Mikrobiomet

Umahro Cadogan a.k.a. The Danish Food Doctor

Mandag d. 22. august 2016

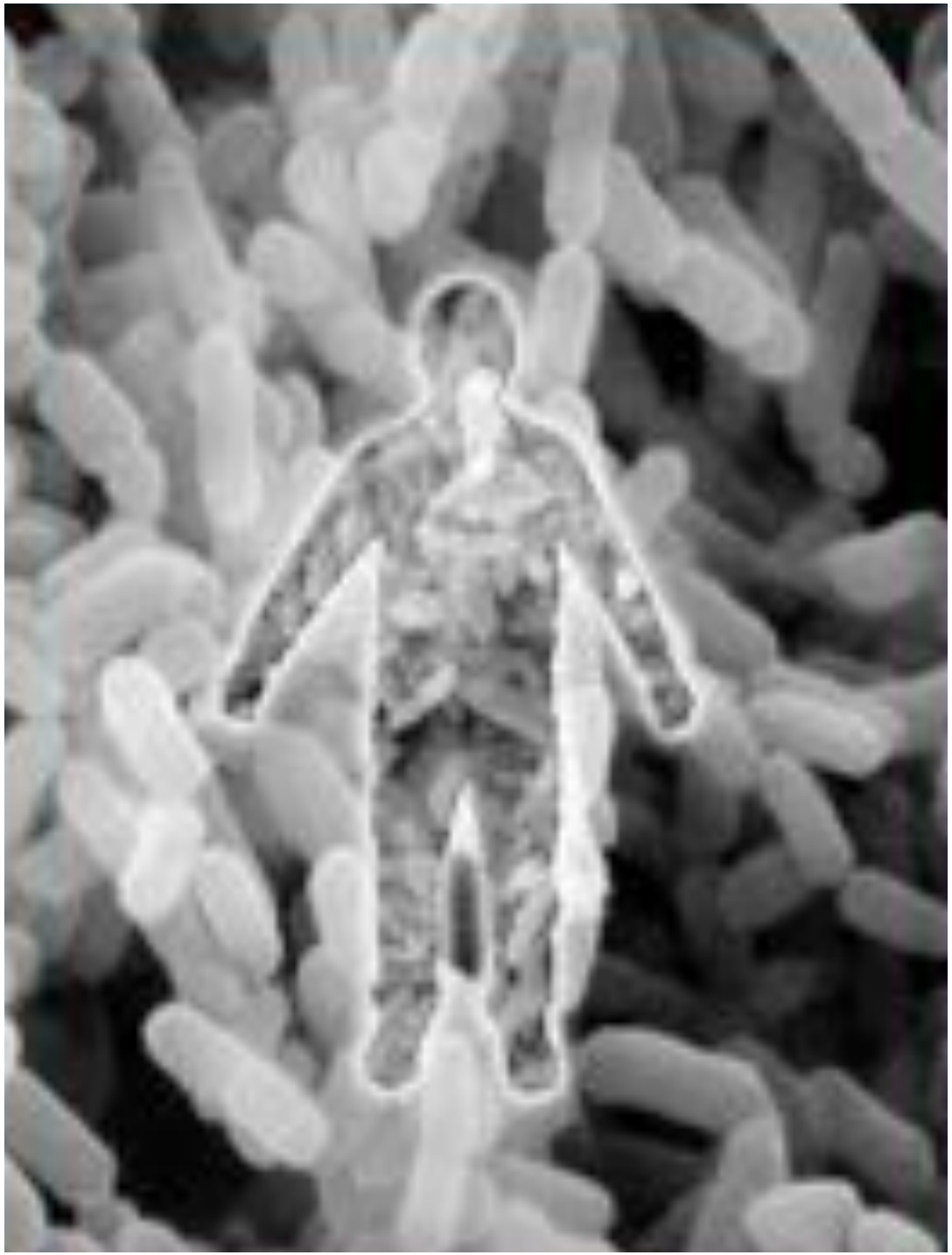
Oversigt

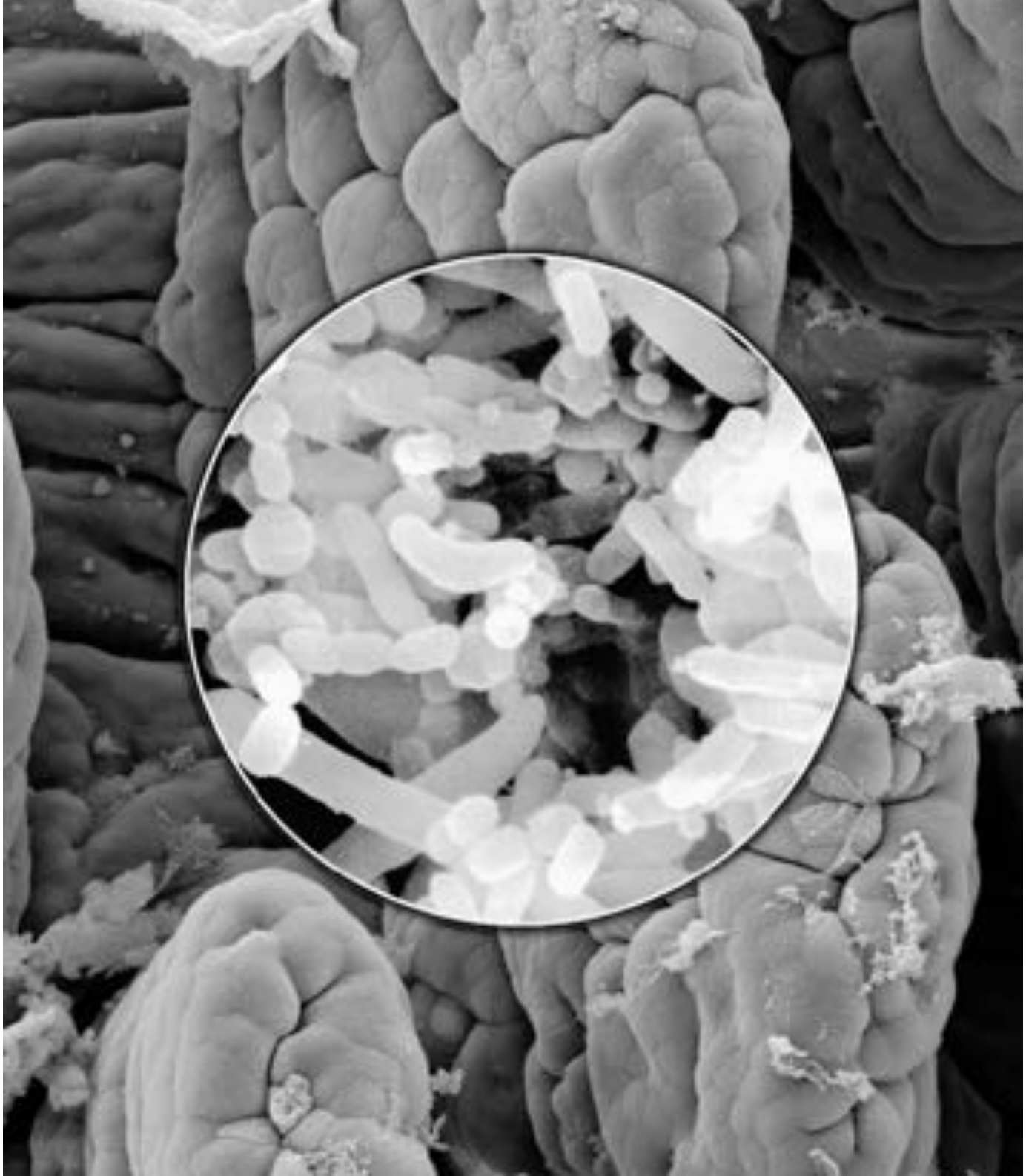
- Hvad er mikrobiomet?
- (Potentielle) virkningsmekanismer
- Dokumenterede effekter af specifikke probiotika
- Et par eksempler
  - Atopisk sygdom
  - Autoimmunsygdomme
  - Psyken
  - Fedme og vægt
- Hvad er godt?
- Hvad er dårligt?
- Hvordan kan jeg hjælpe dig?
- Spørgsmål

Du er i undertal


The Economist
The Catholic church's unholy mess
Paul Ryan: the man with the plan
Generation Xhausted
China, victim of the Olympics?
On the origin of specie
AUGUST 18TH–24TH 2012
Economist.com
Microbes maketh man
How 90% of the cells in your body are bacteria, the benefits of faecal transplants and other things you would rather not know before breakfast


The Human
Microbiome
Project





Din krops celler er i undertal

Ca. 10^{13} celler i menneskekroppen: 100.000.000.000.000 celler

$2x10^{13}$ - 10^{14} mikroorganismer i dit mavetarmsystem: 200.000.000.000.000 - 1.000.000.000.000.000

1:2 - 1:10 forhold menneskeceller:mikrober

Hvem er gæsterne?

De 200.000.000.000.000 - 1.000.000.000.000.000 mikrober i dit mavetarmsystem er et ekstra organ/system

- Lige så stor indflydelse på kroppen som lever, nyrer o.s.v.

De lever af den mad du spiser og påvirkes af hvad du gør

Hvem bor dernede?

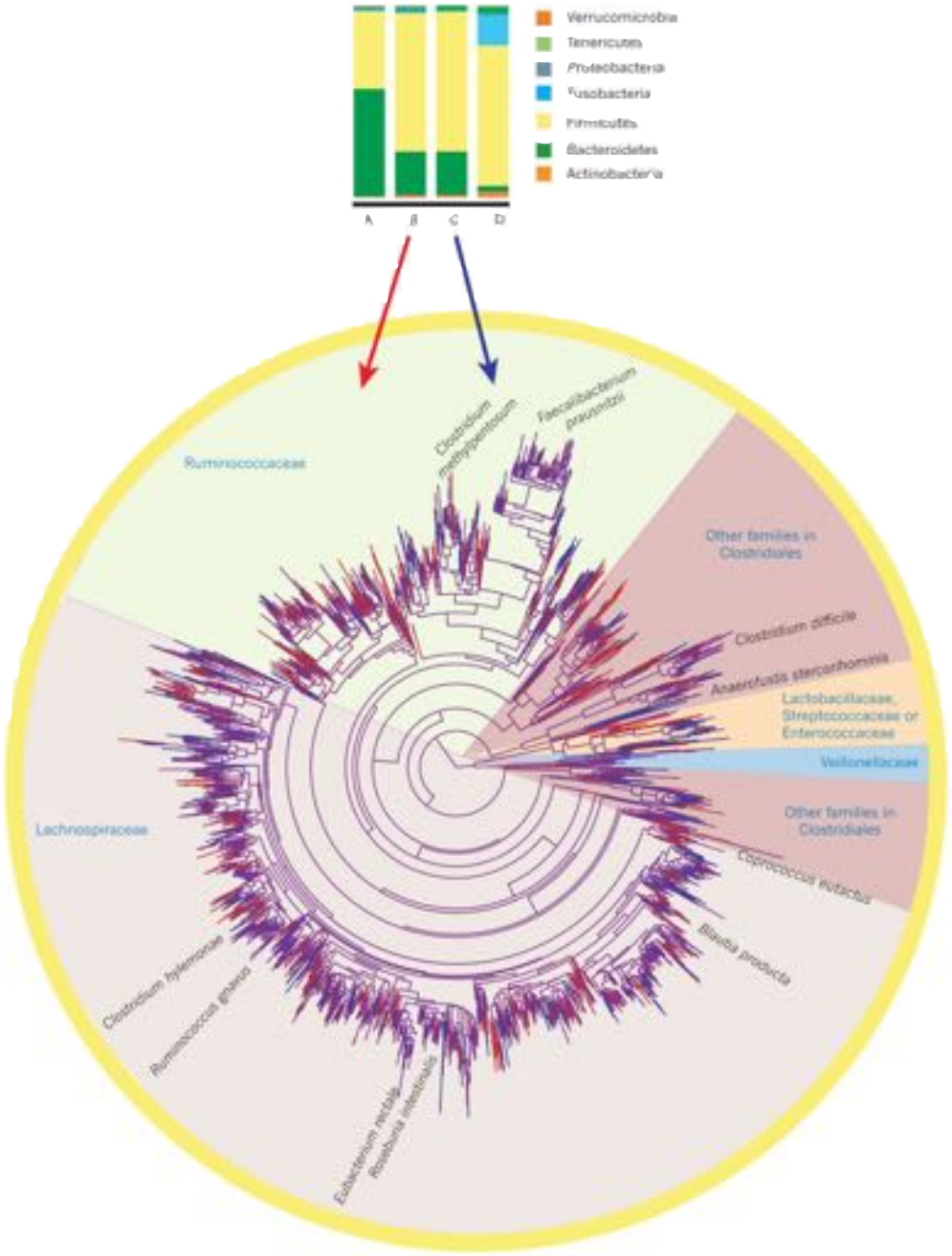
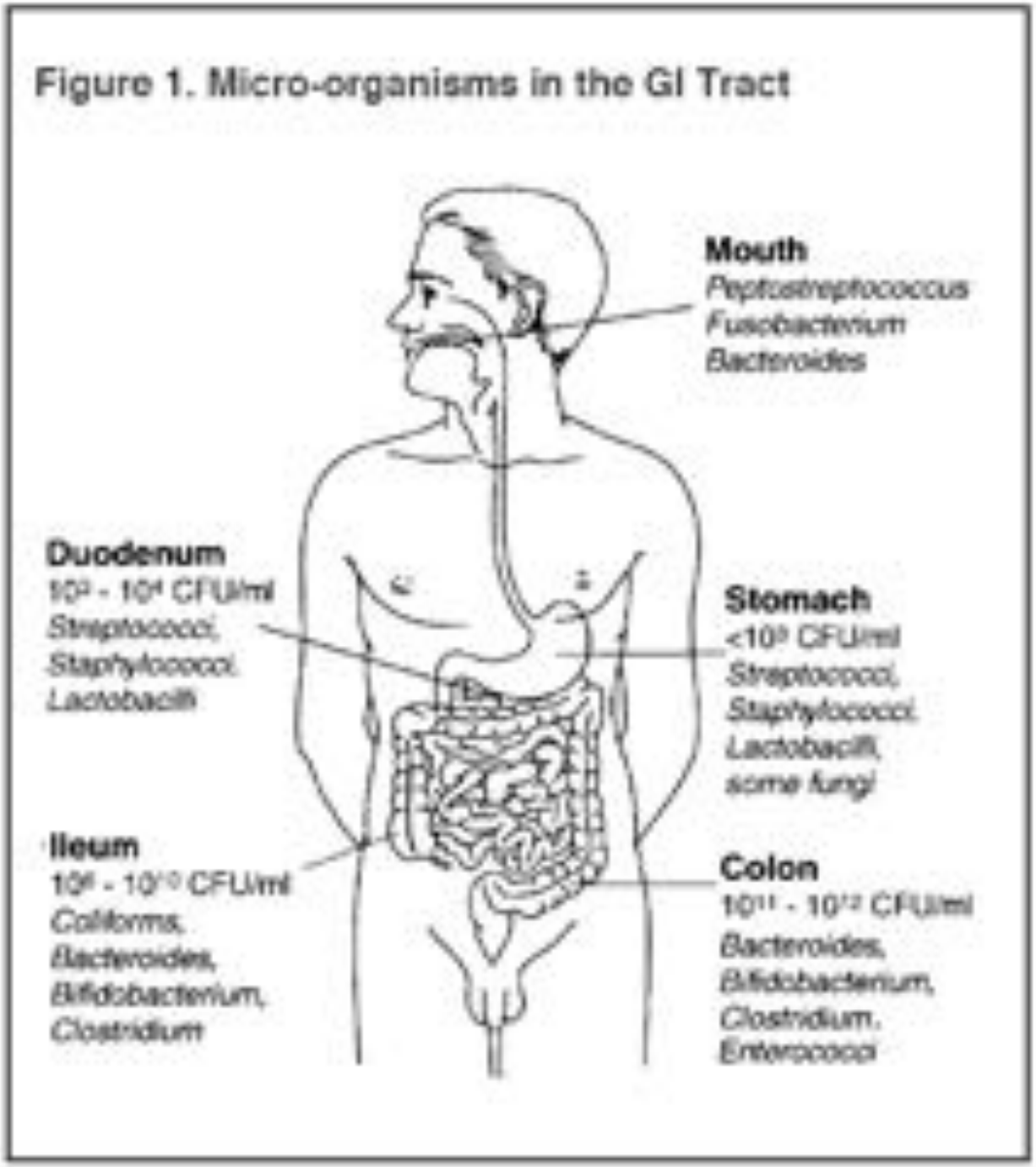
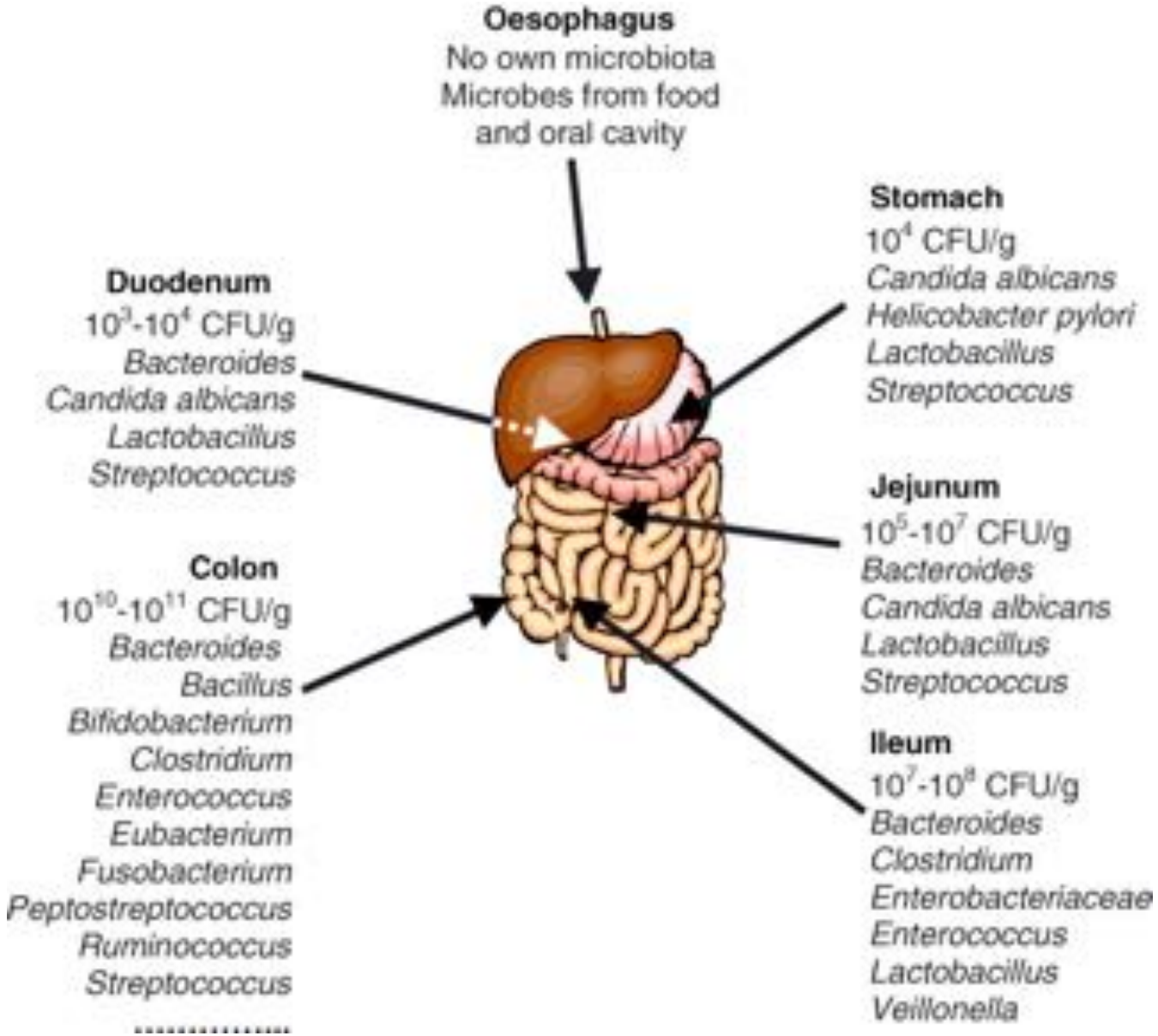
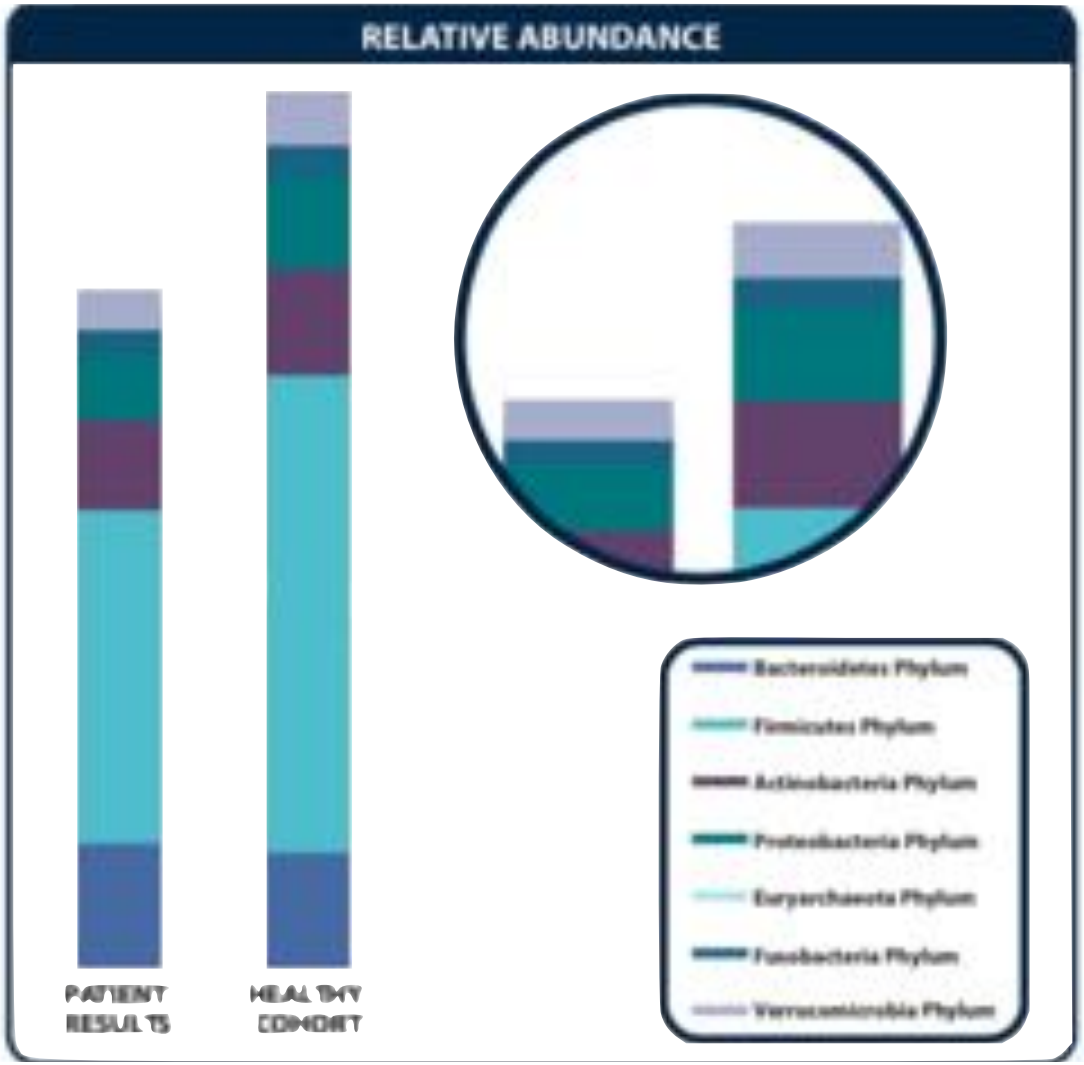


Figure 1. Micro-organisms in the GI Tract

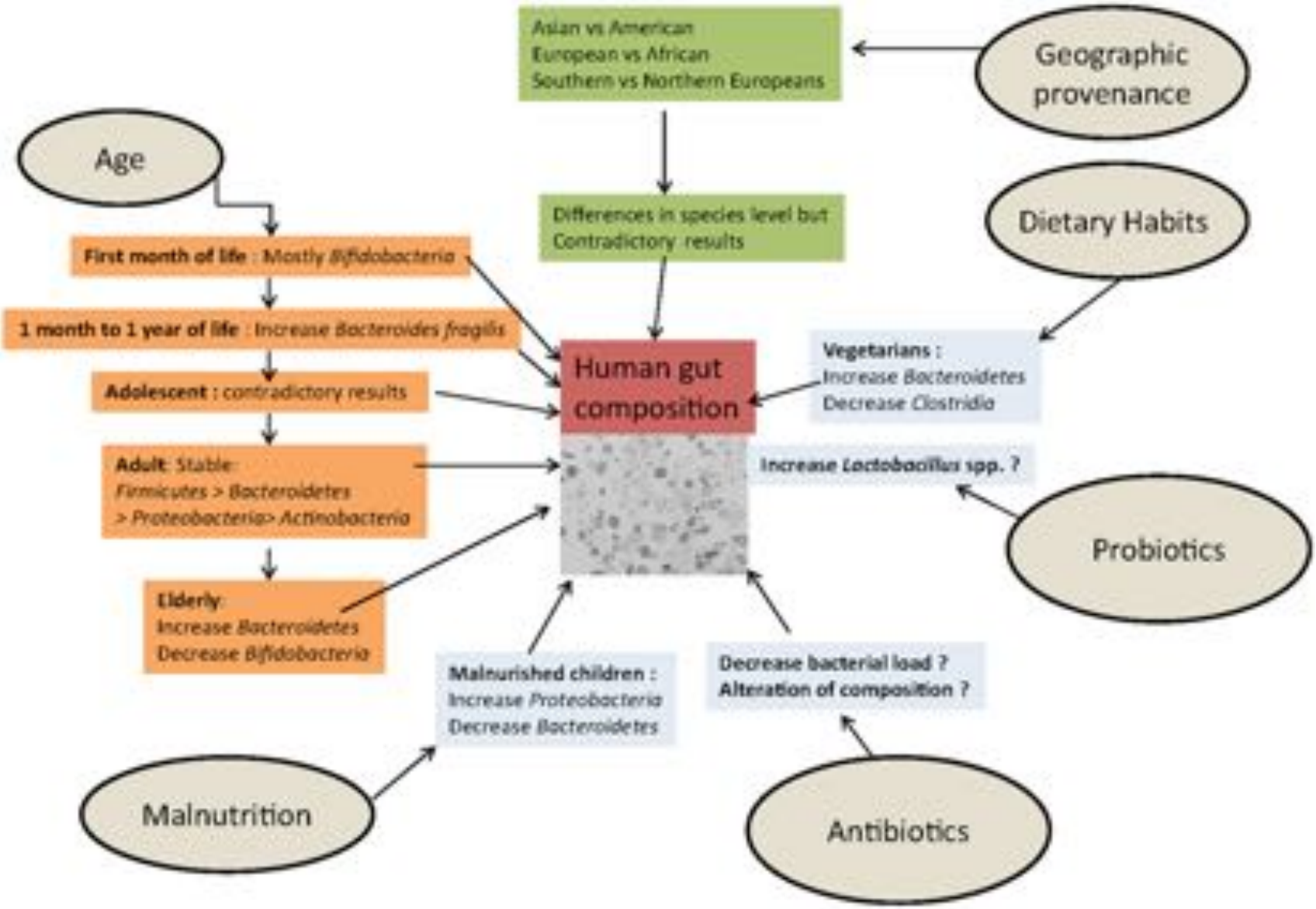



Oesophagus
No own microbiota
Microbes from food
and oral cavity
Stomach
10^4 CFU/g
Candida albicans
Helicobacter pylori
Lactobacillus
Streptococcus
Duodenum
10^3-10^4 CFU/g
Bacteroides
Candida albicans
Lactobacillus
Streptococcus
Jejunum
10^5-10^7 CFU/g
Bacteroides
Candida albicans
Lactobacillus
Streptococcus
Colon
10^{10}-10^{11} CFU/g
Bacteroides
Bacillus
Bifidobacterium
Clostridium
Enterococcus
Eubacterium
Fusobacterium
Peptostreptococcus
Ruminococcus
Streptococcus
Ileum
10^7-10^8 CFU/g
Bacteroides
Clostridium
Enterobacteriaceae
Enterococcus
Lactobacillus
Veillonella

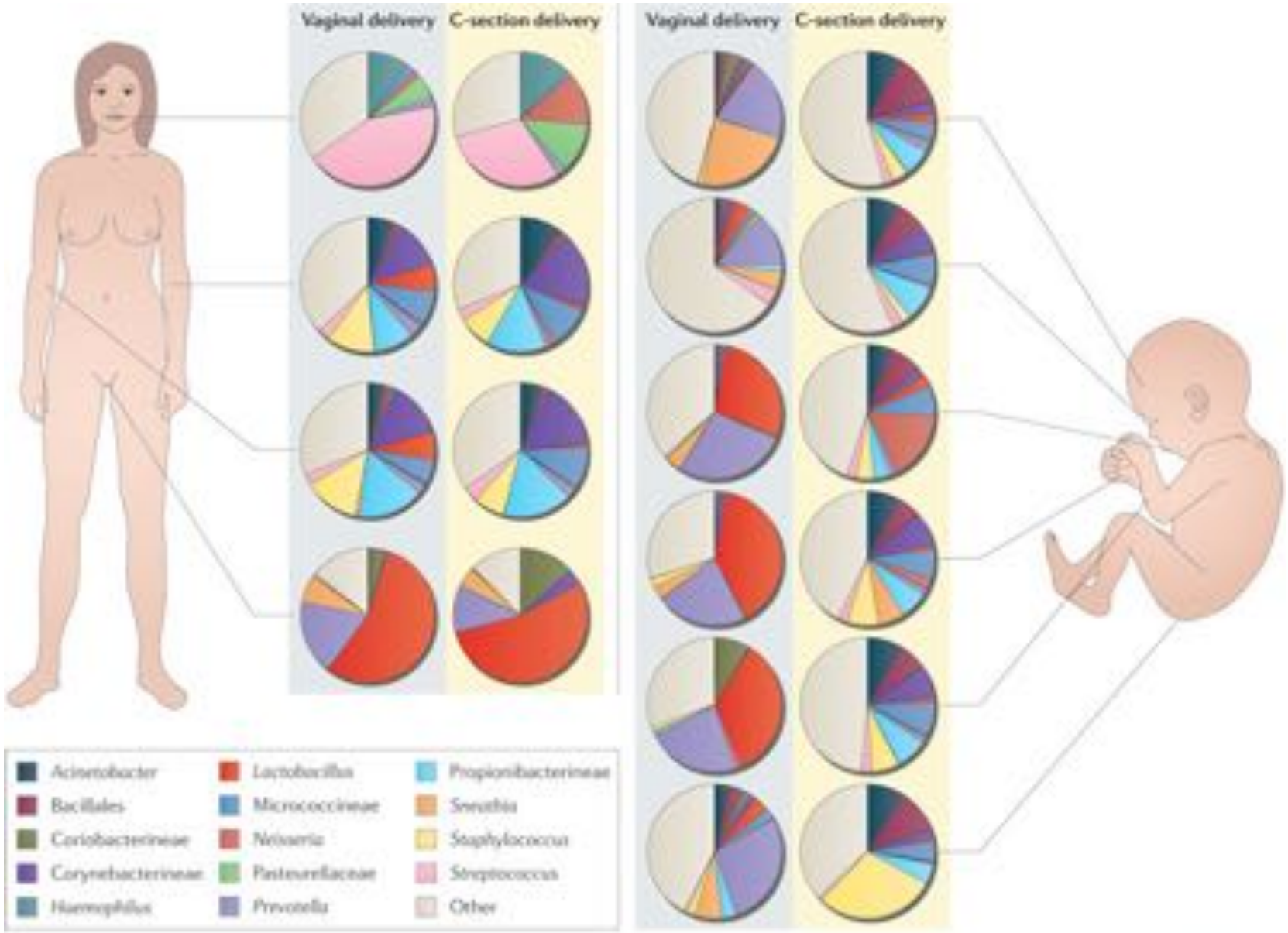
Monokultur eller diversitet?



Du og miljøet bestemmer



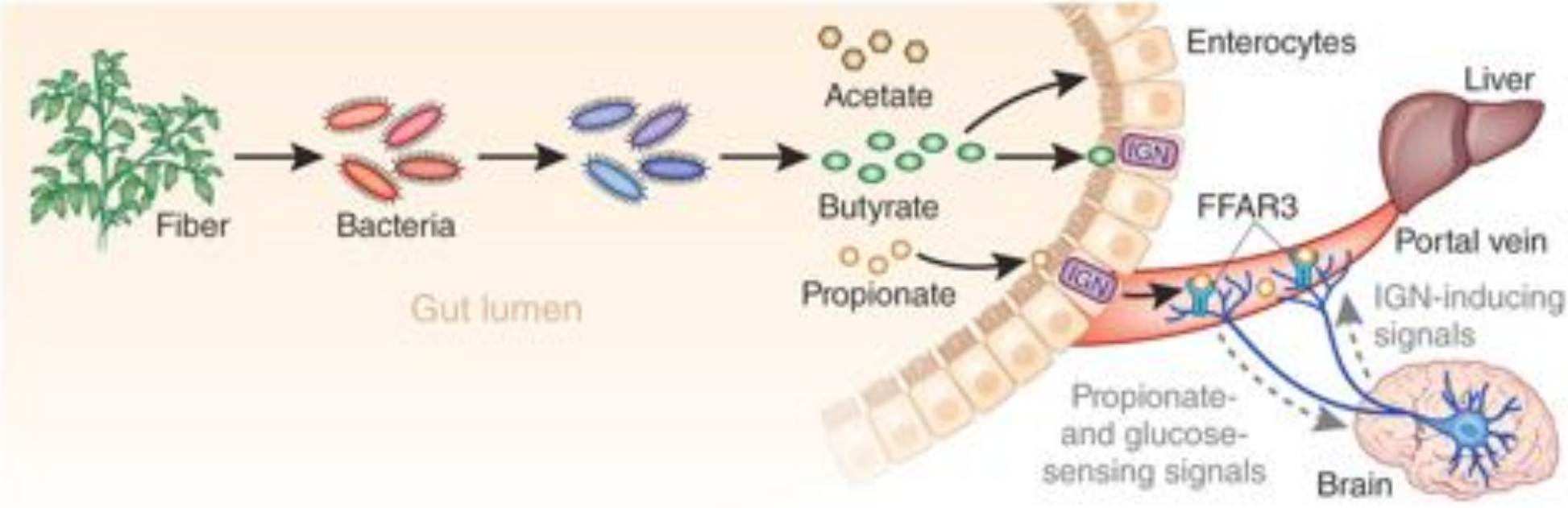
Hvordan blev du født?



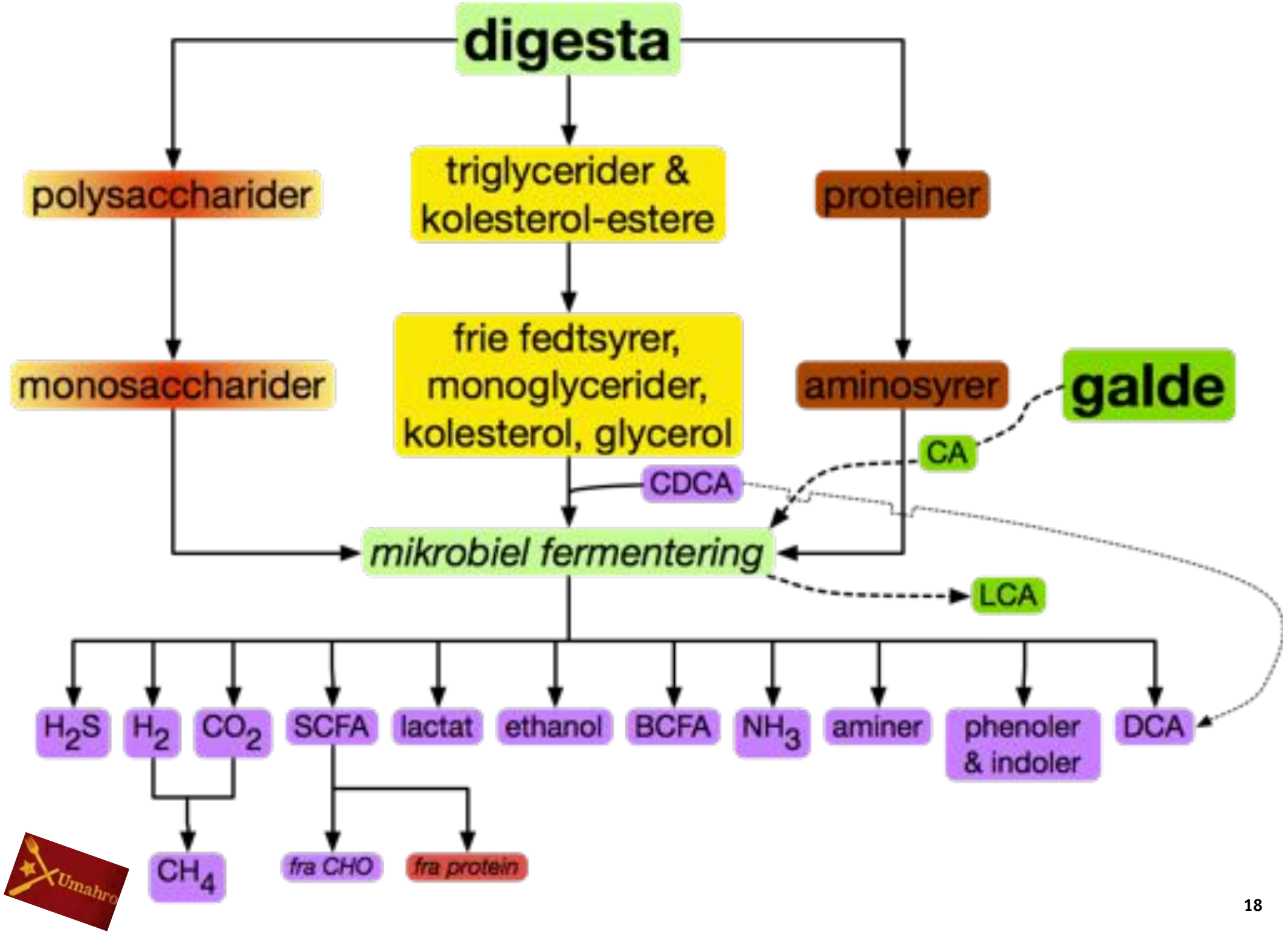
Nature Reviews | Microbiology

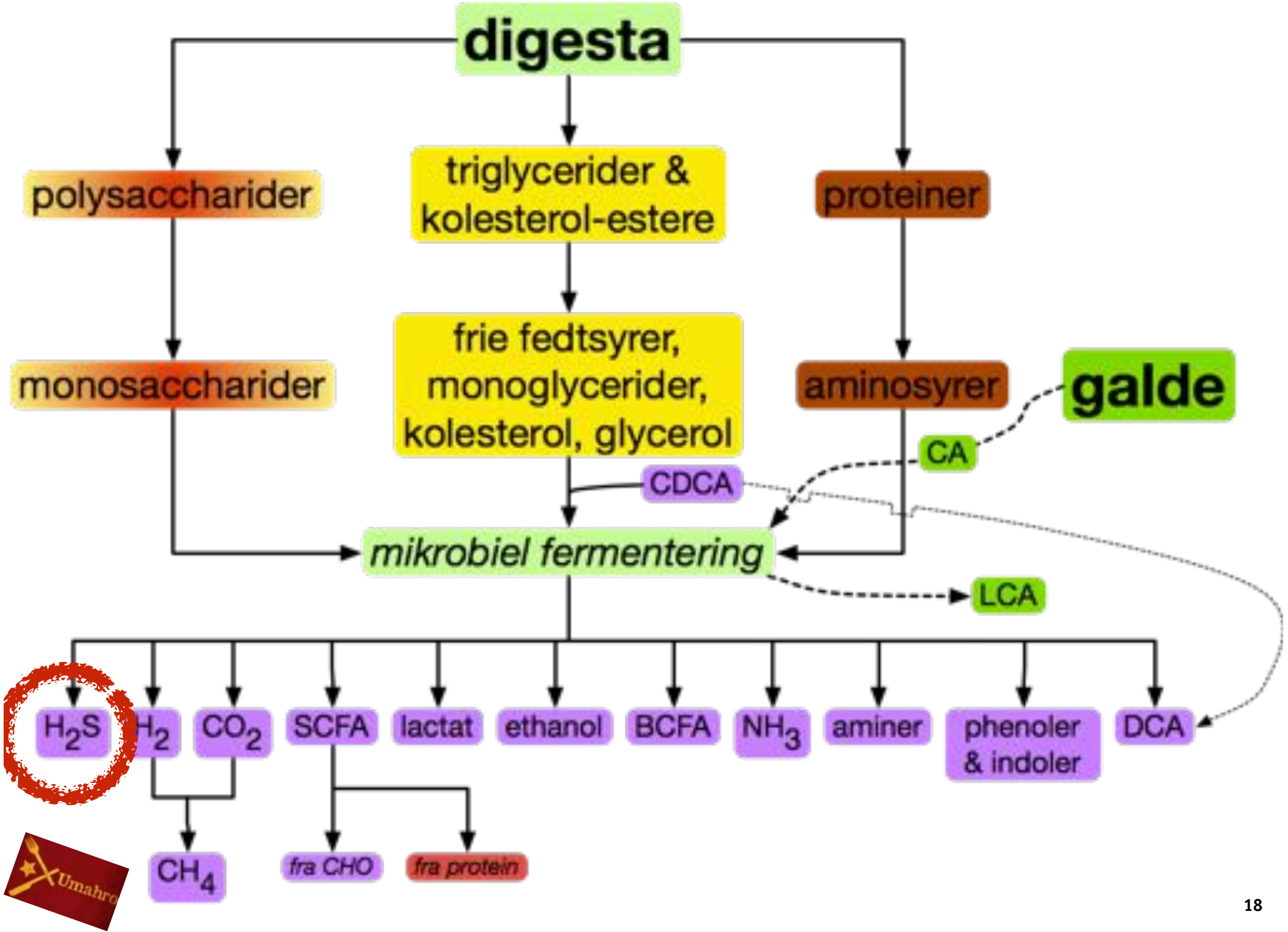
(Potentielle) virkningsmekanismer

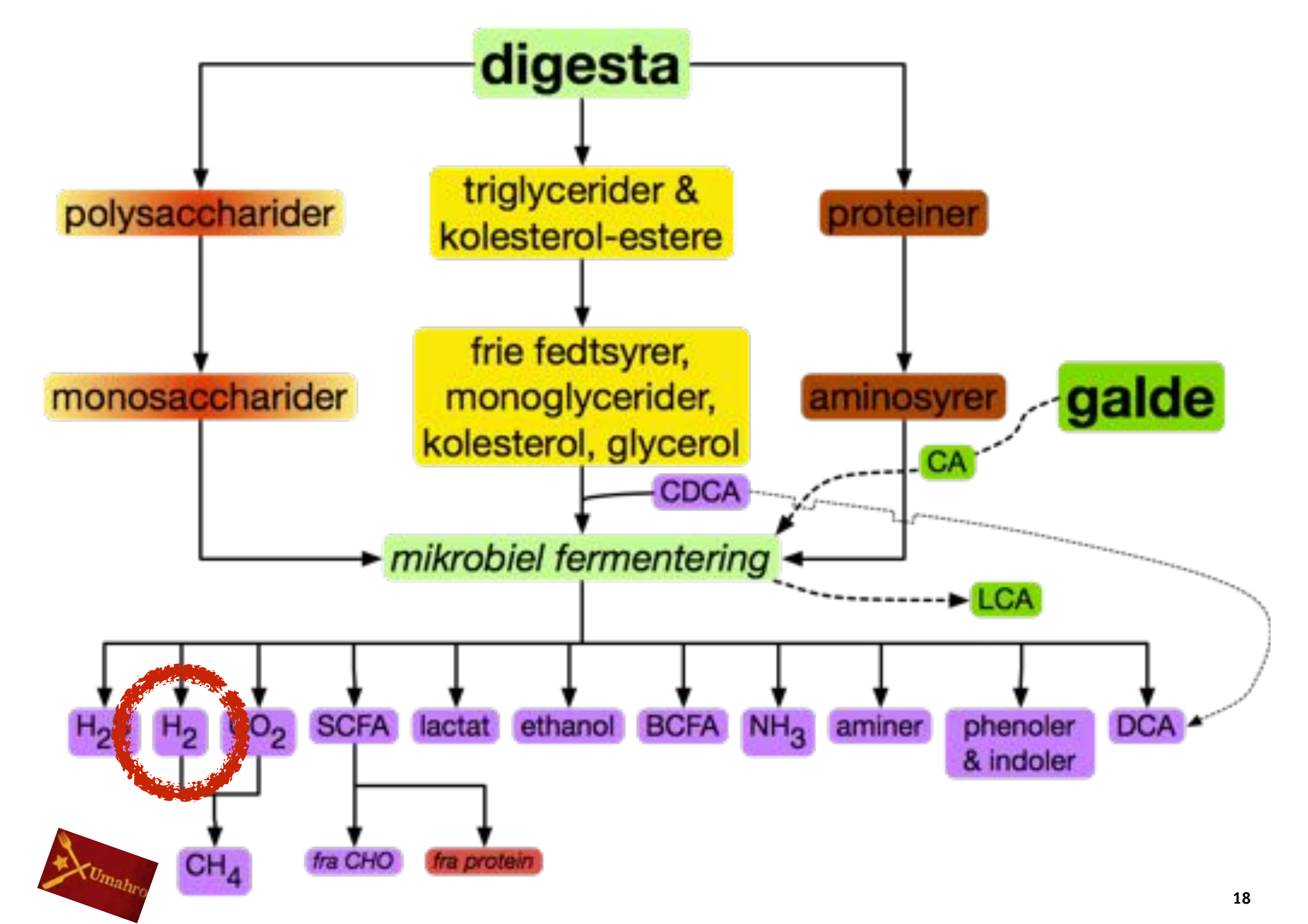
Kortkædede fedtsyrer

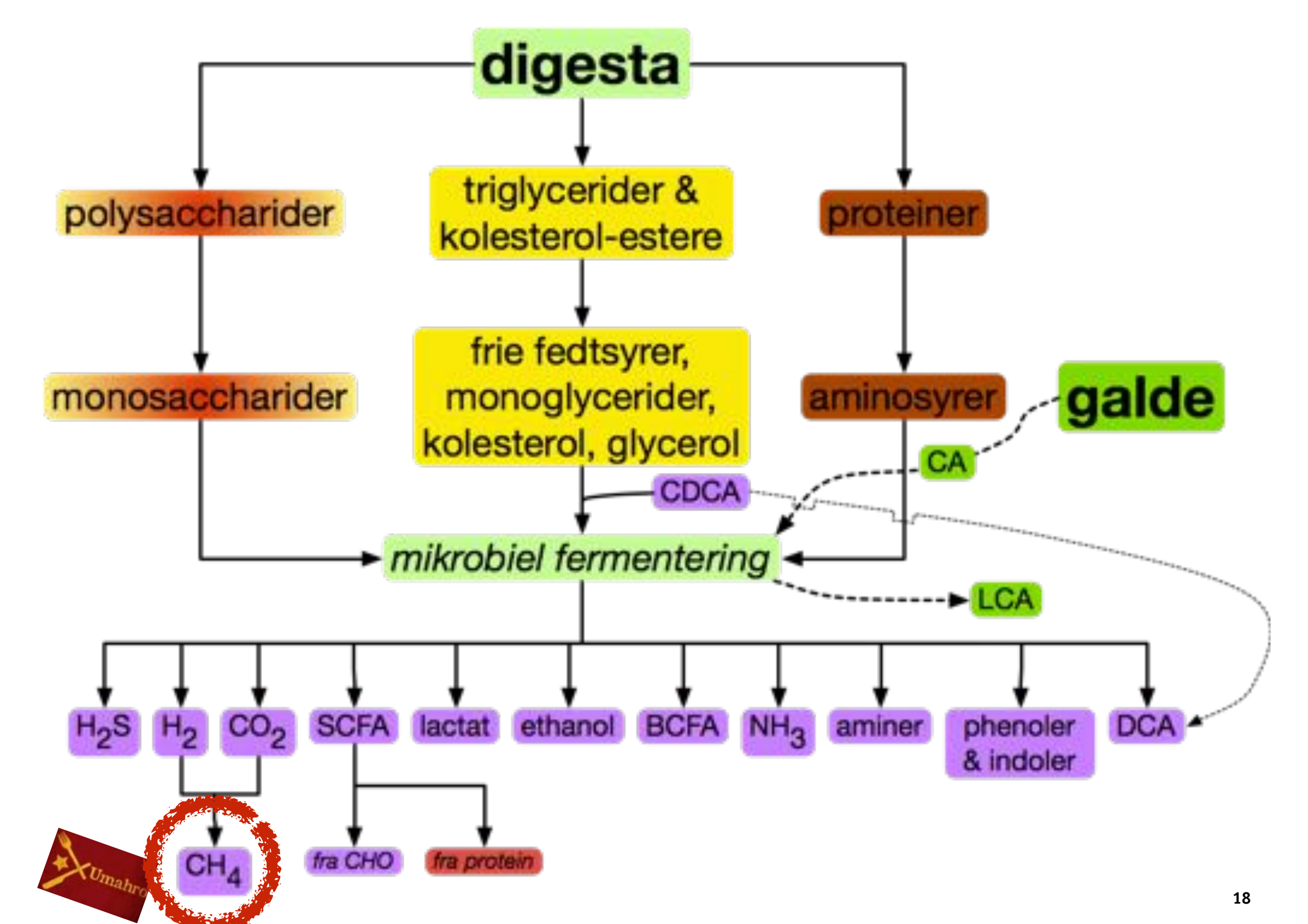


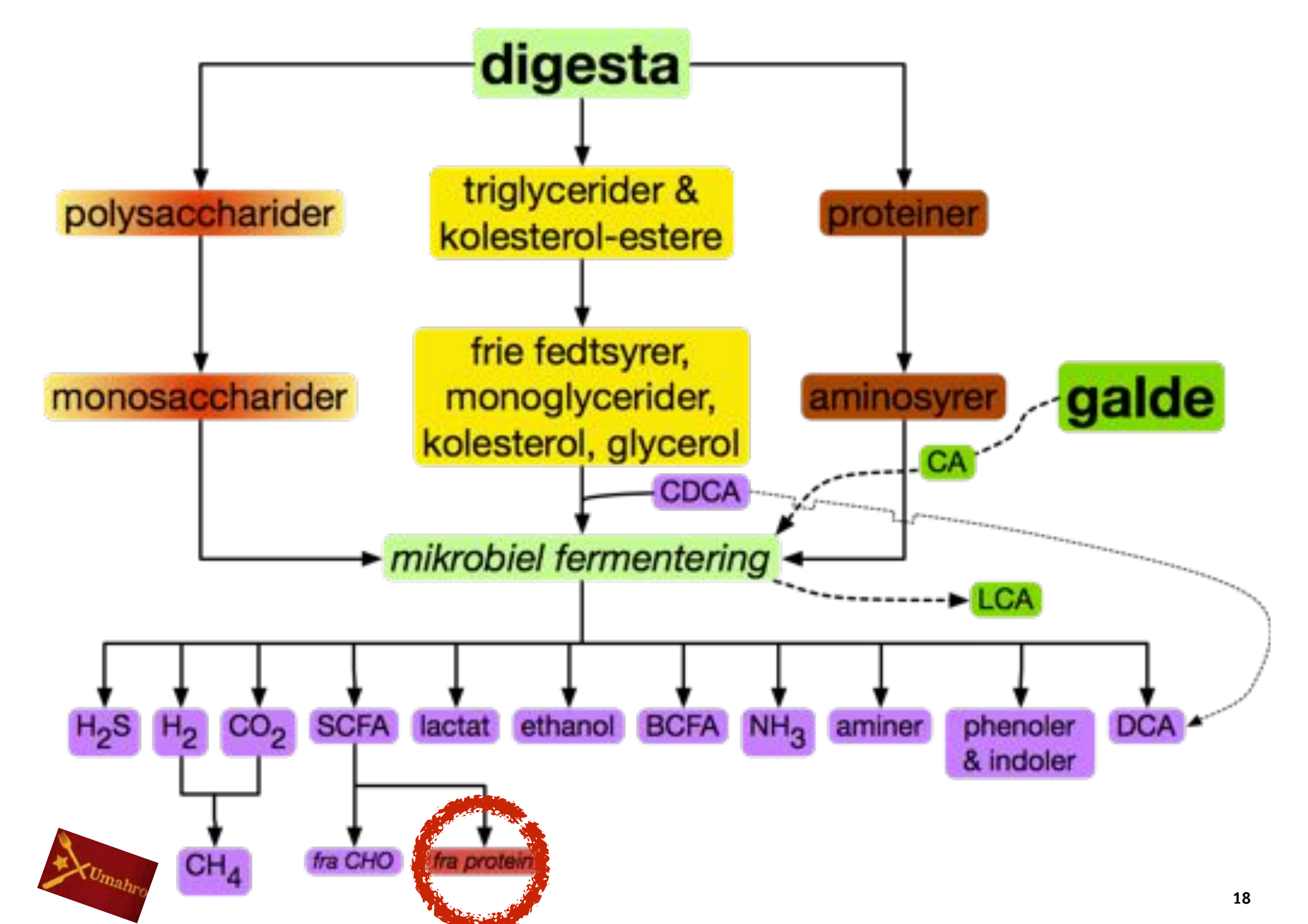
Hvad laver din tarmflora?

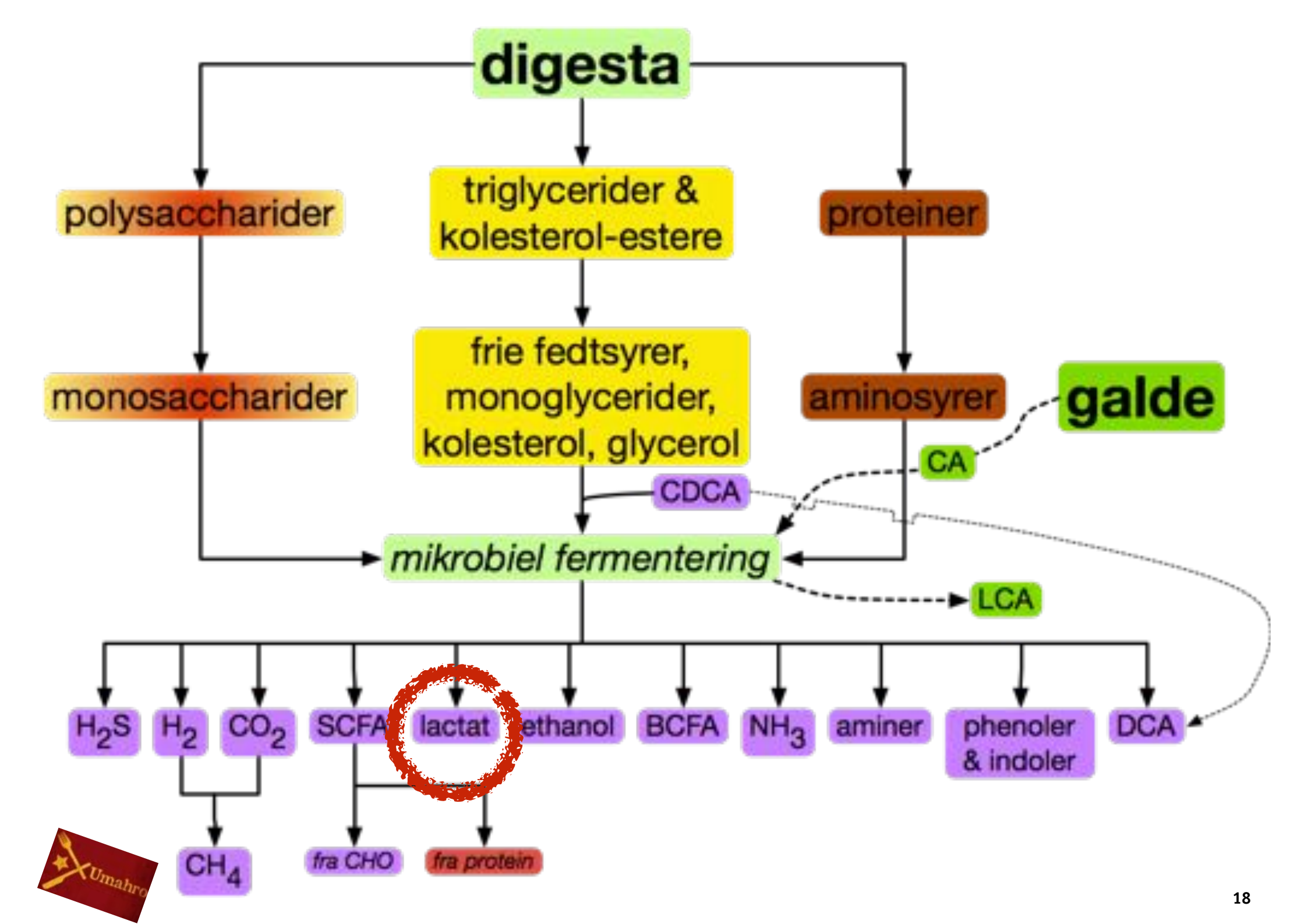

digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein

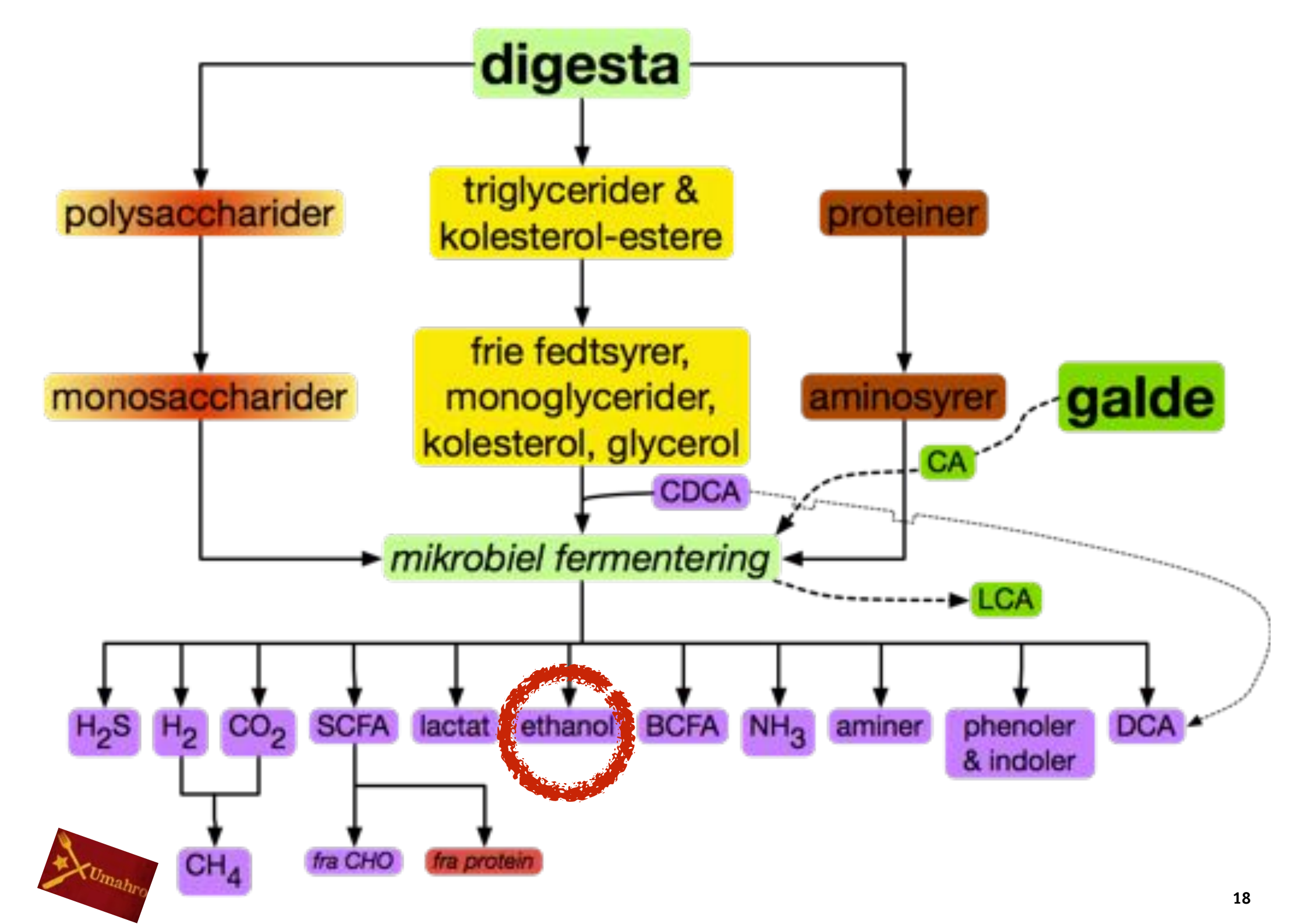

digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein

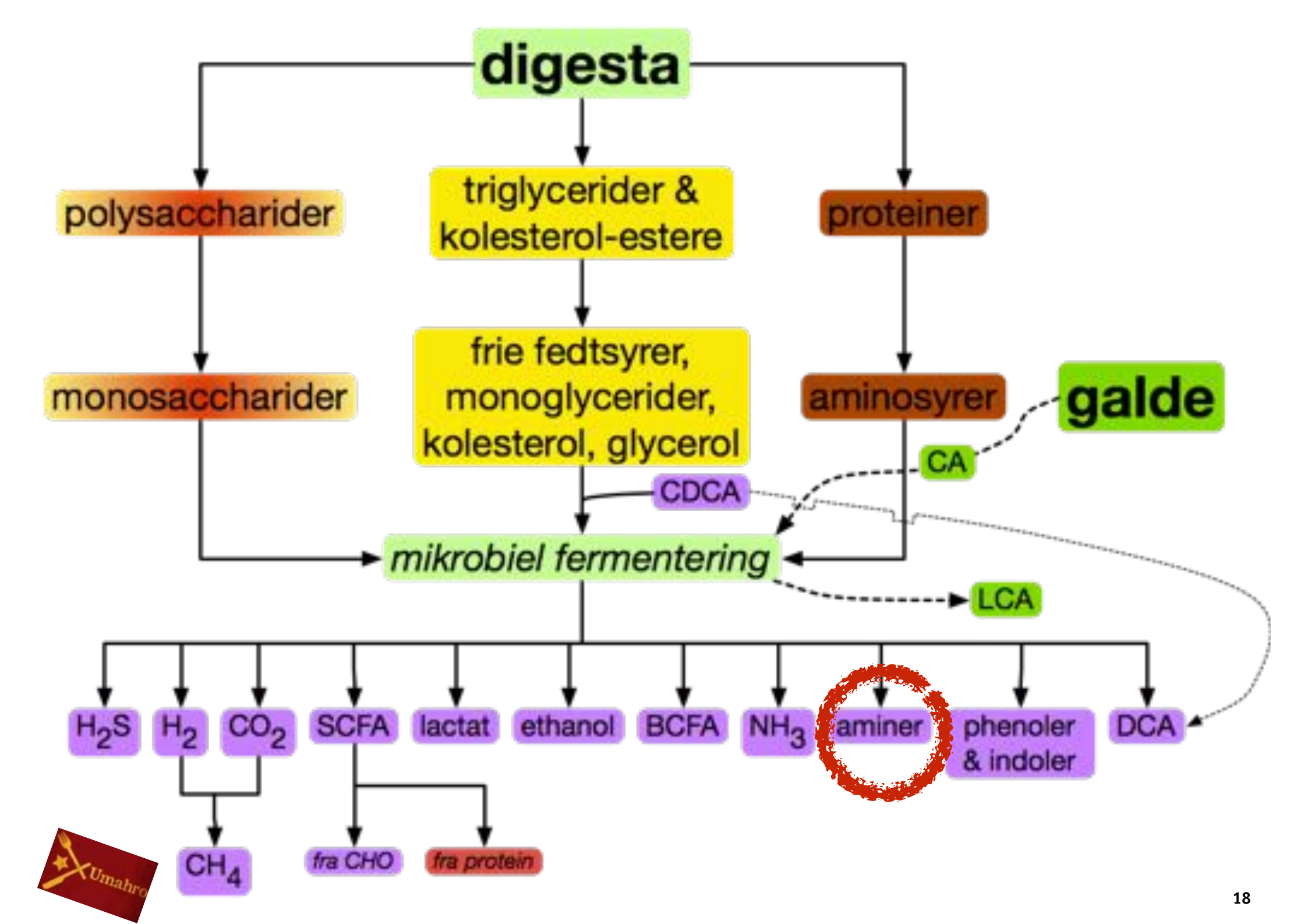

digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H_2
H_2
O_2
SCFA
lactat
ethanol
BCFA
NH_3
aminer
phenoler & indoler
DCA
CH_4
fra CHO
fra protein

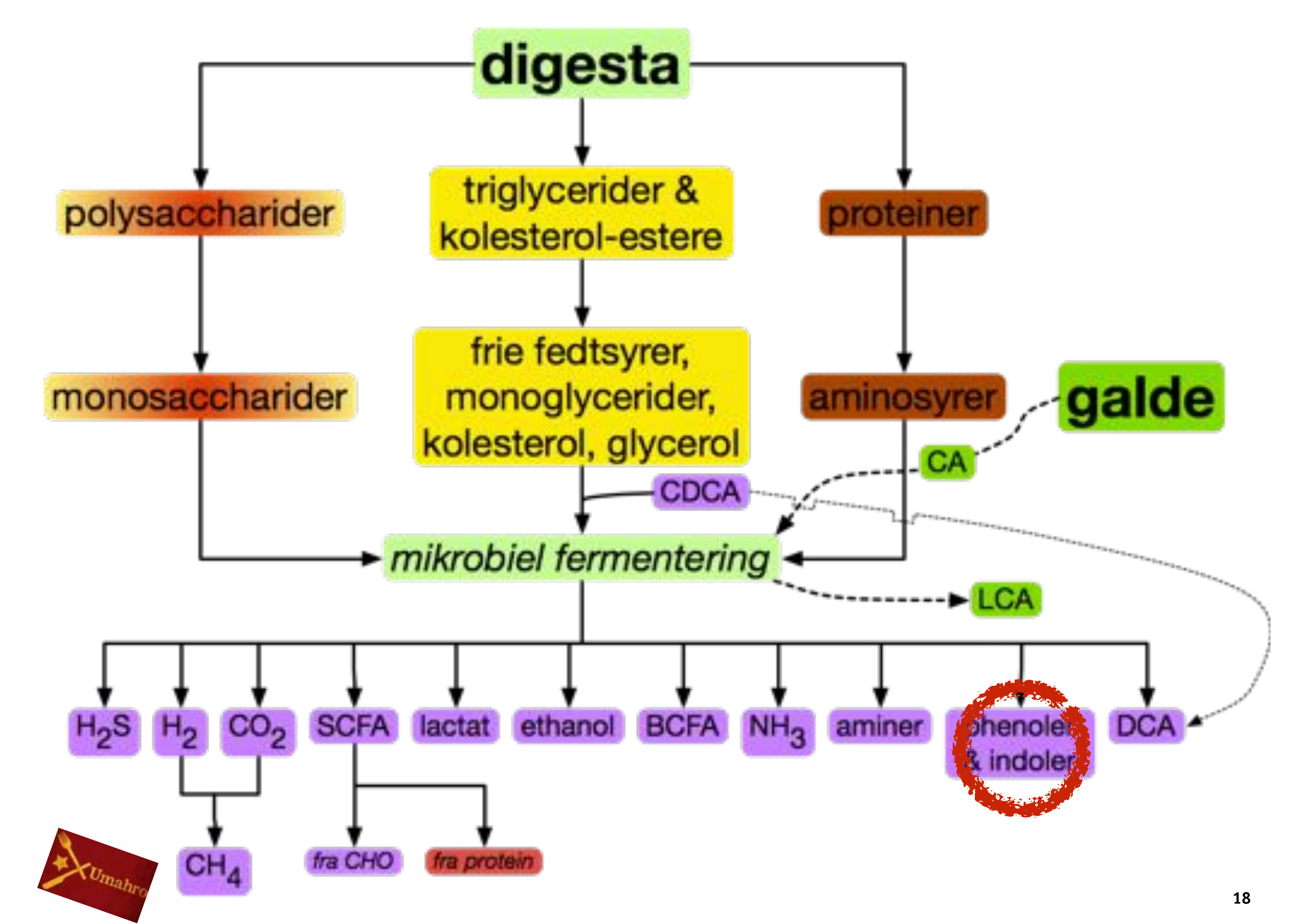

digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein

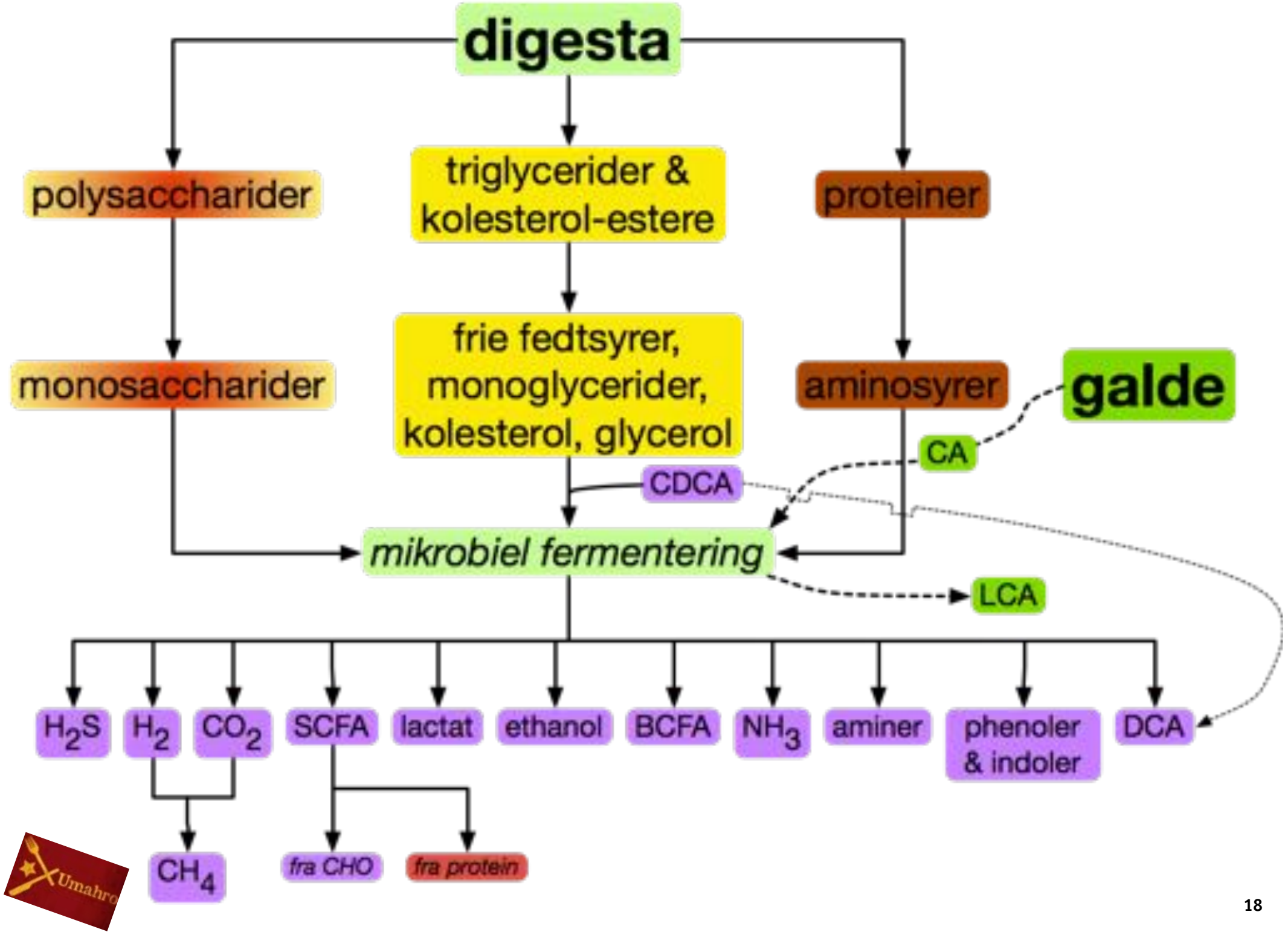

digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein
Umahro

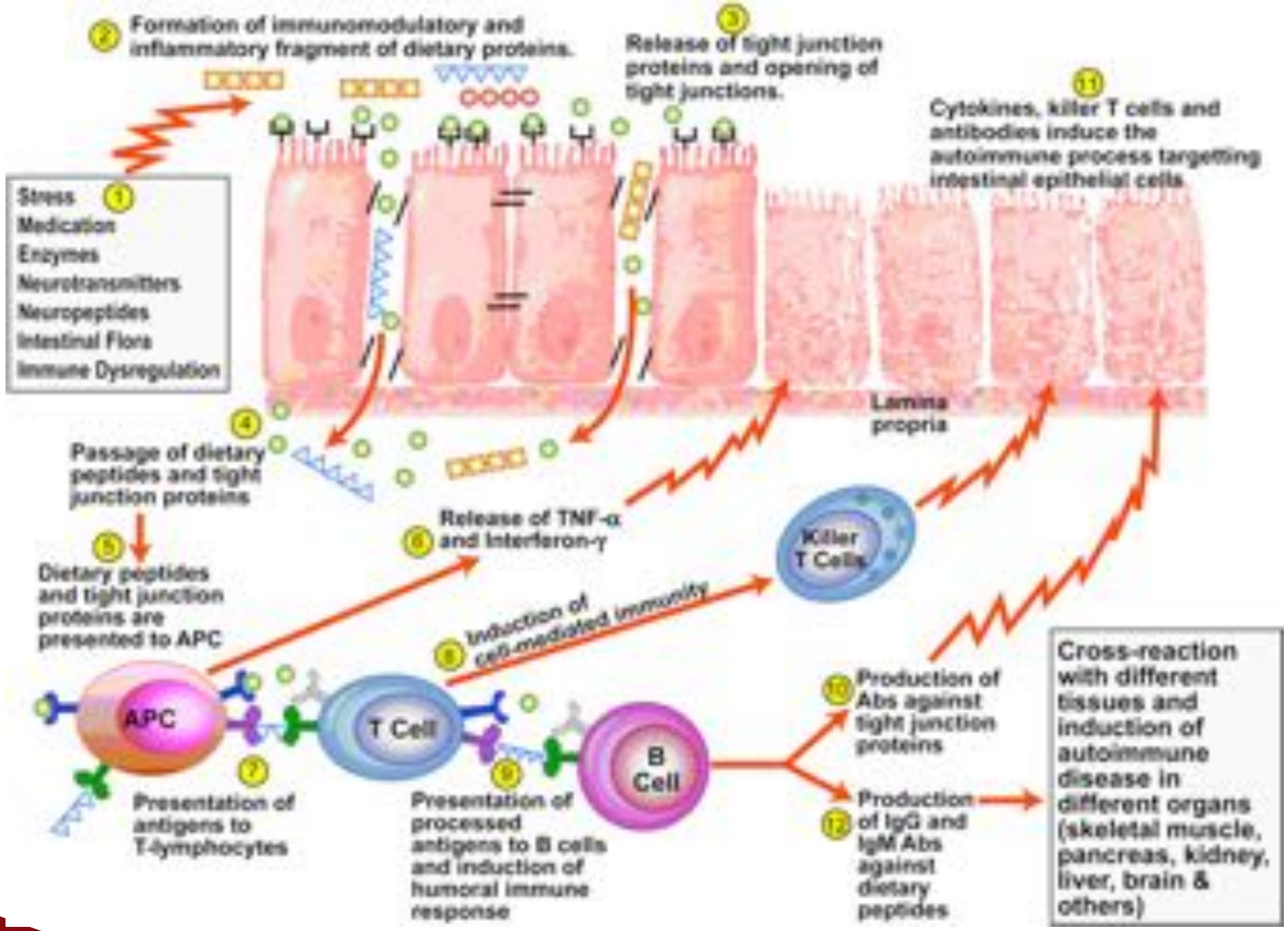

digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein


digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein


digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein


digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
DCA
CH4
fra CHO
fra protein


digesta
polysaccharider
triglycerider & kolesterol-estere
proteiner
monosaccharider
frie fedtsyrer, monoglycerider, kolesterol, glycerol
aminosyrer
galde
CA
CDCA
mikrobiel fermentering
LCA
H2S
H2
CO2
SCFA
lactat
ethanol
BCFA
NH3
aminer
phenoler & indoler
DCA
CH4
fra CHO
fra protein


2 Formation of immunomodulatory and inflammatory fragment of dietary proteins.
3 Release of tight junction proteins and opening of tight junctions.
11 Cytokines, killer T cells and antibodies induce the autoimmune process targeting intestinal epithelial cells
Stress
Medication
Enzymes
Neurotransmitters
Neuropeptides
Intestinal Flora
Immune Dysregulation
1
Lamina propria
4 Passage of dietary peptides and tight junction proteins
5 Dietary peptides and tight junction proteins are presented to APC
6 Release of TNF-α and interferon-γ
Killer T Cells
8 Induction of cell-mediated immunity
APC
T Cell
B Cell
7 Presentation of antigens to T-lymphocytes
9 Presentation of processed antigens to B cells and induction of humoral immune response
10 Production of Abs against tight junction proteins
12 Production of IgG and IgM Abs against dietary peptides
Cross-reaction with different tissues and induction of autoimmune disease in different organs (skeletal muscle, pancreas, kidney, liver, brain & others)

“Ubudne gæster”?

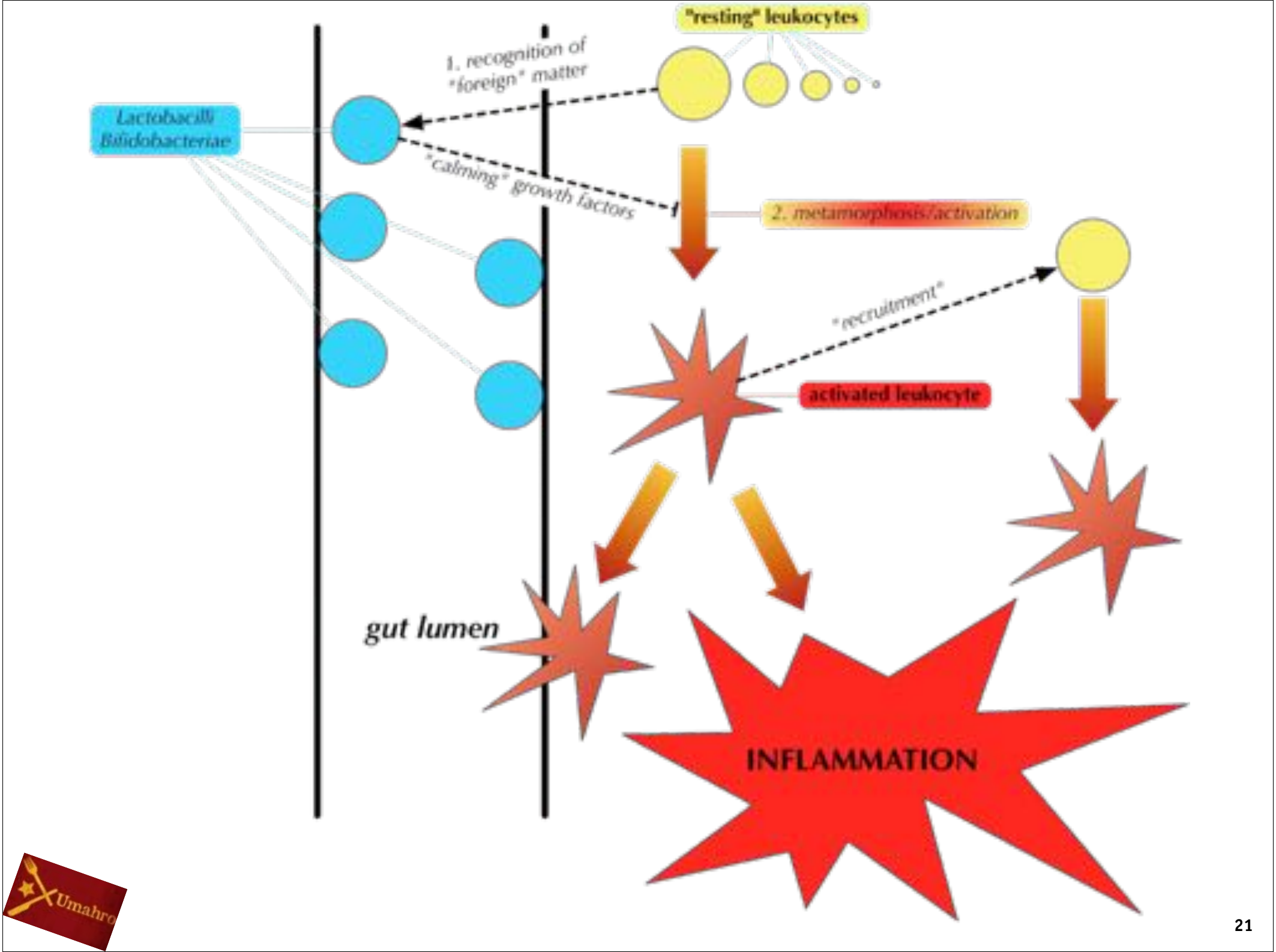
"Ubudne gæster"?

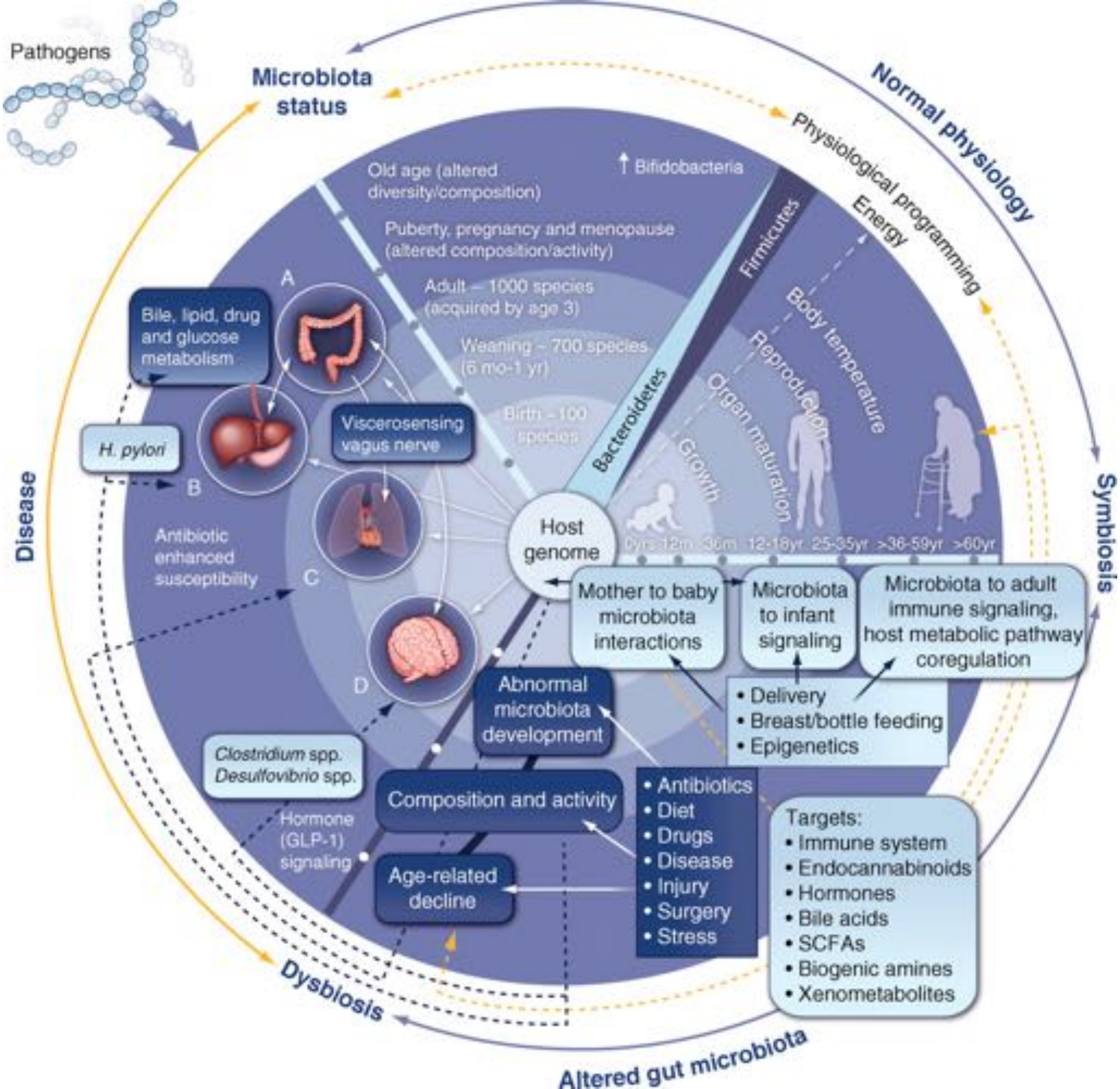
"Ubudne gæster"?

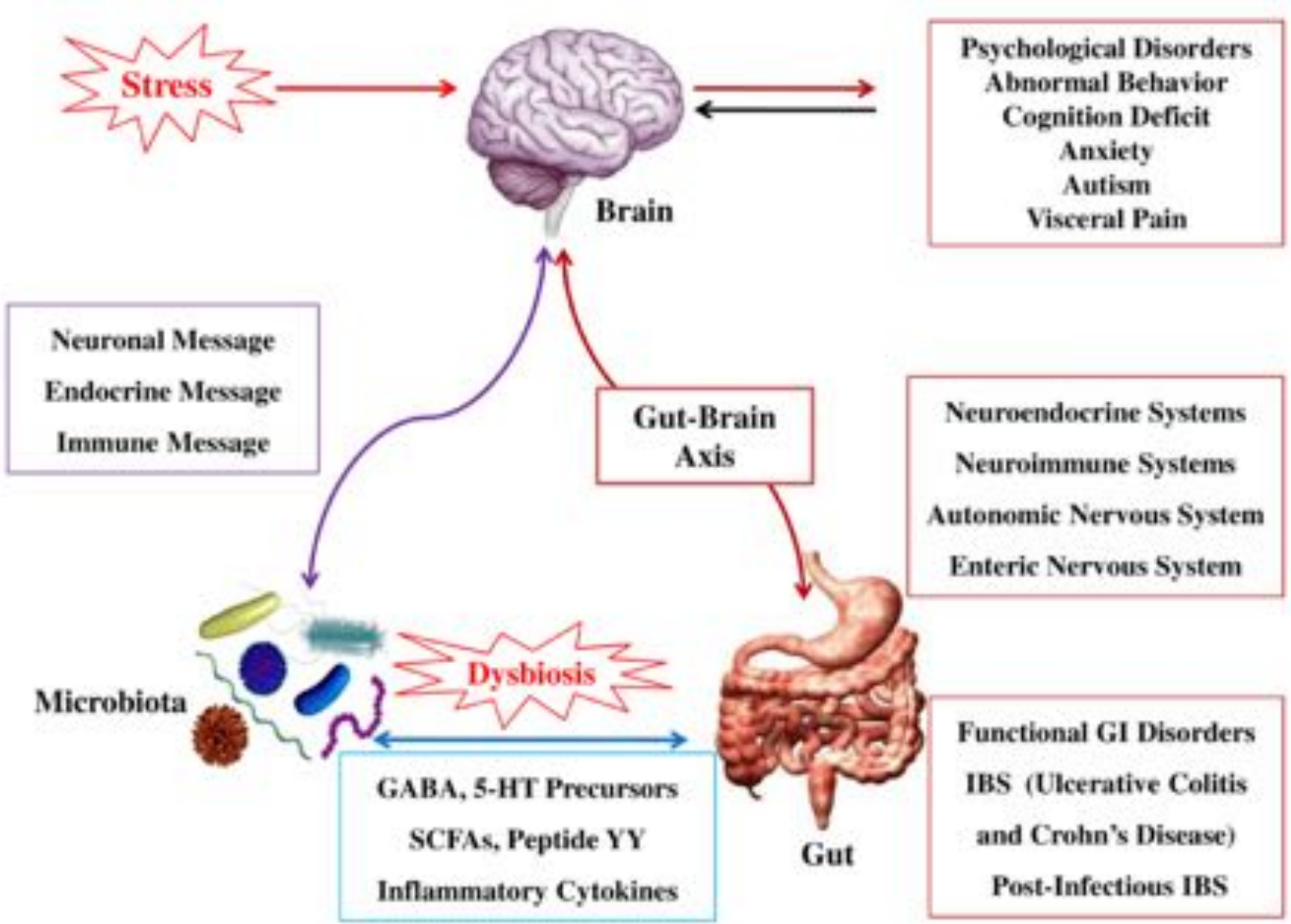
"Ubudne gæster"?

"Ubudne gæster"?

"Ubudne gæster"?


"resting" leukocytes
1. recognition of "foreign" matter
Lactobacilli Bifidobacteriae
"calming" growth factors
2. metamorphosis/activation
"recruitment"
activated leukocyte
gut lumen
INFLAMMATION


Pathogens
Microbiota status
Normal physiology
Physiological programming
Energy
Body temperature
Reproduction
Organ maturation
Growth
Old age (altered diversity/composition)
↑ Bifidobacteria
Puberty, pregnancy and menopause (altered composition/activity)
Adult ~ 1000 species (acquired by age 3)
Weaning ~ 700 species (6 mo-1 yr)
Birth ~ 100 species
Firmicutes
Bacteroidetes
A
Bile, lipid, drug and glucose metabolism
H. pylori
B
Viscerosensing vagus nerve
Antibiotic enhanced susceptibility
C
D
Host genome
0yrs 12m 36m 12-18yr 25-35yr >36-59yr >60yr
Mother to baby microbiota interactions
Microbiota to infant signaling
Microbiota to adult immune signaling, host metabolic pathway coregulation
• Delivery
• Breast/bottle feeding
• Epigenetics
Abnormal microbiota development
Clostridium spp.
Desulfovibrio spp.
Hormone (GLP-1) signaling
Composition and activity
Age-related decline
• Antibiotics
• Diet
• Drugs
• Disease
• Injury
• Surgery
• Stress
Targets:
• Immune system
• Endocannabinoids
• Hormones
• Bile acids
• SCFAs
• Biogenic amines
• Xenometabolites
Disease
Symbiosis
Dysbiosis
Altered gut microbiota



Thakur AK, Shakya A, Husain GM, Emerald M, Kumar V (2014) Gut-Microbiota and Mental Health: Current and Future Perspectives. J Pharmacol Clin Toxicol 2(1):1016.

Dokumenterede effekter af specifikke probiotika

Hvilke arter er der god dokumentation på?

Bifidobacterium BB12

Lactobacillus acidophilus LA-5

Lactobacillus GG (LGG)

Lactobacillus reuteri (RC-14)

Lactobacillus rhamnosus GR-1

Lactobacillus casei L. CASEI 431

Lactobacillus F-19

Streptococcus thermopiles TH-4

Lactobacillus fermentum PCC

Saccharomyces boulardii

Escherichia coli Nissle

Hvad er også interessant?

Bacillus arter

Bacteroides arter

Jordbakterier

Fækale bakterieblandinger

Helminther

Kvalitetskriterier

Mindst 10 milliarder CFU dagligt til behandling

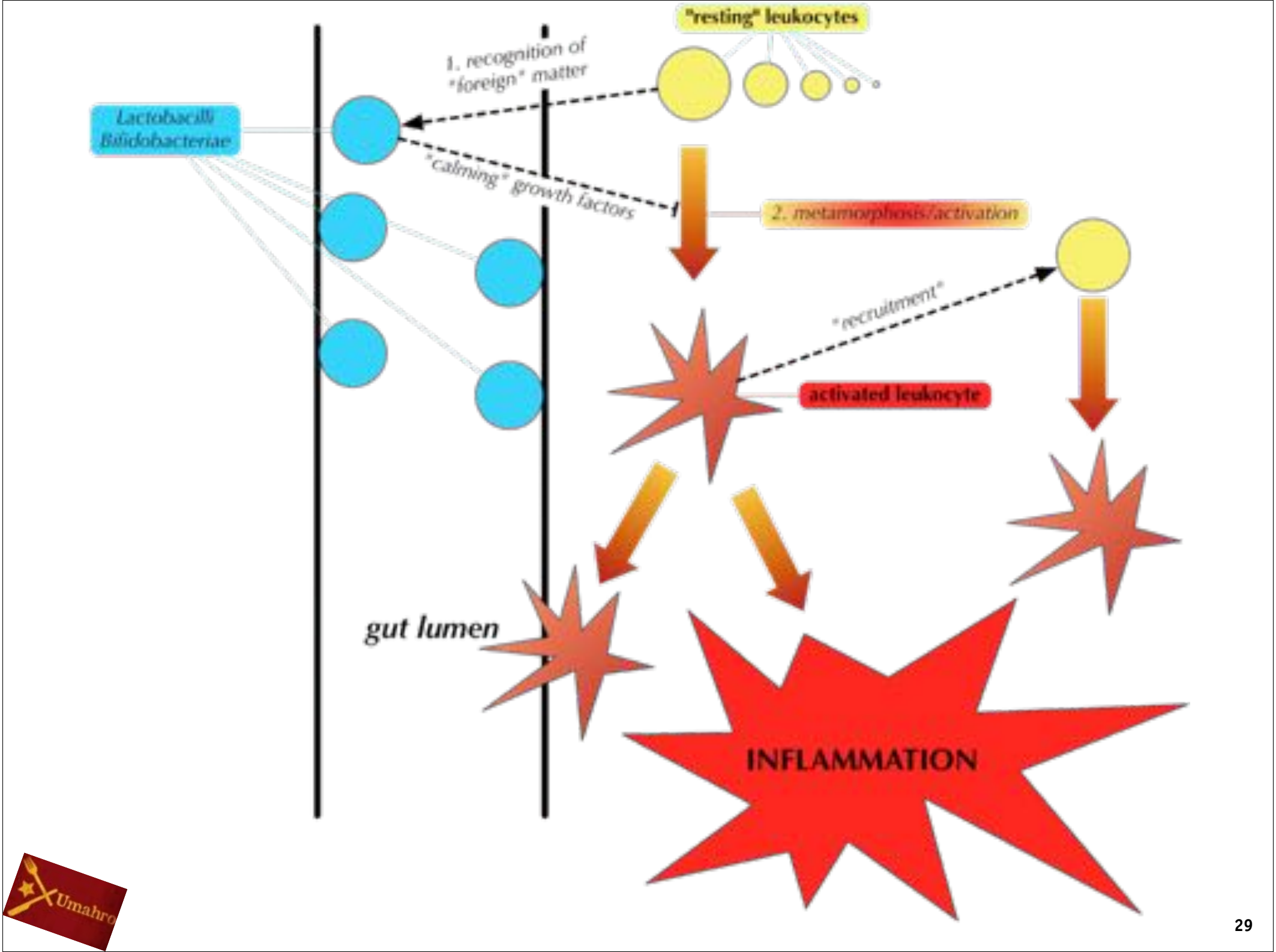
Både *Lactobacillus* og *Bifidobacterium* arter

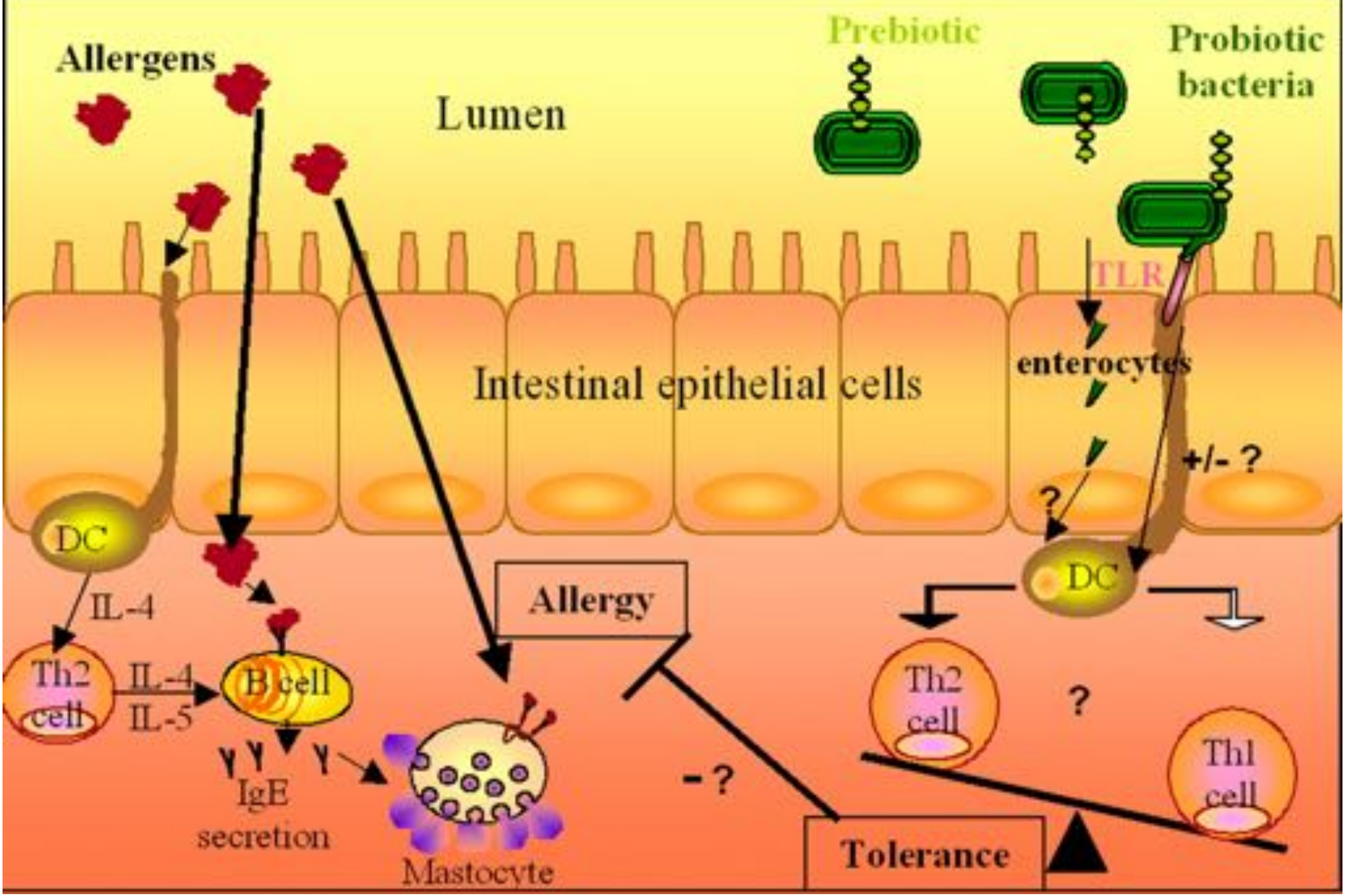
Også gerne andre arter efter behov

Humane bakterier

Istand til at overleve mavesyre og galde

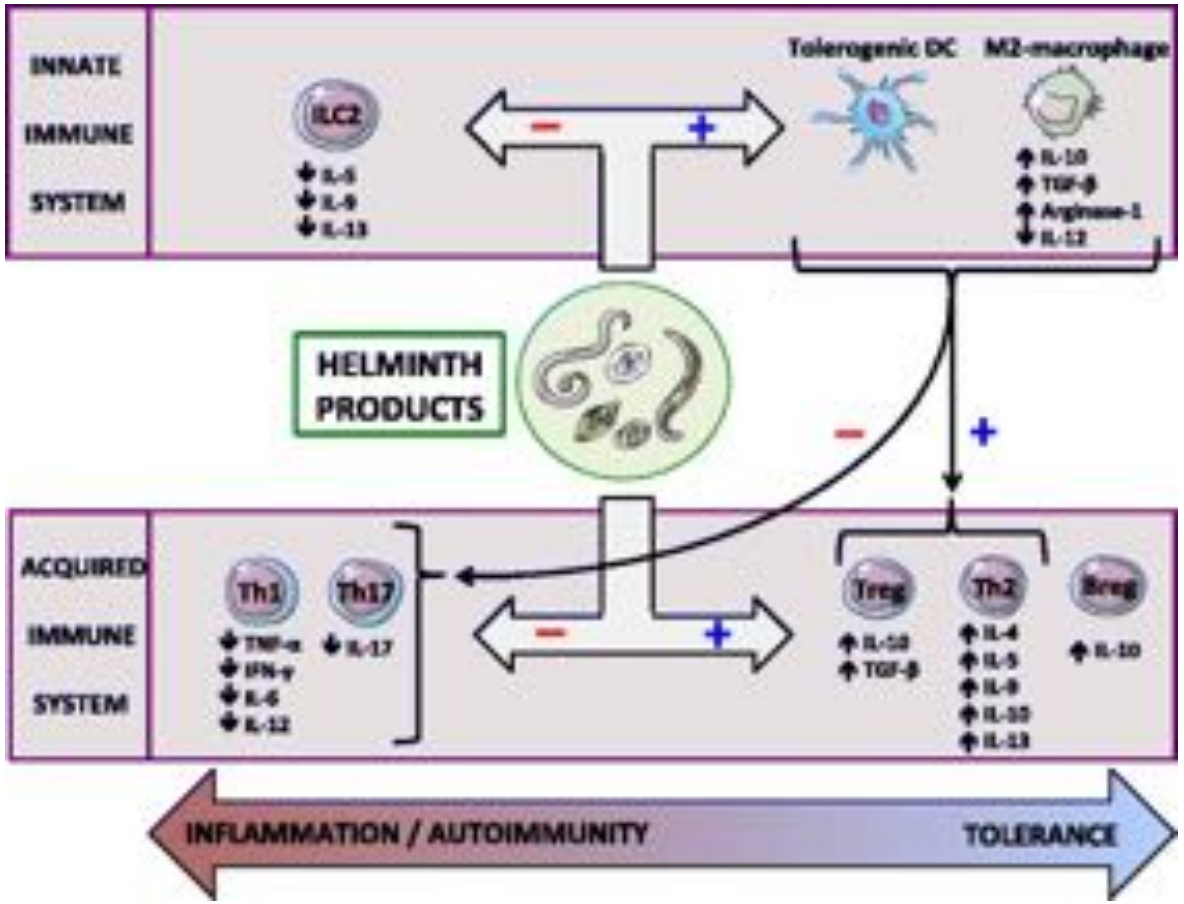
Atopisk sygdom


"resting" leukocytes
1. recognition of "foreign" matter
Lactobacilli
Bifidobacteriae
"calming" growth factors
2. metamorphosis/activation
"recruitment"
activated leukocyte
gut lumen
INFLAMMATION

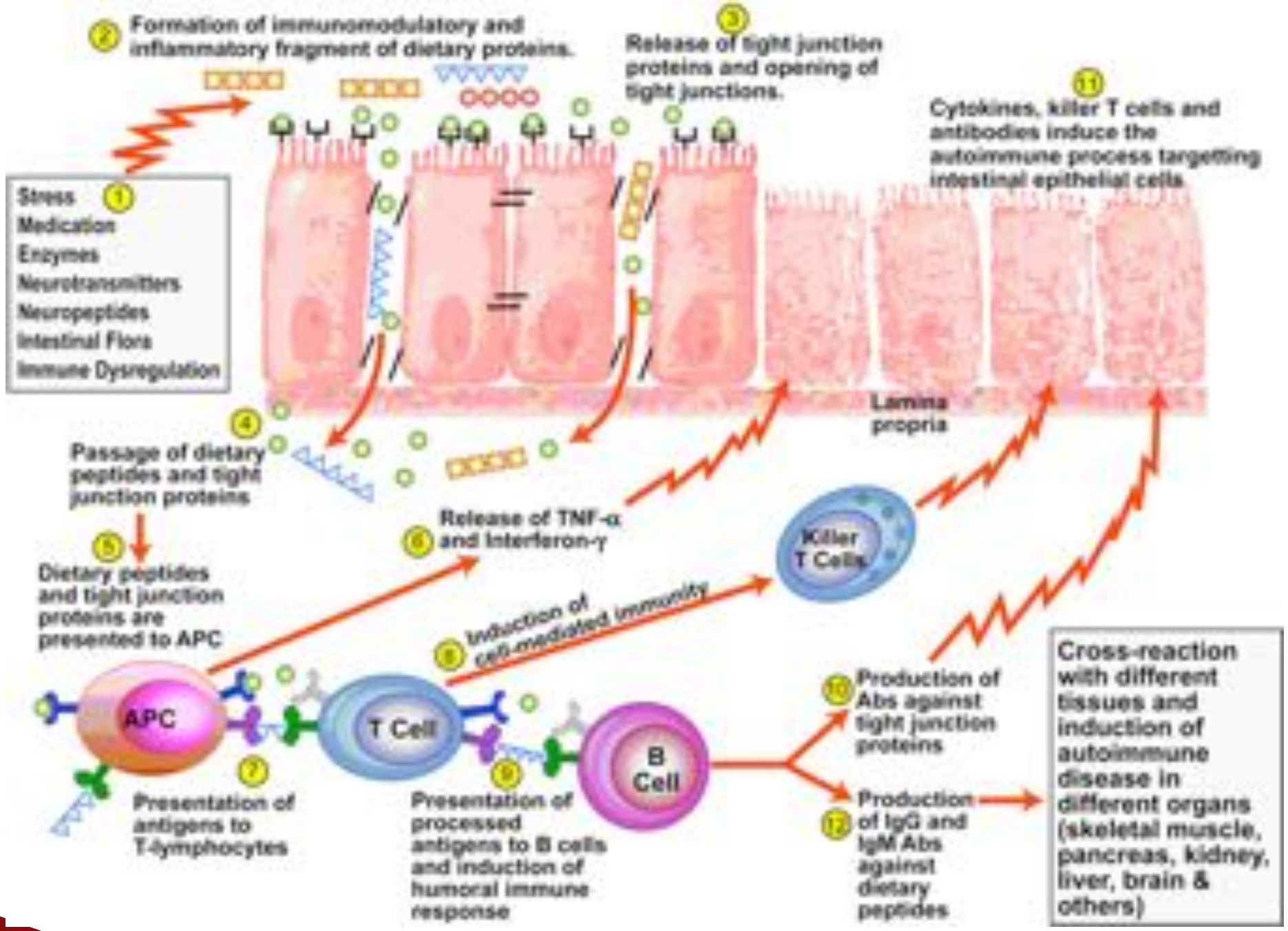


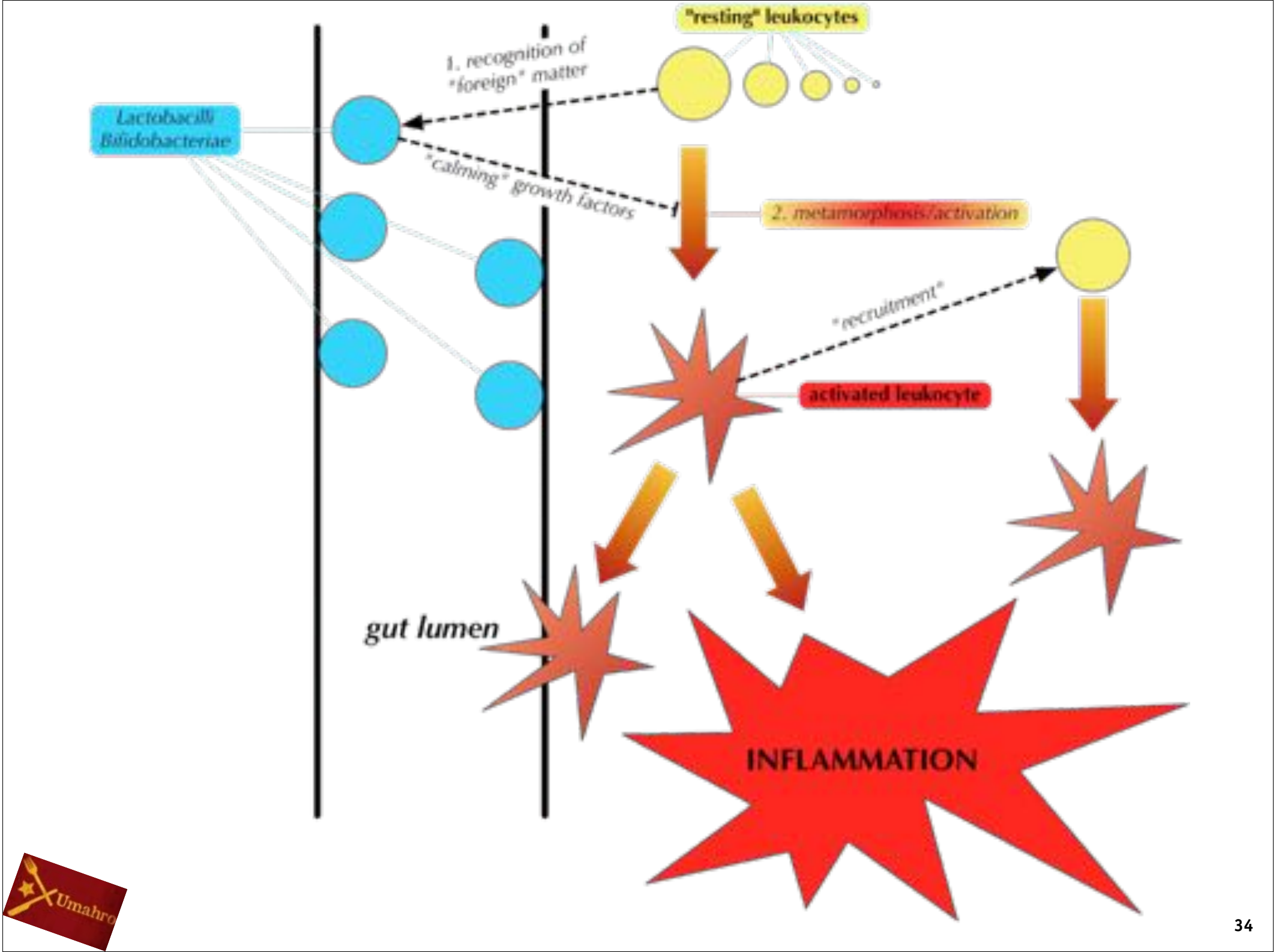
www.jleukbio.org/content/89/5/685/F3.expansion.htmlypositiveparenting.org/wp-content/uploads/2015/04/benefits-probitotics-and-prebiotics.jpg

Worms to the rescue?

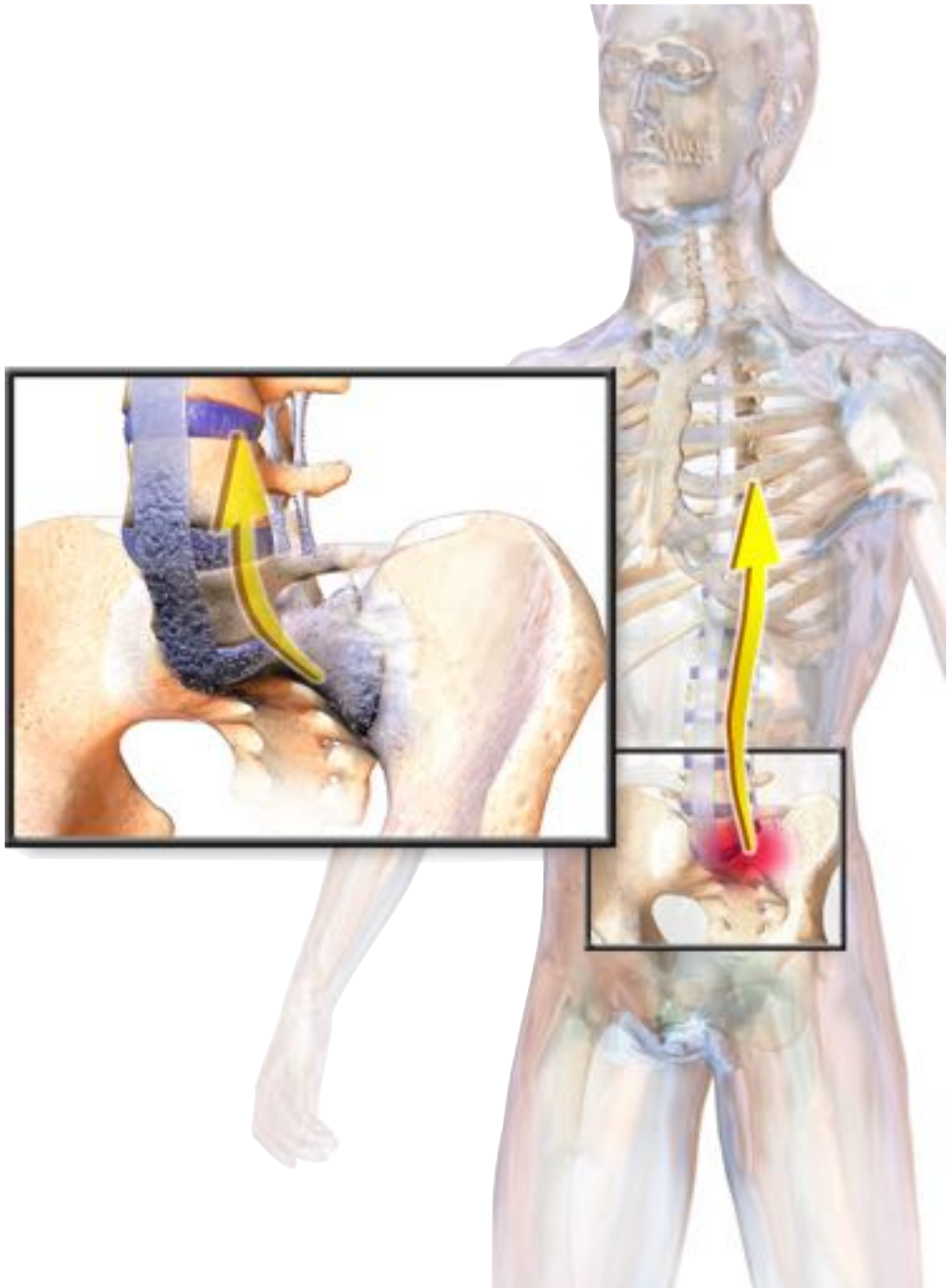


Autoimmunsygdomme

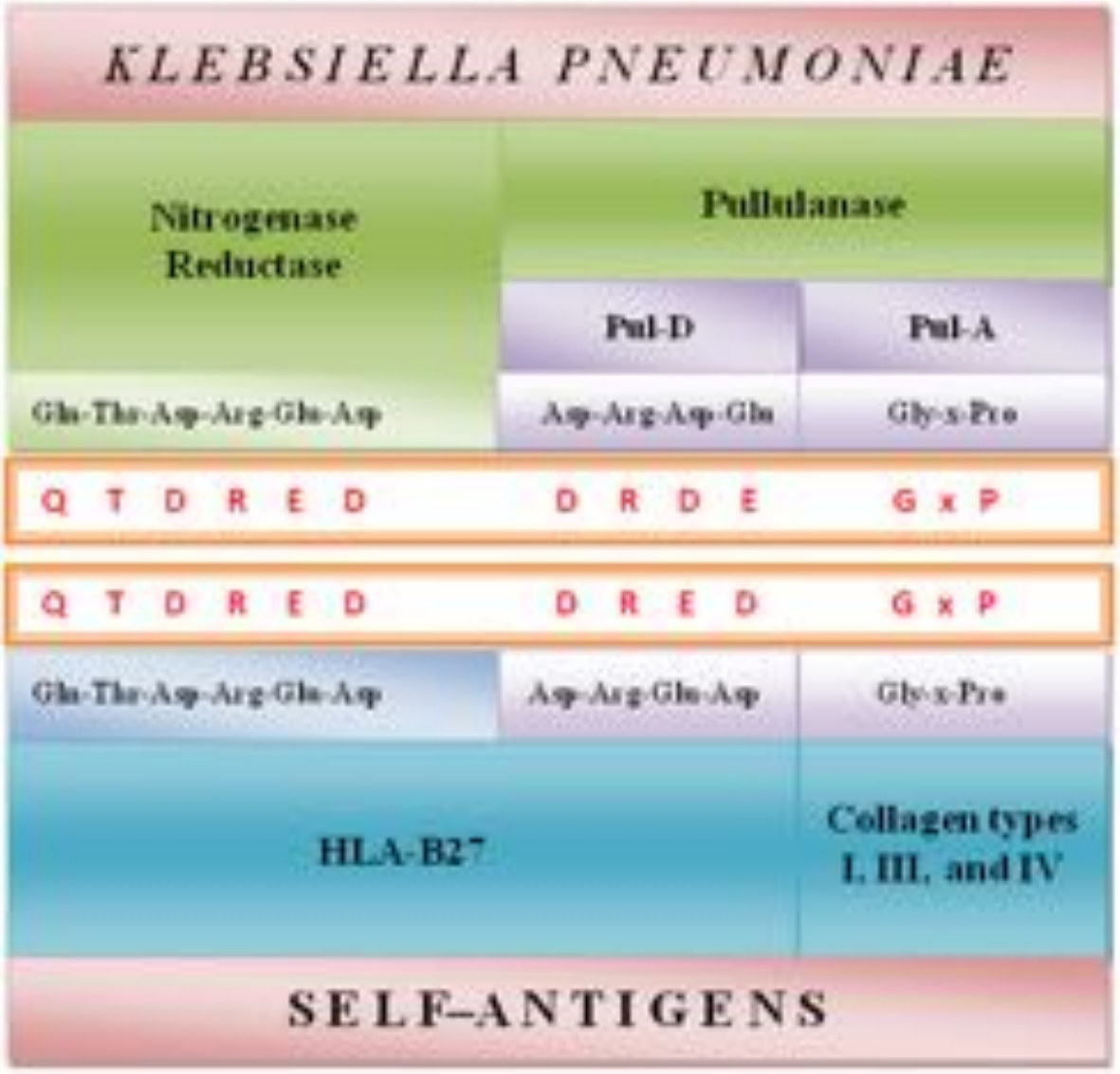

2 Formation of immunomodulatory and inflammatory fragment of dietary proteins.
3 Release of tight junction proteins and opening of tight junctions.
11 Cytokines, killer T cells and antibodies induce the autoimmune process targeting intestinal epithelial cells
Stress
Medication
Enzymes
Neurotransmitters
Neuropeptides
Intestinal Flora
Immune Dysregulation
1
Lamina propria
4 Passage of dietary peptides and tight junction proteins
5 Dietary peptides and tight junction proteins are presented to APC
6 Release of TNF-α and interferon-γ
Killer T Cells
8 Induction of cell-mediated immunity
APC
T Cell
B Cell
7 Presentation of antigens to T-lymphocytes
9 Presentation of processed antigens to B cells and induction of humoral immune response
10 Production of Abs against tight junction proteins
12 Production of IgG and IgM Abs against dietary peptides
Cross-reaction with different tissues and induction of autoimmune disease in different organs (skeletal muscle, pancreas, kidney, liver, brain & others)


"resting" leukocytes
1. recognition of "foreign" matter
Lactobacilli Bifidobacteriae
"calming" growth factors
2. metamorphosis/activation
"recruitment"
activated leukocyte
gut lumen
INFLAMMATION

morbus Bechtrew



Krydsreaktioner p.g.a. Klebsiella ved HLA-27B



Hindawi Publishing Corporation
Clinical and Developmental Immunology
Volume 2013, Article ID 872632, 9 pages
http://dx.doi.org/10.1155/2013/872632

Review Article

The Link between Ankylosing Spondylitis, Crohn's Disease, *Klebsiella*, and Starch Consumption

Taha Rashid,[1] Clyde Wilson,[2] and Alan Ebringer[1]

[1] *Analytical Sciences Group, Kings College, 150 Stamford Street, London SE1 9NH, UK*
[2] *Department of Pathology and Microbiology, Kings Edward VII Memorial Hospital, 7 Point Finger Road, Paget DV04, Bermuda*

Correspondence should be addressed to Alan Ebringer; alan.ebringer@kcl.ac.uk

Received 22 October 2012; Accepted 23 April 2013

Academic Editor: Chung Tei Chou

Both ankylosing spondylitis (AS) and Crohn's disease (CD) are chronic and potentially disabling interrelated conditions, which have been included under the group of spondyloarthropathies. The results of a large number of studies support the idea that an enteropathic pathogen, *Klebsiella pneumoniae*, is the most likely triggering factor involved in the initiation and development of these diseases. Increased starch consumptions by genetically susceptible individuals such as those possessing HLA-B27 allelotypes could trigger the disease in both AS and CD by enhancing the growth and perpetuation of the *Klebsiella* microbes in the bowel. Exposure to increased levels of these microbes will lead to the production of elevated levels of anti-*Klebsiella* antibodies as well as autoantibodies against cross-reactive self-antigens with resultant pathological lesions in the bowel and joints. Hence, a decrease of starch-containing products in the daily dietary intake could have a beneficial therapeutic effect on the disease especially when used in conjunction with the currently available medical therapies in the treatment of patients with AS and CD.

1. Introduction

Ankylosing spondylitis (AS) is regarded as the prototype of seronegative spondyloarthropathies (SpAs) that comprise a group of spondylitis-associated conditions. Other disease entities of SpA include reactive arthritis, psoriatic arthritis, undifferentiated SpA, and arthritis associated with inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC) [1]. SpAs are interrelated conditions which share certain associated clinical, laboratory, radiological, and genetic manifestations such as inflammatory back pain caused by spondylitis/sacroiliitis, as well as asymmetric oligoarthritis, enthesopathy, anterior uveitis, positive family history, and association with HLA-B27 genes, but without positivity for the rheumatoid factors.

Although patients with CD usually present with clinical features of bowel involvement, the characteristic presentation in those with AS and spondylitis-associated CD is progressive inflammatory backache with or without other SpA-associated features [2].

Both AS and CD affect early age groups and have a worldwide distribution. There are at least one million individuals in the United Kingdom who suffer from some features of AS. The negative impact of AS on the employment [3] and the psychological [4] status of patients with this disease has been well established. The disease in CD can also have an impact on the social status and work abilities of patients, especially in women [5]. Because of these negative impacts on the general health and welfare status of patients with AS and CD, with certain drawbacks of the currently used medical treatments, a search for the causative factor and an alternative therapeutic measure involving eradication of the cause could be helpful in the management of patients with these diseases.

2. Genetic Background of AS and CD

A positive family history is one of the key points in defining the characteristics of patients with SpA. In a family study of AS probands and healthy controls in an Icelandic population, it has been shown that there is evidence which might support the existence of common genetic components for AS and IBD. The study demonstrated a risk ratio of 3.0 and 2.1 in the first and second-degree relatives, respectively, for the occurrence of AS in families of probands with IBD, and with

Hindawi Publishing Corporation
Clinical and Developmental Immunology
Volume 2013, Article ID 872632, 9 pages
http://dx.doi.org/10.1155/2013/872632

Review Article

The Link between Ankylosing Spondylitis, Crohn's Disease, *Klebsiella*, and Starch Consumption

Taha Rashid,[1] Clyde Wilson,[2] and Alan Ebringer[1]

[1] *Analytical Sciences Group, Kings College, 150 Stamford Street, London SE1 9NH, UK*
[2] *Department of Pathology and Microbiology, Kings Edward VII Memorial Hospital, 7 Point Finger Road, Paget DV04, Bermuda*

Correspondence should be addressed to Alan Ebringer; alan.ebringer@kcl.ac.uk

Received 22 October 2012; Accepted 23 April 2013

Academic Editor: Chung-Pei Hsu

Both ankylosing spondylitis (AS) and Crohn's disease (CD) are chronic and potentially disabling interrelated conditions which have been included under the group of spondyloarthropathies. The results of a large number of studies support the idea that an enteropathic pathogen, *Klebsiella pneumoniae*, is the most likely triggering factor involved in the initiation and development of these diseases. Increased starch consumptions by genetically susceptible individuals such as those possessing HLA-B27 allelotypes could trigger the disease in both AS and CD by influencing the growth and perpetuation of the *Klebsiella* microflora in the bowel. Consumption of starch fosters the *Klebsiella* microbes which lead to the production of elevated levels of *Klebsiella* antibodies which are autoantibodies against cross-reactive tissue antigens with resultant pathological lesions in the bowel and joints. Hence, a decrease of starch-containing products in the daily dietary intake could have a beneficial therapeutic effect on the disease especially when used in conjunction with the currently available medical therapies in the treatment of patients with AS and CD.

- >95% AS patienter har Klebsiella IgA & IgG
- Klebsiella lever i høj grad af kulhydrater
- En kulhydratfattig kost kan mindske mængden af Klebsiella i mavetarmsystemet

1. Introduction

Ankylosing spondylitis (AS) is regarded as the prototype of seronegative spondyloarthropathies (SpAs) that comprise a group of spondylitis-associated conditions. Other disease entities of SpA include reactive arthritis, psoriatic arthritis, undifferentiated SpA, and arthritis associated with inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC) [1]. SpAs are interrelated conditions which share certain associated clinical, laboratory, radiological, and genetic manifestations such as inflammatory back pain caused by spondylitis/sacroiliitis, as well as asymmetric oligoarthritis, enthesopathy, anterior uveitis, positive family history, and association with HLA-B27 genes, but without positivity for the rheumatoid factors.

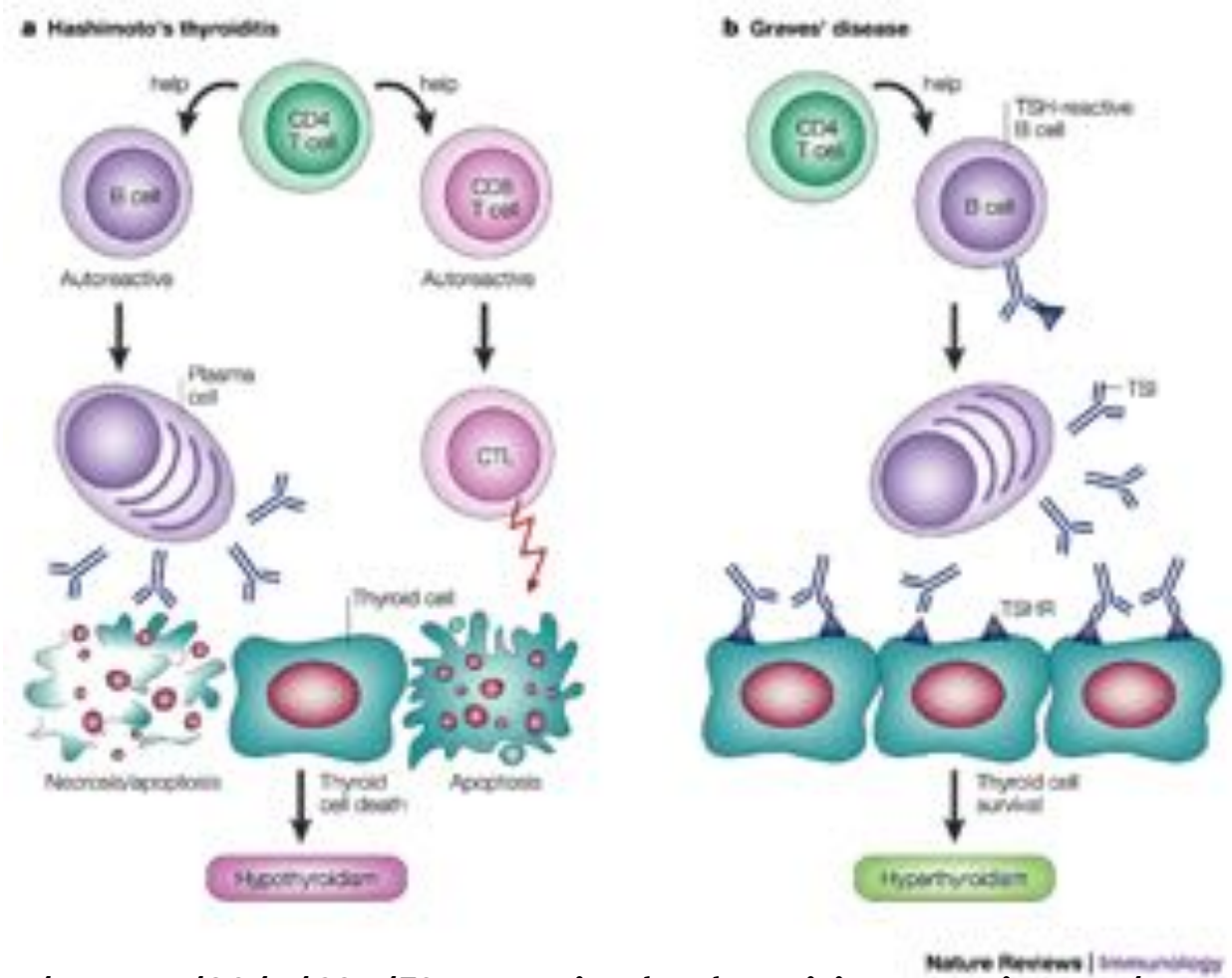
Although patients with CD usually present with clinical features of bowel involvement, the characteristic presentation in those with AS and spondylitis-associated CD is progressive inflammatory backache with or without other SpA-associated features [2].

Both AS and CD affect early age groups and have a worldwide distribution. There are at least one million individuals in the United Kingdom who suffer from some features of AS. The negative impact of AS on the employment [3] and the psychological [4] status of patients with this disease has been well established. The disease in CD can also have an impact on the social status and work abilities of patients, especially in women [5]. Because of these negative impacts on the general health and welfare status of patients with AS and CD, with certain drawbacks of the currently used medical treatments, a search for the causative factor and an alternative therapeutic measure involving eradication of the cause could be helpful in the management of patients with these diseases.

2. Genetic Background of AS and CD

A positive family history is one of the key points in defining the characteristics of patients with SpA. In a family study of AS probands and healthy controls in an Icelandic population, it has been shown that there is evidence which might support the existence of common genetic components for AS and IBD. The study demonstrated a risk ratio of 3.0 and 2.1 in the first and second-degree relatives, respectively, for the occurrence of AS in families of probands with IBD, and with

Hashimoto's (autoimmun thyroidea-betændelse)



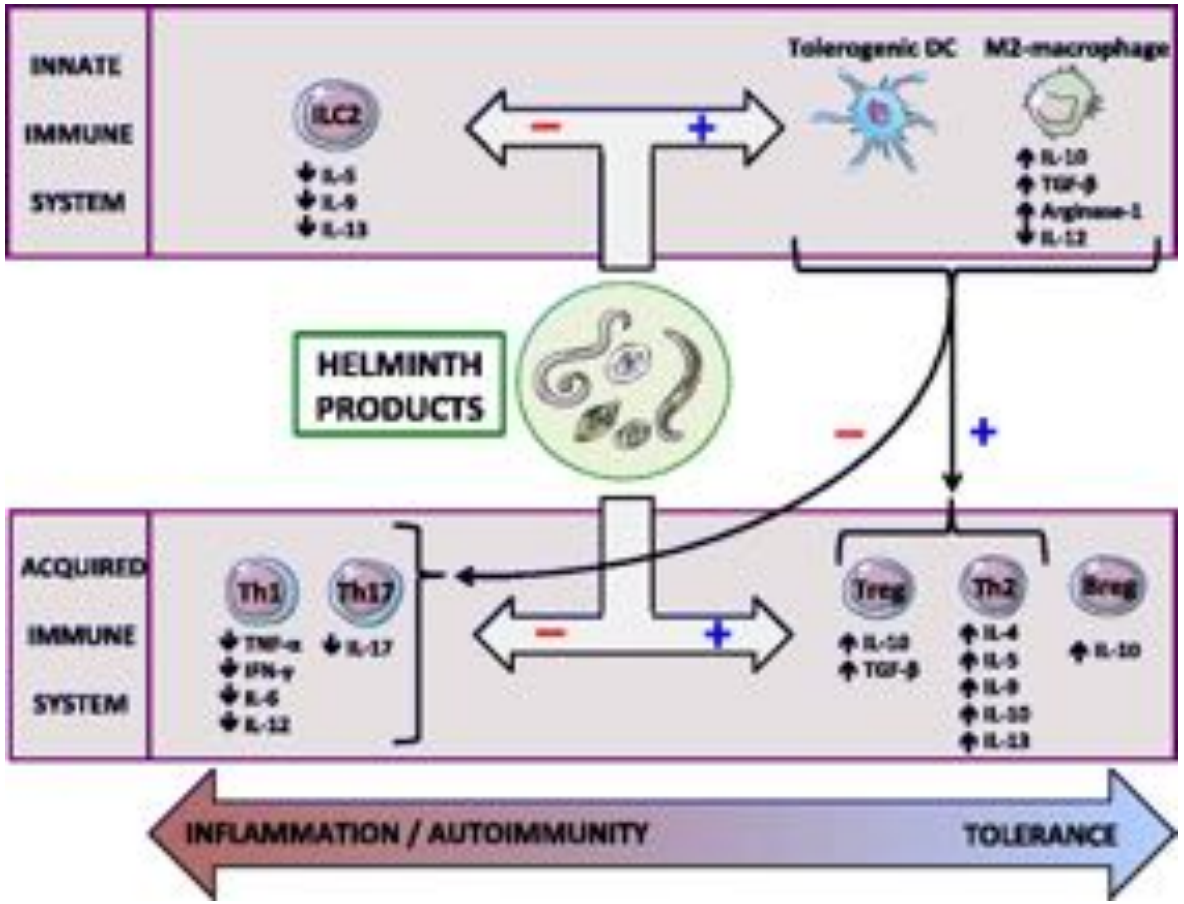
www.jleukbio.org/content/89/5/685/F3.expansion.htmlypositiveparenting.org/wp-content/uploads/2015/04/benefits-probitotics-and-prebiotics.jpg

Eradication of Blastocystis hominis prevents the development of symptomatic Hashimoto's thyroiditis: a case report

In this case report we describe a 49 year-old man who presented with chronic urticaria, angioedema and soft stool consistency. During diagnostic examinations Hashimoto's thyroiditis was found even though the patient never had clear symptoms of this disease. *Blastocystis hominis* was isolated through a stool microbiologic examination, implicating that this parasite can cause the development of Hashimoto's thyroiditis and chronic urticaria. After two-weeks treatment with metronidazole the *Blastocystis hominis* was eradicated, then urticaria and angioedema disappeared. During the four years of follow-up, the patient presented without any symptoms, whereas thyroid hormones were normalized and anti-thyroid antibodies declined. For the first time in the literature we show that eradication of *Blastocystis hominis* can prevent the development of both symptomatic Hashimoto's thyroiditis and chronic urticaria.

Rajïc B. et al. The Journal of Infection in Developing Countries, North America, 9, jul. 2015. Available at: www.jidc.org/index.php/journal/article/view/26230132/1350.

Worms to the rescue?



Psyke, humør, adfærd, indlæring og udvikling

"Psykobiotika"

"... we define a psychobiotic as a live organism that, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness. As a class of probiotic, these bacteria are capable of producing and delivering neuroactive substances such as gamma-aminobutyric acid and serotonin, which act on the brain-gut axis. Preclinical evaluation in rodents suggests that certain psychobiotics possess antidepressant or anxiolytic activity. Effects may be mediated via the vagus nerve, spinal cord, or neuroendocrine systems. So far, psychobiotics have been most extensively studied in a liaison psychiatric setting in patients with irritable bowel syndrome, where positive benefits have been reported for a number of organisms including *Bifidobacterium infantis*. Evidence is emerging of benefits in alleviating symptoms of depression and in chronic fatigue syndrome. Such benefits may be related to the anti- inflammatory actions of certain psychobiotics and a capacity to reduce hypothalamic-pituitary-adrenal axis activity ..."

T.G. Dinan et al. Psychobiotics: A Novel Class of Psychotropic. BIOL PSYCHIATRY 2013;74:720–726. http://dx.doi.org/10.1016/j.biopsych.2013.05.001

"Psykobiotika"

"... we define a psychobiotic as a live organism that, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness. As a class of probiotic, these bacteria are capable of producing and delivering neuroactive substances such as gamma-aminobutyric acid and serotonin, which act on the brain-gut axis. Preclinical evaluation in rodents suggests that certain psychobiotics possess antidepressant or anxiolytic activity. Effects may be mediated via the vagus nerve, spinal cord, or neuroendocrine systems. So far, psychobiotics have been most extensively studied in a liaison psychiatric setting in patients with irritable bowel syndrome, where positive benefits have been reported for a number of organisms including *Bifidobacterium infantis*. Evidence is emerging of benefits in alleviating symptoms of depression and in chronic fatigue syndrome. Such benefits may be related to the anti- inflammatory actions of certain psychobiotics and a capacity to reduce hypothalamic-pituitary-adrenal axis activity ..."

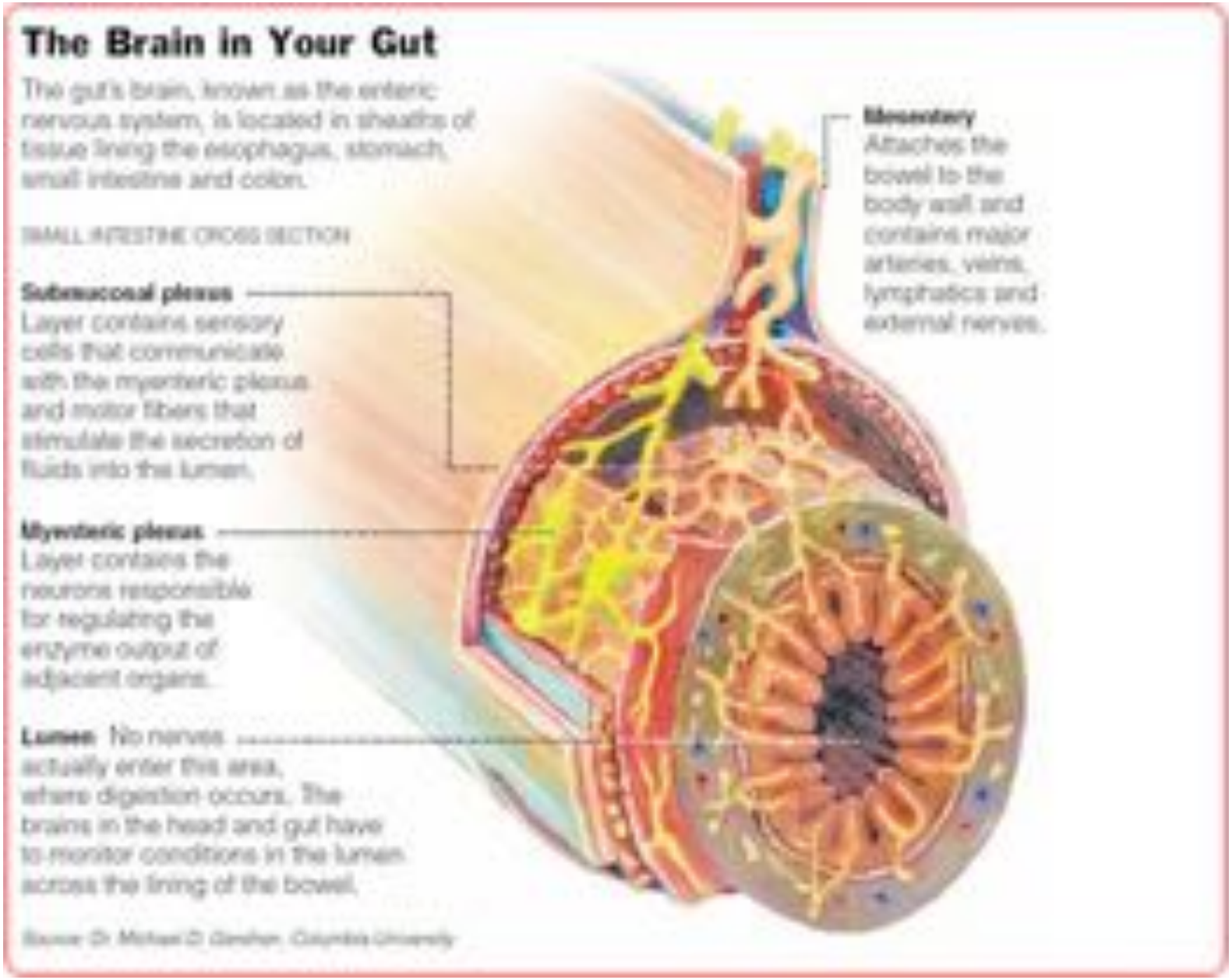
T.G. Dinan et al. Psychobiotics: A Novel Class of Psychotropic. BIOL PSYCHIATRY 2013;74:720–726. http://dx.doi.org/10.1016/j.biopsych.2013.05.001

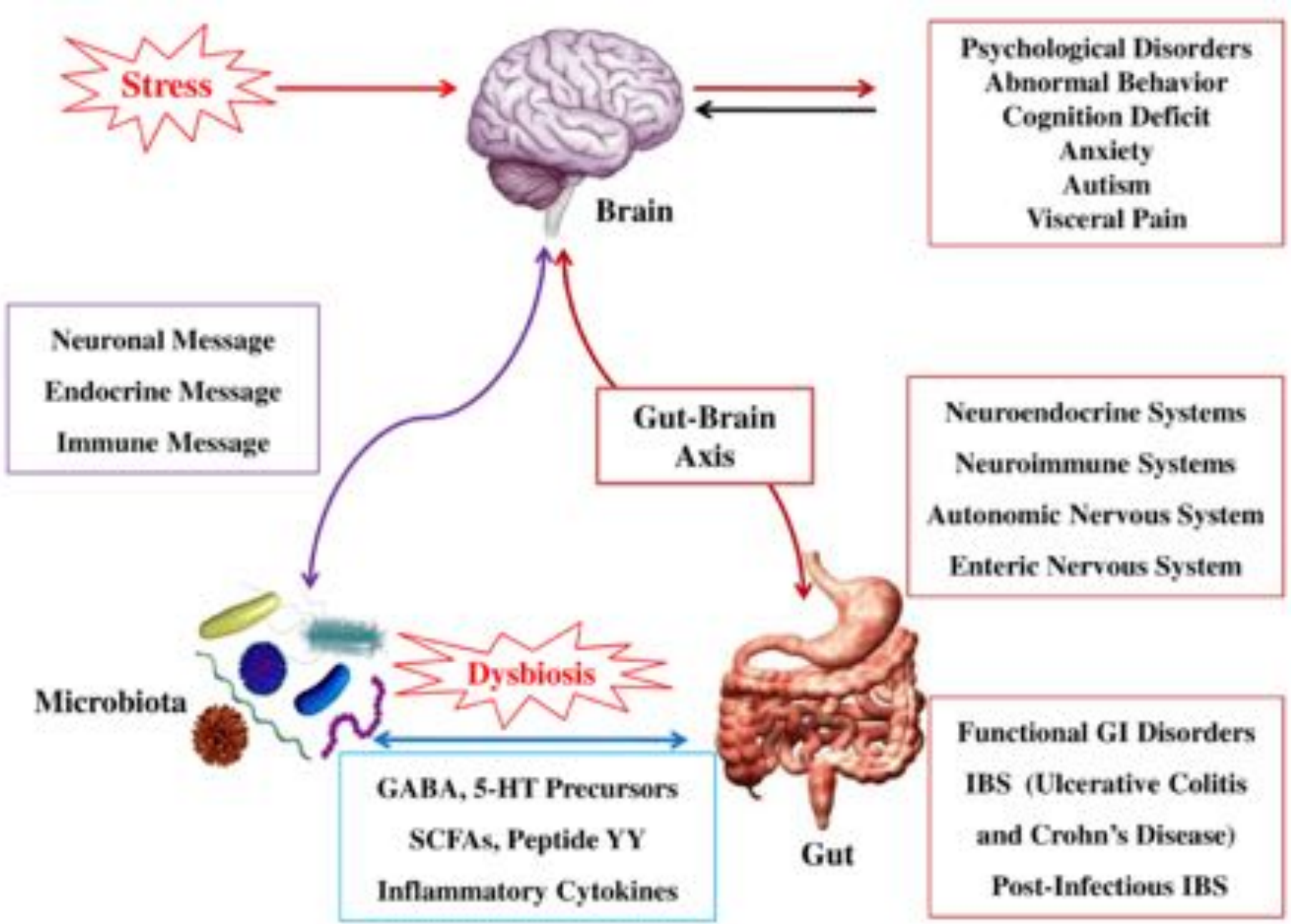
...vi definerer "psykobiotika" som levende organismer, der, når de indtages i tilstrækkelige mængder, har en gavnlig effekt i patienter der lider af psykiatriske lidelser ... Effekterne kan medieres via vagus nerven, rygmarven eller neuroendokrine systemer ...

"Psykobiotika"

"... we define a psychobiotic as a live organism that, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness. As a class of probiotic, these bacteria are capable of producing and delivering neuroactive substances such as gamma-aminobutyric acid and serotonin, which act on the brain-gut axis. Preclinical evaluation in rodents suggests that certain psychobiotics possess antidepressant or anxiolytic activity. Effects may be mediated via the vagus nerve, spinal cord, or neuroendocrine systems. So far, psychobiotics have been most extensively studied in a liaison psychiatric setting in patients with irritable bowel syndrome, where positive benefits have been reported for a number of organisms including *Bifidobacterium infantis*. Evidence is emerging of benefits in alleviating symptoms of depression and in chronic fatigue syndrome. Such benefits may be related to the anti- inflammatory actions of certain psychobiotics and a capacity to reduce hypothalamic-pituitary-adrenal axis activity ..."

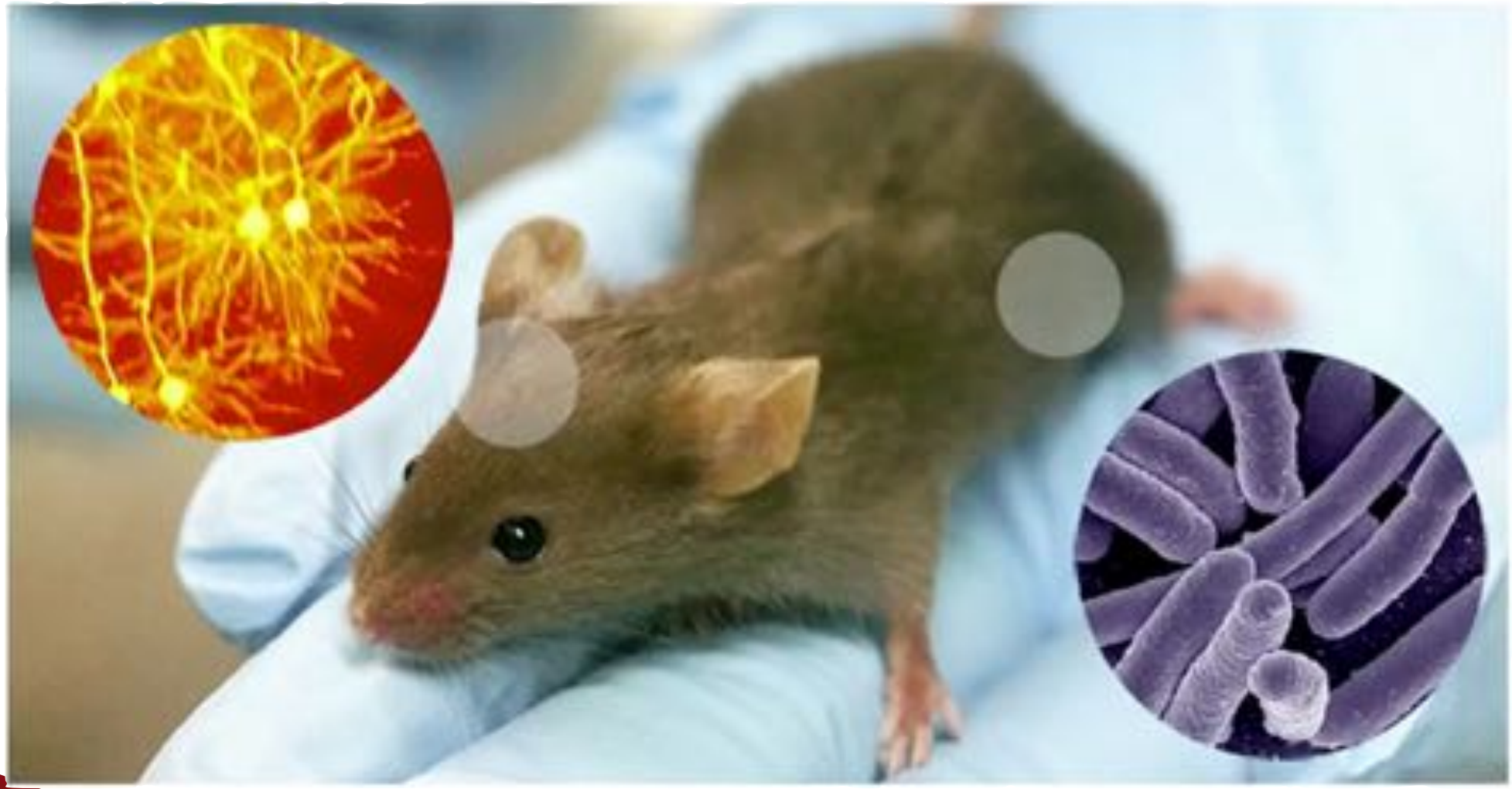
T.G. Dinan et al. Psychobiotics: A Novel Class of Psychotropic. BIOL PSYCHIATRY 2013;74:720–726. http://dx.doi.org/10.1016/j.biopsych.2013.05.001


The Brain in Your Gut
The gut's brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.
SMALL INTESTINE CROSS SECTION
Submucosal plexus
Layer contains sensory cells that communicate with the myenteric plexus and motor fibers that stimulate the secretion of fluids into the lumen.
Myenteric plexus
Layer contains the neurons responsible for regulating the enzyme output of adjacent organs.
Lumen No nerves actually enter this area, where digestion occurs. The brains in the head and gut have to monitor conditions in the lumen across the lining of the bowel.
Source: Dr. Michael D. Gershon, Columbia University
Mesentery
Attaches the bowel to the body wall and contains major arteries, veins, lymphatics and external nerves.



Thakur AK, Shakya A, Husain GM, Emerald M, Kumar V (2014) Gut-Microbiota and Mental Health: Current and Future Perspectives. J Pharmacol Clin Toxicol 2(1):1016.

Tarmflora påvirker neurologisk/mental udvikling



Mind-Altering Microbes: How The Microbiome Affects Brain and Behaviour. Elaine Hsiao @TEDxCaltech

Differences between the gut microflora of children with autistic spectrum disorders and that of healthy children

Abstract: Children with autistic spectrum disorders (ASDs) tend to suffer from severe gastrointestinal problems. Such symptoms may be due to a disruption of the indigenous gut flora promoting the overgrowth of potentially pathogenic micro-organisms. The faecal flora of patients with ASDs was studied and compared with those of two control groups (healthy siblings and unrelated healthy children). Faecal bacterial populations were assessed through the use of a culture-independent technique, fluorescence in situ hybridization, using oligonucleotide probes targeting predominant components of the gut flora. The faecal flora of ASD patients contained a higher incidence of the *Clostridium histolyticum* group (*Clostridium* clusters I and II) of bacteria than that of healthy children. However, the non-autistic sibling group had an intermediate level of the *C. histolyticum* group, which was not significantly different from either of the other subject groups. Members of the *C. histolyticum* group are recognized toxin-producers and may contribute towards gut dysfunction, with their metabolic products also exerting systemic effects. Strategies to reduce clostridial population levels harboured by ASD patients or to improve their gut microflora profile through dietary modulation may help to alleviate gut disorders common in such patients

Helena MRT Parracho, Max O Bingham, Glenn R Gibson and Anne L McCartney

Gastrointestinal Microflora Studies in Late-Onset Autism

Some cases of late-onset (regressive) autism may involve abnormal flora because oral vancomycin, which is poorly absorbed, may lead to significant improvement in these children. Fecal flora of children with regressive autism was compared with that of control children, and clostridial counts were higher. The number of clostridial species found in the stools of children with autism was greater than in the stools of control children. Children with autism had 9 species of *Clostridium* not found in controls, whereas controls yielded only 3 species not found in children with autism. In all, there were 25 different clostridial species found. In gastric and duodenal specimens, the most striking finding was total absence of non—spore-forming anaerobes and microaerophilic bacteria from control children and significant numbers of such bacteria from children with autism. These studies demonstrate significant alterations in the upper and lower intestinal flora of children with late-onset autism and may provide insights into the nature of this disorder.

Sidney Finegold et. al.

Desulfovibrio species are potentially important in regressive autism

Autism is a complex disorder with no specific diagnostic test so the disease is defined by its characteristics including cognitive defects, social, communication and behavioral problems, repetitive behaviors, unusual sensitivity to stimuli such as noise, restricted interests, and self stimulation. The incidence of this disease has increased remarkably in recent years and was 110/10,000 children (~1%) in multiple areas of the US in 2007. The financial burden on families and communities is enormous. In terms of predisposing factors, heredity plays a role in some subjects, but it is clear that environmental factors are also important. Environmental toxins can affect the immune system adversely. Intestinal bacteria are recognized by a few investigators as potentially important and we have proposed that certain antimicrobial drugs may be a key factor in modifying the intestinal bacterial flora adversely, selecting out potentially harmful bacteria that are normally suppressed by an intact normal intestinal flora. We had felt that clostridia in the gut might be involved in autism because they are virulent organisms and spore-formers; spores would resist antibacterial agents so that when antibiotics were discontinued the spores would germinate and by toxin production or another mechanism lead to autism. However, a recent study of ours employing the powerful pyrosequencing technique on stools of subjects with regressive autism showed that *Desulfovibrio* was more common in autistic subjects than in controls. We subsequently confirmed this with pilot cultural and real-time PCR studies and found siblings of autistic children had counts of *Desulfovibrio* that were intermediate, suggesting possible spread of the organism in the family environment. *Desulfovibrio* is an anaerobic bacillus that does not produce spores but is nevertheless resistant to aerobic and other adverse conditions by other mechanisms and is commonly resistant to certain antimicrobial agents (such as cephalosporins) often used to treat ear and other infections that are relatively common in childhood. This bacterium also produces important virulence factors and its physiology and metabolism position it uniquely to account for much of the pathophysiology seen in autism. If these results on *Desulfovibrio* are confirmed and extended in other studies, including treatment trials with appropriate agents and careful clinical and laboratory studies, this could lead to more reliable classification of autism, a diagnostic test and therapy for regressive autism, development of a vaccine for prevention and treatment of regressive autism, tailored probiotics/prebiotics, and important epidemiologic information.

Sidney Finegold et al. Med Hypotheses. 2011 Aug;77(2):270-4. Epub 2011 May 17.

Short-term benefit from oral vancomycin treatment of regressive-onset autism

In most cases symptoms of autism begin in early infancy. However, a subset of children appears to develop normally until a clear deterioration is observed. Many parents of children with "regressive"-onset autism have noted antecedent antibiotic exposure followed by chronic diarrhea. We speculated that, in a subgroup of children, disruption of indigenous gut flora might promote colonization by one or more neurotoxin-producing bacteria, contributing, at least in part, to their autistic symptomatology. To help test this hypothesis, 11 children with regressive-onset autism were recruited for an intervention trial using a minimally absorbed oral antibiotic. Entry criteria included antecedent broad-spectrum antimicrobial exposure followed by chronic persistent diarrhea, deterioration of previously acquired skills, and then autistic features. Short-term improvement was noted using multiple pre- and post-therapy evaluations. These included coded, paired videotapes scored by a clinical psychologist blinded to treatment status; these noted improvement in 8 of 10 children studied. Unfortunately, these gains had largely waned at follow-up. Although the protocol used is not suggested as useful therapy, these results indicate that a possible gut flora-brain connection warrants further investigation, as it might lead to greater pathophysiologic insight and meaningful prevention or treatment in a subset of children with autism.

Sandler RH et. al. J Child Neurol. 2000 Jul;15(7):429-35

www.ncbi.nlm.nih.gov/pubmed/10921511

Fedme og overvægt

Vægtforøgelse efter fækaltransplantation

BRIEF REPORT

Weight Gain After Fecal Microbiota Transplantation

Neha Alang[1] and Colleen R. Kelly[2]

[1]Department of Internal Medicine, Newport Hospital, and [2]Division of Gastroenterology, Center for Women's Gastrointestinal Medicine at the Women's Medicine Collaborative, The Miriam Hospital, Warren Alpert School of Brown University, Providence, Rhode Island

Fecal microbiota transplantation (FMT) is a promising treatment for recurrent *Clostridium difficile* infection. We report a case of a woman successfully treated with FMT who developed new-onset obesity after receiving stool from a healthy but overweight donor. This case may stimulate further studies on the mechanisms of the nutritional-neural-microbiota axis and reports of outcomes in patients who have used non-ideal donors for FMT.

Keywords. *Clostridium difficile* infection; fecal microbiota transplantation; gut microbiota; obesity.

Clostridium difficile infection (CDI) is characterized by a high recurrence rate after treatment. Fecal microbial transplantation (FMT) is a promising approach to recurrent CDI that is being increasingly used clinically, although data remain limited on the full spectrum of possible adverse effects. We report a case of significant weight gain in a woman after FMT from an overweight stool donor.

CASE REPORT

A 32-year-old female with recurrent CDI underwent FMT at our center. She had initially presented several months previously with a 2- to 3-week history of diarrhea and abdominal pain after antibiotic treatment for bacterial vaginosis and exposure to a family member who had CDI. She was treated empirically for CDI by her primary care physician with a 10-day course of oral metronidazole with only partial improvement. Her diarrhea and abdominal pain escalated after completing the metronidazole treatment, and her stool tested positive for *Clostridium difficile* toxin polymerase chain reaction (PCR). She was treated with a 14-day course of oral vancomycin. Testing done around the same time showed *Helicobacter pylori* infection (positive fecal antigen). Nausea and abdominal pain persisted after treatment of the CDI, so the *H. pylori* was treated with a course of triple therapy (amoxicillin, clarithromycin, and proton pump inhibitor). Her abdominal pain and diarrhea escalated again a few weeks later, and her stool tested positive for *C. difficile* toxin PCR. She was treated with a 12-week tapering course of oral vancomycin with improvement, but diarrheal symptoms recurred again within 2 weeks of completing the course, and she was prescribed a course of rifaximin with *Saccharomyces boulardii*. Around this time, she underwent esophagogastroduodenoscopy, which showed persistence of *H. pylori* infection. She had no significant past medical history and had always been of normal weight. Review of systems was positive for diarrhea, and there was frustration over her ongoing diarrheal symptoms. Her weight before FMT was stable at 136 pounds (body mass index of [BMI] 26). Physical examination was unremarkable.

After extensive discussion, the patient elected to undergo fecal transplant. As per the patient's request, her 16-year-old daughter was chosen as the stool donor. At the time of FMT, her daughter's weight was ~140 pounds (BMI of 26.4), but it increased later to 170 pounds. Her daughter had no other health problems, and screening for human immunodeficiency virus 1 and 2, syphilis, and viral hepatitis A, B, and C, *C. difficile*, *Giardia lamblia*, and routine stool culture for enteric pathogens were negative. The patient was retreated for *H. pylori* with quadruple therapy (metronidazole, tetracycline, bismuth, and proton pump inhibitor), and the FMT was performed 2 weeks later via colonoscopy. A total of 600 cc of the suspension of donor stool in sterile water was infused through the colonoscope starting in the terminal ileum. The colon and the terminal ileum appeared normal at the time of the procedure. She improved and did not suffer a further CDI recurrence after FMT.

The patient presented again 16 months after FMT, and reported an unintentional weight gain of 34 pounds. She weighed 170 pounds and had become obese (BMI of 33). She had not lost any weight over the months she was being treated for CDI. She had

Received 24 November 2014; accepted 28 November 2014.

Correspondence: Neha Alang, MBBS, Internal Medicine, Newport Hospital, 11 Friendship St, Newport, RI 02840 (nalang@lifespan.org)

Open Forum Infectious Diseases

Vægtforøgelse efter fækaltransplantation

CA. 15 KG VÆGTFORØGELSE PÅ 16 MÅNEDER EFTER FÆKALTRANSPLANTATION FRA OVERVÆGTIG TEENAGEDATTER

BRIEF REPORT

Weight Gain After Fecal Microbiota Transplantation

Neha Alang[1] and Colleen R. Kelly[2]

[1]Department of Internal Medicine, Newport Hospital, and [2]Division of Gastroenterology, Center for Women's Gastrointestinal Medicine at the Women's Medicine Collaborative, The Miriam Hospital, Warren Alpert School of Brown University, Providence, Rhode Island

Fecal microbiota transplantation (FMT) is a promising treatment for recurrent *Clostridium difficile* infection. We report a case of a woman successfully treated with FMT who developed new-onset obesity after receiving stool from a healthy but overweight donor. This case may stimulate further studies of the mechanisms of the nutritional-neuroendocrinological axis and reports of outcomes in patients who have used non-ideal donors for FMT.

Keywords. *Clostridium difficile* infection; fecal microbiota transplantation; gut microbiota; obesity.

Clostridium difficile infection (CDI) is characterized by a high recurrence rate after treatment. Fecal microbial transplantation (FMT) is a promising approach to recurrent CDI that is being increasingly used clinically, although data remain limited on the full spectrum of possible adverse effects. We report a case of significant weight gain in a woman after FMT from an overweight stool donor.

CASE REPORT

A 32-year-old female with recurrent CDI underwent FMT at our center. She had initially presented several months previously with a 2- to 3-week history of diarrhea and abdominal pain after antibiotic treatment for bacterial vaginosis and exposure to a family member who had CDI. She was treated empirically for CDI by her primary care physician with a 10-day course of oral metronidazole with only partial improvement. Her diarrhea and abdominal pain escalated after completing the metronidazole treatment, and her stool tested positive for *Clostridium difficile* toxin by polymerase chain reaction (PCR). She was treated with a 10-day course of oral vancomycin. Testing around the same time showed *Helicobacter pylori* infection (positive fecal antigen). Nausea and abdominal pain persisted after treatment of the CDI, so the *H. pylori* was treated with a course of triple therapy (amoxicillin, clarithromycin, and proton pump inhibitor). Her abdominal pain and diarrhea escalated again a few weeks later, and her stool tested positive for *C. difficile* toxin PCR. She was treated with a 12-week tapering course of oral vancomycin with improvement, but diarrheal symptoms recurred again within 2 weeks of completing the course, and she was prescribed a course of rifaximin with *Saccharomyces boulardii*. Around this time, she underwent esophagogastroduodenoscopy, which showed persistence of *H. pylori* infection. She had no significant past medical history and had been of normal weight. Review of systems was positive for diarrhea and there was frustration over her ongoing diarrheal symptoms. Her weight before FMT was stable at 136 pounds (body mass index of [BMI] 26). Physical examination was unremarkable.

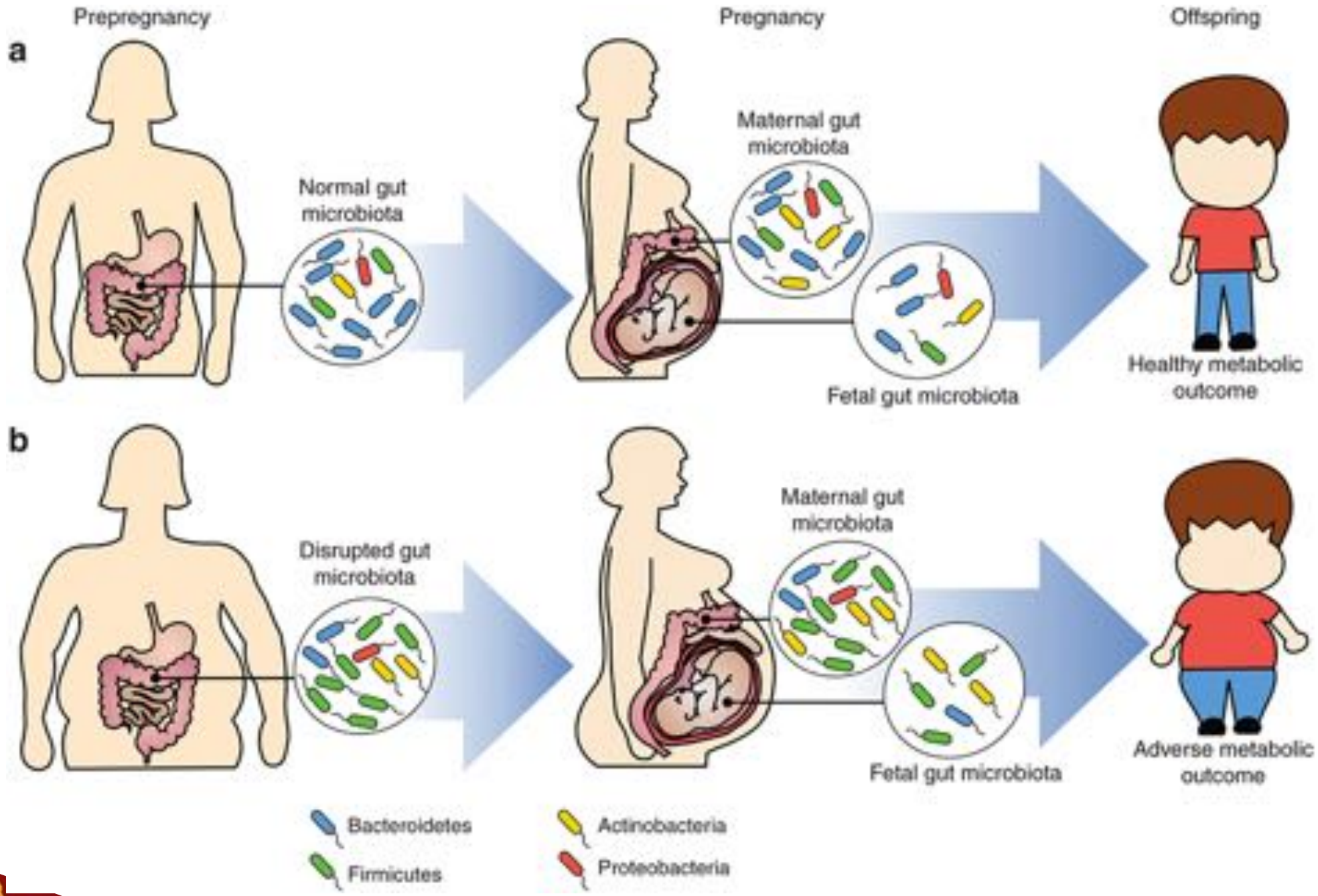
After extensive discussion, the patient elected to undergo fecal transplant. At the patient's request, her 16-year-old daughter was chosen as the stool donor. At the time of FMT, her daughter's weight was ~140 pounds (BMI of 26.4), but it increased later to 170 pounds. Her daughter had no other health problems, and screening for human immunodeficiency virus 1 and 2, syphilis, and viral hepatitis A, B, and C, *C. difficile*, *Giardia lamblia*, and routine stool culture for enteric pathogens were negative. The patient was retreated for *H. pylori* with quadruple therapy (metronidazole, tetracycline, bismuth, and proton pump inhibitor), and the FMT was performed 2 weeks later via colonoscopy. A total of 600 cc of the suspension of donor stool in sterile water was infused through the colonoscope starting in the terminal ileum. The colon and the terminal ileum appeared normal at the time of the procedure. She improved and did not suffer a further CDI recurrence after FMT.

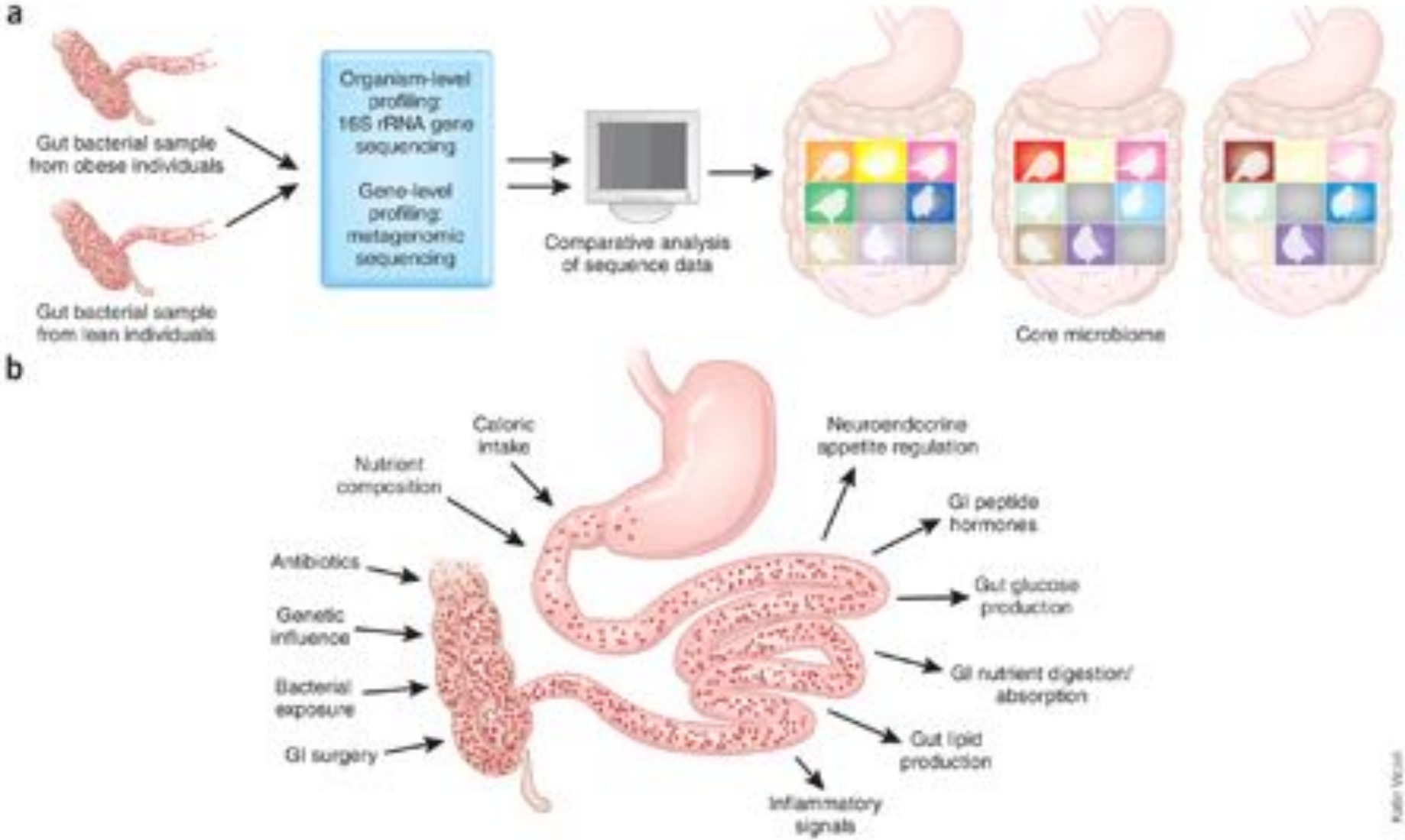
The patient presented again 16 months after FMT, and reported an unintentional weight gain of 34 pounds. She weighed 170 pounds and had become obese (BMI of 33). She had not lost any weight over the months she was being treated for CDI. She had

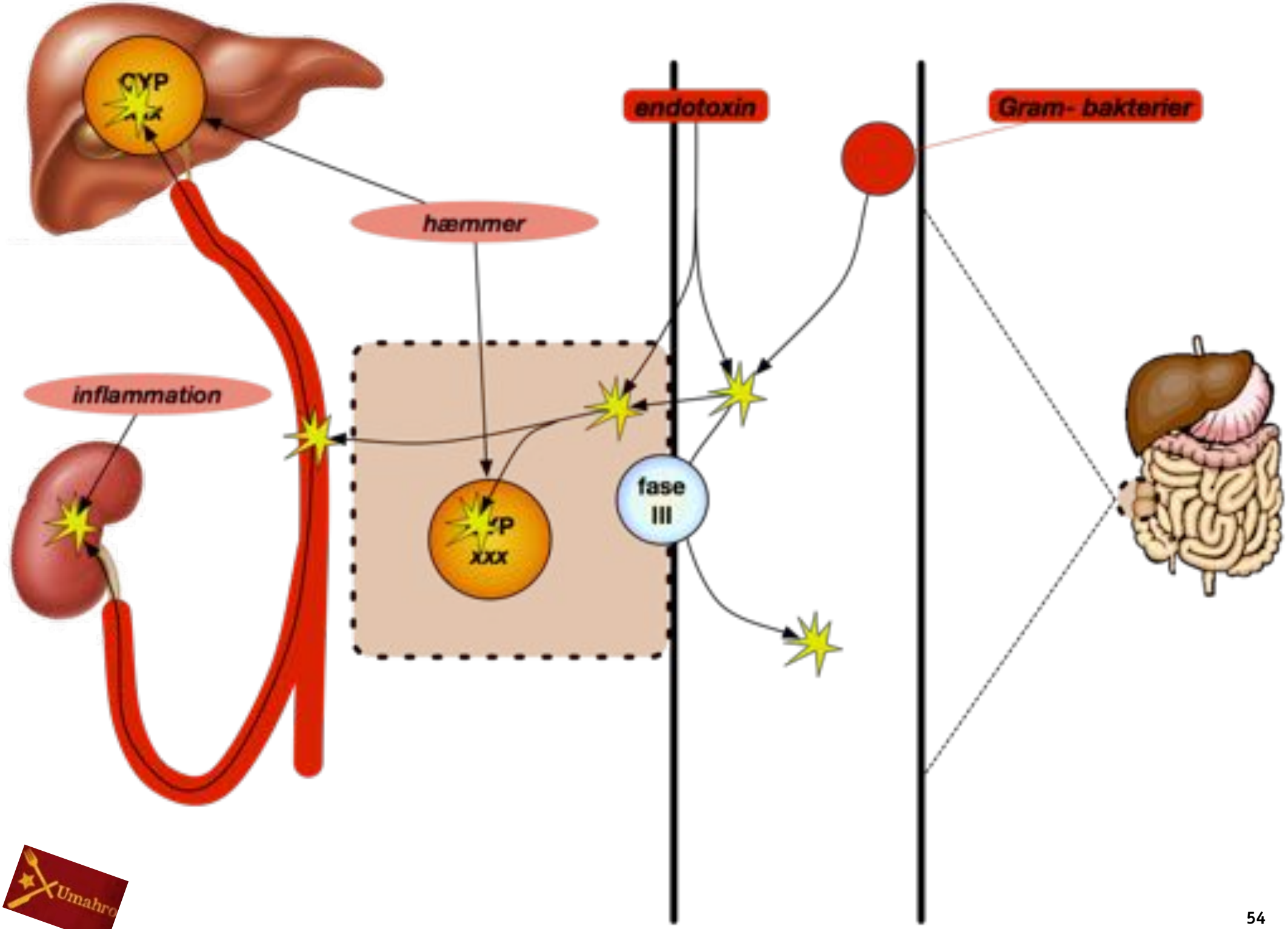
Received 24 November 2014; accepted 28 November 2014.

Correspondence: Neha Alang, MBBS, Internal Medicine, Newport Hospital, 11 Friendship St, Newport, RI 02840 (nalang@lifespan.org)

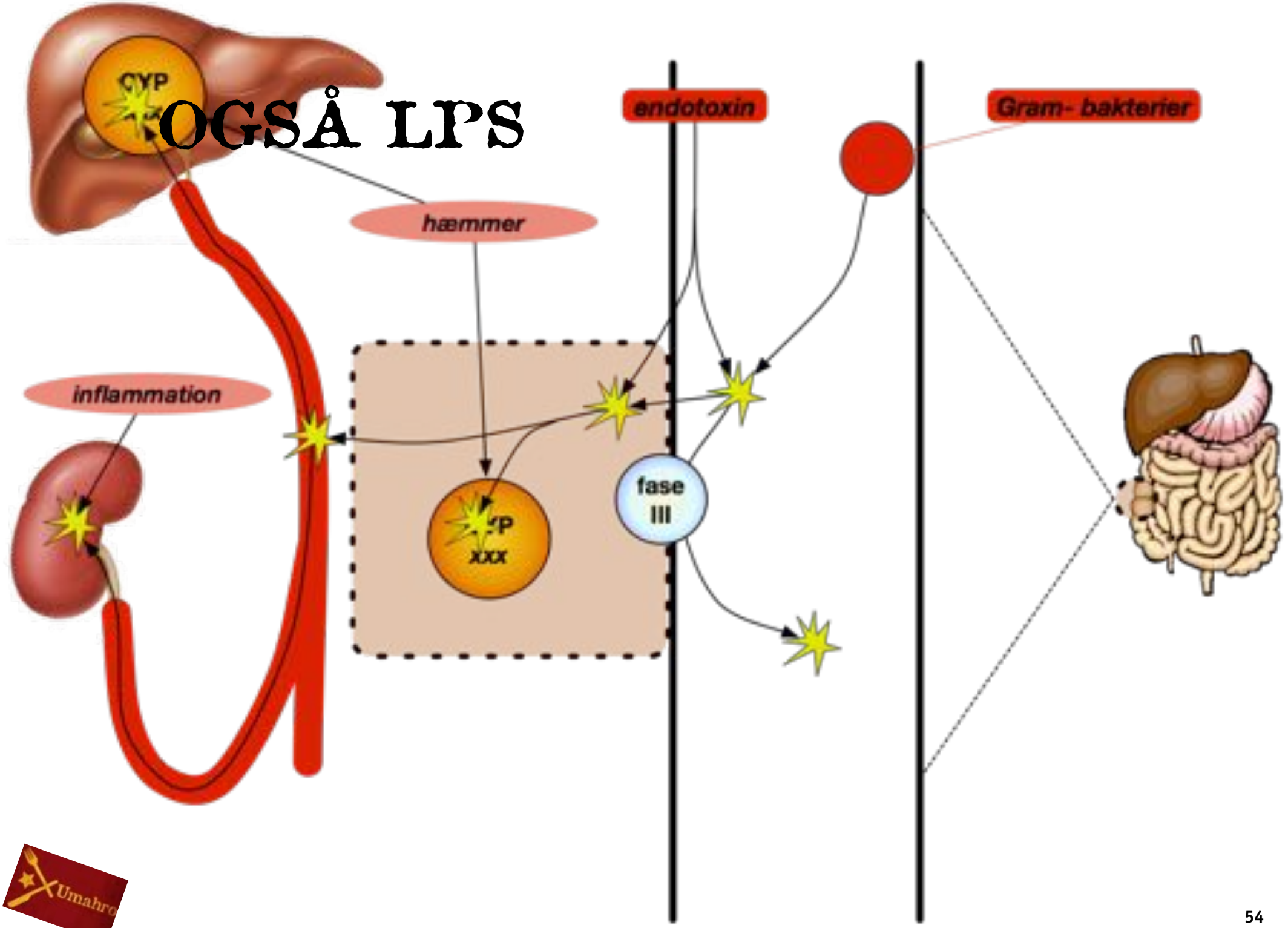
Open Forum Infectious Diseases


Prepregnancy
Pregnancy
Offspring
a
Normal gut microbiota
Maternal gut microbiota
Fetal gut microbiota
Healthy metabolic outcome
b
Disrupted gut microbiota
Maternal gut microbiota
Fetal gut microbiota
Adverse metabolic outcome
Bacteroidetes
Firmicutes
Actinobacteria
Proteobacteria

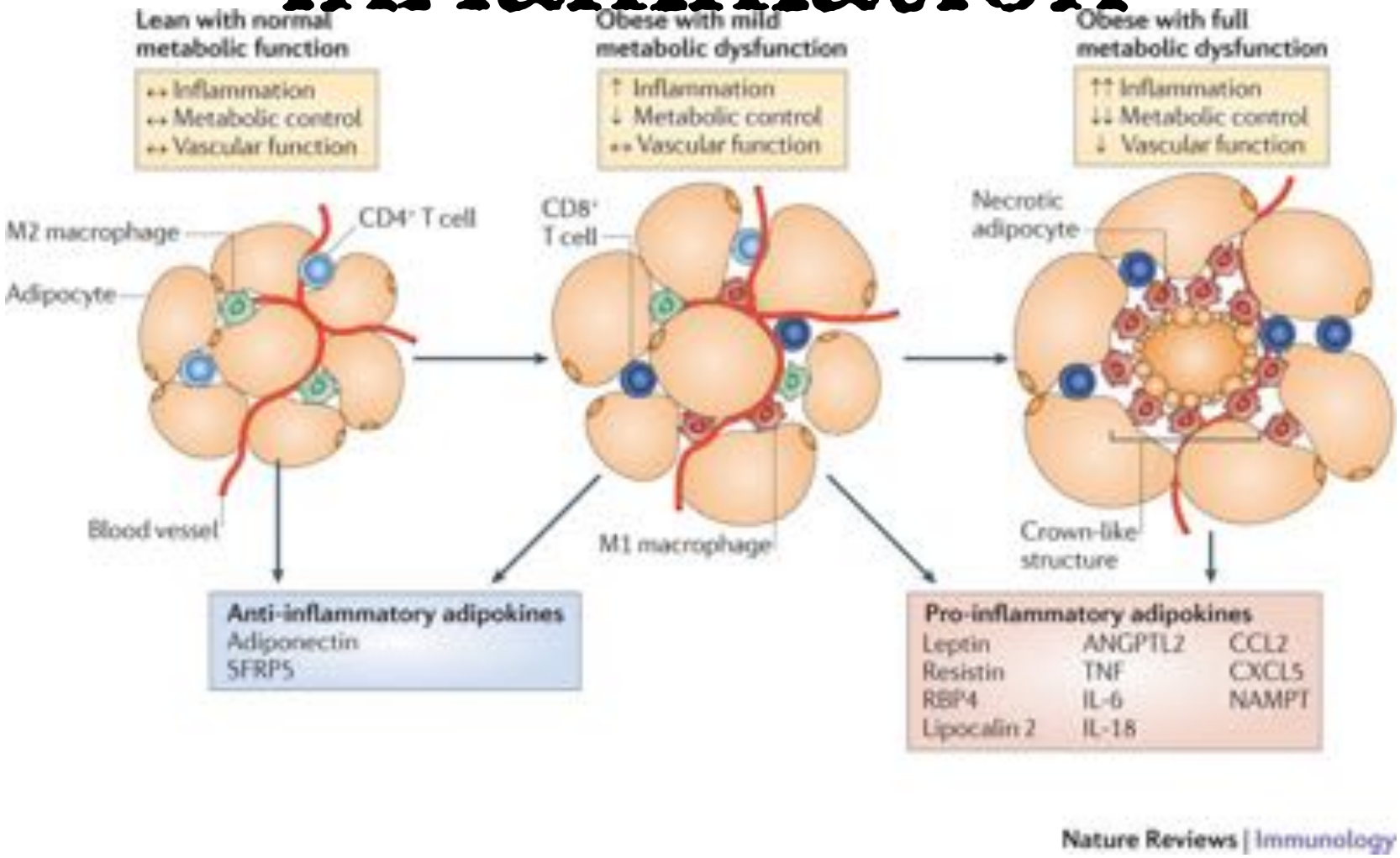

a
Gut bacterial sample from obese individuals
Gut bacterial sample from lean individuals
Organism-level profiling: 16S rRNA gene sequencing
Gene-level profiling: metagenomic sequencing
Comparative analysis of sequence data
Core microbiome
b
Caloric intake
Nutrient composition
Antibiotics
Genetic influence
Bacterial exposure
GI surgery
Neuroendocrine appetite regulation
GI peptide hormones
Gut glucose production
GI nutrient digestion/ absorption
Gut lipid production
Inflammatory signals

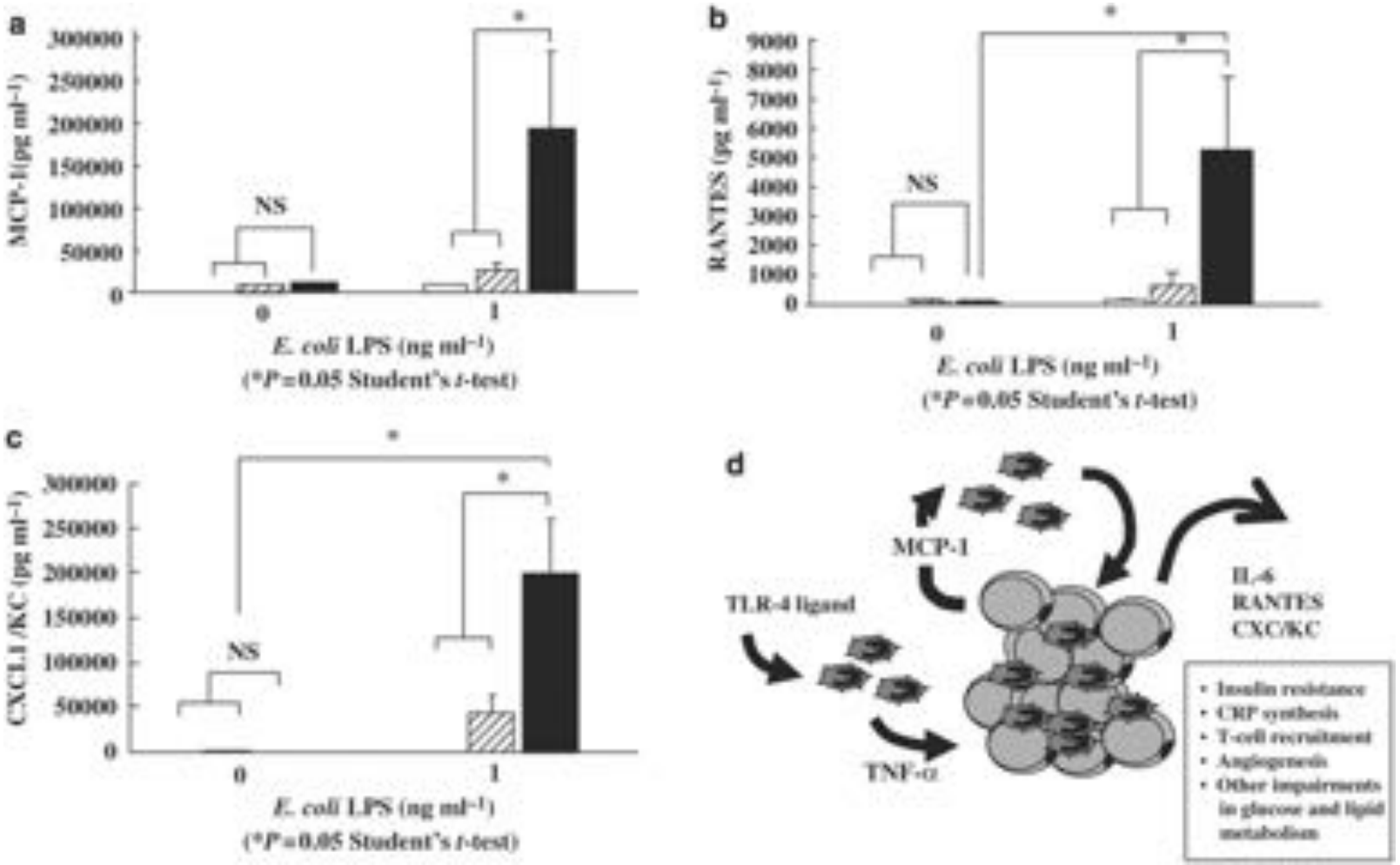

CYP
endotoxin
Gram- bakterier
hæmmer
inflammation
fase
III
xxx

OGSÅ LPS


CYP
endotoxin
Gram- bakterier
hæmmer
inflammation
fase
III
CYP
xxx

Fedtvæv og inflammation

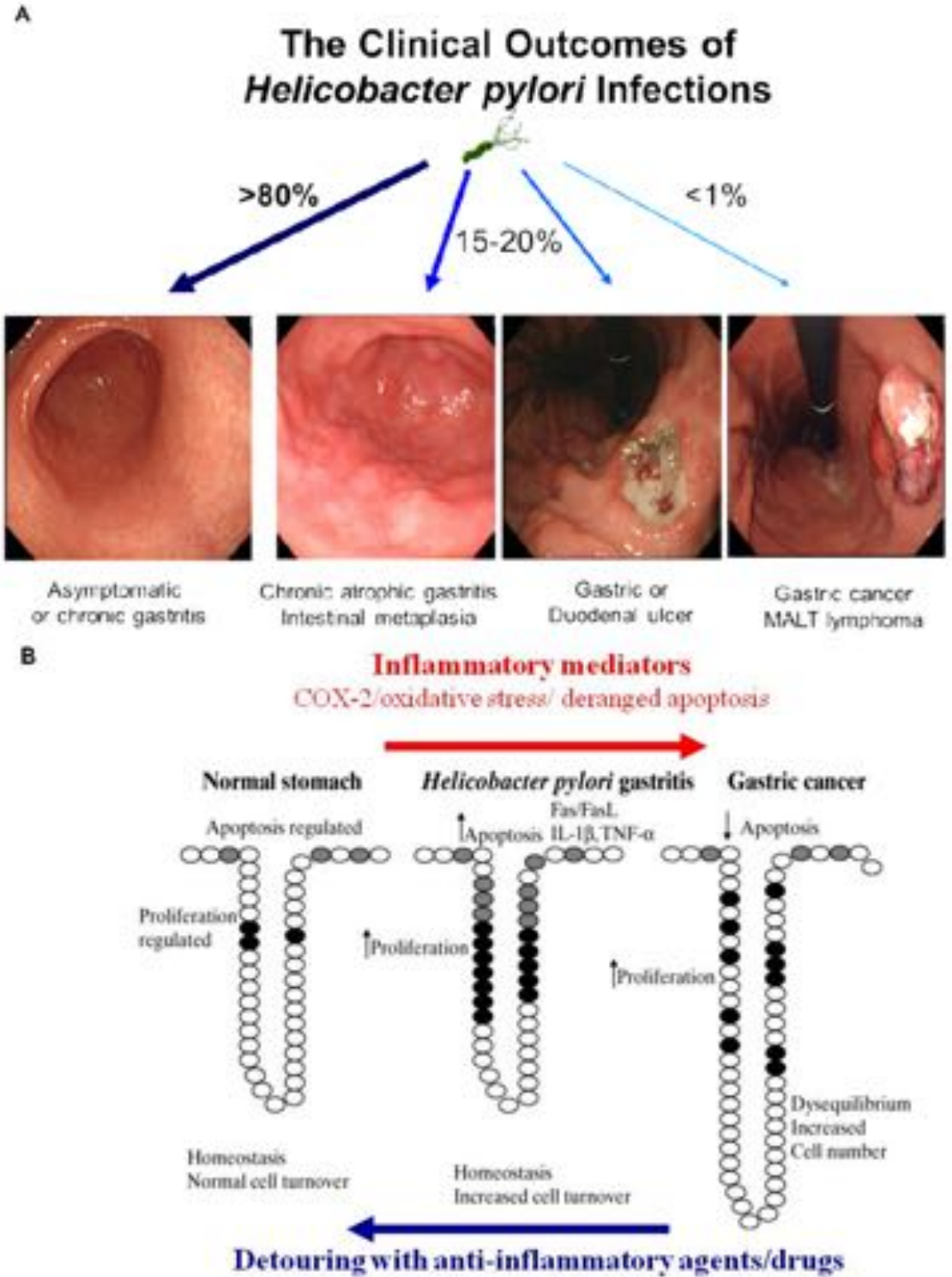


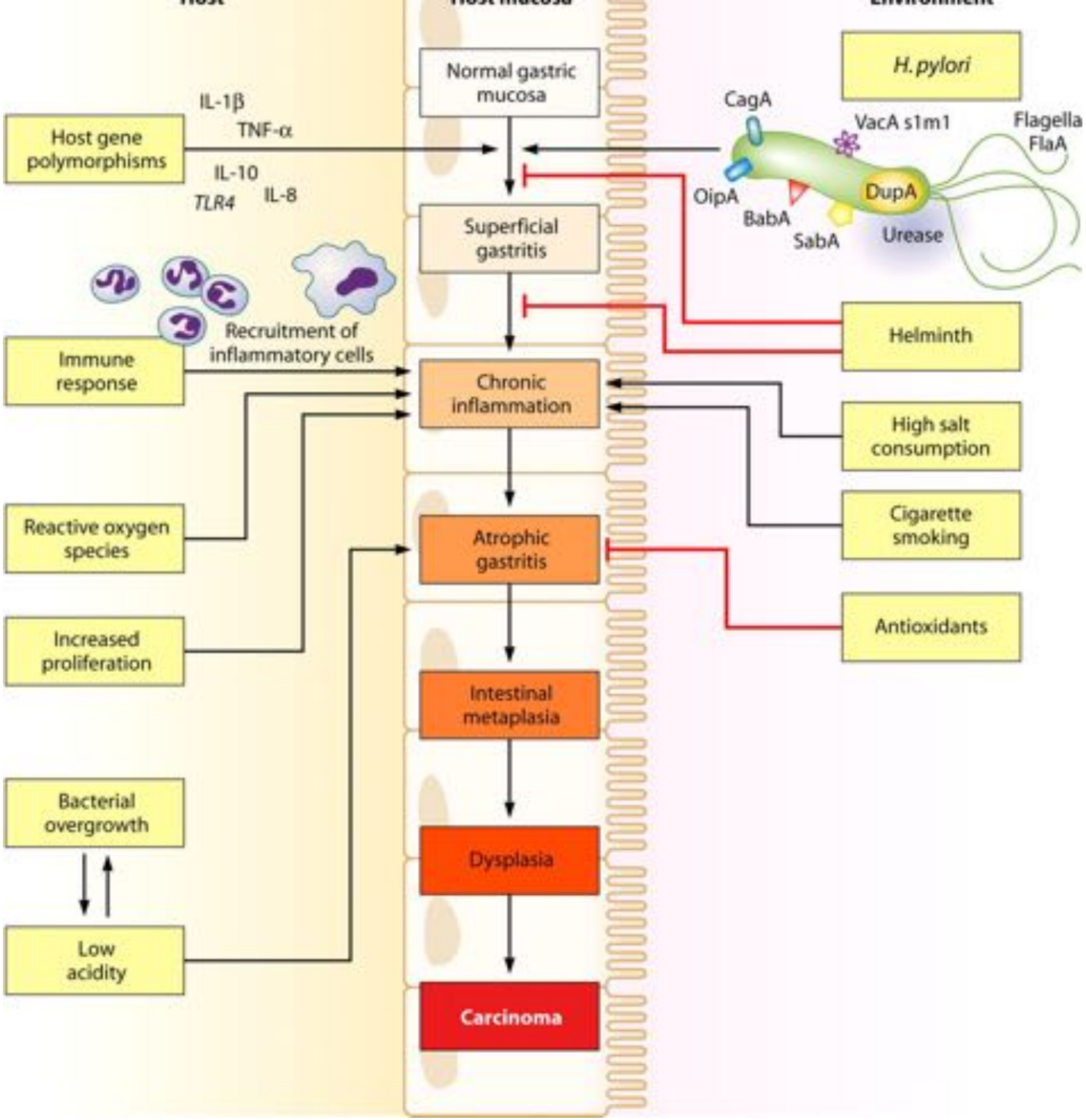


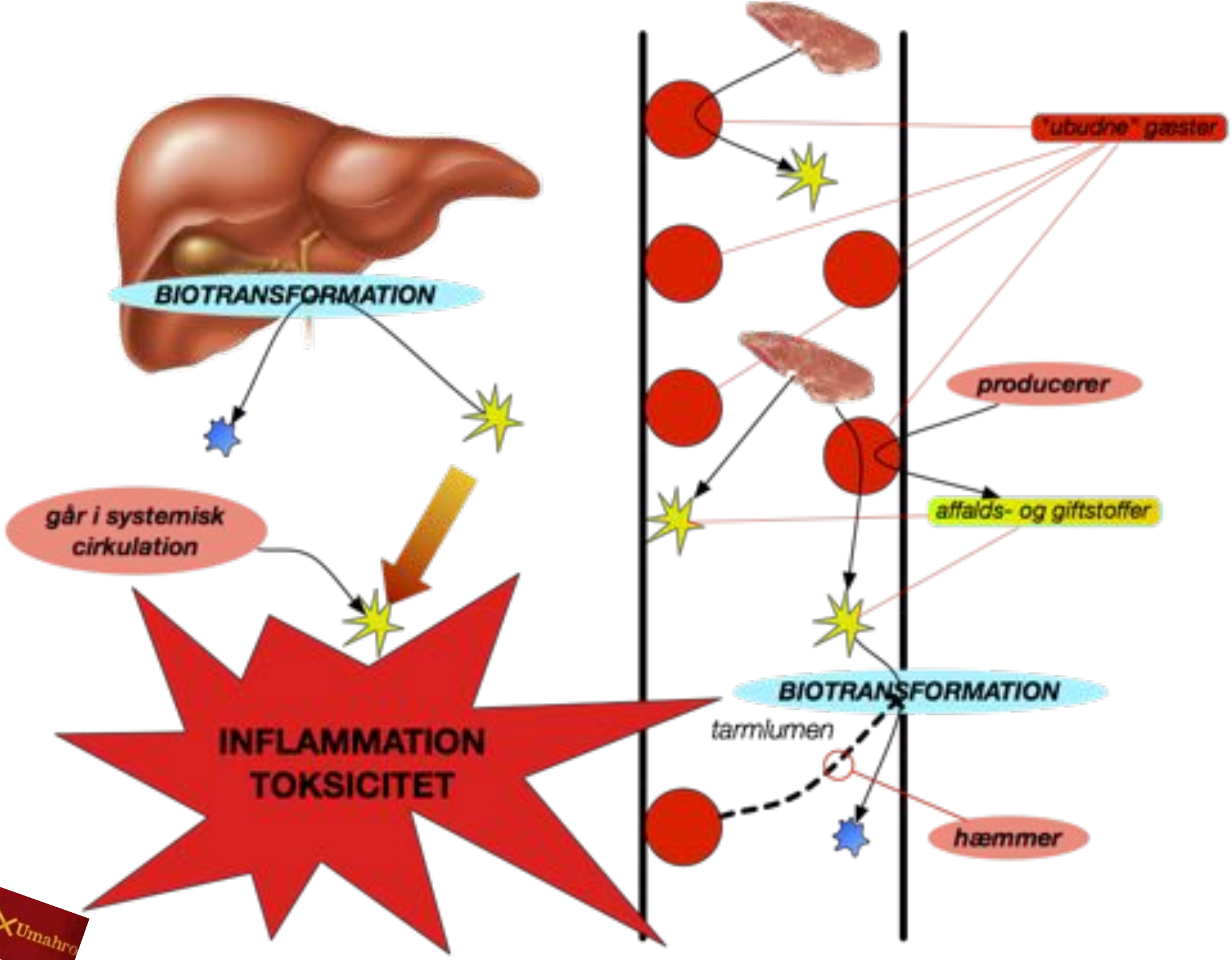
www.nature.com/ijo/journal/v32/n11/full/ijo2008153a.html

Kræft

www.mdpi.com/2072-6694/3/3/3018/htm




Normal gastric mucosa
H. pylori
CagA
VacA s1m1
Flagella FlaA
OipA
BabA
SabA
DupA
Urease
IL-1β
TNF-α
IL-10
TLR4
IL-8
Host gene polymorphisms
Superficial gastritis
Recruitment of inflammatory cells
Immune response
Helminth
Chronic inflammation
High salt consumption
Reactive oxygen species
Cigarette smoking
Atrophic gastritis
Increased proliferation
Antioxidants
Intestinal metaplasia
Bacterial overgrowth
Dysplasia
Low acidity
Carcinoma


"ubudne" gæster
BIOTRANSFORMATION
producerer
affalds- og giftstoffer
går i systemisk cirkulation
BIOTRANSFORMATION
tarmlumen
INFLAMMATION
TOKSICITET
hæmmer

Dietary and enviromental compounds	Microbial products	Known effect on host
Non-digestible carbohydrates	SCFAs	• Microbiota modulation • Cellular differentiation; apoptosis • Inflammation
Phytochemicals	Phenolic acids; isothiocyanates	• Xenobiotic detoxification • Microbiota modulation • Cellular differentiation; apoptosis • Inflammation
Protein	NOCs; ammonia	• ROS production; genotoxicity
	Polyamines	• Inflammation • ROS production; genotoxicity
	Hydrogen sulphide	• Inflammation • ROS production; genotoxicity
Fat ⇢ Bile acids	Taurine	• Microbiota modulation
	Secondary bile acids	• Microbiota modulation • Cellular differentiation; apoptosis • ROS production; genotoxicity
Xenobiotics	Carcinogens	• ROS production; genotoxicity
Ethanol	Acetaldehyde	• ROS production; genotoxicity

www.nature.com/nrmicro/journal/v12/n10/images/nrmicro3344-f4.jpg

Nature Reviews | Microbiology

Probiotiske fødevarer

Mad der indeholder gavnlige tarmbakterier

- Fødevarer med jord på!
- Yoghurt
  - Uden tilsat sukker
  - Gerne hjemmelavet
- Andre syrnede mejeriprodukter
- Råmælk
- Ost
- Surkål og andre gærede grøntsager
- Kombucha
- Kefir
- Miso
- Surdejsbrød
- Natto
- Fødevarer beriget med probiotiske bakterier

Præbiotika

Hvad er præbiotika?

Komponenter i fødevarer der (selektivt) nærer den gavnlige tarmflora

NB: Vi er endnu ikke helt sikre på lige præcis hvordan en gavnlig tarmflora ser ud

Fibre, resistent stivelse, kulhydrater

Protein kan også omsættes af tarmbakterier…men ikke nødvendigvis til noget gavnligt

Typer af præbiotika

Fructaner: Inulin og fruktooligosakkarider

Beta-glukaner

Galaktoologisakkarider

Laktose

Laktulose

Pektin

Mannaner: Glukomannan, galaktomannan og mannanoligosakkarider

Resistent stivelse

Fra tang: Alginat, agar agar og carrageenan

Xylooligosakkarider

Polyoler: Xylitol, maltitol, erytrithol

Mandler

Galaktaner: Arabinogalaktan

Harpiks

Præbiotiske fødevarer

Fuldkorn i alle afskygninger

Rodfrugter

Alle de grønne blade

Grøntsager af *Allium* familien

Grøntsager af korsblomstfamilien

Bælgfrugter i alle afskygninger

Bær i alle afskygninger

Frugter i alle afskygninger

Mandler og tildels andre nødder og kerner

Fødevarer, medicinske fødevarer og kosttilskud tilsat præbiotika

Hvordan kan jeg hjælpe dig?

Hvad arbejder jeg med?

Fra usund til sund

Fra syg til rask

Fra sund til supersund

Peak performance og sportsernæring

“Helsegastronomi”

Foredrag

Konsulentarbejde i virksomheder og organisationer

Sundhedsrevolutionær hold 12

14 måneders online og live forløb

Bliv din egen sundhedsekspert og/eller en endnu bedre sundhedsekspert for dem du hjælper, behandler og rådgiver

14 moduler på 4 uger med video, skrift, opgaver

Live webinarer til hvert modul

Personlig session inden og efter forløbet

Løbende 1-til-1 sparring og supervision på rådgiver- og behandler-niveau

Sundhedsrevolutionær hold 12

Starter mandag d. 12. september 2016, slutter november 2017

God pris ved tilmelding indenfor 48 timer

SIDSTE HOLD FOR NU OG I NUVÆRENDE FORM

Hjælp til selvhjælp

Hvis du vil være din egen sundhedsekspert

Oplagt hvis du gerne vil have virkelig godt styr på dine helbredsproblemer

- Fra syg til rask eller raskere
- Fra usund til sund
- Fra sund til supersund
- Peak performance

Rådgiver-behandler

Oplagt hvis du arbejder med at gøre og hjælpe andre med at blive raske og/eller bibevare deres sundhed

Behandler, såsom læge, ernæringsterapeut, kostvejleder, fysioterapeut, akupunktør, osteopat, kiropraktor

Rådgiver og inspirerer andre, såsom træner, personlig træner, HR ansvarlig, socialrådgiver o.s.v.

Rådgiver-behandler

Send mig en mail eller SMS, så vi kan finde tid til en indledende snak om, hvorvidt Sundhedsrevolutionær hold 12 er noget for dig...

UM@UMAHRO.COM

31328178

SPØRGETID!

HELLO@UMAHRO.COM

31328178 indtil 15. august hvor min PA er tilbage fra ferie