IL MICROBIOTA: INTRODUZIONE

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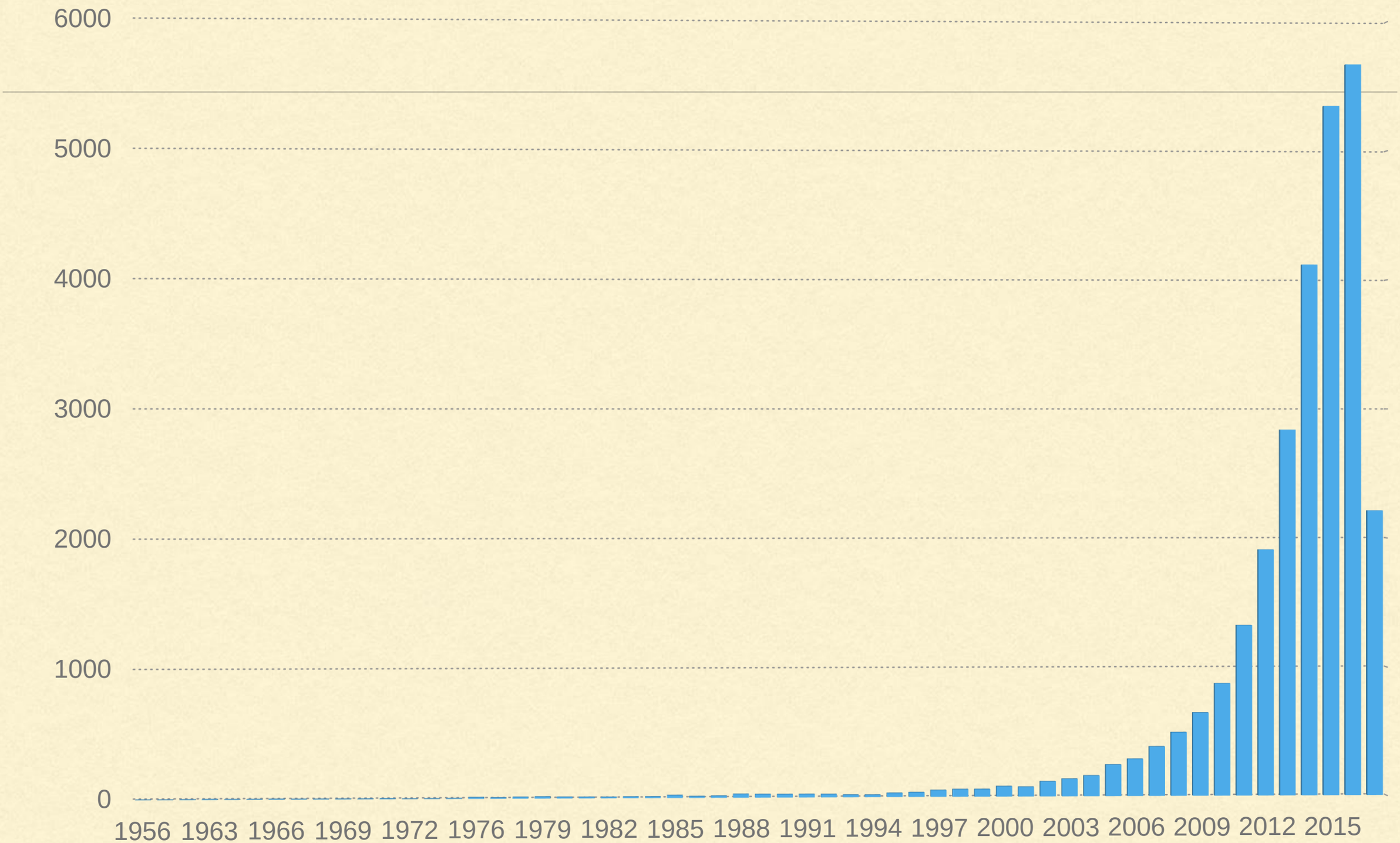
MICROBIOTA & PUB MED



GLOSSARIO

Microbiota: è l'insieme dei microrganismi simbiotici che convivono con l'organismo umano senza danneggiarlo. Flora batterica intestinale o microflora.

Microbioma: è l'insieme del patrimonio genetico e delle interazioni ambientali della totalità dei microrganismi di un definito ambiente

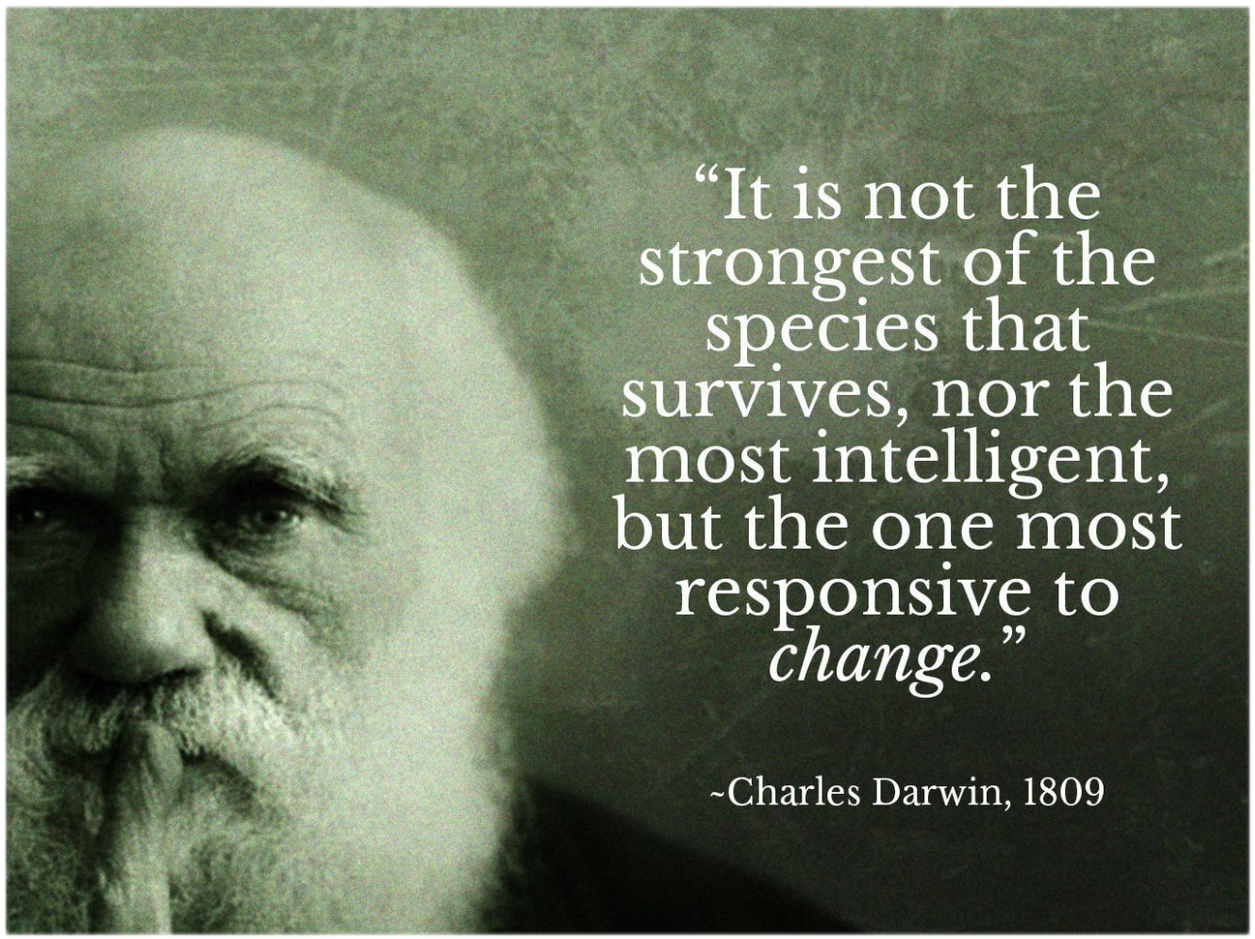
Tassonomia: classificazione dei batteri

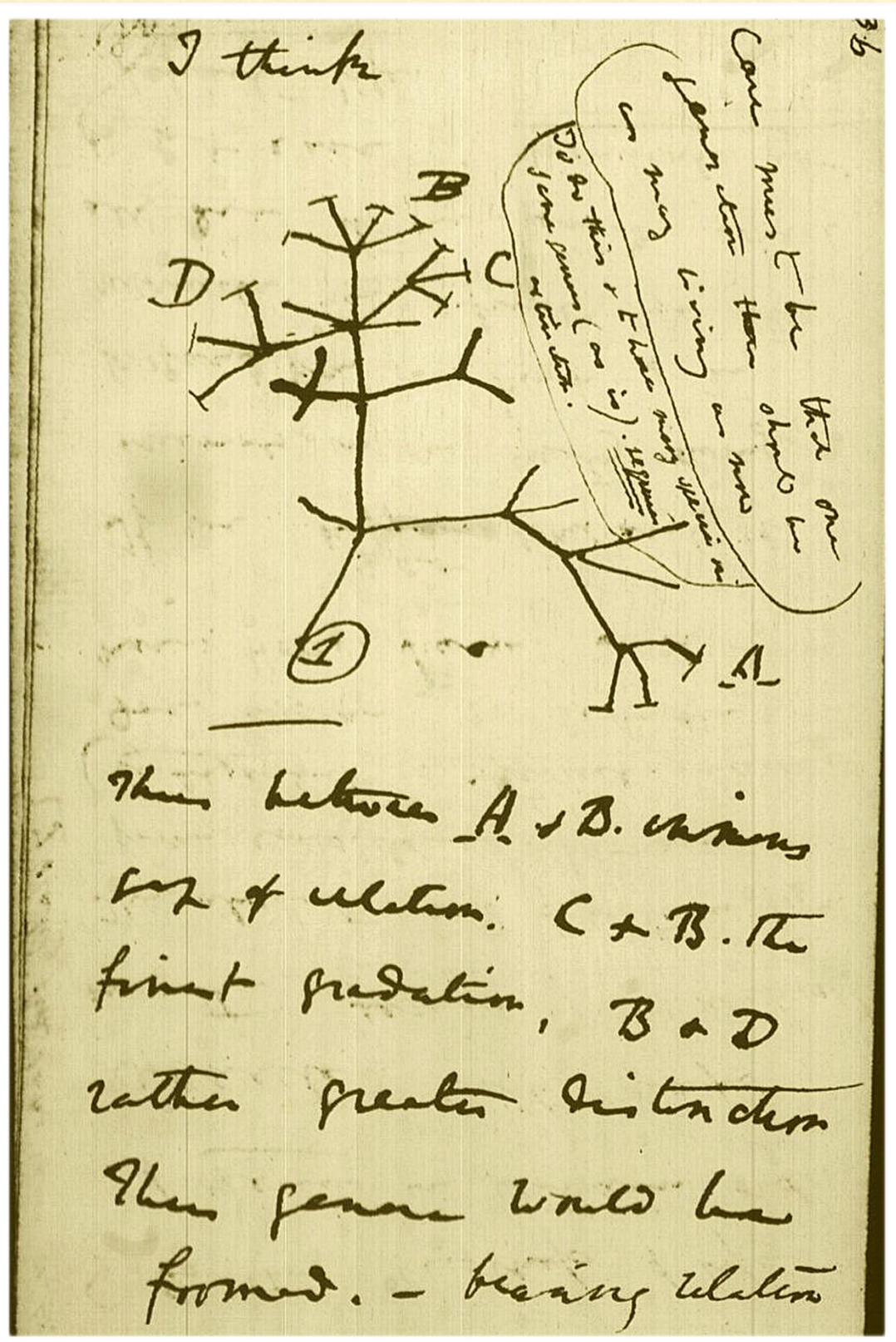
Example of *Akkermansias* taxonomic tree:

Phylum	Class	Order	Family	Genus	Species
Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	*Akkermansia*	*A. muciniphila*

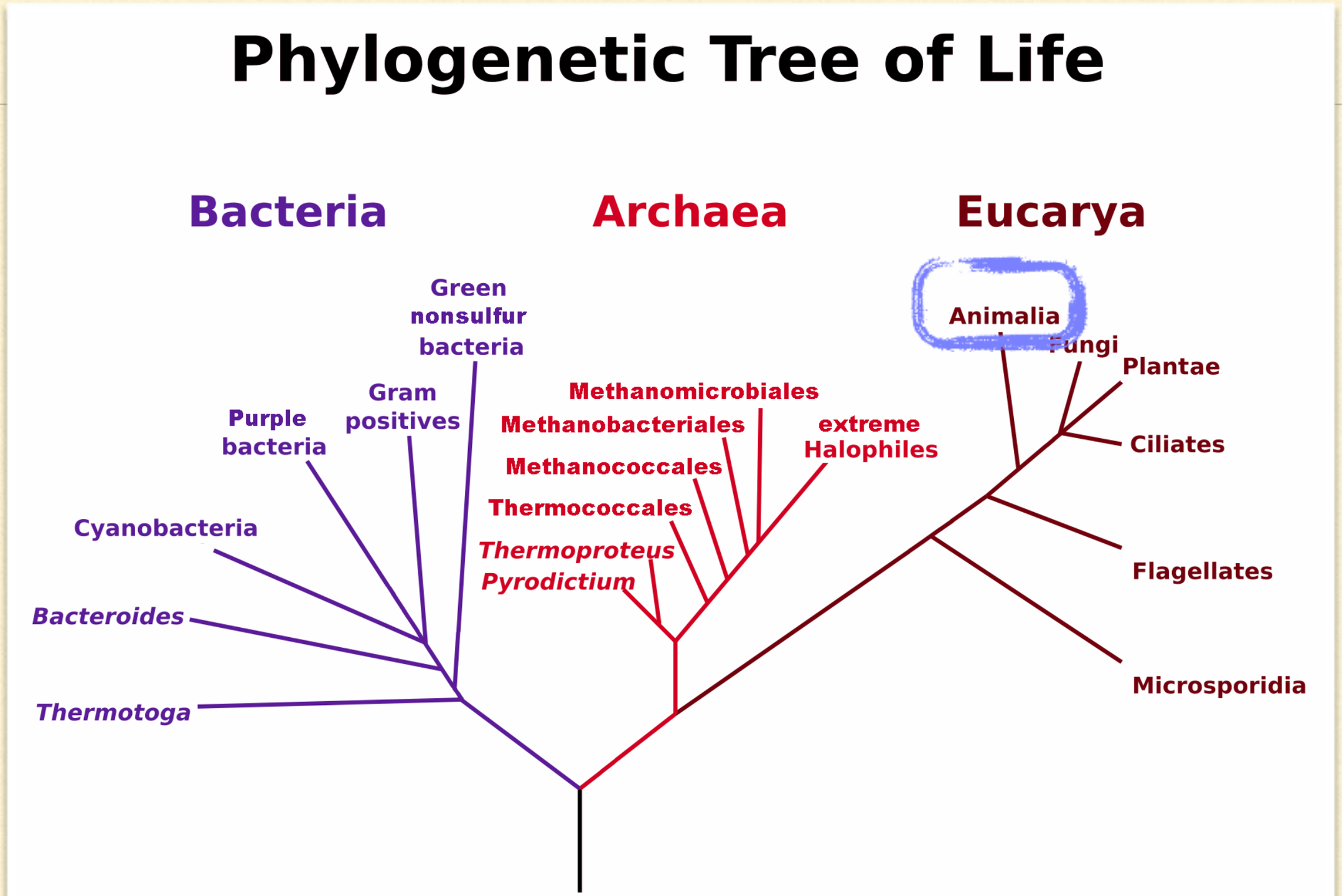
INIZIO

CHARLES DARWIN

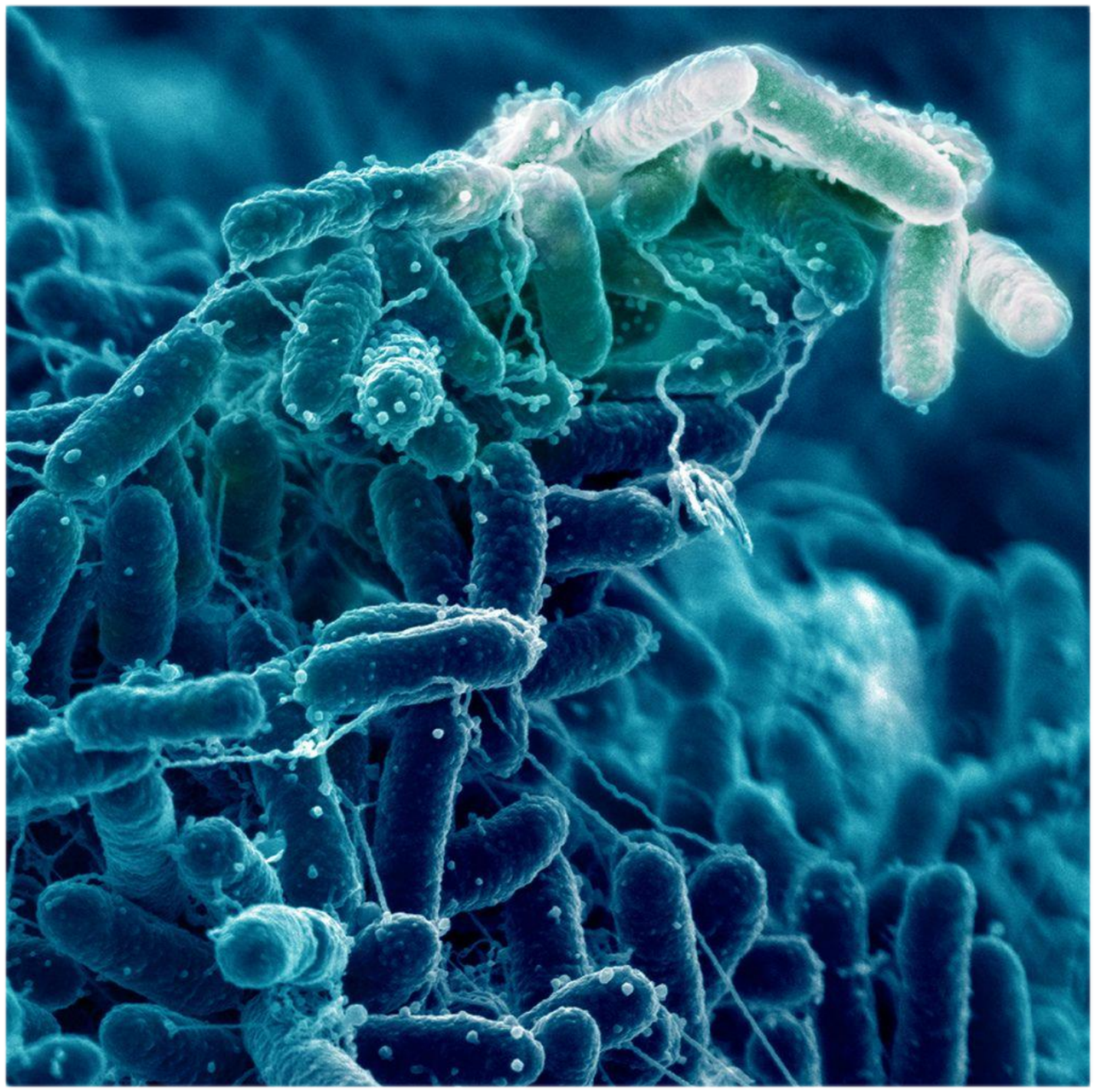




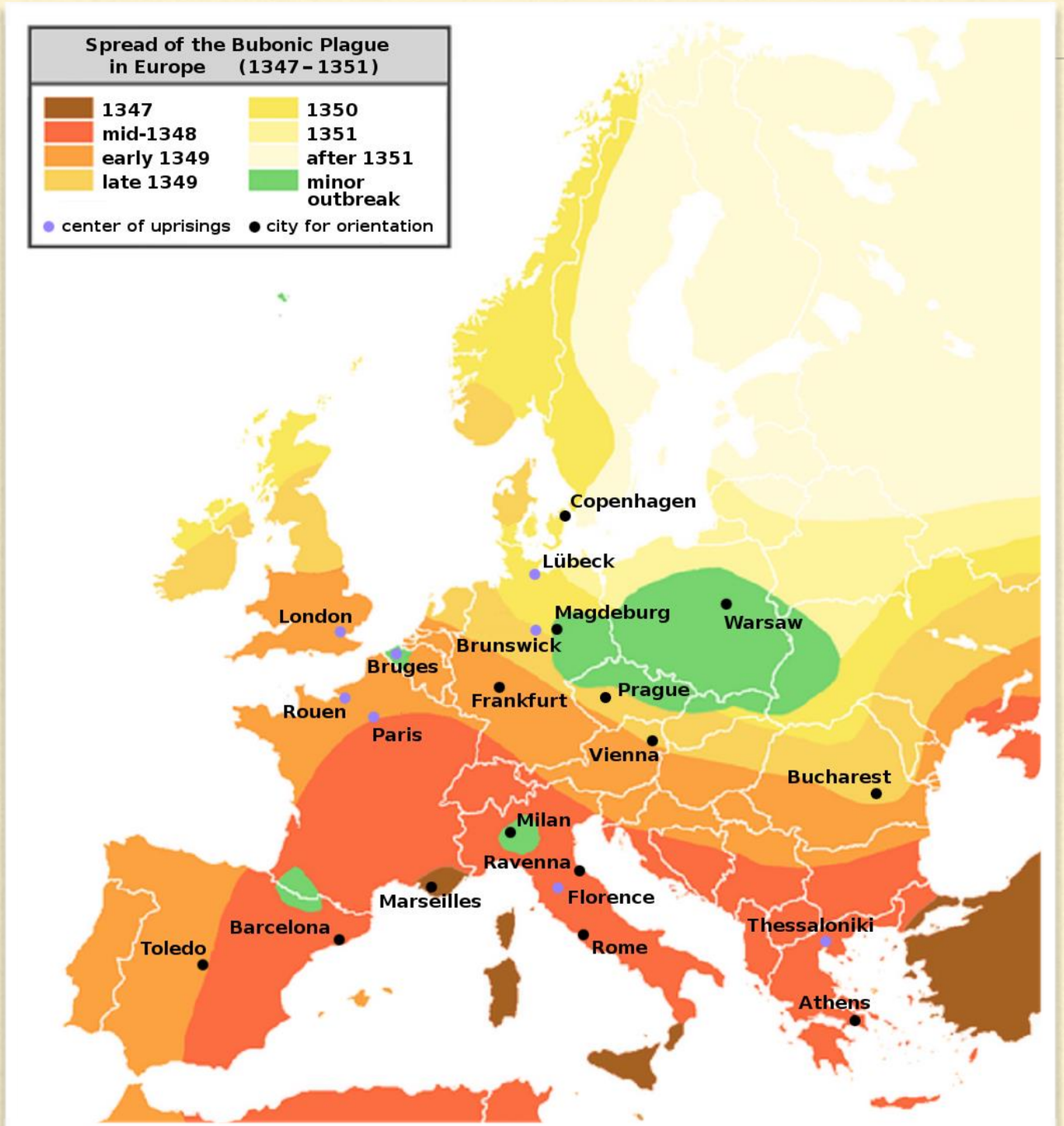
L'ALBERO DELLA VITA



MICROBI, GERMI, BATTERI, VIRUS, PARASSITI



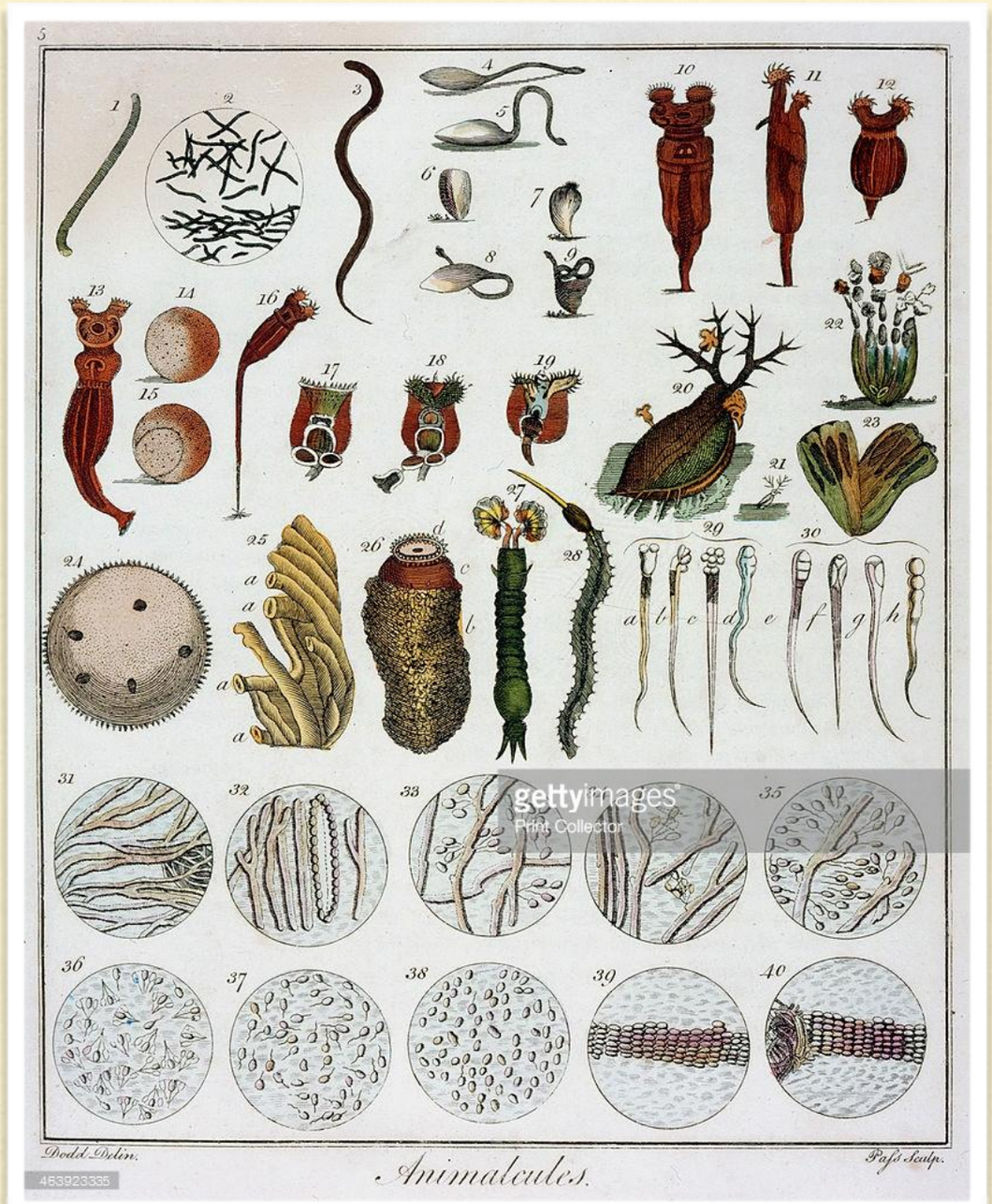
MICROBI E STORIA

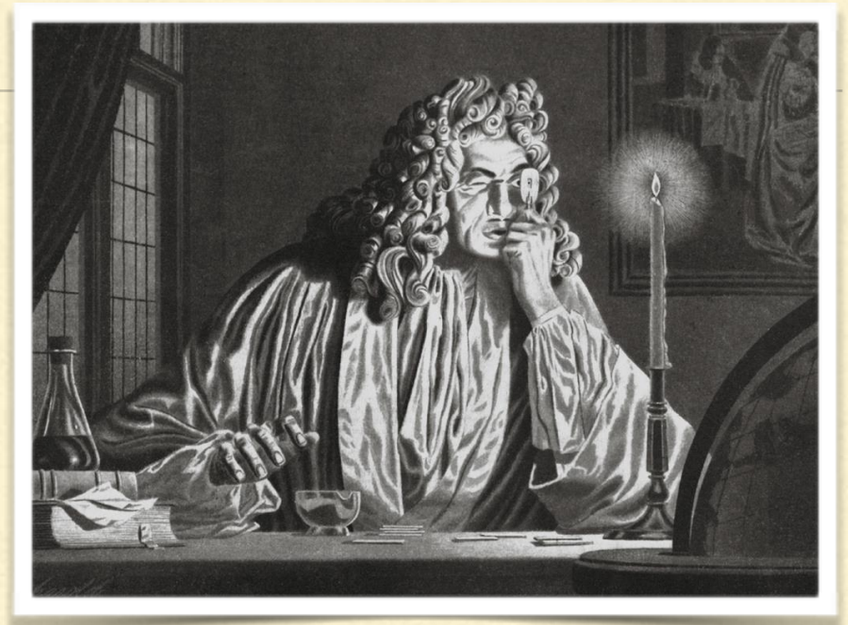


la microbiologia si è sempre interessata ai microrganismi patogeni.

per troppo tempo abbiamo visto i microrganismi solo come fonte di malattie

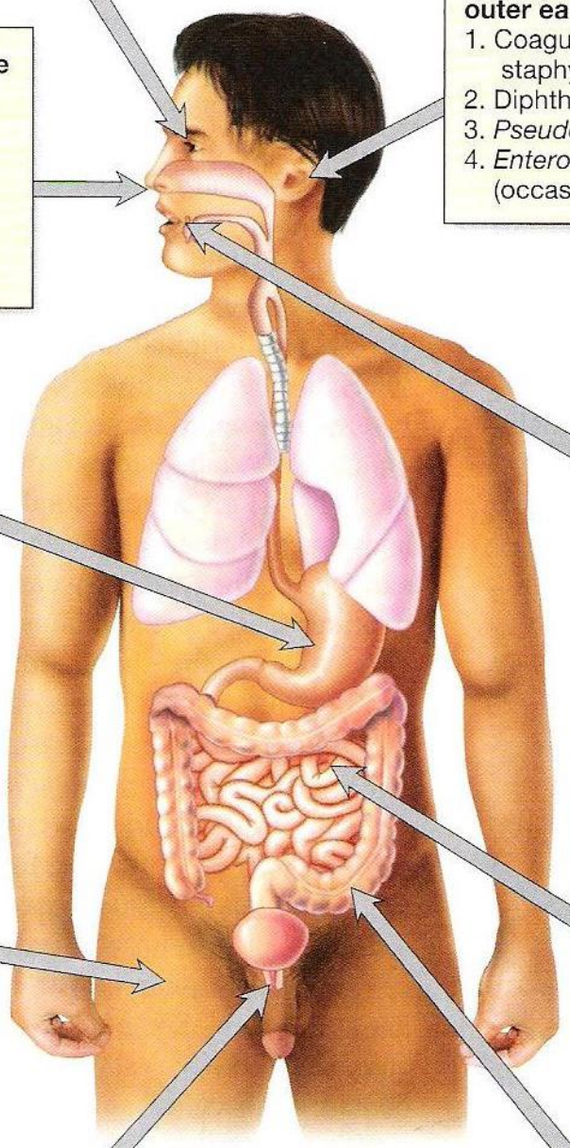
ANTONI VAN LEEUWENHOEK
1676





Animalcules

MICROBIOTA



Normal microbiota of the conjunctiva
1. Coagulase-negative staphylococci
2. *Haemophilus* spp.
3. *Staphylococcus aureus*
4. *Streptococcus* spp.

Normal microbiota of the nose
1. Coagulase-negative staphylococci
2. Viridans streptococci
3. *Staphylococcus aureus*
4. *Neisseria* spp.
5. *Haemophilus* spp.
6. *Streptococcus pneumoniae*

Normal microbiota of the outer ear
1. Coagulase-negative staphylococci
2. Diphtheroids
3. *Pseudomonas*
4. *Enterobacteriaceae* (occasionally)

Normal microbiota of the stomach
1. *Streptococcus*
2. *Staphylococcus*
3. *Lactobacillus*
4. *Peptostreptococcus*

Normal microbiota of the mouth and oropharynx
1. Viridans streptococci
2. Coagulase-negative staphylococci
3. *Veillonella* spp.
4. *Fusobacterium* spp.
5. *Treponema* spp.
6. *Porphyromonas* spp. and *Prevotella* spp.
7. *Neisseria* spp. and *Branhamella catarrhalis*
8. *Streptococcus pneumoniae*
9. Beta-hemolytic streptococci (not group A)
10. *Candida* spp.
11. *Haemophilus* spp.
12. Diphtheroids
13. *Actinomyces* spp.
14. *Eikenella corrodens*
15. *Staphylococcus aureus*

Normal microbiota of the skin
1. Coagulase-negative staphylococci
2. Diphtheroids (including *Propionibacterium acnes)*
3. *Staphylococcus aureus*
4. *Streptococcus* spp.
5. *Bacillus* spp.
6. *Malassezia furfur*
7. *Candida* spp.
8. *Mycobacterium* spp. (occasionally)

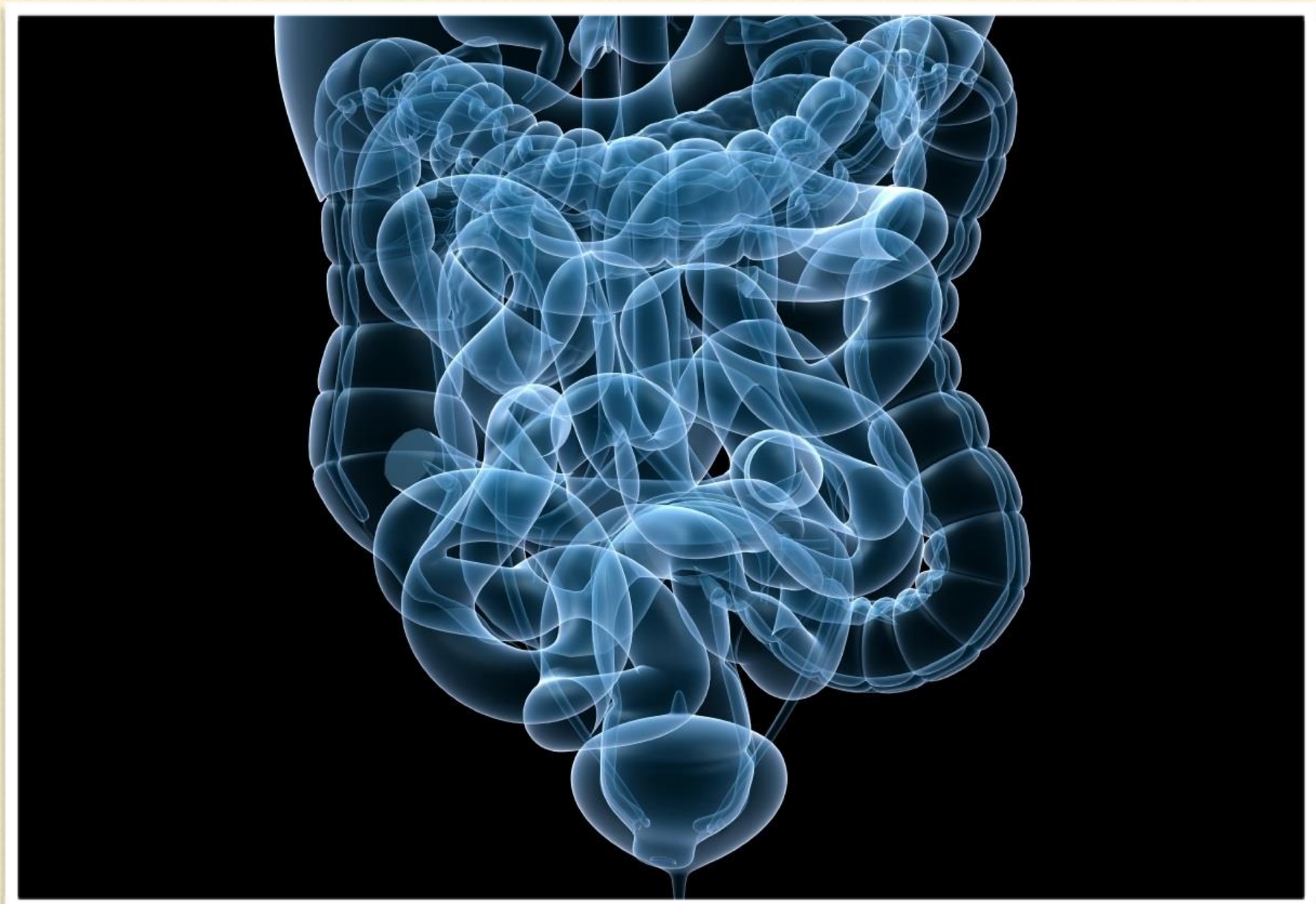
Normal microbiota of the small intestine
1. *Lactobacillus* spp.
2. *Bacteroides* spp.
3. *Clostridium* spp.
4. *Mycobacterium* spp.
5. *Enterococci*
6. *Enterobacteriaceae*

Normal microbiota of the urethra
1. Coagulase-negative staphylococci
2. Diphtheroids
3. *Streptococcus* spp.
4. *Mycobacterium* spp.
5. *Bacteroides* spp. and *Fusobacterium* spp.
6. *Peptostreptococcus* spp.

Normal microbiota of the vagina
1. *Lactobacillus* spp.
2. *Peptostreptococcus* spp.
3. Diphtheroids
4. *Streptococcus* spp.
5. *Clostridium* spp.
6. *Bacteroides* spp.
7. *Candida* spp.
8. *Gardnerella vaginalis*

Normal microbiota of the large intestine
1. *Bacteroides* spp.
2. *Fusobacterium* spp.
3. *Clostridium* spp.
4. *Peptostreptococcus* spp.
5. *Escherichia coli*
6. *Klebsiella* spp.
7. *Proteus* spp.
8. *Lactobacillus* spp.
9. Enterococci
10. *Streptococcus* spp.
11. *Pseudomonas* spp.
12. *Acinetobacter* spp.
13. Coagulase-negative staphylococci
14. *Staphylococcus aureus*
15. *Mycobacterium* spp.
16. *Actinomyces* spp.

DENTRO DI NOI...



NON DOBBIAMO ESSERE RAZZISTI

The human gut microbiota: stability and diversity

Medicine

There are more than **3 MILLION MICROBIAL GENES** in our gut microbiota

150 TIMES more genes than in the **HUMAN GENOME**[1]

APPROXIMATE **WEIGHT OF THE TOTAL GUT MICROBIOTA**[1]

OUR GUT MICROBIOTA EVOLVES THROUGHOUT OUR ENTIRE LIFE and is the result of a variety of influences:[1-2]

GENETICS · STRESS · HYGEINE PRACTICES · MODE OF DELIVERY · DRUGS/ ANTIBIOTICS · DIET · INFECTIONS · SURGERY · ENVIRONMENT

The composition of **GUT MICROBIOTA IS UNIQUE** to each individual, **just like our FINGERPRINTS**[1]

EFFECT OF ANTIBIOTICS ON GUT MICROBIOTA[1-12]

The **GUT MICROBIOTA** is the name for the microbe population living in the intestine. It is estimated to contain at least 1800 genera and 15,000-36,000 species, most of which have never been successfully cultured.

The gut microbiota has co-evolved with its host over millenia and provides benefits to its host including digestion, nutrient production, detoxification and immunity.

One of the ways pathogens and commensals interact with their host is via the expression of microbe-associated molecular patterns (MAMPs) which diffuse through the mucus layer and stimulate pattern-recognition receptors (PRRs) of dendritic cells, M cells and intestinal epithelial cells (IECs). In normal healthy individuals the gut microbiome is diverse and with an abundance of beneficial bacteria which promotes protective intestinal immune responses.

INTESTINAL EPITHELIAL CELLS (IECs) act as a physical barrier that prevents commensals from entering the lamina propria and integration of microbial signals. Tight junctions form a continuous intercellular barrier between IECs and regulate selective movement of solutes across the epithelium.

GOBLET CELLS secrete mucin (Muc2). They respond to the gut microbiome by increasing mucin production, increasing Muc2 sulfate incorporation (increase resistance to enzymatic degradation of mucus) and inhibit pathogen adherence.

MUCUS LAYER is a major mediator of IEC–commensal interactions. It consists of two layers of secreted mucin. The inner layer is sense and devoid of commensal bacteria. The outer layer is more loose and houses commensal bacteria and antimicrobial proteins. The mucus layer prevents IECs from direct contact with commensal bacteria and their molecular components.

Commensals promote strengthening of the mucus barrier.

GUT MACROPHAGES develop a non-inflammatory profile and do not produce pro-inflammatory cytokines in response to MAMPs.

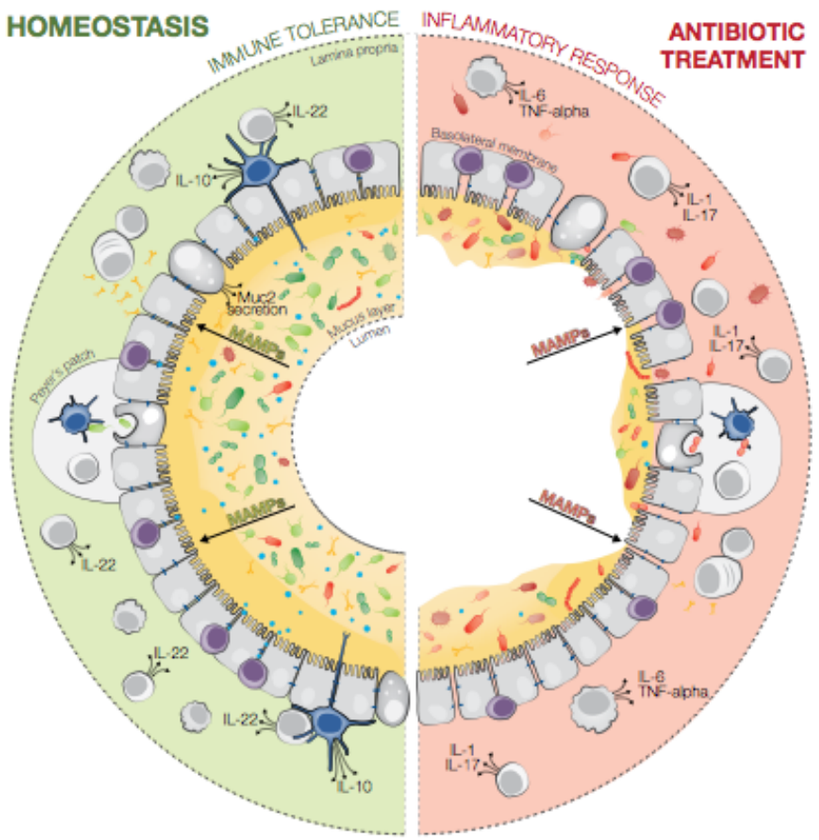
DENDRITIC CELLS protect against infection while maintaining immune tolerance by producing high levels of anti-inflammatory cytokines, e.g. IL-10.

MICROFOLD CELLS (M cells) transport bacteria and bacterial antigens to immune cells.

INTRAEPITHELIAL LYMPHOCYTES are influenced by the gut microbiota via MAMPs and secrete antimicrobial proteins, e.g. defensins, cathelicidins, C-type lectins.

T CELLS produce protective cytokines, e.g. IL-22.

PLASMA CELLS produce large amounts of secretory IgA, which impairs pathogenic bacterial attachment to mucosal epithelium, therefore interfering with pathogenicity.



Antibiotic administration results in significant reduction in **GUT MICROBIOTA** size and diversity. This is seen as increased colonisation by antibiotic-resistant bacterial species, e.g. *Clostridium difficile*, *Candida albicans*, salmonella, *C. perfringens* type A, *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, and reduction in butyrate-producing species, e.g. *Faecalibacterium*, *Subdoligranulum*, and uncultered *Ruminococcaceae*, *Roseburia*, *Coprococcus* and *Lachnospiraceae*.

Studies have shown that while much of the diversity eventually recovered, there were still several species that failed to recover after four years, suggesting that even a short course of antibiotics may cause permanent changes to gut microbiome.

Health implications for low-diversity gut microbiota include inflammatory bowel disease, autoimmune disease, allergies, obesity, cancer, mental illness and autism.

INTESTINAL EPITHELIAL CELL (IEC) barrier function is altered due to changes in MAMP concentrations.

Reduced expression of tight junction proteins leads to increased intestinal permeability and enhanced bacterial penetration into the lamina propria. This can set off a vicious cycle of inflammation and pro-inflammatory immune responses leading to destruction of tight gap junctions and IEC apoptosis, increased permeability and more inflammation.

Shifts in the the intestinal microbiota induce defects in mucin production and alterations in MAMP concentrations.

A defective **MUCUS LAYER** can lead to increased MAMP diffusion, commensal contact with IECs and commensal translocation to underlying lamina propria.

Hyper-stimulation of IECs and commensal translocation lead to further disruption of intestinal homeostasis and further host pathology and inflammation.

GUT MACROPHAGES adopt an inflammatory phenotype and produce IL-6 and TNF-alpha which drives inflammation and cell damage.

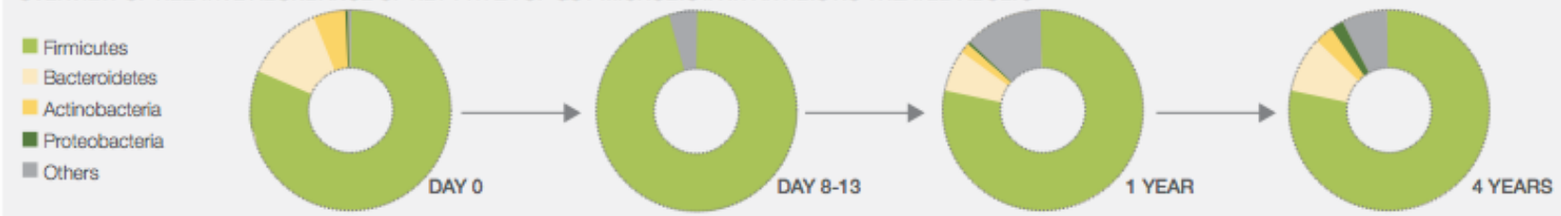
INTRAEPITHELIAL LYMPHOCYTES respond to changes in MAMP concentrations through decreased secretion of antimicrobial proteins. This may promote inflammation and increased susceptibility to intestinal diseases.

T CELLS decrease secretion of protective cytokines and increase secretion of pro-inflammatory cytokines

DENDRITIC CELLS protect against infection while maintaining immune tolerance by producing high levels of anti-inflammatory cytokines, e.g. IL-10.

MICROFOLD CELLS (M cells) transport pathogenic bacteria and bacterial antigens to immune cells which promotes an inflammatory immune response.

OVERVIEW OF RELATIVE ABUNDANCE OF KEY PHYLA OF GUT MICROBIOTA IN ANTIBIOTIC TREATED ADULTS[11-13]



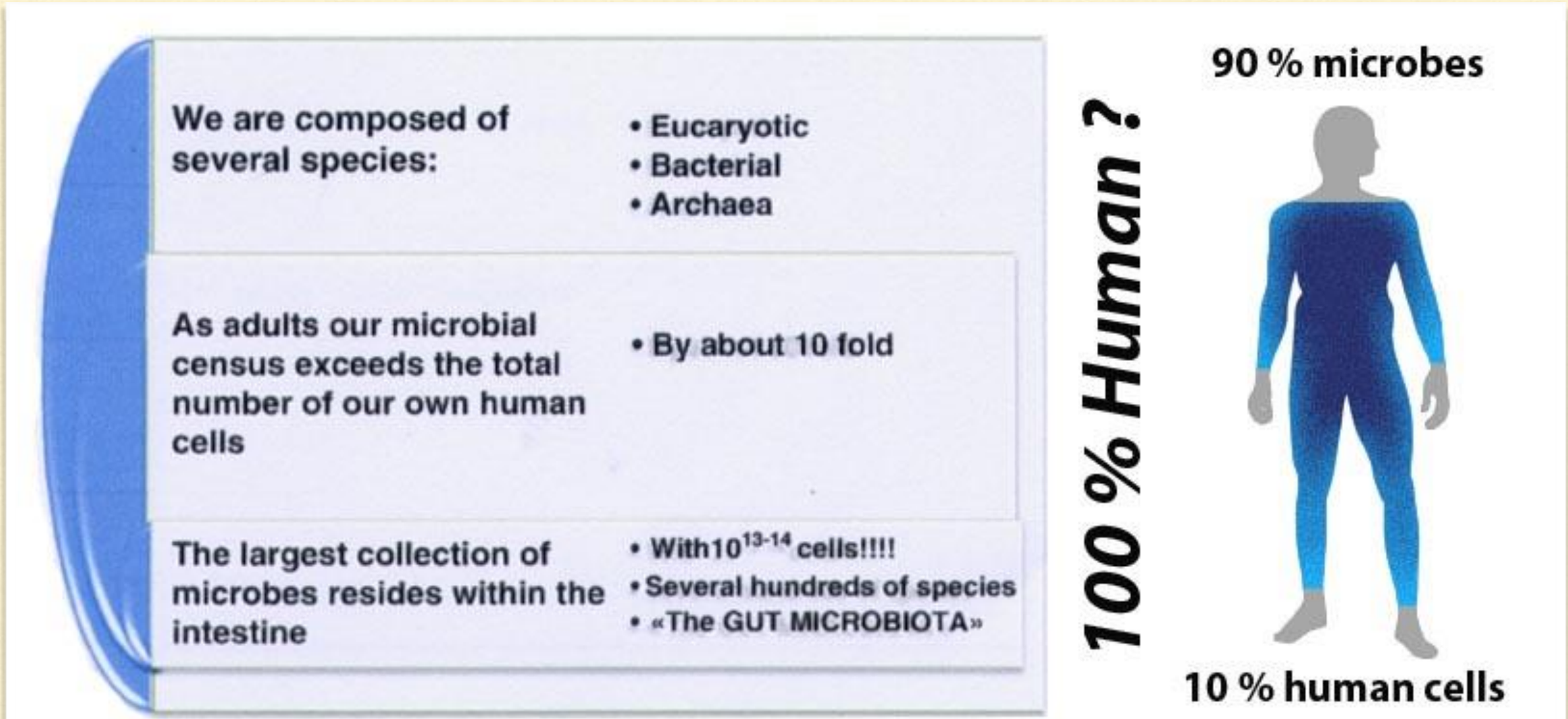
The gut microbiota of individuals who have been treated with antibiotics experiences massive shifts in diversity, which may cause permanent changes to phyla distribution.

Dramatic decline in bacteroidetes and actinobacteria can be observed immediately after antibiotic treatment.

Even after four years, the microbiota is yet to recover its former diversity and distribution.

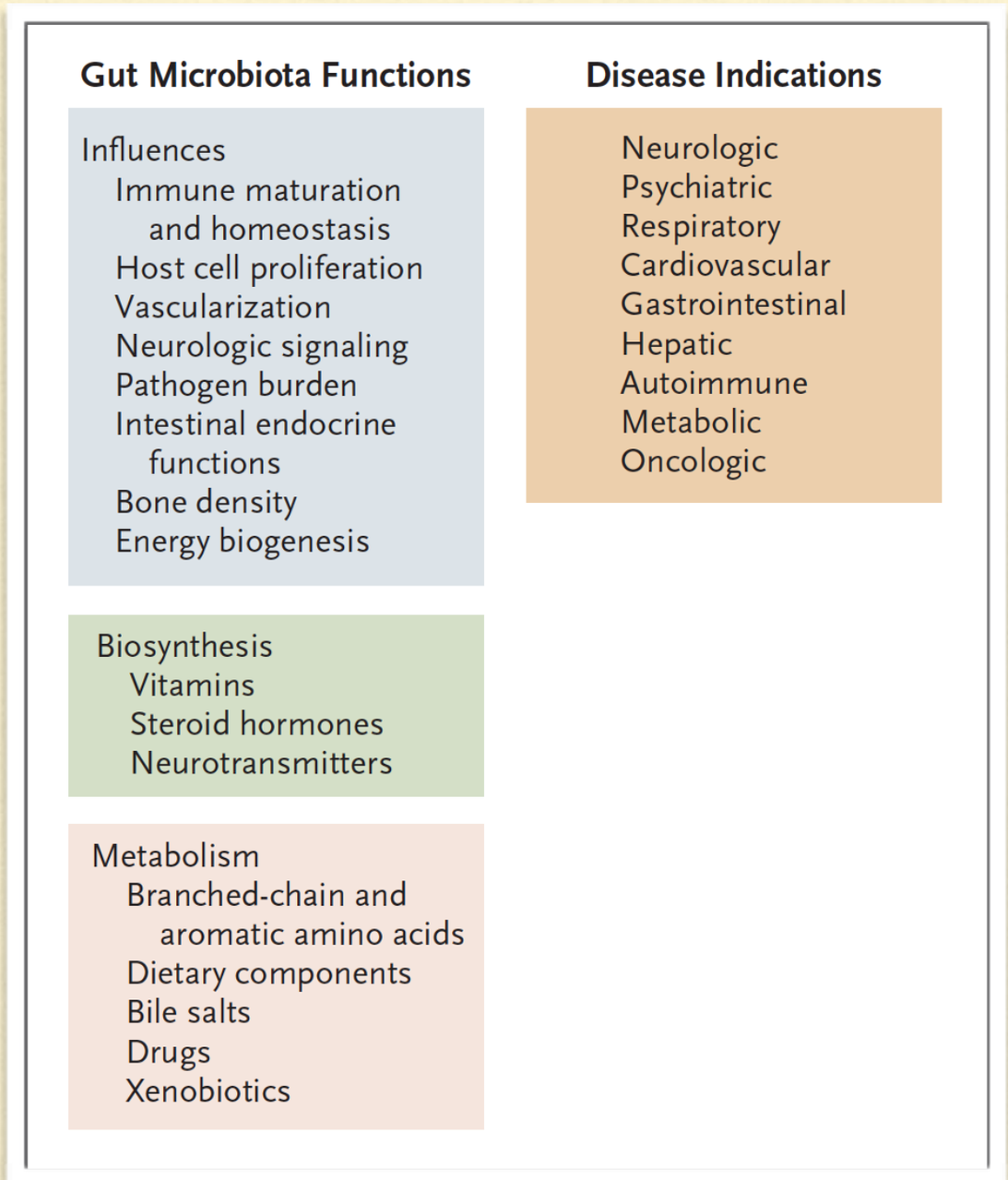
Interestingly, there is a significant increase in proteobacteria. All proteobacteria are gram-negative, with an outer layer of lipopolysaccharides which is strongly associated with inflammation. Members of the Proteobacteria phylum include escherichia, salmonella, vibrio, helicobacter, and yersinia.

COSA SIAMO? UMANI?



MICROBIOTA

essenziale per la biosintesi degli aminoacidi, vitamine, neurotrasmettitori, ormoni, per la digestione delle fibre alimentari in acidi grassi a catena corta



The Human Intestinal Microbiome in Health and Disease

Susan V. Lynch, Ph.D., and Oluf Pedersen, M.D., D.M.Sc.

N ENGL J MED 375;24 NEJM.ORG DECEMBER 15, 2016

MASSIMA VALORIZZAZIONE

Merda d'Artista, 275mila euro all'asta

Sull'etichetta la scritta 'Prodotta e inscatolata nel 1961'

Redazione ANSA

MILANO

07 dicembre 2016
12:28

(ANSA) - MILANO, 7 DIC - Una delle famose scatolette di 'Merda d'artista' di Piero Manzoni è stata venduta al prezzo di 275 mila euro, compresi i diritti d'asta, presso la casa milanese "Il Ponte', dove si è tenuta una vendita di Arte Moderna e Contemporanea. Si tratta del record mondiale d'asta per una di queste scatolette di latta, del diametro di 6,5 centimetri e 4,5 d'altezza, sulle quali compare l'etichetta: 'Merda d'Artista. Contenuto netto gr.30. Conservata al naturale.

Prodotta e inscatolata nel maggio 1961'. Piero Manzoni (Soncino, 1933 - Milano 1963) ne produsse 100, firmate e numerate (quella venduta ieri è la n. 69).

In realtà non si sa se l'etichetta dica il vero circa il contenuto, in quanto nessuna scatoletta è mai stata aperta, semplicemente perché un gesto simile le avrebbe fatto perdere il suo valore, che negli anni è andato sempre più crescendo, essendo ritenuto uno dei maggiori esempi di "provocazione artistica" della storia.

ADESSO

IL FUTURO