Il Microbioma Umano
dalla ricerca alla clinica attraverso i big data

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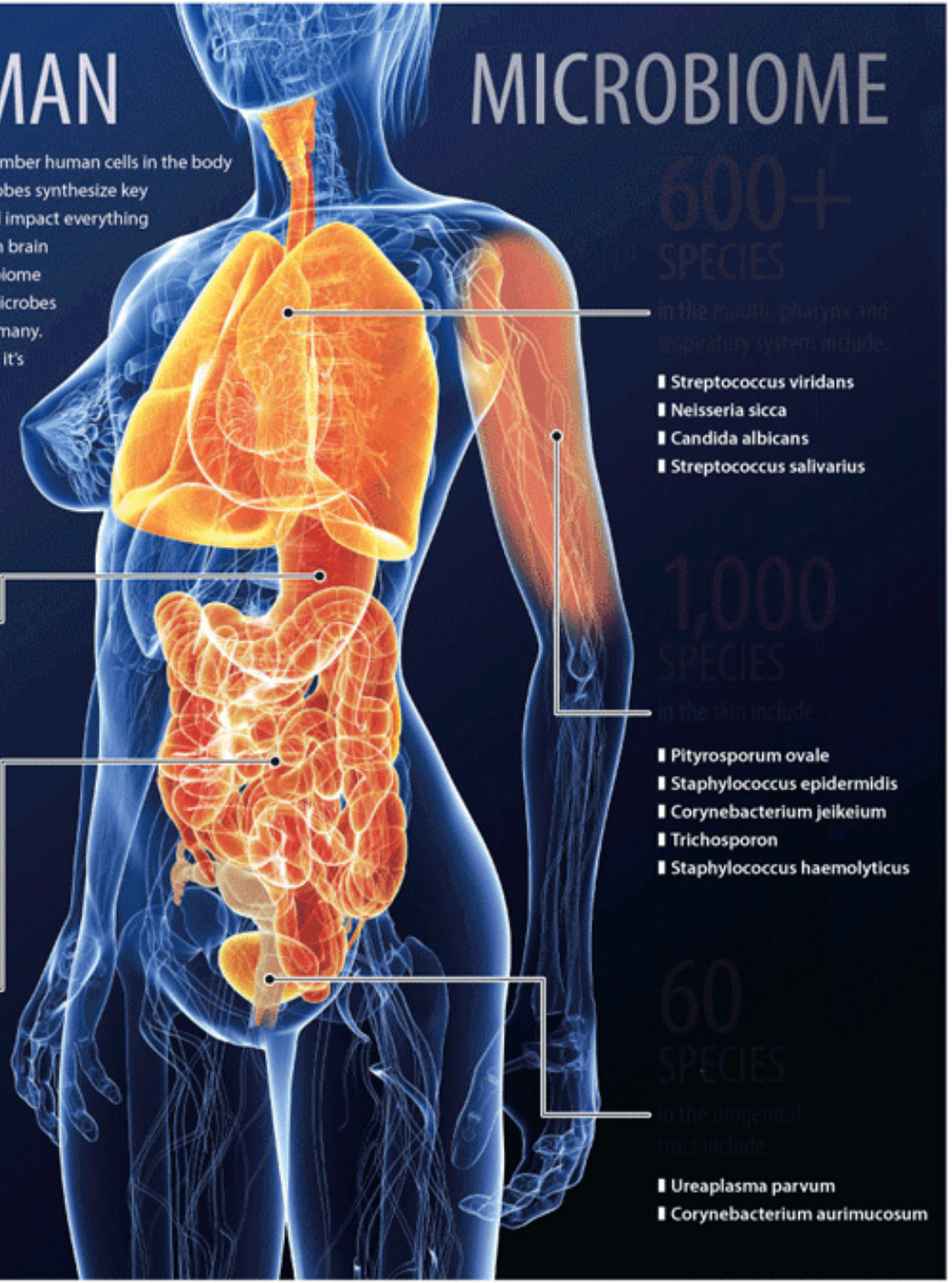
POLICLINICO TOR VERGATA

THE HUMAN MICROBIOME

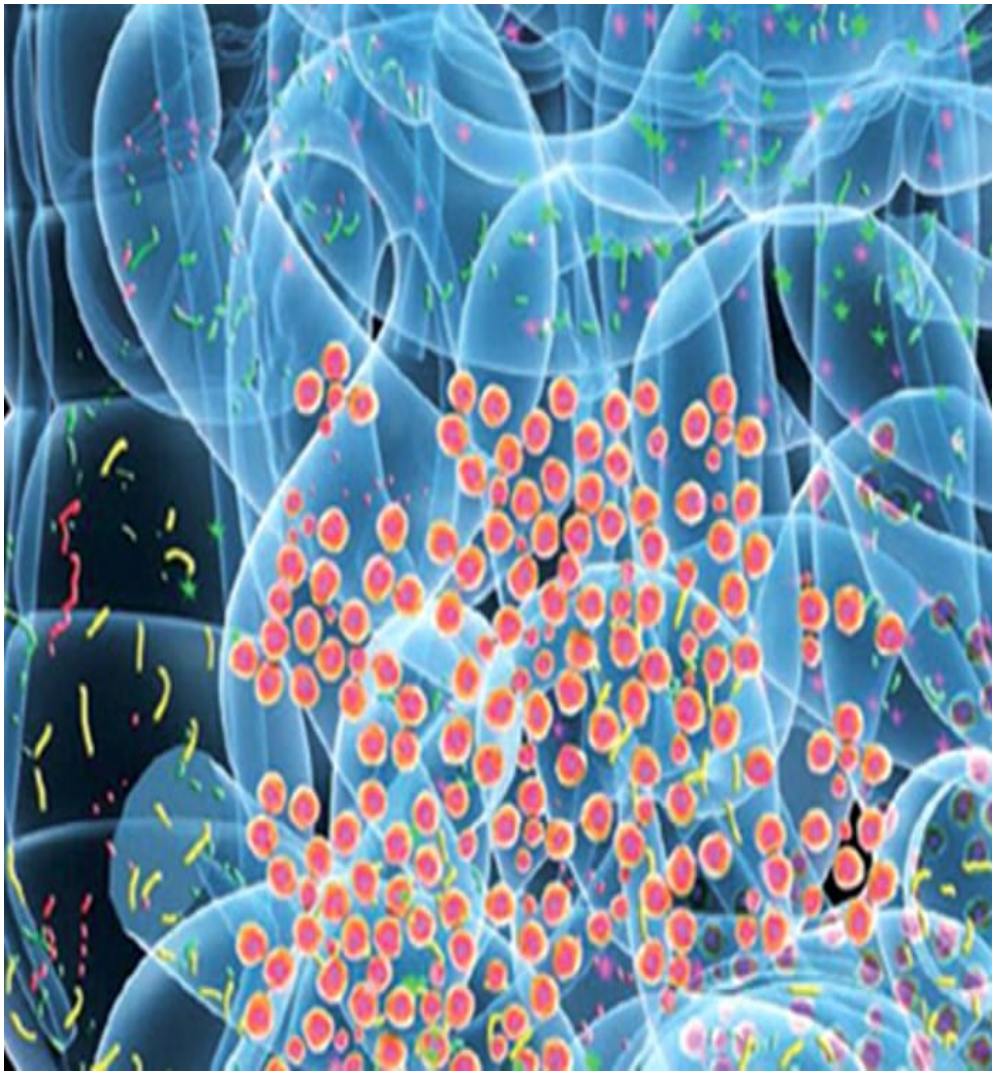
Bacteria, fungi, and viruses outnumber human cells in the body by a factor of 10 to one. The microbes synthesize key nutrients, fend off pathogens and impact everything from weight gain to perhaps even brain development. The Human Microbiome Project is doing a census of the microbes and sequencing the genomes of many. The total body count is not in but it's believed over 1,000 different species live in and on the body.



SOURCES: NATIONAL INSTITUTES OF HEALTH, SCIENTIFIC AMERICAN; HUMAN MICROBIOME PROJECT

Dean Tweed • POSTMEDIA NEWS / IMAGE: Fotolia

Microbiota e Microbioma



COMPOSIZIONE

Ogni individuo ha uno specifico

«microbial fingerprint»

FUNZIONI

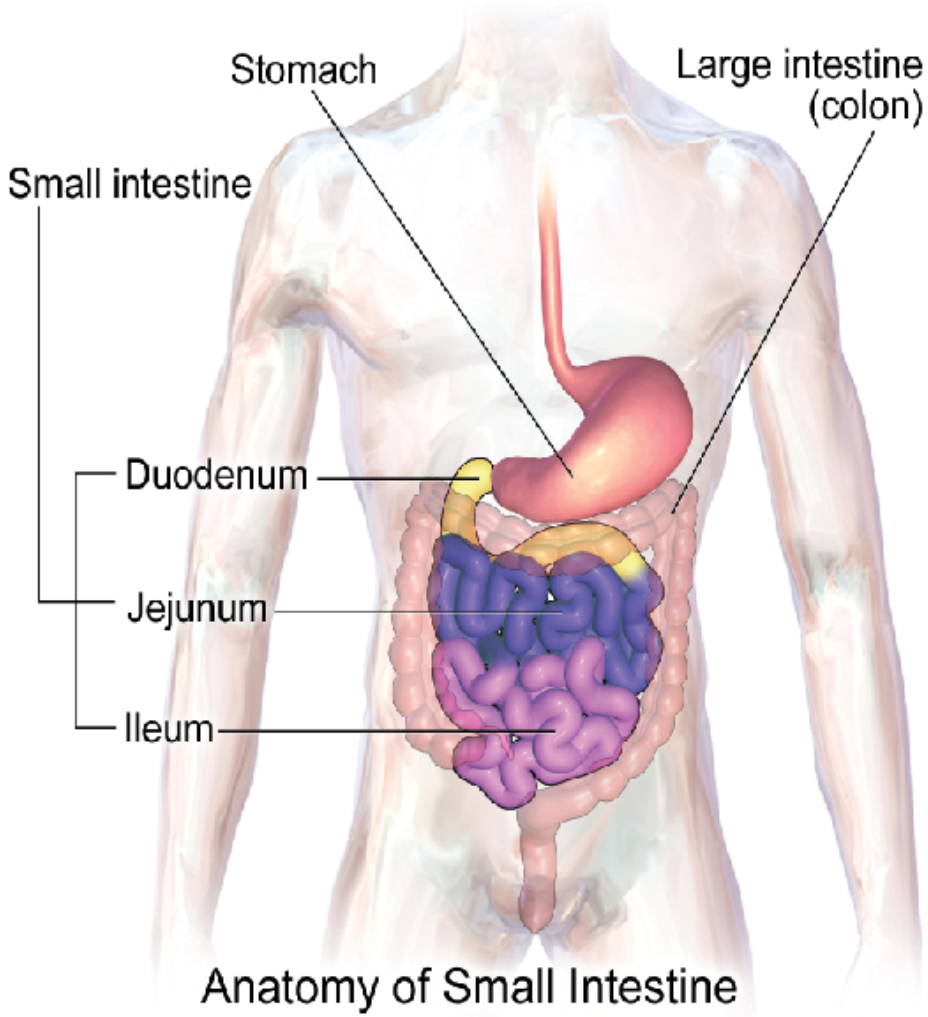
- Strutturale (mantenimento integrità della barriera intestinale);
- Assorbimento dei nutrienti;
- Metabolismo;
- Difesa;
-Sviluppo e regolazione dell'immunità

MICROBIOME DISTRIBUTION IN HUMAN GUT SYSTEM

Stomach 10^2
Lactobacillus
Candida
Streptococcus
Heliobacter pylori
Peptostreptococcus

Duodenum 10^2
Streptococcus
Lactobacillus

Jejunm 10^2
Streptococcus
Lactobacillus



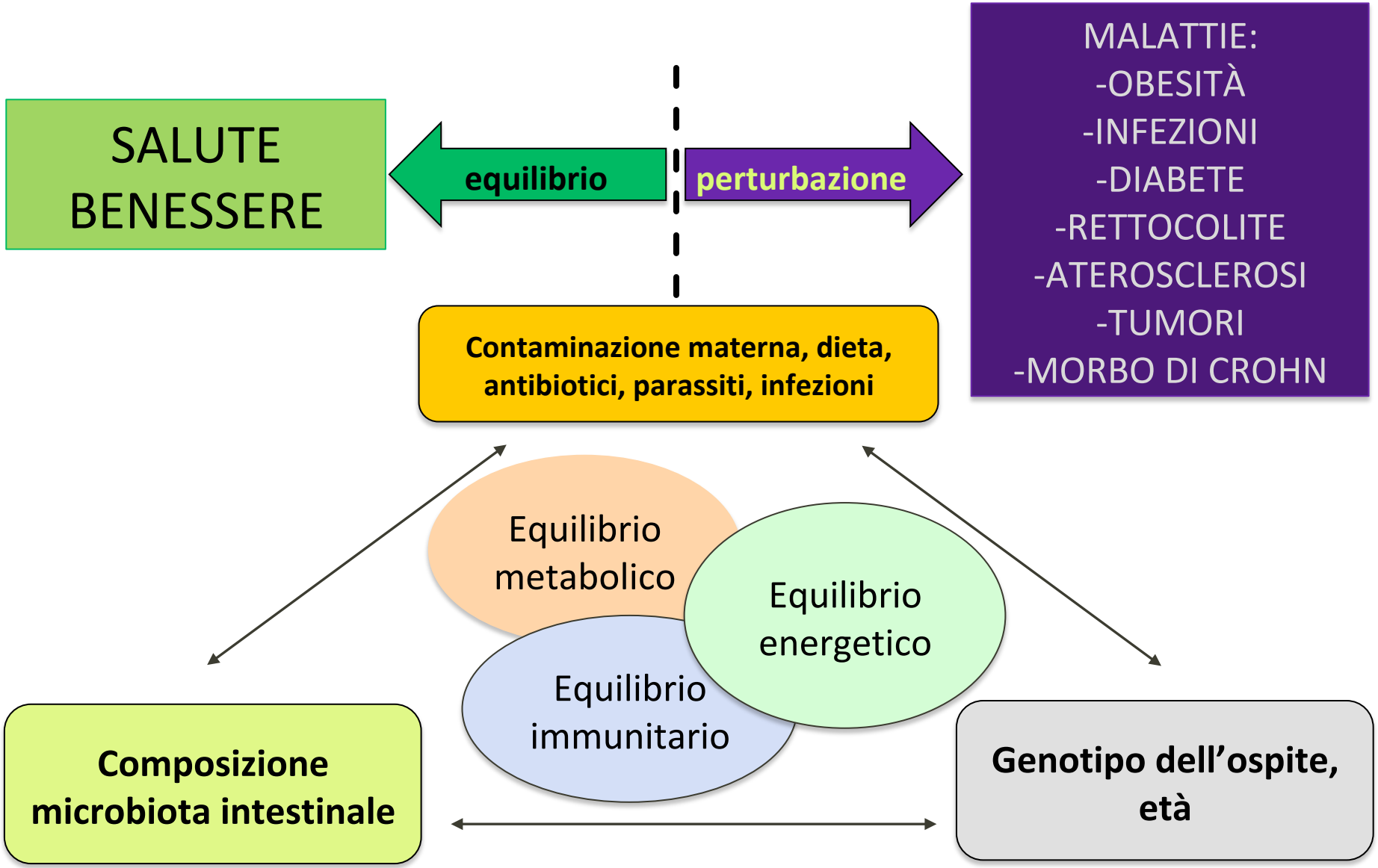
Anatomy of Small Intestine

Proximal ileum 10^2
Streptococcus
Lactobacillus

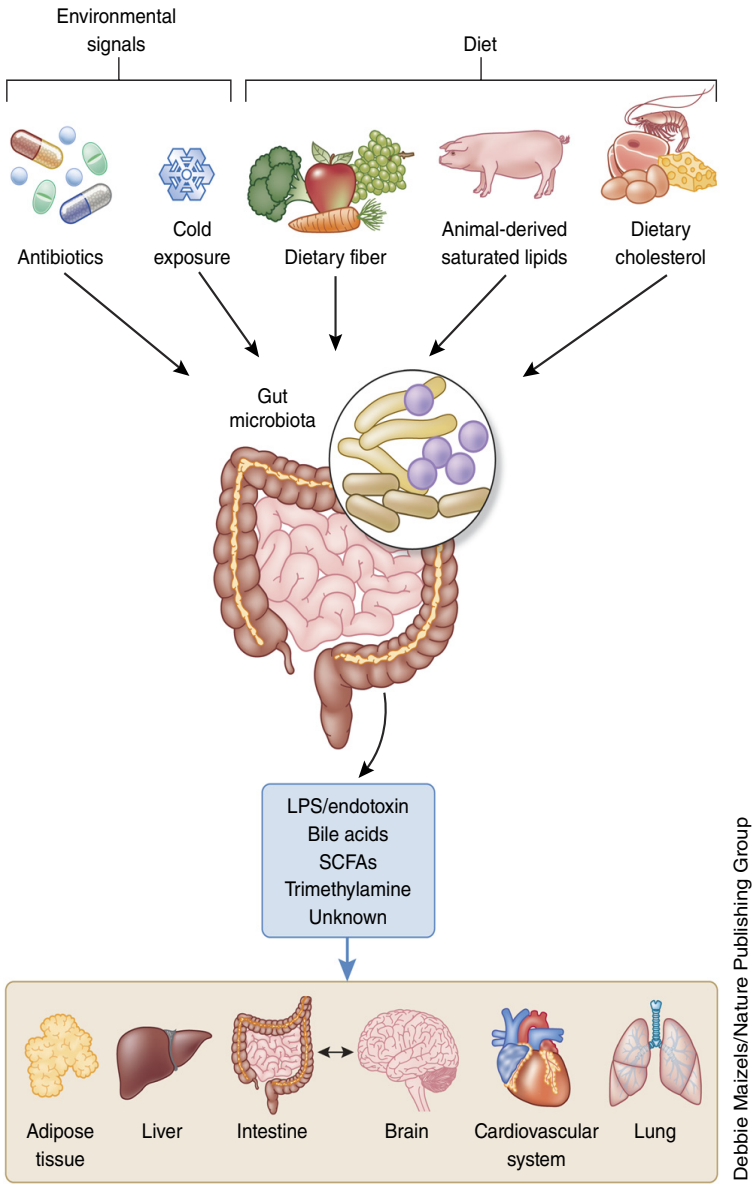
Distal ileum 10^8
Clostridium
Streptococcus
Bacteroides
Actinomycinae
Corneybacteria

Colon 10^{12}
Bacteroides
Clostridium
Bifidobacterium
Enterobacteriacae

Un ecosistema in equilibrio

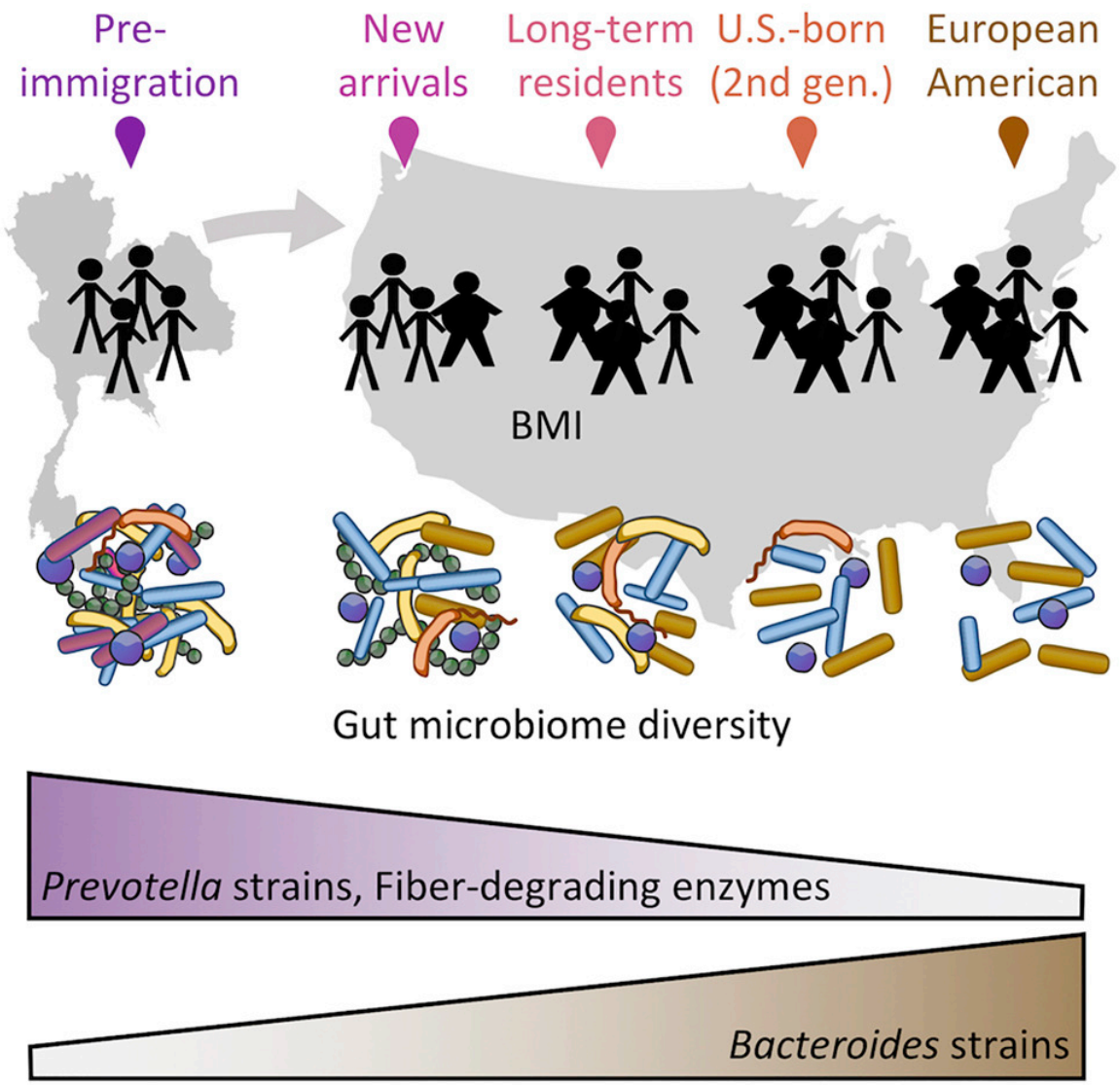


Ambiente e Microbiota



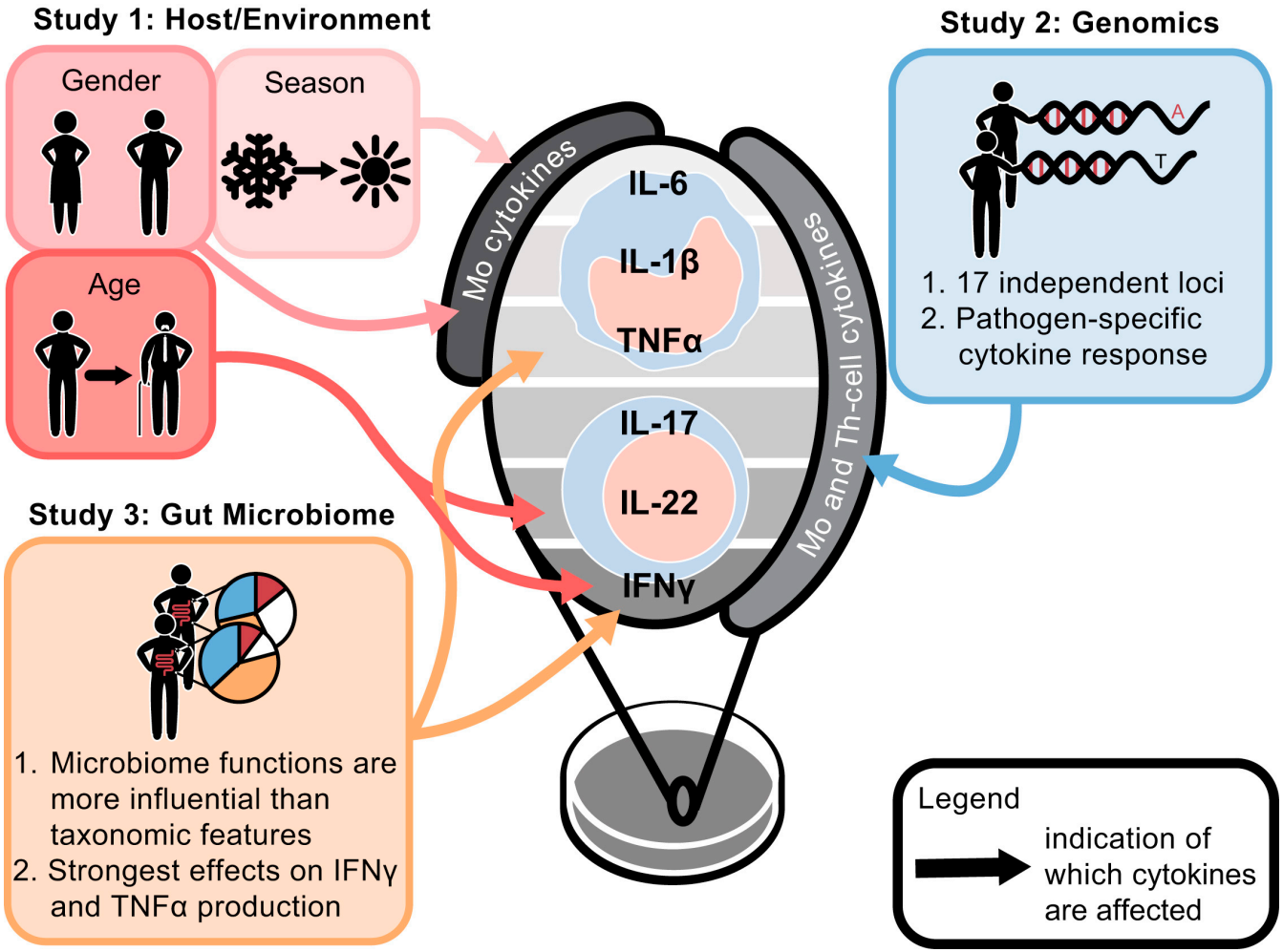
Schroeder and Backhed Nature Medicine 2016

L'immigrazione occidentalizza il microbioma umano



Cell Volume 175, Issue 4, Pages 962-972.e10 (November 2018)

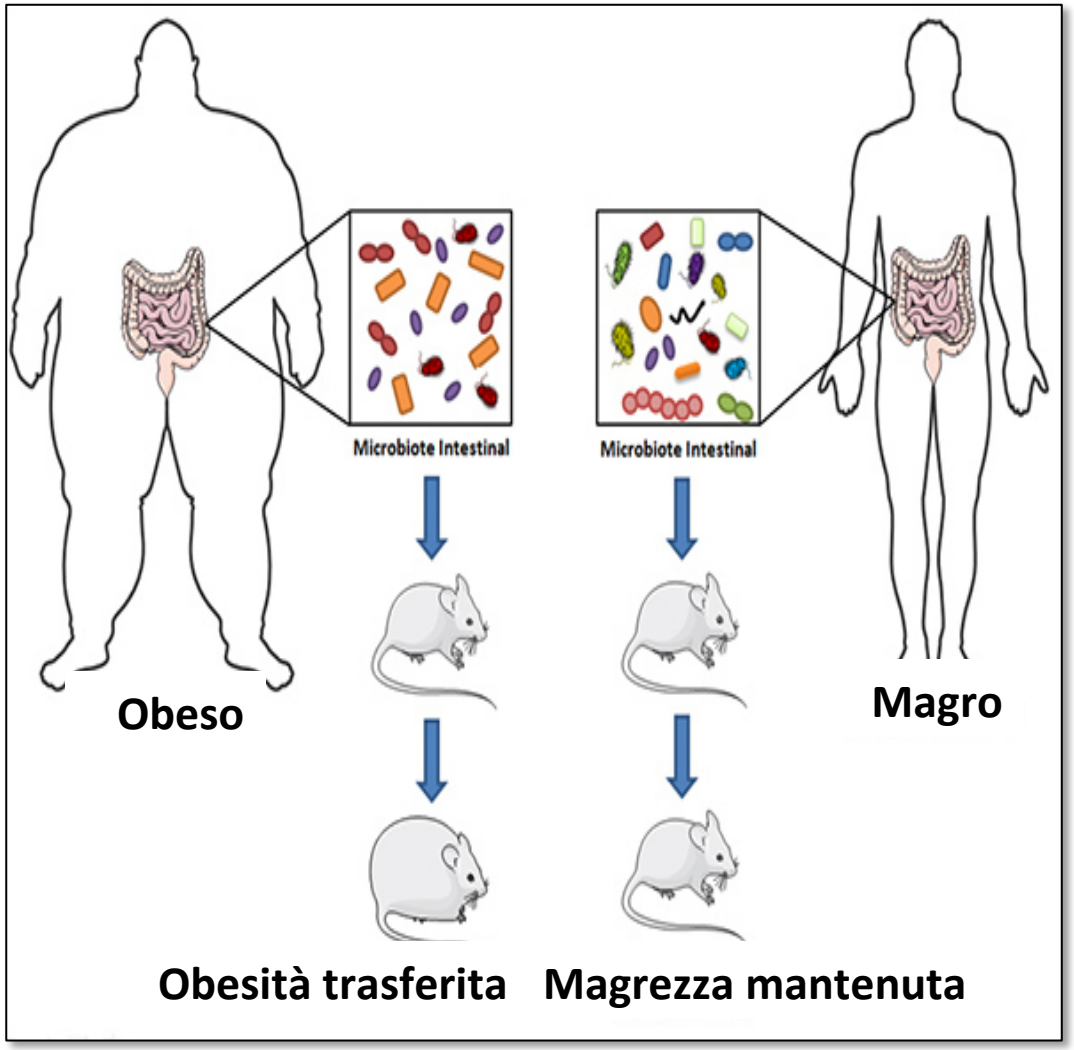
MICROBIOMA INTESTINALE E INFIAMMAZIONE SISTEMICA
Funzioni del microbioma più influenti della tassonomia



Cell 2016 167, 1125-1136.e8DOI: (10.1016/j.cell.2016.10.020)

Microbiota intestinale e Malattie

MICROBIOMA INTESTINALE ED OBESITA': EFFETTI CAUSALI

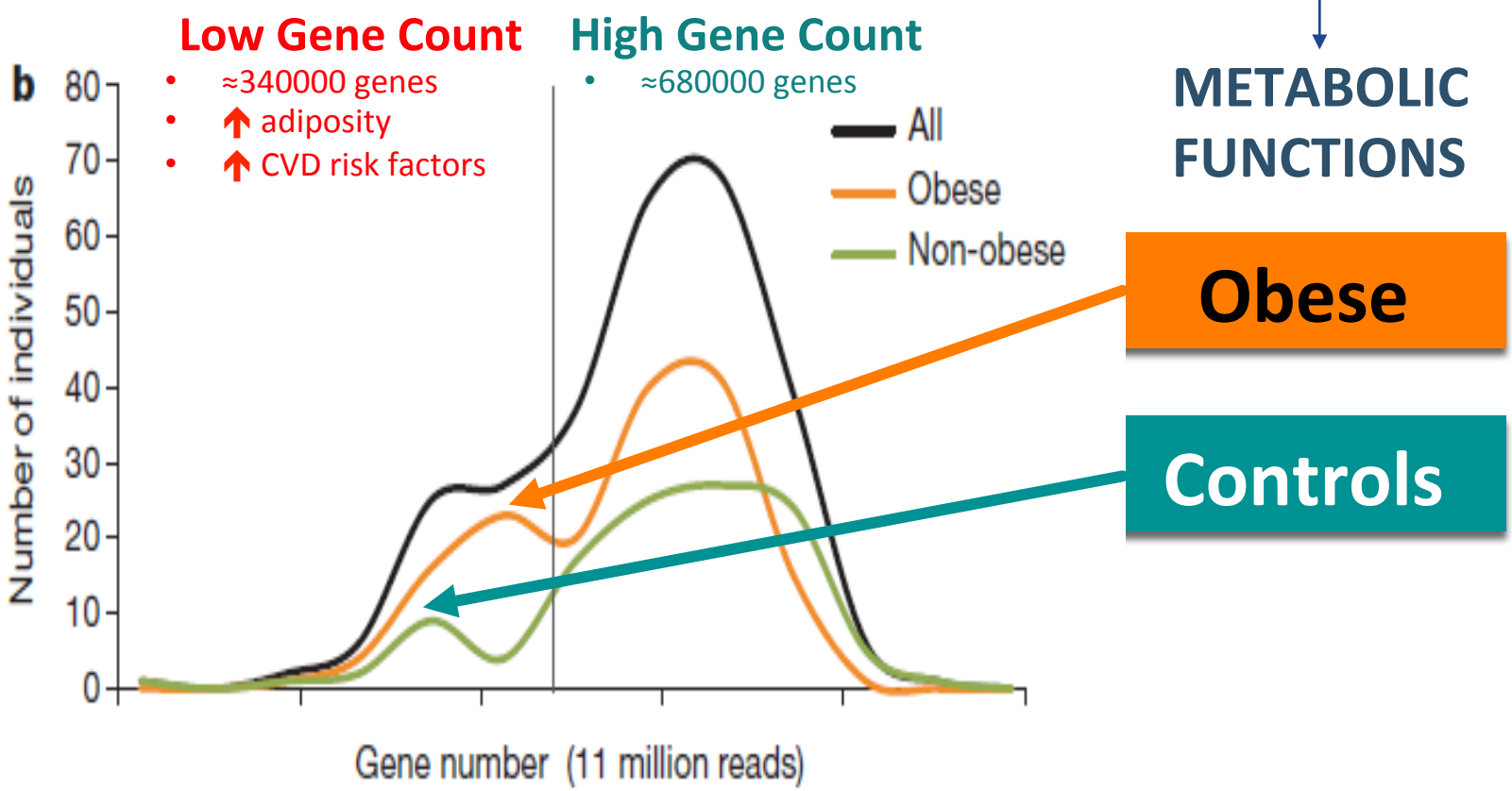


Turnbaugh PJ et al Nature. 2006

Richness of human gut microbiome correlates with metabolic markers

Emmanuelle Le Chatelier[1]*, Trine Nielsen[2]*, Junjie Qin[3]*, Edi Prifti[1]*, Falk Hildebrand[4,5], Gwen Falony[4,5], Mathieu Almeida[1], Manimozhiyan Arumugam[2,3,6], Jean-Michel Batto[1], Sean Kennedy[1], Pierre Leonard[1], Junhua Li[3,7], Kristoffer Burgdorf[2], Niels Grarup[2], Torben Jørgensen[8,9,10], Ivan Brandslund[11,12], Henrik Bjørn Nielsen[13], Agnieszka S. Juncker[13], Marcelo Bertalan[13], Florence Levenez[1], Nicolas Pons[1], Simon Rasmussen[13], Shinichi Sunagawa[6], Julien Tap[1,6], Sebastian Tims[14], Erwin G. Zoetendal[14], Søren Brunak[13], Karine Clément[15,16,17], Joël Doré[1,18], Michiel Kleerebezem[14], Karsten Kristiansen[19], Pierre Renault[18], Thomas Sicheritz-Ponten[13], Willem M. de Vos[14,20], Jean-Daniel Zucker[15,16,21], Jeroen Raes[4,5], Torben Hansen[2,22], MetaHIT consortium†, Peer Bork[6], Jun Wang[3,19,23,24,25], S. Dusko Ehrlich[1] & Oluf Pedersen[2,26,27,28]

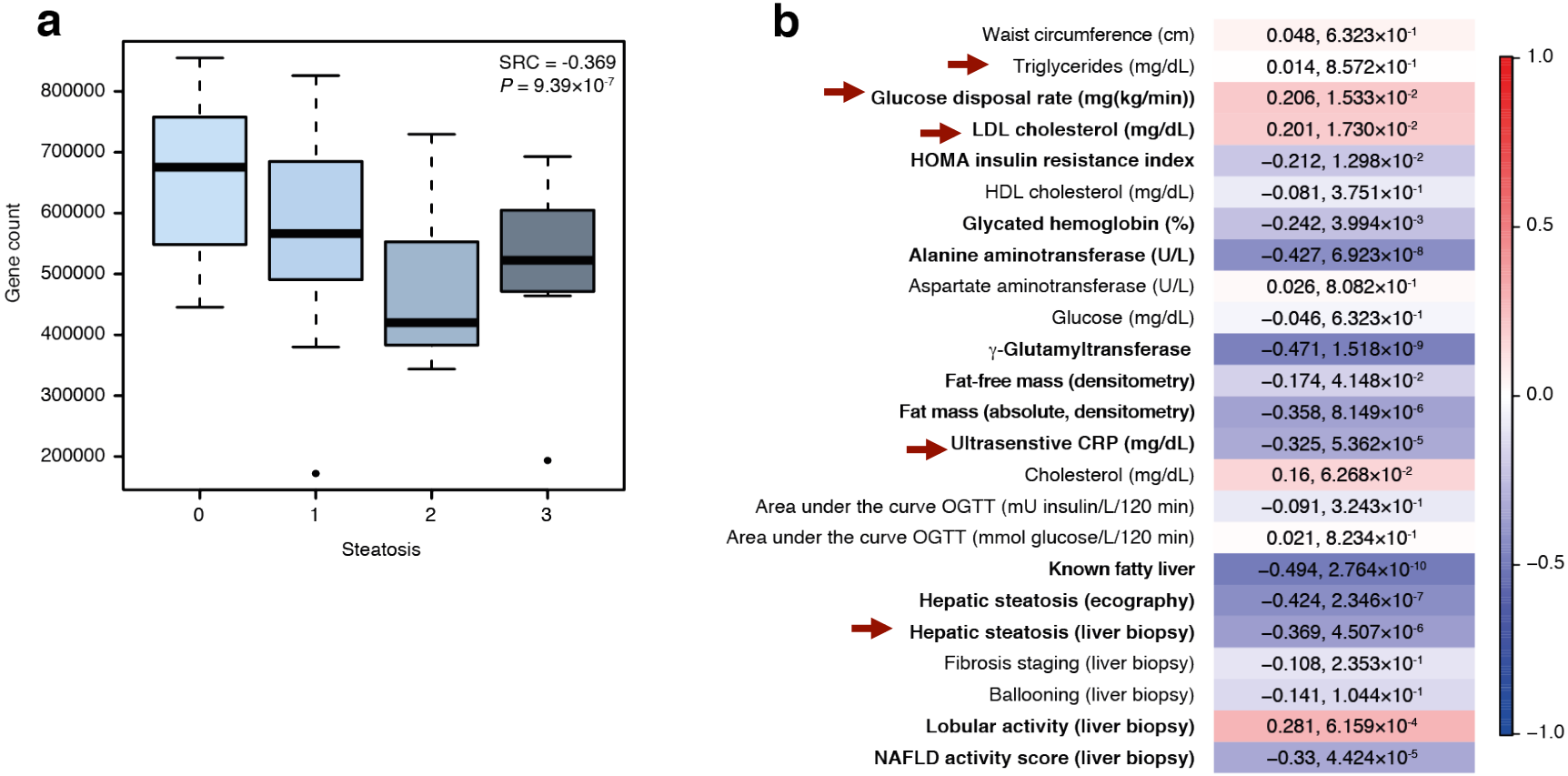
RICHNESS
↓
GENES
↓
METABOLIC FUNCTIONS



E Le Chatelier *et al. Nature* **500**, 541-546 (2013) doi:10.1038/nature12506

nature

Association of Low Microbial Gene Richness with Steatosis (A) and metabolic variables (B)

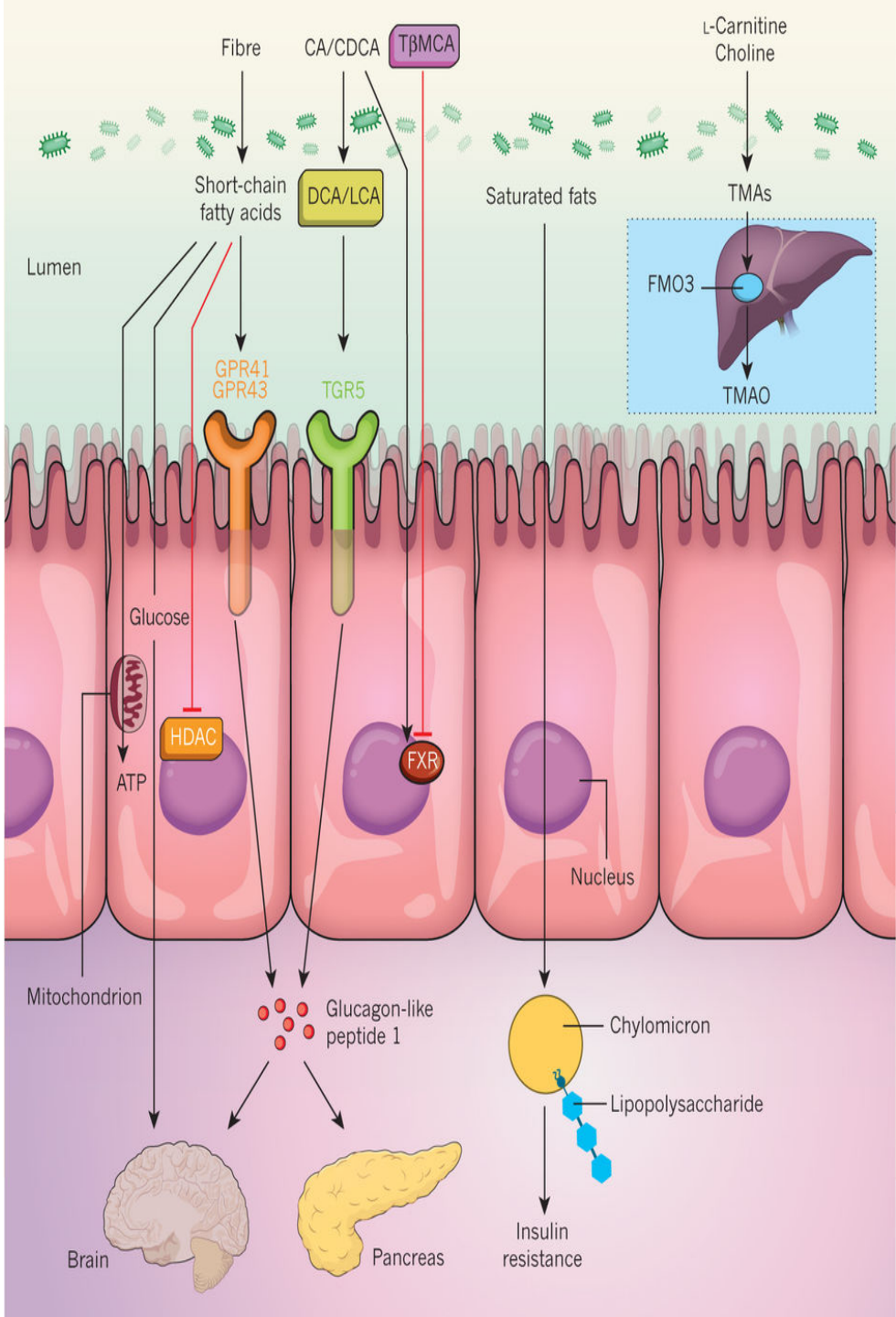


Hoyles, Fernández-Real, Federici,… Burcelin, Dumas, *Nature Medicine* 2018

High microbial gene richness = metabolic health: how?

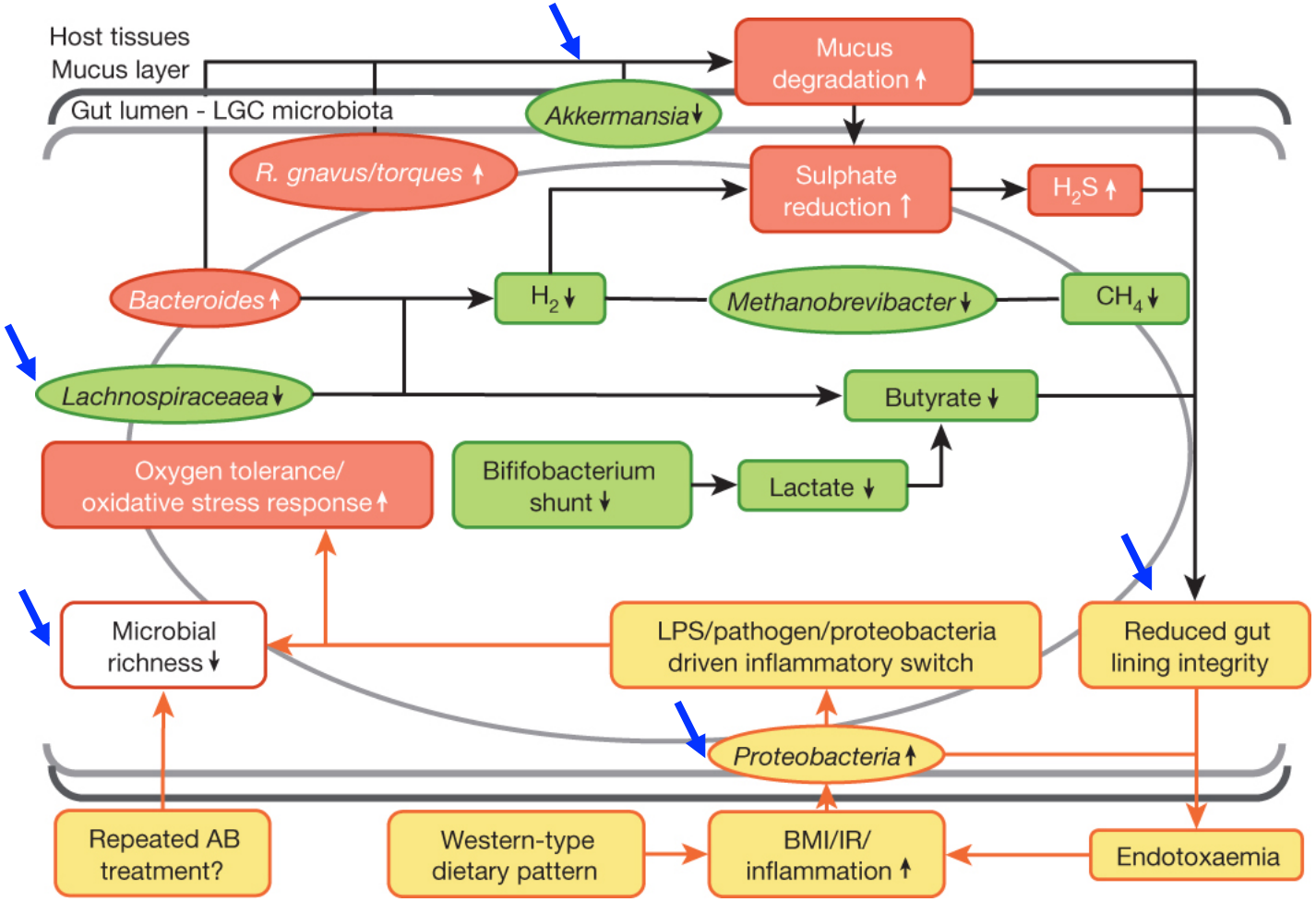
ENDOCRINE SIGNALS

INVASIVE SIGNALS



Sonnenburg and Backhed Nature 2016

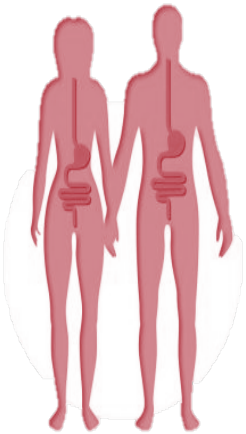
Functional and phylogenetic shifts in the LGC microbiome.



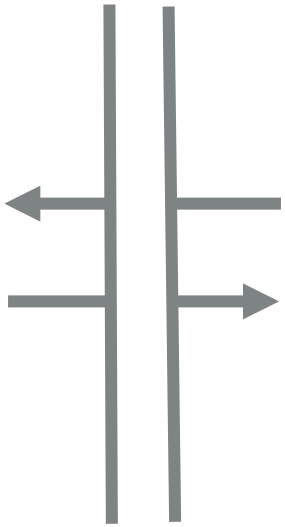
E Le Chatelier *et al. Nature* **500**, 541-546 (2013) doi:10.1038/nature12506

nature

UNA VISIONE FUTURIBILE



OSPITE



MICROBIOMA

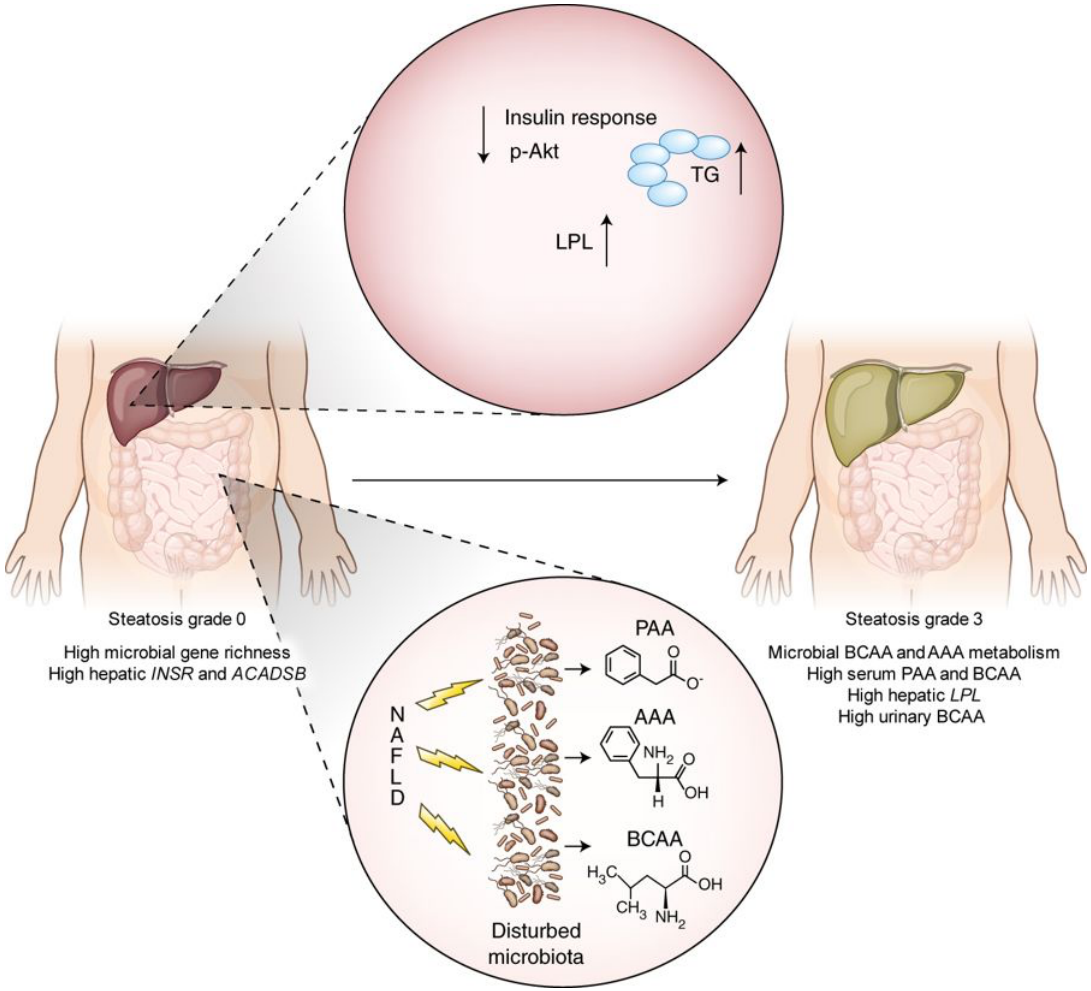
SISTEMA IMMUNITARIO/ METABOLISMO

BARRIERA/ ASSORBIMENTO

COMPOSIZIONE / FUNZIONE

DAL MICROBIOMA:
BIOMARCATORI E OBIETTIVI TERAPEUTICI

Il fenilacetato (PAA), un metabolita di origine microbica è un potenziale biomarcatore di NAFLD

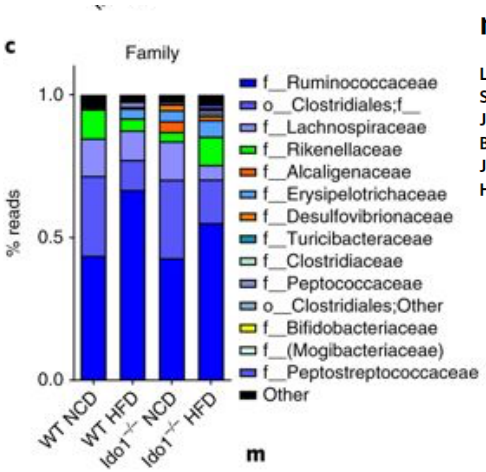


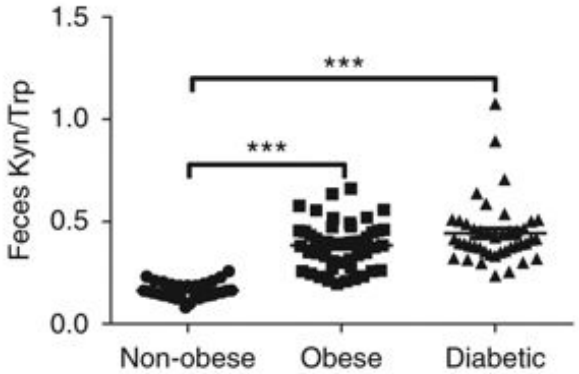
Hoyles, Fernández-Real, Federici,… Burcelin, Dumas, *Nature Medicine* 2018

nature medicine LETTERS
https://doi.org/10.1038/s41591-018-0060-4

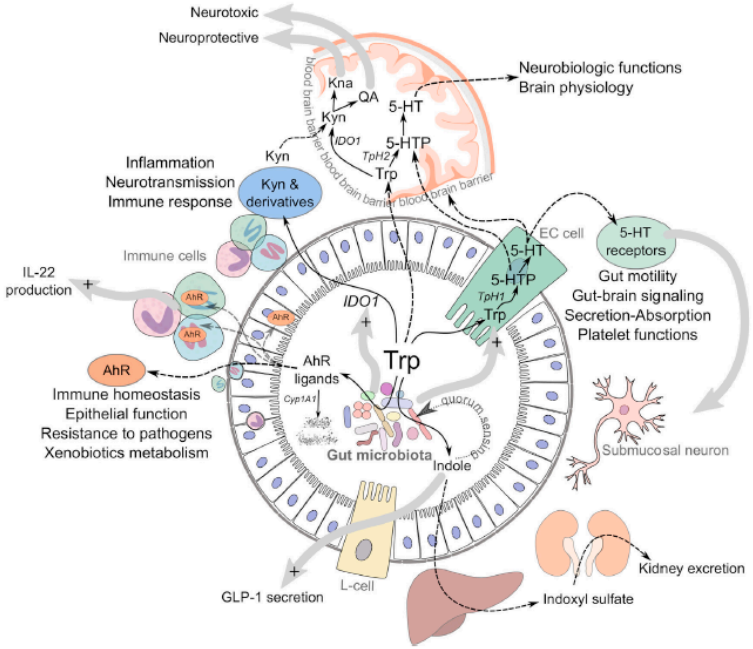
Genetic deficiency of indoleamine 2,3-dioxygenase promotes gut microbiota-mediated metabolic health

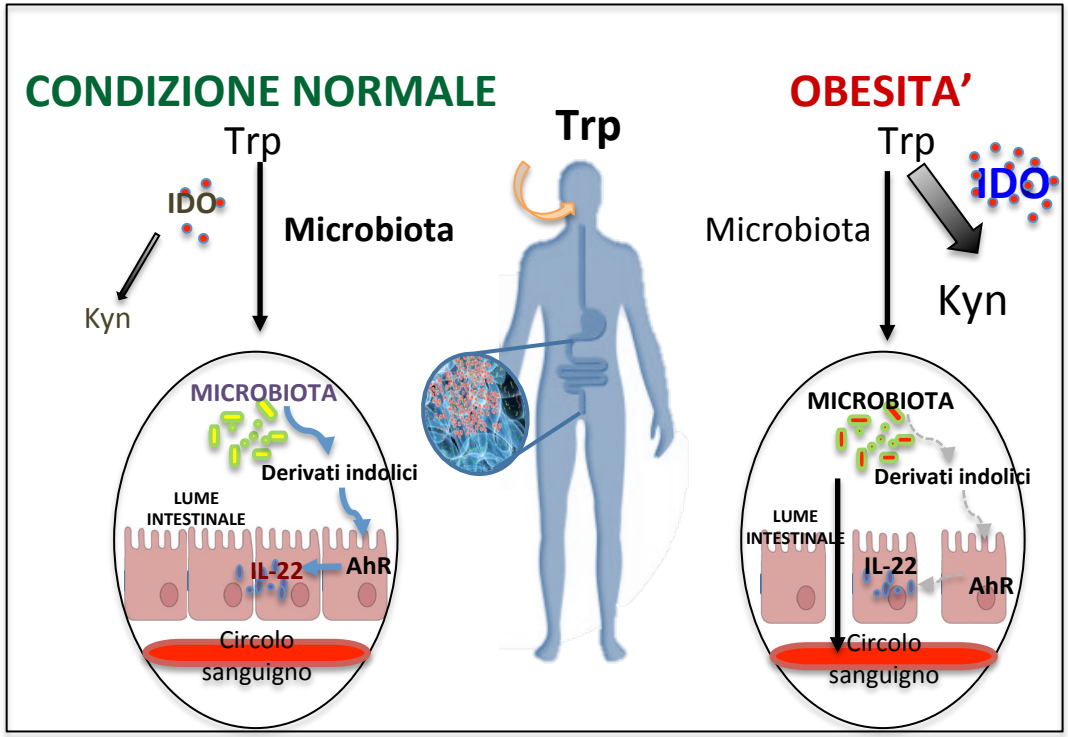
Ludivine Laurans[1], Nicolas Venteclef[2], Yacine Haddad[1], Mouna Chajadine[1], Fawaz Alzaid[2], Sarvenaz Metghalchi[1], Bruno Sovran[3], Raphael G. P. Denis[4], Julien Dairou[5], Marina Cardellini[6], Jose-Maria Moreno-Navarrete[7,8], Marjolene Straub[9], Sarah Jegou[9], Claire McQuitty[9], Thomas Viel[1], Bruno Esposito[1], Bertrand Tavitian[1], Jacques Callebert[10], Serge H. Luquet[4], Massimo Federici[6], José Manuel Fernandez-Real[7], Remy Burcelin[11], Jean-Marie Launay[10], Alain Tedgui[1], Ziad Mallat[1,12], Harry Sokol[3,9,13] and Soraya Taleb[1*]





Indoleamina 2,3-Diossigenasi (IDO)

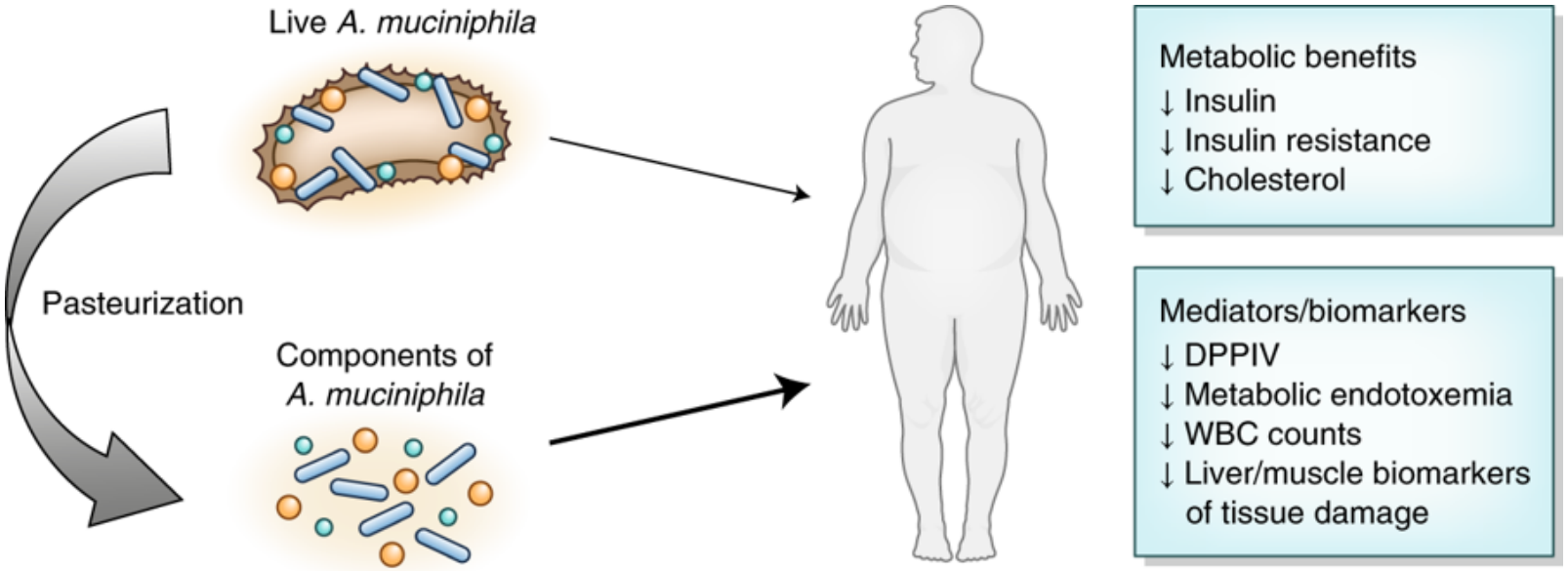




LETTERS
https://doi.org/10.1038/s41591-019-0495-2
nature medicine

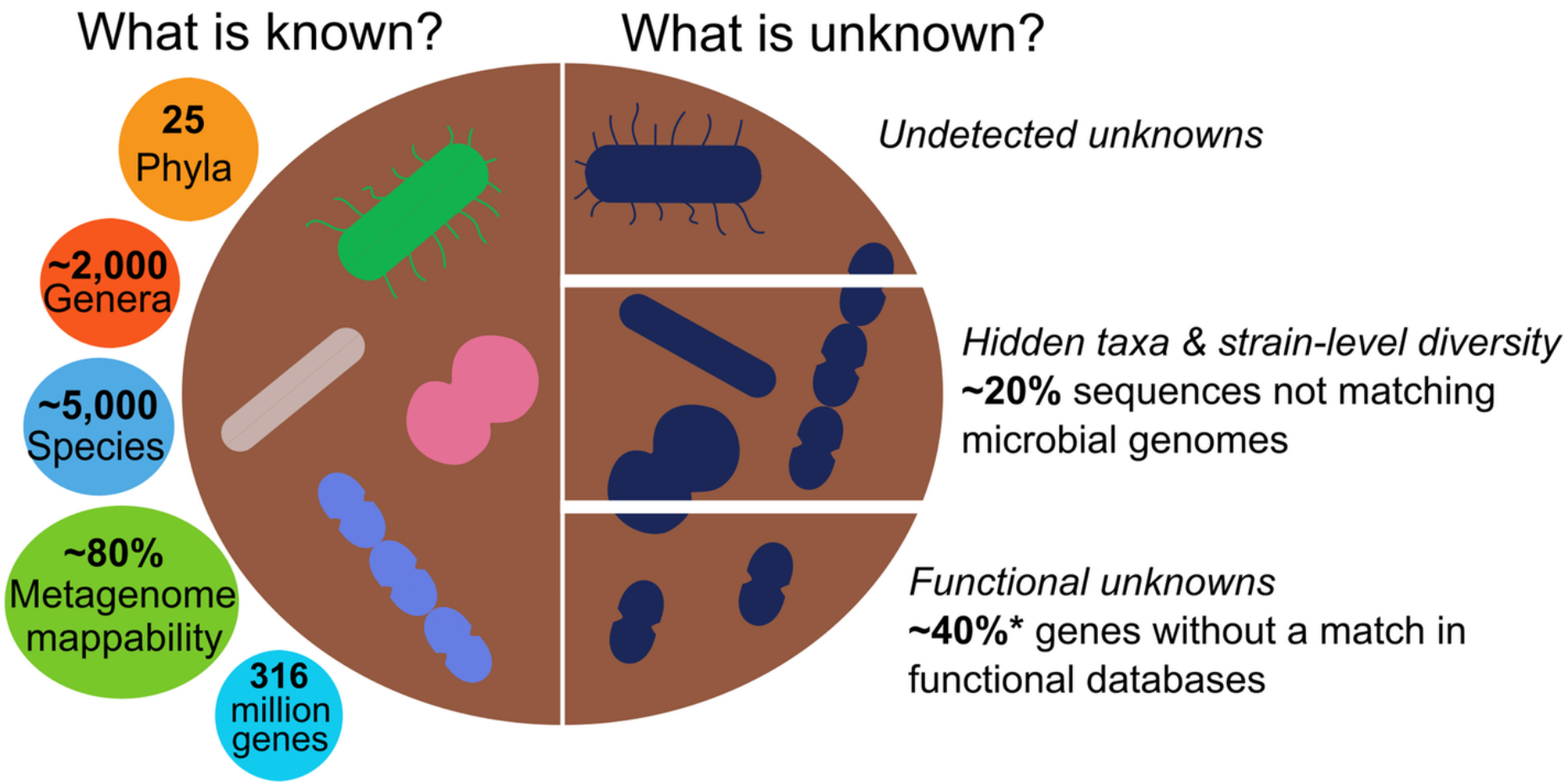
Supplementation with *Akkermansia muciniphila* in overweight and obese human volunteers: a proof-of-concept exploratory study

Clara Depommier[1,9], Amandine Everard[1,9], Céline Druart[1], Hubert Plovier[1], Matthias Van Hul[1], Sara Vieira-Silva[2,3], Gwen Falony[2,3], Jeroen Raes[2,3], Dominique Maiter[4,5], Nathalie M. Delzenne[6], Marie de Barsy[4,5,10], Audrey Loumaye[4,5,10], Michel P. Hermans[4,5,10], Jean-Paul Thissen[4,5,10], Willem M. de Vos[7,8,10] and Patrice D. Cani[1*]



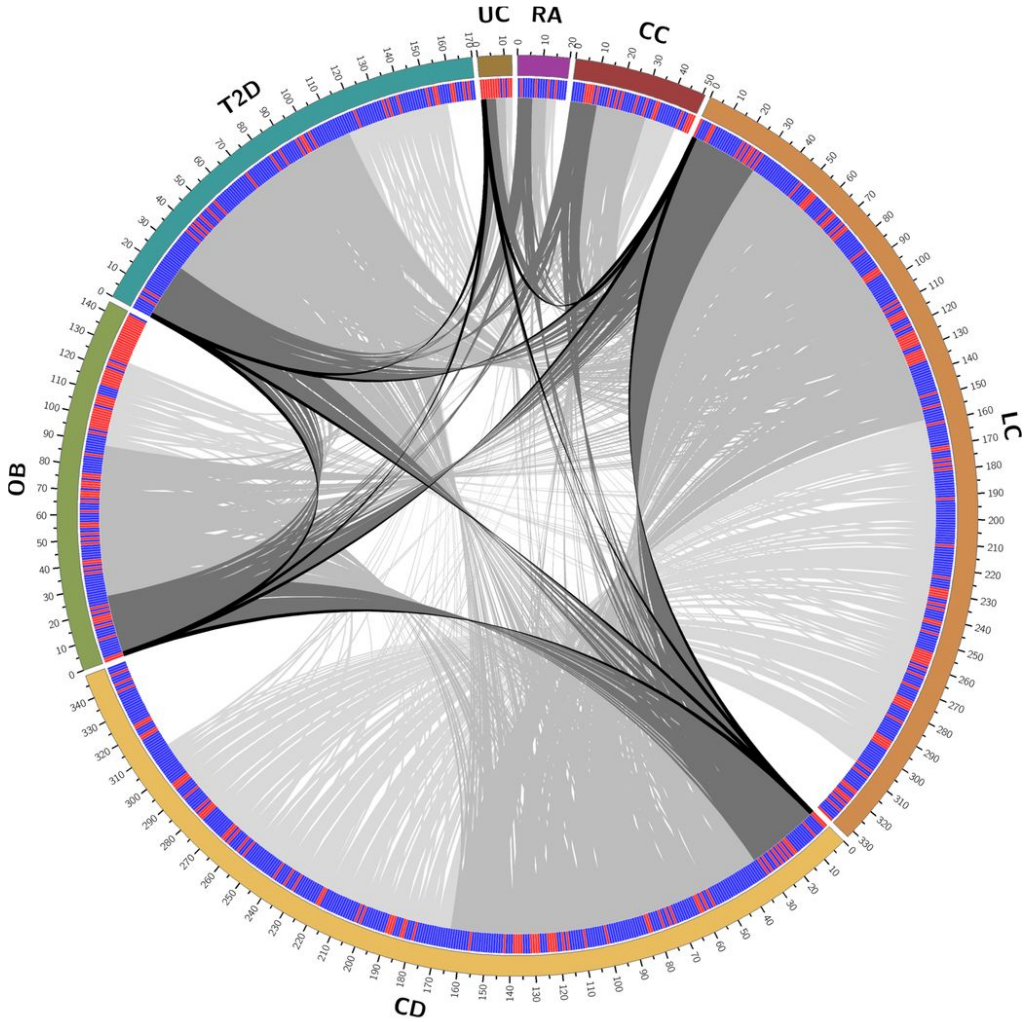
Nature Medicine 2019

The human microbiome



BMC Biol. 2019 Jun 12;17(1):48.

FATTORI COMUNI E DISTINTI DEL MICROBIOMA UMANO IN MALATTIE CRONICHE NON TRASMISSIBILI (NCDs)



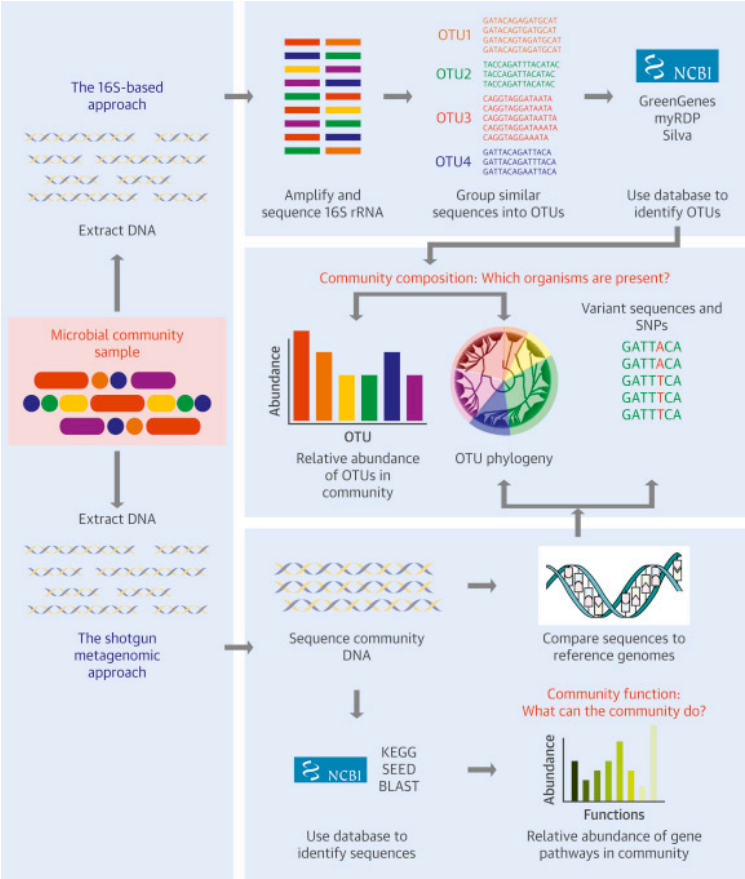
Outer ring colors
- Rheumatoid arthritis (RA)
- Colorectal cancer (CC)
- Liver cirrhosis (LC)
- Crohn's disease (CD)
- Obesity (OB)
- Type II diabetes (T2D)
- Ulcerative colitis (UC)

Inner ring colors
- Increased in cases
- Decreased in cases

Arc colors
- 5 diseases
- 4 diseases
- 3 diseases
- 2 diseases
- 1 disease

Courtney R. Armour et al. mSystems 2019; doi:10.1128/mSystems.00332-18

MICROBIOMA INTESTINALE E MALATTIE



Schroeder and Backhed Nature Medicine 2016

PROCEDURE OPERATIVE STANDARDIZZATE:

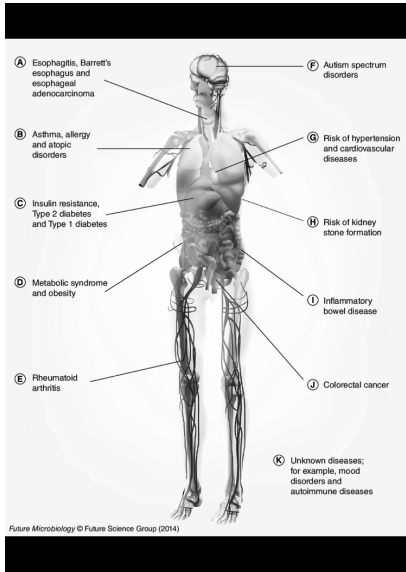
- 16S RNA vs shotgun metagenomics
- Tassonomia vs Genomica Funzionale (basata sull'effetto fisiologico dei prodotti genici)
- Approccio Statistico (FDR, PCA, RF, diversity, etc)

USO APPROPRIATO:

- Specie come obiettivi farmacologici?
- Dati Genomici per diagnosi e personalizzazione delle malattie?

DEFINIZIONE DEI CRITERI DI FISIOLOGIA/NORMALITA'

- Biobanca di soggetti italiani
- Confronto con bio-banche europee
- es. UK BioBank 500.000 soggetti



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