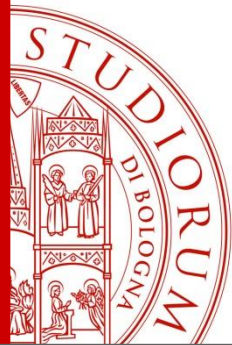


PERSONALIZED INTERVENTION STRATEGIES TO KEEP A HEALTH PROMOTING GUT MICROBIOTA CONFIGURATION IN THE ELDERLY

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Brussels, 30-31 May 2016



DEMOGRAPHIC AGEING IS A EU KEY SOCIETAL CHALLENGE

- EU population aged 65y is projected to increase from 17.4% to nearly 30% by 2060 while population aged over 80y and is predicted to triple during this period.
- Life expectancy continues to rise but healthy life years do not increase at the same rate, and the time spent in ill health will be even longer in future

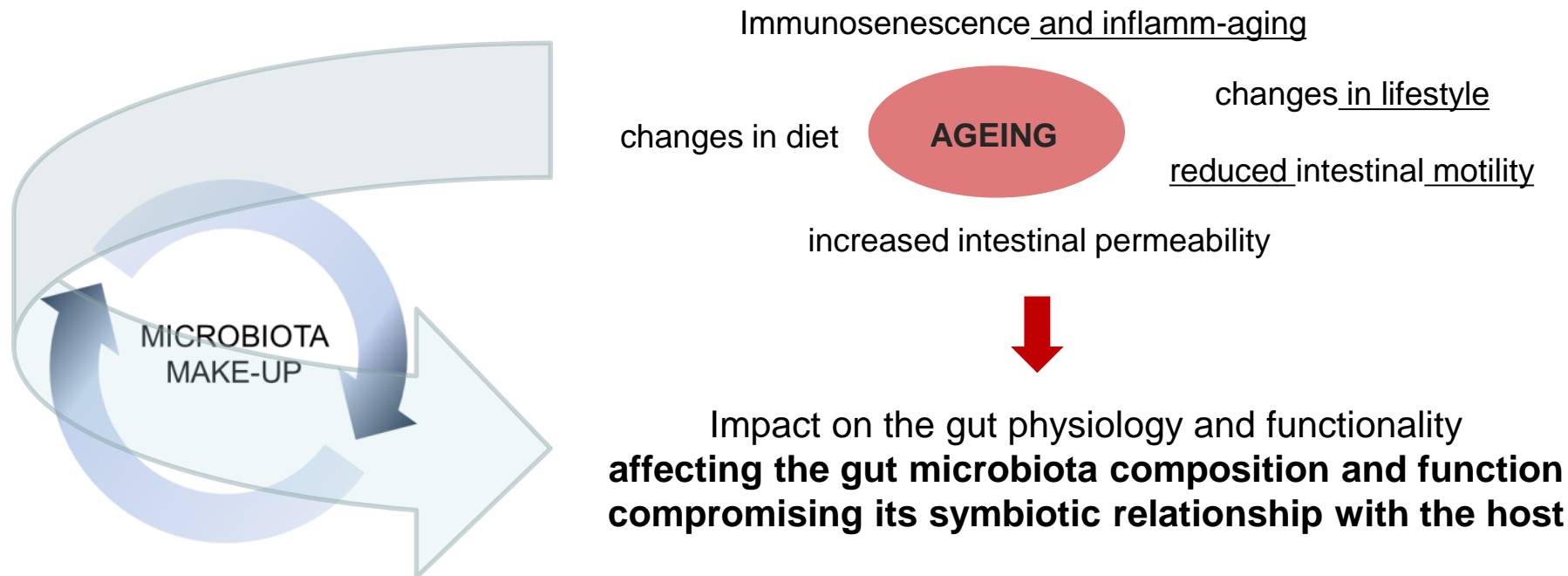
Gap between life expectancy and healthy life years

- High pressure on public health and care services

Crucial to identify appropriate strategies to help population age healthy

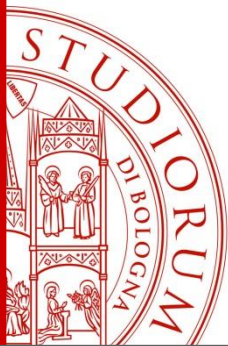


PATHOPHYSIOLOGY OF AGEING

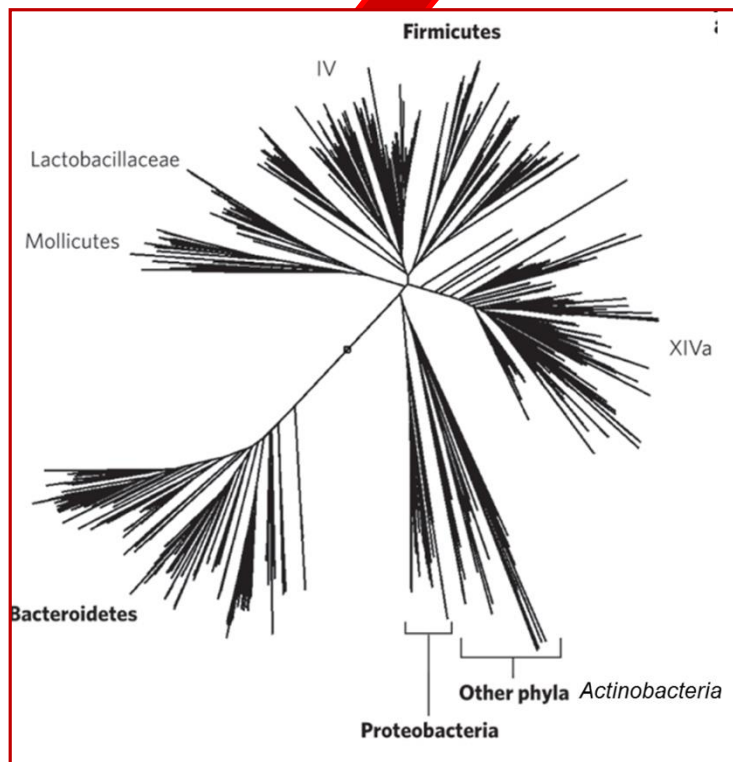


AGED-TYPE MICROBIOTA

PRO-INFLAMMATORY CONSORTIUM THAT PROMOTES THE PROCESS OF
“INFLAMM-AGING” BY ESTABLISHING A SELF-SUSTAINED
INFLAMMATORY LOOP DETRIMENTAL FOR HOST LONGEVITY



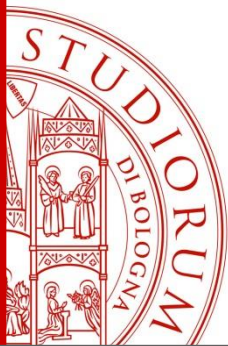
PHYLOGENETIC DIVERSITY



> 1000 species

10 (out of 100) bacterial phyla

- Firmicutes, Bacteroidetes : 90%
- Actinobacteria, Proteobacteria, Fusobacteria and Verrucomicrobia : 10%



FUNCTIONAL DIVERSITY

MICROBIOME

(collective genome of the
microbiota)



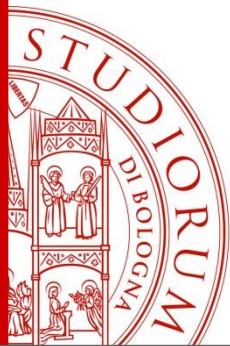
10^6 GENES

58% KNOWN

- carbohydrate metabolism (CAZymes)
- energy metabolism
- amino acid metabolism
- biosynthesis of secondary metabolites
- metabolism of cofactors and vitamins

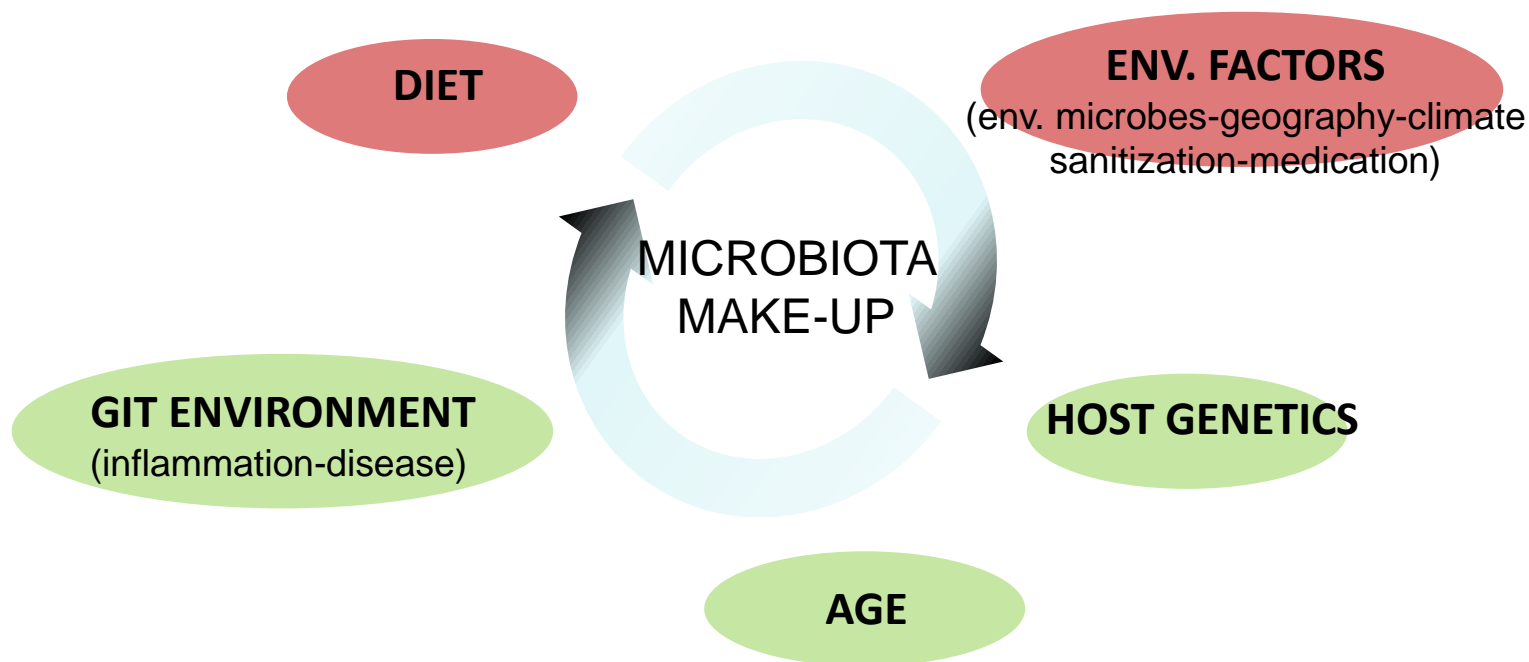
42% UNKNOWN

Schloissing et al, Nature 2013

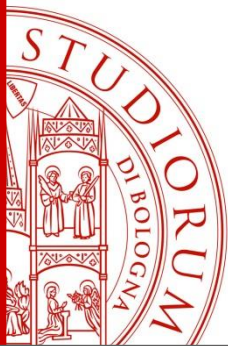


MICROBIOTA PLASTICITY

THE INDIVIDUAL MICROBIOTA COMPOSITION CONTINUOUSLY CHANGES IN RESPONSE TO **EXTRINSIC** AND **INTRINSIC** VARIABLES

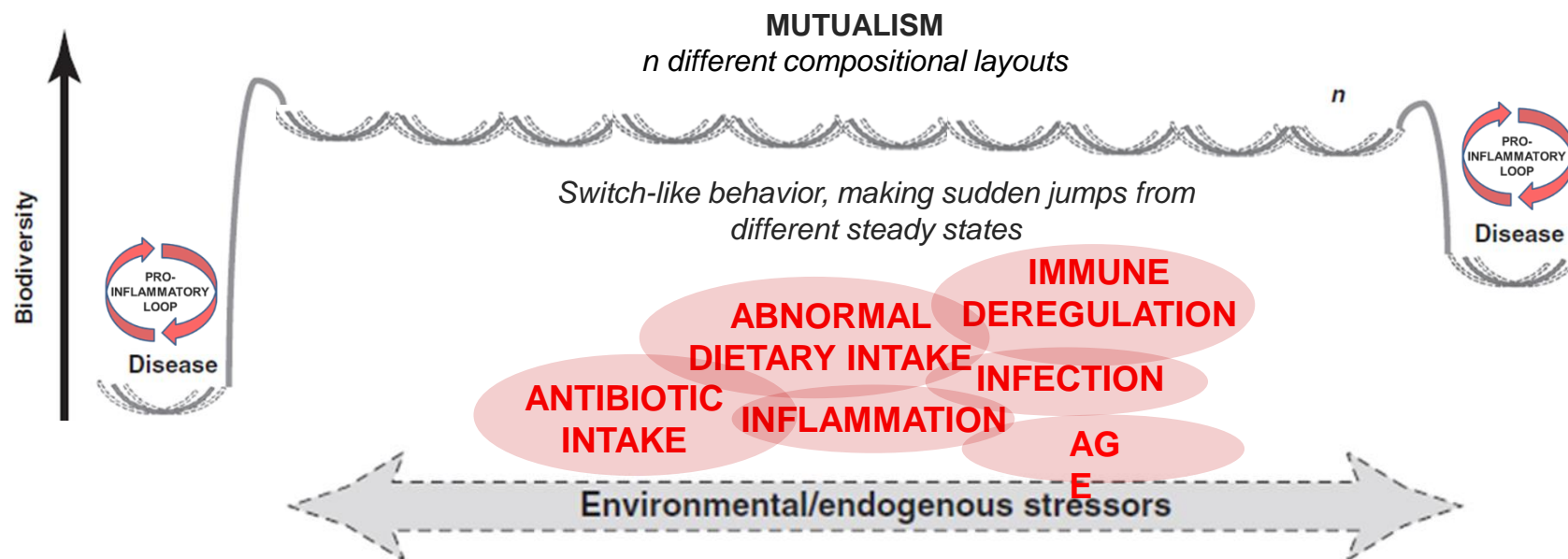


IN A MUTUALISTIC CONTEXT, THE PLASTICITY OF THE HUMAN MICROBIOTA GUARANTEES A RAPID ADAPTATION OF THE SUPER-ORGANISM IN RESPONSE TO DIET CHANGES, AGE, ETC
there is a strong selection towards a readily changeable individual microbiome profile



MUTUALISM BREAKDOWN

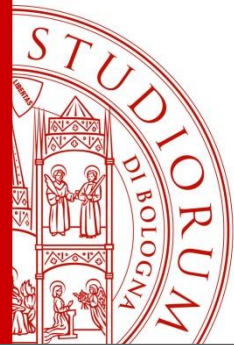
the GM is a multistable system with a variable fraction at 40% of the total community



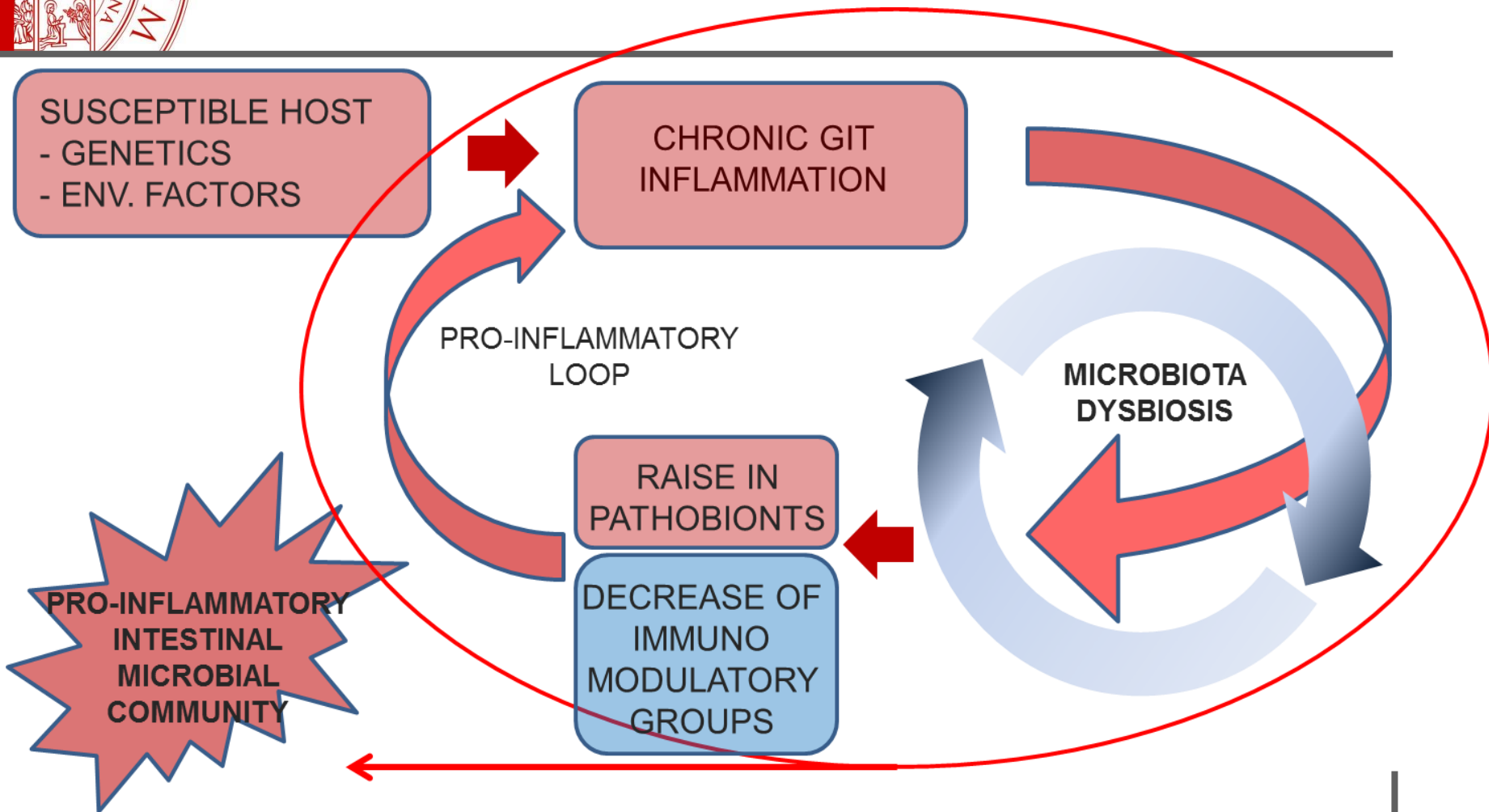
RUPTURE OF THE GM-HOST MUTUALISTIC AGREEMENT AND
COMPROMISED HOST ENERGY BALANCE AND IMMUNE
HOMEOSTASIS

Faith et al, Science 2013

Candela et al, Trends Microbiol. 2012



GM AND INFLAMMATION



THE GM DESCRIBES AN ADAPTIVE TRAJECTORY ALONG HUMAN AGING



GUT MICROBIOTA CHANGES ITS PHYLOGENETIC AND FUNCTIONAL PROFILE FROM INFANCY TO ELDERLY PROVIDING THE HOST WITH **ECOLOGICAL SERVICES CALIBRATED FOR EACH STAGE OF LIFE**

Candela et al., Critical Rev Microbiol, 2013

ELDERLY-TYPE MICROBIOTA

What happens to the human GM with ageing?

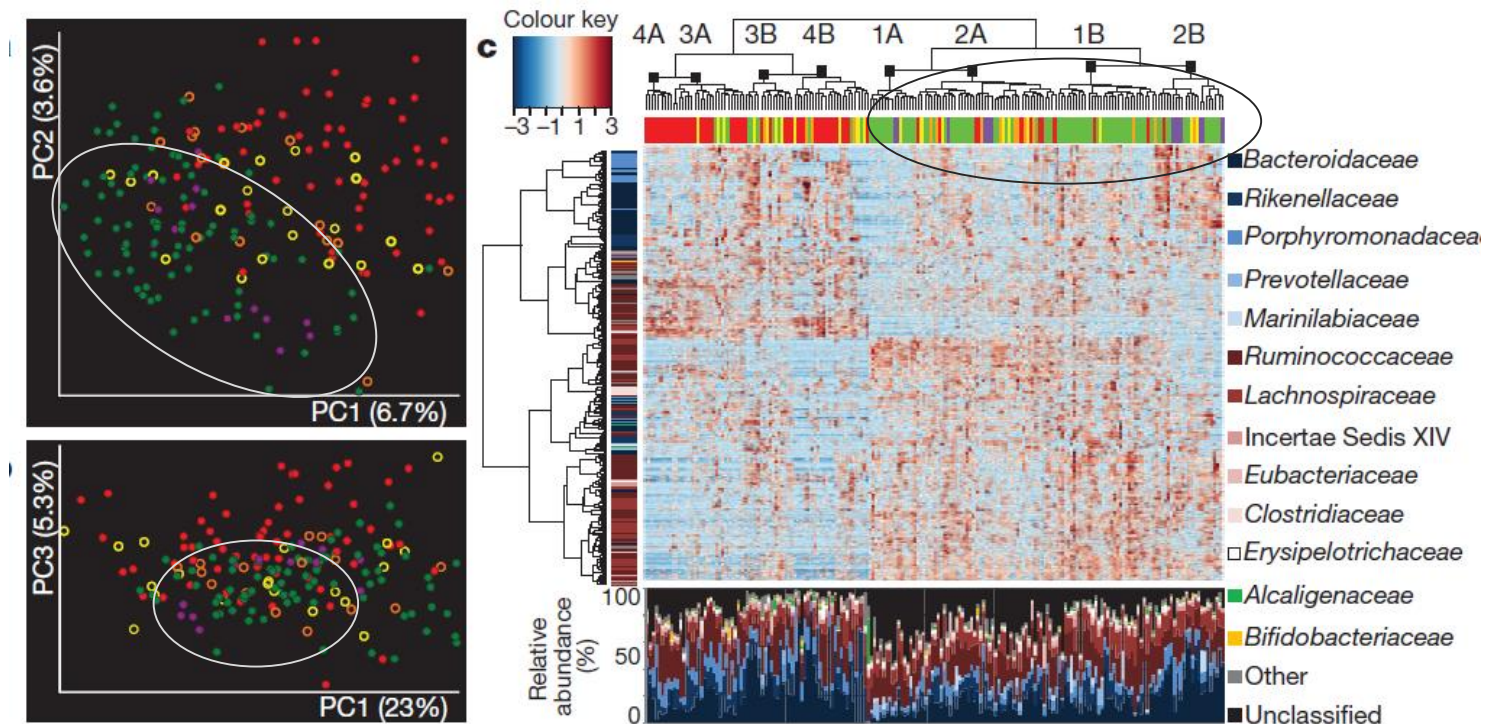
When does microbiome start to change in the healthy elderly?

Do the adaptive gut microbiome changes complement human ageing?

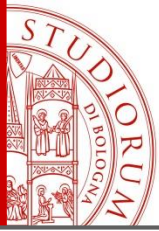


HEALTHY ELDERLY (78 Y) SHOW A MICROBIOTA STRUCTURE COMPARABLE TO THE ONE OF YOUNG ADULTS (35 Y)

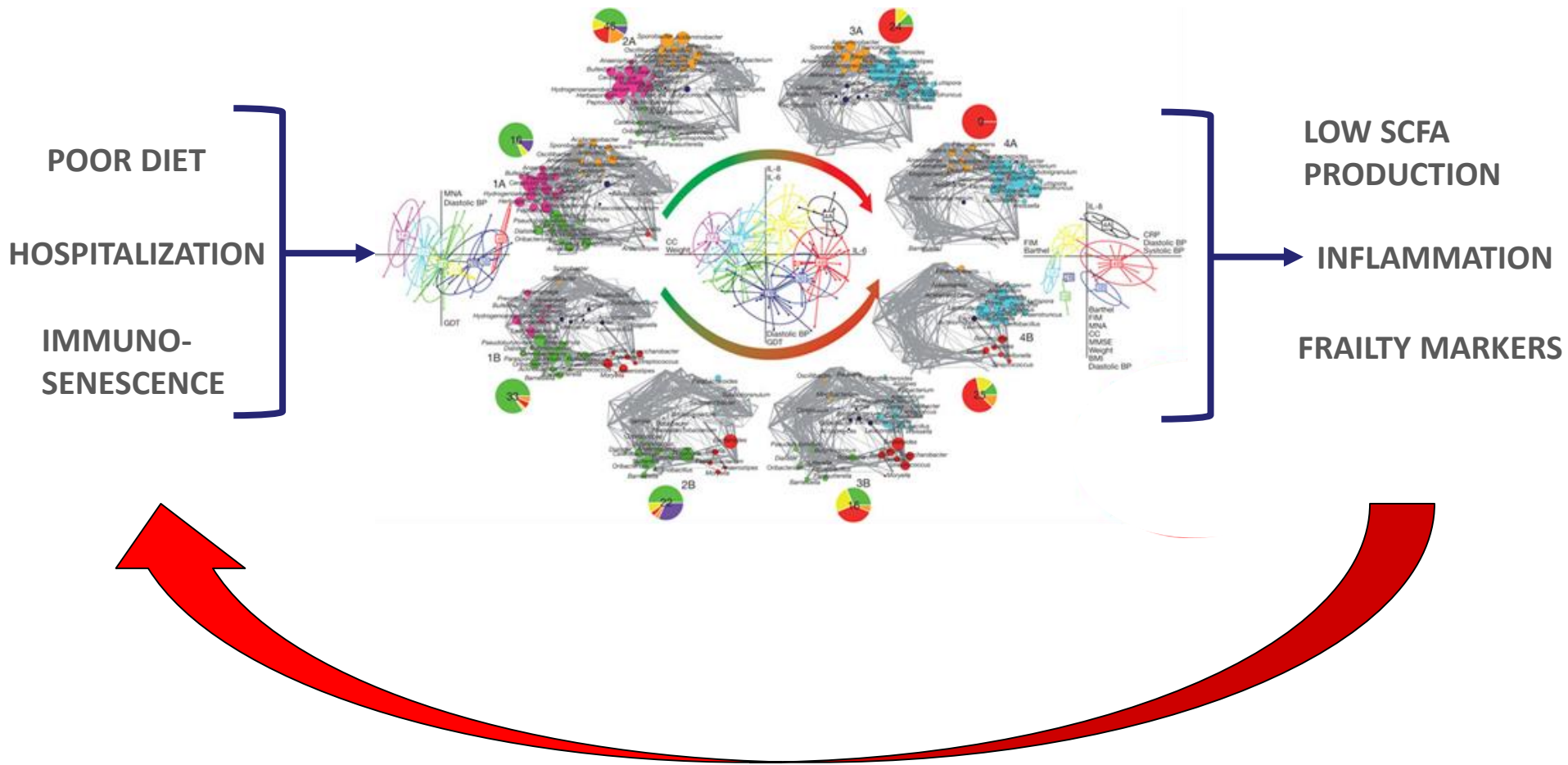
ONLY FRAIL ELDERLY SHOW A COMPROMISED MICROBIOME STRUCTURE

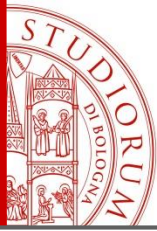


Claesson et al., Nature, 2012



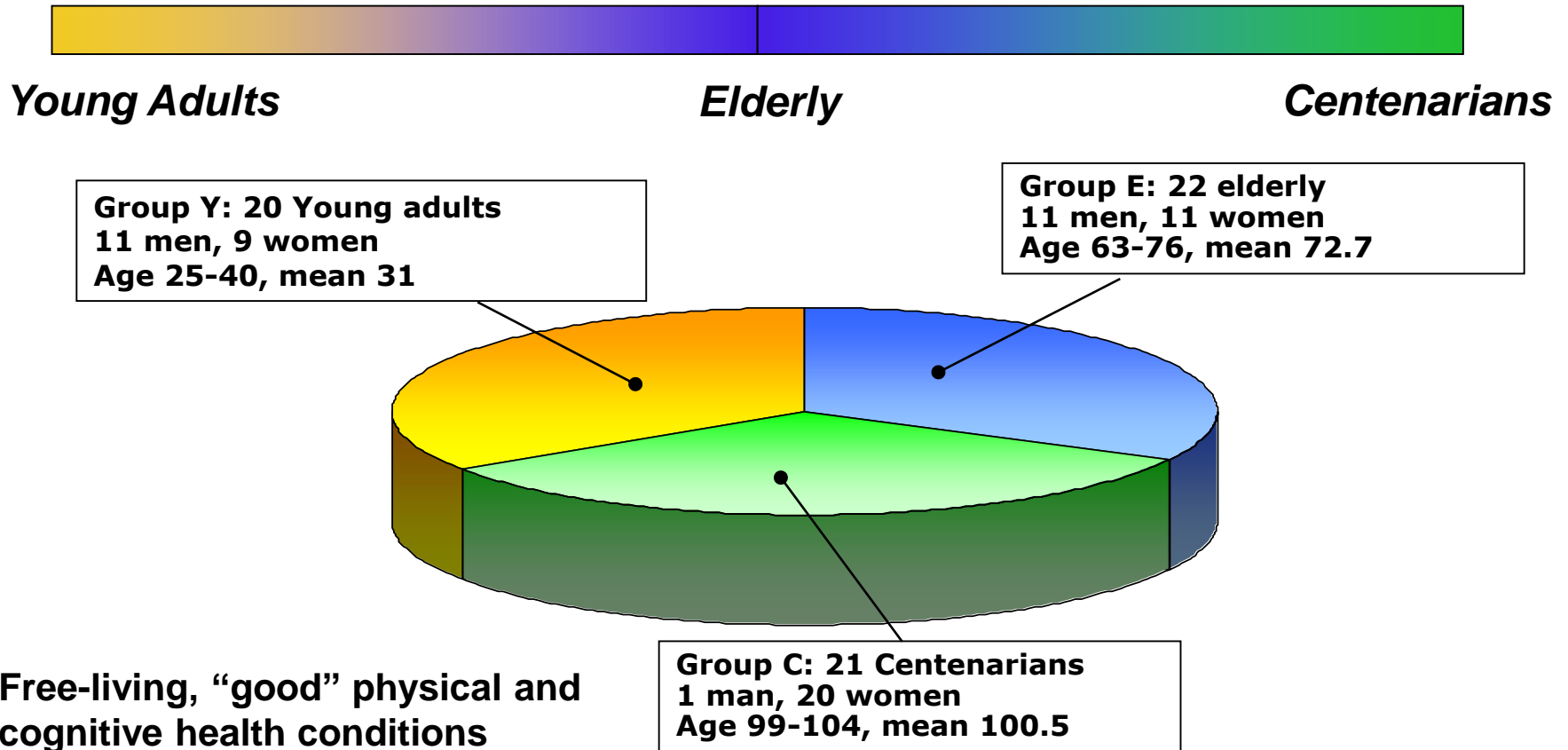
DIETARY CHANGES AND FRAILTY-RELATED FACTORS FORCE MICROBIOME DYSBIOSIS WHICH COMPROMISES THE HEALTH OF THE ELDERLY





COMPARATIVE STUDY OF THE GM STRUCTURE IN HEALTHY CENTENARIANS, ELDERLY AND YOUNG ADULTS

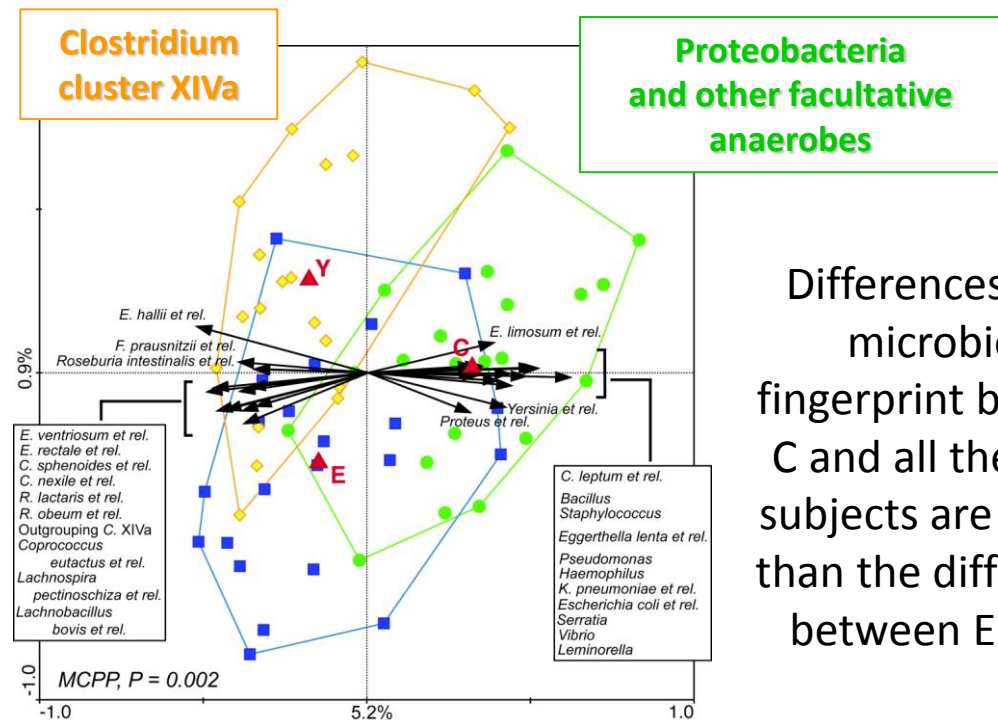
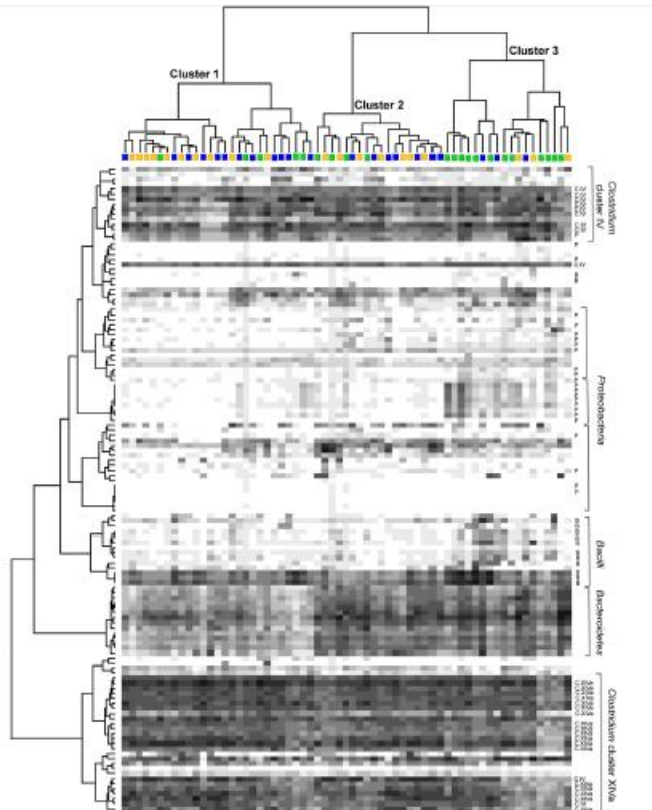
Genetically unrelated



Biagi et al., 2010, PlosONE, Collino et al., PlosOne 2013

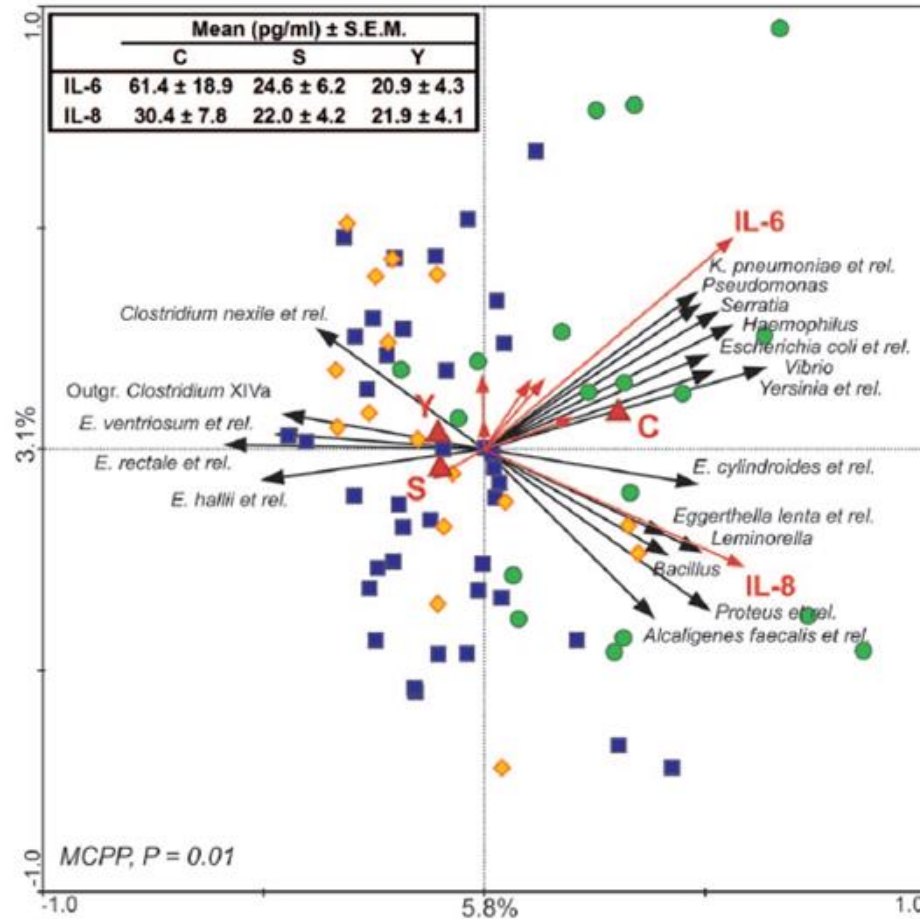
GM CHANGES IN HEALTHY PEOPLE ARE NOT LINEAR WITH AGE

HIERARCHICAL CLUSTERING AND RDA SHOW THAT **CENTENARIANS** TEND TO GROUP TOGETHER WHILE NO SEPARATION WAS OBSERVED BETWEEN **ELDERLY** AND **YOUNG** ADULTS



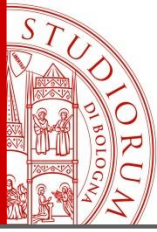
Differences in the microbiota fingerprint between C and all the other subjects are greater than the differences between E and Y

BLOOD PRO-INFLAMMATORY CYTOKINES



8.9% of the total variability of the GM can be related to the pattern of pro-inflammatory cytokines

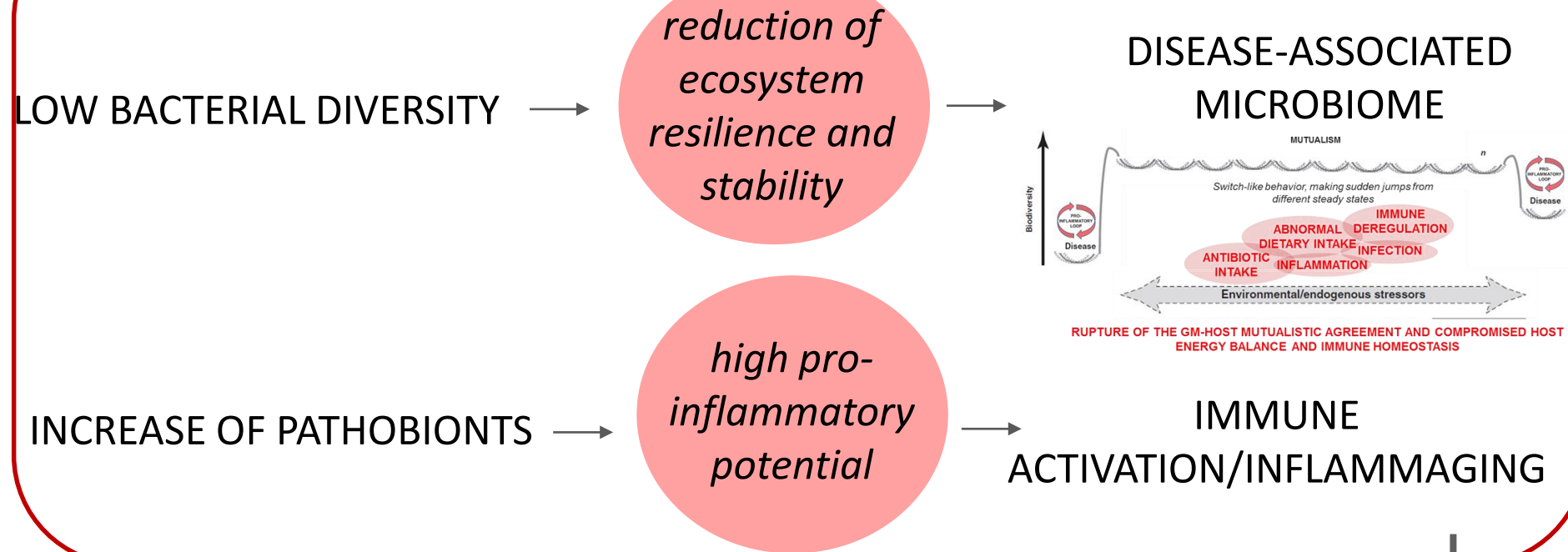
GM LAYOUT IN CENTENARIANS MATCHES WITH AN OVERALL INFLAMMATORY ASSET

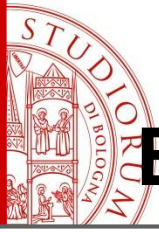


THE CENTENARIAN GM APPEARS AS DYSBIOTIC

TRACES OF STRUCTURAL AND FUNCTIONAL CHARACTERISTICS WITH THE POTENTIAL TO COMPROMISE HOST METABOLIC AND IMMUNE HOMEOSTASIS

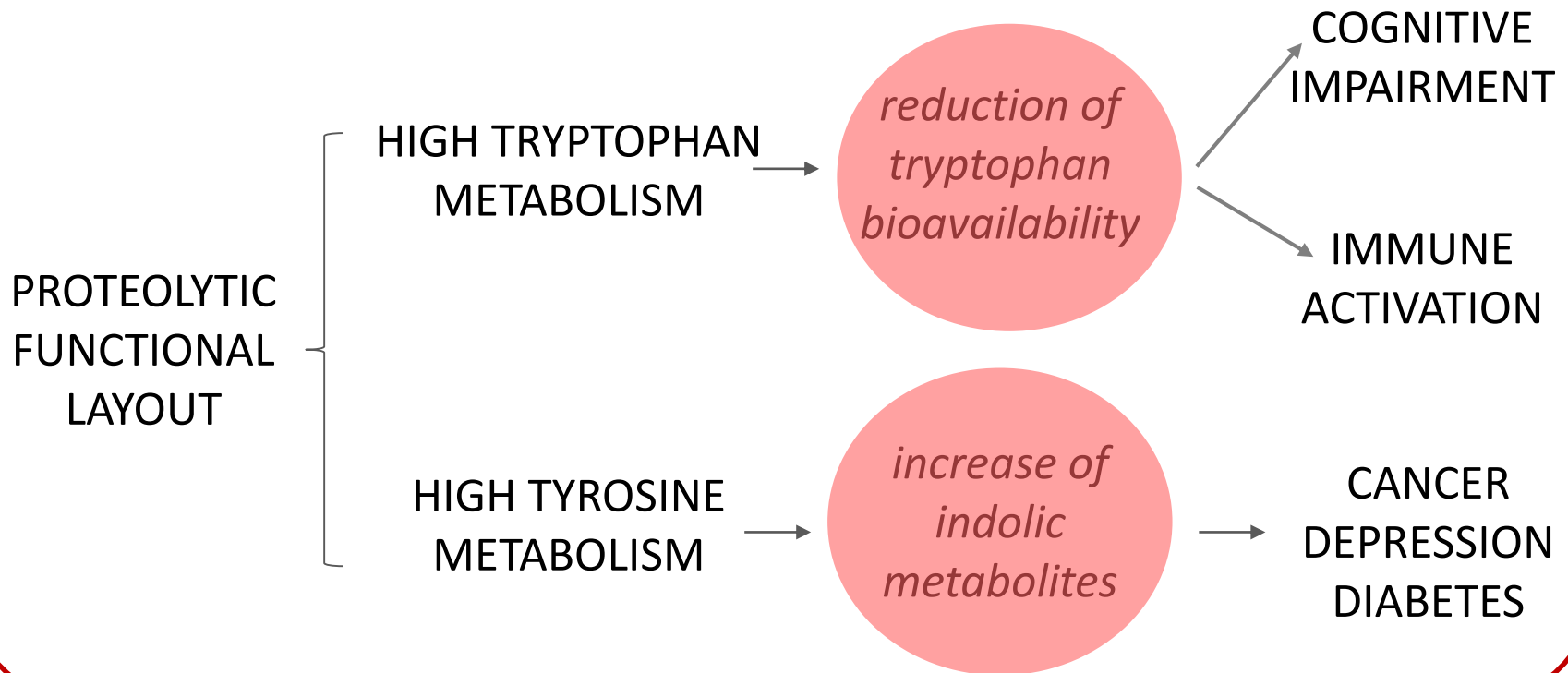
dysbiotic structural features





THE CENTENARIAN GM SHOWS AN ENRICHMENT IN PROTEOLYTIC FUNCTIONS

dysbiotic functional features



Rampelli et al., 2013, Aging

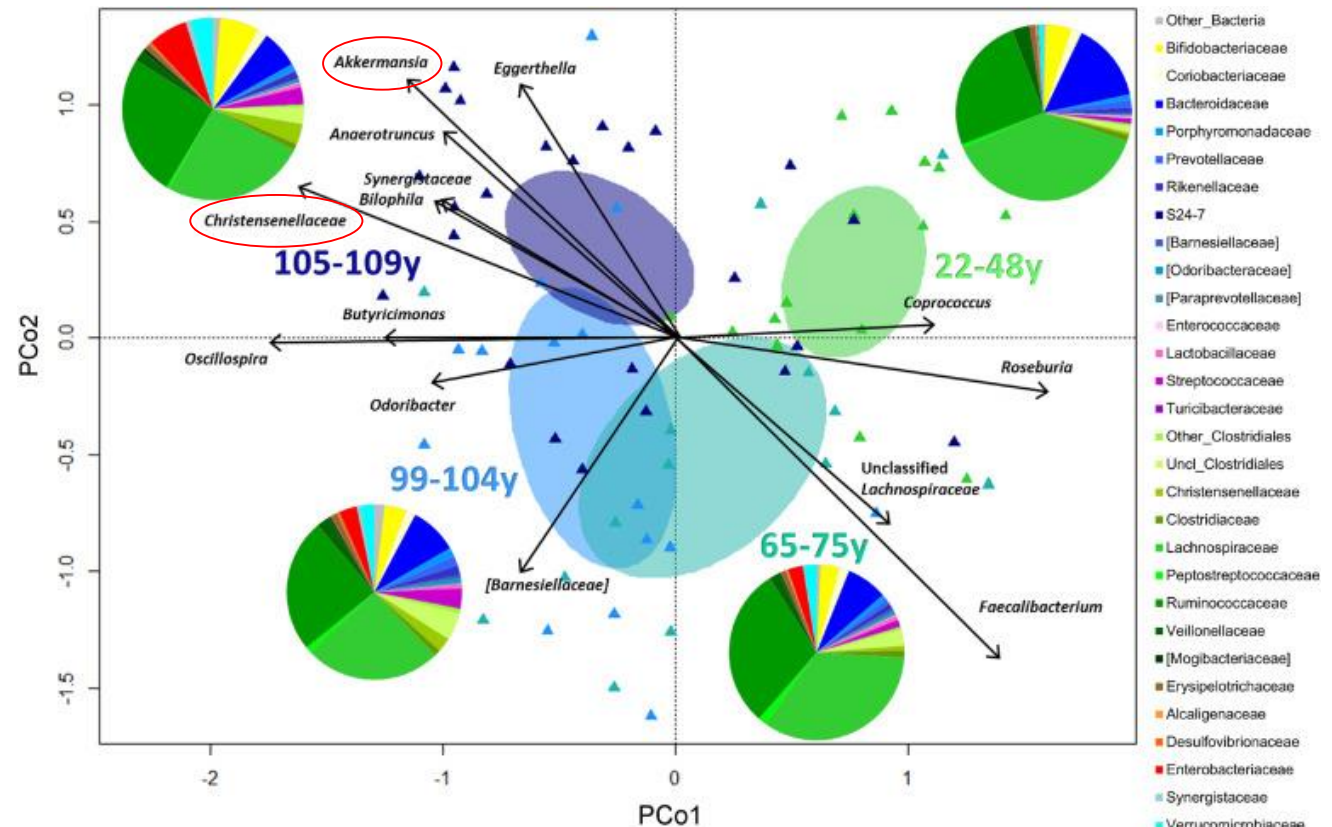
GM AND EXTREME LONGEVITY

Semi-supercentenarians (105-109y)

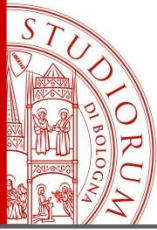
Increasing abundance
of subdominant species

Rearrangement in their
co-occurrence network

Enrichment of health
associated groups
which might support
health maintenance
during aging



Biagi et al., 2016, Curr. Biol.



GM MODULATION STRATEGIES

Improvement of the healthy status in the elderly by modulating the GM functions

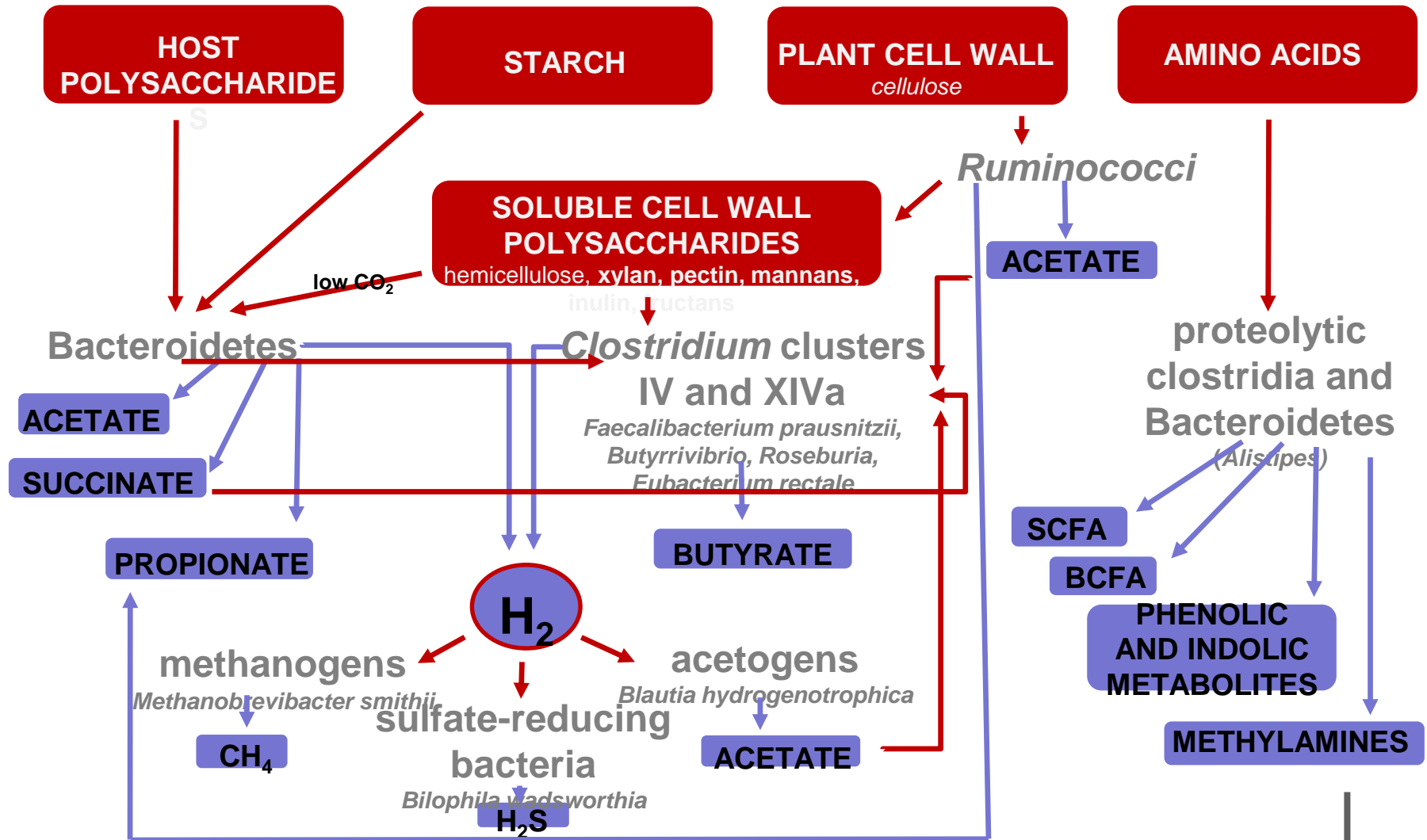


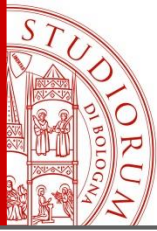
Development of elderly tailored intervention strategies to support/recover a balanced health promoting GM compositional and functional layout:

- Prebiotics
- Probiotics (next generation probiotics)
- Functional foods
- Dietary approaches (whole diet, FP7 KBBE NuAGE)

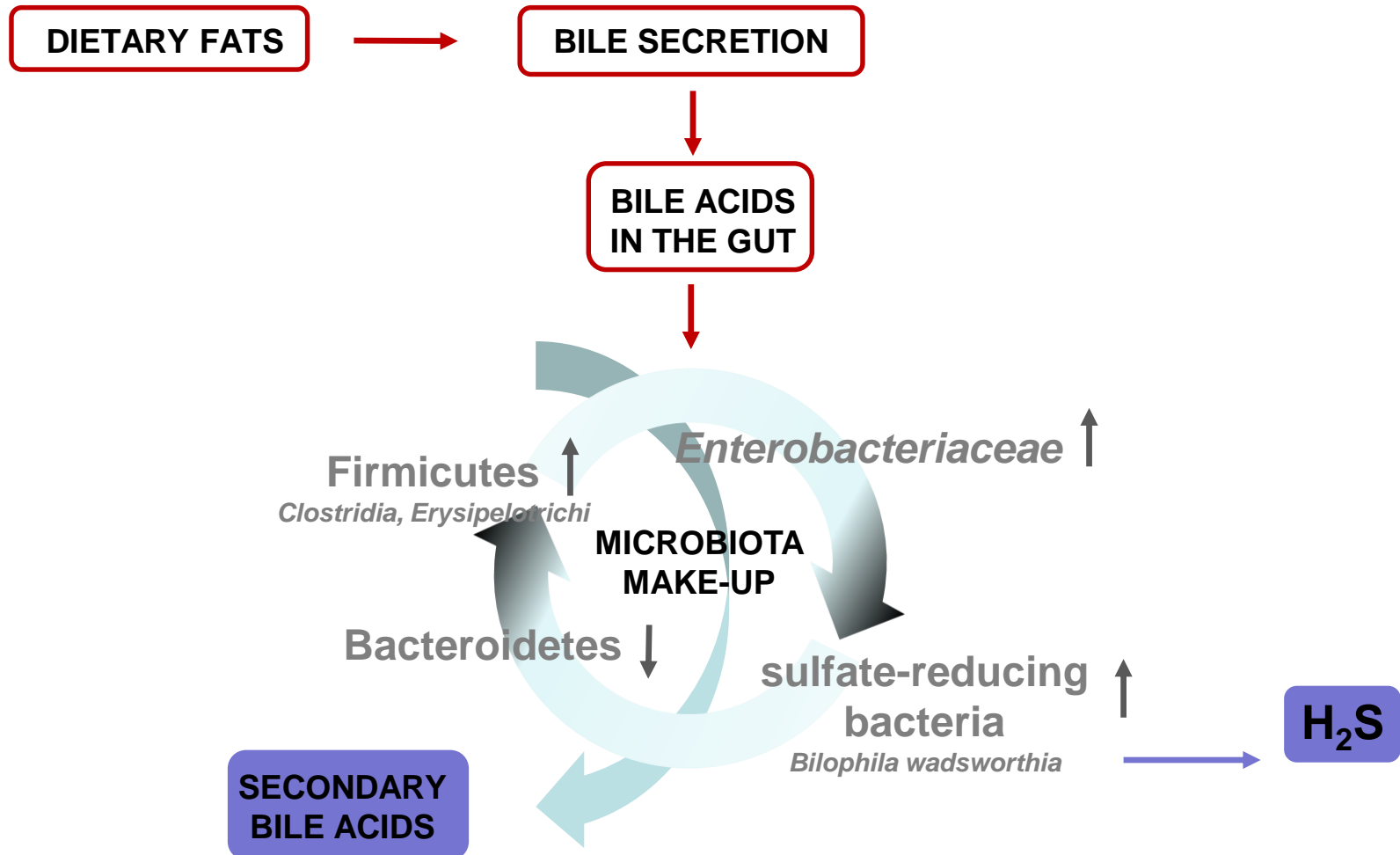


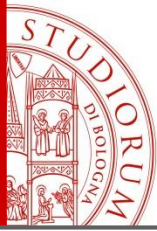
DIETARY COMPONENTS: SYNTROPHIC MICROBIAL NETWORKS





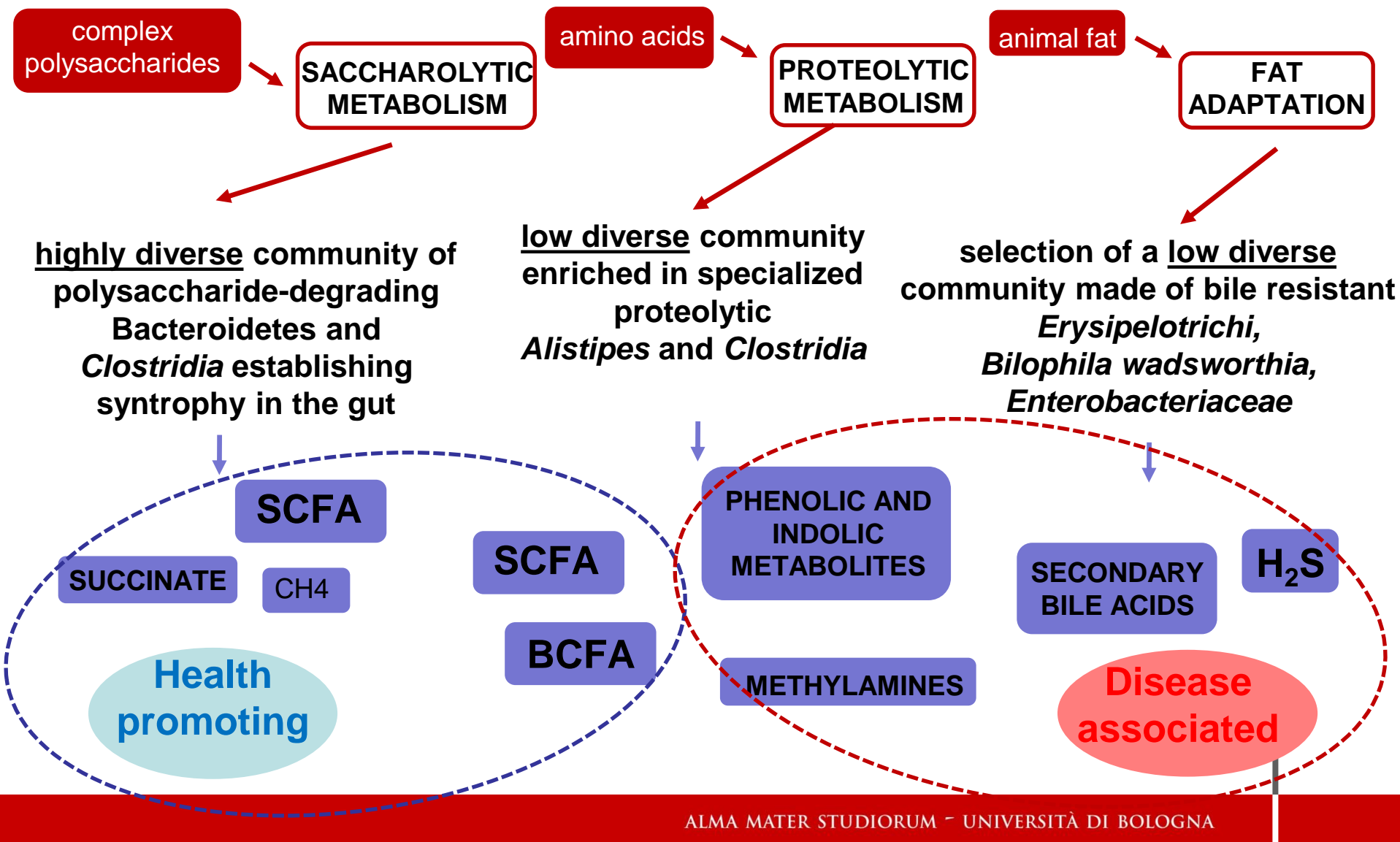
IMPACT OF DIETARY FAT ON THE GUT MICROBIAL COMMUNITIES

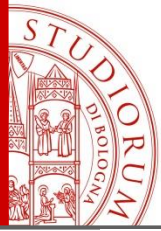




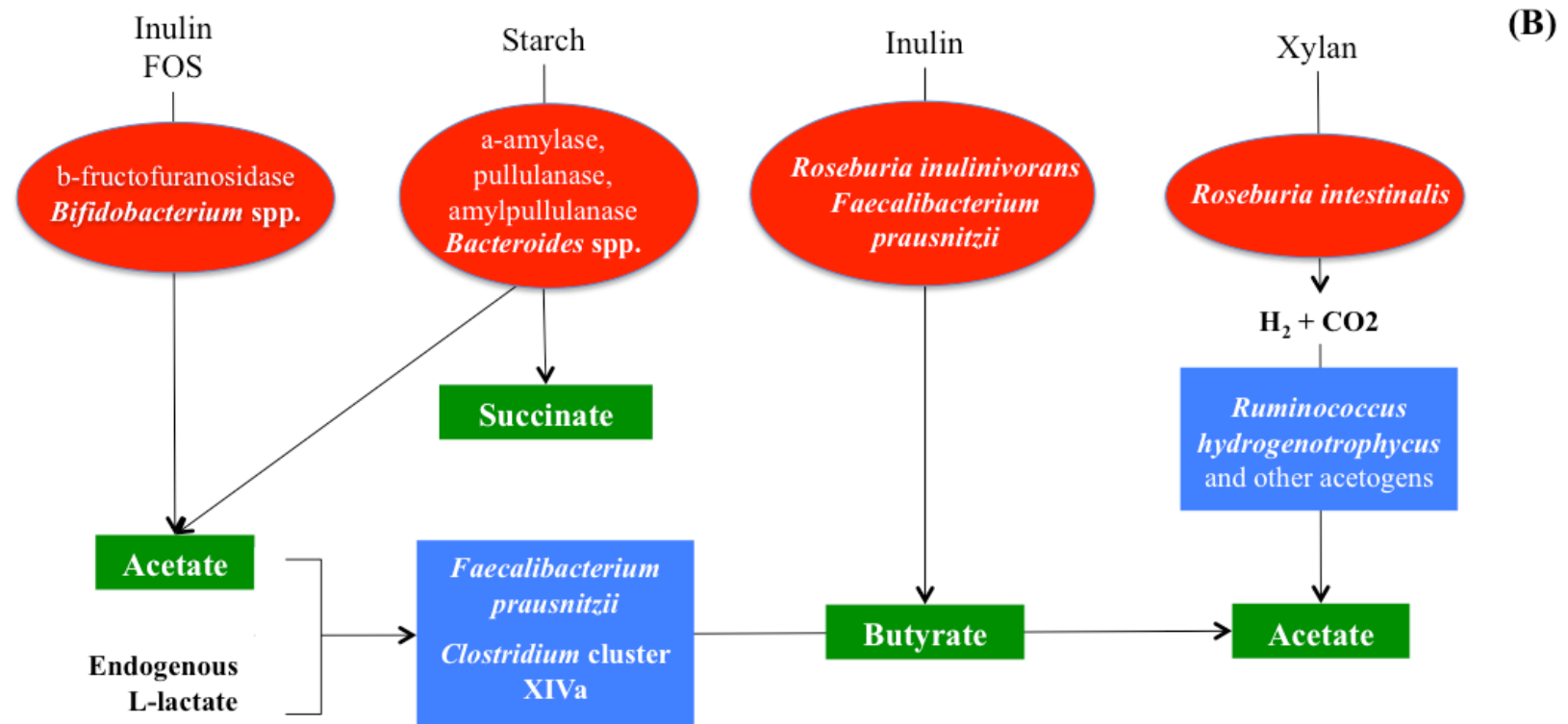
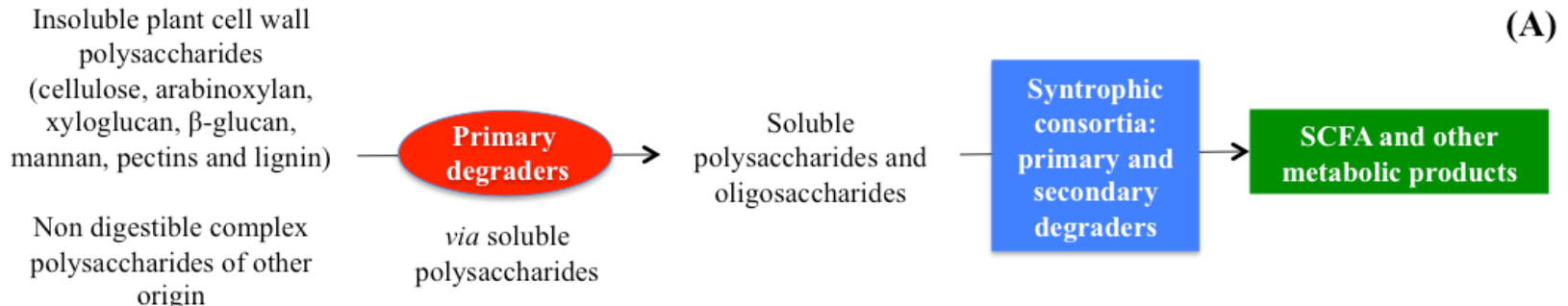
GM-HOST CO-METABOLIC LAYOUTS

diet regulates microbiota composition and metabolic output with a final impact on host physiology

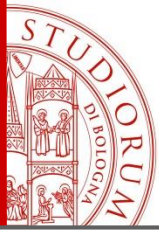




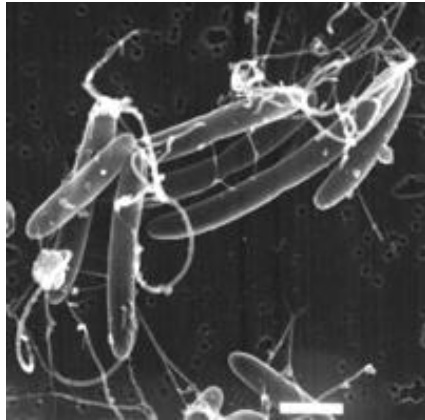
PREBIOTICS FERMENTATION IN HUMAN GUT



NEXT GENERATION PROBIOTICS

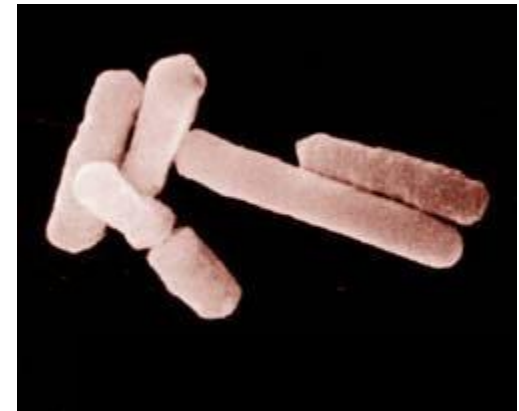


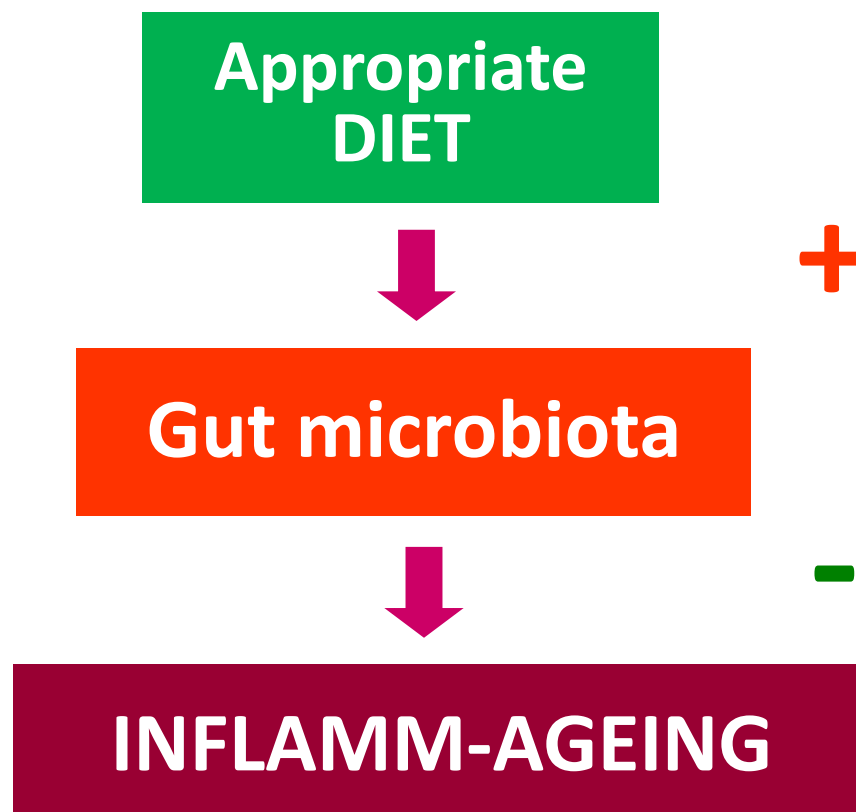
Faecalibacterium prausnitzii



Roseburia

Bacteroides





New dietary strategies addressing the specific needs of the elderly population for healthy ageing in Europe

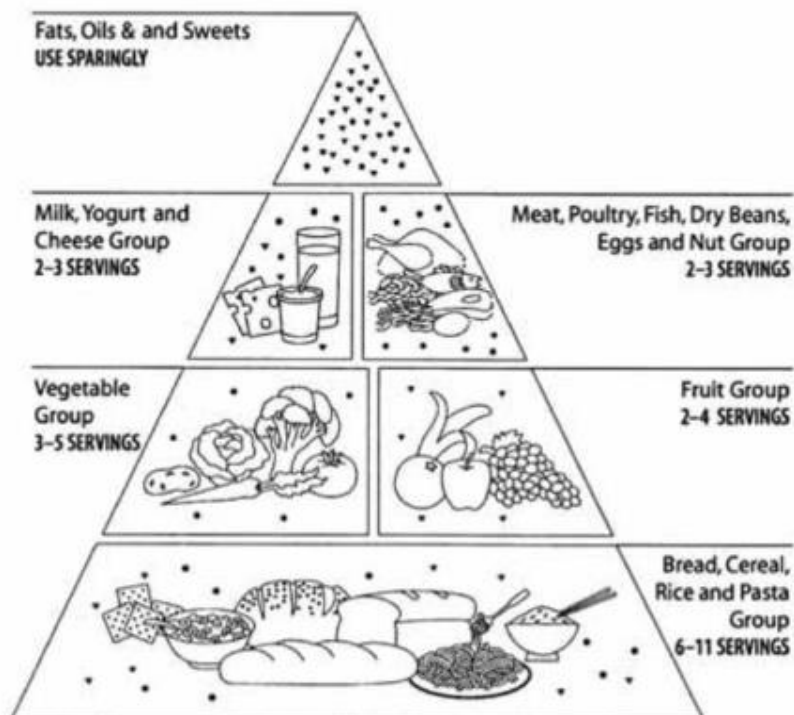
FP7 NUAGE

NUAGE recruited subjects (65-79 years of age)

A total of **1250 individuals** categorized as not frail or **prefrail** were recruited in **5 European countries** (Italy, France, UK, The Netherlands and Poland), and divided into 2 groups:

1. followed a **whole “mediterranean” ad hoc fortified/modified diet**
2. continued its own diet (**control group**)

Original Food Guide Pyramid

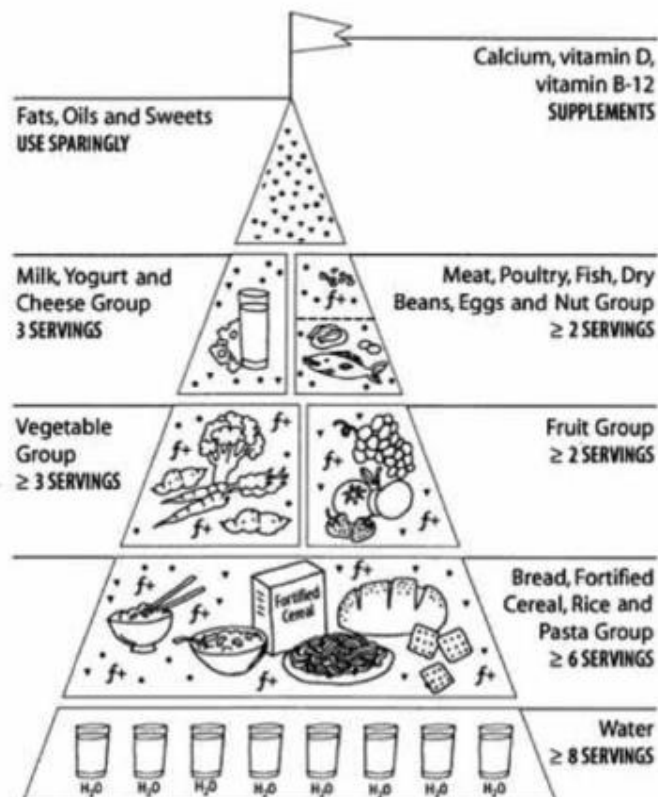


• Fat (naturally occurring and added)

▼ Sugars (added)

These symbols show fat and added sugars in foods.

Modified Food Pyramid for 65+ Adults



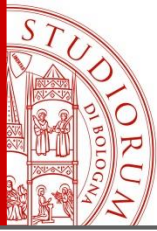
• Fat (naturally occurring and added)

▼ Sugars (added)

f+ Fiber (should be present)

These symbols show fat, added sugars and fiber in foods.

Fig.4. The NuAge modified **Food Guide 65+ Pyramid** for the elderly has a narrower base (to reflect a decrease in energy needs), while emphasizing nutrient-dense foods, fibre and water. In addition, **nutrient-specific supplements** are appropriate for many older people.



NUAGE “OMICS”

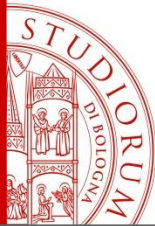
BEFORE AND AFTER 1Y DIETARY INTERVENTION

A variety of parameters have been measured (hematological profiles, immunology and inflammation, cognition, genetics, body composition)

- **Transcriptomics**
- **Metabolomics, lipidomics**
- **GM metagenomics**
- **Genetics**
- **Epigenetics**

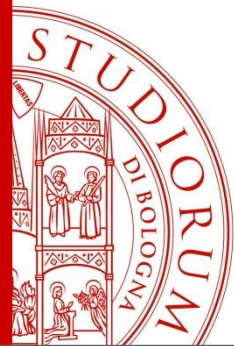
Systems biology approach

Database analysis is ongoing



CONCLUSIONS

- ✓ The elderly of today are very different from those of 20y ago: the emerging wave of more educated people over 65y implies a greater % of older adults paying more attention to their diet
- ✓ Age-specific and up-to-date dietary and lifestyle recommendations for elderly in EU are not easy to find
- ✓ Older adult population is very heterogeneous (simply referring to people aged +65y is not appropriate)
- ✓ Improving the GM profile in elderly is a target to reduce their risk for inflammation and metabolic disorders
- ✓ Design of elderly-tailored innovative functional foods (soups, drinks, dairy and bakery products, finger foods, snacks, 3D printed foods), counteracting the age related increase of pro-inflammatory pathobionts and sustaining the immune homeostasis
- ✓ Consolidation of knowledge about the elderly-microbiome interactions, including the gut-brain axis (how inflammatory and metabolic stimuli from the gut can contribute to cognitive impairment)
- ✓ Longitudinal studies to follow healthy older adults into very old age and validate the outcomes of the dietary intervention



THANKS FOR YOUR ATTENTION

