibiotics

Sensitive and Simplified Detection of Antibiotic Influence on the Dynamic and Versatile Changes of Fecal Short-Chain Fatty Acids

Xiaoya Zhao, Zhenzuo Jiang, Fan Yang, Yan Wang, Xiumei Gao, Yuefei Wang, Xin Chai, Guixiang Pan, Yan Zhu

Published: December 1, 2016 • https://doi.org/10.1371/journal.pone.0167032

PLOS ONE

- Short-chain fatty acids (SCFAs), produced by anaerobic fermentation of mainly indigestible dietary carbohydrates by gut microbiota, have a profound influence on intestinal function and host energy metabolism. **The total amount, types and distribution of nearly all fecal SCFAs were significantly altered during the administration and even after withdrawal of the antibiotics** in rats.

nat
neu

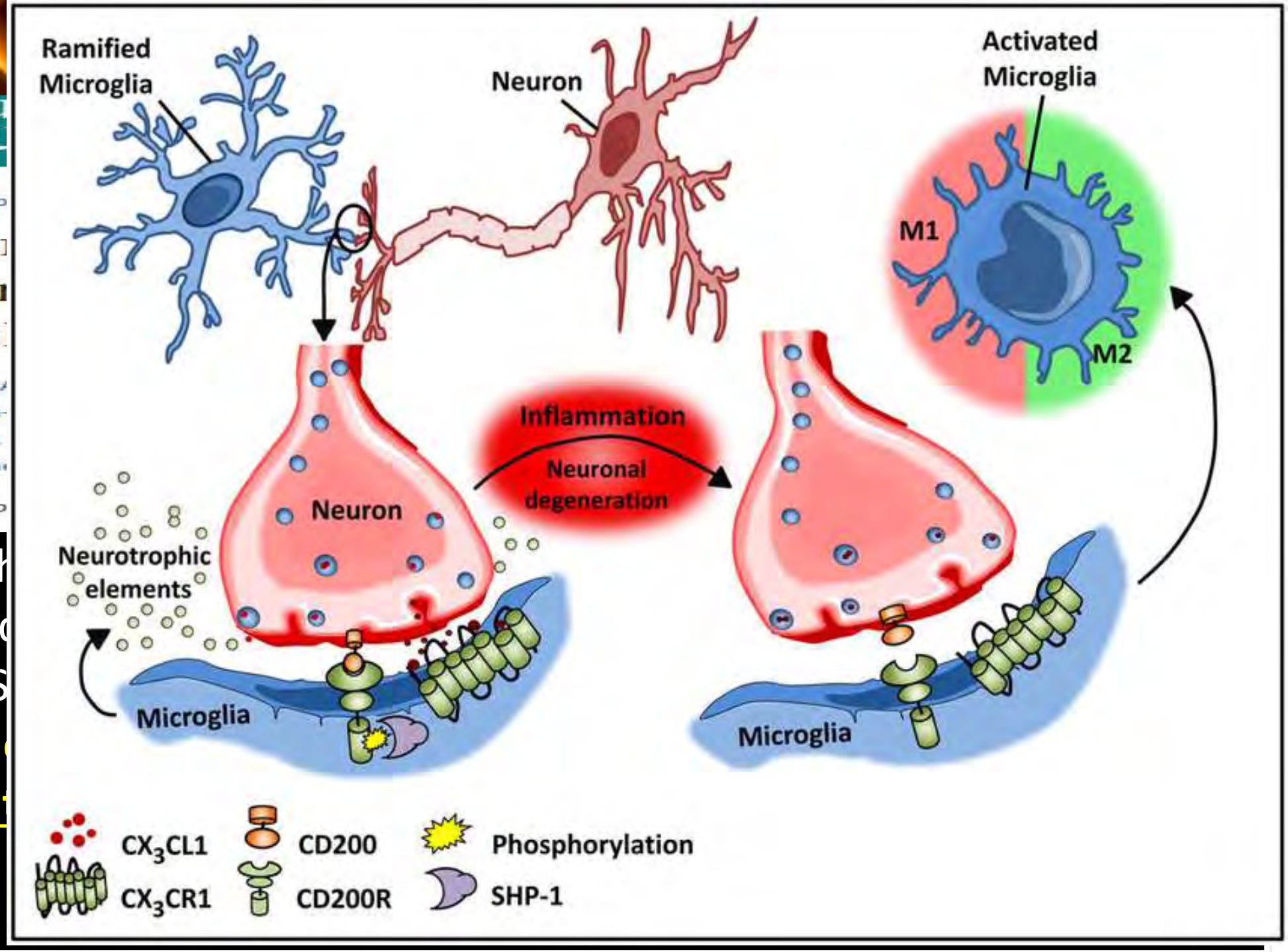
Article Pub

Host
matu
the C

Daniel Erny,
Hadas Keren-
Utermöhlen,
Bärbel Stech

Nature Neuro

- We determined th
fermentation proc
deficient for the S
GF conditions. **Th**
microglia matura
rectified to some



Autism and microbiome

frontiers in Psychiatry

SYSTEMATIC REVIEW ARTICLE

Front. Psychiatry, 17 July 2019 | https://doi.org/10.3389/fpsyt.2019.00473

Association Between Gut Microbiota and Autism Spectrum Disorder: A Systematic Review and Meta-Analysis

Mingyu Xu[1], Xuefeng Xu[2], Jijun Li[3] and Fei Li[1,4*]

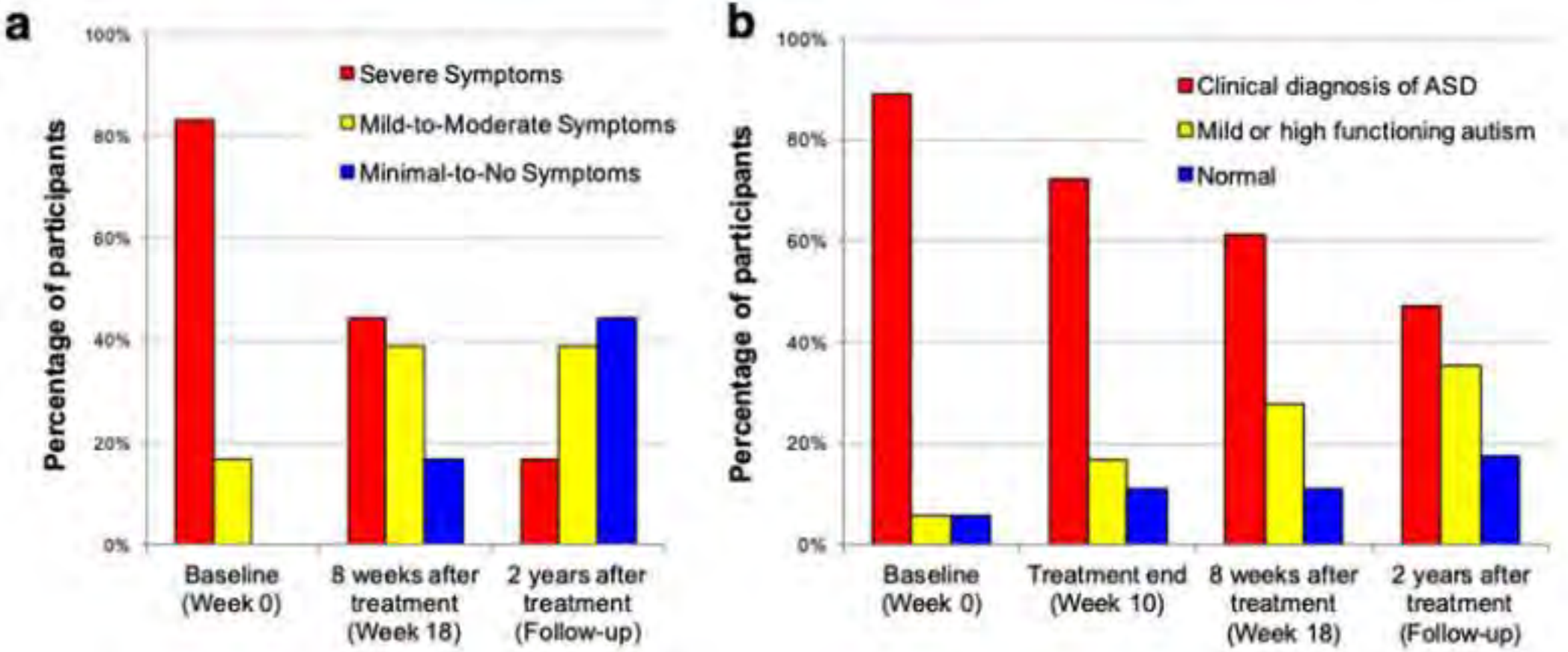
- We analyzed nine studies, including 254 patients with ASD, and found that children with ASD had lower percentages of Akkermansia, Bacteroides, Bifidobacterium, and Parabacteroides and a higher percentage of Faecalibacterium in the total detected microflora compared to controls. In contrast, children with ASD had lower abundance of Enterococcus, Escherichia coli, Bacteroides, and Bifidobacterium and higher abundance of Lactobacillus. **This meta-analysis suggests an association between ASD and alteration of microbiota composition** and warrants additional prospective cohort studies to evaluate the association of bacterial changes with ASD symptoms, which would provide further evidence for the precise microbiological treatment of ASD.

Autism and microbiome

SCIENTIFIC REPORTS

Figure 2

From: Long-term benefit of Microbiota Transfer Therapy on autism symptoms and gut microbiota



Nobel Conferen

eting of the
el Assembly
Stockholm,
SE

gain, the
robiome is
ognized as
the
grammer!

SUE

Probiotics and Microbiome

NUTRITION™

- **Polyols**

Erythritol is a sweet antioxidant

Gertjan J.M. den Hartog, Ph.D., Agnes W. Boots, Ph.D., Aline Adam-Perrot, Ph.D.†, Fred Brouns, Ph.D., Inge W.C.M. Verkooijen, M.Sc., Antje R. Weseler, Ph.D., Guido R.M.M. Haenen, Ph.D., Aalt Bast, Ph.D.

Erythritol was shown to be an excellent HO• radical scavenger and an inhibitor of 2,2′-azobis-2-amidinopropane dihydrochloride–induced hemolysis but inert toward superoxide radicals. The reaction of erythritol with hydroxyl radicals resulted in the formation of erythrose and erythrulose by abstraction of a carbon-bound hydrogen atom. Erythritol displayed an endothelium-protective effect and, in accordance with the in vitro experiments, erythrose was found in the urine of erythritol-consuming rats.

Xylitol- “Prebiotic”

Prebiotic potential of L-sorbose and xylitol in promoting the growth and metabolic activity of specific butyrate-producing bacteria in human fecal culture FREE

Tadashi Sato ✉, Shiro Kusuhara, Wakae Yokoi, Masahiko Ito, Kouji Miyazaki

FEMS Microbiology Ecology, Volume 93, Issue 1, 1 January 2017, fiw227, https://doi.org

- Dietary low-digestible carbohydrates (LDCs) affect gut microbial metabolism, including the production of short-chain fatty acids. Fecal suspensions from five healthy males were anaerobically incubated with various LDCs. L-Sorbose and xylitol markedly promoted butyrate formation in cultures. Bacterial 16S rRNA gene-based denaturing gradient gel electrophoresis **analyses of these fecal cultures revealed a marked increase in the abundance of bacteria closely related to the species Anaerostipes hadrus or A. caccae or both, during enhanced butyrate formation from L-sorbose or xylitol.**

Polyols- “Prebiotics”

molecular oral

Metabolome analyses using capillary electrophoresis time-of-flight mass spectrometry revealed that a number of **nucleic intermediates and constituents of the extracellular matrix, such as nucleotide sugars, were decreased by erythritol** in a dose-dependent manner.

Polyols- “Prebiotics”

J Periodontol. 2014 Jun; 85(6): e212–e223.
PMID
Published online 2014 Mar 4. doi: 10.1902/jop.2014.130455

Xylitol, an Anticaries Agent, Exhibits Potent Inhibition of Inflammatory Responses in Human THP-1-Derived Macrophages Infected With *Porphyromonas gingivalis*

Eunjoo Park,* Hee Sam Na,* Sheon Min Kim,* Shannon Wallet,† Seunghee Cha,‡ and Jin Chung*

Inhibits cytokine inflammation

Increase nitric oxide production

Inhibits *P. gingivalis* attachment

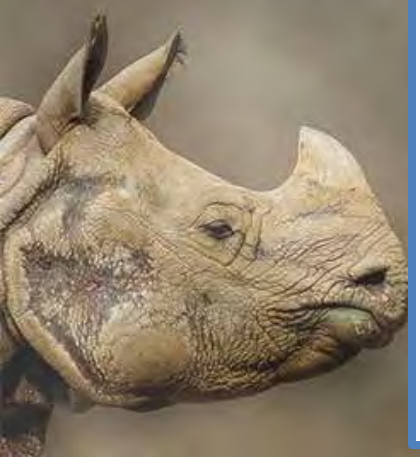
Increases phagocytosis of *E. coli* and *P. gingivalis*

Polyols- “Prebiotics”

Polyols are the prebiotics- now for the probiotics for oral disease

2530 Clinical Trials- Probiotics

“No research!” Pubmed?



PubMed | probiotic trials | Search

Create RSS | Create alert | Advanced | Help

Format: Summary | Sort by: Most Recent | Per page: 20 | Send to

Best matches for probiotic trials:

The effects of **probiotic** and synbiotic supplementation on metabolic syndrome indices in adults at risk of type 2 diabetes: study protocol for a randomized controlled trial.
Kassaian N et al. **Trials**. (2017)

Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial-PROSPECT: a pilot trial.
Cook DJ et al. **Trials**. (2016)

The effect of a novel **probiotic** on metabolic biomarkers in adults with prediabetes and recently diagnosed type 2 diabetes mellitus: study protocol for a randomized controlled trial.
Palacios T et al. **Trials**. (2017)

Switch to our new best match sort order

Search results

Items: 1 to 20 of 2530

Page 1 of 127 Next > Last >>

1. Utility of **Probiotics** for Maintenance or Improvement of Health Status in Older People - A Scoping Review.
Setbo E, Campbell K, O'Cuiv P, Hubbard R.
J Nutr Health Aging. 2019;23(4):364-372. doi: 10.1007/s12603-019-1187-9.
PMID: 30932135
Similar articles

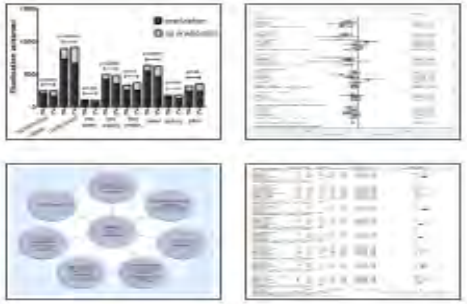
Filters: Manage Filters

Sort by:

Best match | Most recent

Results by year

PMC Images search for *probiotic trials*

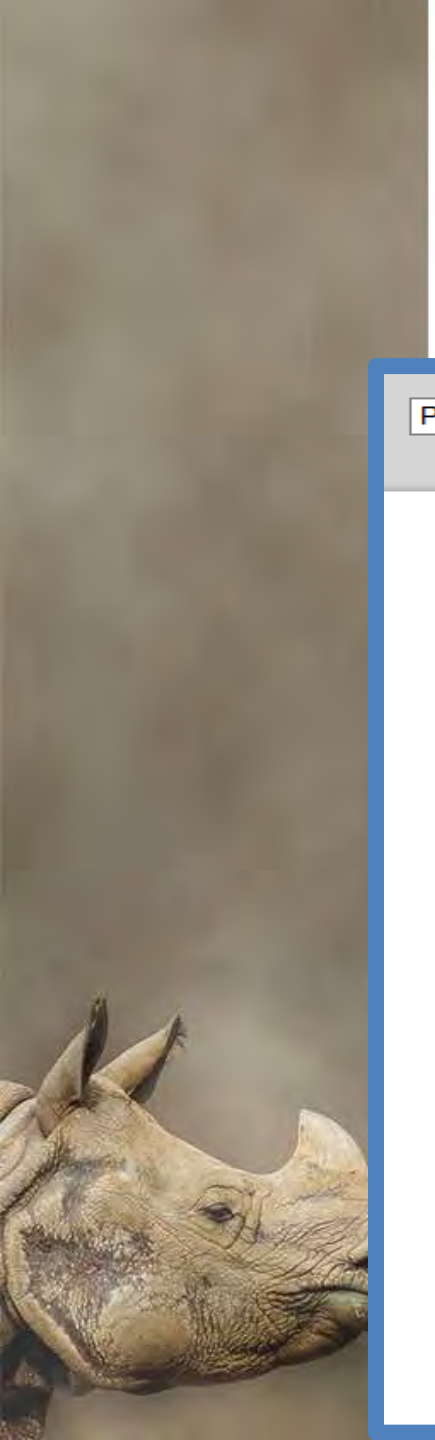


See more (125)...

Titles with your search terms

Pubmed- Probiotics articles

20672 articles on probiotics



PubMed | probiotics | Search

Create RSS | Create alert | Advanced | Help

Format: Summary | Sort by: Most Recent | Per page: 20 | Send to | Filters: Manage Filters

Best matches for probiotics:

Probiotics for Gastrointestinal Conditions: A Summary of the Evidence.
Wilkins T et al. Am Fam Physician. (2017)

Probiotic supplementation in sports and physical exercise: Does it present any ergogenic effect?
Coqueiro AY et al. Nutr Health. (2017)

Probiotics in Inflammatory Bowel Disease.
Abraham BP et al. Gastroenterol Clin North Am. (2017)

Switch to our new best match sort order

Sort by: Best match | Most recent

Results by year

Download CSV

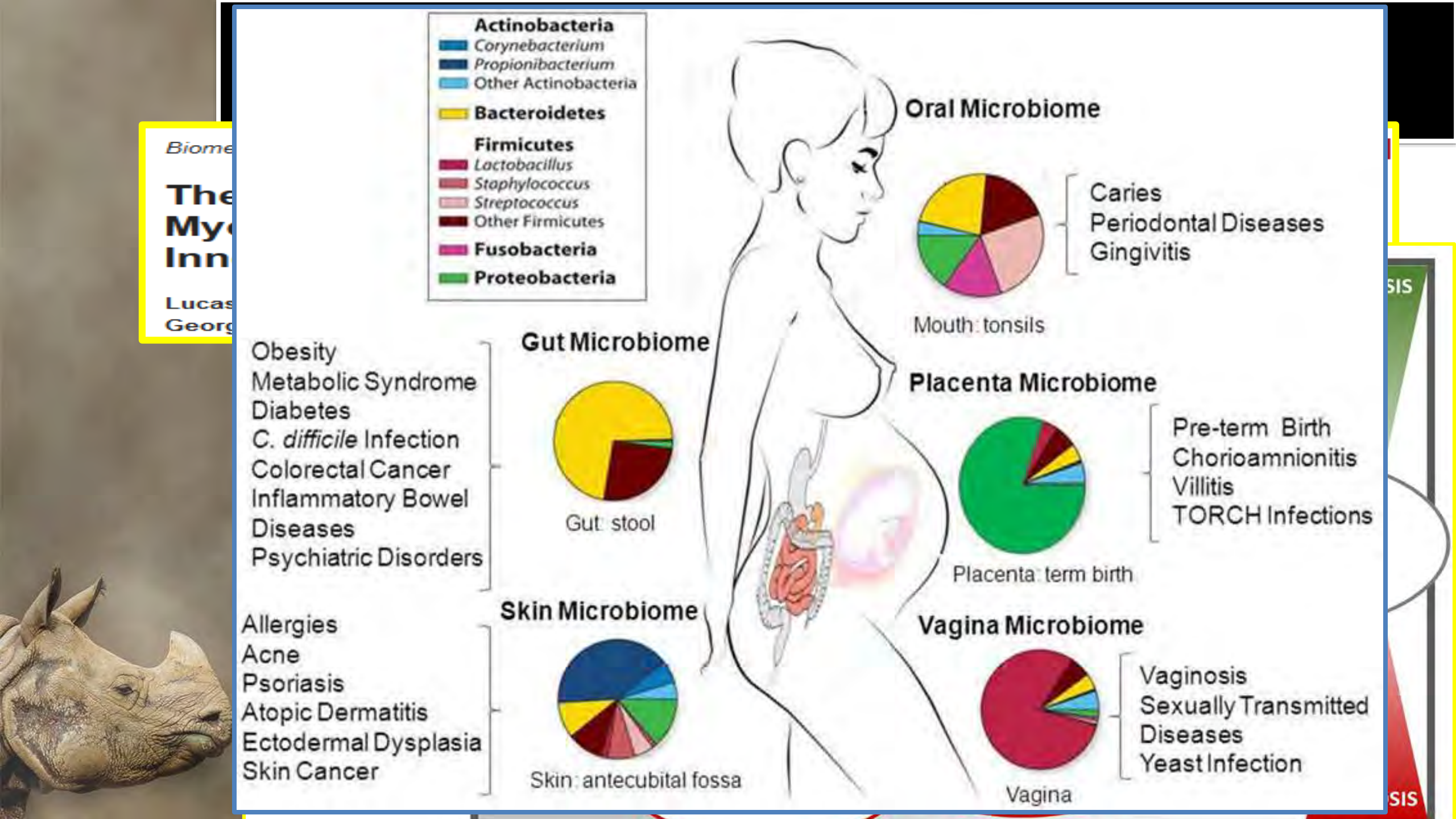
Search results

Items: 1 to 20 of 20672

<< First | < Prev | Page 1 of 1034 | Next > | Last >>

1. Effects of oral probiotic supplements on vaginal microbiota during pregnancy: a randomised, double-blind, placebo-controlled trial with microbiome analysis.
Husain S, Allotey J, Drymoussi Z, Wilks M, Fernandez-Felix BM, Whiley A, Dodds J, Thangaratinam S, McCourt C, Prosdocimi EM, Wade WG, de Tejada BM, Zamora J, Khan K, Millar M.
BJOG. 2019 Apr 1. doi: 10.1111/1471-0528.15675. [Epub ahead of print]
PMID: 30932317
Similar articles

Related searches
probiotics prebiotics
probiotics review
probiotics children
probiotics obesity
probiotics irritable bowel


Actinobacteria
Corynebacterium
Propionibacterium
Other Actinobacteria
Bacteroidetes
Firmicutes
Lactobacillus
Staphylococcus
Streptococcus
Other Firmicutes
Fusobacteria
Proteobacteria
Oral Microbiome
Caries
Periodontal Diseases
Gingivitis
Mouth: tonsils
Gut Microbiome
Obesity
Metabolic Syndrome
Diabetes
C. difficile Infection
Colorectal Cancer
Inflammatory Bowel Diseases
Psychiatric Disorders
Gut: stool
Placenta Microbiome
Pre-term Birth
Chorioamnionitis
Villitis
TORCH Infections
Placenta: term birth
Skin Microbiome
Allergies
Acne
Psoriasis
Atopic Dermatitis
Ectodermal Dysplasia
Skin Cancer
Skin: antecubital fossa
Vagina Microbiome
Vaginosis
Sexually Transmitted Diseases
Yeast Infection
Vagina

Probiotics and Dysbiosis- Reviews

Medicina Oral
Patología Oral
y Cirugía Bucal

Med Oral Patol Oral Cir Bucal. 2017 May; 22(3): e282–e288.
Published online 2017 Apr 8. doi: 10.4317/medoral.21494

PMCID: PMC5432076
PMID: 28390121

Probiotics and oral health: A systematic review

Maria Seminario-Amez,[1] Jose López-López,[2] Albert Estrugo-Devesa,[2] Raul Ayuso-Montero,[3] and Enric Jané-Salas[2]

Fifteen articles were considered for this review. Of which, 12 were RCTs of good / high quality (Jadad scale), two meta-analysis and one systematic review.

The literature reviewed suggests probiotics usage could be beneficial for the maintenance of oral health, due to its ability to decrease the colony forming units (CFU) counts of the oral pathogens. However, randomized clinical trials with long-term follow-up periods are needed to confirm their efficacy in reducing the prevalence/incidence of oral infectious diseases.

Periodont… …atic

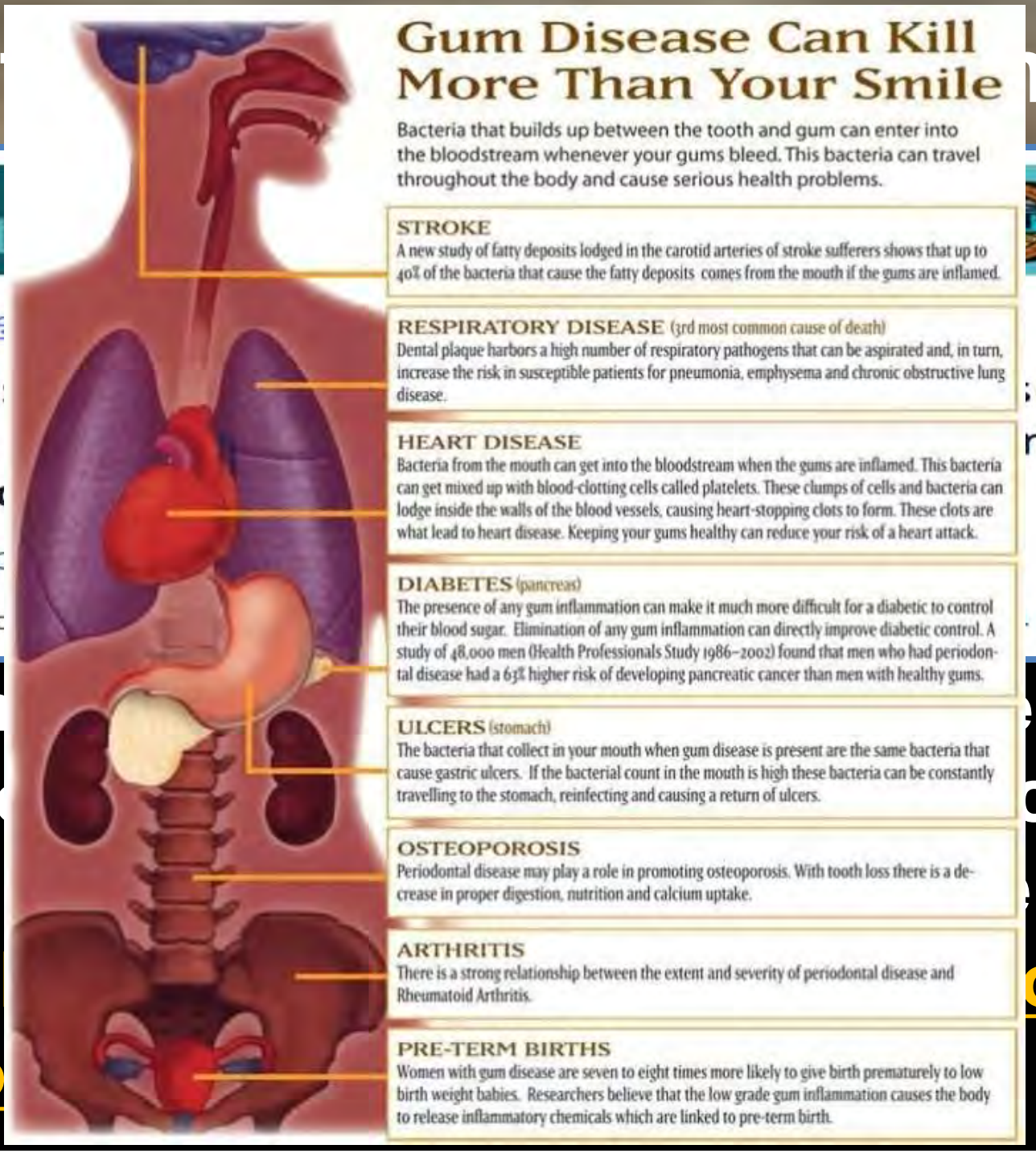
JOURNAL OF Periodont…

ORIGINAL ARTICLE

Periodontal di… …set of systemic comorbidities … …n 18-year retrospective …

Dan Zhao, Zhe Zhen, …

First published: 08 Octo…



Gum Disease Can Kill More Than Your Smile

Bacteria that builds up between the tooth and gum can enter into the bloodstream whenever your gums bleed. This bacteria can travel throughout the body and cause serious health problems.

STROKE
A new study of fatty deposits lodged in the carotid arteries of stroke sufferers shows that up to 40% of the bacteria that cause the fatty deposits comes from the mouth if the gums are inflamed.

RESPIRATORY DISEASE (3rd most common cause of death)
Dental plaque harbors a high number of respiratory pathogens that can be aspirated and, in turn, increase the risk in susceptible patients for pneumonia, emphysema and chronic obstructive lung disease.

HEART DISEASE
Bacteria from the mouth can get into the bloodstream when the gums are inflamed. This bacteria can get mixed up with blood-clotting cells called platelets. These clumps of cells and bacteria can lodge inside the walls of the blood vessels, causing heart-stopping clots to form. These clots are what lead to heart disease. Keeping your gums healthy can reduce your risk of a heart attack.

DIABETES (pancreas)
The presence of any gum inflammation can make it much more difficult for a diabetic to control their blood sugar. Elimination of any gum inflammation can directly improve diabetic control. A study of 48,000 men (Health Professionals Study 1986–2002) found that men who had periodontal disease had a 63% higher risk of developing pancreatic cancer than men with healthy gums.

ULCERS (stomach)
The bacteria that collect in your mouth when gum disease is present are the same bacteria that cause gastric ulcers. If the bacterial count in the mouth is high these bacteria can be constantly travelling to the stomach, reinfecting and causing a return of ulcers.

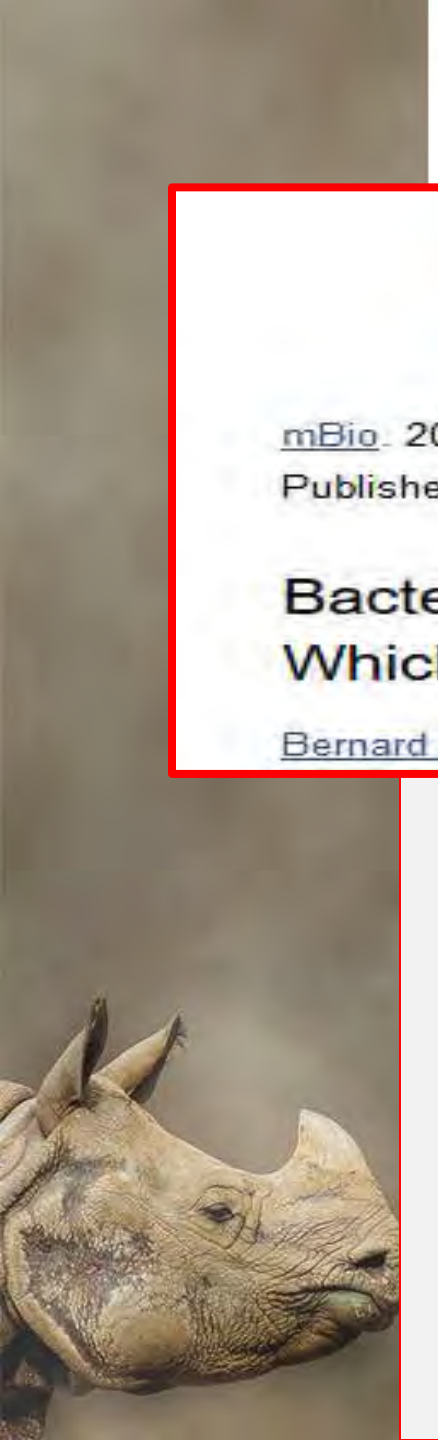
OSTEOPOROSIS
Periodontal disease may play a role in promoting osteoporosis. With tooth loss there is a decrease in proper digestion, nutrition and calcium uptake.

ARTHRITIS
There is a strong relationship between the extent and severity of periodontal disease and Rheumatoid Arthritis.

PRE-TERM BIRTHS
Women with gum disease are seven to eight times more likely to give birth prematurely to low birth weight babies. Researchers believe that the low grade gum inflammation causes the body to release inflammatory chemicals which are linked to pre-term birth.

Within the lim… …ective cohort study, our fin… …ce that **periodontal** … …e extent reflects the … **of common systemic co…**

Bacteria in Carotid Artery Plaque



mBio. 2014 May-Jun; 5(
Published online 2014 Ju

Bacteria Prese
Which May Cor

Bernard B. Lanter, Karin

Atheroscle
within arter
of peripher
s. Emergin
may play a

atheros
were a
eubacte

Probiotics and *P. gingivalis*

Journal of
PERIODONTAL RESEARCH

ORIGINAL ARTICLE

Probiotics alter the immune response of gingival epithelial cells challenged by *Porphyromonas gingivalis*

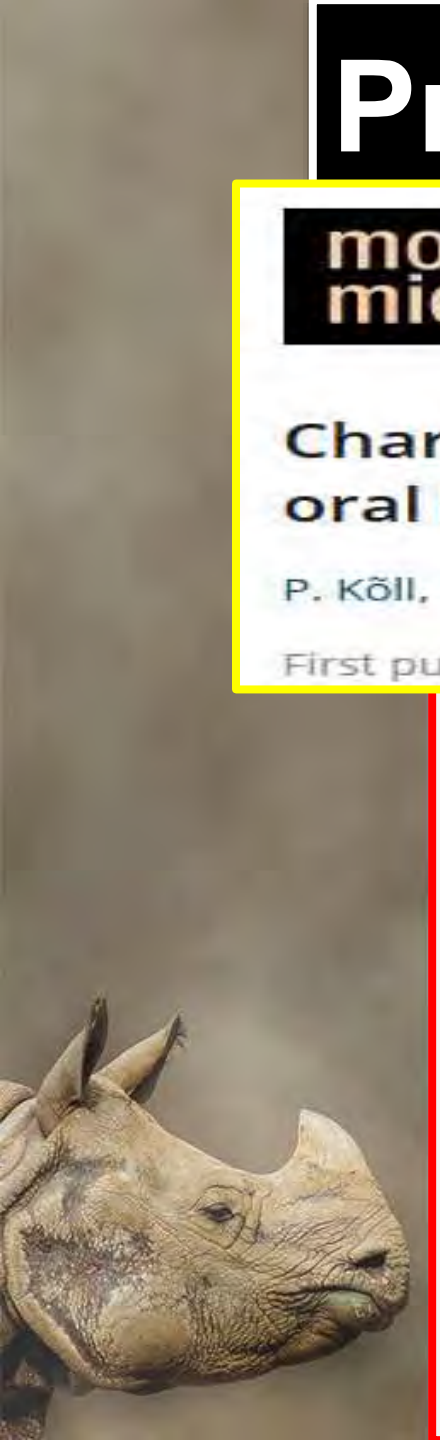
Emmanuel Albuquerque-Souza, Danilo Balzarini, Ellen S. Ando-Suguimoto, Karin H. Ishikawa, Maria R. L. Simionato, Marinella Holzhausen, Marcia P. A. Mayer

First published: 04 October 2018 | https://doi.org/10.1111/jre.12608

Probiotics reduce the adherence of ***P. gingivalis***, the leakage and the systemic effects of periodontal disease!

periodontitis.

Probiotics and *P. gingivalis*



molecular oral microbiology

Characterization
oral health

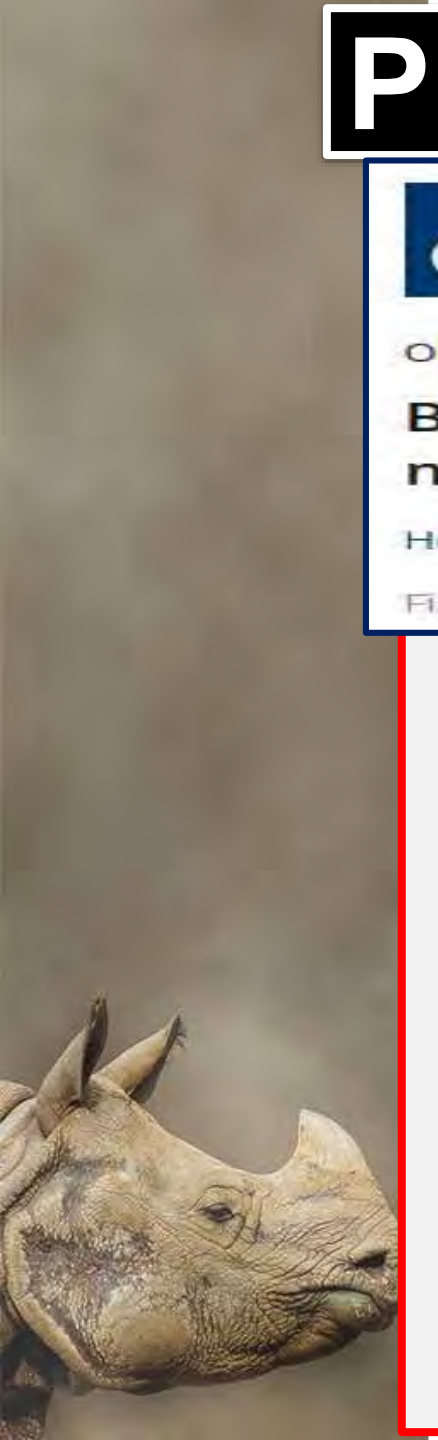
P. Kõll, R. Mändar, H. Marco

First published: 12 February

Incredibly important!

The study
lactobacilli of 10 species, isolated from healthy humans. The majority of strains suppressed the growth of *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Prevotella intermedia*, and *Streptococcus mutans*.

Probiotics and *P. gingivalis*



European Journal of Oral Sciences

Original Article

Bifidobacteria inhibit the growth of *Porphyromonas gingivalis* but not of *Streptococcus mutans* in an in vitro biofilm model

Heli Jäsberg, Eva Söderling, Akihito Endo, David Beighton, Anna Haukioja

First published: 06 April 2016 | https://doi.org/10.1111/eos.12266 | Cited by: 5

All bifidobacteria integrated well into the subgingival biofilms composed of *Porphyromonas gingivalis*, *Actinomyces naeslundii*, and *Fusobacterium nucleatum* and decreased significantly only the number of *P. gingivalis* in the biofilms. The integration of bifidobacteria into the supragingival biofilms containing *Streptococcus mutans* and *A. naeslundii* was less efficient, and bifidobacteria did not affect the number of S. mutans in biofilms.

Alzheimer's and *P. gingivalis*

Oral infections with P. gingivalis- A.D.

Journal of Oral Microbiology

Taylor & Francis
Taylor & Francis Group

J Oral Microbiol. 2019; 11(1): 1563405.
Published online 2019 Jan 29. doi: 10.1080/20002297.2018.1563405

PMCID: PMC6352933
PMID: 30728914

Assessi… determi…

Sim K. Singh

How about antibiotics?

Oral infections with Porphyromonas gingivalis, or introduction of its lipopolysaccharide (LPS), in various mouse models has **demonstrated the development of key neuropathological hallmark lesions defining AD. These are extracellular amyloid-beta plaques, phosphorylated tau, neurofibrillary tangles, widespread acute and chronic inflammation, blood–brain barrier defects** together with the clinical phenotype showing impaired learning and spatial memory. Live P. gingivalis and its LPS (commercial or from 'microbullets') are powerful peripheral and intracerebral inflammatory signaling initiators, and this has direct implications on memory and lesion development.

Obesity and Cancer

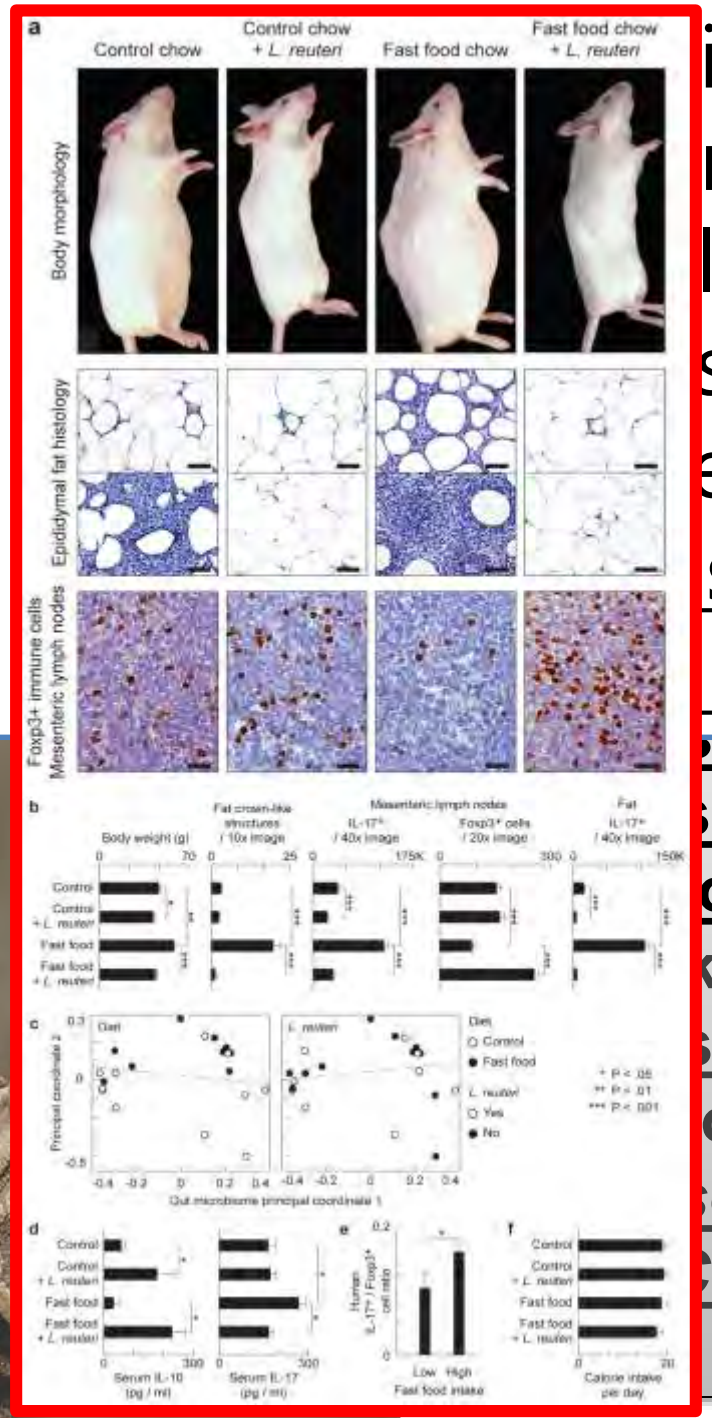
Cancer Epidemiology, Biomarkers & Prevention

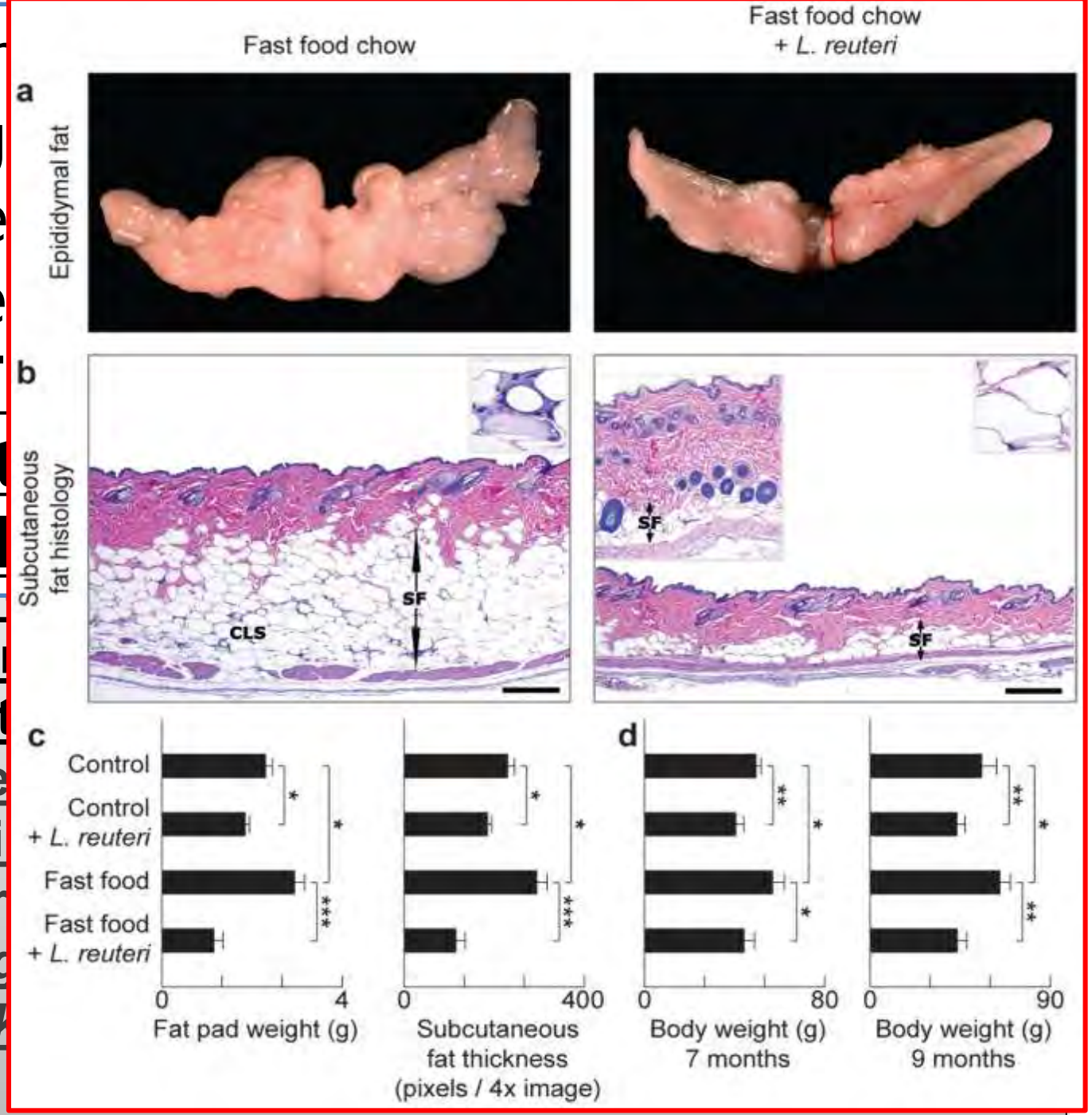
Obesity and Risk for Second Malignant Neoplasms in Childhood Cancer Survivors: A Case–Control Study Utilizing the California Cancer Registry

Diana J. Moke, Ann S. Hamilton, Leena Chehab, Dennis Deapen, and David R. Freyer

Obesity is a known modifiable risk factor associated with adverse outcomes in children with cancer. We sought to determine whether obesity during childhood cancer treatment increases risk for second malignant neoplasms (SMN). **There was a significantly increased risk for SMN among patients who were obese at both diagnosis and EOT [aOR, 4.44 (1.37–14.34)].** This study suggests that obesity during childhood cancer treatment may be associated with increased risk for SMNs, particularly among those obese throughout therapy.

iscovered th
nt to chang
le and pre
sociated we
eline diet. T
sferable int
CD4+ T cel
sed immunity a
ominal fat wit
king contrast, e
stern chow inhi
o test whether
en fat patholog
CC 6475 in drink





Perio and Probiotics

Journal of
PERIODONTAL RESEARCH

Original Article

Topical treatment with probiotic *Lactobacillus brevis* CD2 inhibits experimental periodontal inflammation and bone loss

T. Maekawa, G. Hajishengallis

- Mice topically treated **with L. brevis CD2 displayed significantly decreased bone loss and lower expression of tumor necrosis factor, and interleukin-1β, -6 and -17A as compared to placebo-treated mice.** Moreover, L. brevis CD2-treated mice displayed lower counts of anaerobic bacteria but higher counts of aerobic bacteria than placebo-treated mice.

frontiers in Microbiology

Front Microbiol. 2018; 9: 2976.
Published online 2018 Dec 21. doi: 10.3389/fmicb.2018.02976
PMCID: PMC6308121
PMID: 30619112

Bacteroides fragilis Prevents *Clostridium difficile* Infection in a Mouse

- The ov
  comm
  disrupt
  difficile
  protect
  microb
  epithel

Literally **hundreds of studies have demonstrated that probiotics protect** all of us from disease! Published in all the top journals!

Quigley ? et al. *Clinical and Transl*
DOI 10.1038/s41424-018-0057-9

CORRESPONDE

'Brain Foggi Probiotics A

Eamonn M. M. Quigley MD

The problems with this pa
conflate two separate ent
overgrowth (SIBO), ar
pathogenesis of their pat
be made clear that many
the biochemical machine
gases. The authors
Bifidobacterium) pr

Is Yogurt A Health Food or a Junk Food?

Dannon Light & Fit Greek Nonfat Yogurt Blueberry*:
Cultured Grade A Nonfat Milk**, Water, Blueberry Puree, Fructose**, Modified Corn Starch**, Natural Flavor, Carmine, Sucralose, Malic Acid**, Potassium Sorbate, Acesulfame Potassium, Sodium Citrate**.
*this yogurt is not organic
**ingredient may be derived from or produced with GMOs

Yoplait Light Red Raspberry Yogurt*:
Cultured Grade A Nonfat Milk**, Raspberries, Modified Corn Starch**, Sugar**, Kosher Gelatin, Citric Acid**, Tricalcium Phosphate, Natural Flavor**, Potassium Sorbate, Acesulfame Potassium, Sucralose, Red #40, Vitamin A Acetate***, Vitamin D3***.
*this yogurt is not organic
**ingredient may be derived from or produced with GMOs
***synthetic vitamins

Activa Greek Orchard Peach Yogurt*:
Cultured Grade A Nonfat Milk**, Peaches, Sugar**, Fructose**, Water, Modified Corn Starch**, Natural Flavor**, Pectin, Fruit Juice and Vegetable Juice (for color)**, Carrageenan, Sodium Citrate**, Lactic Acid**, Vitamin D3***, Calcium Citrate**.
*this yogurt is not organic
**ingredient may be derived from or produced with GMOs
***synthetic vitamin

More info at FOODBABE.COM

- **This**

that were NOT covered, Fake News?? 30 experimental subjects- sick, 8 controls..

Mouthrinse

Journal of International Society of Preventive & Community Dentistry

JISPCD

J Int Soc Prev Community Dent. 2015 May; 5(Suppl 1): S44–S48.
doi: 10.4103/2231-0762.156153

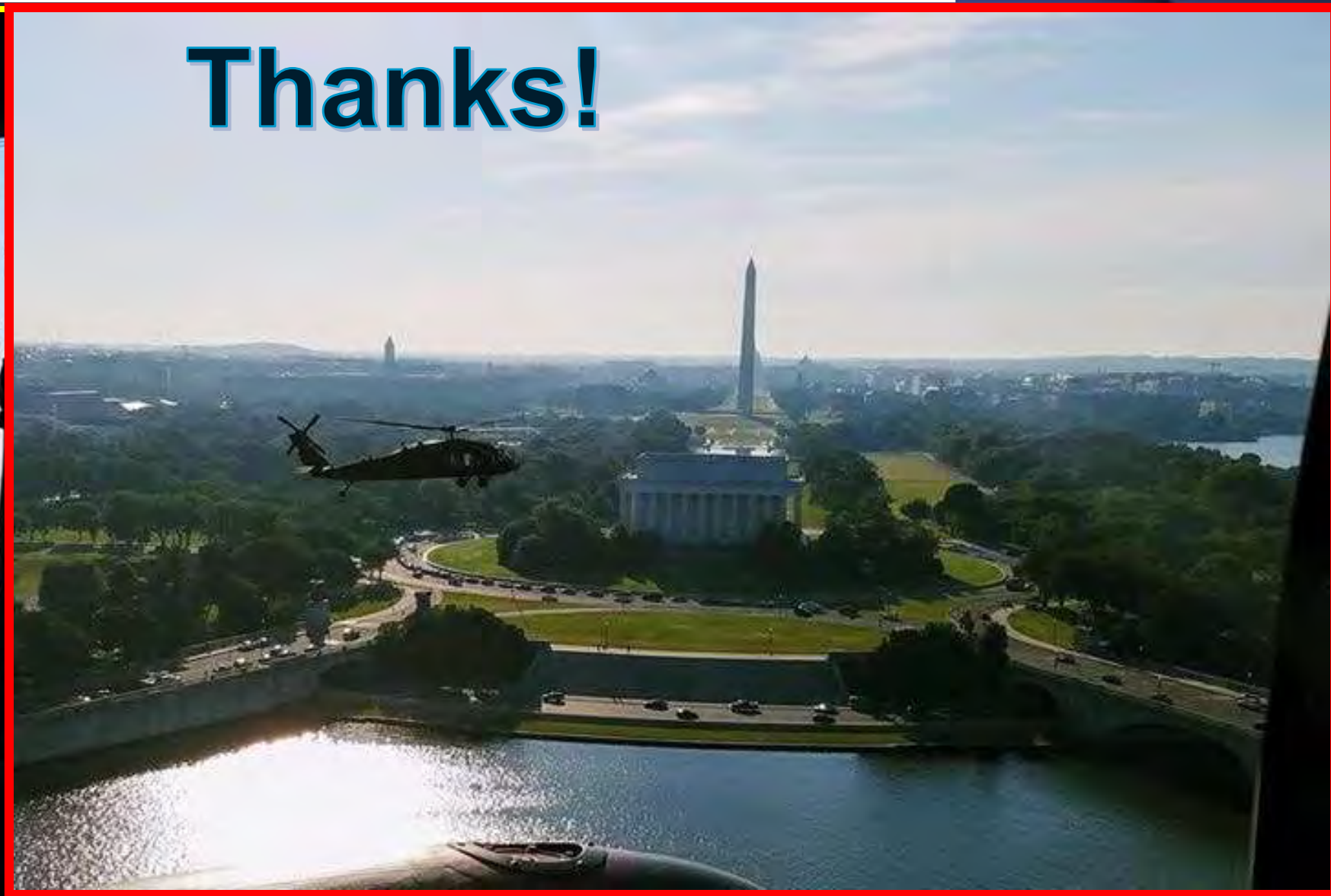
Effectiveness of probiotic, chlorhexidine and fluorid
Streptococcus mutans – Randomized, single-blind,

Chlorhexidine, sodium fluoride, and probiotic m
reduce plaque S. mutans levels. Probiotic mout
effective and equivalent to chlorhexidine and s
fluoride mouthwashes. Thus, probiotic mouthw
be considered as an effective oral hygiene regin

sodium fluoride mouthwash, and group 4- 10 ml of prob

- The ana
  were na
  and 68

Chris- back home…. Yay!!



Reading Materials:

LUPINE PUBLISHERS
https://www.lupinepublishers.com/index.php

Interventions in Pediatric Dentistry Open Access Journal

DOI: 10.32474/IPDOAJ.2019.03.000158

ISSN: 2637-6636

Review Article

Pediatric Oral Systemic Health: From Fetus to Adolescence

Mark Cannon* and John Peldyak

Division of Dentistry, Department of Clinical Otolaryngology, Northwestern University, Chicago, IL, USA

***Corresponding author:** Mark Cannon, Division of Dentistry, Department of Clinical Otolaryngology, Northwestern University, Chicago, IL, USA

Reading Materials:

https://doi.org/10.33805/2572-6978.123
Volume 3 Issue 1 | PDF 123 | Page 6

D:\Edelweiss Documentation\logos\Logo\CompanyLogo_EdelweissPublications.png

EDELWEISS PUBLICATIONS
OPEN ACCESS

Dental Research and Management

Review Article

ISSN 2572-6978

The Prevention and Treatment of Neural Arterial Gingival Simplex

Cannon L Mark[1*] and Peldyak N John[2]

Affiliation

[1]Division of Dentistry, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA

[2]Dentistry practitioner in Mt. Pleasant, Michigan, USA

[*]**Corresponding author:** Mark L Cannon, Professor, Division of Dentistry, Department of Otolaryngology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA, Tel: 847-899-6720, E-mail: drmarkcannon@outlook.com

ARM & HAMMER
ADULT TOOTHBRUSH KIT
17 99
palsrewards
Buy 1, Get the 2nd for 50% Off!
Arm and Hammer Dental Care
Solutions for Dogs

SOURI
RMY

Learn m

A Lot More!

Thanks