



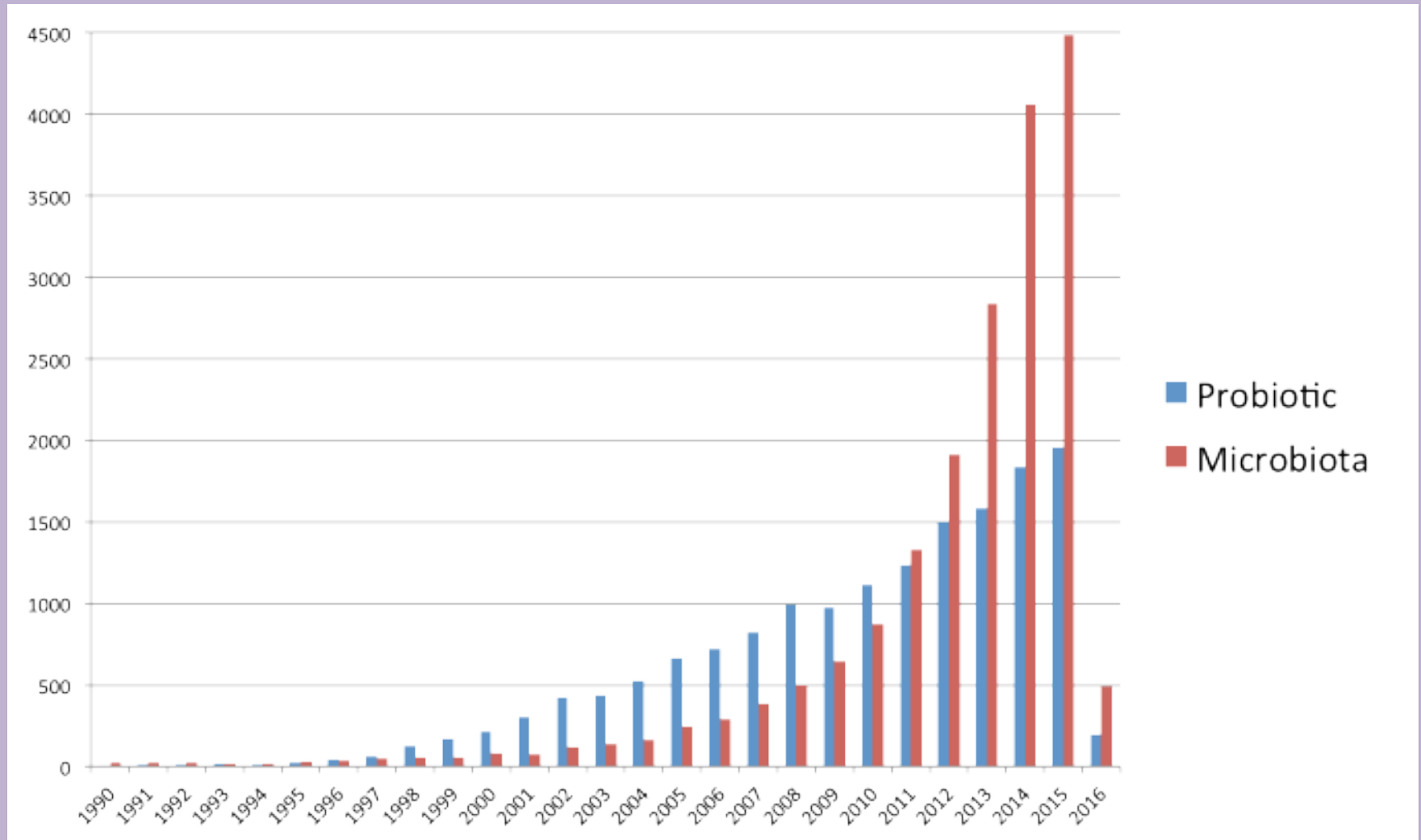
İNTESTİNAL MİKROBİYOTA 2016 VE ROMATOLOJİK HASTALIKLAR

Prof. Dr. Ener Çağrı DİNLEYİCİ
Eskişehir Osmangazi Üniversitesi Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları Anabilim Dalı
26 Mart 2016, Antalya

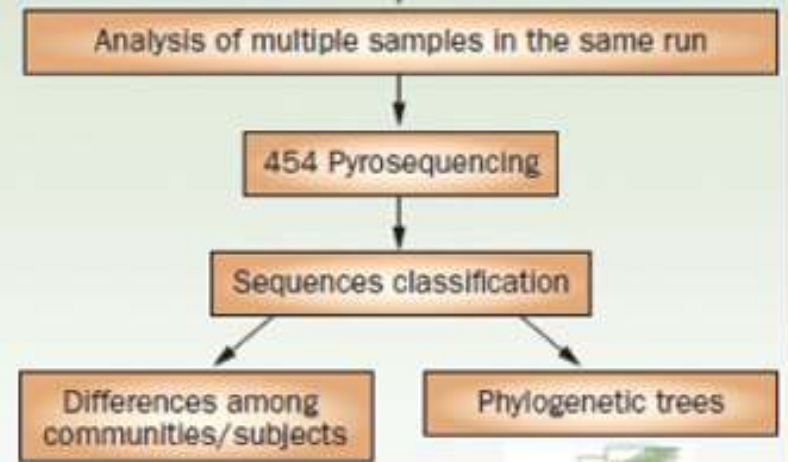
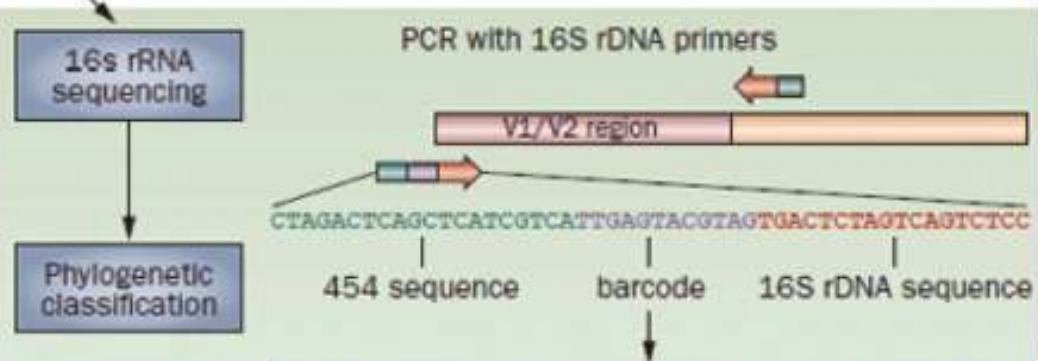
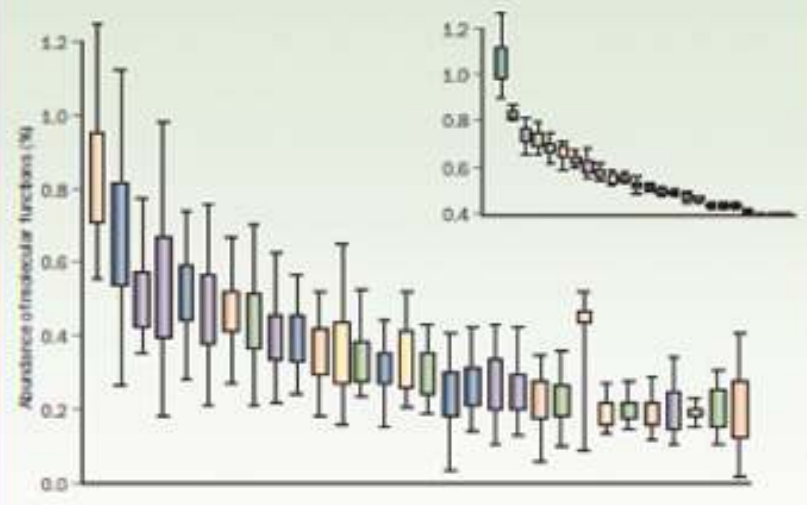
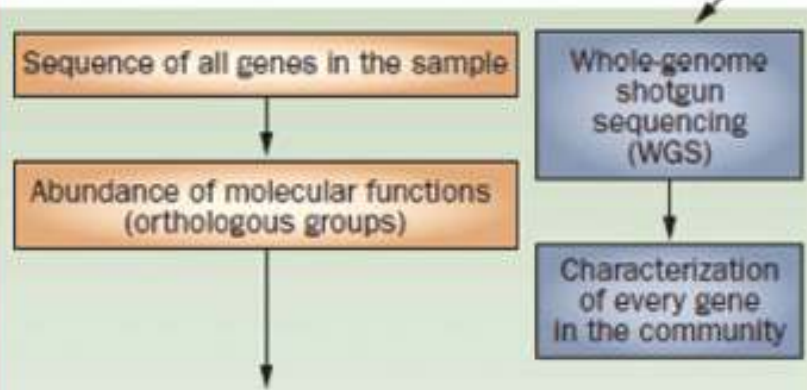
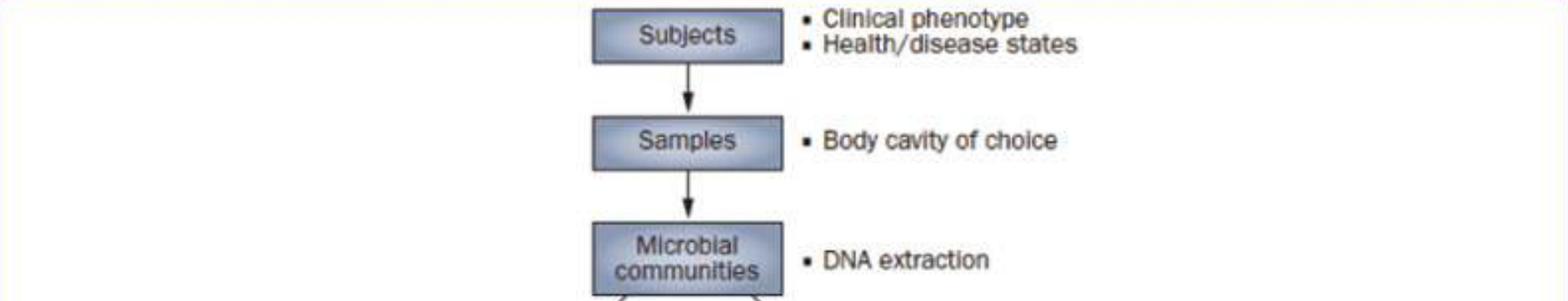




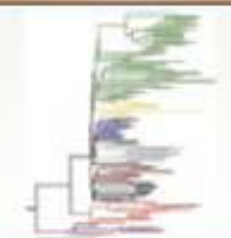
PROBİYOTİK/MİKROBİYOTA PubMed







| | |
|---------|-----------------------|
| Phylum | Firmicutes |
| Class | Bacilli |
| Order | Lactobacillales |
| Family | Lactobacillaceae |
| Genus | <i>Lactobacillus</i> |
| Species | <i>L. acidophilus</i> |



Bacteria to Human cells ratio (B/H) is based on one historical back-of-the-envelope estimate

PNAS, 2010: "With the greatest quantity and diversity found in the lower gastrointestinal tract (Nature, 2007). **One-hundred trillion bacteria** representing hundreds of species"

Nature, 2007: "The microbes that live inside and on us (the microbiota) **outnumber our somatic and germ cells by an estimated 10-fold...**(Science, 2006)"

Science, 2006: "Our body surfaces are home to microbial communities whose aggregate membership outnumbers our human somatic and germ cells by **at least an order of magnitude...** (Science, 2005)"

Wikipedia (Human microbiome): "...Bacterial cells are much smaller than human cells, **and there are at least ten times as many bacteria as human cells in the body** (approximately 10^{14} versus 10^{13}) (Savage, 1977, Berg, 1996)"

Trends Microbiol., 1996: "In summary, there are **ten viable indigenous bacteria in the GI tract for every cell in the human body:** 10^{14} total GI bacteria compared with 10^{13} total cells making up the human body (Savage, 1977)"

Science, 2005: "The adult human intestine is home to an almost inconceivable number of microorganisms. The size of the population - up to 100 trillion... and is **~10 times greater than the total number of our somatic and germ cells** (Savage, 1977)"

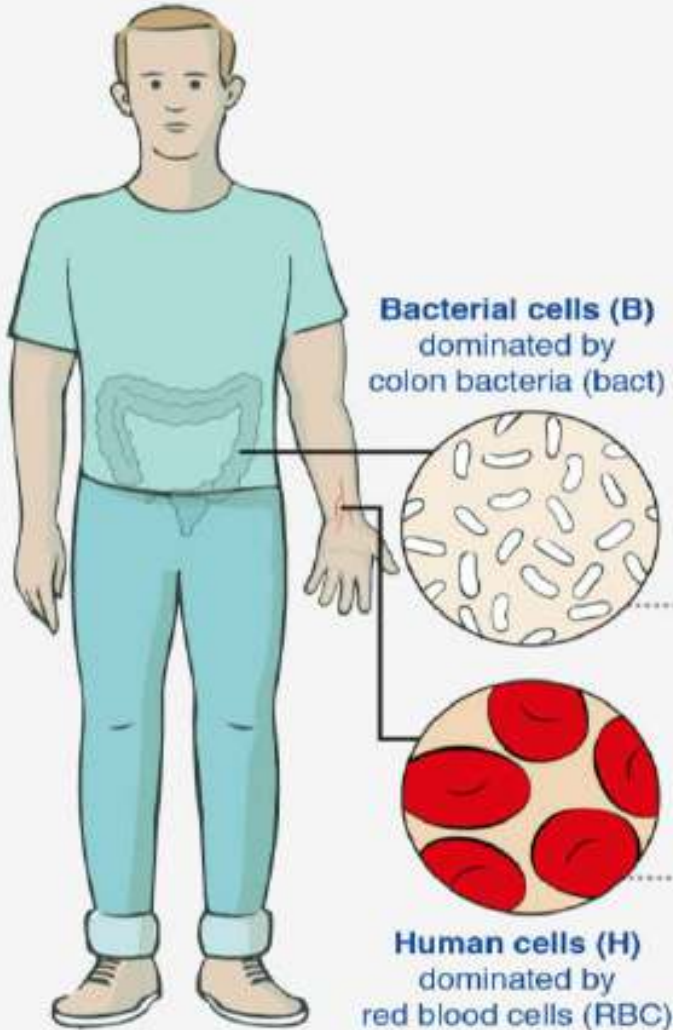
Savage, Annu. Rev. Microbiol., 1977

"The adult human organism is said to be composed of approximately 10^{13} eukaryotic animal cells (Dobzhansky, 1971)... The various body surfaces and the gastro intestinal canals of human may be colonized by as many as 10^{14} indigenous prokaryotic and eukaryotic microbial cells (Luckey, 1972)... From another point of view, therefore, **the normal human organism can be said to be composed of over 10^{14} cells, of which only about 10% are animal cells.**"

Luckey, Am. J. Clin. Nutr., 1972

"Adult man carries 10^{12} microbes associated with his epidermis and **10^{14} microbes** in his alimentary tract (Fig.1). The latter number is **based upon 10^{11} microbes/g contents of an alimentary tract with a capacity of approximately 1 liter.**"

İNTESTİNAL MİKROBİYOTA



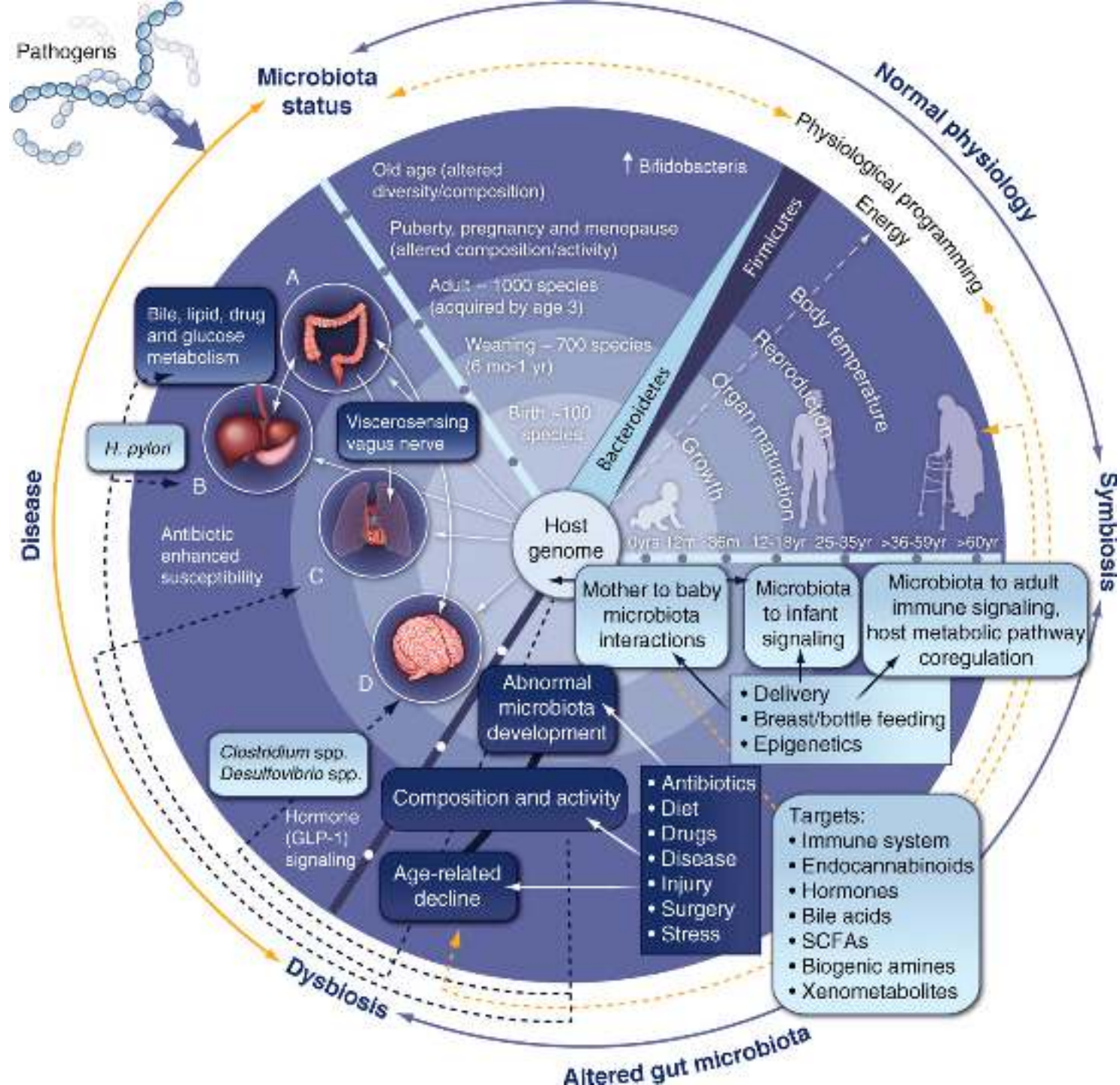
1972 estimate (Luckey, Am. J. Clin. Nutr.)

used all gastrointestinal (GI) tract volume

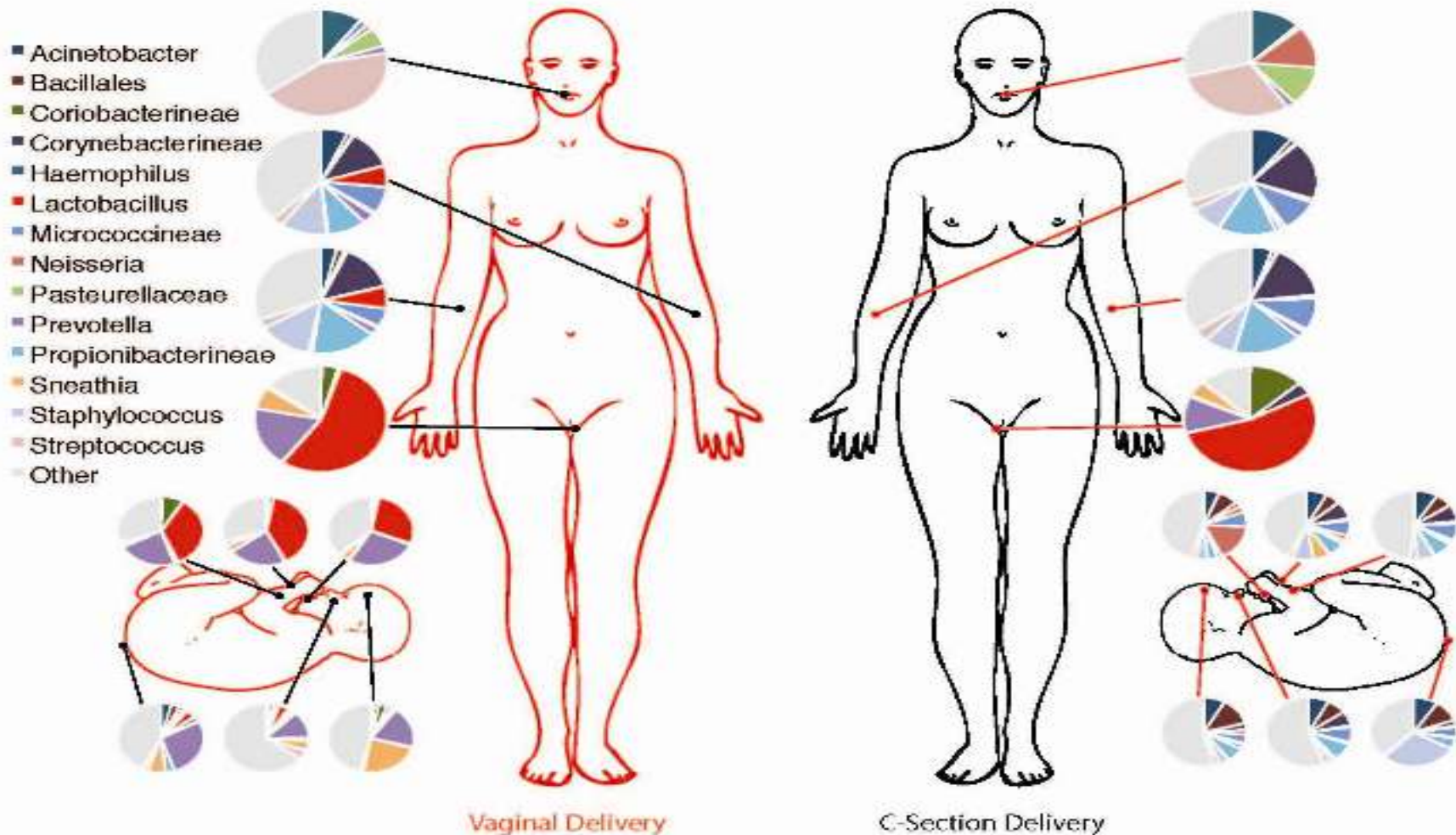
$$\frac{B}{H} = \frac{(V_{GI} \sim 1L) \times (n_{bact} \sim 10^{14} \text{ cells/L})}{\sim 10^{13} \text{ no primary reference}} \approx 10$$

2015 estimate (Current study)

$$\frac{B}{H} = \frac{(V_{colon} \approx 0.4L) \times (n_{bact} \approx 10^{14} \text{ cells/L})}{(V_{blood} \approx 5L) \times (n_{RBC} \approx 5 \times 10^{12} \text{ cells/L})} \approx 1$$



İNTESTİNAL MİKROBİYOTA



İNTESTİNAL MİKROBİYOTA

Mother



Vaginally born/Breast feed

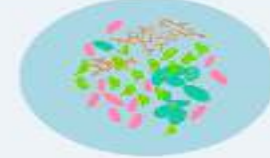


Vaginally born/Bottle feed

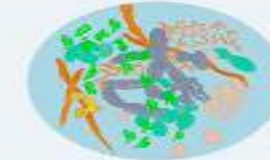
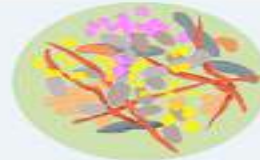


C-section

4 days



4 month

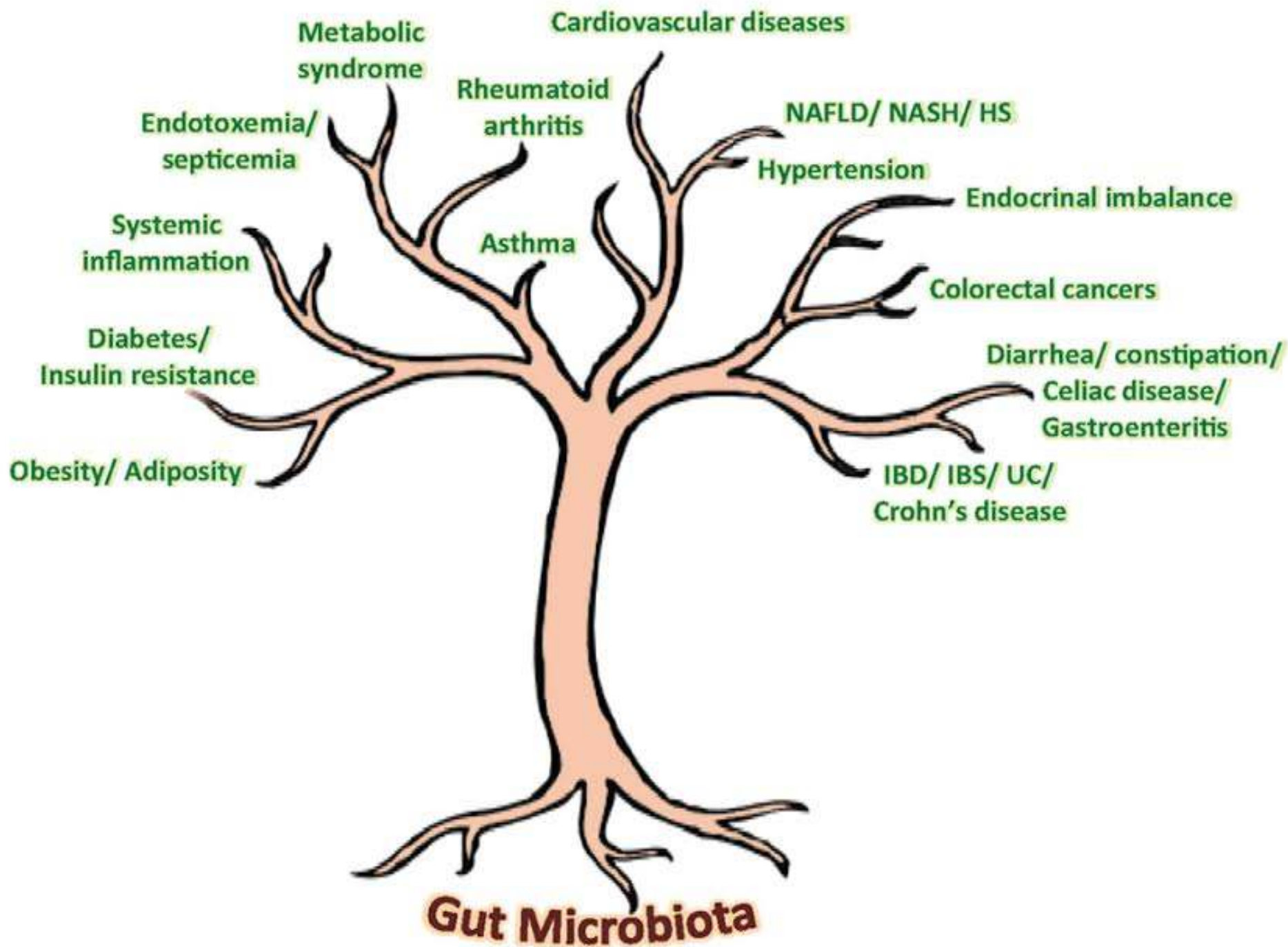


12 month



"Anne st;
fakirin ocuęunu
malntrisyondan,
zenginin ocuęunu
obeziteden
korur.."

Dr.House



DISBIYOSIS



İNTESTİNAL MİKROBİYOTA

Obesite-Diabetes 2016

- *Faecalibacterium*
- *Bifidobacterium,*
- *Lactobacillus,*
- *Coprococcus,*
- *Methanobrevibacter*

OBESİTE ilişkili durumlar ve kardiyovasküler hastalıkların sıklığında azalma sağladığı gösterilmiş.

Mezenterik viseral yağ dokuda bakteri DNA örnekleri saptanmış

(omentum ve diğer viseral adipoz doku örneklerinde yok)

RALSTONIA PICKETTI

Gram negatif çomak, proteobakter

RALSTONIA PICKETTI

- 1- Viseral dokuda *R. picketti* yükü ile sistemik inflamasyon arasında pozitif korelasyon mevcut
- 2- Fecal *R. picketti* düzeyi ile insülin rezistansı olduğu gösterilmiş.
- 3- Deneysel çalışmada 4 hafta süre ile oral *R. picketti* içeren gavaj alan ratlarda kilo alımının olduğu, OGTT'nin bozulduğu gösterilmiş.
- 4- *R. picketti* için geliştirilmiş AŞI uygulanan ratlarda insülin rezistansı gelişiminde azalma!!

EUBACTERIUM HALLII

- 1- Bağırsak mikrobiyotasından elde edilmiş yeni bir probiyotik ?
- 2- Deneysel çalışmada 8 hafta süre ile E. hallii verilmesinin insülin sensitivitesi üzerine olumlu etkisinin olduğu gösterilmiş.
- 3- Kısa zincirli yağ asitleri ve fekal mikrobiyota üzerine olumlu etkileri gösterilmiş.

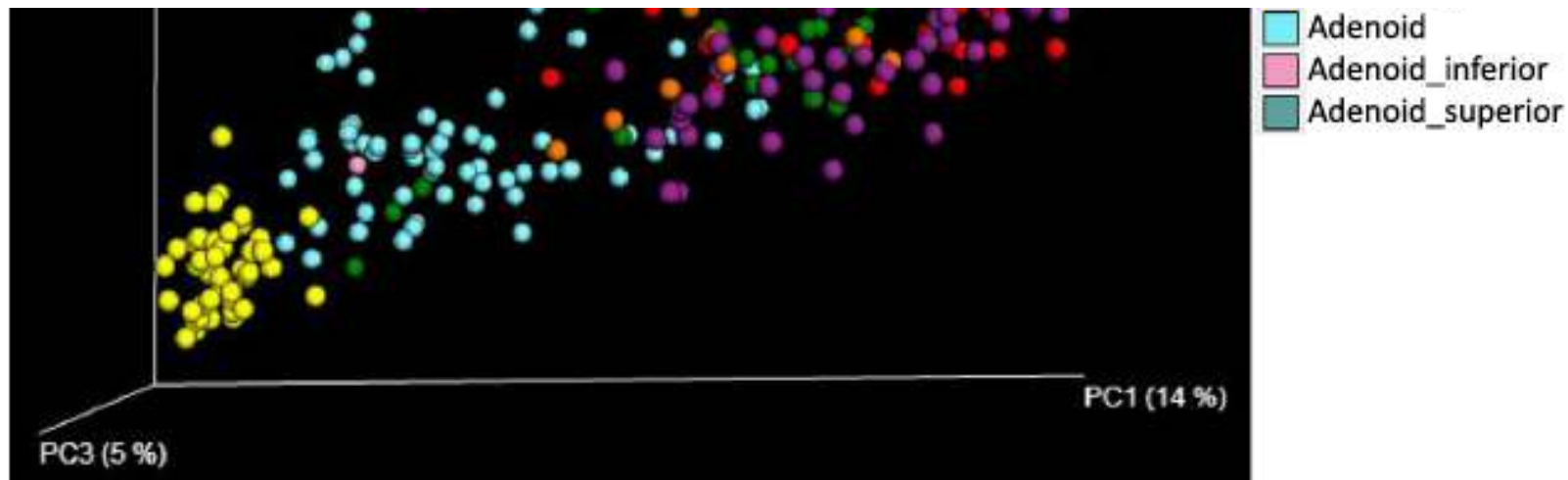
2014'de Faz 1 ve 2 çalışmalarına başlandı

The Infant Nose

Introducing the Respiratory Tract to the World

The Nasopharyngeal Microbiota: An Important Window of Opportunity

American Journal of Respiratory and Critical Care Medicine Volume 190 Number 3 | August 1 2014



Unraveling the Influence of Gut Microbes on the Mind

5 May 2015

M. J. Friedrich

JAMA[®]
The Journal of the American Medical Association



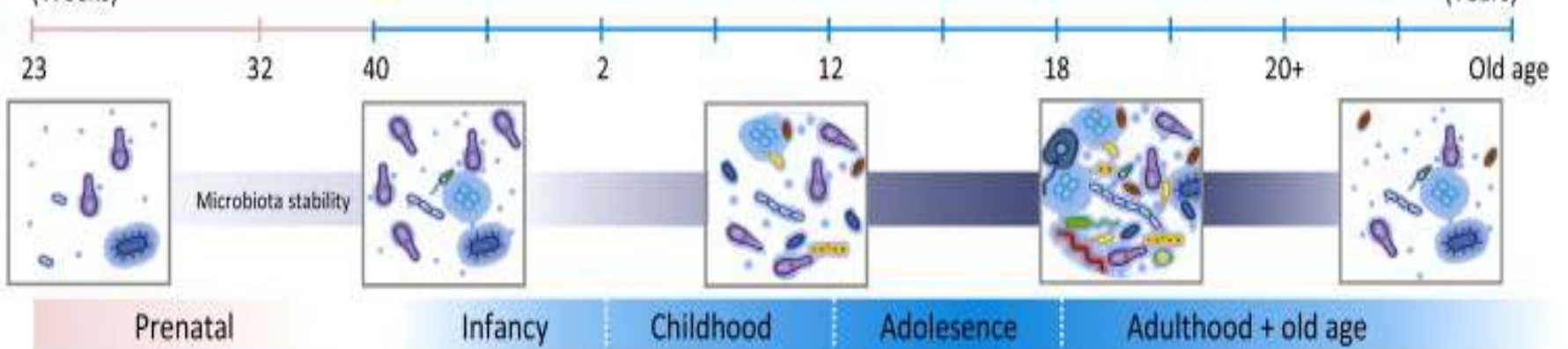
THE DAILY BEAST



David Perlmutter, MD

The Cure for Brain Diseases Is in Your Gut

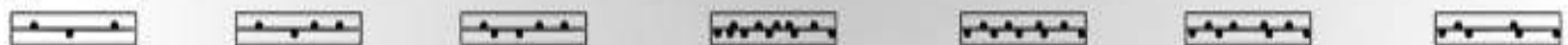
28 April 2015



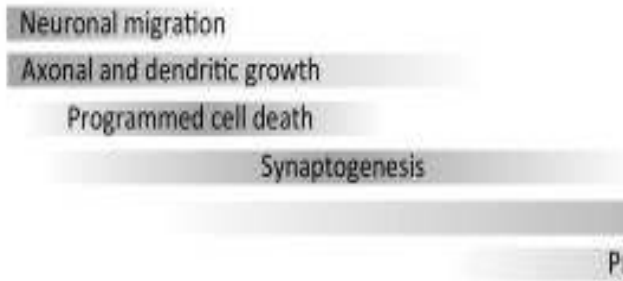
Neuronal complexity through the lifespan



Synaptic density



Stages of brain development



Age of onset of mental disorders



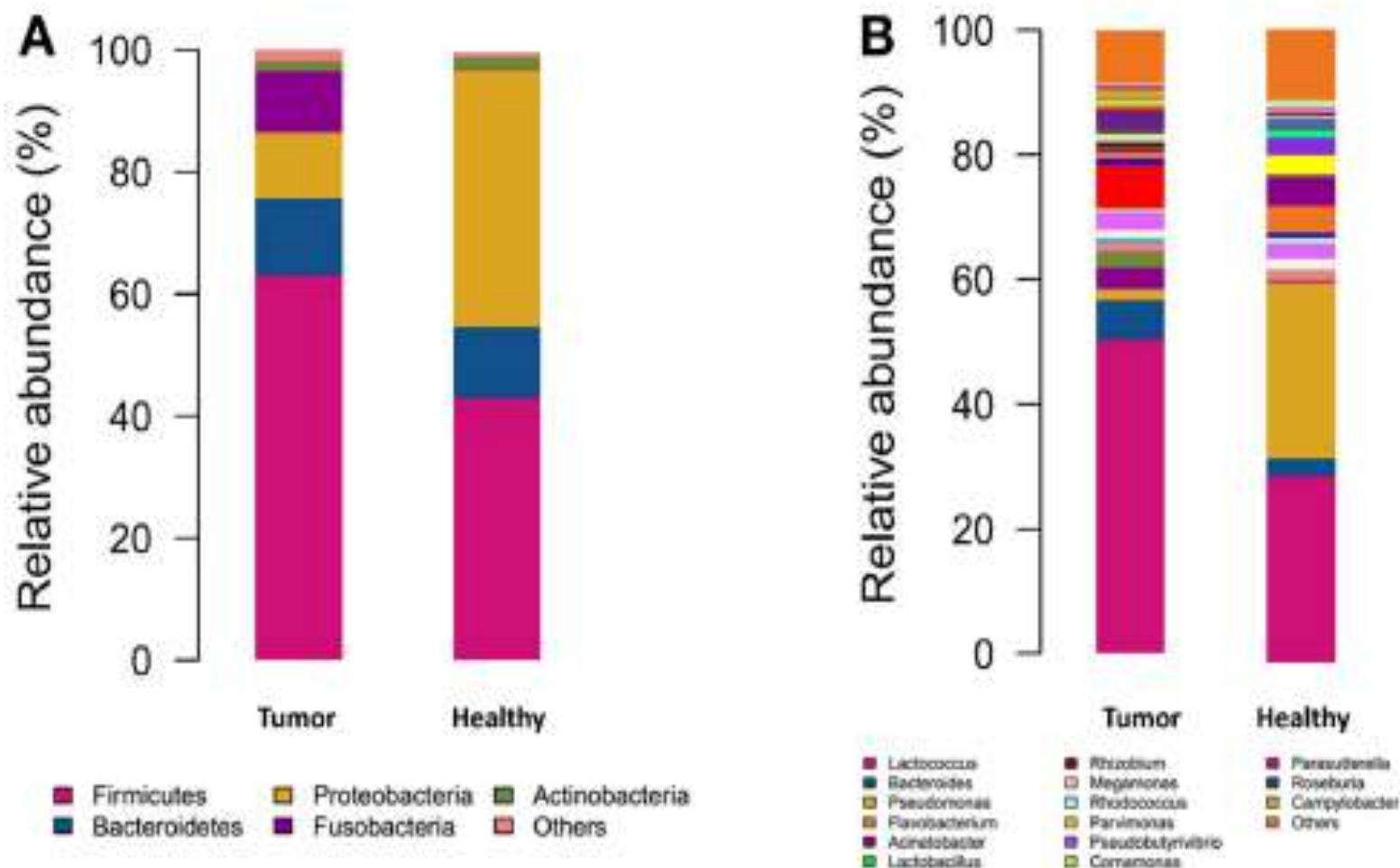
ÖYLE GÜZEL İÇİME
ATARIM KI
KENDİNİ YIRTSA
RUHU DUYMAZ
SEBASTIAN @SoyleSebastian
■■■



Microbiota disbiosis is associated with colorectal cancer

Zhiguang Gao[†], Bomin Guo[†], Renyuan Gao[†], Qingchao Zhu and Huanlong Qin^{*}

Department of General Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China

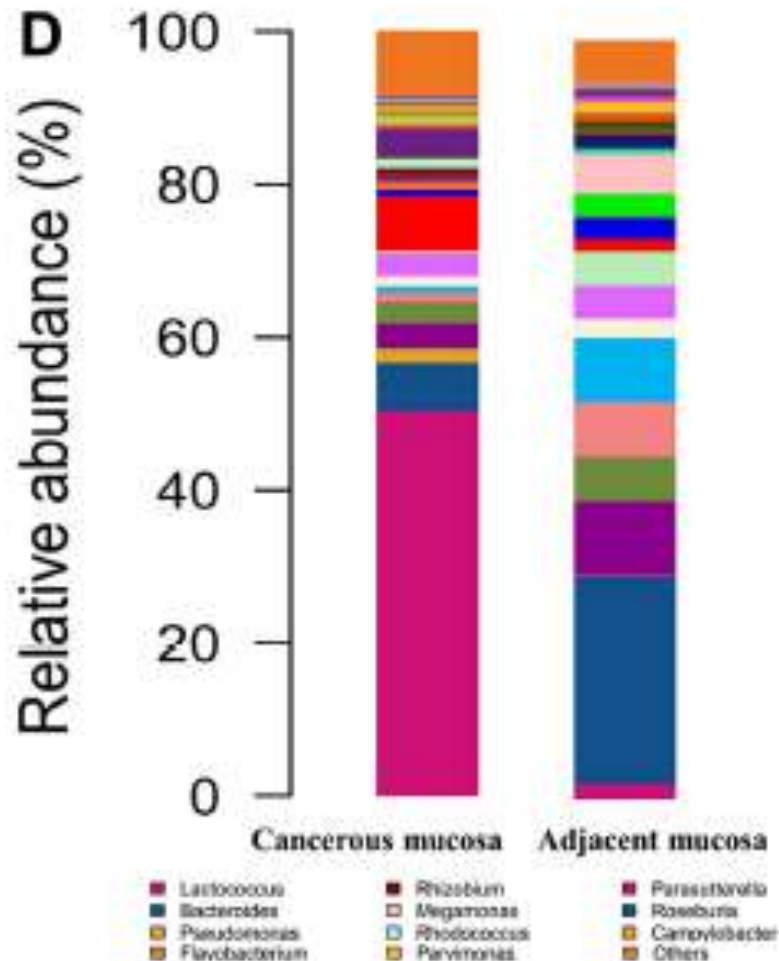
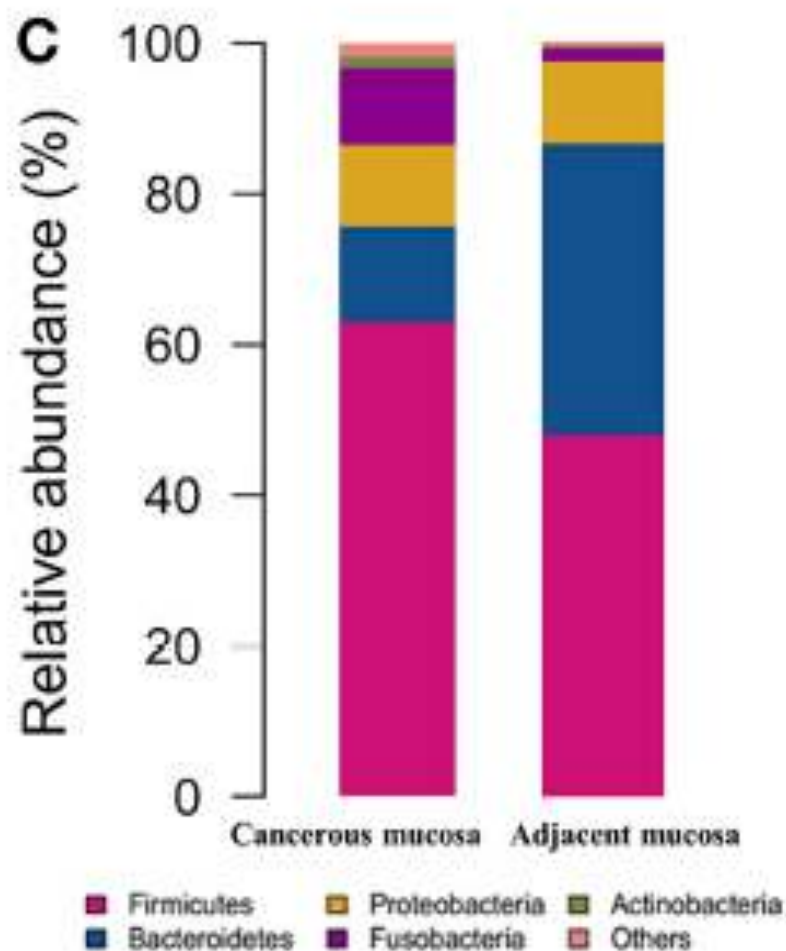




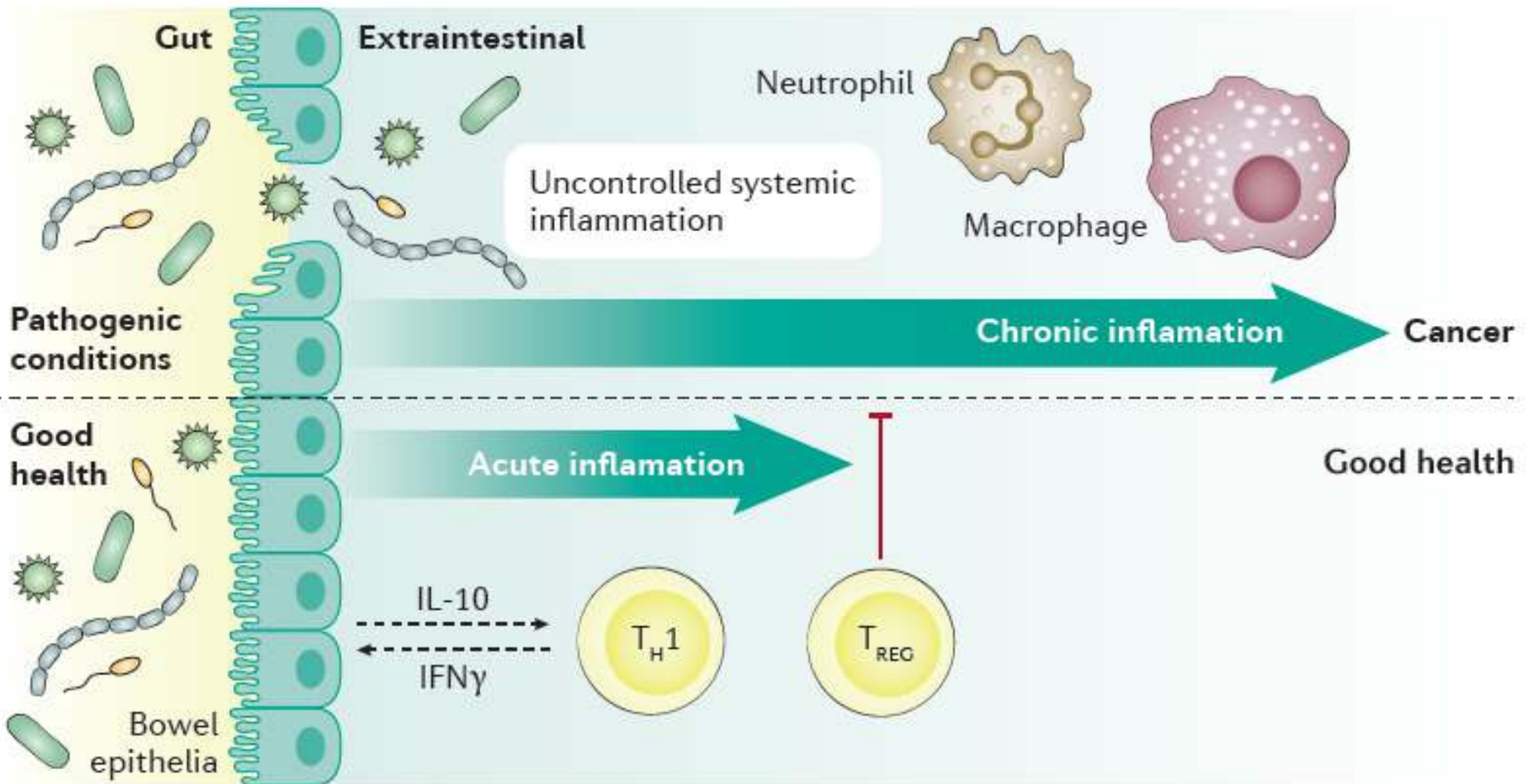
Microbiota disbiosis is associated with colorectal cancer

Zhiguang Gao[†], Bomin Guo[†], Renyuan Gao[†], Qingchao Zhu and Huanlong Qin^{*}

Department of General Surgery, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China



Microbes offer engineering



ANTİBİYOTİK İLİŞKİLİ İSHAL



**Amaç:
Hastalıkları
oluşmadan
Önlemek!!!!**



ANTİBİYOTİK İLİŞKİLİ İSHAL





CLOSTRIDIUM DIFFICILE



GASTROİNTESTİNAL HASTALIKLAR

- **TEKRARLAYAN *C. DIFFICILE* ENFEKSİYONLARI**
 - 273 OLGUDA %90 BAŞARI SAĞLANMIŞ, YAN ETKİ YOK.
- **İDİYOPATİK KONSTİPASYON**
- **İRRİTABL BAĞIRSAK SENDROMU**
- **İNFLAMATUAR BAĞIRSAK HASTALIKLARI**

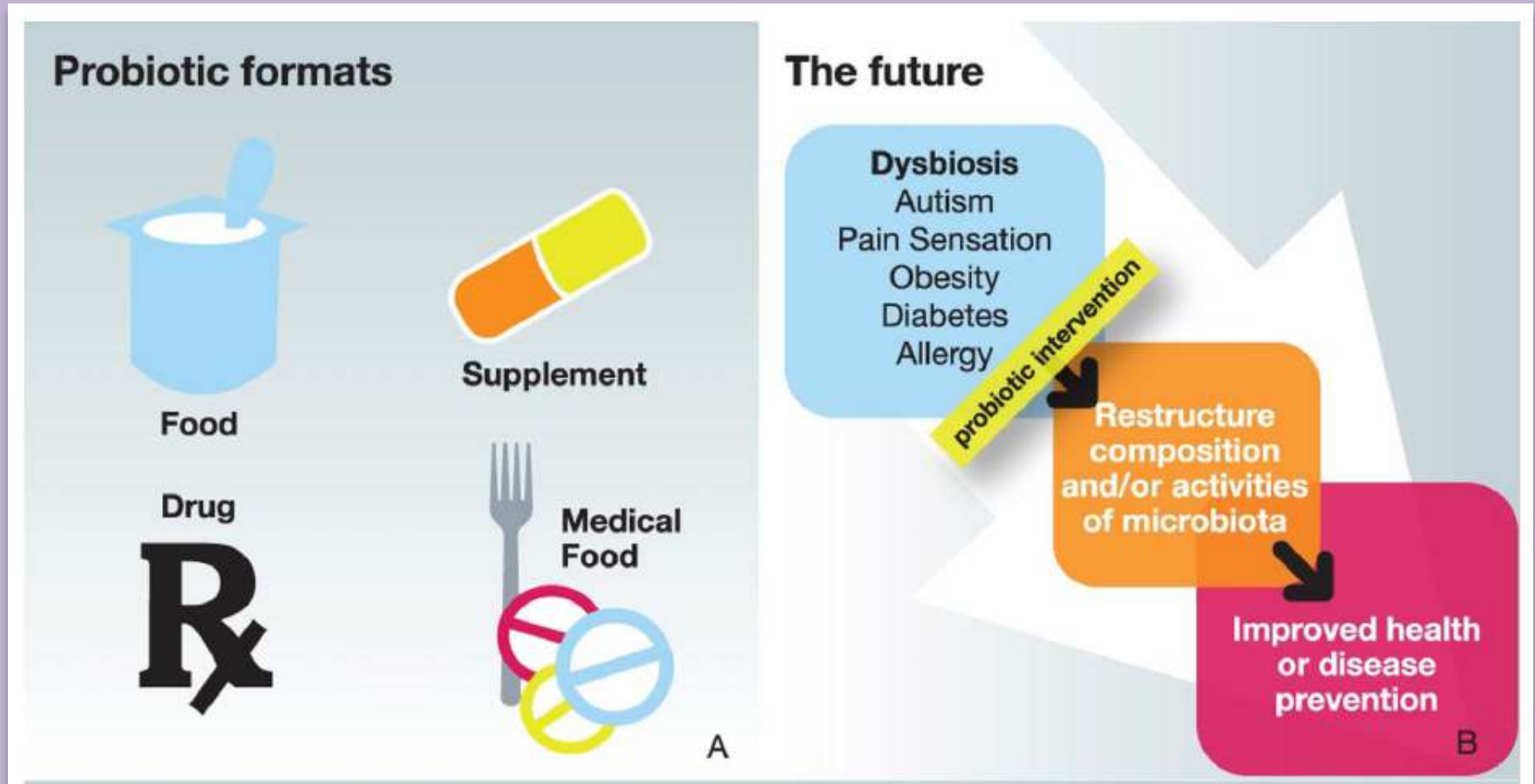
NON- GASTROİNTESTİNAL HASTALIKLAR

- OTİZM
- KRONİK YORGUNLUK SENDROMU
- ALKOLİK KARACİĞER HASTALIĞI
- FİBROMYALJİ
- ITP
- METABOLİK SENDROM
- MULTİPL SKLEROZ
- PARKİNSON HASTALIĞI

- EVRENSEL DONÖRLERDEN DONDURULMUŞ GAYTA
- SENTETİK GAYTA (REPOOPULATE): 33 bakteri
- 3 BAKTERİ İÇEREN FORMÜLLER
 - *Bacteriodes ovatus, fragilis, thetatoitaomicron*)
- FT KAPSÜLLERİ (CRAPSULES)
 - ICAAC 2014'de C. difficile'de başarı %93-100
- GAYTA BANKACILIĞI

FEKAL TRANSPLANTASYON-GELECEK?





Health and clinical targets addressed by studies on orally administered probiotics conducted in human subjects of different ages

PROBİYOTİKLER





Re

ate

Recommend

Immune r

Allergy

Atopic

Treat

Preve

Radiation

Vaginosis

Recommend

Liver dise

Hepatic

encepha

Nonalco

liver dise

Nonalcoholic fatty

liver disease in children

Alcoholic liver disease

C

VSL#3, LGG

C

VSL#3, LGG, *L. acidophilus*, *L. bulgaricus*, *B. bifidum*, *B. longum* with oligosaccharides

58,59

59

59

60,61

62-64

8-12

8,9,13,15,16

17

8-17

← YANLIŞ

ÇOK YANLIŞ →

MICROBIOTA RESTORATION?



The Microbiome

A voyage to (our inner) Lilliput

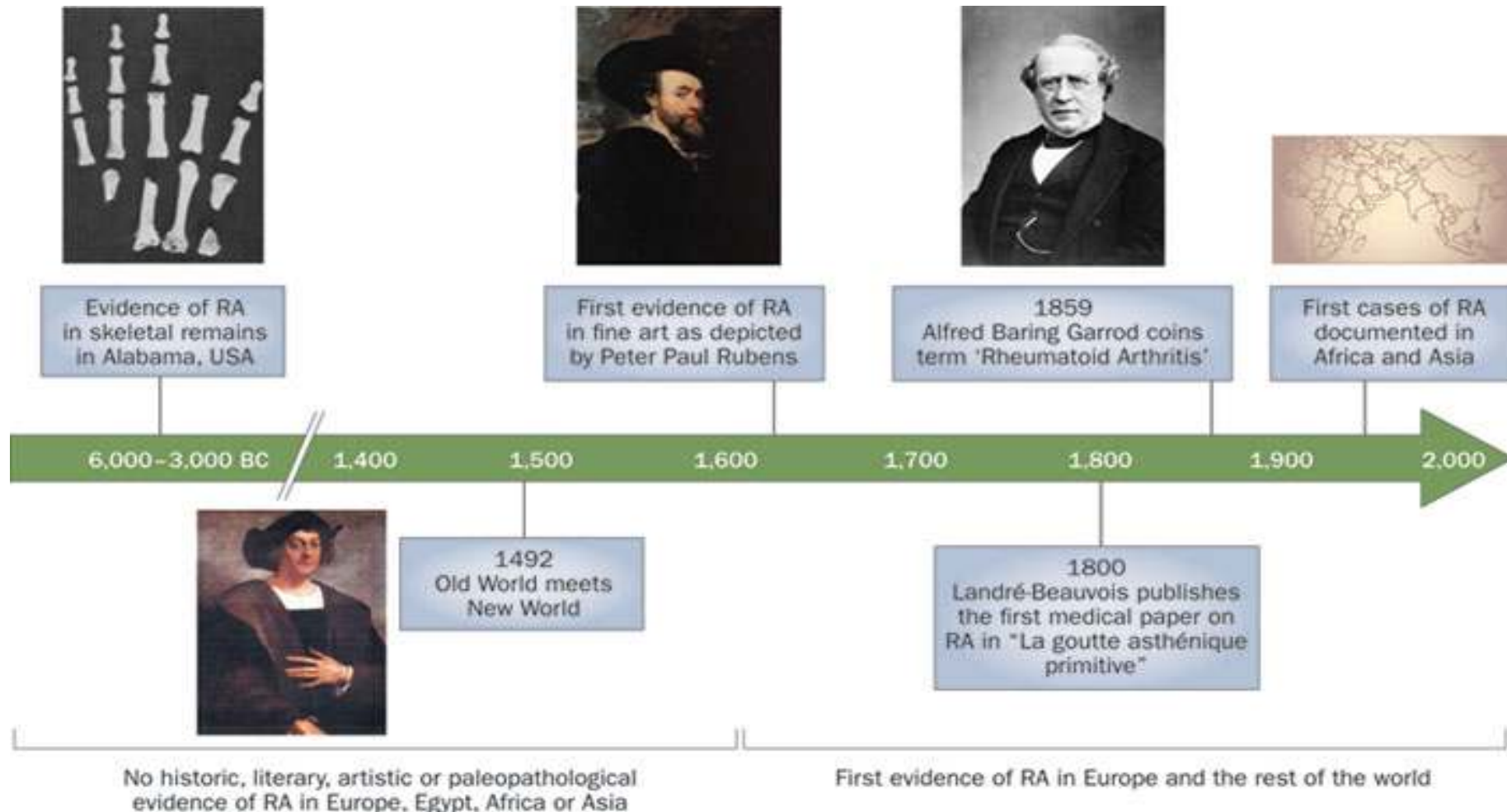
by Jose U. Scher, MD, Steven B. Abramson, MD



I could not sufficiently wonder at the intrepidity of these diminutive mortals, who durst venture to mount and walk upon my body [...] without trembling at the very sight of so prodigious a creature as I must appear to them.

—Jonathan Swift, describing Gulliver's reaction to the Lilliputians, Gulliver's Travels

Figure 1 Historical, literary, artistic and paleopathological evidence of RA as a New World disease that has ‘spread’ to the rest of the world



Host genetics

Mutations in
NOD2, *IL23R*,
ATG16L and *IGRM*

Lifestyle

Diet
Stress



Early colonization

Birth in hospitals
Altered exposure
to microbes



Medical practices

Vaccination use
Antibiotic
Hygiene



Dysbiosis

Disease

↑ T_H1 , T_H2 and T_H17 cells

Health

↑ T_{Reg} cells

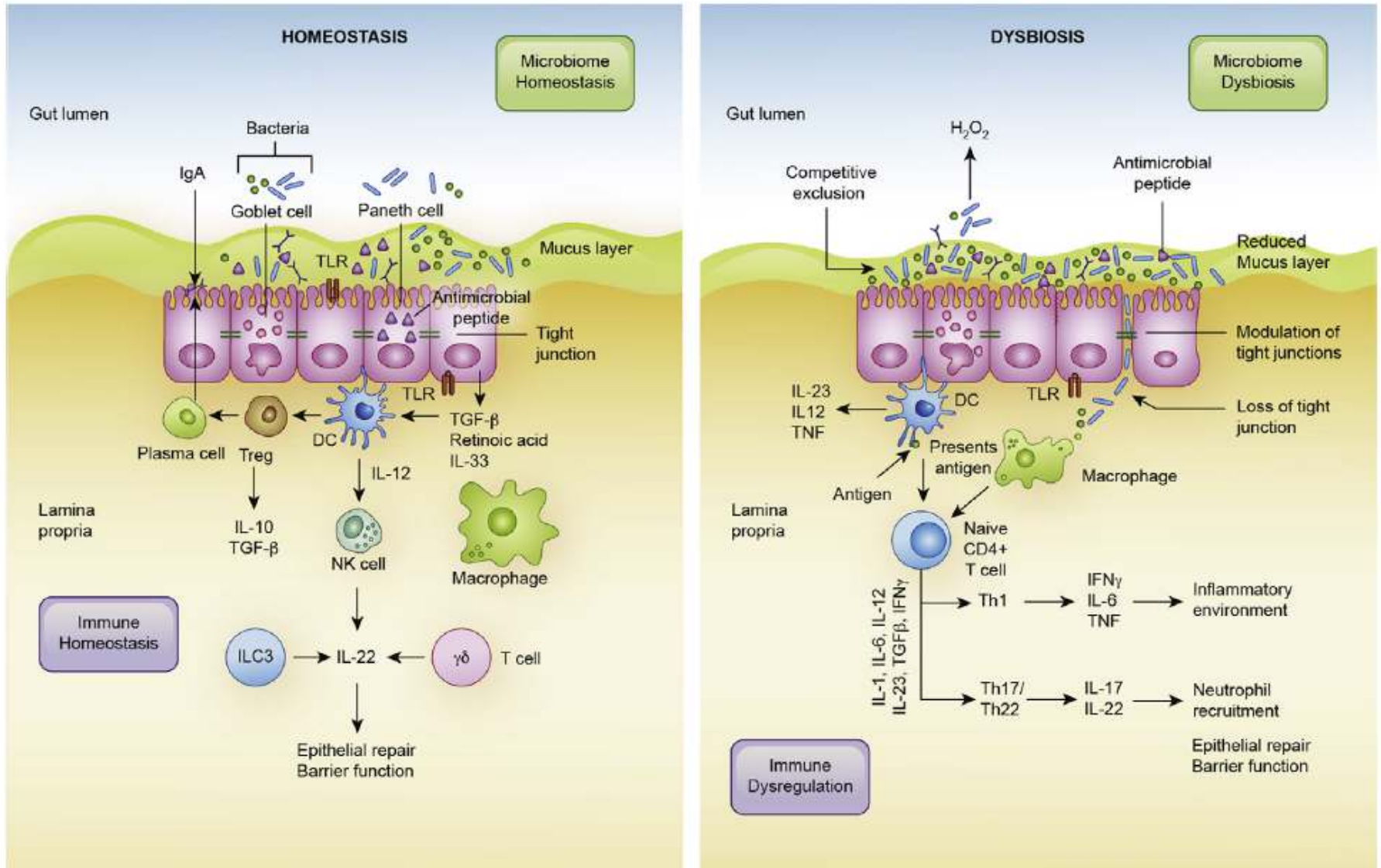


Fig. 1. The microbiome and mucosal immune mechanisms involved in intestinal homeostasis and dysbiosis.

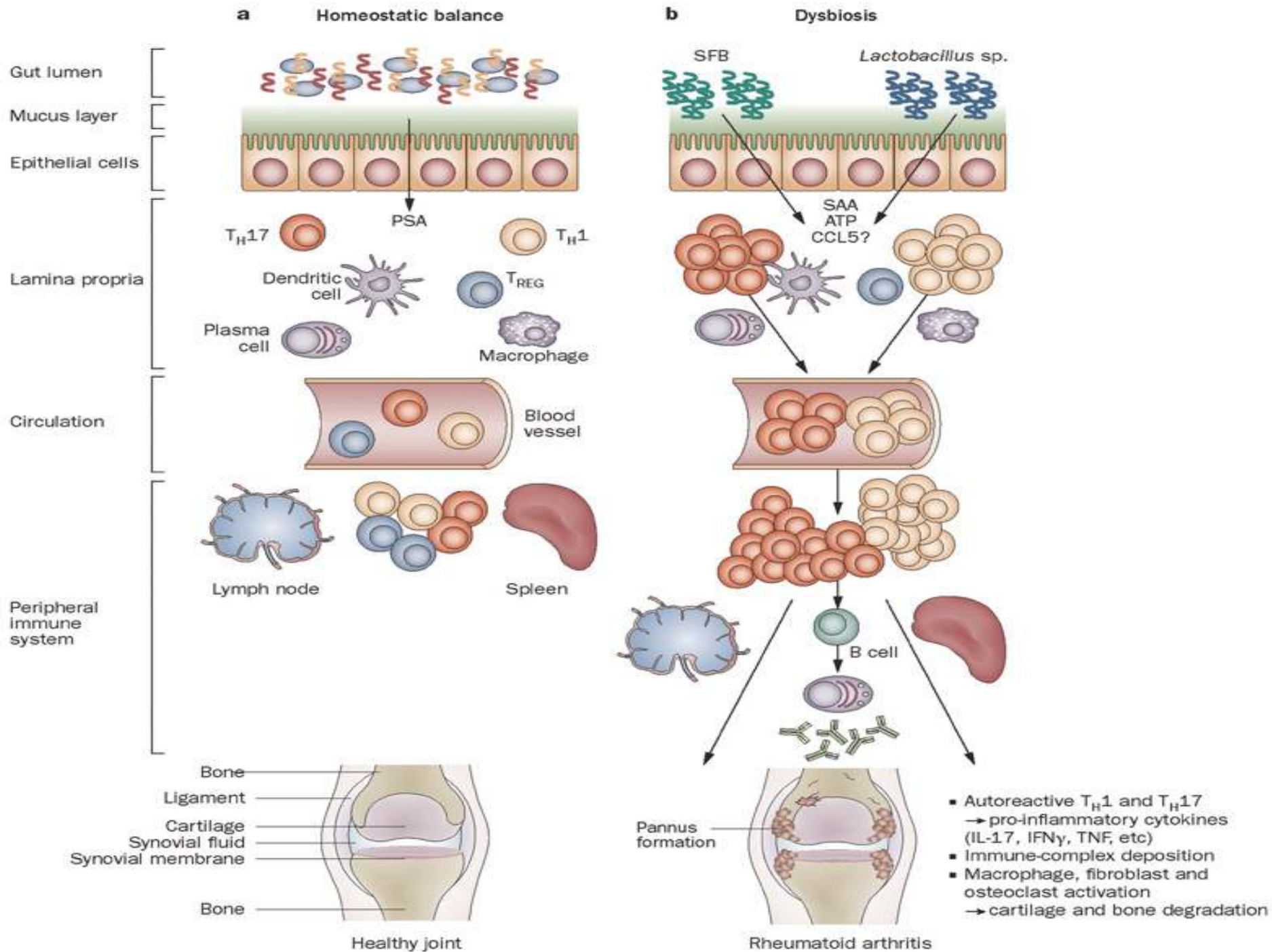
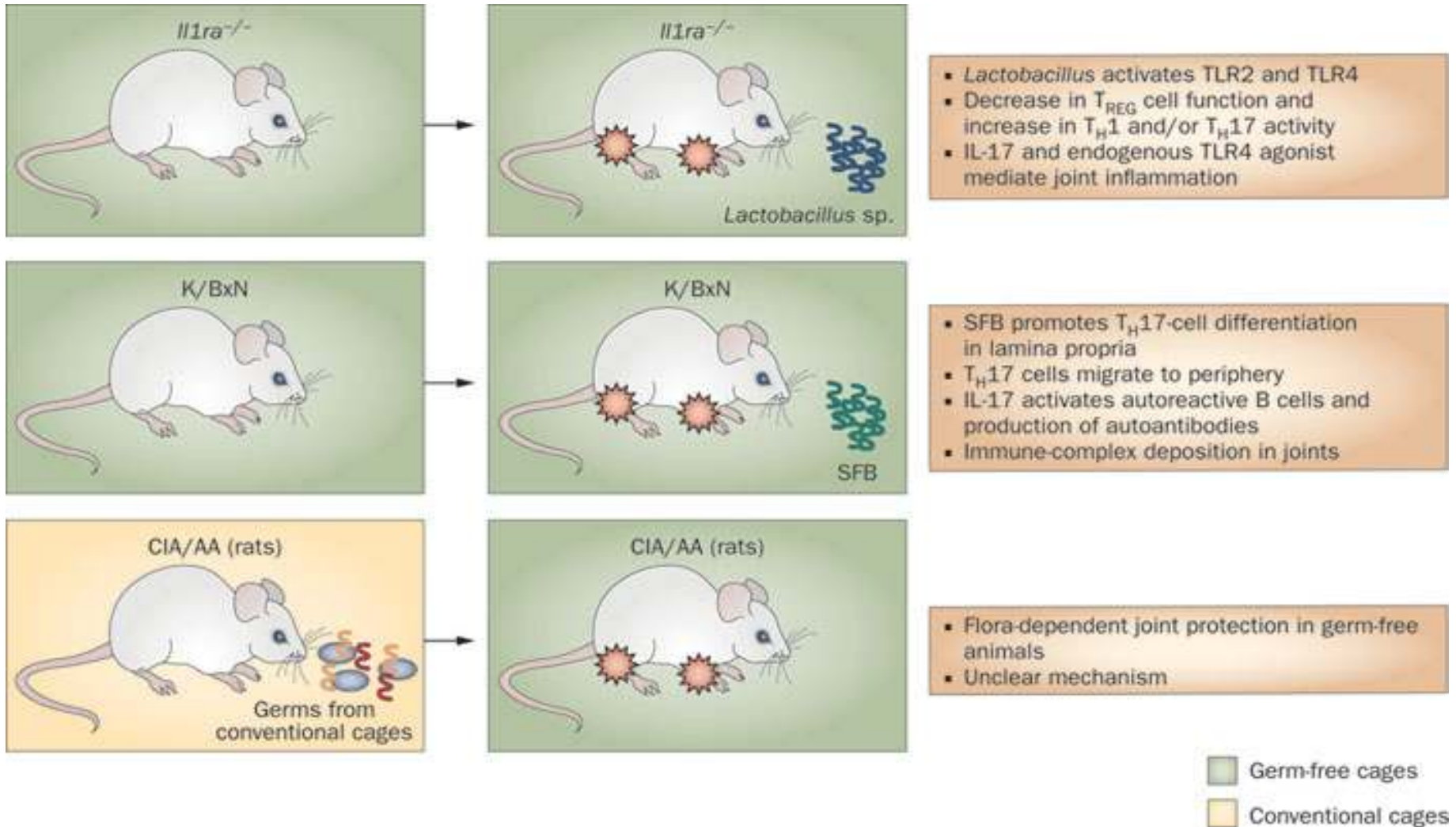


Figure 4 Multiple animal models of inflammatory arthritis have demonstrated that the gut microbiota is critical for the development of disease



- *Lactobacillus* activates TLR2 and TLR4
- Decrease in T_HREG cell function and increase in T_H1 and/or T_H17 activity
- IL-17 and endogenous TLR4 agonist mediate joint inflammation

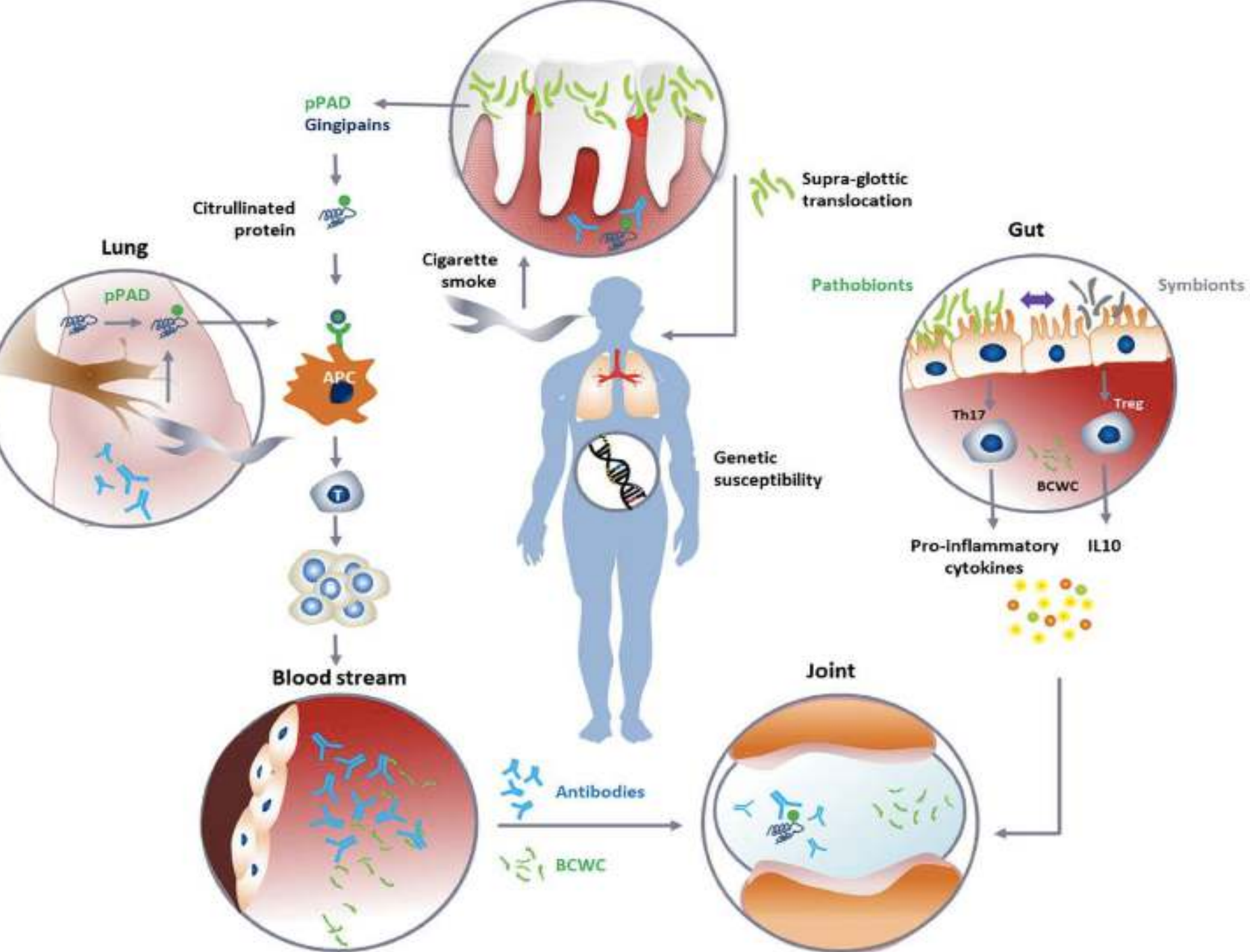
- SFB promotes T_H17-cell differentiation in lamina propria
- T_H17 cells migrate to periphery
- IL-17 activates autoreactive B cells and production of autoantibodies
- Immune-complex deposition in joints

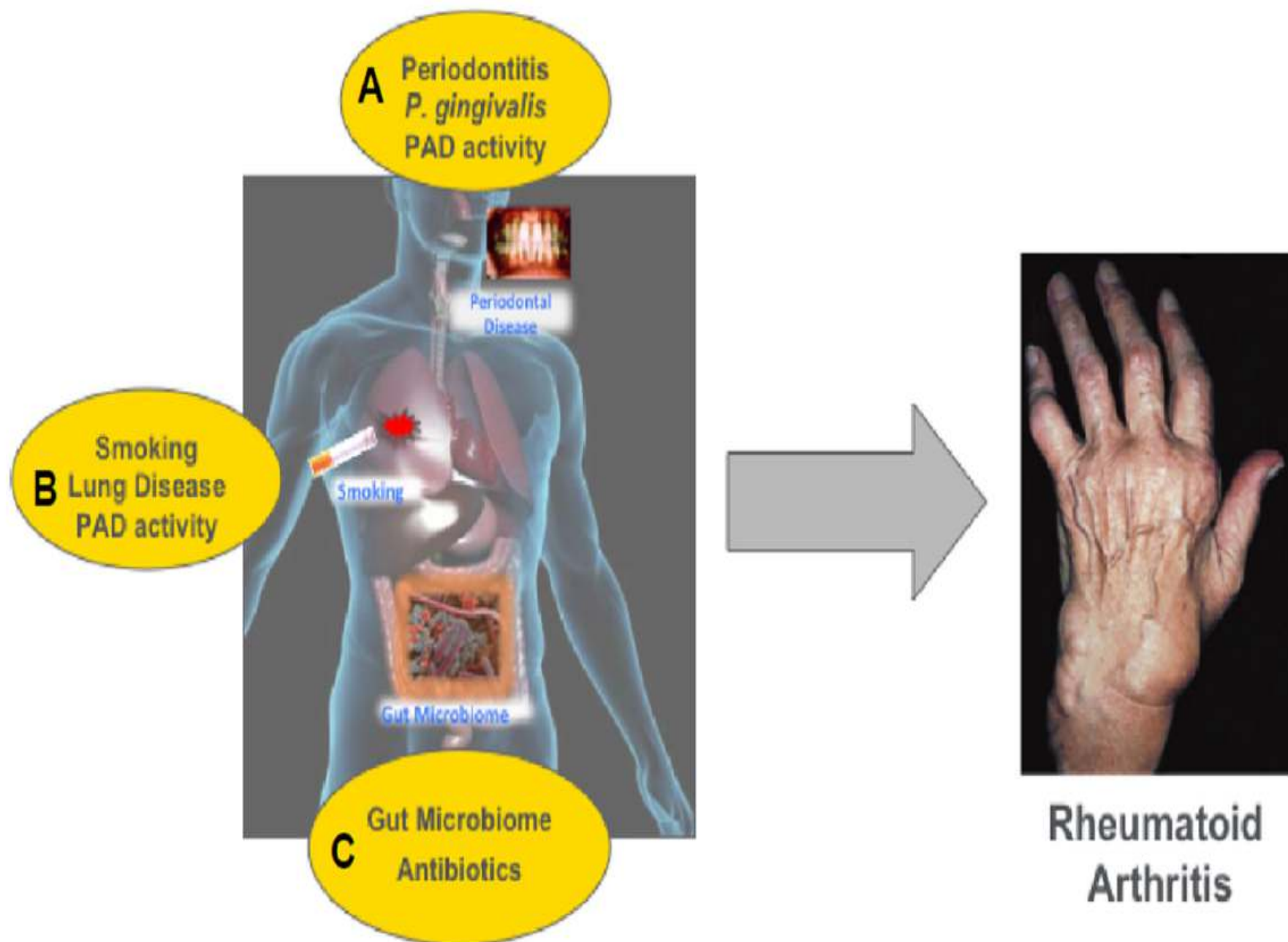
- Flora-dependent joint protection in germ-free animals
- Unclear mechanism

Table 1: Recent Evidence on the Link Between *P. gingivalis* and RA

| Study | Evidence |
|--|---|
| Wegner N, et al. <i>Arthritis Rheum.</i> 2010 | Peptidyl arginine deiminase, type I from <i>P. gingivalis</i> citrullinates human fibrinogen and α -enolase. |
| Kinloch AJ, et al. <i>Arthritis Rheum.</i> 2011 | Human α -enolase induces autoimmunity and arthritis in DR4 mice. |
| Lundberg, et al. <i>Arthritis Rheum.</i> 2008; Mikuls TR, et al. <i>Int Immunopharmacol.</i> 2009 | Antibodies to <i>P. gingivalis</i> (CEP-1, PPAD) are significantly higher in RA patients and correlate with the presence of anti-citrullinated protein antibodies. |
| Mikuls TR, et al. <i>Arthritis Rheum.</i> 2012; Hitchon CA, et al. <i>J Rheum.</i> 2011 | Immune response to <i>P. gingivalis</i> is also higher in individuals at risk for RA. |
| Scher JU, et al. <i>Arthritis Rheum.</i> 2012 | New-onset DMARD-naive RA present with advanced periodontal disease. Evidence of <i>P. gingivalis</i> in new-onset RA by both 16S rRNA and serology, with data showing 55% abundance of <i>P. gingivalis</i> (16S rRNA) in new-onset RA and about 35–60% anti- <i>P. gingivalis</i> Abs (serology) in early RA. |



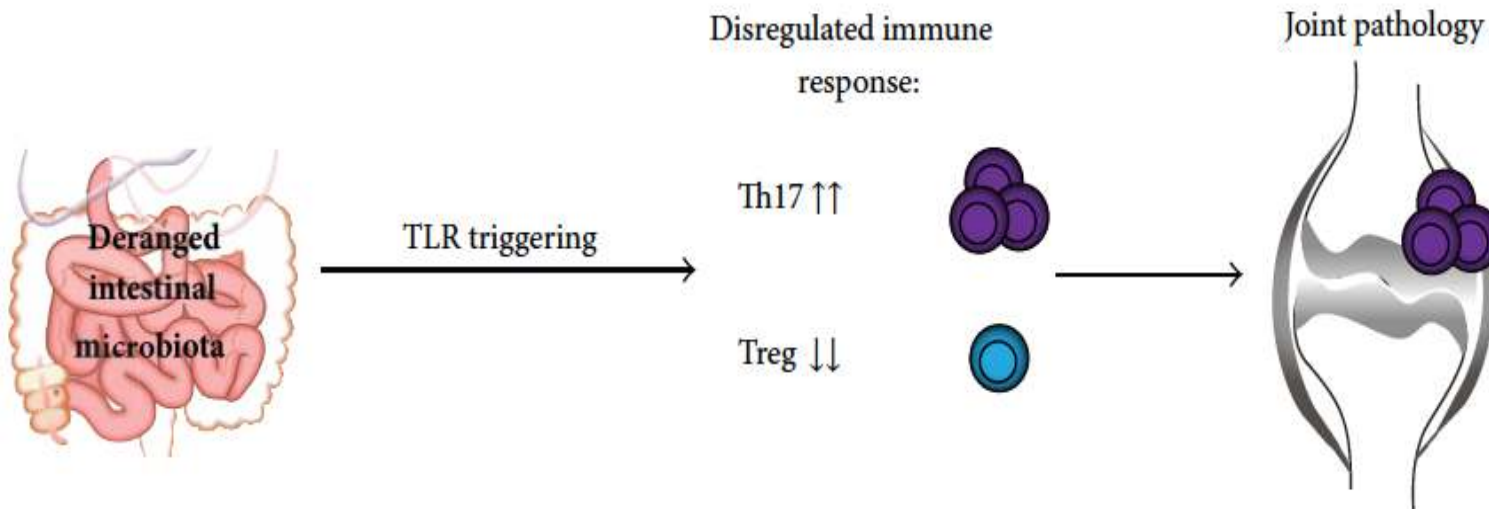




Review Article

Toll-Like Receptor Mediated Modulation of T Cell Response by Commensal Intestinal Microbiota as a Trigger for Autoimmune Arthritis

Journal of Immunology Research



Gut Microbiota Regulates K/BxN Autoimmune Arthritis through Follicular Helper T but Not Th17 Cells

Katharine E. Block^{*,†,‡}, Zhong Zheng^{†,‡}, Alexander L. Dent[§], Barbara L. Kee^{*,¶} and Haochu Huang^{*,†,‡}

+ Author Affiliations

Address correspondence and reprint requests to Dr. Haochu Huang, University of Chicago, Department of Medicine/Section of Rheumatology, Knapp Center for Lupus and Immunology Research, 924 East 57th Street, Chicago, IL 60637. E-mail address: hhuang@bsd.uchicago.edu

Abstract

The bacterial community that colonizes mucosal surfaces helps shape the development and function of the immune system. The K/BxN autoimmune arthritis model is dependent on the microbiota, and particularly on segmented filamentous bacteria, for the autoimmune phenotype. The mechanisms of how the gut microbiota affects arthritis development are not well understood. In this study, we investigate the contribution of two T cell subsets, Th17 and follicular helper T (Tfh), to arthritis and how microbiota modulates their differentiation. Using genetic approaches, we demonstrate that IL-17 is dispensable for arthritis. Antibiotic treatment inhibits disease in IL-17-deficient animals, suggesting that the gut microbiota regulates arthritis independent of Th17 cells. In contrast, conditional deletion of Bcl6 in T cells blocks Tfh cell differentiation and arthritis development. Furthermore, Tfh cell differentiation is defective in antibiotic-treated mice. Taken together, we conclude that gut microbiota regulates arthritis through Tfh but not Th17 cells. These findings have implications in our understanding of how environmental factors contribute to the development of autoimmune diseases.



This Article

Published online before print
January 18, 2016, doi:
10.4049/jimmunol.1501904

The Journal of Immunology
January 18, 2016
1501904

► **Abstract Free Full Text (PDF)**

- **Classifications**

AUTOIMMUNITY

- **Article Usage Stats**

Article Usage Statistics

- **Services**

Alert me when this article is cited

Alert me if a correction is posted

Similar articles in this journal

Similar articles in PubMed

Download to citation manager

[© Get Permissions](#)

+ **Citing Articles**

+ **Google Scholar**

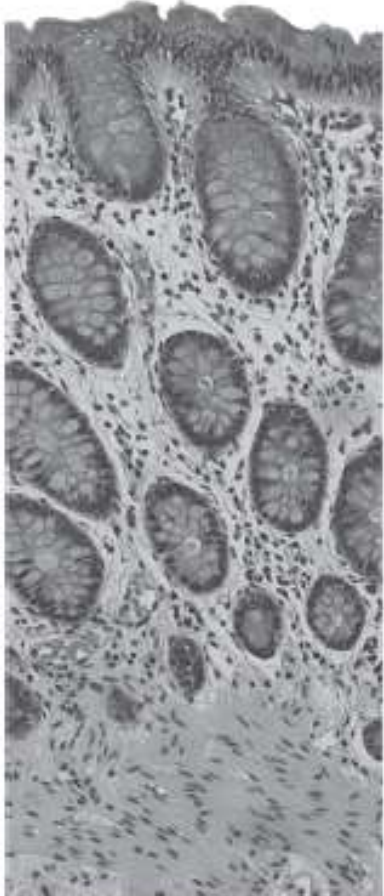
+ **PubMed**



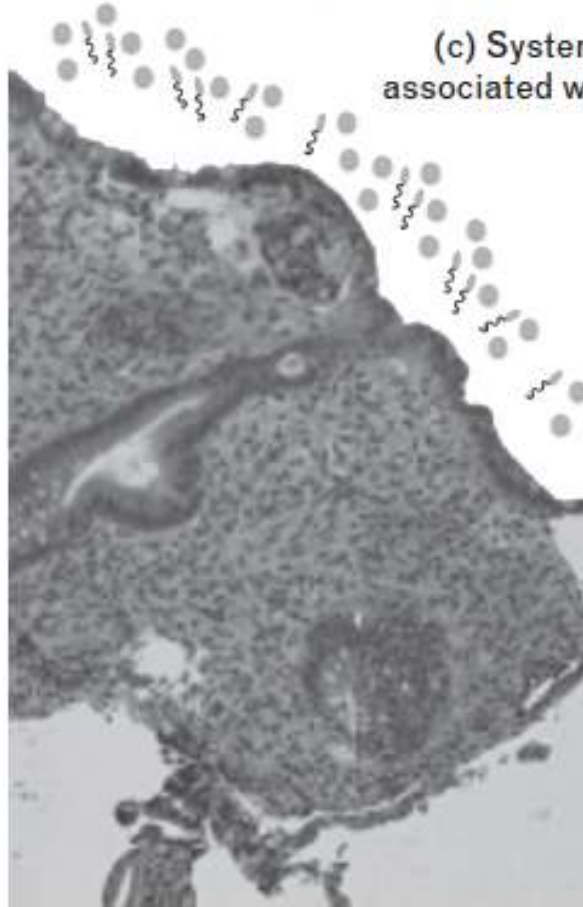
The Journal of
Immunology

ARTRİT

(a) Healthy intestine is populated with commensal microbiota



(b) Intestinal inflammation is associated with dysbiosis.



(c) Systemic inflammation can be associated with intestinal inflammation.



(d) But does intestinal inflammation or dysbiosis cause systemic inflammation?



(e) And is altering the microbiota an effective therapeutic option for treating systemic inflammation?



Rheumatoid Arthritis

| | |
|--|---|
| Cross-sectional analysis of faecal and oral microbiota | <p>↑ Gram +, while ↓ Gram – [9]</p> <p>Negative correlation between <i>Haemophilus</i> spp and serum antibody levels.</p> <p>↑ <i>Lactobacillus salivarius</i></p> <p>Homeostasis restored after DMARDs</p> |
| Cross-sectional case-control study, oral microbiota | ↑ <i>Tannerella forsythia</i> and <i>Streptococcus anginosus</i> [10] |

Psoriatic arthritis

| | |
|--|---|
| PsA, skin psoriasis and HC, faecal samples | <p>PsA patients showed: [14]</p> <p>↓ bacterial diversity, resembles dysbiosis in IBD</p> <p>↓ <i>Akkermansia</i>, <i>Ruminococcus</i>, <i>Pseudobutyrvibrio</i>, <i>Coprococcus</i> spp.</p> |
|--|---|

Spondyloarthritis

| | |
|--|---|
| Children with ERA and HC, faecal samples and blood | <p>ERA patients showed: [15]</p> <p>↓ bacterial diversity, resembles dysbiosis in IBD</p> <p>↑ <i>Akkermansia muciniphila</i>, <i>Bifidobacterium</i></p> <p>↓ <i>Faecalibacterium prausnitzii</i> and <i>Lachnospiraceae</i> spp</p> <p><i>fragilis</i> subgroup and <i>Eubacterium rectale</i>-<i>Clostridium rectale</i> subgroup.</p> |
|--|---|

| | |
|---|--|
| Faecal <i>Lactobacillus</i> community analysis; analysis from patients with disease for <6 months | <p>↑ <i>L. salivarius</i>, <i>L. iners</i> and <i>L. ruminis</i> [13]</p> <p>↑ richness, evenness and Shannon-Wiener index of intestinal <i>Lactobacillus</i> spp.</p> <p><i>L. mucosae</i> was absent in HC</p> |
|---|--|

Psoriatic arthritis

PsA, skin psoriasis and HC, faecal samples

PsA patients showed:

[14]

↓ bacterial diversity, resembles dysbiosis in IBD

↓ *Akkermansia*, *Ruminococcus*, *Pseudobutyrvibrio*, *Coprococcus* spp.

Spondyloarthritis

Children with ERA and HC, faecal samples and blood

ERA patients showed:

[15]

↓ bacterial diversity, resembles dysbiosis in IBD

↑ *Akkermansia muciniphila*, *Bifidobacterium*

↓ *Faecalibacterium prausnitzii* and *Lachnospiraceae* spp

Spondyloarthritis (MA Khan, Section Editor)

Current Rheumatology Reports

February 2015, 17:10

First online: 08 February 2015

Spondyloarthritis and the Microbiome: New Insights From an Ancient Hypothesis

Julia Manasson, Jose U. Scher 

CONCISE REPORT

Patients with ankylosing spondylitis have been breast fed less often than healthy controls: a case–control retrospective study

J Montoya,¹ N B Matta,¹ P Suchon,^{2,3} M C Guzian,¹ N C Lambert,⁴ J P Mattei,¹
S Guis,¹ M Breban,^{5,6,7} J Roudier,^{1,4} N Balandraud^{1,4}

Montoya J, et al. *Ann Rheum Dis* 2015;**0**:1–4. doi:10.1136/annrheumdis-2015-208187



Full Length

Systemic sclerosis is associated with a unique colonic microbial consortium

Elizabeth R. Volkman M.D., M.S.^{1,*}, Yu-Ling Chang M.S.², Nashla Barroso¹, Daniel E. Furst M.D.¹, Philip P. Clements M.D.¹, Alan H. Gorn M.D.¹, Bennett E. Roth M.D.¹, Jeffrey L. Conklin M.D.¹, Terri Getzug M.D.¹, James Borneman Ph.D.³, Dermot P. B. McGovern M.D., Ph.D.⁴, Maomeng Tong Ph.D.², Jonathan P. Jacobs M.D., Ph.D.¹ and Jonathan Braun M.D., Ph.D.²

DOI: 10.1002/art.39572

© 2015, American College of Rheumatology

Issue



Arthritis & Rheumatology
Accepted Article (Accepted, unedited articles published online and citable. The final edited and typeset version of record will appear in future.)

SEARCH

In this issue

Advanced > Saved Searches >

ARTICLE TOOLS

- Get PDF (1607K)
- Save to My Profile
- E-mail Link to this Article
- Export Citation for this Article
- Get Citation Alerts
- Request Permissions

Share |

- 17 hasta SSc (%88 kadın; medyan yaş 52.1 yıl
- Sağlıklı kontroller ile hem çekum hem sigmoid mikrobiyota kompozisyonları farklı.
- SSc hastalarında
 - *Faecalibacterium* ve *Clostridium* ↓
 - *Fusobacterium* ve γ -*Proteobacteria* ↑
 - *Bifidobacterium* ve *Lactobacillus* (??) ↑
 - GIS semptomları olanlarda *Bacteroides fragilis* azalması ve *Fusobacterium* artışı

- Patogenezde rolü olabilir mi?
- Autoreactive CD4+ T cells ve patojenik APS antikorlarının gelişiminde rolü?


Antiphospholipid Syndrome (D Erkan, Section Editor)

Current Rheumatology Reports

January 2015, 17:472

First online: 05 December 2014

The Role of the Gut Microbiota in the Pathogenesis of Antiphospholipid Syndrome

[William E. Ruff](#), [Silvio M. Vieira](#), [Martin A. Kriegel](#) 

| Intervention | Study type | Outcome | Reference |
|---|--|---|-----------|
| Juvenile chronic arthritis | | | |
| <i>Lactobacillus GG</i> , daily for 14 days | Randomised, double-blinded, probiotics, $n = 10$ | No clinically beneficial effect | [29] |
| Rheumatoid arthritis | | | |
| <i>Lactobacillus rhamnosus GG</i> , twice daily for 12 months | RCT probiotics, $n = 8$; placebo, $n = 13$ | No significant differences | [30] |
| <i>Bacillus coagulans</i> , daily for 60 days | RCT probiotics, $n = 22$; placebo, $n = 22$ | No significant differences | [31] |
| <i>L. rhamnosus</i> , <i>L. reuteri</i> , twice daily for 12 weeks | RCT probiotics, $n = 15$; placebo, $n = 11$ | No significant differences | [32**] |
| <i>L. casei</i> with maltodextran, daily for 8 weeks | RCT probiotics, $n = 22$; placebo, $n = 24$ | Significant decreases: serum CRP, IL-12, TNF α ; tender/swollen joints, DAS28; significant increase: serum IL-10 | [33,34] |
| Vegan, low-fat diet, <i>ad libitum</i> 4 weeks | Noncontrolled, single-blinded study, $n = 24$ | No significant differences in ESR, CRP, RF levels; significant decrease in pain assessment, joint tenderness and swelling | [35] |
| Mediterranean diet 6 months | Nonrandomised, controlled study intervention, $n = 75$; controls, $n = 55$ | No significant changes in ESR, CRP or IL-6 levels; significant improvement in global patient and pain assessments | [36] |
| 3 weeks Mediterranean diet or standard hospital meals, 3 weeks, then 9 weeks Mediterranean diet | Randomised, controlled, single-blinded study intervention, $n = 29$; controls, $n = 27$ | Significant decrease in serum CRP, swollen joint counts, DAS28 score, HAQ, patient pain VAS | [37] |
| 2 weeks Mediterranean diet or fasting (calorie restriction) | Nonrandomised fasting, $n = 22$; Mediterranean, $n = 28$ | No change in CRP, decrease in DAS28 score in both groups | [38] |

Spondyloarthritis

| | | | |
|---|---|----------------------------|------|
| <i>Lactobacillus</i> spp., <i>Bifidobacterium</i> spp. daily for 12 weeks | RCT probiotics, $n=65$; placebo, $n=69$ | No significant differences | [39] |
|---|---|----------------------------|------|

| | | | |
|---|---|----------------------------|------|
| <i>Streptococcus salivarius</i> , <i>Bifidobacterium lactis</i> , <i>L. acidophilus</i> twice daily for 12 weeks | RCT probiotics, $n=32$; placebo, $n=31$ | No significant differences | [40] |
|---|---|----------------------------|------|

Juvenile idiopathic arthritis

| | | | |
|--|---|--|------|
| Exclusive enteric nutrition (EEN) for two 7-week blocks | Single patient brief report, as part of ongoing clinical trial | Decreased joint swelling and improved function, lasting several months, stopped infliximab treatment | [41] |
|--|---|--|------|

26 MART 2016

International Journal of
Rheumatic Diseases



International Journal of Rheumatic Diseases 2016; 19: 8–20

REVIEW ARTICLE

Does the buck stop with the bugs?: an overview of microbial dysbiosis in rheumatoid arthritis

Pulukool SANDHYA,¹ Debashish DANDA,¹ Disha SHARMA^{2,3} and Vinod SCARIA^{2,3}

¹*Department of Clinical Immunology and Rheumatology, Christian Medical College, Vellore, Tamil Nadu,* ²*GN Ramachandran Knowledge Center for Genome Informatics, CSIR Institute of Genomics and Integrative Biology (CSIR-IGIB), and* ³*Faculty of Life Sciences, Academy of Scientific and Innovative Research (AcSIR), Delhi, India*





PROBAGE STUDY GROUP



Eur J Pediatr (2013) 172:459–464
DOI 10.1007/s00431-012-1903-5

ORIGINAL ARTICLE

The effect of a multispecies synbiotic mixture on the duration of diarrhea and length of hospital stay in children with acute diarrhea in Turkey: Single blinded randomized study

Ener Çağrı Dinleyici • Nazan Dalgıç • Sirin Güven •
Metehan Ozen • Ates Kara • Vefik Arıca
Özge Metin-Timur • Mesut Sancar • Zafer Kurugöl •
Gonul Tanır • Didem Öztürk • Selime Aydoğdu •
Murat Tutanc • Makbule Eren • Yvan Vandenplas

Beneficial Microbes, 2015 online

ARTICLE IN PRESS



Saccharomyces boulardii CNCM I-745 reduces the duration of diarrhoea, length of emergency care and hospital stay in children with acute diarrhoea

E.C. Dinleyici^{1*}, A. Kara², N. Dalgıç³, Z. Kurugöl⁴, V. Arıca⁵, O. Metin⁶, E. Temur⁷, O. Turel⁸, S. Guven⁹, O. Yasa¹⁰, S. Bulut⁴, G. Tanır⁶, A.S. Yazar⁹, A. Karbuç⁵, M. Sancar¹¹, M. Erguven¹⁰, G. Akca³, M. Eren¹², M. Ozen¹³ and Y. Vandenplas¹⁴

- **FACID Study**
- 10 children (3-4 years age group) with acute infectious diarrhea due to **rotavirus**
- 6 healthy children (3-4 years age group)
- Rotavirus group received *probiotics*, 250 mg twice daily for **5 days**.
- Fecal samples obtained from Sb group and healthy children at Day 0, Day 3, Day 5, Day 10, Day 30.



.join.fna



.join.fna



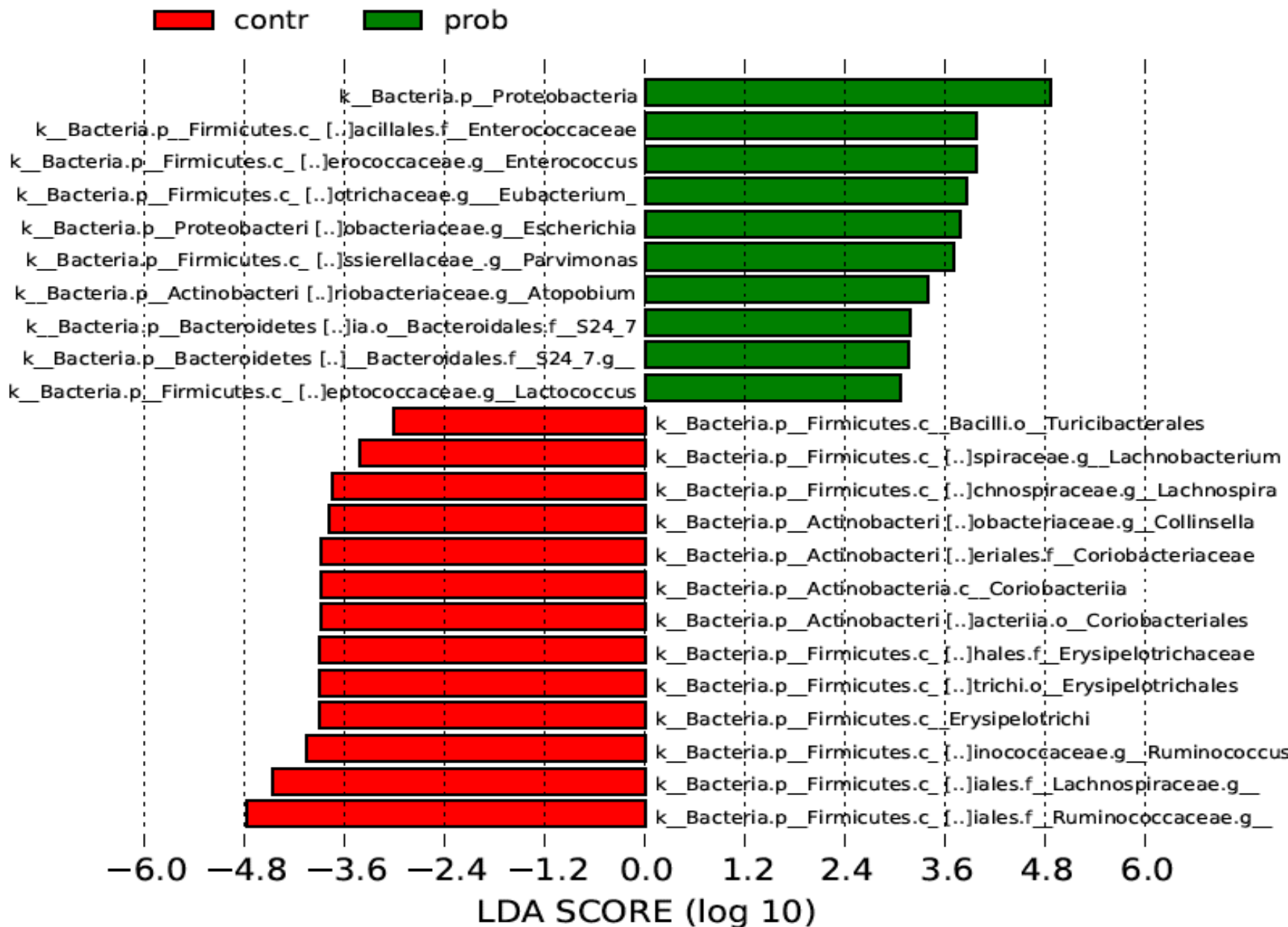
.join.fna



.join.fna



.join.fna





Beneficial Microbes, 2015; 6(6): 775-781



Effects of synbiotic on anthropometry, lipid profile and oxidative stress in obese children

N. Ipar¹, S. Durmus Aydogdu², G. Kilic Yildirim², M. Inal³, I. Gies⁴, Y. Vandenplas⁴ and E.C. Dinleyici^{1*}

¹*Eskisehir Osmangazi University Faculty of Medicine, Department of Pediatrics, 26480 Eskisehir, Turkey;* ²*Eskisehir Osmangazi University Faculty of Medicine, Department of Pediatrics, Nutrition and Metabolism Unit, 26480 Eskisehir, Turkey;* ³*Eskisehir Osmangazi University Faculty of Medicine, Department of Biochemistry, 26480 Eskisehir, Turkey;* ⁴*Department of Pediatrics, UZ Brussel, Vrije Universiteit Brussel, Laarbeeklaan 101, 1090 Brussels, Belgium; enercagri@gmail.com*

Received: 2 February 2015 / Accepted: 29 April 2015

© 2015 Wageningen Academic Publishers

RESEARCH ARTICLE

MİKROBİYOTA İLE İLGİLİ ÇALIŞMALARI MUTLAKA TAKİP EDİN...

